

Ms. Heather Cook,  
Investigating Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
5<sup>th</sup> Floor,  
St. James's Buildings,  
79 Oxford Street,  
Manchester,  
M1 6FQ.

<b>General Medical Council</b>	
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24<sup>th</sup> June 2011

Subject: **G.R.B. Skinner MD (Hons), DSc, FRCPath, FRCOG,**

Dear Ms. Cook,

I understand that Dr. G.R.B. Skinner is to be subjected to a further "Fitness to Practise Hearing" on 28<sup>th</sup> and 29<sup>th</sup> July 2011.

I strongly believe that Dr. Skinner must be permitted to continue treating thyroid patients. This belief is based on my own thyroid history, which I would ask you and your fellow Hearing panellists to read and consider most carefully:

- [redacted] after a thorough examination which included a thyroid scan I was diagnosed as hypothyroid and told that I would require lifelong treatment.

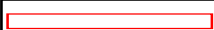
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• The Hippocratic Oath requires doctors to "do no harm". Both the NHS GP and the NHS endocrinologist quoted above caused me harm and suffering by blatantly and maliciously disregarding a serious medical condition previously diagnosed abroad. Had I felt less unwell at the time, I would certainly have reported both of them to the GMC as clearly unfit to practise.

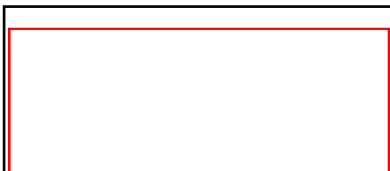
• By contrast, Dr. Skinner's exemplary treatment of my thyroid condition since  has restored me to good health.

There is an old Jewish saying that "a man who saves one life saves the world". Dr. Skinner has saved not only my life but, I know, that of many other thyroid patients who were also failed by the blind adherence of the NHS to a thyroid function test which is clearly unfit for purpose.

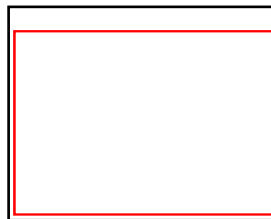
If the Fitness to Practise Directorate is genuinely interested in patient care, it should

- recommend that Dr. Skinner be allowed to continue treating thyroid patients,
- call a halt to the increasingly Kafkaesque harassment of this exemplary doctor, and
- instigate an urgent investigation into the inept and callous state of thyroid care in the NHS.

Yours sincerely,



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GMC FITNESS TO PRACTISE PANEL

30/06/2011

00630622

Dear Sirs,

Re: Dr G R B Skinner

Hearing to be held from the 28<sup>th</sup> of July onward at Manchester.

I am writing to you to express my deep concern that Dr Skinner has to face a Fitness to Practise Panel.

I am a patient of Dr Skinner's, and I can't begin to tell you how much his care for me has changed my life for the better.

I have suffered all my life from symptoms of hypothyroidism (without knowing). This has resulted in a catalogue of disasters for me -

[Redacted]

[Redacted] I could go on and on. Doctors in the past have maintained that they could not help me, my blood results are within the so called "normal range", and they have always intimated that I was a PROBLEM patient.

After much research on my part, I determined that I was indeed hypothyroid, and I began to treat myself with thyroxine. This is not a desirable course of action, but suffering people will do anything to feel better. Because I saw the need for medical supervision, I eventually went to see Dr Skinner with the prior approval of my GP.

Dr Skinner (along with my GP) has overseen an increase in my thyroxine medication over a period of some months. I am now taking in Armour Thyroid the equivalent of [Redacted] mcg levothyroxine daily.

The change in my health has been remarkable. I have energy and a zest for life that I have never known. I have a sense of humour at last.

[Redacted]

[Redacted] I am no longer a burden on the NHS or a constant visitor to the surgery. Life has become worth living at last.

My GP is delighted at the change in me. He shakes his head in wonder at me.

I am so grateful to Dr Skinner for his rational approach to this disease. He has compassion for the patients that he sees and has displayed much determination and courage in continuing to treat them (despite much opposition). He is an excellent doctor and an outstanding human being.

Why do doctors so rigidly adhere to this so called "gold standard" of a blood test? This thinking flies in the face of rationality. I was very ill and thyroxine cured me. If I had not been in need of thyroxine supplement, then taking this amount of thyroxine daily would have landed me in hospital, instead of which I am now a fully functioning person.

I am a registered nurse. I would be willing to attend the hearing to speak on Dr Skinner's behalf. If doctors like him are unable to practise medicine according to their own consciences and medical understanding, what will happen to people like me? We cost the NHS a fortune, when we can so easily and cheaply be cured. We suffer terribly and the majority of the medical profession will not hear us when we ask for help.

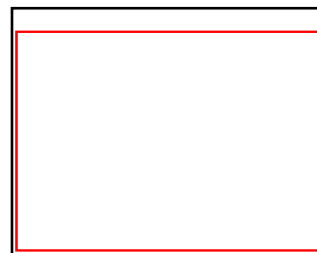
Without doctors like Dr Skinner, people suffering with undiagnosed hypothyroidism, those with so called normal blood values, will buy their thyroxine supplies over the internet and treat themselves, because there will be no other option for them.

Surely these discrepancies in opinion call for research, not castigation of individuals.

Yours faithfully



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1/7/2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester.  
M3 3AW.

Dear Madam,

**RE: DR GORDON SKINNER**

I write in connection with & to support Dr G. Skinner in the upcoming hearing (28/29 July & 1/2/3/ August 2011).

I initially was seen by Dr Skinner at his [redacted] clinic in [redacted] [redacted]. Until that time I had spent many years [redacted] enduring poor & ever deteriorating health coupled with poor treatment which consisted of undiagnosed, misdiagnosis & ultimately severe under medication. My quality of life was zero! Most of it being confined to my home unable to sometimes get up out of bed.

In the [redacted] that Dr Skinner has been treating me my health has improved to the point that I can now function normally, I feel consistently well & have a life again which both myself & family never thought would be possible again.

I am completely dismayed that yet again the GMC are seeing fit to haul Dr Skinner through another unfair & needless process when it would be far better for all concerned if he were allowed to get on & treat/make

better the ever increasing amount of patients referred to him. It is my hope that this latest hearing will see the end of the continued 'hounding'.

Following each appointment with Dr Skinner he always informs my GP of his recommendations & to date my GP has been happy to follow his advice.

Not only does Dr Skinner carry out his job properly but he also treats patients with respect & consideration & as the individuals that they are & most importantly is never dismissive.

When it comes to Thyroid issues Dr Skinner's knowledge is second to none & I feel most fortunate he is in charge of the Thyroid issues I have & definitely have no wish to be returned to the mercy of sub-standard care, which I had been used to.

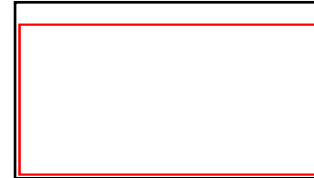
Yours faithfully,

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29<sup>th</sup> June, 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Ms. Cook,

Letter of support for:

**Dr. Gordon R.B. Skinner**  
**Review Hearing, 28<sup>th</sup>/29<sup>th</sup> July & 1<sup>st</sup>/2<sup>nd</sup>/3<sup>rd</sup> August, 2011**

**I give Dr. Skinner my whole hearted support.**

I first consulted Dr. Skinner around [ ] years ago, but unfortunately during [ ] my health steadily declined despite my T3 medication and my GP would not increase the dose because my blood test results were still within range and my GPs only suggestion was that I [ ] I was very ill.

My symptoms [ ]

[ ] All symptoms I had had around [ ] years ago before I consulted a doctor in [ ] who diagnosed hypothyroidism. (I later transferred to be a patient of Dr. Skinner [ ] My GP finally suggested I see a different doctor in the practice, which I did and she felt it would be an excellent idea to have a further consultation with Dr. Skinner.

After a lengthy consultation with Dr. Skinner, when he checked my blood pressure, felt the skin on my hands, looked at tongue size, took my pulse, took my temperature, felt my thyroid and asked many questions, he suggested an increased dose of [ ] mcg per day and wrote to my GP to ask if they would prescribe this for me. My GP did and I have returned to good health. [ ]

I will add here that over the years, apart from occasionally checking my blood pressure, no other doctor has carried out any of the above checks i.e., pulse, skin, thyroid etc., and they have relied totally and utterly on blood test results. Blood test ranges that are now questioned

world-wide. Europe and the USA have much narrower ranges than the UK, hence one could be treated or have an increased dose in Germany, but not in the UK.

Without Dr. Skinner, I would be very ill and struggling to carry out every day tasks, whereas now I am full of energy and am spending a lot of time at my daughter's who has a new baby. There is no way, at the beginning of this year, that I could have possibly have helped her.

**I can't possibly thank Dr. Skinner enough.**

The GMC are carrying out a five day review on his conditions, conditions that should have ended in November, 2011. (FTP D19/7 – Maximum period of 3 years under the Medical Act). This has been extended to 3 years and nine months which was not stated at the above hearing.

The GMC's FTP sanctions were of an administrative nature.

at the conclusion of the hearing, this was the statement made by the Fitness to Practise Panel (Sunday 11.11.2007):-

**"The Panel has taken full account of the mitigation submitted on your behalf. It has read the numerous testimonials submitted by both patients and colleagues and has noted the testimony of the 17 patients who have given evidence on your behalf, and that of Dr Ahmad, who assists you at the Louise Lorne Clinic. It is clear that you are a caring and compassionate doctor whose overwhelming concern is the care and wellbeing of your patients, many of whom have pleaded that you should be allowed to continue to practise" (Page D19/3, paragraphs F, G and H) ..... and, "A large body of evidence has been submitted throughout this case demonstrating that many patients have benefited from the medication that you have prescribed" (Page D19/4, Paragraph A).**

I would like you to take the above quote into consideration along with my testimonial and also the testimonials from all his patients. We need doctors like Dr. Skinner, doctors whose main concern is to make their patients well. There are hundreds of references that support Dr. Skinner's treatments and there are doctors who are now beginning to realise that the blood tests don't tell the whole story and that each patient is an individual.

***UK Guidelines for the Use of Thyroid function tests, "The document should be considered as guidelines only; it is not intended to serve as a standard of medical care. The doctors concerned must make the management plan for an individual patient."***

The Association for Clinical Biochemistry, British Thyroid Association, British Thyroid Foundation. UK Guidelines for the Use of Thyroid Function Tests. Guidelines Development Group: 2006. (p.5))

To repeat my first sentence, "I give Dr. Skinner my whole hearted support" – medicine needs such a dedicated, selfless man whose main concern is his patient's health and wellbeing and to return them to full health.

**Thousands of patients would be left in a state of ill-health if it were not for the Dr. Skinner's of this world!**

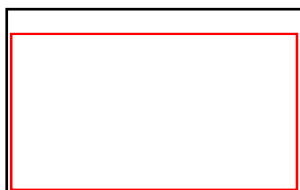
Doctors have said to me that the symptoms sound like hypothyroidism, but they can't treat because the blood tests are within range and later on, I cannot increase your dose because the blood tests are within range. 'There is none so blind as those who will not see'. From the Bible, specifically Jer. 5:21 (King James version): "Hear now this, O foolish people, and without understanding; which have eyes, and see not; which have ears, and hear not."

The doctors who complained to the GMC that brought about the 2007 FTP are the ones who should have their registration scrutinized.

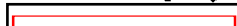
In my eyes and that of my family who have also been treated and returned to full health by him, Dr. Skinner fully complies with the Hippocratic Oath and should be free to practise medicine without GMC conditions.

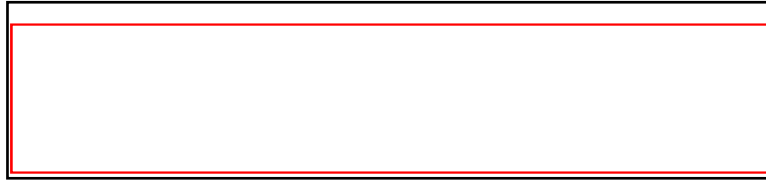
I trust the GMC will adhere to their slogan of, 'Ensuring good medical Practice', because Dr. Skinner is not just a good practitioner, he is an excellent practitioner.

Yours sincerely,



cc Mr. Ralph Shipway, ~~XXXX~~





2 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER  
M3 3AW

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Dear Ms Cook

**Re: Dr Gordon Skinner - Review Hearing 28 July 2011**

I am writing to you - once more - in support of Dr Skinner. I have been writing to you to express my admiration of his technical skill, medical judgment and straightforward commonsense since 2006 ! Why is his outstanding capability and service to countless hypothyroid sufferers still in any question whatsoever?

My wife suffered with hypothyroidism for [redacted] years until Dr Skinner gave her appropriate doses of thyroxine, which restored her to full health in a matter of months. Read that sentence again, and ask yourself how YOU would feel if that were a member of YOUR family.

[redacted] years of 'half life' for want of being prescribed adequate doses of thyroxine! Recovery within months! Does this not shout out as skilled treatment by a professional who has specialised in the area of hypothyroidism? Someone whose close understanding of this disease should be made known widely rather than be called into question for incomprehensible reasons?

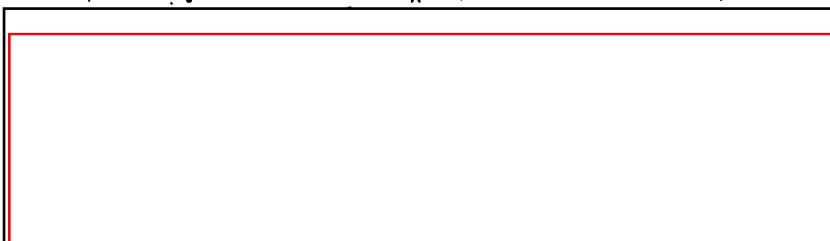
Do you want even one more person to be deprived of the prime of their life because a blood test result falls within arbitrary limits despite the countless symptoms of acute hypothyroidism?

Dr Skinner has restored full and active life to thousands of people who, without his considered treatment, would have continued in the 'half life' to which they were condemned by GPs who slavishly adhered to the Blood Test Guidelines for individuals suffering from hypothyroidism, ignoring the obvious symptoms displayed by their patients simply because the Guidelines said they were 'well'.

Both my wife and I are totally indebted to Dr Skinner. And our daughter too, whose health has improved immeasurably since becoming his patient. And other members of our family. And several friends and acquaintances. That is just our immediate experience. This is repeated countless times across the country.

Please stop reviewing or in any way questioning the medical capability of Dr Skinner. Rather, recognise the huge positive contribution he has made to the well-being of so many hypothyroid sufferers and leave him free to carry on his good work

Yours sincerely



[Redacted]

3/7/11

Dear Heather Cook,

I understand that Dr Skinner is to go before the GMC again on the 28th, 29th July and 1st 2nd and 3rd August at the General Medical Council Oxford Street Manchester and that the Hearing is for the GMC to assess what to do now that Dr Skinner's 3 years of condition are finished.

I am writing to show my utmost support for Dr Skinner. I have suffered for years with [Redacted]

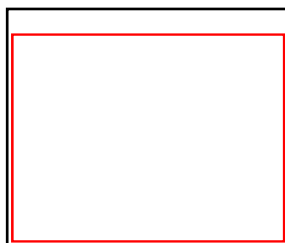
[Redacted] I have had test after test and although a variety of 'possible' diagnosis have been given no treatment could be offered and my life was to continue on this downward spiral of ill health. [Redacted]

Last year a friend said she had been reading in detail about Hypothyroidism having been diagnosed herself (She is one of those people whose bloods were outside the normal range) and was certain I had it. When I looked into it I was really shocked at the detailed similarities between my symptoms and Hypothyroidism. I visited my very supportive doctor who did the blood tests again, but again the reading was in the 'normal' range. I was so struck by the symptoms however, and decided to take this possibility further. I asked my doctor if he would refer me if I found an endocrinologist who would take my symptoms seriously despite my blood results and he agreed. My husband and I looked at information on various consultants and realised it was going to be very difficult to be taken seriously. After days of searching we found information regarding Dr Skinner which showed he might take us seriously, and within weeks I went to see him.

On arriving at the surgery I was asked to complete an information sheet regarding symptoms and had my blood pressure checked. Dr Skinner and I then discussed my many symptoms and my medical history. He was very open about the GMC and the reasons for their actions. After a forty five minute medical and lots of questions Dr Skinner decided to try me on a very low thyroxine dose. He was pleased to know I was fully involving my doctor. The dose was gradually raised with regular checkups. I am now at a level of dose that is beginning to give me my life back. I have vastly reduced symptoms (it has only been [Redacted] months) and in some cases the symptoms have disappeared altogether. I am no longer wondering what on earth is wrong with me and feel like I used to years ago. I cannot emphasise enough how devastating life changing my symptoms have been, and equally, how wonderful and life changing the remarkable improvement in my condition is. Without the support of Dr Skinner and my GP, my life, and that of my husband and young family would still be being devastated by my illness.

Yours Sincerely

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02 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
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M3 3AW

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Dear Ms Cook

I am writing in support of Dr Gordon Skinner whose case comes up on 28<sup>th</sup> July - 3<sup>rd</sup> August.

Although I am not a patient of Dr Skinner's I have read a lot about his work. This doctor appears to care about his patients and is willing to step outside the guidelines in order to help them to become well. If only others were willing to do this I'm sure there would be far fewer disabled and chronically sick people about.

Thyroid illness is a complicated business and does not fit into the neat little reference range that most doctors are forced to adhere to. I [redacted]

[redacted] was told that having an underactive thyroid, which would be the result of this treatment, was easy to treat, I'd just have to take a little white pill every day for the rest of my life and I'd be fine. For some that may be the case but for me it wasn't [redacted]

[redacted] Everybody is different and needs to be treated individually and other factors have to be taken into account i.e. adrenal function, and other nutrients. Dr Skinner works with his patients and tests for these things and prescribes natural thyroid products which work better for some people. I'd like to have the opportunity to try these things. [redacted]

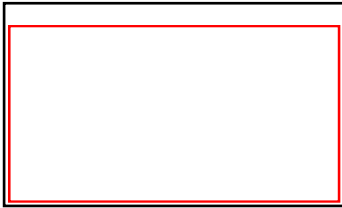
[redacted]

To accuse this doctor and others like him of not being fit to practise is outrageous and will discourage other doctors from trying to help their patients. I believe I could regain some of my health with the help of someone like Dr Skinner but unless he is allowed to continue his work that is never going to happen.



Galileo spent the last ten years of his life under house arrest for believing the earth moved round the sun at a time when no-one else did. He was right and everyone else was wrong. Please don't let history repeat itself.

Yours sincerely



c.c.   
Ralph Shipway

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester M3 3AW

Dear Heather,

Re Dr GRB Skinner

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I write to express my support for Dr Skinner and the work he is doing for those patients who, like myself, were – and still are – being dismally failed by the endocrinology profession's over-reliance on TSH tests as a means of diagnosing thyroid deficiency conditions.

To give thyroid medication to patients who are not hypothyroid would indeed be a dangerous and irresponsible thing for any doctor to do. But Dr Skinner only prescribes thyroid medications to patients whose signs and symptoms clearly indicate hypothyroidism.

There are, astonishingly, those in the UK medical profession who claim that, if a patient has a level of TSH which is within the normal range, then that patient cannot be hypothyroid. This claim displays a level of medical ignorance which I – a mere patient – find both staggering and shocking. TSH tests are indeed a very useful diagnostic aid but a TSH test is designed *only* for detecting primary hypothyroidism (i.e. hypothyroidism caused by thyroid production problems). A TSH test *only* measures levels of Thyroid Stimulating Hormone, so it cannot identify other causes of hypothyroidism, i.e. those causes unrelated to thyroid production levels. For example, a TSH test;

1. cannot detect hypothyroidism caused by cells' ability to uptake T4 being reduced because their thyroid receptors are not functioning correctly. This is a common problem in CFS patients. (See attached paper; 'A Guide To RNase L: Thyroid and RNase L')

2. cannot detect hypothyroidism caused when anything prevents cells from efficiently converting T4 into T3.

If we, Dr Skinner's patients, were not – as some endocrinologists claim – suffering from hypothyroidism, then that begs the question; Why, when we take the hormones Dr Skinner prescribes for us, do we not all start displaying the signs and symptoms of hyperthyroidism? Why, instead, are the majority of us being returned to full health? These facts clearly demonstrate that these allegations against Dr Skinner are totally unfounded.

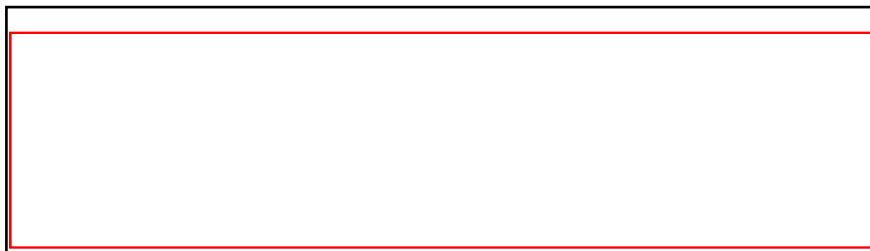
Some endocrinologists also claim that the dramatic improvements Dr Skinner is achieving are just placebo effects. This directly contradicts their other claim - that what Dr Skinner is doing is dangerous! If we were *not* hypothyroid, then us taking thyroid hormones would *not* have a placebo effect, it would *not* make us feel better, it would make us *more ill*, for we would rapidly become *hyper*thyroid!

The most important *fact* for the Fitness to Practice Panel to note is that we, Dr Skinner's patients, are *not* becoming *hyper*thyroid as a result of his treatment - most of us are being restored to full health! Isn't that what doctors are *supposed* to do?

I ask that the GMC Fitness to Practice Panel now bring to an end this relentless persecution of Dr Skinner. I ask that they close this case and instead, direct the GMC to turn its attention to the national disgrace whereby the endocrinology profession is failing so many thousands of CFS patients. Because of endocrinologists' over-reliance on TSH results - a test which can *only* detect thyroid *production* problems - endocrinologists are failing to diagnose the other causes of hypothyroidism.

Endocrinologists are also - again because of their over-reliance on TSH tests - failing to prescribe adequate amounts of thyroid medication to many patients who have been diagnosed with primary hypothyroidism. It is obvious from the positive results of Skinner's work with such patients, that there are people with primary hypothyroidism who also have a secondary form of hypothyroidism. For such patients, to merely bring their TSH levels down to 'normal' levels does make them well - patients with hypothyroidism at cellular level, for example, seem to require significantly higher dosages of thyroid medication than patients who just have primary hypothyroidism.

Yours sincerely,

A large rectangular box with a red border, used to redact the signature of Mr Ralph Shipway.

cc.  Mr Ralph Shipway

## A Guide To RNase L: Thyroid and RNase L by Cort Johnson

*Englebienne, P., Verhas, M., Herst, C. and K. De Meirleir. 2003. Type I interferons induce proteins susceptible to act as thyroid receptor (TR) corepressors and to signal the TR for destruction by the proteasomes: possible etiology for unexplained chronic fatigue. Medical Hypotheses 60, 175-180.*

*This article is unbelievably complex; hopefully this synopsis is correct on the basic points.*

CFS patients are biochemically euthyroid (normal thyroid function) but the severe fatigue they present clinically suggests they are hypothyroid (low thyroid). CFS patients also suffer from a dysregulated part of the immune system (Interferon) which can result in severe fatigue. In this article the authors propose that the severe fatigue seen in CFS patients, and in patients with cancer, hepatitis and MS undergoing IFN  $\alpha/\beta$  treatments, is caused by an IFN induced repression or destruction of the thyroid receptors (TR's). Since the inhibition of TR activity levels does not effect thyroid hormone production this presents a scenario in which patients appear biochemically euthyroid but are clinically hypothyroid; i.e. the signal is there - its just not getting through.

The genesis of this problem occurs during the induction of 2-5OAS-like proteins (p30, p56/p59) called 2-5OASL by type I IFN's (IFN  $\alpha/\beta$ ). These protein were discovered in 1995 but their function remains unknown. (*An examination of the catalytic regions of the 2-5OAS and 2-5OASL proteins revealed subtle differences that probably account for 2-5OASL's inability to act like 2-5OAS; i.e. to cut up ATP and form 2-5A*). A 'BLAST' search of the NCBI database indicated that the 2-5OASL proteins share a 96% homology with a thyroid interacting protein (TRIP) - TRIP 14. (Interestingly this protein only interacts with proteins in cells grown without thyroid hormone (?)).

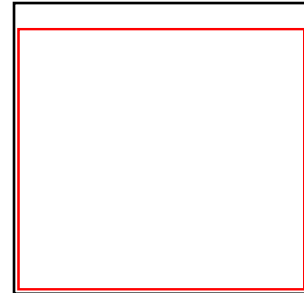
In the cell the thyroid receptor is typically bound to another receptor - the retinoid x receptor. Proteins are able to activate or repress thyroid receptor activity by binding to the binding domains found on both of these receptors. Thus two binding domains need to be filled to effect thyroid receptor activity. While the 2-5OASL proteins contain the motif needed to interact with these binding domains they appeared to only have one of them. A further amino acid scan identified, however, another motif (SCAN) which appears to be able to bind with the other. Thus the p30 and p56/59 OASL proteins appear to be able to engage with and repress thyroid receptor functioning.

An 'e-motif' search of the amino acid domains of the OASL proteins revealed the presence of motifs on the p56/50 OASL's that interact with ubiquitin proteins. Ubiquitins target proteins for destruction by (26S) proteasomes. The ubiquitin system of protein degradation plays an important role in the regulation of the cell cycle, signal transduction, gene transcription and endocytosis. (*Endocytosis is the incorporation of an extracellular substance into a cell such as when dendritic cells, macrophages and phagocytes ingest all or parts of invaders.*) This suggests that after binding to thyroid receptors the p56/59 OASL proteins could target them for destruction with their ubiquitin motifs.

**Conclusion:** the authors propose that the fatigue seen in CFS and in those patients given IFN  $\alpha/\beta$  treatments is caused when increased IFN  $\alpha/\beta$  activity causes the 2-5OASL proteins to either repress thyroid receptor activity (p30 or p56/59) or target the TR's (p56/p59) for destruction by proteasomes. Since the signal from the thyroid hormone is unable get through to the cells nucleus these patients remain biochemically euthyroid but clinically hypothyroid.

*(One wonders why the body would have IFN target the thyroid receptor? What positive function could this serve? Perhaps the fatigue generated is an important part of the body telling itself to rest?)*

Contact: Cort Johnson at



1st July 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Madam,

I am writing in support of Dr. Gordon Skinner who is to go before the G.M.C. on the 28th July, 2011.

I have been a patient of Dr. Skinner's since [redacted], when I was [redacted] years old, and during this time he has treated me in a kind and professional manner bringing me back to the good health I have today. Prior to seeing Dr. Skinner my health was not being improved by N.H.S. treatment for Hypothyroidism and I was severely suffering. Dr. Skinner has restored me to a healthy functioning life.

Yours faithfully,

[redacted]

[redacted]

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Monday, 04 July 2011

The General Medical Council  
St. James Building  
79 Oxford Street  
Manchester  
M1 6FQ

Dear Ms Cook,

**Ref. GMC Hearing Re Dr. G.R.B. Skinner (GMC Reference 0726922)**  
**to be held 28<sup>th</sup> July 2011 onwards**

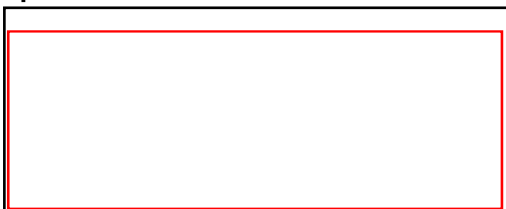
I wish to inform the GMC that I fully support Dr. GRB Skinner in both his work as a Private Medical Practitioner and his modus operandi in this role. He has helped many patients, of which my wife is just one, achieve a return to better health and has not harmed any patients or put them at risk. The same cannot be said for the many endocrinologists and GP's whose intransigence has resulted in their patients seeking Dr. Skinner.

I implore the GMC to allow Dr. Skinner to continue unfettered in his supporting and life saving work.

Yours faithfully,

Copies to:

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Mr Ralph Shipway  
5, Great College Street  
Westminster  
London  
SW1P 3SJ

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6 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester, M3 3AW

Cc: [redacted]  
Mr Ralph Shipway

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Dear Ms Cook

**Re: Support for Dr Gordon Skinner**

I am writing to express my support for Dr Skinner and urge the GMC to allow him to continue his crucial work in treating thyroid patients in the UK.

I became ill in early [redacted] with [redacted]  
[redacted] Blood testing revealed that I was "within  
reference range" for all variables, and thus there was nothing wrong with me. A  
range of GP's and two consultants told me there was nothing they could do to  
treat me. [redacted]  
[redacted]

My physical condition steadily declined through [redacted] and [redacted] I resigned from  
my job in [redacted] feeling that I was unable to  
[redacted] I spent the remainder of [redacted] researching treatments for chronic  
fatigue syndrome (CFS) / ME, with little success. I steadily lost hope in being well  
again. I was too ill to consider working full time and I started to anticipate being  
on long-term disability benefit.

In early [redacted] I became aware that hormonal imbalances were a possible cause  
of CFS/ME and I began to research this issue. I noticed that the symptoms of  
CFS/ME and those of hypothyroidism were almost identical, and I started to  
suspect that hypothyroidism was the underlying cause of my illness. I quickly  
learned of Dr Skinner's work and reputation in this field. I went to see him in  
[redacted] and he immediately diagnosed me as being hypothyroid. Despite  
blood tests which showed I had normal thyroid chemistry, Dr Skinner showed me  
my clear physical signs of hypothyroidism [redacted]  
[redacted]

[redacted] None of the doctors I had previously consulted  
had even bothered to do a physical examination and were thus unaware of most  
of these clinical signs.

Dr Skinner prescribed thyroxine and later Armour thyroid, and after taking it for several months I have made significant progress in recovering from my illness. Many of the symptoms have disappeared and others have significantly lessened. I expect to be fully recovered within the next several months. Dr Skinner has repeatedly advised a gradual and cautious use of thyroid replacement medication despite my eagerness to accelerate the process with higher dosages.

Because my thyroid chemistry was within the "normal" reference range for the standard tests (i.e. TSH and FT4 tests), I was essentially written off by the medical profession until I found Dr Skinner. He recognised that I was clinically hypothyroid despite having "normal" thyroid chemistry and was prepared to treat me and my symptoms rather than my blood tests. I now look forward to a healthy and happy future rather than a life of chronic illness and incapacity.

Dr Skinner's advice and treatment is desperately needed by thyroid patients in the UK. I urge you to allow him to continue his critical work. Please contact me if you require any further information (contact details below).

Sincerely,



[REDACTED]

Investigation Officer  
Heather Cook  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER M3 3AW

2 July 2011

Dear Ms Cook

Re: Dr Gordon Skinner – Hearing July/August 2011

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I wrote to the GMC voicing my views in support of Dr Skinner in 2007 and am shocked to find myself having to do it all over again. I am nearly [REDACTED] now and dictating this as my writing these days is very difficult to read.

[REDACTED]. In our day we always believed the disgrace of appearing before the GMC was reserved for doctors who harmed their patients. Nothing could be further from the truth in the case of Dr Skinner who is a wonderful man.

Both my daughter, [REDACTED] and her daughter [REDACTED] have been recipients of his excellent care. Indeed, I became hypothyroid some years ago and on the strength of their treatment regimes my GP treated me in the same way and I too recovered. You could say I am now a patient of Dr Skinner's by proxy! Anyway I'm very grateful to have had 'his' treatment.

We are a thyroid family and I could never understand why this was not taken into account when family members became ill and could not get treatment. It took [REDACTED] years for [REDACTED] despite it being apparent even to me that she had all the signs and symptoms in the book. She was very unwell for a long time but the blood tests always said she was normal. Rubbish. Normal she was not.

Fortunately, once treated by Dr Skinner, Sue was able to see clearly for the first time that my granddaughter [REDACTED] was also desperately in need of treatment. [REDACTED] was lucky. Her blood tests showed her to be very unwell and she rapidly became a patient of Dr Skinner – with excellent effect. [REDACTED]

[REDACTED]

There is clearly something wrong with the test for hypothyroidism. In my day it was clearly apparent from the signs and symptoms if a patient had the condition. These days they can have them till they are blue in the face but if the test says they are alright, no treatment. I think relying just on a blood test is a very poor medicine. Indeed, I think it is a scandalous state of affairs. Thank goodness for Dr Skinner.

My son-in-law recounts with utter relief the first consultation my daughter had with him. It lasted over an hour and during that time the most thorough history, test evaluation, examination and discussion took place. This was a complete contrast to the useless consultations [REDACTED] had had with endocrinologists and doctors over the [REDACTED] long years. Thanks to Dr Skinner, [REDACTED] made a brilliant recovery and has been well ever since.

In conclusion I can only say that I think there is something very badly wrong with endocrinologists today and with their teaching of thyroid medicine. NHS doctors are terrified of coming before you if they ignore the diagnostic blood test and consequently fail to treat their patients. Endocrinologists go on to diagnose them with ME and the endocrinology gravy train is then guaranteed. SHAMEFUL. What is the GMC doing about it?

Yours sincerely, [REDACTED]

[redacted]  
Miss Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
MANCHESTER M3 3AW

4 July 2011-07-02

Dear Miss Cook

Re: Dr Gordon Skinner

My sister [redacted] has told me that her doctor, Dr Skinner, has got to appear before the GMC again. I'm very sorry to hear this as it upset our family a lot when it happened last time, fearing he would no longer be able to treat his patients.

By all accounts from [redacted] and my niece, [redacted] who is also his patient, he is a wonderful doctor who transformed their lives when he gave them the correct treatment. [redacted] in particular had a dreadful experience, being unable to get any treatment at all for her hypothyroidism over an [redacted] year period.

[redacted]

This is how bad it gets for patients without hope when they cannot get any treatment, or even the right treatment, for such a common condition. I gather that with both [redacted] and [redacted] they fell foul of some blood test or other which decreed they didn't qualify for treatment. It blows your mind when you see people so ill being turned away by the medical profession for something as stupid as THAT. It is cruel and unnecessary. It makes you want to scream with frustration.

We are a medical family and also a thyroid family – but even that is no use, it would appear, when things are really bad. My father [redacted] would turn in his grave if he could see what is going on now. Getting treatment is like getting blood out of a stone.

Is the GMC in a position to do something about all this?? If [redacted] went from being so ill, SO quickly; what about all the others in this world in the same position? Surely the GMC are perfectly placed to look into this situation. It is all so hushed up. You wonder what is going on.

Clearly the one person who must be saved to continue his amazingly successful work is Dr Skinner. Our family love him and we haven't even met him! Please ensure that nothing happens to prevent him continuing to treat his patients. He is a wonderful doctor. You need someone out there who gets his patients better.

Yours sincerely, [redacted]  
[redacted]  
[redacted]

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[REDACTED]

6 July 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

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Dear Ms Cook

**Dr G Skinner**

This letter is in support of Dr Gordon Skinner.

I became a patient of Dr Skinner a [REDACTED] ago because of the problems in getting effective treatment for hypothyroidism through my NHS general practitioner.

It is vital to me that my illness is treated properly so that I can continue to pursue my career, earn a living, and look after my family properly, for which I need good health, energy and a clear mind. My general practitioner was unable to provide an effective treatment: he was prepared to leave me with [REDACTED] [REDACTED], as he believed my hypothyroidism resolved despite evidence to the contrary. Therefore, I researched doctors with specialist knowledge of hypothyroidism and asked to be referred to Dr Skinner, although I did not know him, or of him, beforehand.

I have found that Dr Skinner is an intelligent, professional, caring doctor who has an excellent understanding of thyroid problems and the experience to provide suitable treatment. Dr Skinner's analytical approach, and thorough consideration of all the evidence available, meant that he was able to provide a much more effective treatment. He went into much more detail, asked for far more information, and spent longer considering the best solution before coming to a

[redacted]

recommendation. After only a couple of months, I feel much better than I had after [redacted] of treatment with my GP: [redacted]

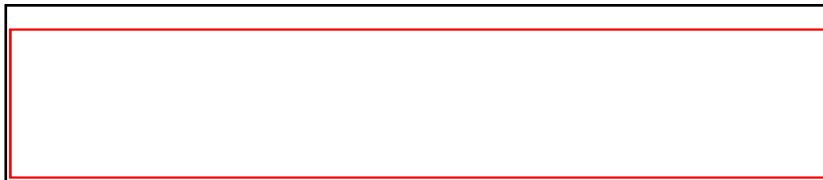
[redacted]

I feel that Dr Skinner should be employed as an example of good practice. He should be invited to teach the new generation of doctors how to properly evaluate all the information available and tailor their treatment to each individual, rather than jump to the standard treatment and hold to that whether it works or not.

Yours sincerely

[redacted]

[redacted]



Investigation Officer  
Heather Cook  
Fitness to Practice Directorate  
General Medical Council  
MANCHESTER M3 3AW

3 July 2011

Dear Ms Cook

**Re: Hearing for Dr Gordon Skinner - July 28/29 & August 1,2,3**

I am the son of [redacted] the brother of [redacted] and the good friend of [redacted] all of whom are patients of Dr Skinner.

I would like to testify to the hearing of the excellent treatment they all received from Dr Skinner. My mother tried consistently over [redacted] years to get treatment for her under-active thyroid. Again and again she was prevented from receiving it by the blood test, taken repeatedly, which always indicated that her health was normal, when it most certainly wasn't. As a consequence she could get not treatment. As a family we were mystified because she was clearly so very unwell and struggling. Eventually she was diagnosed [redacted] which outraged her as they told her then there was no further treatment she could have. She knew it was her thyroid and the whole awful thing ruined her life for [redacted] years.

In [redacted] she heard about Dr Skinner and was referred to him. In a remarkably short time he restored her to normal again. All it took was a drug called Thyroxine which he gave to her in appropriate doses - which apparently the NHS are barred from doing above a certain level. All I can say is that it was like watching her coming back to life.

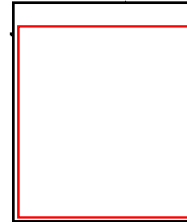
Our family holds Dr Skinner in the highest esteem. He treated my sister [redacted] with the same success. When my then girlfriend, [redacted] was diagnosed [redacted] she was devastated. Fortunately I was able to get my mother to talk to her about her experiences and she too then went on to see Dr Skinner with excellent results. It seems so simple if you know what you're doing, as Dr Skinner clearly does. What on earth is wrong with a system that condemns so many people to a life of misery, without treatment, all for want of passing the great blood test?

I can only ask why a man who has such success treating patients, is in danger of losing his livelihood by appearing before the GMC? What about all the doctors who failed my family? Will you be holding them to account for withholding treatment? I find the whole thing baffling. Dr Skinner is a remarkable man for whom I have the utmost respect.

Yours sincerely, [redacted]



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05/07/2011

**Testimonial with regard to Dr GRB Skinner**

Heather Cook  
Investigation Officer

Dear Madam

I was diagnosed by my general practioner in [redacted] with an underactive thyroid.  
I was prescribed Thyroxine, although my blood results returned into the perceived normal range, I was still experiencing many distressing symptoms associated with the condition.

Fortunately I was referred to Dr Skinner in [redacted], he performed a physical examination and painstakingly went through my symptoms.

In place of Thyroxine Dr Skinner prescribed Armour Thyroid medication.  
I was started on a low dose, and after as little as [redacted] weeks or so, I was showing a marked improvement with many of the symptoms subsiding.

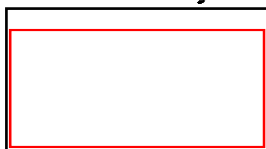
My progress in the following months was carefully monitored by Dr Skinner, as my dose of natural thyroid hormone was increased to the correct level for me.

I was returned to full health because of Dr Skinner's extensive knowledge and care.  
I am extremely grateful to him.

I remain in good health and continue with the natural thyroid hormone instead of thyroxine.

Dr Skinner continues to monitor me on an annual basis.

Yours faithfully



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6th July, 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms. Cook,

**Testimonial for Dr. Gordon R.B. Skinner**  
**Review Hearing 28<sup>th</sup> July to 3<sup>rd</sup> August.**

Dr. Skinner has, over the years, helped my family where other doctors have failed.

1) Firstly, he saw my daughter [redacted]  
[redacted] Her health was rapidly going downhill [redacted]

Dr. Skinner prescribed thyroid medication for her and the improvement in her health was dramatic. She has never looked back since.

2) Secondly, my wife was so ill for so many years and I went with her to GP appointments where they actually said it appeared like hypothyroidism, but the blood tests said otherwise. I was seriously worried [redacted]

After finally seeing another doctor, the GP said my wife looked so classically hypothyroid, she couldn't understand why on earth no-one would give her a trial of thyroxine. Eventually, my wife saw Dr. Skinner and after some time he changed her medication to T3. It is no exaggeration to say that my wife could have ended up in a wheelchair without his help and thanks to him she resumed a normal life until the last couple of years when her health again declined dramatically. The whole family were very worried about her, but eventually, earlier this year her GP referred her back to

Dr. Skinner and I am pleased to say that as a result she has now reversed the terrible decline in her health purely through dosage changes.

3) My younger daughter also saw Dr. Skinner because she had symptoms of hypothyroidism. [redacted]

[redacted] She was treated with thyroxine and is now well [redacted]  
[redacted]

My wife and two daughters have had excellent treatment from Dr. Skinner over the years and he deserves to be allowed to give other patients the same care. In fact he should be applauded for the fantastic work he is doing. Those who are against the proper treatment of this terrible condition should be the ones whose performance is questioned.

Yours sincerely,

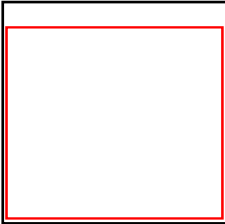
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Copies to Mr. Ralph Shipway

[redacted]



  
Heather Cook,  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

6 July 2011

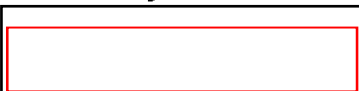
Dear Ms Cook,

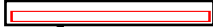
I request that you remove any conditions on Dr G. R. B. Skinner's registration forthwith and cancel the review hearing that is due to take place at the end of July/ beginning of August so that this excellent and outstanding doctor would then be able to use this time to diagnose and treat additional patients and restore their health and lives.

I know that Dr Skinner is a brilliant doctor and I speak from personal experience as he rescued my twin sister and I from the severe and debilitating symptoms that had resulted from our under treated hypothyroidism (as a result of NHS doctors decreasing our thyroxine treatment on the basis of our TSH results). Dr Skinner evaluated us carefully and patiently, asking questions and carrying out a clinical examination. Furthermore, NHS experts were forced to admit that we did require the treatment and dose of Natural Desiccated Thyroid treatment e.g. Armour Thyroid that Dr Skinner prescribed for us thus endorsing Dr Skinner's diagnosis and treatment.

Many other patients have benefitted from Dr Skinner's skill as a medical practitioner, at the last GMC hearing, with reference to Dr Skinner, the GMC Panel stated "It is clear that you are a caring and compassionate doctor whose overwhelming concern is the care and wellbeing of your patients, many of whom have pleaded that you should be allowed to continue to practise." [Fitness to Practise hearing, November 2007, Page D19/3, Paragraphs F, G and H of transcript]... and, "A large body of evidence has been submitted throughout this case demonstrating that many patients have benefitted from the medication that you have prescribed." [Fitness to Practise hearing, November 2007, Page D19/4, Paragraph A].

I would be most grateful for confirmation of receipt of this letter.  
Yours sincerely,



cc. Dr G. R. B. Skinner,  
cc.   
cc. Mr Ralph Shipway.

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**WITNESS TESTIMONY IN SUPPORT OF DR GORDON R B SKINNER MD, DSc, FRCOG,  
FRCPath**



FAO: Heather Cook, Investigation Officer  
Fitness to Practise Directorate, General Medical Council  
3 Hardman Street, Manchester, M3 3AW

Dear Ms Cook

I have written to the GMC previously in support of Dr Skinner. He is an exceptional doctor and I say this with complete confidence because he saved the lives of both my daughters. Therefore, in order that you understand just how grateful myself and my family are to Dr Skinner, I enclose a full testimonial which describes exactly how he helped my daughters recover from severe hypothyroidism, after their medication had been drastically reduced by their GP. I think it is important that you know that his treatment and care of my daughters has meant that they have fully recovered their health.

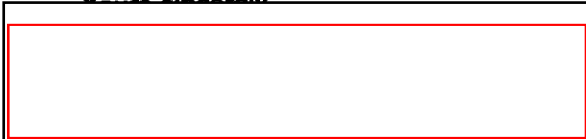
I also think it is important that you know that the treatment regime recommended by Dr Skinner ie [treatment with natural desiccated thyroid] was later endorsed in writing by two eminent endocrinologists. This endorsement was made available to the FTP panel during the hearing in 2007.

[Redacted]  
I personally met hundreds of patients who had been helped by Dr Skinner. It therefore came as no surprise that at the end of the hearing, the panel conceded that, *"It is clear that you are a caring and compassionate doctor whose overwhelming concern is the care and wellbeing of your patients, many of whom have pleaded that you should be allowed to continue to practise."* [Fitness to Practise hearing, November 2007, Page D19/3, Paragraphs F, G and H of transcript]..... and, *"A large body of evidence has been submitted throughout this case demonstrating that many patients have benefitted from the medication that you have prescribed."* [Fitness to Practise hearing, November 2007, Page D19/4, Paragraph A]

What did come as a surprise or rather a shock was that conditions were placed on Dr Skinner for three years and that a further hearing is to take place at your offices at St James's Building, Oxford Street, Manchester, for 5 days commencing 28<sup>th</sup> of July 2011 until 3<sup>rd</sup> August 2011 in respect of these conditions.

[Redacted]  
[Redacted] I should like to receive confirmation that this letter, together with the enclosed statement of truth and fact will be presented to the panel at the above hearing.

Yours sincerely,



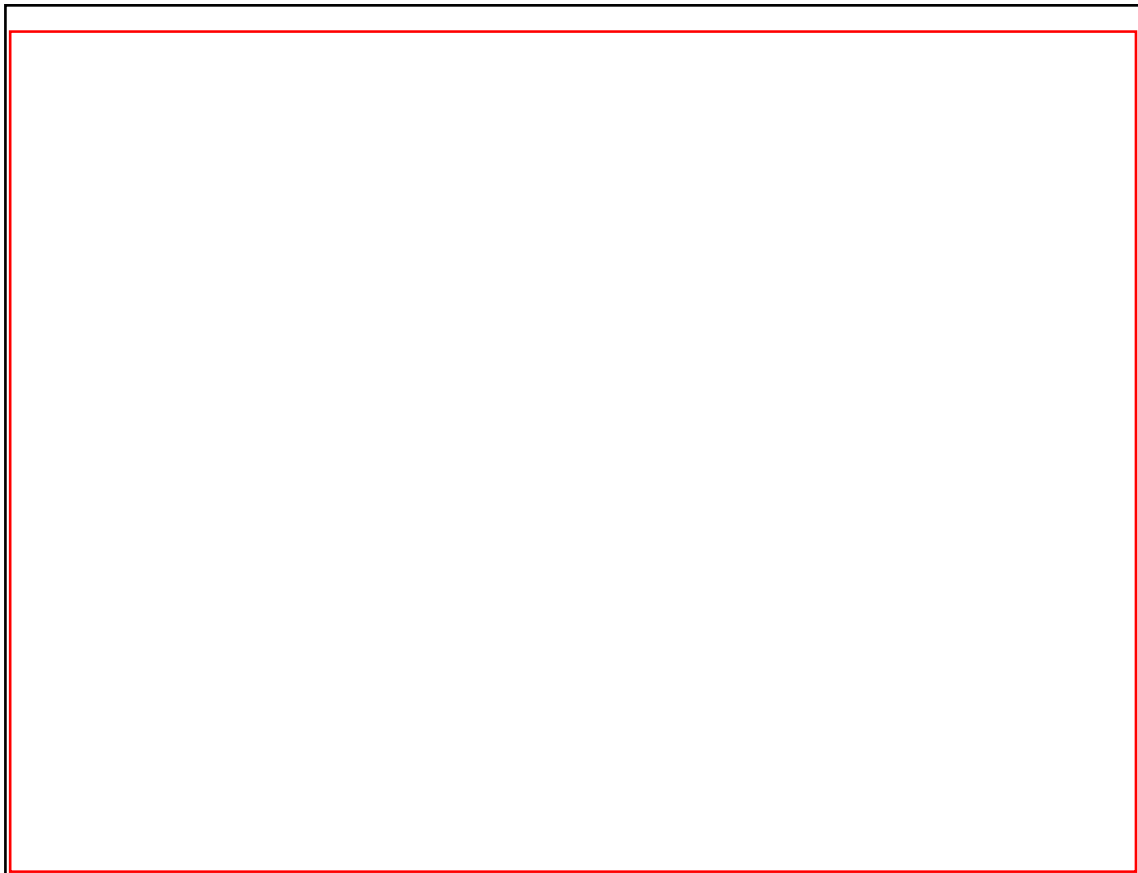
cc. Dr G. R. B. Skinner, [Redacted] Mr Ralph Shipway.

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**STATEMENT OF TRUTH AND FACT RE DR. G R B SKINNER MD (HONS) DSc FRCPath  
FRCOG**

This statement of truth and fact has been written in full support of Dr G R B Skinner and is to be presented as evidence at the forthcoming review hearing due to commence at the GMC Fitness to Practise Directorate, Manchester on the 28th of July 2011.

I am the mother of identical twin daughters. Both daughters developed hypothyroidism in childhood, one after the other. It was some time before the first twin was diagnosed, since her condition was not recognised by the GPs at that time. However, eventually a diagnosis of hypothyroidism was made following a consultation with a paediatrician. Diagnosis of the second twin (who developed hypothyroidism a couple of years after the first twin) was made by the same paediatrician. This paediatrician prescribed thyroxine, which he said would be required for the rest of their lives. Were it not for his care, neither of my daughters would have developed normally, either physically or mentally.



They went to the local surgery where they begged for another blood test as something was very wrong. When the blood test results came back this time, they showed that my daughters had both become seriously under treated for their hypothyroidism and their dosage was partially re-instated immediately. Later, as a result of further blood tests, the GPs would not contemplate increasing the dosage further, to the original amount, even though my daughters remained very unwell and continued to present with numerous

[redacted] My daughters continued to decline and due to their many symptoms including [redacted]  
[redacted].

My daughters were desperate and they wrote to several doctors who had an interest in hypothyroidism including Dr Skinner. He responded almost immediately and said that he would see them, provided they were referred by their GP. This was around [redacted].

I accompanied my daughters to the local surgery where I requested an appointment to see their GP. My daughters were so very ill [redacted]  
[redacted] On seeing the GP, I told her that her treatment of my daughters just wasn't working and that there was a doctor who might be able to help. We provided her with contact details of Dr Skinner and she referred both my daughters to him.

In [redacted] my daughters were taken to see Dr Skinner. Dr Skinner was a revelation. He first of all listened to what they had to say, he then questioned them further with regard to their signs, symptoms and family history and carried out a thorough examination. He was sympathetic and kindly and over the coming months, made necessary adjustments to their dosage and to their medication and put them on the road to recovery.

My daughters are now well again thanks to Dr Skinner and the story doesn't end there,  
[redacted]

[redacted] None of the above would have been possible if it were not for Dr Skinner and his treatment regime. My family and I cannot thank him enough.

My daughters continue to thrive and It should be noted that Dr Skinner's treatment regime was subsequently endorsed in writing by two eminent endocrinologists, so in my view, there can be no doubt regarding the quality of care provided by Dr Skinner or his competence as a physician.

I write this statement of truth and fact and declare it to be an accurate and factual account of what has happened in relation to my daughters.

[redacted]  
cc. Dr G. R. B. Skinner, [redacted] Mr Ralph Shipway.

Heather Cook,  
Investigation Officer  
Fitness to Practise Directorate, GMC

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6/7/2011

Dear Ms Cook

RE: DR GORDON R B SKINNER MD, DSc, FRCOG, FRCPath

I am writing this letter in support of Dr Gordon Skinner whose review hearing is due to take place late July, early August 2011. I felt it necessary to write to you to let you know that Dr Skinner is an excellent, caring and compassionate doctor, who has treated both my daughters for severe hypothyroidism and returned them to good health.

My daughters became hypothyroid during childhood, but later in [redacted] when adults, their medication was gradually reduced by their GP due to concerns of suppressed TSH following blood tests. This reduction continued, until they were being prescribed half their original dosage. They both began experiencing hypothyroid symptoms within days of reducing their medication until many months later, their situation became desperate. This dreadful state of affairs continued until [redacted] [redacted] during which time they both became extremely ill.

It took referral to Dr Skinner by their GP, for things to improve. Dr Skinner was kindly and sympathetic towards my daughters and were it not for his professionalism and his care and treatment of my daughters over the next couple of years, I dread to think what would have become of them. As it is, as already stated he has returned them to good health.

During the IOP and FTP hearings [redacted] [redacted] there appeared to be an attempt to discredit Dr Skinner's methods, yet NHS endocrinologists had endorsed the treatment regime that Dr Skinner had begun with my daughters. In addition, not once have I seen or heard a witness say that Dr Skinner has harmed them, yet I have become very aware of the thousands of patients he has helped. This was further endorsed by, the FTP panel in November 2007, who stated that "A large body of evidence has been submitted throughout this case demonstrating that many patients have benefitted from the medication that you have prescribed." (FTP TRANSCRIPT Page D19/4, Paragraph A)

Therefore, I have to say that whilst the GMC has a job to do in regulating doctors, in the case of Dr Skinner, I really do not understand why he was brought before the GMC and pursued in such a manner in the first place. He has helped so many patients regain their health. He is also exceptional in that he is a research scientist of some renown – thus his care of his patients is meticulous. Dr Skinner is a doctor that the medical profession can be proud of and one that helps to uphold and maintain the reputation of the medical profession in general, as such he is to be valued.

Would you now be so kind as to pass on this letter of support of Dr Skinner to the review panel and confirm its receipt?

Yours sincerely

[redacted]

cc. Dr G. R. B. Skinner, [redacted] Mr Ralph Shipway [RadcliffeleBrasseur]

[redacted]  
Heather book  
Investigation officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman St,  
Manchester  
M3 3AW

4-7-11

General Medical Council	
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Dear Madam.

Dr. Gordon Skinner

I was extremely sorry to learn that there is another 'Fitness to Practice Hearing' scheduled for Dr. Skinner.

This gentleman is a truly exceptional being, notwithstanding that he has reached retirement age - his duty is to ~~be~~ make thyroid sufferers well, regardless of the guidelines laid down by the British Thyroid Association and the RCP, which keep many (mainly women) in ill-health.

I was completely ignorant of the function of the thyroid gland, but, believe me, over the past [redacted] years I have had a quick learning curve, what with being undiagnosed + misdiagnosed [redacted]  
[redacted]  
[redacted]

[redacted] I cannot believe the incompetence. Initially I was extremely grateful for levothyroxine, but since the [redacted] month new symptoms appeared gradually.

To cut a long story short, I added T3 to T4, and the result was amazing.

and I felt a return to good health.

I still had a few things to be remedied & I consulted Dr. Skinner, he was the only doctor ( [redacted] ) who looked at my tongue [redacted]. No other medical person did this previously, neither did they have a clue what was wrong with me.

Thyroid UK has been a godsend to me & I am extremely sorry for all those for whom levothyroxine is not working - it takes an enormous toll on relationships, marriages, work etc, when GPs/Endocrinologists state the symptoms are not connected to thyroid.

In my case - all new symptoms were caused by synthetic TH alone.

Dr. Skinner is one of the doctors of the "Old School" wherein the patient's wellbeing is at the front.

It would be wonderful if Dr Skinner + [redacted] <sup>could</sup> pass on their immense expertise to all our younger doctors.

Dr. Skinner's book also informed me of the reasons I most probably became [redacted]

His book makes enormous sense & he is a brave person.

He should have an Honour given for helping others, ~~to~~ instead of having a "fitness to practice hearing".

Yours sincerely



[redacted]  
12 July 2011

Heather Cook, Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester, M3 3AW

Dear Ms Cook,

Re: Dr Gordon R B Skinner MD DSc FRCPath FRCOG – Hearings in July and August.

It must be difficult for someone, medical practitioner or not, who has not suffered from a long term Thyroid problem, left untreated by GP and specialist alike - sometimes for years - to understand our sheer anger, frustration and downright disbelief, that once again the GMC is investigating Dr Skinner.

This is a terrible use of time and resources all round. The outcome will be that instead of Dr Skinner being able to concentrate on his patients, who rely on his skill, care, dedication and professionalism to get and keep them well, he will, yet again, have to devote some of his precious time to the GMC hearing. This is lamentable.

As far as I can tell he has done his utmost to comply with the GMC's conditions of practice; if you contact his surgery as a prospective patient you receive a number of pages explaining these conditions, which he insists have to be adhered to to see him. I am not one of his patients but if I lived in the UK I would go out of my way to try to be one.

I found his book: *'Diagnosis and management of Hypothyroidism'* to have been invaluable. I was one of those people with 'normal' thyroid blood test results. I was not well and was getting worse. Neither my GP (insisting on depression) nor an Endocrinologist would consider treatment – a scenario repeated in the UK perhaps hundreds if not thousands of times - but armed with information from his book I persevered. I was lucky; I was finally seen by a young Endocrinologist at a well regarded Hospital in [redacted] Fortunately for me, although sceptical, she listened, was curious and was prepared to look beyond 'normal'!. Exactly what Dr Skinner does! The surgeon [redacted] was amazed I had been left so long - untreated! This is what is happening today, many Doctors and even Endocrinologists are obsessed with 'normal' laboratory results, unable, or afraid, to look beyond their noses or computer screens at the clinical signs staring them in the face.

I have absolutely no doubt you have had complaints about Dr Skinner, **but how many of these complaints come from patients he has treated? How many?** It is extraordinary and disgraceful the lengths some so called medical professionals will go to try to discredit a college whose work they disagree with. It is even more incredible that the GMC allows itself to be sucked into this cesspit of spite – and unfortunately this is not an isolated case.

Wake up! It is patients, their care and wellbeing that should be your priority, not the (anonymous) blinkered, out of touch vested interests of a tiny minority of so called experts.

Yours sincerely, [redacted]  
[redacted]

CC [redacted] Mr Ralph Shipway 53



[redacted]  
[redacted]  
Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

[redacted]  
13th July 2011

**Dr. Gordon R B Skinner – Review 28th July**

Dear Ms. Cook,

Please accept this letter in support of Dr. Skinner. Since the hearing is a review I believe patient evidence should now be treated as **evidence of fact**.

For [redacted] years from [redacted] I suffered [redacted]  
[redacted]

I had numerous medications and extensive investigations. I was referred to an endocrinologist who carried out a number of thyroid function tests, the results were always in the middle of the reference intervals. He was adamant I was euthyroid, because the blood test said so!

I asked my GP for a referral to Dr. Skinner, after a detailed consultation he said he thought I might be hypothyroid and I was started on [redacted] µg thyroxine. [redacted]  
[redacted]

My improvement since then has been enormous. By [redacted] I had fully recovered physically, mental capabilities although not as sharp as they could be had dramatically improved. I was taking [redacted] µg Levothyroxine (L-T4) plus [redacted] µg Liothyronine (L-T3) daily which put my TSH and fT3 figures well outside their respective reference intervals.

I was profoundly ill whilst "biochemically euthyroid" and I am now healthy whilst "biochemically hyperthyroid". These terms are of course nonsense. It is the patient that is euthyroid, hypothyroid or hyperthyroid - not the bloody blood test. This clinical picture and biochemistry points to a form of hormone resistance, the patient produces sufficient hormone but is unable to fully utilize it. Various types of thyroid hormone resistance are known, such as mutations to the gene that produces the beta-1 thyroid hormone receptor and polymorphisms in deiodinase genes. These patients usually have an abnormal thyroid profile (they will only get a referral if their thyroid profile is abnormal).

Hormone resistance with a "normal" thyroid profile is a fascinating and rewarding subject for any doctor to undertake. One would hope it would spur endocrinologists into enthusiastic research rather than firing off malicious, flippant and false accusations against colleagues who put their patients ahead of their egos. In the absence of any helpful contribution from the endocrinologist establishment I attach two research projects I have undertaken in order to debunk the assertion that prescribing L-T3 is either unnecessary or dangerous and to reveal the aetiology of my form of hypothyroidism. It's a pity that Dr. Skinner's accusers could not have got off their backsides and made a similar contribution to thyroid patient care.

Yours faithfully,

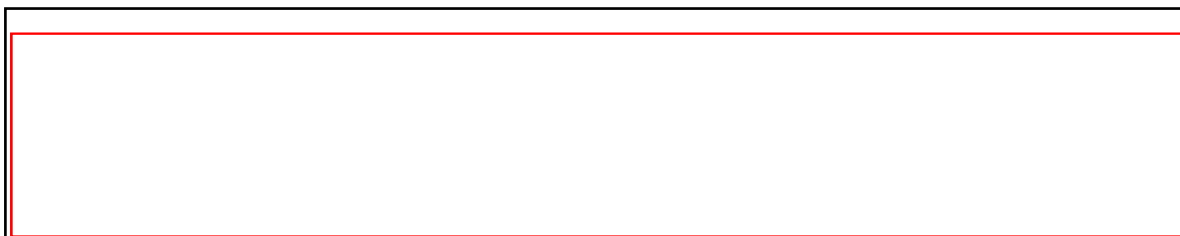
[redacted]

### **Safety and Effectiveness of Liothyronine**

The prescribing of Liothyronine Sodium (L-T3) as treatment for hypothyroidism has been criticized as unsafe and unnecessary. Nonetheless, it is prescribed by many physicians and is a preferred treatment option for a large body of patients. It is hypothesized that some patients may be less able to convert T4 to T3 (impaired deiodinase activity).

A 1999 study published in the New England Journal of Medicine demonstrated improved mood and neuropsychological function in patients who had 50µg L-T4 replaced by 12.5µg L-T3. A number of follow-up studies proved inconclusive. These trials used an average baseline L-T4 dose in the range of 100µg to 130µg L-T4, which many thyroid patients and physicians would regard as inadequate. None of these trials targeted patients who have, or might be expected to, respond to combined L-T3 / L-T4 treatment. A 2009 study carried out in Bristol demonstrated superior results for combined L-T3 / L-T4 treatment in patients with a specific polymorphism of the DIO2 deiodinase gene. This polymorphism has no effect on circulating thyroid hormone levels.

It is claimed that L-T3 therapy exposes patients to wildly fluctuating levels of hormone which puts them at risk, particularly from coronary events. The elimination half-life of L-T3 in adults is often inaccurately claimed to be 24 hours, in practice it is closer to 2½ days as per the attached document from the FDA. In any event these figures represent the levels of T3 detected by the specific assay used and not the body's response to the hormone. L-T3 goes through many stages, including binding to serum transport proteins, cellular transport, binding to thyroid hormone receptors and the thyroid response element of the DNA, production of mRNA and translation into proteins which finally are available for metabolic action. All of these actions take time and effectively act as buffers. The TSH of patients taking twice daily L-T3 does not fluctuate. I may drink a large glass of water and discover its elimination half-life is quite brief. I am not placed at risk by my erratic ingestion of H<sub>2</sub>O.



Extract from DailyMed which provides high quality information about marketed drugs including FDA labels. DailyMed is a service provided by the United States National Library of Medicine.

#### **LIOTHYRONINE SODIUM - liothyronine sodium tablet**

##### **CLINICAL PHARMACOLOGY**

The mechanisms by which thyroid hormones exert their physiologic action are not well understood. These hormones enhance oxygen consumption by most tissues of the body, increase the basal metabolic rate and the metabolism of carbohydrates, lipids and proteins. Thus, they exert a profound influence on every organ system in the body and are of particular importance in the development of the central nervous system.

##### **Pharmacokinetics**

Since liothyronine sodium (T3) is not firmly bound to serum protein, it is readily available to body tissues. The onset of activity of liothyronine sodium is rapid, occurring within a few hours. Maximum pharmacologic response occurs within 2 or 3 days, providing early clinical response. The biological half-life is about 2-1/2 days.

T3 is almost totally absorbed, 95 percent in 4 hours. The hormones contained in the natural preparations are absorbed in a manner similar to the synthetic hormones.

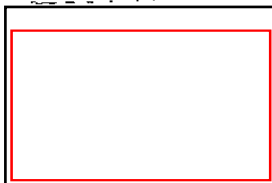
Liothyronine sodium has a rapid cutoff of activity which permits quick dosage adjustment and facilitates control of the effects of overdosage, should they occur.

The higher affinity of levothyroxine (T4) for both thyroid-binding globulin and thyroid-binding prealbumin as compared to triiodothyronine (T3) partially explains the higher serum levels and longer half-life of the former hormone. Both protein-bound hormones exist in reverse equilibrium with minute amounts of free hormone, the latter accounting for the metabolic activity.









3<sup>rd</sup> July 2011

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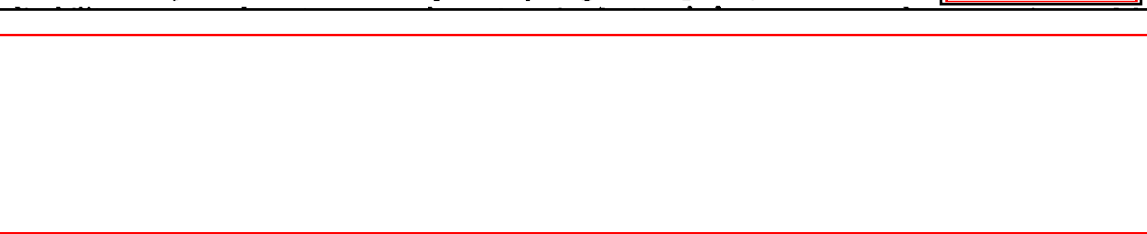
**RE: DR GORDON SKINNER MD, BSC FRCPath FRCOG - GMC HEARING**

I am writing to register my support for Dr Skinner in his GMC hearing.

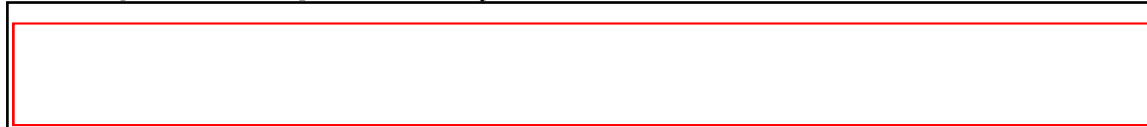
In [redacted], aged [redacted] I became unwell, [redacted]

[redacted] I visited my GP who conducted blood tests, and I was informed that my thyroid result had come back "borderline" underactive. I was asked to come back in six weeks for another test, which I was told had come back "normal". I was diagnosed with [redacted] [redacted] and told that there was nothing doctors could do for me other than send me to a support group. My thyroid was not mentioned any more at that point, and no one informed me what the symptoms of having an underactive thyroid even were. During all the time I had an ME diagnosis, I struggled with various different GPs who "didn't believe in it" and thought it must all be "in my head".

I slowly came to terms with the fact that my health would probably be poor for the rest of my life, and I may not be able to complete my degree or get a job afterwards. [redacted]



Eventually, I reached a point where my health was at its' lowest [redacted]



[redacted] During one of these appointments, the GP suggested I should have my thyroid tested. Although the results came back "normal" once again, this gave me the push I needed to look into what the symptoms of an underactive thyroid actually were. When I saw the list, I was amazed to see that I had the vast majority of symptoms mentioned. During my research, I came across Dr Skinner's name, and asked my GP to refer me to him, which she did. [redacted]



Dr Skinner was the first doctor who actually listened to what I had to say. He gave me an examination, something other doctors had not done. He took my concerns seriously and did not talk down to me or make me feel intimidated. At the end of my first, hour long, appointment with Dr Skinner, he diagnosed me with an underactive thyroid. The next week, I started on medication. Since that appointment in [redacted] I have got my life back. I was able to return to

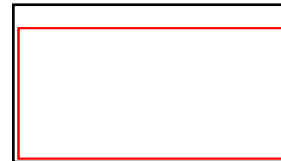
work, and start a second job. [redacted]  
[redacted] I cannot thank Dr Skinner enough for all the help  
he has given me.

Yours Sincerely,

[redacted]



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10<sup>th</sup> July, 2011

Ms. Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
GMC  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook,

**Testimonial for Dr. G. R. B. Skinner**  
**Review Hearing of 28<sup>th</sup> July – 3<sup>rd</sup> August, 2011.**

Dr. Skinner diagnosed me with hypothyroidism around ☐ years ago. I was returned to good health and since that time, my GP has prescribed my thyroid medication.

I found Dr. Skinner to be a caring, compassionate doctor who asked me a lot of questions about how I felt and what my symptoms were. He also checked blood pressure, pulse, temperature, etc and also did blood tests.

I hope other patients can continue to benefit from Dr. Skinner's experience and his exceptional knowledge of this debilitating illness.

Yours sincerely,

**Copies sent to:**  
**Mr. Ralph Shipway**

10 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
Manchester M3 3AW

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**Re: Dr Gordon Skinner – appearing @ the GMC 28/29 July, 1/2/3 August**

Dear Ms Cook

For many years my mother had been suffering an 'unknown' illness that was making her so very unwell that we, as a family, were actually surprised she could live from day to day.

[redacted] the symptoms were lengthy and on-going. They had lasted [redacted] years. She felt this was her life. To all those who knew her this was quite unacceptable.

What I/we didn't know at the time, and what her doctors never picked up (quite shamefully in my opinion), was that she suffered from hypothyroidism. She was left untreated by every doctor she approached.

One evening I was discussing my mother's plight with a friend of mine, [redacted] [redacted] Describing her symptoms she instantly recognised them as her own and told me of Dr Skinner and how he had transformed her life, having herself suffered from similar debilitating symptoms.

**Quite simply: Dr Skinner saved my mother's life.**

Armed with her test results, Dr Skinner listened to my mother, questioned, queried, evaluated and only then diagnosed and prescribed. She spent a long time with him, and was impressed by his thoroughness. My mother did not fall into the 'you have hypothyroidism' blood test results. There are many, many of us that do not. This is not unusual for hypothyroid patients (if anyone would study the clinical evidence thoroughly). However doctors in the UK will not treat patients if they do not fall into the "normal" categories.

I also have hypothyroidism. I too did not pass the infamous blood tests. However I am very lucky and have a broad minded doctor who saw the results of Dr Skinner's treatment (initially obtained privately) positively. She continues to treat me, even though I do not fall into the "NHS rules and regulations".

I would very much like you to take into account that thyroid medicine is NOT an exact science. CLINICAL diagnosis is by far the most important than any statutory blood test. Doctors need to look at the patient and diagnose his or her symptoms, NOT whether or not they fit into a, to be frank, quite ridiculous set of 'rules' set out by people (yes, they are actually doctors) who do not really understand the condition.

Hypothyroid conditions are not ME. It may be easy for a doctor to put this simple label on something they do not understand or cannot spend the funds on to get to the bottom of, but this leaves too many patients untreated, with quite unacceptable lives. Hypothyroidism is treatable, very successfully as my mother and I can attest to.

Please do not allow the medical profession to 'bully' Dr Skinner simply because they do not have the knowledge, clinical experience and expertise that he has gained studying this very debilitating illness. It exists. Recognise it. Allow diligent, intelligent doctors, such as Dr Skinner, to treat it the way it can be treated.

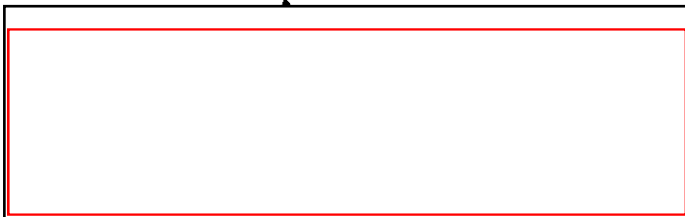
Dr Skinner should be recognised for the value he is to people such as me and my mother. His treatment methods should be evaluated and adopted for the wider good.

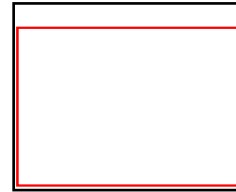
That I have to write again to support such an excellent doctor and clinician renders me speechless.

Dr Skinner has my full and wholehearted support. Without him not only would I not have my mother but I too would be very ill.

Please remember the patients' lives he has changed for the better, indeed saved, when you are discussing these quite ridiculous charges at the GMC.

Yours sincerely





8th July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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Dear Ms Cook,

I am writing this letter in support of Dr Gordon Skinner, who will be having to attend a review hearing at the GMC offices in Manchester from 28th July to 3rd August 2011.

I am one, of no doubt many people for whom Dr Skinner has been a life saver. He was willing to treat me as a whole person and not just a set of blood tests, which thyroid patients in the know, know are at best a general guide and at worst totally useless.

There was a Welsh case last year in which the woman was in a Myxedema coma (thyroid coma)...with "subclinical" thyroid blood tests...the report authors concluded that this woman must have had a much higher PRESET level which made her well and able to function. They concluded also that CLINICAL observations must be given much higher credence...something which Dr Skinner has always done...why then is he having to defend his actions YET AGAIN????!!!!

In 2010 there was also a paper published from Ninewells hospital in Dundee which showed that some people have a defective D102 gene which prevents them from converting the biologically inactive T4 into the biologically active T3...despite "apparently" adequate levels of T4 circulating in the blood stream. Therefore TFT's will never show what is actually happening at a cellular level where the actions occur.

I went through hell to be diagnosed and treated, despite having classic symptoms including a



I saw Dr Skinner in [redacted] (and yes i had a letter of referral from my Gp practice) and since then my life has changed dramatically. He diagnosed my thyroid condition and has prescribed thyroid medication which includes both thyroxine and Natural Dessicated Thyroid products (which are regulated by the US Pharmacopia & FDA) and they have turned my life around. The biggest improvement after my physical health has been my mental health. I cannot describe the feelings when i was reaching the optimal levels for me...it is nothing

short of miraculous. [redacted]

[redacted]

My Gp has acknowledged the vast improvement in my health but refuses to prescribe any thyroid medication for me,i suspect for fear of being in Dr Skinner's shoes. In my view he is a hero and has been willing to stand against the consensus of the Endocrinology field in the UK...a consensus doesn't equate to being right!!!! Even the most conservative members of that field in the US have been astounded at the "guidelines" coming from the BTA. These guidelines state that people shouldn't be suspected of having hypothyroidism until their TSH is over 10...most Western countries have lowered their ranges with many experts in the field thinking that around a TSH of 1 is probably nearer the truth. The BTA's actions are going to consign even more people to a miserable existence. I wish to make the panel members who will sit on Dr Skinner's hearing aware that if they continue to carry out this witch hunt and i cannot be monitored and treated by Dr Skinner then i will explore all avenues available to me through the Human Rights Act and will take legal action if necessary.

My Gp and I have debated the "opinions" of the opposing sides in the field of thyroidology but I am going to go with my EXPERIENCE and all i can say is i'd rather live for [redacted] years as i am today than [redacted] years as i felt before...and i think that says it all.

Yours Sincerely

[redacted]

cc [redacted]  
Mr Ralph Shipway

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
5th Floor, St James Buildings  
79 Oxford Street  
Manchester M1 6FQ

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12 July 2011

Dear Ms Cook,

**Re: Dr G R B Skinner, [REDACTED] - Fitness To Practise Hearing**

My mother, [REDACTED], is one of Dr Skinner's patients. She will be writing separately to provide her perspective on Dr Skinner's treatment of her case. However, I wish to provide my own assessment of her care and treatment prior to her first consultation with Dr Skinner and whilst under his care.

In about [REDACTED], my mother was diagnosed with hypothyroidism following a thyroid function test. Later testing confirmed that she has [REDACTED]. The standard treatment for hypothyroidism, Thyroxine, had limited effect despite her blood levels attaining somewhat higher than "normal" values. Her condition was referred to as a form of thyroxine resistance, or persistent hypothyroidism. Treating her with an "excess" of thyroid hormone in both T4 and T3 form was seen as both responsible and necessary for the treatment of her condition.

Later thyroid function tests showed that her T4 levels had risen to the mid-thirties and her TSH was completely suppressed. Despite this, she remained clinically hypothyroid. The consultant physicians that she saw maintained her at a high level of T4 because they recognised that it brought her some relief. However, a clear strategy for moving forward in the treatment of her condition never materialised. I attribute this, in the main, to a lack of continuity in her care arising from attendance at hospital clinics where, at each appointment, she would see a different doctor.

With my mother in a poor state of health, we attended Dr Skinner's clinic in [REDACTED]. Dr Skinner was thorough in taking my mother's medical history and in examining her. His consideration that higher levels of thyroid hormone would be necessary for the treatment of her persistent hypothyroidism was of no surprise as it confirmed what had previously been diagnosed on several occasions. As noted, she was already on a higher level than would be tolerated by a more restrictive regime i.e. one solely based on blood test results.

Adding T3 to the existing dose of T4 which my mother was taking produced an improvement in her health but not to any great extent. It was only after trying this approach that the use of an animal-sourced thyroid extract was considered. With an incremental change in dose over some time, coupled with Dr Skinner's attention to the detail of her care, my mother's health and quality of life began to improve to the point where she is now active and able to walk several miles at a time.

Throughout this, and continuing to this day, Dr Skinner has required that he be provided with regular blood test results, as well as seeing my mother for regular checks. He has been nothing less than attentive, thorough and successful in his approach -- to his credit and my mother's benefit.

The improvement in my mother's health, which has been sustained over several years, cannot be underestimated in its impact of her quality of life. It is too easy to take for granted the ability to simply be able to leave the house and take a walk on a summer's day. Or, indeed, to simply feel well, without thought for what a chronic health condition is like for the sufferer, day-by-day.

Therefore, I am deeply concerned to learn that Dr Skinner is being criticised on the basis of his approach to treatment of hypothyroidism, an approach which has led to my mother's good health today. To think that a distant tribunal may reach a decision which casts my mother back into the poor health from which she has escaped is of great concern.

Frankly, I am worried as to what the hearing might mean for her as I doubt, in the event of a negative outcome for Dr Skinner, that the architects of that outcome would be offering any help.

It seems to me that any consideration of Dr Skinner's approach to the treatment of hypothyroidism cannot exclude the success which he has in that approach. It cannot exclude the reality of people who do not respond to "satisfactory" levels of thyroid hormone. It most certainly cannot exclude the patients who depend on Dr Skinner's approach, to the benefit of their health.

I think that is the question the committee must take into account in its decision-making process: Cui Bono? To whose benefit?

I hope the answer will be to the benefit of my mother, and others like her.

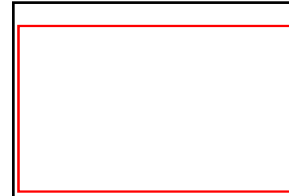
Thank you.

Yours sincerely,

[Redacted signature]

[Redacted name]

Cc: [Redacted]  
*Ralph Shipway, 5 Great College Street, Westminster, London, SW1P 3SJ*



9<sup>th</sup> July, 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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Dear Ms. Cook,

**Testimonial for Dr. Gordon Skinner's Review Hearing,  
28<sup>th</sup> July to 3<sup>rd</sup> August, 2011**

In 2007, I wrote a testimonial for Dr. Skinner's Fitness to Practise Hearing. My gratitude to Dr. Skinner is still the same today as it was then and I will always be grateful to him for his diagnosis and subsequent treatment of my illness.

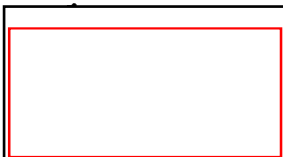
Dr. Skinner started me on Thyroxine, but later changed my prescription to Armour Thyroid and from that moment on, my recovery was complete.

I strongly believe had it not been for him, that I would have certainly been on state benefits as I would have been unfit for work, whereas I completed my degree and went into full time employment. I have also been able to enjoy life, something I was unable to do for many years.

My GP now prescribes Armour Thyroid for me.

Dr. Skinner gave me back my life.

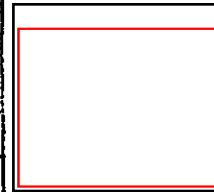
Yours sincerely



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Heather Cook  
Investigation Offices  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester

14<sup>th</sup> July 2011

Dear Ms Cook

Re: Hearing with the GMC and Dr. Skinner on 28<sup>th</sup>, 29<sup>th</sup> July and 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> August

Well, where do I start? Quite simply, Dr. Skinner has saved my life.

This is certainly not a statement that I give to everyone one I meet but I truly believe that I would not be alive today if it was not for this individuals help and advice.

I would like to share my experience with you in the hope that it goes some way to explaining what an incredible man Dr. Skinner is.

I had been suffering [redacted]  
[redacted] Trying to explain how I felt during this time is extremely difficult but I guess 'rock bottom' would be appropriate.

Whenever I felt remotely like prizing myself from the bed, I would visit my GP with the hope that he would wave a magical wand and I would be cured – but time after time it was not to be. Don't get me wrong, he was supportive but his verdict was that I was suffering with

[redacted]  
[redacted]  
[redacted] He turned his attention to the possibility of having thyroid issues, therefore proceeded to do tests which came back as 'within the normal range', so nothing further progressed on that front.

I used the word 'we' in my previous paragraph because my whole family and close friends were heavily involved in assisting me through this horrible period of my life. I was walking along a very fine line by now – did I or did I not want to continue living.



My daughter-in-law had read an article in a National newspaper which explained the symptoms of Hypothyroid and it read exactly how I was feeling. She gave me and my husband the article to read.

I could not put the paper down. If someone had asked me to describe how I felt with my illness then it would be identical to this article and other people were suffering in the same way. In a perverse sort of way, I was happy that someone else was suffering like me because I felt I was an isolated case but no – and reading on there was this individual called Dr. Skinner who could help.

My husband immediately contacted the GP who in turn referred me to Dr. Skinner. We drove to [redacted] for the appointment under duress because I still felt very ill.

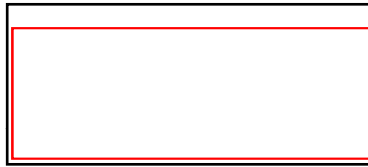
To cut a long story short, this marvellous man had me feeling better within [redacted] WEEKS of seeing him. He had diagnosed my illness as hypothyroid and prescribed me with Armour which I continue to take. I have now returned to full health and live a normal life.

I feel indebted to Dr. Skinner for what he has done for me and in turn my family and friends who were affected during this time as well. He is an incredible individual and a true professional and to think of him not being able to help people who suffer in the same way as I did would be an absolute travesty.

I would sincerely hope that you view this hearing in the manner it should be and allow Dr. Skinner to continue to practice and to save lives like he has done with mine.

Yours faithfully

[redacted]



Telephone: 


Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

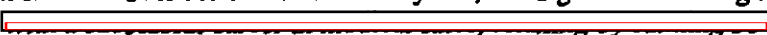
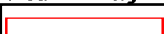
Wednesday, July 13, 2011

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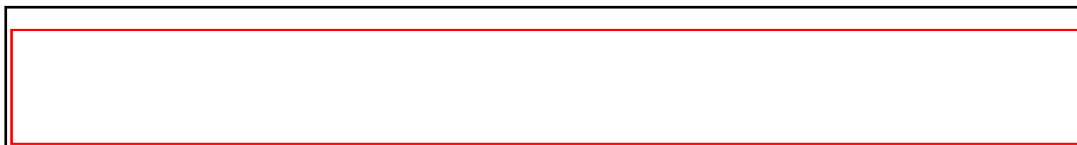
Dear Ms Cook

It has been brought to my attention that you have once again called Dr Gordon Skinner to appear before the General Medical Council and I write to protest at your victimization of this exceptional clinician.

I first became a patient of his in  when, after years of chronic fatigue, I was told that there was nothing wrong me and therefore there was nothing further that the NHS would offer.

This was despite that fact that over the course of a few years, I had gone from being a fit and healthy woman   to a person who was unable to function in any normal way – just getting out of bed was a major achievement.

At my first consultation, Dr Skinner took a full history and examined me carefully – something which had not been done for more than a decade – and listened carefully to my tale of woe.



[REDACTED]

I fail to understand how it is acceptable to diagnose [REDACTED] in the face of normal biochemistry and without confirmation by ultrasound, while it appears to be unacceptable to diagnose hypothyroidism when there is a wealth of symptoms but two markers (TSH and T4) are within the reference range.

When I eventually made my way to Dr Skinner, for the first time I found someone who seemed to accept how ill I felt and was prepared to offer a solution.

At his suggestion, I started to take a very small dose of thyroxine, building up gradually,

[REDACTED]  
[REDACTED]  
It took much longer, and the addition of liothyronine, before I began to feel well enough to be capable of picking up the tattered threads of my life, but throughout my return to health (albeit with a need for thyroid hormones), Dr Skinner has been both supportive and very careful.

Every consultation includes an examination; blood tests for TSH, T4 and free T3 are required at least annually.

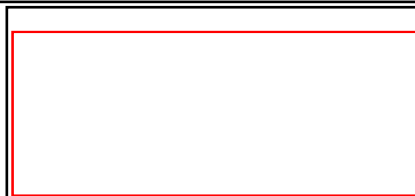
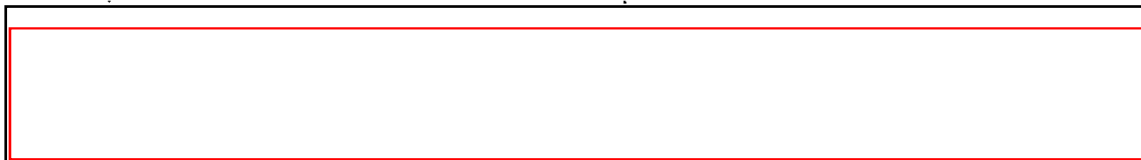
I am reliant on Dr Skinner for my continuing good health, and I could not be in the hands of a better medical practitioner. It is time that the GMC recognized his skill – and his courage in putting his own livelihood in danger for the benefit of his patients – and stopped persecuting him.

I look forward to hearing that you will clear Dr Skinner of any mal-practice, and allow him the freedom to treat people as they require.

Yours sincerely

[REDACTED]

[REDACTED]

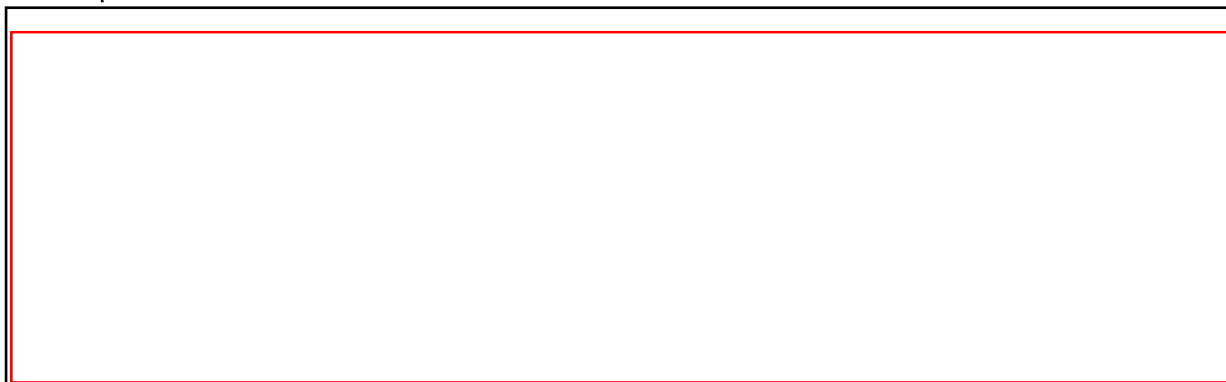


13<sup>th</sup> July 2011

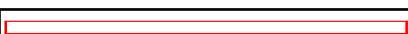

To: Heather Cook, Investigations Officer, GMC Manchester


I am writing in full support for Dr. Skinner, his professional care has transformed me from a sick person, who was unable to do even simple things, into a well person. Before my diagnosis and treatment, I effectively had no life and was increasingly unable to work, (even part-time) or care for my daughter.

My symptoms were many and these effectively made it impossible to lead a normal life. These symptoms included:



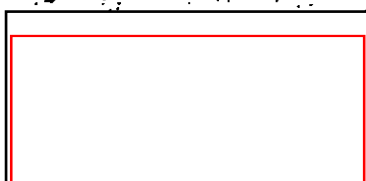
 I considered myself disabled.

All these symptoms,  had been present consistently for over  years prior to my diagnosis. However, without exception all of these symptoms have disappeared following successful treatment and I am now able to live a normal life..

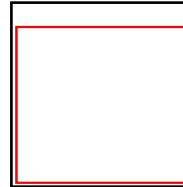
I chose Dr Skinner because I understood him to be one of the best in this field. I have always been someone who goes to the best available specialist. Having met Dr. Skinner and been under his care now for over  years – I still consider him to be a thoroughly professional practitioner and one who takes his patient's care very seriously. I am also incredibly grateful to him for restoring my health and giving me back my life.. One cannot put a price on health and one cannot replace years that should have been spent enjoying one's family....

I am looking forward to attending the hearing.

Signed,



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14.07.2011

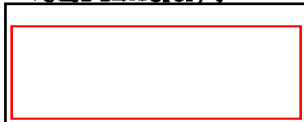
Dear Ms Cook,

I was astonished that two days were put aside for the meeting about Dr Skinner's status with the GMC since it was quite obvious at the completion of his hearing in 2007 that he was a caring doctor, well thought of by his patients and that he achieved excellent results. It was admitted in the Determination (D19/3) that he is "a caring and compassionate doctor whose overwhelming concern is the care and wellbeing of [his] patients". I expected that this final meeting would be a formality and therefore very brief.

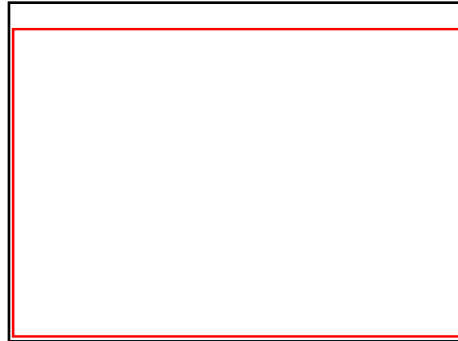
I was even more astonished when I learned that there were three more days set aside for the hearing. What waste of time and money! What unfair strain on Dr Skinner! Can the GMC target those doctors who do not diagnose hypothyroidism rather than those who do. In the Determination it was stated (D19/4) "a profession's most valuable asset is its collective reputation and the confidence that it inspires in members of the public". I maintain that the GMC falls short of this in the constant harassment of Dr Skinner.

I hope that his excellent results are now to be the main consideration.

Yours sincerely,



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15 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook

Re: Dr Skinner Hearing in Manchester 29<sup>th</sup> July-3<sup>rd</sup> August 2011-07-15

I have been a patient of Dr Skinner for the past  months and am writing to place on record my gratitude for what Dr Skinner has done for me in getting me the appropriate treatment for my Thyroid.

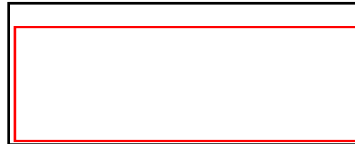
months ago prior to seeing Dr Skinner I was a shadow of who I am today   
 Dr Skinner wrote to my GP to suggest the appropriate amounts of Thyroxine I should take. Within  months my energy and vitality for life had returned and my blood tests showed and satisfied my GP that I was taking the right amount of Thyroxine.

I am really feeling the benefit of living a more normal life.

If you require further amplification please do e-mail or telephone me at the details above.

Yours faithfully

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14/7/11

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

General Medical Council	
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Dear Ms Cook,

I am writing to support Dr Skinner's case, as he is appearing again at another hearing in August.

I have been treated by him since  with Armour thyroid, without which I would not be able to function. This is with my GP's consent. My late father was also helped by Dr Skinner many years ago.

I feel that Dr Skinner's work for his thyroid patients is highly commendable! Hypothyroidism does not seem to be addressed properly by many doctors and Dr Skinner has brought many people peace of mind and understanding. Several people in my family have this disease, which is very debilitating and often goes undiagnosed for many years, leaving us suffering and without fulfilling our potential.

My blood tests proved from the start without doubt, that I was hypothyroid. However, Dr Skinner taught myself and my GP that I need to have a T4 test at the top of the normal range, or a little over in order to feel well. Also that I was a non-convertor and needed T3 as well as thyroxine. Dr Skinner



prescribes Armour thyroid for me, which is not available on the NHS and should be.

I know that some people have many debilitating symptoms of hypothyroidism, but a 'normal' blood test result and that Dr Skinner has been able to help them too by listening to symptoms and by their appearance.

I fully support Dr Skinner's work and expertise and without him, myself and many people would continue to suffer from hypothyroidism, which ruins lives and can lead to premature death. I could not survive without Armour thyroid.

I hope this letter will help him.

Yours sincerely,

Heather Cook,  
Investigation Officer,  
Fitness to Practice Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester,  
M3 3AW

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15.7.11

Dear Heather Cook,

Ref. Dr. Skinner and thyroid treatments of:

Elisabeth Murray Klaar (15.11.1973)

Janet Murray Klaar (10.10.1944)

During  my older daughter  became ill

Over the next  she became increasingly weak.

[redacted] she became aware of the work done by Dr. Skinner, and after studying about the thyroid gland and its function decided to go to ask his advice. She was prescribed Armour thyroid replacement by him and within a few weeks of taking it began to improve. [redacted]

Due to the lack of recognition of her condition [redacted] was severely disabled and very ill from the age of [redacted] to [redacted] years - half of her life! If she had not continued to search for answers to her condition and by chance heard of Dr Skinner, who assisted so dramatically in her recovery, she would be still living a half-life rather than functioning as an almost fully fit young woman. The result of his prescription of Armour Thyroid for her has enabled her recovery. A few years ago she attempted to change to Thyroxine. Her GP at that time was supportive of Dr Skinner prescription of Armour, but [redacted] wanted to move to a treatment which was more accepted by other GP practices in the event that she might need to move away from the area and join a new practice. However the Thyroxine combined with T3 was very unsuccessful for her with many of her old symptoms reappearing so she returned to using Armour and since then she has slowly improved again.

[redacted]

[redacted] This was all purely a dream years ago, but without Dr Skinner's intervention could never have become a reality. Our gratitude to him for all he has given our daughter is immense.

It was during [redacted] when I began to become very tired. [redacted]

[redacted]

Following a visit to a GP at my practice, who could not find anything the matter, I asked for a referral to visit Dr Skinner. (This particular GP had organised blood tests for me which showed an increase in my thyroid antibodies.) Dr. Skinner took blood tests and a family history, noting that my mother, grandmother and great aunts all had had thyroid problems by having goitres. He made observations about how he perceived me physically and prescribed for me a very slowly increasing dose of Thyroxine. Within months I was feeling well again and more than able to return to my job [redacted]

[redacted]

Dr. Skinner prescribed for me a very low dose of T4 initially and my health began to improve remarkably. [redacted]  
to notice the return of the previous [redacted]

[redacted] I began to fear once again that I would not be able to work. After a discussion with Dr. Skinner he added some T3 to my prescription, and a few weeks later I had returned to my normal self. The combination of T4 and T3 helps me immensely and with it I can lead a normal life and meet the challenges of my work and family.

Dr. Skinner has at all times treated me in an exemplary manner. He has ensured that tests are taken regularly to support his treatment and that all records of my visits to him are sent to my GP. I have no support from my GP for my treatment and certainly none from the local endocrinologist. My GP refuses to do blood tests for my

thyroid which I find quite unreasonable. She tells me that to do so would mean that she would be 'collaborating' with Dr. Skinner. However I consider that her first concern should be my health and not her political situation. If she truly doubted his work so much then surely she is remiss in not taking blood tests from me and thus examining and ensuring the good state of my health?

Without Dr Skinner prescribing for me I fear that I would not have been able to continue the work that I was doing [redacted]  
[redacted] Dr. Skinner has not only been able to help me, but he has totally turned round my daughter's life when no other doctor would treat her at all, [redacted] might never recover and would have to put up with it!

I am exceptionally grateful to Dr. Skinner for all that he has done for us and am greatly saddened that he finds himself in this situation. I am also very concerned for the treatment of other thyroid patients who may need his skills in the future, but in particular I am concerned that my own daughter will not lose her newly found health and have to return to the abysmally restricted life she had before he began to help her, for her health now has to be maintained because she has a young family to care for.

I sincerely hope that a way can be found for him to not only be able to treat his patients but also to work alongside other interested doctors so that his knowledge can be discussed and developed further. One of the most saddening aspects of our family's story has been the lack of interest, and at times antagonism, shown by any GP as to how the health of a young person could have changed so dramatically. [redacted]  
[redacted]

[redacted] This apparent blinkered lack of interest of the medical profession is very worrying to me for the future of all medicine.

Yours sincerely,

[redacted]

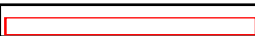
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

16<sup>th</sup> July 2011

Dear Sir/Madam

Dr Gordon Bruce Skinner

General Medical Council	
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 'Thyroid Patient Advocacy' (TPA) [www.tpa-uk.org.uk](http://www.tpa-uk.org.uk) (Registered Charity No. 1138608). TPA is an independent, user-led, organisation established to ensure that all thyroid disease sufferers are given a correct diagnosis and receive effective treatment. TPA campaigns for better education in diagnostics and treatment and provides extensive support and guidance for all sufferers. TPA also runs a large Internet Thyroid Support Forum (2380 members - and rising)

I am not one of Dr Skinner's patients, but over the years, I have been made fully aware of the great work that he does in helping hundreds of sufferers of the symptoms of hypothyroidism to regain their optimal health and of his devotion to helping all those being left to suffer. The majority of members who register to join our Support Group do so because they continued to suffer under the present NHS diagnosing and treatment protocol because they were being denied a diagnosis or refused a choice thyroid hormone replacement.

Of necessity, new members are asked to introduce themselves by writing a little about their medical history, giving a reason for joining the group. Many being left so ill they have had to leave paid employment and surviving on State Benefits. The majority tell of their months (often years) of continued suffering because their doctors tell them they do not have a thyroid problem because their thyroid function test (TFTs) results are within the 'normal' reference range. The majority of NHS doctors do not take into account symptoms or signs; they do not perform a thorough clinical examination; they do not make an adequate assessment of the patient's condition based on the patient's history and symptoms. Their diagnosis and treatment is based on the results of TFTs in isolation, which follows the recommendation laid down by the British Thyroid Association and Society of Endocrinology statement on the BTA web site [http://www.british-thyroid-association.org/news/Docs/thyroid\\_statement.pdf](http://www.british-thyroid-association.org/news/Docs/thyroid_statement.pdf)

- ***"The Clinical Committee of the Society for Endocrinology and the British Thyroid Association recommend the use of sensitive and specific blood tests as the only method for the precise diagnosis of thyroid dysfunction and for the monitoring of treatment with approved medications".***

... which goes against the recommendations laid down by the GMC and DoH.

- ***...the GMC state: "Good clinical care must include: an adequate assessment of the patient's conditions, based on the history and symptoms and, if necessary, an appropriate examination; "***

- ...the DOH state: " Blood tests are useful in helping diagnose hypothyroidism but should not be used in isolation and other factors must be taken into account such as the absence or presence of symptoms. This is why at present it is considered good medical practice to rely upon clinical history and examination, in addition to blood tests, in the diagnosis of this condition.

I know that Dr Skinner follows the recommendations laid down by the GMC and the DoH and it is because of this that TPA highly recommends our members get a referral to see Dr Skinner and the reason why we asked Dr Skinner to become one of the medical advisers to the TPA support forum.

There would be no need for thyroid support forums if patients were getting well within the NHS diagnosing and treatment protocol. TPA is not in isolation in the UK, there is also 'The British Thyroid Foundation', 'Thyroid UK', 'Thyroid Disease UK' and 'Thyroid Help', plus the large number of local support groups, having tens of thousands of sufferers between them.

Doctors are becoming more and more afraid of being arraigned before the GMC if they dare to go outside of the BTA, RCP 'Statement on the Diagnosing and Management of Primary Hypothyroidism'. They use the RCP recommendations in that statement to cover ALL forms of hypothyroidism, even those suffering with peripheral resistance to thyroid hormones at the cellular level, and who should be treated with T3, and not T4. Many members report on the forum that their doctors tell them they dare not give them a diagnosis if their TFT's are shown to be 'normal', or will not prescribe T3, even though this is indicated for specific patients. Instead, as a consequence, doctors are prescribing many and varied prescriptions for the various on-going symptoms, including selective serotonin reuptake inhibitors (SSRI's) and antidepressants.

Dr Skinner is one of the very few medical practitioners who fully understands the functioning of the endocrine system and the greater thyroid system in particular, and one of the few doctors who has the knowledge and capability of helping those suffering the symptoms of hypothyroidism back to normal health once more.

I fully support Dr Gordon Skinner because I have knowledge of the medical history of hundreds of individual members when they first joined the support forum, and who asked their GP to give them a referral to see him. I have seen these members regain their health fully, enabling them to go back into paid employment. Potentially, had these members not been referred to him and left within the care of the NHS, they would still be suffering.

On 3<sup>rd</sup> July 2011 the Mail on Sunday published an article entitled "For 12 Years I was the Victim of The Great Thyroid Scandal". [http://www.tpa-uk.org.uk/mail\\_on\\_sunday.pdf](http://www.tpa-uk.org.uk/mail_on_sunday.pdf). The response from readers has been nothing less than staggering. Every Sunday morning I receive the Statistics for the TPA web site showing the previous weeks activity. The week before publication, the statistics showed that the week ending 3<sup>rd</sup> July, the number of unique visitors was 3510 (usually between 3000 and 3500). From the 3<sup>rd</sup> July to 10<sup>th</sup> July, the number of unique visitors rose dramatically to a staggering 8272 – an increase of just under 5000 visitors. Over 100 new members joined the TPA forum, and I personally received over 500 messages asking for more information about the diagnosing and treatment choice for those with symptoms of hypothyroidism who are being left to suffer. Our stock of Thyroid Information Packs ran out and we had to print another 500 as an emergency measure. Needless to say, Dr Skinner has my unqualified support and I can only ask that this letter be taken into consideration in reviewing his current situation.

Yours very sincerely

[Redacted Signature]

Cc: [Redacted] PhD, and Mr Ralph Shipway,

[Redacted]

#### Unique visitors in each day

Multiple hits with the same IP, user agent and access day, are considered a single visit

Number of unique visitors 3510

Different days in logfile 8

26/Jun/2011	330 (9.4%)
27/Jun/2011	539 (15.4%)
28/Jun/2011	644 (18.3%)
29/Jun/2011	576 (16.4%)
30/Jun/2011	536 (15.3%)
01/Jul/2011	507 (14.4%)
02/Jul/2011	330 (9.4%)
03/Jul/2011	48 (1.4%)

#### Unique visitors in each day

Multiple hits with the same IP, user agent and access day, are considered a single visit

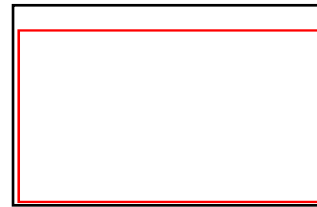
Number of unique visitors 8272

Different days in logfile 8

03/Jul/2011	1825 (22.1%)
04/Jul/2011	1735 (21.0%)
05/Jul/2011	1258 (15.2%)
06/Jul/2011	1093 (13.2%)
07/Jul/2011	909 (11.0%)
08/Jul/2011	792 (9.6%)
09/Jul/2011	600 (7.3%)
10/Jul/2011	60 (0.7%)



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16<sup>th</sup> July, 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester, M3 3AW

Dear Heather,

**Re. Gordon R B Skinner MD, DSc, FRCPath, FRCOG**

I have pleasure in writing in support of Dr. Skinner.

I have been a patient of Dr. Skinner for [redacted] Prior to seeing him I had been suffering from [redacted]

[redacted]

[redacted] After carrying out extensive tests an endocrinologist could find nothing wrong and said he was unable to help. My GP also said she was unable to recommend any treatment at that time.

I consider myself very fortunate to have heard about Dr. Skinner [redacted]  
[redacted] My GP was happy to refer me to him and when I saw Dr. Skinner he immediately correctly diagnosed my problem as hypothyroidism. As soon as I took the full dose of the medication he had prescribed my energy returned and I was able to live and work as I had before. The quality of my life and my general health has improved immeasurably. From my experience it would therefore seem perverse to challenge the right of Dr. Skinner to continue to practise since he has effectively diagnosed and treated my problem when no other health professional had helped me in any way.

I have found Dr. Skinner to be supportive and generous with his time. He is a very experienced, knowledgeable and skilled practitioner and in my opinion it would be a great loss to the profession if he were no longer able to practise.

Yours sincerely,



[REDACTED]

Heather Cook,  
Investigation Officer,  
Fitness to Practice Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

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17<sup>th</sup> July 2011

**Re: DR GORDON SKINNER MD, BSC FRCPATH FRCOG - - GMC HEARING**

I am not one of Dr. Skinner's patients but one of the nearly 2 400 hypothyroid members of the TPA-UK and I would like to file a letter of support for him in the hope that it will be taken into account at his forthcoming GMC hearing.

I have met Dr. Skinner on several occasions over the years and my impression of him is that he is not only extraordinarily knowledgeable in the diagnostic and treatment of thyroid disease, but has a no-nonsense approach to both, and he is caring deeply about his patients.

[REDACTED]

[REDACTED] My own GP told me for [REDACTED] years that all my rather severe clinical symptoms were caused by [REDACTED] and my thyroid gland was working just fine.... As it turned out, he was wrong. I suffer from autoimmune thyroiditis - [REDACTED] long years of unnecessary suffering! Although my GP was apologetic when I finally got correctly diagnosed, he told me in no uncertain terms that his hands had been tied. He was following the dictates of the RCP, BTA et al and to diagnose me hypothyroid and treat me on the basis of clinical symptoms and family history alone - disregarding biochemical "evidence" - was asking more than his job was worth (my words, not his) - Is this the kind of care we should have to put up with from our doctors?

'First do no harm' ..... - Is it not doing harm to close your eyes to the suffering of your patients for fear of being victimized and dragged in front of the GMC like Dr. Skinner? Has a single one of Dr. Skinner's patients' complaint to have been harmed by him in any way? If not - why has he been summoned to yet another hearing by the GMC?

The majority of NHS doctors do not perform a thorough clinical examination ; they do not make assessments taking into account a patient's medical history and symptoms.... they look at their computer screens and diagnose and treat according to the numbers they find there, disregarding the patient in front of them. I have found myself at the receiving end of such treatment for years, and I read almost daily on the TPA forum near identical accounts of such appalling medial "care".

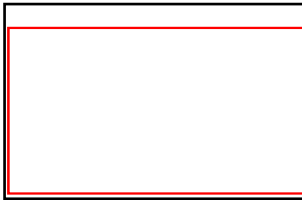
I know that Dr. Skinner does assess each patient based on his or her medical history and symptoms and – unlike the majority of his colleagues - he performs a physical examination, as any good doctor should. He takes blood results into account, of course, but does so in addition to looking at clinical signs and symptoms, history and the results of a physical examination. I know this to be true, because I got feed-back from several of my hypothyroid friends and acquaintances to whom I have recommended Dr. Skinner. They are all doing well now.

I fully support Dr. Skinner and wish I could attend his hearing in person. This won't be possible, but he has my continuing trust and very best wishes for a favourable outcome.

Sincerely yours,

CC:

Mr Ralph Shipway,  
5 Great College Street,  
Westminster,  
London,  
SW1P 3SJ



Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

15<sup>th</sup> July 2011

Dear Ms Cook

**Gordon R B Skinner MD**

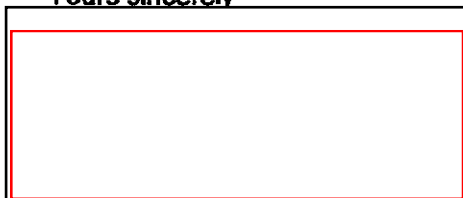
I would like to take this opportunity to draw your attention to the very positive impact Dr Skinner has made to my wife's long-term wellbeing and our family life.

Since Dr Skinner commenced treatment in , the ongoing care and consideration he gave my wife has led to a sustained improvement in her general health.

I can testify that from the first consultation, Dr Skinner showed my wife a high degree of empathy and subsequently presented a personalised care plan – something that some of the UK's noted physicians failed to deliver. In a very short time, my wife's health significantly improved; a situation that continues to this day.

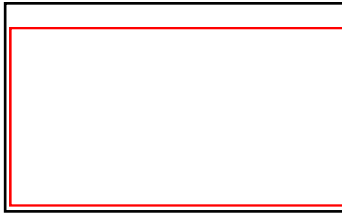
I have no hesitation in confirming that Dr Skinner is an extremely attentive physician, dedicated to applying his experience solely towards his patient's long-term welfare.

Yours sincerely



cc -   
Mr R Shipway

General Medical Council	
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Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

15<sup>th</sup> July 2011

Dear Ms Cook

**Gordon R B Skinner MD**

Prior to my GP's referral to Dr Skinner in [redacted], I had consulted with six other physicians. Unfortunately for me, my many debilitating symptoms of thyroid dysfunction were coupled with entirely normal thyroid function tests; deeming me not suitable for thyroid hormone replacement.

Without that treatment my symptoms escalated, [redacted]  
[redacted]

Thankfully, Dr Skinner's clinical expertise and a daily dose of Thyroxine have rapidly returned me to excellent health.

Quite simply, I depend upon Dr Skinner not just for ongoing monitoring of my thyroid status, but my continued and most precious wellbeing.

Yours sincerely

[redacted signature box]

cc -

[redacted]

Mr R Shipway

17<sup>th</sup> July 2011

FAO Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW.

General Medical Council	
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Dear Ms Cook,

My daughter, [REDACTED], has been a patient of Dr Gordon Skinner since [REDACTED] and is reliant on him for the prescriptions and care that have kept her in good health for the last [REDACTED] years.

[REDACTED] suffered from increasing exhaustion from [REDACTED] and, despite seeing NHS specialists over the course of [REDACTED] years, was offered no diagnosis or treatment. During this time blood tests showed her thyroid levels to be low but still borderline within 'normal range'. By the start of [REDACTED] Julie was experiencing constant, severe [REDACTED]. She was unable to work for over [REDACTED] months and in danger of losing her job.

I was given Dr Gordon Skinner's details through a chance contact and took [REDACTED] to see him in [REDACTED]. At this time [REDACTED] had been advised by her GP to come back for further blood tests in a few more weeks when her thyroid levels had dropped the fraction necessary to receive NHS treatment. It was clear to her family, however, that she couldn't wait for treatment any longer. [REDACTED]

[REDACTED] Dr Skinner diagnosed [REDACTED] was suffering a number of symptoms of under active thyroid and began immediate treatment with thyroxine. My daughter's condition improved within a few days, although it took a number of months for her to regain full health.

Dr Skinner has provided continued care and maintained Julie's health for [REDACTED] years and through two pregnancies. I am convinced that without his sensible, clinical based judgement and support I would not have my grandson [REDACTED]

[REDACTED] Following Dr Skinner's treatment Julie had the energy to take on a new, demanding career in [REDACTED]

The General Medical Council's interference in Dr Skinner's work has caused my daughter great stress. [REDACTED]

[REDACTED]

On a separate note, the experience of my partner, who suffers from an under active

thyroid following surgery, has also been negative. She receives NHS prescriptions but finds her thyroxine levels are regularly cut down following blood tests to bring her within 'normal range'. [redacted]  
[redacted]

Yours Sincerely

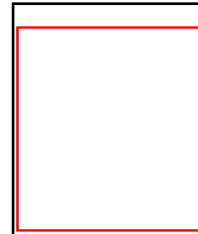
[redacted]

[redacted]

cc Mr. Ralph Shipway, radcliffes leBrasseur, 5, Great College St, Westminster, SW1P 3SJ

cc [redacted]





16<sup>th</sup> July 2011

Dear Ms Cook,

I understand that Dr Skinner is due to appear before the GMC in July. He has treated my friend , whom I have known since childhood.

had various medical problems and she struggled for a long time as no-one seemed to be able to find their root cause.

However, after struggling for a long time, Dr Skinner started to treat her for an underactive thyroid, and this has radically changed her life.

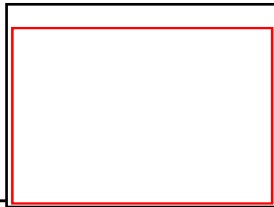
I am glad to say that  is now back to her normal self, thanks to her treatment.

Yours faithfully

Cc

Mr Ralph Shipway

General Medical Council	
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


Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

18 July 2011

Dear Madam

**Gordon Robert Bruce Skinner**  
**GMC Reference Number 6071656**

To avoid confusion please note that I am not acting in a professional capacity but as the husband of  a patient of Dr Skinner.

I refer to my attached letter and to the fitness to practise hearings that Dr Skinner must attend at the end of this month and the beginning of next.

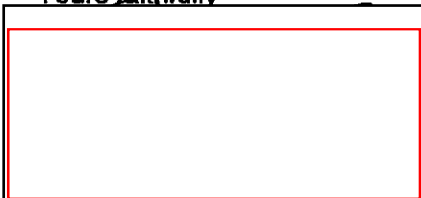
I am both shocked and disappointed that the man who has saved my wife and I from so much pain and suffering must now fight for his professional survival.

How can this be?

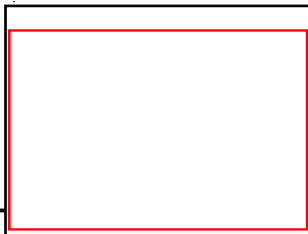
At some point you are going to have to admit that the current guidelines are wrong. It would be better if that happened gradually rather than suddenly (through a successful legal action against the GMC for example). A softening of the GMCs approach might be in its own interest. As would a gradual acknowledgement that a clinical diagnosis of an under active thyroid has as much value as a diagnosis through blood chemistry.

In any event, and regardless of the details, Dr Skinner is making my wife better and it is a pleasure to be guided by him. Both my wife and I have great confidence in Dr Skinner and, as an ambassador of your profession, he is a great asset. It would be deeply unfortunate, for all concerned, if he is not allowed to practise.

Yours faithfully



General Medical Council	
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**General Medical Council**

**By email: [gmc@gmc-uk.org](mailto:gmc@gmc-uk.org)**

18 July 2011

Dear Sirs

**Testing for an underactive thyroid**

**Patient:**

**1. Summary**

- 1.1 Approximately  ago my wife was tested for an under active thyroid. She was told that the blood chemistry showed no thyroid problem. The blood chemistry test seems to be revered by consultants and family GP's alike. Indeed, it was the only method used in diagnosing my wife. The test, unfortunately, was wrong.
- 1.2 I am not a medical professional.  I am not, therefore, qualified to discuss why a blood test which shows only the level of thyroid hormones in the blood, and not in the brain or heart tissue, is appropriate as an exclusive method of testing for an under active thyroid. I am, however, qualified to deal with the facts of a situation, and the evidence presented to me, when I attempt to resolve an issue.
- 1.3 In this letter I will, quite simply, set out the facts and then draw conclusions based on those facts.

**2. Background**

- 2.1 My wife has been tested on many occasions for an underactive thyroid. Nevertheless, her thyroid was declared fit and healthy by two family GPs, one private GP and one private consultant endocrinologist.
- 2.2 The reason for the diagnosis was the result of 's blood test. The test revealed that her free T4 reading was low but the TSH reading was, apparently, perfectly normal.  was told that this is the gold standard test in diagnosing thyroid conditions. Apparently, if  had an underactive thyroid the TSH reading would be high (showing an inversely proportional relationship to the free T4

reading). Because the TSH reading was not high [ ] was told that she had a normal functioning thyroid. Nevertheless [ ] continued to ask, based on her symptoms and family history, whether she might have an underactive thyroid. [ ]'s suggestions were dismissed solely on the basis of her blood test.

2.3

### 3. Test results

### 4. Symptoms

**5. Other relevant factors**

5.1 [redacted]'s family have suffered thyroid problems. Both her maternal great aunt and her mother were diagnosed with an underactive thyroid.

5.2

**6. Diagnosis**

6.1

6.2

**7. Lifestyle**

7.1 If [redacted] had accepted the diagnosis her quality of life would have deteriorated dramatically. I cannot say whether she would have been confined to a wheel chair, or bed ridden, because I cannot support those statements with evidence. However, you are well placed to know whether those outcomes were likely on the basis of an untreated, and deteriorating, under active thyroid.

7.2

7.3

7.4

7.5

7.6

## 8. Treatment

8.1 [ ] I am naturally sceptical. I do not simply accept what I am told without checking and without properly considering and then questioning that advice. To me it seems logical that if the facts of a situation point to a solution then that solution should at least be explored. In this case it was not. The facts of the situation were ignored in place of a set of laboratory results. None of the three GP's involved would prescribe thyroxine sodium. Neither would the endocrinologist.

8.2 There are, I am sure, complicated medical explanations as to why thyroxine sodium should not have been prescribed given the blood test results. Indeed, I have researched and understand many of those reasons. I don't agree with them but do not propose to set out why in this letter. I am not qualified in this area and those thoughts are better articulated by someone who is expertly qualified. Nevertheless, it seemed illogical that nobody would look more closely at [ ]'s symptoms. It was bizarre that nobody would question, as any enquiring mind should, whether there was something missing in the thought process that led to [ ] being prescribed something material to manage her symptoms. At the very least, and with the patient's best interests in mind, I was surprised that none of these professionals even attempted to treat [ ] with thyroxine sodium. Again, I refer to [ ]'s symptoms and ask the question, "Are these symptoms typical of an underactive thyroid?". If they are then why were they ignored? In addition, why was [ ]'s family history ignored? By use of the word "ignored" I do not mean "not considered" I mean "not materially considered" – were these things not as relevant as the blood test results when making the diagnosis?

8.3 I am sure there are many reasons for this lack of action. [ ]  
[ ]. The reason is fear of the law and of regulations. This fear seems to contradict itself. In not treating [ ], should it later occur that she was hypothyroid, all 4 professionals were exposing themselves to a potential action in negligence. If those professionals were simply following their regulatory guidelines then the regulator must answer why those guidelines were in place and how rigidly they were supposed to be followed (and how often the guidelines were monitored and reviewed). If the regulator was then found to be wrong – and should have known that its regulations were wrong but refused to change the regulations – then an action would lie against the regulator and a Judge would decide whether the regulations were correct.

8.4 I leave it to you to decide whether a patient in [ ]'s situation would have – realistically – suffered any harm to her health by being treated with a low dose of thyroxine sodium and being carefully

monitored by her GP. The alternative, as I have explained above, was severe ill health of life changing proportions. As the highest regulating body of medical professionals in this country, you will know whether the thyroid medicine – taken on a trial basis - would have led to any worse condition than [ ] was already destined to endure by the inaction of her professional medical advisors.

## 9. Solution

9.1 Eventually, [ ] found a well qualified medical professional, of consultant status, who knew a great deal about the thyroid. His name is Gordon Skinner. He was prepared to examine [ ] not just on the blood tests, but also on her symptoms. [ ] was told that her symptoms are very much indicative of an underactive thyroid. Indeed, [ ]

[ ]

9.2 [ ] has now taken thyroxine sodium for [ ]. During that time many of her symptoms have disappeared. Even with my lack of medical qualifications it seems unlikely that there is a chance that [ ]'s recovery is pure coincidence and that the 3 GPs and endocrinologist were correct and that the more decisive Dr Skinner was wrong.

9.3 What we are certain of is that since taking the established treatment for an under active thyroid [ ]'s health has improved dramatically. Furthermore, each time the treatment dose has increased more of the symptoms have disappeared. I suppose, in theory, we could test the medicine and decrease it to see if the symptoms re-appear. In the circumstances, you must surely admit that the anecdotal evidence is compelling.

## 10. Conclusions

10.1 Until now I have mostly just stated the facts. Now I must draw conclusions. These follow.

10.1.1 [ ]'s health is improving. Her condition has improved because of the actions taken by Dr Gordon Skinner. Our debt to Dr Skinner is far more than the small fee that she paid him.

10.1.2 Dr. Skinner was prepared to diagnose [ ] on her symptoms. Although he looked carefully at it, he did not attach definitive importance to the thyroid chemistry and he was prepared to prescribe medicine to see if the medication would work. It seemed to me that the motive of Dr Skinner was purely his patient's health. He put his patient's health first – probably before his own reputation and career. It seems to me that the other medical professionals were more concerned about following established rules and regulations. For example, by not questioning the thyroid chemistry.

10.1.3 The 3 GPs and endocrinologist were prepared to do nothing apart from further tests over many months (most to determine what effect the vitamin supplements were having). They took very little action to manage [redacted]'s symptoms in the absence of a diagnosis. In my opinion their actions – or the rules that led to their behaviour – border on Negligence. My greatest concern lies with the endocrinologist who all 3 GPs and [redacted] consulted for his wisdom. His wisdom was clearly lacking. [redacted] left her many consultations – in clinical terms – no better than the day she was referred to him.

10.1.4 The practical inaction of these medical professionals would have degraded the quality of [redacted]'s life, my life, and our daughter's early life. This conclusion is not exaggerated. It is a logical conclusion given my wife's rapid degeneration. Again, please consider whether, in your collective experience of untreated underactive thyroids, this medical condition might have led to my wife being confined largely to a wheel chair or, worse still, bed ridden.

10.1.5 As discussed, there are reasons why thyroid chemistry taken from blood tests have such precedence in the minds of medical professionals in this country. As a non medical professional I can only guess at those reasons. The reasons, whatever they are, will not help the medical profession to do the job that they are supposed to do if they prevent Drs from making sick patients well. Whatever the reasons are they must be dealt with. As a lawyer I am well placed to observe that if the reasons are not dealt with, and the medical profession suffer a kind of analysis paralysis, then they are not fit for purpose. When they are not fit for purpose then Negligence must exist somewhere and litigation is a likely outcome. Change, if it will not come from within, is likely to be forced upon the medical profession. Most likely by patients seeking help from the legal profession. I would hope that this problem – and on review of the internet it seems to be a widespread problem - concerning the diagnosis of underactive thyroids is an unusual problem for an otherwise first rate health service.

## 11. Action

I have not, for the time being, decided what course of action to take. [redacted]

[redacted] I am also aware of the number of potential claimants who are in a far worse position than my wife through years of mis-diagnosis.

Indeed I am very concerned, now that my wife's health is improving, how many other poor souls are suffering in this country through an over reliance being placed on thyroid chemistry. The medical community must confront the issues which prevent the correct diagnosis of thyroid conditions. They must decide whether to place less reliance on thyroid chemistry and more on the symptoms of a patient.

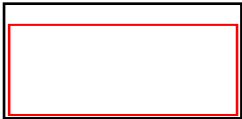
As you must surely be aware, various patient self help groups can be found on the internet. These groups reveal case studies of situations very similar to my wife's. Evidentially, and no doubt scientifically, these

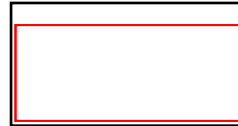


groups could do better in the way they present their evidence. However, they cannot be dismissed when one looks at the sheer numbers beginning to develop and the outspoken Drs in this area of endocrinology.

For the time being my only request is to ask whether you intend to take any action at all to change the regulations and the guidance that you give to the medical profession on the diagnosis and management of thyroid conditions. I would also appreciate your thoughts on the other questions posed within this letter.

Yours faithfully





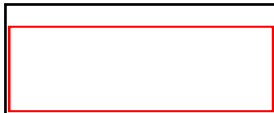
Re Dr Skinner

Dear Ms Cook,

My sister was becoming more and more Zombie like. Although she had been attending her GP, she was being given various diagnoses [redacted]  
[redacted] This went on over a long period. Whilst [redacted]  
[redacted], my sister enumerated her symptoms to the practitioner; a  
[redacted]  
[redacted] said that to him it sounded like thyroid trouble and suggested that she query this with her GP. A blood test showed no positive thyroid trouble. However she was told of Dr Skinner's work with thyroid patients and decided to see him. For [redacted] years since then she has had a new lease of life becoming lively mentally and physically once again. She believed that Dr Skinner saved her life.

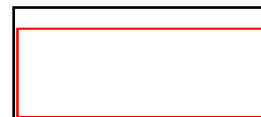
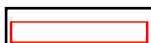
Another sister has also shown a very definite improvement in her quality of life since going to Dr Skinner for treatment. Upholding standards is one thing but vindictive pursuit of someone who is obviously doing good work for people is quite another.

Yours sincerely,



Heather Cook  
Investigation Officer,  
Fitness to Practise Directorate  
General Medical Council,  
3 Hardman St  
Manchester  
M3 3AW

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Ms. Heather Cook  
Investigating Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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18 July 2011

Dear Ms. Cook,

**Fitness to Practice hearing 28 July - 3 August 2011- Dr. Gordon Skinner**

I am writing to you to express my continued support for Dr. Skinner. As stated previously (see attached letter 6/6/2007 and ) he helped me and by extension my family enormously.

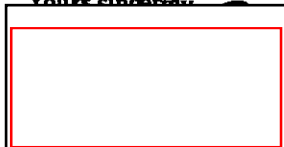
As a result of his compassion and the careful diagnosis and effective treatment of my hypothyroidism he was able to restore my health, which has allowed us to lead a normal family and working life.

Dr. Skinner was the only one who was able to help me, and he could do so precisely because his approach was not exclusively based on blood tests or a one-size-fits-all treatment regime.

I urge you to consider patients like me, for whom he was the last and only chance to be diagnosed and treated correctly.

I sincerely hope that he will be able to continue practicing as we do need doctors like him.

Yours sincerely,



Encl. - My letter to GMC 6/6/2007

cc:



Mr. Ralph Shipway

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
5th Floor, St James Buildings  
79 Oxford Street  
Manchester M1 6FQ

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17 July 2011

Dear Ms Cook,

Re: Dr Gordon Skinner, [REDACTED]

I am writing in support of Dr Skinner, whom I understand will be facing a "Fitness to practise" hearing in the near future.

I think it will be useful to provide some brief information on my circumstances prior to my first consultation with Dr Skinner.

Following several years of ill-health, I was diagnosed with hypothyroidism in [REDACTED] as confirmed by blood tests. Treatment with Thyroxine followed, with limited success despite my blood levels returning to "normal" values. Following referral to a consultant, it was considered that I had a form of thyroxine resistance and I was placed on [REDACTED] mcg T3 daily, on which dose I improved for a time but this did not last.

[REDACTED]

In the absence of a strategy for improving my continuing ill-health, it seemed that I was to be left with a poor quality of life. This was an intolerable situation yet it appeared that there was no alternative.

Several years later, I heard of Dr Skinner and made an appointment to see him. I was required to bring with me a referral from my GP. At the initial consultation, I was given a thorough examination by Dr Skinner and diagnosed to be clinically hypothyroid despite thyroid function tests which indicated that I was "well-replaced".

Dr Skinner's assessment was in accord with the consultants whom I had seen previously.

Dr Skinner's treatment - with varying doses of T3 and T4 initially - was again in accord with previous assessments which I had received. In addition, after some time with no significant improvement, the further option of a natural thyroid extract was tried. This proved successful in improving my condition, over time, with perseverance and with Dr Skinner's attention to the detail of my care.

During the time which I have been his patient, Dr Skinner has paid attention to my blood test results - which he requires on a regular basis - but not to the exclusion of all else. He has been careful in his approach, thorough in his assessments, and has sought to do his best for me, his patient. His approach has been successful and led to an improvement in my health and quality of life. From being virtually housebound I am able to go out and enjoy my life, taking advantage of the fine weather to go for long walks, and to attend to chores. Indeed, I no longer need a car to take me to my GP for my thyroid function test - I walk there.

That I have had this level of health and fitness for the last few years is thanks to Dr Skinner.

All of these events must be seen in context; previous treatment of my condition had left me in a poor state indeed. Dr Skinner's approach was successful. Also, I note that my T4 level in blood tests is lower now than when I was treated, unsuccessfully, by some of the consultants I saw in the NHS.

That Dr Skinner faces a threat to his ability to continue to practise medicine is a source of great concern. It is not the least of it to point out that Dr Skinner has successfully treated those, like myself, who were otherwise left without the care and attention which they deserve. One should be called to account for one's errors, yes, but to be called to account for one's successes is unjust, not to say perverse.

On a personal level, I am of course concerned for myself. If Dr Skinner is unable to practise then I have nowhere to go. I would be returned to the condition I was in before I saw him.

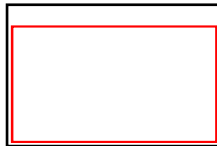
It is not only Dr Skinner facing the hearing, it is people like me.

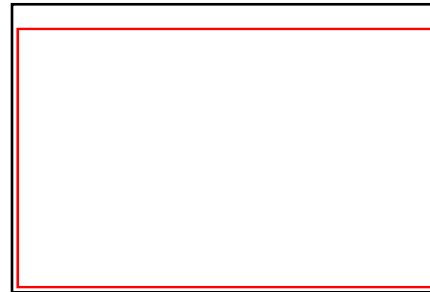
In closing, it is without doubt, and with appreciation, that I can state that Dr Skinner has been nothing less than attentive, thorough and cautious in his care. That his ability to practise has been called into question concerns me because I do not wish to lose a doctor who has helped me, I do not wish to return to the "appropriate" treatment which condemned me to continued poor health.

In considering the case against Dr Skinner, the testimony of people such as myself should not be ignored, as it is we who will be most affected by the outcome.

Thank you.

Yours sincerely,





19 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

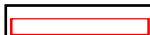
Dear Ms Cook

Re: Dr Skinner Hearing in Manchester 29<sup>th</sup> July-3<sup>rd</sup> August 2011-07-15

My wife, [redacted] has been a patient of Dr Skinner for the past [redacted] months and I am writing to say that only through Dr Skinner's intervention has the correct diagnosis and dosage been managed to be reached with previous GP's only wanting to describe 1/10<sup>th</sup> of what my wife required.

The family and the extended family have all benefitted from the ongoing improvement in my wife's stamina. My wife [redacted]  
[redacted] has her sparkle back.

Yours faithfully



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Heather Cook

Investigation Officer

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**DR GORDON SKINNER MD, BSC FRCPATH FRCOG - GMC HEARING**

Dear Ms Cook,

I wish to place on record my support for Dr. Skinner.

My partner was extremely ill, suffering from undiagnosed hypothyroidism for at least  years, until she was correctly diagnosed and treated by Dr. Skinner.

Rather than go into the whole sorry tale of how she was not diagnosed with hypothyroidism by her family G.P., it is easier to say that after initially suspecting hypothyroidism, her family doctor concluded that this could not be the case because the two tests which were carried out came back 'borderline' and then normal. She was then told she was suffering  and that there was nothing further that could be done for her. As her symptoms progressed she was diagnosed with further, separate illnesses such as

From then onwards my partner tried her best to carry on with her daily life. However, as time progressed so did the severity of her condition. After  years, she became so ill

Meanwhile, I carried on working trying to support both of us and look after my partner. It was at this stage, her symptoms so severe, that she again 'bothered' our local G.P. Again, the G.P. decided that her symptoms matched that of hypothyroidism and so ordered more thyroid function tests, again we were told they were 'normal' (we were later to find out that this meant 0.1 below a reference range). At this juncture we looked into what the symptoms of hypothyroidism actually were. We were amazed; every single symptom that my partner was suffering from was a symptom of

hypothyroidism. Surely, this couldn't be a coincidence? Instead of suffering from a whole range of disparate illnesses, there was one illness which manifested itself with all of these symptoms.

My partner then asked her G.P to refer her to Dr. Skinner, which she did. It was from here that her life began to turn around. Dr. Skinner listened carefully to my partner as she told him of her symptoms and carried out a clinical examination of her, something that I had seen no other doctor do for my partner (and believe me, at this point we had seen many, many doctors, including a rheumatologist, neurologist, countless G.P.s and a junior doctor in A&E when she was admitted with a suspected pulmonary embolism due to the severity of her symptoms). This, in conjunction with her blood tests, allowed Dr. Skinner to diagnose her as hypothyroid. He prescribed thyroxine, which my partner began to take.

That initial visit was [redacted] ago. Since that time my partner's health has increased beyond any description. It has not been an overnight cure, but gradually, she has returned to the person she was when we first met. She was able to return to her part-time job [redacted]

[redacted] I could barely have imagined her being able to walk to the top of our street one year ago!

Many of our friends and family members have commented on how amazing the turn-around has been. Even just looking at her, they comment how well she looks in comparison with [redacted] ago. They also ask if I am angry that she was not diagnosed earlier. I must admit, I am a little. However, this is tempered by the fact that I am so grateful that she has returned to health – something which neither of us thought was possible. We owe all of this to Dr. Skinner. If he did not possess the expertise and professionalism that he does then I can honestly say that I do not know what we would have done.

I could never put into words how grateful I am to Dr. Skinner for what he has done for my partner. He really has changed both of our lives. I am deeply, deeply saddened and worried that Dr. Skinner has to defend himself at the GMC for helping people like my partner. I would be very interested to know who has brought about these proceedings and why. It seems, to me, unbelievably perverse that the one doctor that has actually helped my partner return to health after years of suffering is the one doctor who has to defend himself in this manner.

Should you require any further information of me then please do not hesitate to contact me at the address supplied.

Yours Sincerely,

[redacted]



15<sup>th</sup> July 2011

Heather Cook,  
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Dear Ms Cook,

Re: Dr Gordon Skinner

I am writing to you in respect of Dr Gordon Skinner who has a Hearing at the GMC starting on 28<sup>th</sup> July, 2011.

Thyroid UK provides information and resources to promote effective diagnosis and appropriate treatment for people with thyroid disorders in the UK and part of our work is helping people who contact us via telephone, letter, email and via our HealthUnlocked support website.

Our membership has grown steadily over the years and one of the main problems patients have in respect of their health is that their GP or endocrinologist (should they ever get to see one) does not listen to them properly and will not partake in shared decision making – something that the present Government is advocating strongly.

Patients do not get very long with their GP – usually 5-8 minutes which is not really long enough to have a meaningful discussion about their thyroid health.

Patients feel that they need more time with a health professional and turn to private practice, which usually gives them at least an hour to have a full discussion about their diagnosis and treatment and come to a joint decision based on this.

Many of our members have visited Dr Skinner having exhausted both the NHS system and private therapists i.e. reflexology; physiotherapy etc. These patients have then become well again due to Dr Skinner's diagnosis, care and treatment. Thyroid UK is often told that patients have been able to return to a "normal" life again including coming off benefits and going back to work.

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[redacted] are extremely concerned that Dr Skinner will not be allowed to continue practising and they will not be able to see him again, causing their health to deteriorate.

There are no NICE Guidelines in respect of thyroid disease. There are Thyroid Function Test Guidelines set in 2007 but it should be noted that a decision was made that patients need not be treated until their TSH level reached above 10 – the UK reference range is around 0.5 – 4.5 or 5.0 – whereas in the United States, endocrinologists recommended that patients are treated if their TSH is above 2.5. Other European countries are following the US way of thinking with Sweden being the latest country to change their views.

The Guidelines do state that doctors can give a trial of levothyroxine but in many cases doctors are too worried to try this and therefore this is one reason patients seek out Dr Skinner.

It should also be noted that there is increasing evidence to show that even when a patient is *within the reference range*, there is an *increased risk of coronary heart disease; high cholesterol; kidney disease; preterm birth and miscarriage; gallstones; infertility; skeletal muscle alterations and pre-eclampsia* – see enclosed research articles.

Some endocrinologists feel that subclinical hypothyroidism (defined as a TSH above the normal range with FT4 and FT3 within the range) should be treated (see enclosed article). One endocrinologist feels that patients actually need to be slightly outside of the range i.e. slightly below the bottom of the TSH range and slightly above the FT4 range – Dr A Toft (a former president of both the British Thyroid Association and RCP of Edinburgh) writes in the BMA book "Understanding Thyroid Disorders", "The consensus is that enough should be given to ensure that levels of T4 in the blood are at the upper limit of normal or slightly elevated and those of TSH at the lower limit of normal, or in some patients undetectable." He has also written an article including this information in Pulse Magazine.

Because of all the research that is coming through now, patients are taking more control and expecting their health providers to listen to them and to try various ways to make their symptoms go away. Dr Skinner is a doctor who listens to them and has success in treating his patients.

Thyroid UK would like the GMC to be aware of all of the above when the Panel makes a decision about the future of Dr Skinner's practice.

Kindly acknowledge receipt of this letter.

Kind regards,

[redacted signature box]

cc

[redacted]

Mr Ralph Shipway

## CLINICAL PERSPECTIVE

# Subclinical Hypothyroidism Is Mild Thyroid Failure and Should be Treated

MICHAEL T. McDERMOTT AND E. CHESTER RIDGWAY

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Subclinical hypothyroidism is defined as an elevated serum TSH level associated with normal total or free  $T_4$  and  $T_3$  values. The overall prevalence has been reported to range from 4–10% in large general population screening surveys (1–5) and from 7–26% in studies of the elderly (1–3, 6–11). Because of the frequency with which this condition is encountered, important questions have been raised regarding its clinical relevance and appropriate management. One of the myths that surrounds subclinical hypothyroidism is that the laboratory profile of an elevated serum TSH and normal free thyroid hormone levels really represents “compensated hypothyroidism.” The reasoning behind this idea is that, since the circulating levels of thyroid hormones are within the normal range with only the serum TSH being elevated, the affected subject is really euthyroid because the increased TSH is stimulating and driving the thyroid gland to produce normal thyroid hormone levels. Certainly, elevated serum TSH levels do stimulate even a diseased thyroid gland to produce and release more thyroid hormone. However, as long as the serum TSH level remains elevated, the thyroid hormone levels are not truly normal for that individual. The clearance kinetics of thyroid hormones and TSH from the circulation actually make such a conclusion inescapable. Because the half-life of  $T_4$  is 7 d and that of  $T_3$  is 1 d, the serum TSH, which has a half-life of less than 1 h, would certainly be expected to return to normal if thyroid hormone levels were, indeed, normal for that individual. An elevated TSH in an individual patient, thus, means that the circulating thyroid hormone concentrations are insufficient, with a few rare exceptions (TSH-secreting tumors, thyroid hormone resistance syndromes). We, indeed, believe that subclinical hypothyroidism represents mild thyroid failure and is a clinically important disorder that has adverse clinical consequences and that should be treated in most, if not all, cases. We will support this position by reviewing the reported objective data regarding its natural history, its clinical manifestations, and the benefits of treatment.

### Natural history

Mild thyroid failure represents an early stage of thyroid disease that will commonly progress to overt hypothyroid-

ism. Progression has, in fact, been reported to occur in approximately 3–18% of affected patients per year (10–17). One study evaluated the natural history of mild thyroid failure in 154 female patients over a 10-yr period; 57% of patients continued to have mild thyroid failure, 34% of patients progressed to overt hypothyroidism, and 9% of patients reverted to a normal TSH level. How many of the 9% had a transient form of thyroiditis such as silent, subacute, or postpartum thyroiditis is unclear (17). The strongest predictors of progression are the presence of antithyroid antibodies, serum TSH values greater than 20  $\mu\text{U}/\text{ml}$ , a history of radioiodine ablation for Graves' disease, a history of external radiation therapy for nonthyroid malignancies, and chronic lithium treatment (10–16).

### Clinical manifestations

**Symptoms.** Mild thyroid failure is often asymptomatic; however, nearly 30% of patients with this condition may have symptoms that are suggestive of thyroid hormone deficiency (2, 18). The Colorado Thyroid Disease Prevalence Study (2) measured serum TSH levels and conducted symptom surveys in over 25,000 state residents. Elevated serum TSH values were found in 9.5% of all subjects and in 8.9% of those who were not already on thyroid hormone therapy (Fig. 1); 75% of these individuals had serum TSH levels in the 5–10  $\mu\text{U}/\text{ml}$  range. In response to a validated survey regarding symptoms of thyroid hormone deficiency, the 2,336 subjects who were identified as having mild thyroid failure significantly more often reported having dry skin (28%;  $P < 0.001$ ), poor memory (24%;  $P < 0.001$ ), slow thinking (22%;  $P < 0.001$ ), muscle weakness (22%;  $P < 0.001$ ), fatigue (18%;  $P < 0.01$ ), muscle cramps (17%;  $P < 0.001$ ), cold intolerance (15%;  $P < 0.001$ ), puffy eyes (12%;  $P < 0.05$ ), constipation (8%;  $P < 0.05$ ), and hoarseness (7%;  $P < 0.05$ ) than did euthyroid subjects. It is important to note that, whereas euthyroid subjects experienced a mean of 12.1% of all listed symptoms, overtly hypothyroid subjects had 16.6% of these symptoms ( $P < 0.05$  vs. euthyroid group), and subjects with mild thyroid failure reported an intermediate 13.7% of the symptoms ( $P < 0.05$  vs. euthyroid group) (Fig. 2). This suggests a “dose effect” between levels of thyroid hormones and symptoms. Consistent with these findings, a Swiss study involving 332 women with hypothyroidism reported that 24% of the 93

Abbreviations: ATA, American Thyroid Association; PCP, primary care provider; RCT, randomized controlled trial.

## THE COLORADO STUDY PREVALENCE OF HIGH TSH LEVELS

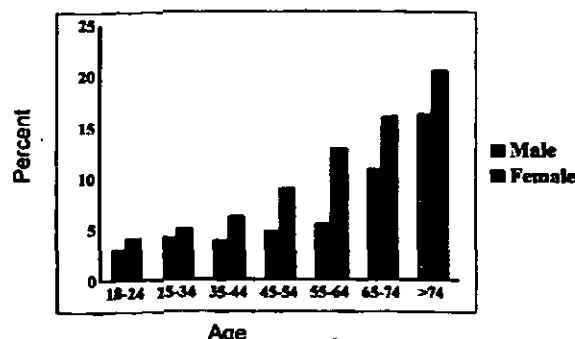


FIG. 1. The Colorado Thyroid Disease Prevalence Study (2). Shown are the age- and gender-specific prevalences of high serum TSH levels found during the screening of 25,862 Colorado state residents in 1995.

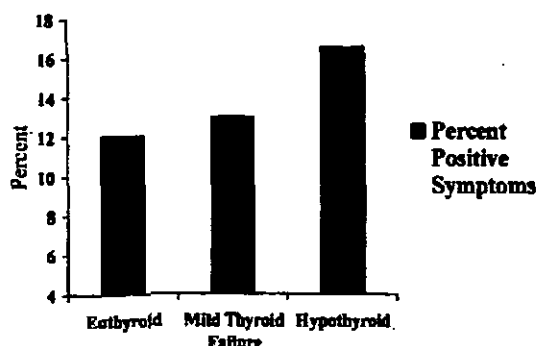


FIG. 2. The Colorado Thyroid Disease Prevalence Study (2). Participants were given a validated survey containing questions regarding symptoms of thyroid hormone deficiency. Of all the symptoms listed, euthyroid subjects ( $n = 22,842$ ) reported having 12.1%, mild thyroid failure patients ( $n = 2,336$ ) had 13.7%, and overtly hypothyroid patients (114) had 16.6%. Compared with the euthyroid subjects, total symptoms reported were significantly higher for both the mild thyroid failure patients ( $P < 0.05$ ) and those with overt hypothyroidism ( $P < 0.05$ ).

subjects with mild thyroid failure exhibited typical symptoms of hypothyroidism (18). These studies also emphasize the difficulty in making the diagnosis of primary hypothyroidism using clinical symptoms alone; euthyroid subjects and patients with mild or overt hypothyroidism all had similar constellations of symptoms. Despite statistical significance in large groups, it can be difficult in an individual patient to distinguish a euthyroid subject from one with either mild or overt thyroid disease.

**Neurobehavioral abnormalities and neuromuscular function.** Other cross-sectional studies have demonstrated evidence of specific neurobehavioral and neuromuscular dysfunction in mild thyroid failure patients (19–31). Depression (19–23), memory loss (2, 19, 24), cognitive impairment (25) and a variety of neuromuscular complaints (26, 27) have all been

reported to occur more frequently in patients with this condition. Objective peripheral nerve dysfunction, manifested by decreased conduction amplitude in peripheral nerves (28), and an abnormal stapedial reflex (29) have been demonstrated in these patients. Skeletal muscle abnormalities, including elevated serum creatine phosphokinase levels (30), increased circulating lactate levels during exercise (26), and repetitive discharges on surface electromyography (27), have also been reported. Finally, there is intriguing evidence that mild thyroid failure in pregnant women may result in reduced intellectual development of their euthyroid offspring (31).

**Cardiac-pulmonary function.** Myocardial function has been reported in multiple studies to be subtly impaired in patients with mild thyroid failure (32–41). Identified functional abnormalities include impaired myocardial contractility (32–40) and diastolic dysfunction (39–41), at rest (32, 34, 37, 39–41) or with exercise (35–39). Myocardial texture has also been shown to be abnormal by videodensitometric analysis (40). In one comprehensive study of exercise capacity (38), patients with mild thyroid failure were shown to have significant impairment of exercise-related stroke volume, cardiac index, and maximal aortic flow velocity. Pulmonary testing in these same patients revealed decreased vital capacity, reduced anaerobic thresholds, and decreased oxygen uptake at the anaerobic threshold (38). These data clearly demonstrate that cardiovascular function in mild thyroid failure is slightly impaired and not identical to that in the euthyroid state. The important question is whether these differences result in clinically significant impairment of performance in affected patients.

**Cardiovascular risk factor.** Mild thyroid failure has been extensively evaluated as a cardiovascular risk factor. The condition has been shown to be associated with increased serum levels of total cholesterol (Fig. 3) and low-density lipoprotein (LDL) cholesterol in most but not all studies (2, 38, 42, 43) and with reduced high-density lipoprotein cholesterol in some studies (38). Some reports have suggested that even high normal serum TSH values may adversely affect serum lipid

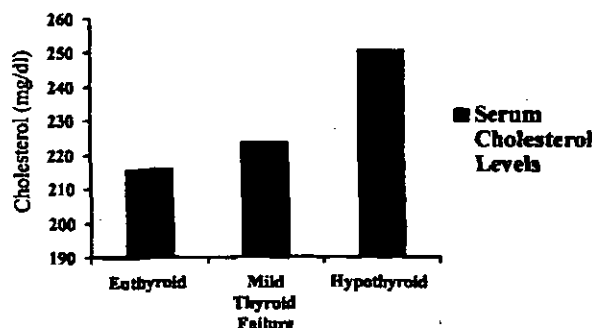


FIG. 3. The Colorado Thyroid Disease Prevalence Study (2). Shown are the mean serum total cholesterol levels in the 22,842 euthyroid subjects (216 mg/dl), the 2,336 mild thyroid failure subjects (224 mg/dl), and the 114 subjects with overt hypothyroidism (251 mg/dl); both thyroid disease groups had statistically higher total cholesterol levels and LDL cholesterol levels (data not shown) than did the euthyroid controls ( $P < 0.001$ ).

and lipoprotein levels (44–46). It has been estimated that an increase in the serum TSH level of 1  $\mu\text{U}/\text{ml}$  is associated with a rise in the serum total cholesterol concentration of 0.09 mmol/liter (3.5 mg/dl) in women and 0.16 mmol/liter (6.2 mg/dl) in men (45). The relationship between TSH and LDL cholesterol seems to be most significant in individuals who have underlying insulin resistance (46). One recent study reported that patients with mild thyroid failure, and even subjects with high normal serum TSH values, have evidence of endothelial dysfunction, manifested by impaired flow-mediated, endothelial-dependent vasodilatation (47). An association between mild thyroid failure and peripheral vascular disease was suggested by an older case-control study involving elderly women (48). A 20-yr follow-up study of the original Whickham Survey found no association between initial hypothyroidism, raised serum TSH levels, or antithyroid antibodies and the development of coronary artery disease (49). In contrast, a more recent report from the Rotterdam Study (9) concluded that patients with mild thyroid failure have a significantly increased prevalence of aortic atherosclerosis and myocardial infarctions. After adjustment for multiple known coronary artery disease risk factors, the

#### Subclinical Hypothyroidism and Myocardial Infarction Attributable Risk in SCH vs All Women

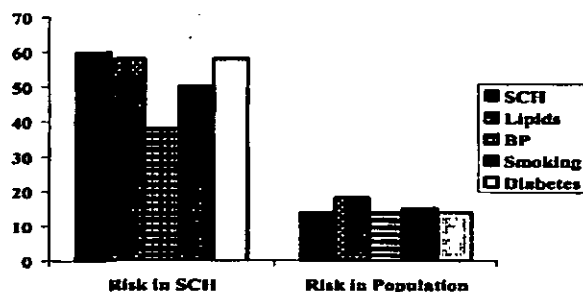


FIG. 4. The Rotterdam Study (9). Analysis of the relationship between subclinical hypothyroidism (SCH) and myocardial infarctions in this study revealed an attributable risk of 60% (SCH contributed to 60% of the myocardial infarctions in the 124 women who had SCH) and a population attributable risk of 14% (SCH was involved in 14% of all myocardial infarctions in the entire group of 1149 women). These risks were similar to those associated with the major recognized cardiovascular risk factors—hypercholesterolemia, hypertension (BP), smoking, and diabetes mellitus.

authors found mild thyroid failure to be an independent and equivalently important risk factor for myocardial infarctions (Fig. 4).

#### Benefits of treatment

Having defined the scope, natural history, clinical features, and potential morbidity of mild thyroid failure, one must next ask whether treatment of the condition has demonstrable benefits. A number of studies have addressed this issue.

**Symptoms.** There have been three randomized controlled trials (RCT) examining the effects of L-thyroxine treatment on general symptoms in subjects with mild thyroid failure (Table 1). Two of these RCTs (33, 34) reported that mild thyroid failure subjects who were treated with L-thyroxine had significantly greater improvement in general hypothyroid symptom scores than did subjects who were treated with placebo (Fig. 5). A third RCT (50) showed no symptomatic treatment benefit; in this study, however, the mean serum TSH level on L-thyroxine treatment was 4.6  $\mu\text{U}/\text{ml}$ , which was at the high end of the normal range. One uncontrolled study also reported a reduction of general somatic complaints after L-thyroxine treatment was instituted (19).

**Neurobehavioral abnormalities and neuromuscular function.** Memory has been shown to improve significantly in one RCT (50) and in two uncontrolled studies in which mild thyroid

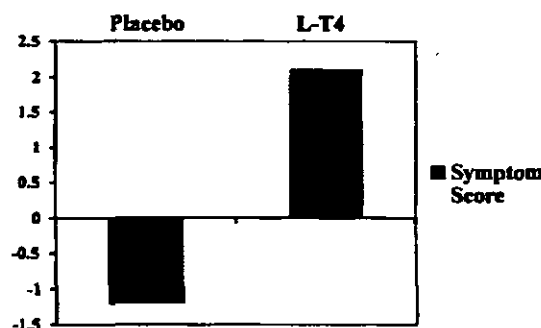


FIG. 5. A RCT of L-thyroxine (L-T4) therapy in subjects with mild thyroid failure (33). Subjects ( $n = 33$ ) were randomly assigned to received L-thyroxine therapy or placebo for a period of 1 yr. L-thyroxine-treated subjects had a significant improvement in their mean symptom score compared with the placebo-treated group ( $P < 0.05$ ).

TABLE 1. Randomized controlled trials investigating the effects of L-thyroxine treatment on general symptoms in patients with mild thyroid failure

Author (Ref.)	n	Design	TSH ( $\mu\text{U}/\text{ml}$ )		Results
			Pre-L-thyroxine	On L-thyroxine	
Cooper (33)	33	Randomized, double-blind, placebo-controlled (1 yr)	10.8	2.6	Symptom score improvement in L-thyroxine group ( $P < 0.05$ )
Nystrom (34)	17	Randomized, double-blind, placebo-controlled crossover (6 months)	7.7	1.9	Symptom score improvement in L-thyroxine group ( $P < 0.01$ )
Jaeschke (50)	32	Randomized, double-blind, placebo-controlled (11 months)	12.3	4.6	Symptom score not improved in L-thyroxine group ( $P = \text{ns}$ ); memory improved ( $P < 0.01$ )

ns, Not statistically significant.

failure patients were given L-thyroxine therapy (19, 24). Other reported benefits from uncontrolled interventional studies include reduction in neuromuscular complaints (19, 27) and normalization of initially abnormal electromyograms (27).

**Cardiac-pulmonary function.** Studies that have examined the effects of L-thyroxine treatment on cardiac function, including one RCT (40), have reported modest but relatively consistent beneficial results (Table 2). Observed responses to treatment have included enhanced cardiac contractility (32-41), improvement of diastolic function (40, 41), and normalization of videodensitometric myocardial texture (40). Increases in pulmonary vital capacity, the anaerobic threshold and oxygen uptake at the anaerobic threshold have also been demonstrated (38).

**Cardiovascular risk factor.** The reported lipid and lipoprotein responses to treatment of mild thyroid failure with thyroid hormone have been somewhat inconsistent (38). A retrospective evaluation suggested that thyroid hormone replacement had very little lipid-lowering effect in patients whose initial TSH values were less than 10  $\mu$ U/ml (51). However, two quantitative literature reviews (42, 43) of the prospective studies examining this issue have concluded that L-thyroxine treatment of patients with mild thyroid failure lowers serum total cholesterol by approximately 0.2-0.4 mmol/liter (7.9-15.8 mg/dl) and LDL cholesterol by about 0.26 mmol/liter (10 mg/dl). The observed cholesterol reductions were greater in patients with inadequately treated overt hypothyroidism (0.44 mmol/liter; 17.4 mg/dl) than in those with untreated spontaneous mild thyroid failure (0.14 mmol/liter; 5.5 mg/dl) and were also greater in patients with higher initial cholesterol levels (43). There have been no reported beneficial effects on high-density lipoprotein cholesterol or triglycerides (42, 43). One intriguing, but uncontrolled, retrospective analysis (52) showed progression of coronary atherosclerosis in subjects on L-thyroxine therapy with elevated serum TSH levels compared with those with normal TSH levels ( $P < 0.02$ ).

**Treatment goals.** Firm data-based guidelines for treatment goals have not yet been established. The distribution of serum TSH values in the normal population is skewed, with the majority of individuals having TSH values at the lower end

of the normal range (53). Recent studies have reported that "high normal" TSH values may be associated with modest increases in serum cholesterol levels (44-46) and that serum cholesterol levels improve when TSH values are reduced from the high end to the low end of the normal range with L-thyroxine supplementation (44). Furthermore, individuals with high normal serum TSH levels may have endothelial dysfunction (47). Thus, although not based on prospective outcomes data, these findings would suggest to us that the optimal goal TSH range for L-thyroxine-treated patients is 0.5-2.0  $\mu$ U/ml.

**Cost-effectiveness and consensus opinion.** Additional support for a decision to treat comes from a recent analysis, which concluded that screening for and treating mild thyroid failure in all adults greater than 35 yr old is as cost-effective as many other screening procedures used in the United States today (54). Finally, we have recently conducted a survey seeking opinions from both primary care providers (PCPs) and members of the American Thyroid Association (ATA) regarding the management of hypothyroidism (55). When presented the case of a 26-yr-old woman with minimally symptomatic mild thyroid failure, the majority of respondents (70% of PCPs and 65% of ATA members) indicated that they would treat the patient if antithyroid antibodies were negative, whereas 95% of ATA members recommended treatment if antibodies were positive. Responses were similar when the case was a 71-yr-old woman with minimally symptomatic mild thyroid failure; the majority (64% of PCPs and 61% of ATA members) chose to treat if antithyroid antibodies were negative, and 92% of ATA members recommended treatment if antibodies were positive.

### Summary

We believe that mild thyroid failure is a common disorder that frequently progresses to overt hypothyroidism. The condition may clearly be associated with somatic symptoms, depression, memory and cognitive impairment, subtle neuromuscular abnormalities, subtle systolic and diastolic cardiac dysfunction, raised serum levels of total and LDL cholesterol, and an increased risk for the development of atherosclerosis. There is documented evidence that many, if not most, of these adverse effects are improved or corrected

TABLE 2. Studies that have investigated the effects of L-thyroxine on cardiac function in patients with mild thyroid failure

Author (Ref.)	n	TSH ( $\mu$ U/ml)		Untreated		L-thyroxine Therapy		Methods*
		Pre-L-thyroxine	On L-thyroxine	Rest	Exercise	Rest	Exercise	
Ridgway (32)	20	28	1.9	↓ MC		↑ MC		1
Cooper (33)	33	10.8	2.6	Normal		↑ MC <sup>b</sup>		1
Nystrom (34)	17	7.7	1.9	↓ MC		↑ MC		1
Bell (35)	18	17.9	3.2	Normal	↓ MC		↑ MC	2
Forfar (36)	10	18.2	3.5	Normal	↓ MC		↑ MC	2
Foides (37)	17	10.3		↓ MC		↑ MC		1,2
Kahaly (38)	20	11.2		Normal	↓ MC		↑ MC	1,3
Arem (39)	8	14.8	3.0	↓ DF	↓ MC		↑ MC	1,3
Monzani (40)	20	5.4	1.2	↓ MC, DF		↑ MC, DF		1,3,4
Biondi (41)	10	8.6	1.7	↓ DF		↑ MC, DF		3

MC, Myocardial contractility; DF, diastolic function.

\* 1, Systolic time intervals; 2, ventriculography; 3, Doppler echocardiography; 4, videodensitometry.

<sup>b</sup> In 5 subjects with initially impaired MC.

when L-thyroxine replacement is instituted. Furthermore, treatment of mild thyroid failure has been reported to be cost-effective. Early treatment may even be justified in asymptomatic individuals to prevent the symptoms of more severe thyroid hormone deficiency that eventually develop as the thyroid gland progressively fails; this is particularly true of antithyroid antibody-positive patients, who have the highest risk of disease progression. For these reasons, we recommend L-thyroxine treatment for the majority of patients with mild thyroid failure, particularly those who have symptoms, other cardiovascular risk factors, goiters, or positive antithyroid antibodies, and in those who are pregnant. However, despite these positive indications that treatment with thyroid hormone carries a benefit, there are many unanswered questions. There are few prospective, randomized placebo-controlled studies that have been performed, a shame when compared with other common disorders such as hypercholesterolemia and osteoporosis. The potential consequences of untreated mild thyroid failure on atherosclerosis in adults and on intellectual potential in infants born to mothers with mild thyroid failure begs for definitive answers about the therapeutic benefits of thyroid hormone replacement. It is no longer scientifically or morally justifiable to argue whether mild thyroid failure is "something" or "nothing." What is clearly needed now are clean, randomized, prospective, and adequately powered trials to provide unequivocal answers to the lingering but critical questions regarding the effects of mild thyroid failure and its treatment on important end points such as intellectual function, ischemic heart disease, and quality of life.

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## References

1. Tunbridge WMG, Evered DC, Hall R, et al. 1977 The spectrum of thyroid disease in a community: The Whickham survey. *Clin Endocrinol (Oxf)* 7: 481-493.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC 2000 The Colorado thyroid disease prevalence study. *Arch Intern Med* 160:526-534.
3. Hollowell J, Braverman LE, Spencer CA, Staehling N, Flanders D, Hannon H Serum TSH, T4, and thyroid antibodies in the United States population: NHANES III. 72nd Annual Meeting of the American Thyroid Association, Palm Beach, FL, 1999; Abstract 213.
4. Guel KW, van Sluisveld IL, Grobbee DE, et al. 1993 The importance of thyroid microsomal antibodies in the development of elevated serum TSH in middle-aged women: associations with serum lipids. *Clin Endocrinol (Oxf)* 39:275-280.
5. Rivolta G, Cerutti R, Colombo R, Miano G, Dionisio F, Grossi E 1999 Prevalence of subclinical hypothyroidism in a population living in the Milan metropolitan area. *J Endocrinol Invest* 22:693-697.
6. Bagchi N, Brown TR, Parish RF 1990 Thyroid dysfunction in adults over age 55 years. A study in an urban U.S. community. *Arch Intern Med* 150:785-787.
7. Sawin CT, Chopra D, Azizi F, Mannix JE, Bacharach P 1979 The aging thyroid. Increased prevalence of elevated serum thyrotropin levels in the elderly. *JAMA* 242:247-250.
8. Lindeman RD, Schade DS, LaRue A, et al. 1999 Subclinical hypothyroidism in a biethnic, urban community. *J Am Geriatr Soc* 47:703-709.
9. Hak AE, Pols HAP, Visser TJ, Drexhage HA, Hofman A, Witteman JCM 2000 Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam study. *Ann Intern Med* 132:270-278.
10. Rosenthal MJ, Hunt WC, Garry PJ, Goodwin JS 1987 Thyroid failure in the elderly: microsomal antibodies as discriminant for therapy. *JAMA* 258:209-213.
11. Parle JV, Franklin JA, Cross KW, Jones SC, Sheppard MC 1991 Prevalence and follow-up of abnormal thyrotropin (TSH) concentrations in the elderly in the United Kingdom. *Clin Endocrinol (Oxf)* 34:77-83.
12. Bastenie PA, Bonnyns M, Vanhaelst L 1985 Natural history of primary myxedema. *Am J Med* 79:91-100.
13. Kabadi UM 1993 Subclinical hypothyroidism. Natural course of the syndrome during a prolonged follow-up study. *Arch Intern Med* 153:957-961.
14. Tunbridge WMG, Brewis M, French JM, et al. 1981 Natural history of autoimmune thyroiditis. *Br Med J* 282:258-262.
15. Vanderpump MPJ, Tunbridge WMG, French JM, et al. 1995 The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol* 43:55-68.
16. Wang C, Crapo LM 1997 The epidemiology of thyroid disease and implications for screening. *Endocrinol Metab Clin North Am* 26:189-218.
17. Huber G, Mitrache C, Guglielmetti M, Huber P, Staub JJ Predictors of overt hypothyroidism and natural course: a long-term follow-up study in impending thyroid failure. 71st Annual Meeting of the American Thyroid Association, Portland, OR, 1998; Abstract 109.
18. Zulewski H, Muller B, Exer F, Miserex AR, Staub JJ 1997 Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. *J Clin Endocrinol Metab* 82:771-776.
19. Monzani F, Del Guerra P, Caraccio N, Prunetti CA, Pucci E, Lual M, et al. 1993 Subclinical hypothyroidism: neurobehavioral features and beneficial effect of L-thyroxine treatment. *Clin Invest* 71:367-371.
20. Tappy L, Randin JP, Schwed P, Wertheimer J, Lemarchand-Beraud T 1987 Prevalence of thyroid disorders in psychogeriatric inpatients. A possible relationship of hypothyroidism with neurotic depression but not dementia. *J Am Geriatr Soc* 35:526-531.
21. Joffe RT, Levitt AJ 1992 Major depression and subclinical (grade 2) hypothyroidism. *Psychoneuroendocrinology* 17:215-221.
22. Haggerty Jr JJ, Stern RA, Mason GA, Beckwith J, Morey CE, Prange Jr AJ 1993 Subclinical hypothyroidism: A modifiable risk factor for depression? *Am J Psychiatry* 150:508-510.
23. Manciet G, Dartigues JE, Decamps A, et al. 1995 The PAQUID survey and correlates of subclinical hypothyroidism in elderly community residents in the southwest of France. *Age Aging* 24:235-241.
24. Baldini IM, Vita A, Maura MC, et al. 1997 Psychological and cognitive features in subclinical hypothyroidism. *Prog Neuropsychopharmacol Biol Psychiatry* 21:925-935.
25. Ganguli M, Burmeister LA, Seaberg EC, Belle S, DeKosky ST 1996 Association between dementia and elevated TSH: a community-based study. *Biol Psychiatry* 40:714-725.
26. Monzani F, Caraccio N, Siciliano G, Manca L, Murri L, Ferrannini E 1997 Clinical and biochemical features of muscle dysfunction in subclinical hypothyroidism. *J Clin Endocrinol Metab* 82:3315-3318.
27. Monzani F, Caraccio N, Del Guerra P, Casolaro A, Ferrannini E 1999 Neuromuscular symptoms and dysfunction in subclinical hypothyroid patients: beneficial effect of L-T4 replacement therapy. *Clin Endocrinol* 51:237-242.
28. Misiunas A, Ravera HN, Faraj G, Faure E 1995 Peripheral neuropathy in subclinical hypothyroidism. *Thyroid* 5:283-286.
29. Goulla DG, Tsilipiridis N, Delaroudis S, et al. 1998 Stapedial reflex: A biological index found to be abnormal in clinical and subclinical hypothyroidism. *Thyroid* 8:583-587.
30. Beyer IW, Karmali R, DeMeester-Mirkin N, Cogan E, Fuss MJ 1998 Serum creatine kinase levels in overt and subclinical hypothyroidism. *Thyroid* 8:1029-1031.
31. Haddow JE, Palomaki GE, Allan WC, et al. 1999 Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 341:549-555.
32. Ridgway EC, Cooper DS, Walker H, Rodbard D, Maloof F 1981 Peripheral responses to thyroid hormone before and after L-thyroxine therapy in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab* 53:1238-1242.
33. Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC 1984 L-thyroxine therapy in subclinical hypothyroidism. *Ann Intern Med* 101:18-24.
34. Nystrom E, Caidahl K, Fager G, Wikkelso C, Lundberg P-A, Lindstedt G 1988 A double-blind cross-over 12-month study of L-thyroxine treatment of women with 'subclinical' hypothyroidism. *Clin Endocrinol* 29:63-76.
35. Bell GM, Todd WT, Forfar JC, et al. 1985 End-organ responses to thyroxine therapy in subclinical hypothyroidism. *Clin Endocrinol (Oxf)* 22:83-89.
36. Forfar JC, Wathen CG, Todd WT, et al. 1985 Left ventricular performance in subclinical hypothyroidism. *CJ Med* 57:857-865.
37. Foldes J, Istvanfy M, Halmagyi M, Varadi A, Gara A, Partos O 1987 Hypothyroidism and the heart. Examination of left ventricular function in subclinical hypothyroidism. *Acta Med Hung* 44:337-347.
38. Kahaly GJ 2000 Cardiovascular and atherogenic aspects of subclinical hypothyroidism. *Thyroid* 10:665-679.
39. Aren R, Rokeby R, Kiefe C, Escalante DA, Rodriguez A 1996 Cardiac systolic and diastolic function at rest and exercise in subclinical hypothyroidism: Effect of thyroid hormone therapy. *Thyroid* 6:397-402.
40. Monzani F, Di Bello V, Caraccio N, et al. 2001 Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. *J Clin Endocrinol Metab* 86:1110-1115.
41. Biondi B, Fazio S, Palmieri EA, et al. 1999 Left ventricular diastolic dysfunction

- tion in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab* 84:2064-2067
42. Tanis BC, Westendorp RGJ, Smelt AHM 1996 Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: a re-analysis of intervention studies. *Clin Endocrinol* 44:643-649
  43. Danese MD, Ladenson PW, Meinert CL, Powe NR 2000 Effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. *J Clin Endocrinol Metab* 85:2993-3001
  44. Michalopoulos G, Alevizaki M, Piperinos G, et al. 1998 High serum cholesterol levels in persons with 'high normal' TSH levels: should one extend the definition of subclinical hypothyroidism. *Eur J Endocrinol* 138:141-145
  45. Bindels AJ, Westendorp RG, Frolich M, Seidell JC, Blokstra A, Smelt AH 1999 The prevalence of subclinical hypothyroidism at different total plasma cholesterol levels in middle aged men and women: a need for case-finding? *Clin Endocrinol* 50:217-220
  46. Bakker SJL, Ter Matten JC, Popp-Snijders C, Slaets JPJ, Heine RJ, Gans ROB 2001 The relationship between thyrotropin and low density lipoprotein cholesterol is modified by insulin sensitivity in healthy euthyroid subjects. *J Clin Endocrinol Metab* 86:1206-1211
  47. Lekakis J, Papamichael C, Alevizaki M, Piperinos G, Marafelia P 1997 Flow-mediated, endothelium-dependent vasodilatation is impaired in subjects with hypothyroidism, borderline hypothyroidism, and high-normal serum thyrotropin (TSH) values. *Thyroid* 7:411-414
  48. Powell J, Zadeh JA, Carter G, Greenhalgh RM, Fowler PB 1987 Raised serum thyrotrophin in women with peripheral arterial disease. *Br J Surg* 74:1139-1141
  49. Vanderpump MP, Tunbridge WM, French JM, et al. 1996 The development of ischemic heart disease in relation to autoimmune thyroid disease in a 20-year follow-up study of an English community. *Thyroid* 6:155-160
  50. Jaeschke R, Guyatt G, Gerstein H, et al. 1996 Does treatment with L-thyroxine influence health status in middle-aged and older adults with subclinical hypothyroidism? *J Gen Intern Med* 11:744-749
  51. Diekman T, Lansberg PJ, Kastelein JJ, Wiensinga WM 1995 Prevalence and correction of hypothyroidism in a large cohort of patients referred for dyslipidemia. *Arch Intern Med* 155:1490-1495
  52. Perk M, O'Neill BJ 1997 The effect of thyroid hormone therapy on angiographic coronary artery disease progression. *Can J Cardiol* 13:273-276
  53. Stockigt J 2000 Serum thyrotropin and thyroid hormone measurements and assessment of thyroid hormone transport. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's the thyroid*, ed 8. Philadelphia: Lippincott Williams and Wilkins; 376-392
  54. Danese MD, Powe NR, Sawin CT, Ladenson PW 1996 Screening for mild thyroid failure at the periodic health examination. *JAMA* 276:285-292
  55. McDermott MT, Haugen BR, Lezotte DC, Seggelke S, Ridgway EC 2001 Management practices among primary care physicians and thyroid specialists in the care of hypothyroid patients. *Thyroid* 11:757-764



# Subclinical Hypothyroidism Is an Independent Risk Factor for Atherosclerosis and Myocardial Infarction in Elderly Women: The Rotterdam Study

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**Background:** Overt hypothyroidism has been found to be associated with cardiovascular disease. Whether subclinical hypothyroidism and thyroid autoimmunity are also risk factors for cardiovascular disease is controversial.

**Objective:** To investigate whether subclinical hypothyroidism and thyroid autoimmunity are associated with aortic atherosclerosis and myocardial infarction in postmenopausal women.

**Design:** Population-based cross-sectional study.

**Setting:** A district of Rotterdam, the Netherlands.

**Participants:** Random sample of 1149 women (mean age  $\pm$  SD,  $69.0 \pm 7.5$  years) participating in the Rotterdam Study.

**Measurements:** Data on thyroid status, aortic atherosclerosis, and history of myocardial infarction were obtained at baseline. Subclinical hypothyroidism was defined as an elevated thyroid-stimulating hormone level ( $>4.0$  mU/L) and a normal serum free thyroxine level (11 to 25 pmol/L [0.9 to 1.9 ng/dL]). In tests for antibodies to thyroid peroxidase, a serum level greater than 10 IU/mL was considered a positive result.

**Results:** Subclinical hypothyroidism was present in 10.8% of participants and was associated with a greater age-adjusted prevalence of aortic atherosclerosis (odds ratio, 1.7 [95% CI, 1.1 to 2.6]) and myocardial infarction (odds ratio, 2.3 [CI, 1.3 to 4.0]). Additional adjustment for body mass index, total and high-density lipoprotein cholesterol level, blood pressure, and smoking status, as well as exclusion of women who took  $\beta$ -blockers, did not affect these estimates. Associations were slightly stronger in women who had subclinical hypothyroidism and antibodies to thyroid peroxidase (odds ratio for aortic atherosclerosis, 1.9 [CI, 1.1 to 3.6]; odds ratio for myocardial infarction, 3.1 [CI, 1.5 to 6.3]). No association was found between thyroid autoimmunity itself and cardiovascular disease. The population attributable risk percentage for subclinical hypothyroidism associated with myocardial infarction was within the range of that for known major risk factors for cardiovascular disease.

**Conclusion:** Subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and myocardial infarction in elderly women.

Overt hypothyroidism, with its accompanying hypercholesterolemia and hypertension, has been found to be associated with cardiovascular disease (1-3). Subclinical hypothyroidism, defined as an asymptomatic state characterized by normal serum concentrations of free thyroxine and elevated serum concentrations of thyroid-stimulating hormone (TSH) (4), is highly prevalent in elderly women (5, 6). Whether subclinical hypothyroidism is related to risk for cardiovascular disease is controversial. Case-control and cross-sectional studies on the association between subclinical hypothyroidism and cardiovascular disease have been done (7-11). Results from these studies are not consistent, but many of the studies were small. The same controversy surrounds thyroid autoimmunity. In the late 1960s and early 1970s, autopsy studies (12, 13) and studies in hospital inpatients (12, 14) suggested that asymptomatic autoimmune thyroiditis was an important risk factor for coronary heart disease. These findings, however, were not confirmed by other studies (7, 8, 11, 15).

In our population-based study, we examined whether subclinical hypothyroidism and thyroid autoimmunity are associated with aortic atherosclerosis and myocardial infarction in elderly women. We conducted our study in a random sample of 1149 postmenopausal women who were participating in the Rotterdam Study.

## Methods

### The Rotterdam Study

The Rotterdam Study is a population-based cohort study designed to assess the occurrence and clarify the determinants of chronic diseases in an aging population (16). The cohort includes 3105 men and 4878 women at least 55 years of age (78% of the eligible population) living in a defined district in Rotterdam, the Netherlands. Baseline data were collected from August 1990 to July 1993. During a home interview, a trained research assistant gathered information on current and past health, medication, lifestyle, and risk factors for chronic diseases. Participants were subsequently invited to visit a research center for clinical examination. The study

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was approved by the medical ethics committee of Erasmus University Medical School, Rotterdam, the Netherlands.

#### Clinical Examination and Laboratory Methods

Height and weight were measured while each participant was wearing indoor clothing without shoes. Body mass index was computed as weight divided by height squared. A trained research assistant measured sitting systolic and diastolic blood pressure with a random-zero sphygmomanometer after 5 minutes of rest, and a standard 12-lead electrocardiogram was obtained (ACTA electrocardiogram recorder, Esoate, Florence, Italy).

Venipuncture was performed, and nonfasting serum samples were collected. The samples were immediately put on ice and were processed within 30 minutes, after which they were kept frozen at  $-20^{\circ}\text{C}$ . We used an automated enzymatic procedure to determine serum total cholesterol level (17). High-density lipoprotein (HDL) cholesterol levels were measured in a similar manner after precipitation of the non-HDL cholesterol fraction. Total protein level was measured by using the biuret method, albumin level was measured by using the bromocresol-green method, and creatinine concentration was measured by using an enzymatic colorimetric method. (All products were manufactured by Boehringer Mannheim, Mannheim, Germany, currently Roche Diagnostics, Basel, Switzerland.) We assayed levels of TSH by using TSH Lumitest (Henning, Berlin, Germany, currently Brahms, Berlin, Germany) (18). When TSH concentrations were abnormal ( $>4.0$  mU/L or  $<0.4$  mU/L), serum free thyroxine levels were measured with an in vitro immunodiagnostic reagent (Ortho-Clinical Diagnostics, Amersham, England, United Kingdom); values between 11 and 25 pmol/L (0.9 and 1.9 ng/dL) were considered normal. Serum antibodies to thyroid peroxidase were assessed by using enzyme-linked immunosorbent assay (Milenia, DPC, Los Angeles, California); test results were considered positive if levels were greater than 10 IU/mL.

#### Thyroid Definitions

Subclinical hypothyroidism was defined as a TSH level greater than 4.0 mU/L in the presence of a normal free thyroxine level (11 to 25 pmol/L [0.9 to 1.9 ng/dL]). Clinical hypothyroidism was defined as a TSH level greater than 4.0 mU/L and a decreased free thyroxine level ( $<11$  pmol/L [ $<0.9$  ng/dL]) (4). Euthyroidism was defined as a normal TSH level (0.4 to 4.0 mU/L).

#### Aortic Atherosclerosis

Aortic atherosclerosis was assessed on a lateral radiographic film of the lumbar spine, which was

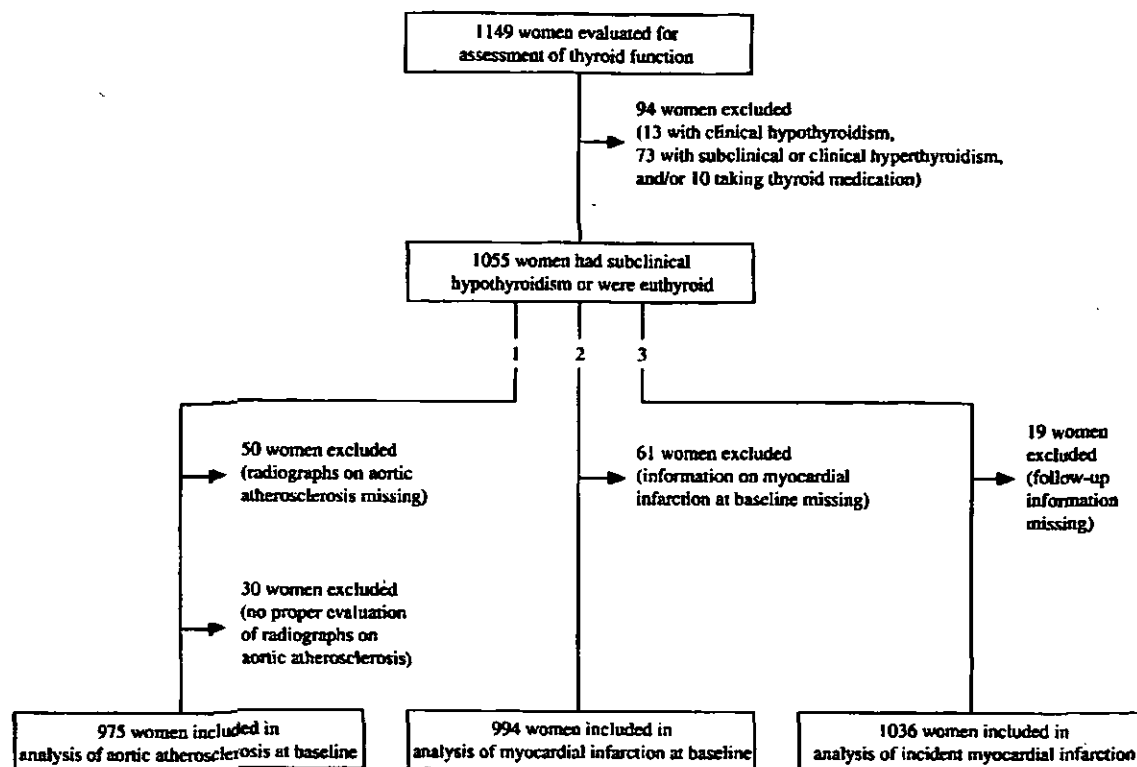
obtained from a fixed distance while the participants were seated. A researcher who was unaware of the participants' thyroid status diagnosed atherosclerosis off-line by detecting calcified deposits in the abdominal aorta, as described elsewhere (19, 20). Calcification was considered present when linear densities were found in an area parallel and anterior to the lumbar spine (L1 to L4). We classified aortic atherosclerosis as mild, moderate, or severe, according to the length of the involved area ( $\leq 1$  cm, 2 to 5 cm, and  $>5$  cm, respectively). Because of a relatively small number of participants in the categories of aortic atherosclerosis, we combined severity grades into two categories—"present" or "absent"—for analysis.

The validity of radiographic assessment of aortic atherosclerosis has been studied by comparing results of this method with data obtained at autopsy. Radiographic assessment was shown to be highly specific, and in most cases visible calcification represented advanced intima atherosclerosis (21). A comparison study involving computed tomography was performed at our department. In 56 unselected elderly persons, aortic calcifications were independently assessed by radiography and computed tomography. Calcifications were detected on abdominal radiography in 32 persons. In all but 1 person, these calcifications were shown to be located in the aorta on the corresponding computed tomography images (20).

Aortic calcification is known to be associated with risk factors for cardiovascular disease (19, 20) and with atherosclerosis at other sites (22) and predicts cardiovascular morbidity and mortality (23, 24). When aortic calcification (as detected by radiography) was compared with coronary artery calcium (as detected by electron-beam computed tomography) in 457 participants in the Rotterdam Study, aortic calcification was present in 3.9% of participants in the lowest tertile of coronary artery calcium, in 13.7% of those in the middle tertile of coronary artery calcium, and in 31.5% of those in the highest tertile of coronary artery calcium ( $P < 0.001$  for trend, adjusted for age and sex). These results indicate that aortic calcification is strongly related to coronary calcification.

#### Myocardial Infarction at Baseline

The presence of myocardial infarction was assessed by self-report and by analysis of the standard 12-lead electrocardiograms, which were stored digitally and were analyzed by using the Modular Electrocardiogram Analysis System (MEANS) (25, 26). For participants who reported myocardial infarction but had no electrocardiographic evidence of it, we collected additional information from their general practitioners or cardiologists. Myocardial infarction



**Figure.** Selection of sample for analysis. 1 = selection of women for analysis of aortic atherosclerosis at baseline; 2 = selection of women for analysis of history of myocardial infarction at baseline; 3 = selection of women for analysis of incident myocardial infarction.

was confirmed if the information in the medical records met standard diagnostic criteria. An experienced cardiologist reviewed the electrocardiograms of participants who had not reported myocardial infarction but had electrocardiographic evidence of it. In these participants, absence of symptoms was confirmed by medical records review. When the cardiologist confirmed myocardial infarction (silent myocardial infarction), it was considered present. We combined both types of myocardial infarction into one variable for analysis. No information on the thyroid status of participants was available at assessment for myocardial infarction.

#### Follow-up Procedures

We collected data on incident myocardial infarction from baseline (1990 to 1993) until 1 April 1996. Fatal and nonfatal events were reported by general practitioners in the research area (in which 85% of the study cohort resides) who cooperate with the Rotterdam Study and provide information through a computerized system. Research physicians verified all information by checking participants' medical records at the general practitioners' offices. In addition, we obtained letters from medical specialists and discharge reports for hospitalized patients. Two

research physicians coded events independently according to the International Classification of Diseases, 10th Revision (27). If the two physicians disagreed, they reached consensus in a separate session. Subsequently, a medical expert in the field reviewed all events coded by the research physicians and verified that all coding rules had been applied correctly. When discrepancies were found between the coding of the medical expert and that of the research physicians, the expert's judgment was considered final. Myocardial infarction was defined as a nonfatal or fatal myocardial infarction (ICD-10 codes I21–I23). When we compared our results with data registered by the nationwide morbidity registry of hospitals, we found that 98% of all incident myocardial infarctions that occurred in Rotterdam Study participants before 1 April 1996 had been detected by our follow-up data collection system.

#### Selection of the Sample for Analysis

The selection of the sample for analysis is shown in the Figure. We determined thyroid status in a random sample of 1149 women after excluding those who took amiodarone, which may nonsystematically alter TSH levels (28). To obtain a reference category that included only euthyroid women (those

**Table 1. Baseline Characteristics of the Study Sample**

Variable	Euthyroid Women (n = 931)*	Women with Subclinical Hypothyroidism (n = 124)†
Mean age ± SD, y	68.9 ± 7.4	69.0 ± 7.9
Mean body mass index ± SD, kg/m <sup>2</sup>	26.7 ± 4.1	27.1 ± 3.8
Mean systolic blood pressure ± SD, mm Hg	138 ± 21	137 ± 22
Mean diastolic blood pressure ± SD, mm Hg	73 ± 11	73 ± 11
Mean total cholesterol level ± SD, mmol/L (mg/dL)	7.0 ± 1.2 (271 ± 46)	6.7 ± 1.0 (259 ± 39)‡
Mean high-density lipoprotein cholesterol level ± SD, mmol/L (mg/dL)	1.5 ± 0.4 (58 ± 15)	1.4 ± 0.4 (54 ± 15)§
Mean total protein level ± SD, g/L	71.0 ± 4.9	71.7 ± 4.7
Mean albumin level ± SD, g/L	42.7 ± 2.4	43.0 ± 2.5
Mean creatinine concentration ± SD, μmol/L (mg/dL)	77.6 ± 13.9 (0.9 ± 0.2)	77.4 ± 14.7 (0.9 ± 0.2)
Smoking status, % (n)		
Never	50 (466)	51 (63)
Past	29 (272)	30 (37)
Current	19 (176)	19 (23)

\* For some euthyroid women, data were missing on body mass index (n = 7), blood pressure and HDL cholesterol level (n = 4), albumin level (n = 2), creatinine concentration (n = 1), and smoking habits (n = 17).

† Data on body mass index, blood pressure, and smoking habits were each missing for 1 woman.

‡ P < 0.05, adjusted for age.

§ P = 0.07, adjusted for age.

whose TSH levels were within the normal range), we excluded women with clinical hypothyroidism (n = 13); those with a decreased TSH level (<0.4 mU/L), which indicated clinical hyperthyroidism (free thyroxine level > 25 pmol/L [>1.9 ng/dL]) or subclinical hyperthyroidism (free thyroxine level, 11 to 25 pmol/L [0.9 to 1.9 ng/dL]) (n = 73); and/or those taking thyroid medication (L-thyroxine or thyrostatic medication [propylthiouracil, carbimazole, or thiamazole]) (n = 10).

Of the 1055 women remaining, we excluded those for whom data were missing (n = 50) or improper (n = 30); therefore, 975 were included in our analysis of aortic atherosclerosis (Figure, selection 1). Data on myocardial infarction at baseline were available for 994 women (Figure, selection 2). At the time of analysis, 19 women had not been completely followed because of linking problems between their general practitioners' medical records and our computerized registration system. Therefore, until 1 April 1996, completed follow-up for analysis of incident myocardial infarction was available for 1036 women, covering an average period (±SD) of 4.6 ± 0.7 years (Figure, selection 3).

#### Statistical Analysis

We used linear regression analysis to compare the age-adjusted continuous baseline characteristics of euthyroid women and women with subclinical hypothyroidism. The chi-square test was used to compare proportions of women who smoked in both groups and to compare proportions of women who had subclinical hypothyroidism and antibodies to thyroid peroxidase according to vascular disease status.

Multivariate logistic regression analysis was used to evaluate the association of aortic atherosclerosis and myocardial infarction as assessed at baseline (history of myocardial infarction) with subclinical hypothyroidism. For women with subclinical hypo-

thyroidism, we computed the risk for incident myocardial infarction (both fatal and nonfatal) during follow-up by using Cox proportional hazards regression analysis. In this analysis, we excluded women with a history of myocardial infarction (n = 79). We adjusted all analyses for age by entering age as a continuous variable in the regression model; we subsequently adjusted analyses for body mass index, cholesterol and HDL cholesterol level, systolic and diastolic blood pressure, and smoking status (never, past, or current). To ensure that comparisons between models were valid, the age-adjusted models included the number of participants for whom information was available on all of the covariates for which the multivariate model was adjusted.

We performed additional analyses after excluding women who took β-blockers (alprenolol, oxprenolol, pindolol, propranolol, timolol, and sotalol) (n = 37) because these drugs may influence TSH levels (29). In addition, we used logistic regression analysis to compare the associations of aortic atherosclerosis and history of myocardial infarction with subclinical hypothyroidism in women who had subclinical hypothyroidism and antibodies to thyroid peroxidase relative to those in euthyroid women who did not have antibodies to thyroid peroxidase. We also used logistic regression analysis to compare the frequency of aortic atherosclerosis and history of myocardial infarction in women with antibodies to thyroid peroxidase and women without antibodies to thyroid peroxidase, independent of thyroid status.

The attributable risk percentage, or etiologic fraction, and the population attributable risk percentage for subclinical hypothyroidism associated with incident myocardial infarction were calculated (30). For purposes of comparison, we calculated the attributable risk percentage and the population attributable risk percentage for the four major, classic risk factors for cardiovascular disease—hypercholes-

terolemia (total cholesterol level  $\geq 8.0$  mmol/L [ $\geq 309$  mg/dL]), hypertension (systolic blood pressure  $\geq 160$  mm Hg and/or diastolic blood pressure  $\geq 95$  mm Hg, and/or antihypertensive medication use), smoking status (current and past compared with never), and diabetes mellitus (use of antidiabetic medication or a random postload glucose level  $>11.1$  mmol/L [200 mg/dL])—associated with incident myocardial infarction in all female participants of the Rotterdam Study ( $n = 4878$ ).

All measures of association are presented with 95% CIs. A  $P$  value less than 0.05 was considered statistically significant. We used SPSS 8.0 for Windows (SPSS, Inc., Chicago, Illinois) for all analyses.

## Results

Before exclusion of clinically hypothyroid women, women with a decreased TSH level, and women using thyroid medication, the prevalence of subclinical hypothyroidism in the study sample was 10.8%. The baseline characteristics of the study sample are shown in Table 1. Women with subclinical hypothyroidism did not differ from euthyroid women with regard to age, body mass index, blood pressure, total protein level, albumin level, creatinine concentration, or smoking status but had significantly lower levels of total cholesterol and borderline significantly lower levels of HDL cholesterol in age-adjusted comparisons.

Table 2 shows the characteristics of participants according to vascular disease status. Fifty-three percent of participants ( $n = 560$ ) had aortic atherosclerosis at baseline, and 7.5% ( $n = 79$ ) had a history of myocardial infarction. Subclinical hypothyroidism was present in 11.8% of women in our sample for analysis. Women who had aortic atherosclerosis and a history of myocardial infarction had a higher prevalence of subclinical hypothyroidism and subclinical hypothyroidism accompanied by antibodies to thyroid peroxidase than those who did not have these diseases. The prevalence of thyroid autoimmunity independent of thyroid status itself did not differ

significantly among the specific subgroups. Among women with subclinical hypothyroidism, concentrations of TSH were higher in those with antibodies to thyroid peroxidase than in those without such antibodies (age-adjusted geometric means, 6.6 mU/L [CI, 6.1 to 7.1 mU/L] and 5.4 mU/L [CI, 5.0 to 5.8 mU/L], respectively;  $P = 0.001$ ). Independent of thyroid status, TSH levels were also higher in women who had antibodies to thyroid peroxidase than in those who did not (geometric means, 2.4 mU/L [CI, 2.2 to 2.6 mU/L] and 1.6 mU/L [CI, 1.5 to 1.7 mU/L], respectively;  $P < 0.001$ ).

Subclinical hypothyroidism was associated with a greater prevalence of aortic atherosclerosis. The odds ratio for aortic atherosclerosis (1.7 [CI, 1.1 to 2.6]) was increased in women with subclinical hypothyroidism (Table 3). Women with subclinical hypothyroidism also had a greater prevalence of myocardial infarction than euthyroid women (odds ratio, 2.3 [CI, 1.3 to 4.0]) (Table 3). Additional adjustment for body mass index, total cholesterol and HDL cholesterol levels, systolic and diastolic blood pressure, and smoking status did not affect these associations, nor did exclusion of participants who used  $\beta$ -blockers (data not shown). During an average follow-up of 4.6 years, 16 women had a first incident myocardial infarction. When we used a Cox proportional hazards regression analysis in women with subclinical hypothyroidism, a statistically non-significant adjusted relative risk of 2.5 (CI, 0.7 to 9.1) was observed for myocardial infarction.

Women with subclinical hypothyroidism and antibodies to thyroid peroxidase had a greater prevalence of aortic atherosclerosis than euthyroid women without antibodies to thyroid peroxidase (odds ratio, 1.9 [CI, 1.1 to 3.6]) (Table 3). The presence of antibodies to thyroid peroxidase increased the odds ratio for a history of myocardial infarction to 3.1 (CI, 1.5 to 6.3) in women who had subclinical hypothyroidism compared with euthyroid women who did not have antibodies to thyroid peroxidase (Table 3). Because only one woman with subclinical hypothyroidism and antibodies to thyroid peroxidase had myocardial infarction during follow-up, we were not

Table 2. Characteristics of Women according to Vascular Disease Status

Characteristic	All Women ( $n = 1055$ )	Women with Aortic Atherosclerosis ( $n = 560$ )	Women with a History of Myocardial Infarction ( $n = 79$ )
Mean age $\pm$ SD, y	68.9 $\pm$ 7.5	70.7 $\pm$ 7.4	71.1 $\pm$ 6.9
Median thyroid-stimulating hormone level (25th, 75th percentile), mU/L	1.7 (1.1, 2.7)	1.7 (1.1, 2.8)	2.0 (1.2, 3.4)
Women with subclinical hypothyroidism, % ( $n$ )	11.8 (124)	13.9 (78)*	21.5 (17)†
Women with subclinical hypothyroidism and antibodies to thyroid peroxidase, % ( $n$ )	5.8 (61)	7.1 (40)*	13.9 (11)†
Women with antibodies to thyroid peroxidase, % ( $n$ )	21.6 (228)	21.4 (120)	26.6 (21)

\*  $P < 0.05$  compared with women without the specific vascular disease status (chi-square test).

†  $P < 0.01$  compared with women without the specific vascular disease status (chi-square test).

**Table 3. Odds Ratios for Aortic Atherosclerosis and Myocardial Infarction\***

Variable	Condition Present	Condition Absent	Odds Ratio (95% CI)†	Odds Ratio (95% CI)‡
	<i>n</i>			
<b>Aortic atherosclerosis</b>				
Women with subclinical hypothyroidism	77	37	1.7 (1.1–2.6)	1.9 (1.2–3.1)
Euthyroid women	474	376	1§	1§
Women with subclinical hypothyroidism and antibodies to thyroid peroxidase	39	16	1.9 (1.1–3.6)	2.2 (1.1–4.3)
Euthyroid women without antibodies to thyroid peroxidase	398	301	1§	1§
<b>Myocardial infarction</b>				
Women with subclinical hypothyroidism	17	99	2.3 (1.3–4.0)	2.3 (1.3–4.2)
Euthyroid women	61	806	1§	1§
Women with subclinical hypothyroidism and antibodies to thyroid peroxidase	11	46	3.1 (1.5–6.3)	3.5 (1.7–7.4)
Euthyroid women without antibodies to thyroid peroxidase	52	660	1§	1§

\* The number of women may not be exactly the same as in Table 2 because data on some covariates were missing.

† Adjusted for present age.

‡ Adjusted for present age, body mass index, cholesterol level, high-density lipoprotein cholesterol level, systolic and diastolic blood pressure, and smoking status (current, past, or never).

§ Reference risk.

able to compute the corresponding risk for incident myocardial infarction. No association was found between the presence of antibodies to thyroid peroxidase and history of myocardial infarction or between aortic atherosclerosis and history of myocardial infarction when thyroid status was not altered (data not shown).

From our data, we calculated an attributable risk percentage of 60 and a population attributable risk percentage of 14 for subclinical hypothyroidism associated with myocardial infarction (Table 4). If subclinical hypothyroidism is assumed to be causally related to myocardial infarction, our findings suggest that it contributed to 60% of cases of myocardial infarction among women affected by subclinical hypothyroidism and that it was involved in the pathogenesis of 14% of all myocardial infarctions in the study sample. For purposes of comparison, the attributable risk percentages and the population attributable risk percentages for hypercholesterolemia, hypertension, smoking, and diabetes associated with myocardial infarction in all female participants in the Rotterdam Study are presented in Table 4.

### Discussion

Our results show that subclinical hypothyroidism is highly prevalent among elderly women and is associated with a greater frequency of aortic atherosclerosis and myocardial infarction. Among women with subclinical hypothyroidism, these associations are slightly stronger in those who have antibodies to thyroid peroxidase. Thyroid autoimmunity itself is not associated with aortic atherosclerosis or myocardial infarction.

One limitation of our study is the cross-sectional nature of the design, which necessitates careful in-

terpretation of the results. The relative risk for myocardial infarction in women with subclinical hypothyroidism in the prospective part of our study was similar to the point estimate in the cross-sectional part of our study. However, the CI was wide and included 1.0. Furthermore, we must consider the fact that elevated TSH levels may be caused by nonthyroidal illness (31, 32). However, we excluded women with a low free thyroxine level and observed that women with subclinical hypothyroidism did not differ from euthyroid women in levels of total protein, albumin, and creatinine. Therefore, it is highly unlikely that nonthyroidal illness affected the validity of our results. Serum samples were obtained only from women who visited the research center. We assume that the nonresponse for the visit to the research center will not depend on subclinical hypothyroidism differently among persons with or without the presence of cardiovascular disease, making selection bias unlikely. Furthermore, follow-up information was not available for all study participants as a result of logistic reasons. Because we have no reason to assume that the relation between subclinical hypothyroidism and myocardial infarction in women with complete follow-up data differs from this association in those without follow-up data, we do not believe that this lack of information influenced the validity of our results.

Approximately 11% of women in our sample had a TSH level greater than 4 mU/L. This prevalence closely resembles that reported in women in the Wickham survey (5), the Framingham Study (6), and a study in community-dwelling elderly persons (33). Among all women in our sample for analysis, 13 (1.1%) had unrecognized overt thyroid failure characterized by an elevated TSH level (>4.0 mU/L) and an abnormal free thyroxine level (<11 pmol/L [0.9 ng/dL]), which is in agreement with reports of prevalence found during screening (4).

These data suggest that our sample is representative of the general population.

Several studies on the association between coronary heart disease and subclinical hypothyroidism have been done. Our results agree with those of previous case-control studies that also showed an association between subclinical hypothyroidism and coronary heart disease in elderly women (9, 10). However, a Finnish study that presented results of men and women together provided no evidence that latent thyroid failure is associated with coronary heart disease (7). Female patients with coronary heart disease were shown to have significantly lower serum levels of TSH than controls; however, subclinical hypothyroidism did not seem to be related to the presence of coronary heart disease (11). In the Wickham survey, no cross-sectional association with ischemic heart disease was observed, but a weak association between minor electrocardiographic changes and minor degrees of hypothyroidism was found in women (8).

Data on atherosclerosis and subclinical hypothyroidism are scarce. A case-control study in elderly women suggested an association between subclinical hypothyroidism and peripheral arterial disease (34). We are the first to describe an association between subclinical hypothyroidism and atherosclerosis as assessed by a noninvasive measurement in a general population sample. Aortic atherosclerosis was diagnosed by radiographic detection of calcified deposits in the abdominal aorta, which has been shown to be a highly specific technique for the measurement of aortic intima atherosclerosis (21). False-negative misclassification may have occurred in our study, but it was probably independent of thyroid status and therefore may have affected our results only by causing us to underestimate the association. Because we found that subclinical hypothyroidism was associated with both atherosclerosis and myocardial infarction, our data may indicate that atherosclerosis is involved in the mechanism by which subclinical hypothyroidism and myocardial infarction are associated.

Several mechanisms that may be involved with the association of subclinical hypothyroidism with atherosclerosis and myocardial infarction can be considered. A common cause of thyroid failure in elderly women is autoimmune thyroiditis (6, 35). It has been suggested that pathologic immune reactivity (for example, immune complex-mediated vascular damage) may be important in the association of autoimmune thyroiditis with coronary heart disease (36). However, the literature on this association is controversial. Some studies have described an association between thyroid autoimmunity and coronary heart disease (9, 10, 12, 14, 37), and other studies have not (7, 8, 11, 15). Different uses of various

**Table 4. Attributable Risk Percentages and Population Attributable Risk Percentages for Subclinical Hypothyroidism and Classic Risk Factors for Cardiovascular Disease Associated with Incident Myocardial Infarction in Women in the Rotterdam Study**

Risk Factor	Age-Adjusted Relative Risk*	Attributable Risk	Population Attributable Risk
			%
Subclinical hypothyroidism	2.5	60	14
Hypercholesterolemia	2.4	58	18
Hypertension	1.6	38	14
Smoking	2.0/1.2†	50/17‡	15
Diabetes mellitus	2.4	58	14

\* Determined by using Cox proportional hazards regression analysis.

† Age-adjusted relative risk and attributable risk percentage for current compared with never smokers.

‡ Age-adjusted relative risk and attributable risk percentage for past compared with never smokers.

generations of antibody assays and different definitions of thyroid autoimmunity may have played a role in these discrepant findings. We found no association between the presence of antibodies to thyroid peroxidase itself and aortic atherosclerosis or myocardial infarction, which weakens the notion that a pathologic immune reactivity is important. We found that associations between subclinical hypothyroidism and aortic atherosclerosis or myocardial infarction were slightly stronger when subclinical hypothyroidism was accompanied by antibodies to thyroid peroxidase. This suggests that subclinical hypothyroidism, which is thought to be more severe and lasting in the presence of thyroid antibodies, contributes to the pathogenesis of cardiovascular disease.

Some authors found a disturbance in the atherogenic lipid metabolism in patients with subclinical hypothyroidism (38–42), whereas other studies did not (43–45). Although in our study the total cholesterol level was higher in women with overt hypothyroidism than in euthyroid women (data not shown), we did not find that total cholesterol level was higher in women with subclinical hypothyroidism than in euthyroid women. High-density lipoprotein and total cholesterol levels provided no pathophysiologic explanation for the association of subclinical hypothyroidism with aortic atherosclerosis and myocardial infarction. Other lipids—such as low-density lipoprotein cholesterol level, enhanced low-density lipoprotein oxidation (46), triglyceride level, and lipoprotein(a) level (42)—may be responsible for the association between subclinical hypothyroidism and cardiovascular disease, but we did not measure these factors.

Other mechanisms that may be involved in the association between subclinical hypothyroidism and cardiovascular disease can be derived from experimental data. In vitro, thyroid hormones inhibit

collagen-induced platelet aggregation (47, 48) and directly relax smooth muscle (49). These effects may be important if thyroid hormones have the same effects in adult humans, although in subclinical hypothyroidism, by definition, levels of thyroid hormones are not decreased. Hypothyroidism is accompanied by a hypercoagulable state (50), increased blood viscosity (51), and a greater plasma concentration of total homocysteine (52); if these factors are also seen in subclinical hypothyroidism, they may account for atherosclerotic and ischemic disorders.

In conclusion, we found that subclinical hypothyroidism is highly prevalent in elderly women and is strongly and independently associated with aortic atherosclerosis and myocardial infarction. The population attributable risk percentage for subclinical hypothyroidism associated with myocardial infarction was within the range of that for known major risk factors for cardiovascular disease. Additional research should be done to determine whether this association can be confirmed in a prospective study. If not, subsequent studies may focus on the effectiveness of possible therapies for subclinical hypothyroidism in elderly women and the desirability of screening such women for this disorder.

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## References

1. Vanhaelst L, Nève P, Chailly P, Bastenie PA. Coronary-artery disease in hypothyroidism. Observations in clinical myxoedema. *Lancet*. 1967;2:800-2.
2. Steinberg AD. Myxoedema and coronary artery disease—a comparative autopsy study. *Ann Intern Med*. 1968;68:338-44.
3. Klein I, Ojamaa K. The cardiovascular system in hypothyroidism. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's the Thyroid*. 7th ed. Philadelphia: Lippincott-Raven; 1996:799-804.
4. Helfand M, Redfern CC. Clinical guideline, part 2. Screening for thyroid disease: an update. American College of Physicians. *Ann Intern Med*. 1998;129:144-58.
5. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Wickham survey. *Clin Endocrinol (Oxf)*. 1977;7:481-93.
6. Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P. The aging thyroid. Thyroid deficiency in the Framingham Study. *Arch Intern Med*. 1985;145:1386-8.
7. Heinonen OP, Gordin A, Aho K, Punsar S, Pyörälä K, Puro K. Symptomless autoimmune thyroiditis in coronary heart-disease. *Lancet*. 1972;1:785-6.
8. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. Lipid profiles and cardiovascular disease in the Wickham area with particular reference to thyroid failure. *Clin Endocrinol (Oxf)*. 1977;7:495-508.
9. Tiethe M, Lupi GA, Gutzwiller F, Grob PJ, Studer H, Burgi H. Borderline low thyroid function and thyroid autoimmunity. Risk factors for coronary heart disease? *Br Heart J*. 1981;46:202-6.
10. Dean JW, Fowler PB. Exaggerated responsiveness to thyrotrophin releasing hormone: a risk factor in women with coronary artery disease. *Br Med J (Clin Res Ed)*. 1985;290:1555-61.
11. Miura S, Iitaka M, Suzuki S, Fukasawa N, Kitahama S, Kawakami Y, et al. Decrease in serum levels of thyroid hormone in patients with coronary heart disease. *Endocr J*. 1996;43:657-63.
12. Bastenie PA, Vanhaelst L, Nève P. Coronary-artery disease in hypothyroidism. *Lancet*. 1967;2:1221-2.
13. Gaspar JA. Postmortem observations on the thyroid in atherosclerosis. *J Am Geriatr Soc*. 1968;16:686-95.
14. Bastenie PA, Vanhaelst L, Bonnyns M, Nève P, Staquet M. Prediagonal hypothyroidism: a risk factor for coronary heart-disease. *Lancet*. 1971;1:203-4.
15. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, et al. The development of ischemic heart disease in relation to autoimmune thyroid disease in a 20-year follow-up study of an English community. *Thyroid*. 1996;6:155-60.
16. Hofman A, Grobbee DE, de Jong PT, van den Ouweland FA. Determinants of disease and disability in the elderly: the Rotterdam Elderly Study. *Eur J Epidemiol*. 1991;7:403-22.
17. van Gent CM, van der Voort HA, de Bruyn AM, Klein F. Cholesterol determinations. A comparative study of methods with special reference to enzymatic procedures. *Clin Chim Acta*. 1977;75:243-51.
18. Tranter T, Herzog R, Gegenheimer L, Luckner PW. A new method for the determination of the bioavailability of thyroid hormone preparations. *Methods Find Exp Clin Pharmacol*. 1994;16:133-40.
19. Witteman JC, Grobbee DE, Valkenburg HA, van Hemert AM, Stijnen T, Hofman A. Cigarette smoking and the development and progression of aortic atherosclerosis. A 9-year population-based follow-up study in women. *Circulation*. 1993;88(5 Pt 1):2156-62.
20. Witteman JC, Grobbee DE, Valkenburg HA, van Hemert AM, Stijnen T, Burger H, et al. J-shaped relation between change in diastolic blood pressure and progression of aortic atherosclerosis. *Lancet*. 1994;343:504-7.
21. Hyman JB, Epstein FM. A study of the correlation between roentgenographic and post-mortem calcifications of the aorta. *Am Heart J*. 1954;48:540-3.
22. Bots ML, Witteman JC, Grobbee DE. Carotid intima-media wall thickness in elderly women with and without atherosclerosis of the abdominal aorta. *Atherosclerosis*. 1993;102:99-105.
23. Witteman JC, Kannel WB, Wolf PA, Grobbee DE, Hofman A, D'Agostino RB, et al. Aortic calcified plaques and cardiovascular disease (the Framingham Study). *Am J Cardiol*. 1990;66:1060-4.
24. Witteman JC, Kok FJ, van Saase JL, Valkenburg HA. Aortic calcification as a predictor of cardiovascular mortality. *Lancet*. 1986;2:1120-2.
25. van Bommel JH, Koss JA, van Herpen G. Methodology of the modular ECG analysis system MEANS. *Methods Inf Med*. 1990;29:346-53.
26. Willemis JL, Abreu-Lima C, Arnaud P, van Bommel JH, Brohet C, Degani R, et al. The diagnostic performance of computer programs for the interpretation of electrocardiograms. *N Engl J Med*. 1991;325:1767-73.
27. International Statistical Classification of Diseases and Related Health Problems, 10th Revision. v 1. World Health Organization. Geneva: World Health Organization; 1992.
28. Harjai KJ, Likata AA. Effects of amiodarone on thyroid function. *Ann Intern Med*. 1997;126:63-73.
29. Brass EP. Effects of antihypertensive drugs on endocrine function. *Drugs*. 1984;27:447-58.



30. Hennekens CH, Buring JE. *Epidemiology in Medicine*. v 1. Boston: Little, Brown; 1987.
31. Wong ET, Bradley SG, Schultz AL. Elevations of thyroid-stimulating hormone during acute nonthyroidal illness. *Arch Intern Med*. 1981;141:873-5.
32. Brent GA, Hershman JM, Braunstein GD. Patients with severe nonthyroidal illness and serum thyrotropin concentrations in the hypothyroid range. *Am J Med*. 1986;81:463-6.
33. Parle JV, Franklyn JA, Cross KW, Jones SC, Sheppard MC. Prevalence and follow-up of abnormal thyrotrophin (TSH) concentrations in the elderly in the United Kingdom. *Clin Endocrinol (Oxf)*. 1991;34:77-83.
34. Powell J, Zadeh JA, Carter G, Greenhalgh RM, Fowler PB. Raised serum thyrotrophin in women with peripheral arterial disease. *Br J Surg*. 1987;74:1139-41.
35. Robuschi G, Safran M, Braverman LE, Graudi A, Roti E. Hypothyroidism in the elderly. *Endocr Rev*. 1987;8:142-53.
36. Mathews JD, Whittingham S, Mackay IR. Autoimmune mechanisms in human vascular disease. *Lancet*. 1974;2:1423-7.
37. Bastenie PA, Vanhaelest L, Golstein J, Smeets P. Asymptomatic autoimmune thyroiditis and coronary heart-disease. Cross-sectional and prospective studies. *Lancet*. 1977;2:155-8.
38. Fowler PB, Swale J, Andrews H. Hypercholesterolaemia in borderline hypothyroidism. Stage of premyxoedema. *Lancet*. 1970;2:488-91.
39. Althaus BU, Staub JJ, Ryff-De Leche A, Oberhansli A, Stahelin HB. LDL/HDL-changes in subclinical hypothyroidism: possible risk factors for coronary heart disease. *Clin Endocrinol*. 1988;28:157-63.
40. Caron P, Calazel C, Parra HJ, Hoff M, Louvet JP. Decreased HDL cholesterol in subclinical hypothyroidism: the effect of L-thyroxine therapy. *Clin Endocrinol (Oxf)*. 1990;33:519-23.
41. Staub JJ, Althaus BU, Engler H, Ryff AS, Trabucco P, Marquardt K, et al. Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on peripheral target tissues. *Am J Med*. 1992;92:631-42.
42. Kung AW, Pang RW, Janus ED. Elevated serum lipoprotein(a) in subclinical hypothyroidism. *Clin Endocrinol (Oxf)*. 1995;43:445-9.
43. Nilsson G, Nordlander S, Larin K. Studies on subclinical hypothyroidism with special reference to the serum lipid pattern. *Acta Med Scand*. 1976;200:63-7.
44. Parle JV, Franklyn JA, Cross KW, Jones SR, Sheppard MC. Circulating lipids and minor abnormalities of thyroid function. *Clin Endocrinol (Oxf)*. 1992;37:411-4.
45. Geul KW, van Sluisveld IL, Grobbee DE, Docter R, de Bruyn AM, Hooykaas H, et al. The importance of thyroid microsomal antibodies in the development of elevated serum TSH in middle-aged women: associations with serum lipids. *Clin Endocrinol (Oxf)*. 1993;39:275-80.
46. Sundaram V, Hanna AN, Koneru L, Newman HA, Falke JM. Both hypothyroidism and hyperthyroidism enhance low density lipoprotein oxidation. *J Clin Endocrinol Metab*. 1997;82:3421-4.
47. Mamiya S, Hagiwara M, Inoue S, Hidaka H. Thyroid hormones inhibit platelet function and myosin light chain kinase. *J Biol Chem*. 1989;264:8575-9.
48. Masaki M, Nishikawa M, Urakami M, Yoshimura M, Toyoda N, Mori Y, et al. 3,3',5'-Triiodothyronine inhibits collagen-induced human platelet aggregation. *J Clin Endocrinol Metab*. 1992;75:721-5.
49. Ishikawa T, Chijiwa T, Hagiwara M, Mamiya S, Hidaka H. Thyroid hormones directly interact with vascular smooth muscle strips. *Mol Pharmacol*. 1989;35:760-5.
50. Chadarevian R, Bruckert E, Ankri A, Beudier I, Giral P, Turpin G. Relationship between thyroid hormones and plasma d-dimer levels. *Thromb Haemost*. 1998;79:99-103.
51. Koltringer P, Eber O, Wakonig P, Klima G, Lind P. Hypothyroidism and the influence on human blood rheology. *J Endocrinol Invest*. 1988;11:267-72.
52. Nedrebo BG, Ericsson UB, Nygaard O, Rafsum H, Ueland PM, Aakvaag A, et al. Plasma total homocysteine levels in hyperthyroid and hypothyroid patients. *Metabolism*. 1998;47:89-93.

**Subclinical hypothyroidism in infertile women: the importance of continuous monitoring and the role of the thyrotropin-releasing hormone stimulation test**

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The aim of our study was to assess the prevalence of subclinical hypothyroidism (SH) after administering a thyrotropin-releasing hormone (TRH) stimulation test among women with normal serum thyroid-stimulating hormone (TSH) levels and various causes of infertility. Eighty-seven infertile women (39 with ovulation disorders and 48 with other causes of infertility) had a TRH stimulation test on day 3 - 7 of their cycle. Exaggerated TSH response ( $>30$  mIU/l at 20, 40 or 60 min) following intravenous injection of 400 microg TRH was defined as SH. The TRH test was performed 2 - 4 months after the first visit to the clinic. We found that the prevalence of SH was significantly higher among women with ovulation disorders (20.5%) than among women with normal ovulation (8.3%). In addition, we found that although basal TSH levels were normal at recruitment, 2 - 4 months later these levels were abnormally high in 8% of the women. All these women had an abnormal TRH test. We recommend performing TRH stimulation testing in women suffering from ovulation disorders who have normal basal TSH levels, followed by repeat assessments of thyroid function to enable treatment with thyroxine in cases with abnormal results.

## Left Ventricular Diastolic Dysfunction in Patients with Subclinical Hypothyroidism

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### ABSTRACT

Although subclinical hypothyroidism is frequently diagnosed, the decision to institute a substitutive therapy with L-T<sub>4</sub> remains controversial. Because the cardiovascular system is considered a main target for the action of thyroid hormone, we investigated whether subclinical hypothyroidism induces cardiovascular abnormalities.

Twenty-six patients (mean age, 36 ± 12 yr) were evaluated by Doppler-echocardiography, whereas a subgroup of 10 patients, randomly selected, were reevaluated after 6 months of L-T<sub>4</sub> substitutive therapy (mean dose, 68 µg daily). Thirty subjects (matched for age, sex, and body surface area) served as controls.

Mean plasma TSH was significantly higher in patients ( $P < 0.001$ ), whereas mean serum free T<sub>4</sub> and free T<sub>3</sub> concentrations, although in the normal range, were significantly lower ( $P < 0.001$  and  $P < 0.005$ , respectively). Blood pressure and heart rate did not differ from control values. Echocardiogram examination showed no abnormalities of the left ventricular morphology and a slight, but not significant, reduction in the systolic function in the patient group. In contrast, Doppler-derived indices of diastolic function showed significant prolongation

of the isovolumic relaxation time ( $94 \pm 13$  vs.  $84 \pm 8$  msec;  $P < 0.001$ ), increased A wave ( $55 \pm 13$  vs.  $48 \pm 9$  cm/sec;  $P < 0.05$ ), and reduced early diastolic mitral flow velocity/late diastolic mitral flow velocity ratio ( $1.4 \pm 0.3$  vs.  $1.7 \pm 0.3$ ;  $P < 0.001$ ). In the subgroup of 10 patients, thyroid hormone profile was normalized by 6 months of L-T<sub>4</sub> substitutive therapy, whereas no changes were observed in the left ventricular morphology. Systolic function was significantly enhanced, as compared with pretreatment values ( $P < 0.01$ ) but did not differ from control values. Also, systemic vascular resistance was significantly decreased by L-T<sub>4</sub> replacement therapy. Assessment of diastolic function showed significant shortening of isovolumic relaxation time ( $77 \pm 15$  vs.  $91 \pm 8$ ;  $P < 0.05$ ), reduction of A wave ( $51 \pm 13$  vs.  $60 \pm 12$ ;  $P < 0.01$ ), and increase of early diastolic mitral flow velocity/late diastolic mitral flow velocity ratio ( $1.7 \pm 0.4$  vs.  $1.3 \pm 0.3$ ;  $P < 0.001$ ). These indices, however, were comparable with those of control subjects.

These findings indicate that subclinical hypothyroidism affects diastolic function and that this abnormality may be reversed by L-T<sub>4</sub> substitutive therapy. (*J Clin Endocrinol Metab* 84: 2064–2067, 1999)

**S**UBCLINICAL hypothyroidism (SHypo) is characterized by variably increased serum TSH concentration with apparently normal serum free T<sub>4</sub> (F-T<sub>4</sub>) and free T<sub>3</sub> (F-T<sub>3</sub>) levels. It occurs in 10–15% of the general population (1).

The clinical presentation of SHypo is nonspecific, and the symptoms are usually subtle, as compared with those of overt hypothyroidism, probably in relation to the intensity and the duration of thyroid hormone deficiency and the age of the patients.

The decision to treat the patients affected by SHypo with substitutive L-T<sub>4</sub> therapy remains controversial (1–3) and mainly dependent on the physician's attitude (to consider the disease as a mild form of tissue hypothyroidism or as a compensate state, in which the increase of TSH is required to maintain normal circulating thyroid hormone concentrations). Indeed, reports on the efficacy of replacement therapy with levothyroxine (L-T<sub>4</sub>) on the lipid abnormalities in the patients with SHypo have shown conflicting results (4–10). However, although it is difficult to establish a cutoff for TSH values that clearly indicates the need to institute a substitutive

therapy with L-T<sub>4</sub>, the treatment is generally recommended in the presence of a serum TSH level of 10 mU/L or more (2, 11, 12). When the TSH level is less than 10 mU/L, the treatment may be indicated in relation to the presence of goiter or antithyroid antibodies to prevent the onset of overt hypothyroidism more than to tissue assessment of thyroid hormone deficiency (1).

Considering the high prevalence of SHypo and the well-established cardiac consequences of altered thyroid status, in the present study, we investigated whether SHypo causes cardiovascular abnormalities. To this aim, we assessed cardiac morphology and function, using noninvasive methods, in patients with SHypo before and after L-T<sub>4</sub> substitutive therapy.

### Subjects and Methods

The study was performed by means of Doppler-echocardiography in 26 patients with SHypo and in 30 normal control subjects.

SHypo was diagnosed on the basis of TSH values above normal (see Table 1), associated with a supranormal response to TRH (ΔTSH above 30 mU/L), and FT<sub>3</sub> and FT<sub>4</sub> in the lower limit of the normal range. Only the patients with stable TSH and thyroid hormone levels for at least 6 months before the enrollment and with a positive test for serum antithyroid peroxidase antibodies were included in the study. TSH and thyroid hormone levels were considered stable if their variations were lower than 20% in three consecutive evaluations performed in the 6 months before study. Patients and normal volunteers had a sedentary life-style, none of them had a history of cardiovascular disease, and all were in sinus rhythm.

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TABLE 1. Characteristics of the study population

	Controls (n = 30)	SHypo patients (n = 26)
Age (yr)	36 ± 11	36 ± 12
Sex (M/F)	6/24	2/24
BSA (m <sup>2</sup> )	1.67 ± 0.17	1.64 ± 0.12
HR (bpm)	71 ± 8	73 ± 9
SBP (mm Hg)	125 ± 12	120 ± 10
DBP (mm Hg)	77 ± 5	78 ± 7
FT <sub>4</sub> (7.7–23.2 pmol/L)	15.3 ± 2.6	9.4 ± 3.0*
FT <sub>3</sub> (3.9–8.8 pmol/L)	6.0 ± 1.2	5.1 ± 1.1*
TSH (0.2–3.0 mU/L)	1.6 ± 0.9	8.6 ± 4.8*

BSA, body surface area; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure.

\*  $P < 0.001$ .

<sup>a</sup>  $P = 0.005$ , vs. control subjects.

A subgroup of 10 patients, randomly selected, was reevaluated after 6 months of L-T<sub>4</sub> therapy, at substitutive doses ranging from 50–100 µg daily, with a mean dose of 68 µg. None of the subjects received any medication during the study, other than L-T<sub>4</sub> for the subgroup of 10 patients previously described.

All subjects gave informed consent before participating in the study, and the protocol was approved by the Ethics Committee of the University of Naples Federico II.

#### Assessment of thyroid status

Evaluation of plasma TSH levels was performed by an ultrasensitive immunoradiometric assay (Bouty, Milan, Italy) with a detection limit of 0.05 mU/L. The intra- and interassay variations were 3.1% and 3.8% at 0.25–50 mU/L. Serum FT<sub>4</sub> and FT<sub>3</sub> were measured using the Lisophase Kits (Bouty). The intra- and interassay variations and sensitivities were 2.9%, 4.7%, and 0.8 pmol/L for FT<sub>4</sub>, respectively, and 4.1%, 5.9%, and 1.0 pmol/L for FT<sub>3</sub>.

#### Doppler-echocardiography

Complete mono- and two-dimensional, and Doppler-echocardiographic analysis was performed by an ultrasound mechanical system equipped with a 3.5-MHz transducer (Apogee CX, Interspec, Inc., Ambler, PA), as previously described (13, 14). The examinations were performed by the same operator for all participants in the study. The investigator reading the echoes was blinded as to whether the recordings he was interpreting were of hypothyroid or normal subjects.

The parameters of systolic and diastolic function, derived by echocardiography and by Doppler examination, were assessed as previously reported (14, 15). Stroke volume was obtained using the method of Teichholz *et al.* (16). Cardiac output (CO) was measured as the product of stroke volume and heart rate. Systemic vascular resistance (SVR) was calculated as follows:  $SVR = [(mPAO - mPRA) / CO] \times 80$ , where mPRA is the mean right atrial pressure, considered equal to zero mm Hg in each subject, and mPAO is the mean aortic pressure, derived by cuff-sphygmomanometer, as diastolic blood pressure + 1/3(systolic-diastolic blood pressure) (17). Furthermore, aortic peak flow velocity and mean aortic acceleration were obtained by the recording of the aortic flow velocimetry. In particular, mean aortic acceleration was obtained by dividing the peak flow velocity by the acceleration time (18).

#### Statistical analysis

All data in the text and tables are reported as the mean ± SD. Comparisons among control subjects and subclinical hypothyroid patients were performed by the two-tailed Student's *t* test for unpaired data, whereas comparisons among the subgroup of 10 subclinical hypothyroid patients, before and 6 months after L-T<sub>4</sub> treatment, were performed using the two-tailed Student's *t* test for paired data. A *P* value less than 0.05 was considered as significant.

#### Results

The clinical characteristics of the study population are shown in Table 1. Patients and normal controls were well matched for

age, sex, and body surface area. Both heart rate and blood pressure were comparable in the two groups. As expected, TSH levels were significantly higher in patients than in controls. FT<sub>3</sub> and FT<sub>4</sub> levels, although in the normal range, were significantly lower in the patients than in control subjects.

As summarized in Table 2, no abnormalities were found in LV morphology and mass in the patients with SHypo.

Table 3 displays Doppler-echocardiographic resting indices of LV systolic and diastolic function. No clear evidence of systolic dysfunction was found in the patient group. The only abnormality was a significant, although mild, decrease in the mean aortic acceleration.

Doppler-derived indices of left ventricular (LV) diastolic filling showed clear abnormalities of myocardial relaxation, as indicated by significant prolongation of the isovolumic relaxation time (Fig. 1) and significant reduction of the early diastolic mitral flow velocity/late diastolic mitral flow velocity (E/A) ratio, mainly accounted for by increased A-wave of mitral flow velocity.

In the subgroup of SHypo patients receiving L-T<sub>4</sub> substitutive therapy for six months, TSH was normalized (from  $9.2 \pm 4.2$  to  $1.7 \pm 1$  mU/L,  $P < 0.005$ ), whereas FT<sub>3</sub> and FT<sub>4</sub> increased (FT<sub>3</sub>: from  $4.5 \pm 1.2$  to  $5.6 \pm 1.4$  pmol/L,  $P < 0.05$ ; FT<sub>4</sub>: from  $9.3 \pm 3.4$  to  $14.4 \pm 3.8$  pmol/L,  $P < 0.005$ ) and were no longer different from the values of control subjects.

As summarized in Tables 4 and 5, L-T<sub>4</sub> substitutive therapy did not induce significant changes in LV morphology. In con-

TABLE 2. Echocardiographic parameters to left ventricular morphology in subclinical hypothyroid patients and in normal subjects

	Controls (n = 30)	SHypo patients (n = 26)
LVEDD (mm)	48 ± 3	47.5 ± 4
LVESD (mm)	30.5 ± 2	30.5 ± 4
Diastolic IVST (mm)	9.2 ± 1.5	9.8 ± 1.7
Diastolic LVPWT (mm)	8.5 ± 1.4	8.9 ± 1.1
LVMi (g)	63 ± 14	66 ± 17

LVEDD, left ventricular end diastolic diameter; LVESD, left ventricle end systolic diameter; IVST, interventricular septum thickness; LVPWT, left ventricle posterior wall thickness; LVMi, left ventricle mass corrected for body surface area.

TABLE 3. Doppler-echocardiographic parameters of left ventricular function in subclinical hypothyroid patients and in normal subjects

	Controls (n = 30)	SHypo patients (n = 26)
Systolic function		
FS (%)	36 ± 4.0	36 ± 4.5
mVCF (circ/sec)	1.3 ± 0.1	1.2 ± 0.2
Mean aortic acceleration (m/sec <sup>2</sup> )	10.1 ± 1.1	9.3 ± 1.4*
Peak aortic flow velocity (cm/sec)	0.9 ± 0.1	0.9 ± 0.2
Cardiac output µL/min	5223 ± 959	5300 ± 1260
SVR (dynes/sec · cm <sup>-5</sup> )	1460 ± 343	1470 ± 372
Diastolic function		
E (cm/sec)	79 ± 11	74 ± 13
A (cm/sec)	48 ± 9	55 ± 13*
E/A ratio	1.7 ± 0.3	1.4 ± 0.3*
IRT (msec)	84 ± 8	94 ± 13*

FS, fractional shortening; mVCF, mean velocity of circumferential fiber shortening; IRT, isovolumetric relaxation time; SVR, systemic vascular resistance.

\*  $P < 0.05$ , vs. control subjects.

<sup>a</sup>  $P < 0.001$ .

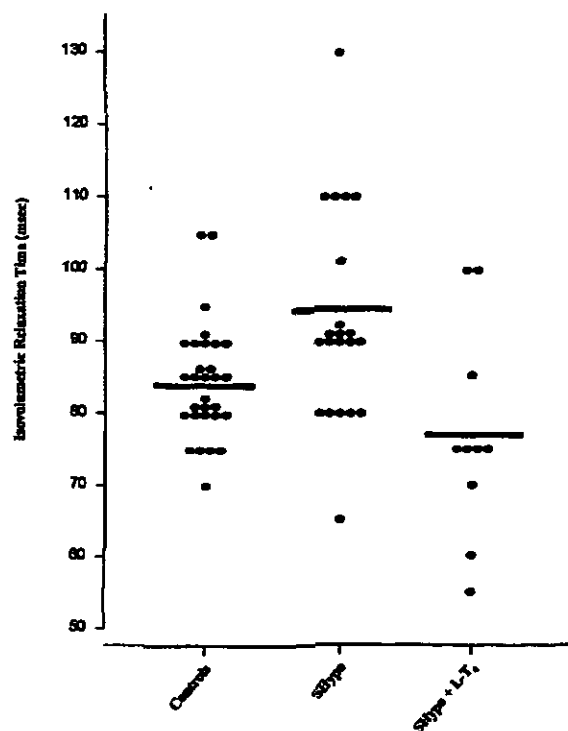


FIG. 1. Individual values of isovolumetric relaxation time (IRT) in controls and in patients with SHypo before (SHypo) and after (SHypo + L-T<sub>4</sub>) L-T<sub>4</sub> replacement therapy.

TABLE 4. Echocardiographic parameters of left ventricular morphology in subclinical hypothyroid patients before and after L-T<sub>4</sub> replacement therapy

	SHypo patients (n = 10)	
	Before therapy	After therapy
LVEDD (mm)	47.5 ± 4	47 ± 3
LVESD (mm)	30 ± 4	28.5 ± 4
Diastolic IVST (mm)	9.8 ± 0.6	9.5 ± 1.1
Diastolic LVPWT (mm)	8.7 ± 0.9	8.4 ± 0.7
LVMi (g)	87 ± 20	82 ± 11

trast, Doppler indices of diastolic function were normalized by L-T<sub>4</sub> therapy, whereas systolic function improved. In particular, the isovolumic relaxation time shortened significantly to values comparable with those of normal subjects (Fig. 1), and the E/A ratio increased significantly. Fractional shortening, mean velocity of circumferential fiber shortening, and mean aortic acceleration were all enhanced by L-T<sub>4</sub> therapy, although they were still in the normal range. Moreover, CO increased slightly, but not significantly, whereas SVR was reduced by L-T<sub>4</sub> treatment, although it was not significantly different from the mean value of the control subjects.

#### Discussion

The results of the present study demonstrate that abnormal LV diastolic filling (suggestive of impaired LV relax-

TABLE 5. Doppler-echocardiographic parameters of left ventricular function in subclinical hypothyroid patients before and after L-T<sub>4</sub> replacement therapy

	SHypo patients (n = 10)	
	Before therapy	After therapy
<b>Systolic function</b>		
FS (%)	37 ± 5	39 ± 7 <sup>a</sup>
mVCF (circ/sec)	1.2 ± 0.2	1.3 ± 0.2 <sup>a</sup>
Mean aortic acceleration (m/sec <sup>2</sup> )	9.3 ± 1.3	11.1 ± 2.3 <sup>a</sup>
Peak aortic flow velocity (cm/sec)	0.9 ± 0.2	0.9 ± 0.1
Cardiac Output (mL)	5330 ± 1840	5806 ± 1758
SVR (dynes/sec · cm <sup>-5</sup> )	1497 ± 415	1361 ± 383 <sup>b</sup>
<b>Diastolic function</b>		
E (cm/sec)	78 ± 12	85 ± 14 <sup>b</sup>
A (cm/sec)	60 ± 12	51 ± 13 <sup>a</sup>
E/A ratio	1.3 ± 0.3	1.7 ± 0.4 <sup>c</sup>
IRT (msec)	91 ± 8	77 ± 15 <sup>b</sup>

<sup>a</sup> P < 0.01 vs. before therapy.

<sup>b</sup> P < 0.05.

<sup>c</sup> P < 0.001.

ation) is a common finding in patients with SHypo and that this abnormality may be reversed by a short-term substitutive L-T<sub>4</sub> therapy.

Cardiac function has been previously evaluated in patients with SHypo, by systolic time intervals, with conflicting results (19–25). Some authors reported prolonged systolic time intervals in SHypo (19–21), which improved after L-T<sub>4</sub> therapy, particularly in those patients with more marked basal abnormalities (20). In contrast, Tseng *et al.* found that the isovolumic contraction time, the pre-ejection period, and the ratio of pre-ejection period to LV ejection time were normal in patients with SHypo (25), as assessed by simultaneous recording of aortic and mitral flow velocities.

Arem *et al.*, using Doppler echocardiography at rest and during exercise in eight patients with SHypo, found normal cardiac structure and function, and mild prolongation of the pre-ejection period during exercise and slightly reduced LV diastolic dimensions at rest (26).

Bell *et al.* showed, by radionuclide ventriculography, that patients with SHypo have normal ejection fraction at rest, with a small (but significant) increase in LV ejection fraction during maximal exercise after L-T<sub>4</sub> therapy (27). Forfar *et al.* also reported a blunted increase in ejection fraction during exercise, with a clear improvement in this parameter after L-T<sub>4</sub> replacement therapy (28). Moreover, Foldes *et al.* found a lower ejection fraction, both at rest and during physical exercise, in patients with SHypo, as compared with normal subjects (29).

The discrepant results reported in previous studies of cardiac involvement in SHypo might be, in part, related to the different patient selection (age, inclusion of patients with previous hyperthyroidism, evaluation of patients with acute or unstable SHypo) and to the different diagnostic criteria (too-large range of TSH levels).

In the present study, we performed a strict selection of patients with stable SHypo, excluding patients with confounding factors particularly affecting the cardiovascular system. The impaired diastolic function in this group of patients suggests that SHypo is a condition of minimal tissue hypothyroidism rather than a compensated state. If this is the case, the patients with SHypo should all be considered as potential candidates for therapy with L-T<sub>4</sub>.

The idea that SHypo should be treated is also supported by a recent study from Perk *et al.*, who found greater progression of left coronary angiographic lesions in hypothyroid patients with TSH levels in the range seen in SHypo, compared with patients whose TSH levels were assiduously maintained in the normal range (30).

An impairment of diastolic function is a common finding in many cardiac diseases, and it often precedes and causes systolic dysfunction (31). It has been documented that 30–40% of heart failure syndromes are secondary to impaired diastolic function (31). Therefore, the diastolic dysfunction observed in the current study could be the prelude to more serious limitations of cardiac function and physical performance. In this regard, our finding may be causally related to the blunted increase of LV ejection fraction during exercise observed in patients with SHypo (27, 28).

There is a seeming discrepancy between the results of the present study and our previous findings in subclinical hyperthyroidism (14). Specifically, both subclinical hyperthyroidism and hypothyroidism patients show similar diastolic abnormalities despite opposite hormonal patterns. However, subclinical hyperthyroidism is associated with mild LV hypertrophy, whose well-known deleterious consequences on diastolic function (31) may prevail over the enhanced relaxation induced by thyroid hormone excess (32). On the other hand, SHypo may impair directly diastolic function by reducing sarcoplasmic calcium ATPase activity, with consequent impairment of ventricular diastolic function (33).

Among the indices of systolic function, only mean aortic acceleration was significantly reduced in the group of patients with SHypo. Therefore, this index seems to be the most susceptible to variations in thyroid hormone levels. Furthermore, in the groups of patients with SHypo treated with replacement L-T<sub>4</sub> therapy, SVR was significantly reduced, which confirms a direct vasodilatory effect of thyroid hormone (34).

Doppler-echocardiography represents a simple and reliable method for the evaluation of morphology and function in patients with SHypo. An additional advantage is its easy repeatability and, therefore, it could be used to serially evaluate the adequacy and efficacy of L-T<sub>4</sub> dose. To support this concept, in the subgroup of patients treated with substitutive doses of L-T<sub>4</sub>, the echo-Doppler evaluation performed after 6 months demonstrated an improvement of cardiac function.

In conclusion, the results of this study show that diastolic function is impaired in patients with stable SHypo. This abnormality is reversible after 6 months of substitutive L-T<sub>4</sub> therapy. Doppler-echocardiography may be considered a reliable method for a cross-sectional and longitudinal assessment of left ventricular diastolic function in patients with SHypo.

## References

1. Singer PA, Cooper DS, Levey EG, Ladenson FW, Braverman LE, Daniels G. 1995 Treatment guidelines for patients with hyperthyroidism and hypothyroidism. *JAMA*. 273:808–812.
2. Cooper DS. 1998 Subclinical thyroid disease: a clinician's perspective. *Ann Intern Med*. 129:135–138.
3. Helfand M, Redfern CC. 1998 Screening for thyroid disease: an update. *Ann Intern Med*. 129:144–158.
4. Caron PH, Calazel C, Pazzi HJ, Haff M, Lonvet JP. 1990 Decreased LDL cholesterol in subclinical hypothyroidism: the effect of L-thyroxine therapy. *Clin Endocrinol (Oxf)*. 33:519–523.
5. Arem R, Patsch W. 1990 Lipoprotein and apolipoprotein levels in subclinical hypothyroidism: effect of levothyroxine in therapy. *Arch Intern Med*. 150:2097–2100.
6. Franklyn JA, Daykin J, Betteridge J, et al. 1993 Thyroxine replacement therapy and circulating lipid concentrations. *Clin Endocrinol (Oxf)*. 38:453–459.
7. Miura S, Iitaka M, Yoshimura H, et al. 1994 Disturbed lipid metabolism in patients with subclinical hypothyroidism: effect of L-thyroxine therapy. *Intern Med*. 33:413–417.
8. Tanis BC, Westendorp GJ, Smelt HM. 1996 Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: a reanalysis of intervention studies. *Clin Endocrinol (Oxf)*. 44:643–649.
9. Yildirimkaya M, Ozata M, Yilmaz K, Kilinc C, Gundogan MA, Kutluay T. 1996 Lipoprotein(a) concentration in subclinical hypothyroidism before and after levo-thyroxine therapy. *Endocr J*. 43:731–736.
10. Danese MD, Powe N, Sawin CT, Ladenson FW. 1996 Screening for mild thyroid failure at the periodic health examination: a decision and cost-effectiveness analysis. *JAMA*. 276:285–292.
11. Mandel SJ, Brent GA, Larsen PR. 1993 Levothyroxine therapy in patients with thyroid disease. *Ann Intern Med*. 119:492–502.
12. Toft AD. 1994 Thyroxine therapy. *New Engl J Med*. 331:174–180.
13. Fazio S, Cittadini A, Sabatini D, et al. 1993 Evidence of biventricular involvement in acromegaly: a Doppler echocardiographic study. *Eur Heart J*. 14:26–33.
14. Fazio S, Biondi B, Carella C, et al. 1995 Diastolic dysfunction in patients on thyroid-stimulating hormone suppressive therapy with levothyroxine: beneficial effect of  $\beta$ -blockade. *J Clin Endocrinol Metab*. 80:2222–2226.
15. Biondi B, Fazio S, Carella C, et al. 1993 Cardiac effects of long-term thyrotropin-suppressive therapy with levothyroxine. *J Clin Endocrinol Metab*. 77:334–338.
16. Teichholz LE, Kreulen T, Herman MV, Gorlin R. 1976 Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence or absence of asynergy. *Am J Cardiol*. 37:7–11.
17. Grossman W. 1986 Cardiac catheterization and angiography. 3rd ed. Philadelphia: Lea & Febiger; 137.
18. Bennett ED, Barclay SA, Davis AJ, Mannering D, Mehta N. 1984 Ascending aorta blood velocity and acceleration using Doppler ultrasound in the assessment of left ventricle function. *Cardiovasc Res*. 18:632–638.
19. Ridgway EC, Cooper DS, Walker H, Rodbard D, Maloof F. 1981 Peripheral responses to thyroid hormone before and after L-thyroxine therapy in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab*. 53:1238–1242.
20. Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC. 1984 L-thyroxine therapy in subclinical hypothyroidism. A double-blind placebo-controlled trial. *Ann Intern Med*. 101:18–24.
21. Nystrom E, Caidahl K, Fager G, Wikkelso C, Lundberg PA, Lindstedt G. 1988 A double-blind cross-over 12-month study of L-thyroxine treatment of women with subclinical hypothyroidism. *Clin Endocrinol (Oxf)*. 29:63–76.
22. Staub JJ, Althaus BU, Engler H, et al. 1992 Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin and thyroid reserve and metabolic impact on peripheral target tissues. *Am J Med*. 92:631–642.
23. Bough EW, Crowley WF, Ridgway EC, et al. 1987 Myocardial function in hypothyroidism: relation to disease severity and response to treatment. *Arch Intern Med*. 138:1476–1480.
24. Ooi TC, Whitlock RML, Frengley PA, Ibbertson HK. 1980 Systolic time intervals and ankle reflex time in patients with minimal serum TSH elevation: response to triiodothyronine therapy. *Clin Endocrinol (Oxf)*. 13:621–627.
25. Tseng KH, Wallfish PC, Persand JA, Gilbert BW. 1989 Concurrent aortic and mitral valve echocardiography permits measurement of systolic time intervals as an index of peripheral tissue thyroid function status. *J Clin Endocrinol Metab*. 69:633–638.
26. Arem K, Rokey R, Kiefe C, Escalante DA, Rodriguez A. 1996 Cardiac systolic and diastolic function at rest and exercise in subclinical hypothyroidism: effect of thyroid hormone therapy. *Thyroid*. 6:397–402.
27. Bell GM, Todd WTA, Forfar JC, et al. 1985 End-organ responses to thyroxine therapy in subclinical hypothyroidism. *Clin Endocrinol (Oxf)*. 22:83–89.
28. Forfar JC, Wathen CG, Todd WT, et al. 1985 Left ventricular performance in subclinical hypothyroidism. *Am J Med*. 57:857–865.
29. Foldes J, Istvanffy M, Halmagyi H, Varadi A, Gara A, Partos O. 1987 Hypothyroidism and the heart. Examination of left ventricular function in subclinical hypothyroidism. *Acta Med Hung*. 44:337–347.
30. Perk M, O'Neill BJ. 1997 The effect of thyroid hormone therapy on angiographic coronary artery disease progression. *Can J Cardiol*. 13:273–276.
31. Grossman W. 1991 Diastolic dysfunction in congestive heart failure. *N Engl J Med*. 325:1557–1564.
32. Mina G, Pizzarello R, Klein I. 1991 Enhanced left ventricular diastolic function in hyperthyroidism: noninvasive assessment and response to treatment. *J Clin Endocrinol Metab*. 73:146–150.
33. Rohrer D, Dillmann WH. 1988 Thyroid hormone markedly increases the mRNA coding for sarcoplasmic reticulum Ca<sup>2+</sup>-ATPase in rat heart. *J Biol Chem*. 263:6941–6944.
34. Ojamaa K, Balkman C, Klein I. 1993 Acute effects of triiodothyronine on arterial smooth muscle cells. *Ann Thorac Surg*. 56:561–567.

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## Interventions for clinical and subclinical hypothyroidism in pregnancy.

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### Abstract

**BACKGROUND:** Over the last decade there has been enhanced awareness of the appreciable morbidity of thyroid dysfunction, particularly thyroid deficiency. Since treating clinical and subclinical hypothyroidism may reduce adverse obstetric outcomes, it is crucial to identify which interventions are safe and effective.

**OBJECTIVES:** To identify interventions used in the management of hypothyroidism and subclinical hypothyroidism in pregnancy and to ascertain the impact of these interventions on important maternal, fetal, neonatal and childhood outcomes.

**SEARCH STRATEGY:** We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (November 2009).

**SELECTION CRITERIA:** Randomised controlled trials (RCTs) that compared a pharmacological intervention for hypothyroidism and subclinical hypothyroidism in pregnancy with another intervention or placebo.

**DATA COLLECTION AND ANALYSIS:** Two review authors assessed trial eligibility and quality and extracted the data.

**MAIN RESULTS:** We included three RCTs of moderate risk of bias involving 314 women. In one trial of 115 women, levothyroxine therapy to treat pregnant euthyroid women with thyroid peroxidase antibodies was not shown to reduce pre-eclampsia significantly (risk ratio (RR) 0.61; 95% confidence interval (CI) 0.11 to 3.48) but did significantly reduce preterm birth by 72% (RR 0.28; 95% CI 0.10 to 0.80). One trial of 30 hypothyroid women compared levothyroxine doses, but only reported biochemical outcomes. A trial of 169 women compared the trace element selenomethionine (selenium) with placebo and no significant differences were seen for either pre-eclampsia (RR 1.44; 95% CI 0.25 to 8.38) or preterm birth (RR 0.96; 95% CI 0.20 to 4.61). None of the three trials reported on childhood neurodevelopmental delay. There was a non-significant trend towards fewer miscarriages with levothyroxine, and selenium showed some favourable impact on postpartum thyroid function and decreased incidence of moderate to advanced postpartum thyroiditis.

**AUTHORS' CONCLUSIONS:** Levothyroxine treatment of clinical hypothyroidism in pregnancy is already standard practice given the documented benefits from earlier non-randomised studies. Whether levothyroxine should be utilised in autoimmune and subclinical hypothyroidism remains to be seen, but it may prove worthwhile, given a possible reduction in preterm birth and miscarriage. Selenomethionine as an intervention in women with thyroid autoantibodies is promising, particularly in reducing postpartum thyroiditis. There is a probable low incidence of adverse outcomes from levothyroxine and selenomethionine. High-quality evidence is lacking and large-scale randomised trials are urgently needed in this area. Until evidence for or against universal screening becomes available, targeted thyroid function testing in pregnancy should be implemented in women at risk of thyroid disease and levothyroxine utilised in hypothyroid women.

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## TSH-Controlled L-Thyroxine Therapy Reduces Cholesterol Levels and Clinical Symptoms in Subclinical Hypothyroidism: A Double Blind, Placebo-Controlled Trial (Basel Thyroid Study)

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This study evaluated the effect of physiological, TSH-guided, L-thyroxine treatment on serum lipids and clinical symptoms in patients with subclinical hypothyroidism. Sixty-six women with proven subclinical hypothyroidism (TSH,  $11.7 \pm 0.8$  mIU/liter) were randomly assigned to receive L-thyroxine or placebo for 48 wk. Individual L-thyroxine replacement (mean dose,  $85.5 \pm 4.3$   $\mu$ g/d) was performed based on blinded TSH monitoring, resulting in euthyroid TSH levels ( $3.1 \pm 0.3$  mIU/liter). Lipid concentrations and clinical scores were measured before and after treatment. Sixty-three of 66 patients completed the study. In the L-thyroxine group ( $n = 31$ ) total cholesterol and low density lipoprotein cholesterol were significantly reduced [ $-0.24$  mmol/liter, 3.8% ( $P = 0.015$ ) and  $-0.33$  mmol/liter, 8.2% ( $P = 0.004$ ), respectively]. Low density lipoprotein cholesterol decrease was more pronounced in patients with TSH levels greater than 12 mIU/liter or elevated

low density lipoprotein cholesterol levels at baseline. A significant decrease in apolipoprotein B-100 concentrations was observed ( $P = 0.037$ ), whereas high density lipoprotein cholesterol, triglycerides, apolipoprotein AI, and lipoprotein(a) levels remained unchanged. Two clinical scores assessing symptoms and signs of hypothyroidism (Billewicz and Zulewski scores) improved significantly ( $P = 0.02$ ).

This is the first double blind study to show that physiological L-thyroxine replacement in patients with subclinical hypothyroidism has a beneficial effect on low density lipoprotein cholesterol levels and clinical symptoms of hypothyroidism. An important risk reduction of cardiovascular mortality of 9–31% can be estimated from the observed improvement in low density lipoprotein cholesterol. (*J Clin Endocrinol Metab* 85: 4860–4866, 2001)

SUBCLINICAL HYPOTHYROIDISM (SCH) has been detected with increasing frequency in recent years and is causing major controversies concerning management and treatment. This syndrome is characterized by the finding of elevated TSH levels in the presence of normal circulating thyroid hormones,  $T_4$  and  $T_3$  (1–3). In a classical epidemiological study the prevalence of SCH was 7.5% in women and 2.8% in men (4). The highest prevalence (up to 16%) was found in elderly women over 60 yr of age (5). It is to be expected that an increasing number of patients with SCH will be detected by the widespread use of TSH measurements, as TSH screening has been shown to be cost-effective (6).

Patients with SCH may present with variable clinical manifestations, showing signs and symptoms of hypothyroidism. SCH has been linked with abnormalities of lipid metabolism [increased serum total cholesterol and low density lipoprotein cholesterol (LDL-C)] (3) associated with increased risk for coronary heart disease, and depression (7, 8). In addition, several target tissues were shown to be affected [e.g. ankle reflex time (9, 10), systolic time intervals (11–16), and PRL levels (10, 13)].

Short-term intervention trials showed a lipid-lowering effect of L-thyroxine in patients with SCH (17–23), which, how-

ever, could not be confirmed in placebo-controlled, double blind studies in rather small groups of patients (13, 14, 24). To evaluate the therapeutic effect of physiological L-thyroxine doses, we initiated a prospective, double blind, placebo- and TSH-controlled study in a larger group of patients with SCH. The aim was to investigate the clinical and lipid-lowering effects of physiological L-thyroxine replacement in patients with confirmed subclinical hypothyroidism.

### Materials and Methods

#### Study population

Between September 1993 and May 1997, 66 women with SCH were enrolled in this prospective study. All patients were examined and followed-up in the Thyroid Research Unit of the Division of Endocrinology, Department of Medicine, University Hospital Basel (Basel, Switzerland). The inclusion criteria were as follows: 18–75 yr old, TSH level more than 5.0 mIU/liter on 2 consecutive blood tests, exaggerated TSH response of more than 35 mIU/liter after oral TRH stimulation, free  $T_4$  concentration within the normal range, and good general health as assessed by a full medical and endocrine work-up. The exclusion criteria were as follows: coronary heart disease, pituitary/hypothalamic disorders, or other nonthyroidal illnesses; thyroid hormone medication up to 3 months before enrollment; lipid-lowering agents within 6 months before enrollment; and obvious or suspected poor compliance. Forty-nine of 66 patients had a postmenopausal hormone status, with identical ratios between the treatment groups (L-thyroxine, 25/33; placebo, 24/33). In patients receiving E replacement therapy (9 in each group) the dose remained unchanged over the entire study period.

Abbreviations: HDL-C, High density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol. SCH, subclinical hypothyroidism.



The underlying thyroid disorders leading to SCH were autoimmune thyroiditis ( $n = 33$ ), Graves' disease ( $n = 22$ ; treated with radioiodine, surgery, or carbimazole), toxic multinodular goiter ( $n = 1$ ; treated with radioiodine), surgically resected goiter ( $n = 6$ ), and idiopathic SCH ( $n = 4$ ). The median time after radioactive iodine therapy before entry into the study was 11.0 yr (range, 1–42 yr). The frequencies of underlying thyroid disorders were equally distributed in the L-thyroxine and placebo groups.

A total of 63 women (mean age,  $58.5 \pm 1.3$  yr) completed the study according to the study protocol, with no serious adverse events reported. The study was terminated early in 2 participants due to previously unknown serious medical comorbidities [endometrial cancer (L-thyroxine group), malignant astrocytoma (placebo group)] and to rapid progression to clinically overt hypothyroidism in 1 L-thyroxine-treated patient. Patients were followed-up until May 1998.

#### Design and organization of the study

We used a prospective, double blind, placebo-controlled trial design. Eligible patients were sequentially assigned to either the L-thyroxine treatment group ( $n = 33$ ) or the placebo group ( $n = 33$ ) according to a predefined randomization list. The study duration for each patient was 50 wk, including a 2-wk run-in phase before starting treatment. During the first 24 wk, the L-thyroxine dose was adapted continuously every 6 wk to achieve optimal physiological hormone replacement with euthyroid TSH levels (i.e. basal TSH concentration within the reference range (0.1–4.0 mIU/liter)). L-thyroxine (Hering Berlin GmbH & Co., Berlin, Germany) was given in the fasting state in tablets of 25, 50, 75, 100, or 125  $\mu$ g active ingredient. The placebo tablets were prepared and packed in an identical manner as the L-thyroxine tablets. The dosage was controlled every 6 wk to ascertain an optimal replacement regimen (mean L-thyroxine dose at the end of the study,  $85.5 \pm 4.3$   $\mu$ g daily; range, 50–125  $\mu$ g; Fig. 1). To guarantee blinding, patients in the placebo group received tablets with dose adjustments in concordance to their randomly assigned patients in the treatment group. Hormone measurements were transmitted to an endocrinologist outside the hospital, who communicated the necessary dose adjustments to the hospital pharmacist, who then mailed the medication of L-thyroxine or placebo to the patients. Compliance to Good Clinical Practice guidelines was assured by exter-

nal study monitoring. The study was approved by the local ethics committee for human studies. All patients gave their written informed consent to participate in the trial.

#### Hormone measurements and tests of peripheral hormone action

Hormone measurements as well as serum lipid measurements were assessed at the baseline visit and at the end of the study after 48 wk. Serum samples were collected in the fasting state, immediately put on ice, and processed within 30 min. Thereafter, they were kept frozen at  $-70^\circ\text{C}$ . To minimize nonspecific variability, all parameters were evaluated twice in a period of 2 wk (before and after treatment); for statistical analysis the results of both measurements were averaged. All laboratory analyses, including biochemical, hematological, and lipid profiles, were conducted at the Department of Central Laboratories at the University Hospital Basel. Lipoprotein(a) levels were measured at the Institute of Clinical Chemistry, State Hospital (St. Gallen, Switzerland). Total cholesterol (reference range, 3.0–5.2 mmol/liter), high density lipoprotein cholesterol (HDL-C; 0.9–2.2 mmol/liter), and triglycerides (0.5–2.3 mmol/liter) were assayed enzymatically by automated procedures (Roche). LDL-C levels (1.6–3.4 mmol/liter) were calculated using the formula of Friedewald. Apolipoprotein AI (0.95–2.0 g/liter) and apolipoprotein B-100 (0.65–1.35 g/liter) were measured using immunonephelometry (Beckman Instruments, Inc./Hybritech, Palo Alto, CA). All lipid concentrations were measured in the fasting state, and no dietary instructions were given. The serum TSH concentration (reference range, 0.1–4.0 mIU/liter) was measured by immunometric assay (Delfia, Wallac, Inc., Turku, Finland). Free  $T_4$  (8.0–23.0 pmol/liter) and total  $T_4$  (1.2–3.1 nmol/liter) were determined by microparticle enzyme immunoassays (IMx, Abbott Laboratories, Inc., Chicago, IL). The degree of clinical hypothyroidism was estimated using the score developed by Billewicz (25) (euthyroidism is indicated by a score of  $\leq -30$  points, borderline hypothyroidism by  $-29$  to  $+24$  points, and clinical hypothyroidism by  $\geq 25$  points) and using the score developed by Zulewski et al. (25) (euthyroidism is indicated by a score of 0–1 point, borderline hypothyroidism by 2–5 points, and clinical hypothyroidism by  $>5$  points, including an age-correcting factor), as previously described (25).

#### Statistical analyses

All data are expressed as the mean  $\pm$  SEM. Unpaired  $t$  test (two-sided) or Mann-Whitney  $U$  test in the case of nonparametric distributions was used to identify demographic variables showing differences among the groups. Differences of frequencies were tested with the  $\chi^2$  test or Fisher's exact test, as appropriate. In the case of significant interaction between treatment and intrasubject effect, treatment effects were compared for each treatment group by paired  $t$  test (two-sided) for normally distributed data and Wilcoxon signed rank test for nonparametric distributions. Levels that were undetectable were assigned a value equal to the lower limit of detection for the assay. All analyses were performed by intention to treat unless otherwise specified. Significance was defined as  $P \leq 0.05$ . Data were analyzed using SPSS for Windows (version 10.0, SPSS, Inc., Chicago, IL).

#### Results

##### Baseline characteristics

Between September 1993 and May 1998, 63 women (mean age,  $58.5 \pm 1.3$  yr) completed the study as foreseen by the study protocol. At baseline the 2 groups of women with SCH (L-thyroxine,  $n = 31$ ; placebo,  $n = 32$ ) were similar with respect to age, body mass index, smoking habits, and E status. The patient groups were also well balanced regarding thyroid hormone concentrations, serum lipid levels, and clinical scores of hypothyroidism. In both groups basal TSH levels were mildly to markedly elevated (range, 5.0–50 mIU/liter) with an exaggerated TSH response of more than 35 mIU/liter after orally administered TRH. Peripheral thyroid

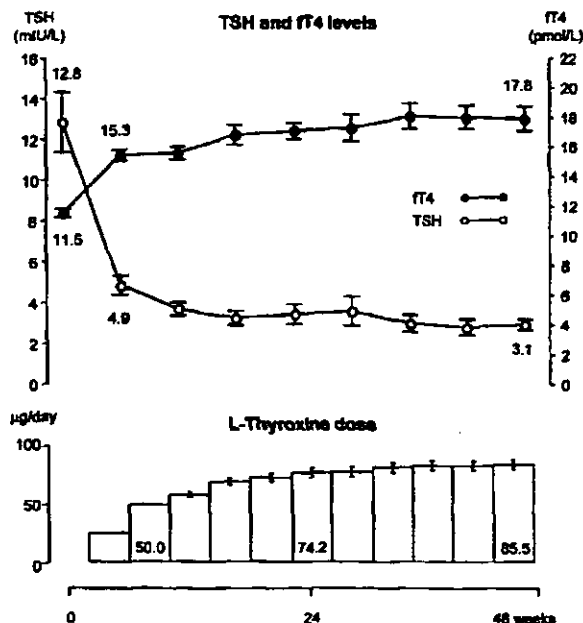


FIG. 1. Change in thyroid hormone levels and L-thyroxine dose during replacement treatment ( $n = 31$ ).

hormone concentrations (fT<sub>4</sub> and T<sub>3</sub>) were within the lower reference range (Table 1).

#### Effect of treatment on thyroid hormone concentrations

The L-thyroxine dose in the treatment group (mean dose, 85.5 ± 4.3 µg daily) was adapted at 6-wk intervals to decrease the TSH concentration to the euthyroid reference range. In all

L-thyroxine-treated patients, TSH concentrations were in the reference range at least for the last 24 wk. The mean serum TSH level at the end of the study was 3.1 ± 0.3 mIU/liter (Fig. 1 and Table 2). No patient had a blunted or absent TSH response to TRH. Peripheral thyroid hormone concentrations (free T<sub>4</sub> and T<sub>3</sub>) increased significantly within the reference range. As expected, no change in any variable of thyroid function occurred in the placebo group (Table 2).

TABLE 1. Baseline characteristics of the patients at enrollment (n = 66)

Characteristics	L-thyroxine group (n = 33)	Placebo group (n = 33)
Age (yr)	57.1 ± 1.8	57.1 ± 1.9
Body mass index (kg/m <sup>2</sup> )	25.6 ± 0.7	26.4 ± 0.7
Smokers (%) <sup>a</sup>	5 (15.1%)	2 (6.1%)
Pre/postmenopausal <sup>a</sup>	8/25	9/24
TSH basal (mIU/liter)	14.4 ± 1.7	11.3 ± 1.0
Free T <sub>4</sub> (pmol/liter)	11.9 ± 0.3	12.2 ± 0.3
Total T <sub>4</sub> (nmol/liter)	2.0 ± 0.1	1.9 ± 0.1
Total cholesterol (mmol/liter)	6.3 ± 0.2	6.0 ± 0.2
LDL-C (mmol/liter)	4.1 ± 0.2	3.7 ± 0.2
HDL-C (mmol/liter)	1.7 ± 0.1	1.5 ± 0.1
Triglycerides (mmol/liter) <sup>b</sup>	1.3 ± 0.1	1.5 ± 0.2
Apolipoprotein AI (g/liter)	1.8 ± 0.1	1.7 ± 0.0
Apolipoprotein B-100 (g/liter)	1.3 ± 0.1	1.2 ± 0.1
Lipoprotein(a) (mg/liter) <sup>b</sup>	247.8 ± 39.9	211.8 ± 42.7
Billewicz score (points) <sup>b</sup>	-25.3 ± 2.7	-27.9 ± 2.4
Zulewski score (points) <sup>b</sup>	2.2 ± 0.3	1.9 ± 0.2

Characteristics at baseline were not significantly different in both treatment groups [analysis was done by intention to treat: significance was determined by unpaired *t* test (two-sided) or by <sup>a</sup> Mann-Whitney *U* test in nonparametric distribution, and <sup>b</sup>  $\chi^2$  test or Fisher's exact test, as appropriate]. Data are mean ± SEM.

#### Effect of treatment on serum lipid concentrations

In all women serum lipid concentrations were measured before and at the end of the study. Significant changes in lipid concentrations could be seen in L-thyroxine-treated patients only, whereas placebo-treated patients showed no significant change during the study period (Table 2). After 48 wk of L-thyroxine treatment total cholesterol levels decreased significantly by -0.24 ± 0.09 mmol/liter (3.8%; *P* = 0.015), whereas LDL-C levels decreased by -0.33 ± 0.11 mmol/liter (8.2%; *P* = 0.004; Fig. 2). Apolipoprotein B-100 levels were significantly reduced (*P* = 0.037). The apolipoprotein B-100/LDL-C ratio did not change after 48 wk of L-thyroxine replacement. In addition, HDL-C levels, triglycerides, and apolipoprotein AI levels as well as lipoprotein(a) concentrations remained unchanged. A comparison of the mean treatment effects between the two treatment groups (L-thyroxine, n = 31; placebo, n = 32) did not reach the level of significance [total cholesterol, *P* = 0.23; LDL-C, *P* = 0.11; HDL-C, *P* = 0.16; triglycerides, *P* = 0.97; apolipoprotein AI, *P* = 0.16; apolipoprotein B-100, *P* = 0.71; lipoprotein(a), *P* = 0.83].

In the subgroup of patients with high TSH concentrations

TABLE 2. Parameters before and after 48 wk of treatment with L-thyroxine or placebo

Parameters	Before treatment	After 48 wk	95% CI (of 3 means)	<i>P</i>
<b>Treatment with L-thyroxine (n = 31)</b>				
TSH (mIU/liter)	12.8 ± 1.4	3.1 ± 0.3	-12.7 to -6.6	<0.001
fT <sub>4</sub> (pmol/liter)	11.6 ± 0.3	17.8 ± 0.8	4.7 to 7.8	<0.001
T <sub>3</sub> (nmol/liter)	2.0 ± 0.1	1.7 ± 0.1	-0.4 to -0.1	<0.001
Total cholesterol (mmol/liter)	6.3 ± 0.2	6.1 ± 0.2	-0.4 to 0.0	0.015
LDL-C (mmol/liter)	4.0 ± 0.2	3.7 ± 0.2	-0.5 to -0.1	0.004
HDL-C (mmol/liter)	1.7 ± 0.1	1.7 ± 0.1	-0.1 to 0.0	0.476
TC/HDL-C ratio	3.8 ± 0.1	3.7 ± 0.1	-0.3 to 0.0	0.131
Triglycerides (mmol/liter) <sup>a</sup>	1.3 ± 0.1	1.3 ± 0.1	-0.2 to 0.1	0.769
Apolipoprotein AI (g/liter)	1.82 ± 0.05	1.76 ± 0.05	-0.1 to 0.0	0.103
Apolipoprotein B-100 (g/liter)	1.25 ± 0.05	1.15 ± 0.05	-0.2 to 0.0	0.037
Lipoprotein(a) (mg/liter) <sup>a</sup>	251.5 ± 41.7	236.5 ± 36.5	-38.8 to 9.0	0.202
Billewicz score (points) <sup>a</sup>	-25.7 ± 2.7	-32.1 ± 2.1	-11.6 to -1.1	0.022
Zulewski score (points) <sup>a</sup>	2.1 ± 0.3	1.5 ± 0.2	-1.1 to -0.1	0.024
<b>Treatment with placebo (n = 32)</b>				
TSH (mIU/liter)	10.7 ± 0.9	9.9 ± 0.6	-1.9 to 0.2	0.108
fT <sub>4</sub> (pmol/liter)	12.0 ± 0.3	12.3 ± 0.4	-0.3 to 0.9	0.316
T <sub>3</sub> (nmol/liter)	1.9 ± 0.1	1.9 ± 0.1	-0.1 to 0.2	0.784
Total cholesterol (mmol/liter)	6.1 ± 0.2	6.0 ± 0.2	-0.3 to 0.1	0.393
LDL-C (mmol/liter)	3.8 ± 0.2	3.7 ± 0.2	-0.3 to 0.2	0.509
HDL-C (mmol/liter)	1.6 ± 0.1	1.6 ± 0.1	0.3 to 0.1	0.210
TC/HDL-C ratio	4.1 ± 0.2	4.0 ± 0.2	-0.2 to 0.1	0.404
Triglycerides (mmol/liter) <sup>a</sup>	1.5 ± 0.2	1.5 ± 0.2	-0.2 to 0.1	0.507
Apolipoprotein AI (g/liter)	1.71 ± 0.05	1.73 ± 0.05	-0.1 to 0.1	0.612
Apolipoprotein B-100 (g/liter)	1.22 ± 0.07	1.17 ± 0.06	-0.1 to 0.0	0.256
Lipoprotein(a) (mg/liter) <sup>a</sup>	217.7 ± 43.6	208.7 ± 44.8	-38.7 to 16.7	0.264
Billewicz score (points) <sup>a</sup>	-28.3 ± 2.5	-30.8 ± 2.5	-8.0 to 3.0	0.382
Zulewski score (points) <sup>a</sup>	2.0 ± 0.2	1.6 ± 0.2	-0.8 to 0.0	0.074

Data are mean ± SEM. Analysis was done per protocol; significance was determined by paired *t* test (two-sided) or by <sup>a</sup> Wilcoxon signed rank test in nonparametric distribution: values at 48 wk compared with baseline.

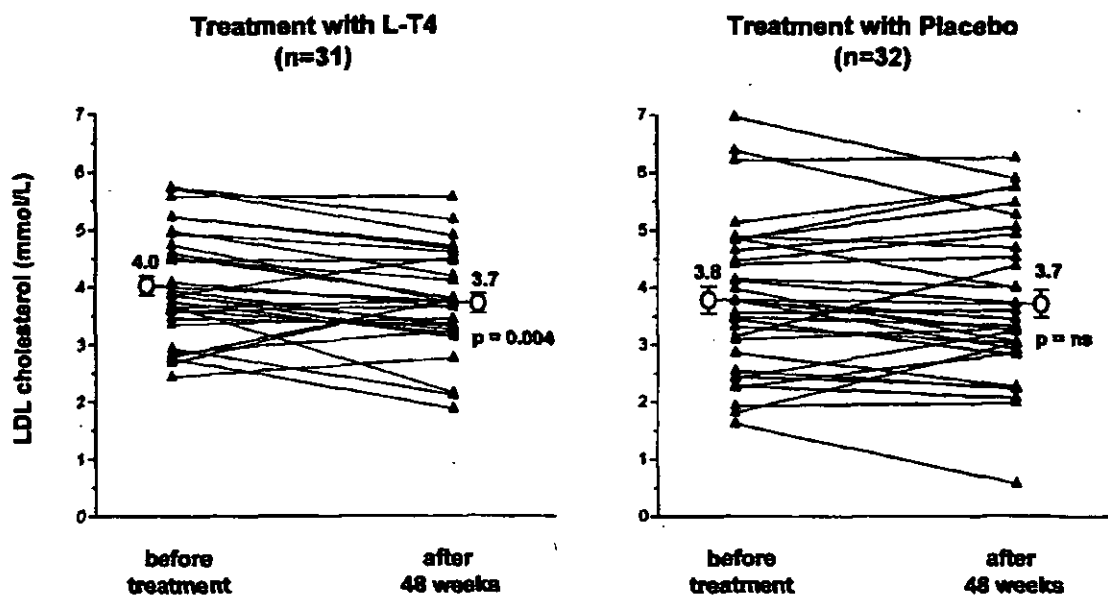


FIG. 2. Individual decrease in serum LDL-C in L-thyroxine ( $n = 31$ ) and placebo ( $n = 32$ ) groups.

(TSH  $>12$  mIU/liter;  $n = 13$ ), L-thyroxine treatment was associated with a decrease in total cholesterol levels by  $-0.29 \pm 0.14$  mmol/liter (4.4%;  $P = 0.06$ ) and a decrease in LDL-C levels by  $-0.37 \pm 0.15$  mmol/liter (8.5%;  $P = 0.03$ ). In patients with lower TSH values (TSH  $\leq 12$  mIU/liter;  $n = 18$ ), slightly lesser improvements in lipid concentrations could be observed [ $-0.20 \pm 0.12$  mmol/liter (3.3%) for total cholesterol and  $-0.31 \pm 0.15$  mmol/liter (8.2%) for LDL-C, respectively; Fig. 3]. The lipid-lowering effect of L-thyroxine was greater in the subset of patients with elevated pretreatment total cholesterol values ( $\geq 6.2$  mmol/liter;  $n = 17$ ) with a mean total cholesterol decrease of  $-0.34 \pm 0.12$  (4.9%;  $P = 0.01$ ). Similarly, a significant treatment effect was observed in patients with elevated pretreatment LDL-C levels ( $\geq 4.0$  mmol/liter;  $n = 13$ ), with a mean LDL-C decrease of  $-0.55 \pm 0.09$  mmol/liter (11.2%;  $P < 0.0001$ ), and for those with elevated pretreatment apolipoprotein B-100 levels ( $>1.35$  g/liter;  $n = 9$ ), with a mean apolipoprotein B-100 decrease of  $-0.22 \pm 0.08$  (13.8%;  $P = 0.02$ ; Table 3).

#### Effect of treatment on clinical scores of hypothyroidism

For clinical assessment, clinical scores of hypothyroidism were determined using two different questionnaires (Billewicz and Zulewski scores) at the baseline visit and at the end of the study. Significant improvement of both questionnaires, assessing clinical signs and symptoms, was found in L-thyroxine-treated patients, in contrast to placebo-treated women ( $P = 0.02$ ; Table 2). A comparison of the mean treatment effects between the two treatment groups (L-thyroxine,  $n = 31$ ; placebo,  $n = 32$ ) did not reach the level of significance (Billewicz score,  $P = 0.31$ ; Zulewski score,  $P = 0.53$ ). Analyzing subsets of patients, an improvement in symptom score was noted only in those T<sub>4</sub>-treated patients with pretreatment TSH levels greater than 12 mIU/liter ( $n = 13$ ; e.g.

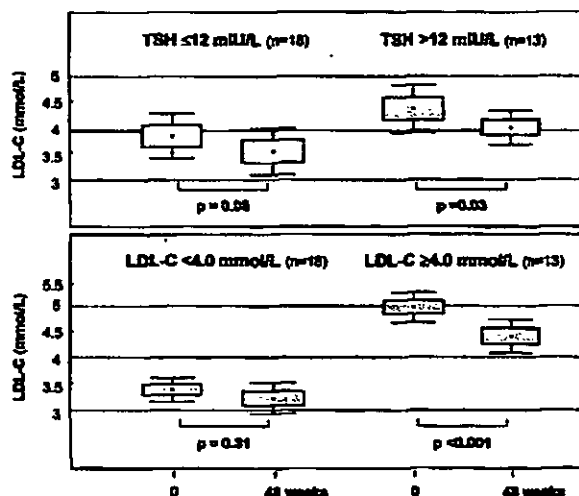


FIG. 3. Effect of L-thyroxine treatment on serum LDL-C in subsets of patients in relation to TSH and LDL-C levels at baseline (points, mean; boxes,  $\pm 1.00$  SE; bars,  $\pm 1.96$  SE).

Billewicz score: at baseline,  $-24.2 \pm 4.6$  points; after L-thyroxine,  $-34.3 \pm 3.4$ ;  $P = 0.049$ ). In contrast, in patients with lower TSH values ( $\leq 12$  mIU/liter;  $n = 18$ ), changes in symptom questionnaires were not significant (e.g. Billewicz score,  $P = 0.21$ ).

#### Discussion

Primary hypothyroidism is a graded phenomenon with different levels of severity, showing a wide interindividual range of clinical and biochemical presentation. The earliest

TABLE 3. Treatment effects in subsets of patients in relation to lipid values at baseline

Parameters		Treatment	n	Before treatment	After 48 wk	P
Total cholesterol	≥6.2 mmol/liter	L-thyroxine	17	7.0 ± 0.1	6.7 ± 0.1	0.01
		Placebo	17	7.0 ± 0.2	6.8 ± 0.2	0.22
	<6.2 mmol/liter	L-thyroxine	14	5.5 ± 0.1	5.4 ± 0.2	0.44
		Placebo	15	5.0 ± 0.2	5.1 ± 0.2	0.66
LDL-C	≥4.0 mmol/liter	L-thyroxine	13	5.0 ± 0.1	4.4 ± 0.2	<0.0001
		Placebo	13	5.1 ± 0.2	5.0 ± 0.2	0.92
	<4.0 mmol/liter	L-thyroxine	18	3.4 ± 0.1	3.2 ± 0.2	0.31
		Placebo	19	2.9 ± 0.2	2.8 ± 0.2	0.53
Apolipoprotein B-100	>1.35 g/liter	L-thyroxine	9	1.6 ± 0.1	1.4 ± 0.1	0.02
		Placebo	10	1.6 ± 0.1	1.5 ± 0.1	0.07
	≤1.35 g/liter	L-thyroxine	22	1.1 ± 0.0	1.1 ± 0.1	0.43
		Placebo	22	1.1 ± 0.0	1.0 ± 0.1	0.41

Data are given as mean ± SEM. Analysis was done per protocol; significance was determined by *t* tests (two-sided) or by Wilcoxon signed rank test in nonparametric distribution.

form of hypothyroidism, called SCH or mild thyroid failure, is defined by an increased serum TSH level in the presence of normal concentrations of circulating thyroid hormones (26). Although the original definition is based solely on biochemical criteria, it is well recognized that some individual patients may present with symptoms and signs of hypothyroidism (10, 13, 14, 25).

The Whickham study, an extensive population-based survey, showed a prevalence of mild thyroid failure of 7.5% in women and 2.8% in men (4). Based on these data, it can be estimated that at least 20 million people in the European Union and over 14 million in the United States are affected by this syndrome. The number of patients diagnosed is increasing due to the widespread use of TSH measurements (6, 27, 28).

However, the need for treatment of SCH is still a matter of debate. The aim of our study was to investigate the clinical and metabolic effects of L-thyroxine replacement in patients with SCH. Therefore, we used a double blind and placebo-controlled study design. Throughout the study continuous TSH monitoring and adaptation of the L-thyroxine dose were performed to guarantee physiological thyroid hormone replacement. To the best of our knowledge this is the only study that combines a double blind design with randomization by matched pairs (either L-thyroxine or placebo group) and TSH-guided dose adaptations throughout the entire trial period.

In the thyroxine treatment group, the mean serum TSH concentration was 12.8 ± 1.4 mIU/liter before and 3.1 ± 0.3 mIU/liter after treatment, whereas TSH levels remained unchanged in the control group. As expected, free T<sub>4</sub> levels increased within the reference range in parallel to the L-thyroxine dose adjustment. Dose adaptations were necessary in most patients for the first 24 wk of treatment before reaching a steady state condition (L-thyroxine dose after 48 wk, 85.5 ± 4.3 µg daily; range, 50–125 µg). SCH and confounding supraphysiological therapeutic effects were excluded in all patients, in contrast to other studies in which overtreatment could be assumed at least in some subjects (14, 19, 29).

In SCH, major discrepancies concerning the effect on lipoprotein concentrations have been described in the literature. Several researchers found serum lipid concentrations, mainly total cholesterol levels, within the normal range. Others detected elevated total cholesterol or LDL-C concentra-

tions, especially in smokers (3, 10, 30–32). In addition, increases in HDL-C and apolipoprotein AI concentrations were found (33); however, the reported changes were not consistent.

Using a double blind, placebo-controlled study design, we found significant decreases in total and LDL-C levels. This is the first randomized trial that clearly demonstrates that elevated serum lipid levels, mainly total and atherogenic LDL-C levels, are lowered by thyroid hormone replacement in patients with mild thyroid failure. L-thyroxine therapy resulted in a decrease in mean serum cholesterol by 3.8% (0.24 mmol/liter) and in LDL-C by 8.2% (0.33 mmol/liter), respectively. Two previously published randomized trials showed only minimal and nonsignificant reductions of total cholesterol levels during L-thyroxine therapy and no data for LDL-C (13, 14). A further placebo-controlled study found a LDL-C reduction of 3.6% (0.13 mmol/liter) after T<sub>4</sub> replacement, which, due to the smaller sample size, did not reach statistical significance (24). Conversely, our data are in accordance with 2 recent meta-analyses that calculated a beneficial effect of L-thyroxine on serum cholesterol concentrations (29, 34). In a quantitative review of 13 intervention trials Danese and co-workers (19, 29) reported a similar reductions total cholesterol and LDL-C levels, with mean decreases of 0.20 and 0.26 mmol/liter, respectively. Thus, the results from the present double blind study are in agreement with those of several uncontrolled intervention trials in the current literature.

HDL-C, triglycerides, lipoprotein(a), as well as apolipoprotein AI levels were not changed after 48 wk of L-thyroxine supplementation, whereas apolipoprotein B-100 concentrations showed a significant decrease during thyroid hormone replacement. As the apolipoprotein B-100/LDL cholesterol ratio did not change, the LDL particle size remained unchanged. Thus, the LDL-C reduction during L-thyroxine replacement therapy did not result in a depletion of LDL-C, and thus smaller and more atherogenic LDL particles.

In the present study a slightly better improvement in LDL-C levels could be seen in patients with TSH levels more than 12 mIU/liter. When analyzed according to pretreatment LDL-C levels, serum LDL-C was reduced in all patients with cholesterol levels of 4.0 mmol/liter or more (mean reduction of 11.2%). Similarly, a significant decrease in serum values

was observed in patients with elevated total cholesterol levels (*i.e.*  $\geq 6.2$  mmol/liter) and elevated apolipoprotein B-100 levels (*i.e.*  $> 1.35$  g/liter) at baseline, but not in the subgroups with lower values. Thus, a risk-stratified therapeutic approach for patients with SCH with impending thyroid failure or elevated serum lipid levels can be advocated.

Based on published data from the Seven Countries Study (35) and the Munster Heart Study (PROCAM) (36) and adapted to LDL-C concentrations, we estimated the relative risk reduction in coronary heart disease mortality. A mean decrease in serum LDL-C of  $-0.33$  mmol/liter, as documented in all L-thyroxine-treated patients, corresponds to an important risk reduction of 17%. When we analyzed different subgroups of L-thyroxine-treated patients according to TSH and LDL-C levels at baseline, the estimated risk reduction ranged from 9–31% in relation to the observed decrease in LDL-C ( $-0.17$  to  $-0.60$  mmol/liter). The lowest estimated risk reduction was found for the group of patients with basal LDL-C levels below 4.0 mmol/liter and TSH levels of 12 mU/liter or less; the highest reduction was calculated for the subgroup with LDL-C and TSH levels above these limits.

Hence, mild thyroid failure must be considered as another risk factor contributing to the development of atherosclerosis and coronary heart disease. Several cross-sectional studies suggested an association between SCH or autoimmune thyroid disease and atherosclerosis (37). Furthermore, a recently published population-based study has given evidence that SCH itself may be an independent risk factor for atherosclerosis and myocardial infarction in elderly women (38). However, these findings were not confirmed by other investigations (39, 40). Further mechanisms are suggested to be involved in the association between mild thyroid failure and cardiovascular disease. These include a hypercoagulable state (41) and endothelial effects of thyroid hormones (42). However, controlled long-term studies evaluating cardiovascular morbidity and mortality as end points would be needed to definitively confirm our conclusions.

In addition to the change in lipid and lipoprotein levels, significant improvement of clinical signs and symptoms of hypothyroidism assessed by two separate clinical scores (Billewicz and Zulewski scores) (25) could be demonstrated. These results are in accordance with two controlled trials documenting clinical and metabolic improvements in patients with mild thyroid failure treated with thyroid hormones (13, 14).

Smokers with mild thyroid failure were shown to have markedly more pronounced metabolic signs and symptoms of peripheral tissue hypothyroidism than nonsmokers, including a worse lipid profile (30). In the present study only a low percentage of patients were smokers. Based on the finding of a significant improvement of the atherogenic lipid and lipoprotein profile in mainly nonsmokers, an even more beneficial effect of physiological L-thyroxine therapy can be anticipated in smokers with SCH.

The decision to treat patients with mild thyroid failure is based on the fact that some symptoms may be reversed by hormone supplementation and that therapy prevents progression to the overt stage of hypothyroidism (43–45). Furthermore, L-thyroxine therapy is indicated in special clinical conditions, such as goiter, thyroidectomy, depression, infer-

tility, and endocrine ophthalmopathy. Regarding our findings of a definite improvement in the plasma lipoprotein profile, we advocate replacement therapy in patients with mild thyroid failure and hypercholesterolemia, in particular in the presence of other cardiovascular risk factors, such as smoking. Overdose with unphysiological (not TSH-controlled) T<sub>4</sub> treatment can produce overt or mainly subclinical hyperthyroidism with TSH suppression. It has been shown that endogenous SCH may be associated with adverse effects, such as mild clinical signs of hyperthyroidism and impaired quality of life (46), induction of atrial fibrillation (47), acceleration of osteoporosis, or possibly dementia and Alzheimer's disease (48). Therefore, fine-tuning of T<sub>4</sub> replacement therapy with the goal of restoring the serum TSH concentration to a physiological level is mandatory.

In conclusion, we demonstrate by this double blind study that SCH has negative clinical and metabolic effects in affected patients. Physiological, TSH-guided, L-thyroxine treatment can improve LDL-C and total cholesterol levels and clinical signs and symptoms of hypothyroidism, and thereby may reduce morbidity and mortality in patients with this common syndrome.

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#### References

1. Cooper DS 1991 Subclinical hypothyroidism. London: Mosby-YearBook
2. Surks MI, Ozcampo E 1996 Subclinical thyroid disease. *Am J Med* 100:217–223
3. Ross DS 2000 Subclinical hypothyroidism. In: Braverman LE, Utiger RU, eds. *Werner and Ingbar's the thyroid*, 8th Ed. New York: Lippincott-Williams & Wilkins; 1001–1006
4. Tunbridge WM, Evered DC, Hall R, et al. 1977 The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 7:481–493
5. Sawin CT, Chopra D, Azizi F, Mannix JE, Bacharach P 1979 The aging thyroid. Increased prevalence of elevated serum thyrotropin levels in the elderly. *JAMA* 242:247–250
6. Danese MD, Powe NR, Sawin CT, Ladenson PW 1996 Screening for mild thyroid failure at the periodic health examination: a decision and cost-effectiveness analysis. *JAMA* 276:285–292
7. Haggerty Jr JJ, Stern RA, Mason CA, Beckwith J, Morey CE, Prange Jr AJ 1993 Subclinical hypothyroidism: a modifiable risk factor for depression? *Am J Psychiatry* 150:508–510
8. Monzani F, Del Guerra P, Caraccio N, et al. 1993 Subclinical hypothyroidism:

- neurobehavioral features and beneficial effect of L-thyroxine treatment. *Clin Invest* 71:367-371
9. Ooi TC, Whitlock RM, Frengley PA, Ibbertson HK 1980 Systolic time intervals and ankle reflex time in patients with minimal serum TSH elevation: response to triiodothyronine therapy. *Clin Endocrinol (Oxf)* 13:621-627
  10. Staub JJ, Althaus BU, Engler H, et al. 1992 Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on peripheral target tissues. *Am J Med* 92:631-642
  11. Burckhardt D, Staub JJ, Kraentlin M, Raeder E, Engel U, Cloppenburg P 1978 The systolic time intervals in thyroid dysfunction. *Am Heart J* 95:187-196
  12. Ridgway EC, Cooper DS, Walker H, Rodbard D, Maloof F 1981 Peripheral responses to thyroid hormone before and after L-thyroxine therapy in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab* 53:1238-1242
  13. Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC 1984 L-Thyroxine therapy in subclinical hypothyroidism. A double-blind, placebo-controlled trial. *Ann Intern Med* 101:18-24
  14. Nystrom E, Calafat K, Fager G, Wikkelso C, Lundberg PA, Lindstedt G 1988 A double-blind cross-over 12-month study of L-thyroxine treatment of women with 'subclinical' hypothyroidism. *Clin Endocrinol (Oxf)* 29:63-75
  15. Arem R, Rokky R, Kiefe C, Escalante DA, Rodriguez A 1996 Cardiac systolic and diastolic function at rest and exercise in subclinical hypothyroidism: effect of thyroid hormone therapy. *Thyroid* 6:397-402
  16. Monzani F, Di Bello V, Caraccio N, et al. 2001 Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. *J Clin Endocrinol Metab* 86:1110-1115
  17. Arem R, Patach W 1990 Lipoprotein and apolipoprotein levels in subclinical hypothyroidism. Effect of levothyroxine therapy. *Arch Intern Med* 150:2097-2100
  18. Bogner U, Arntz HR, Peters H, Schleusener H 1993 Subclinical hypothyroidism and hyperlipoproteinemia: indiscriminate L-thyroxine treatment not justified. *Acta Endocrinol (Copenh)* 128:202-206
  19. Franklyn JA, Daykin J, Betteridge J, et al. 1993 Thyroxine replacement therapy and circulating lipid concentrations. *Clin Endocrinol (Oxf)* 38:453-459
  20. Arem R, Escalante DA, Arem N, Morrisett JD, Patach W 1995 Effect of L-thyroxine therapy on lipoprotein fractions in overt and subclinical hypothyroidism, with special reference to lipoprotein(a). *Metabolism* 44:1559-1563
  21. Diekmann T, Lansberg PJ, Kastelein JJ, Wiersinga WM 1995 Prevalence and correction of hypothyroidism in a large cohort of patients referred for dyslipidemia. *Arch Intern Med* 155:1490-1495
  22. Yildirimkaya M, Ozata M, Yilmaz K, Kilinc C, Gundogan MA, Kutluy T 1996 Lipoprotein(a) concentration in subclinical hypothyroidism before and after L-thyroxine therapy. *Endocr J* 43:731-736
  23. Michalopoulos G, Alevizaki M, Piperopoulos G, et al. 1998 High serum cholesterol levels in persons with 'high-normal' TSH levels: should one extend the definition of subclinical hypothyroidism? *Eur J Endocrinol* 138:141-145
  24. Jaeschke R, Goyatt G, Gerstein H, et al. 1996 Does treatment with L-thyroxine influence health status in middle-aged and older adults with subclinical hypothyroidism? *J Gen Intern Med* 11:744-749
  25. Zulewski H, Muller B, Exer P, Miserez AR, Staub JJ 1997 Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. *J Clin Endocrinol Metab* 82:771-776
  26. Bigos ST, Ridgway EC, Kourides IA, Maloof F 1978 Spectrum of pituitary alterations with mild and severe thyroid impairment. *J Clin Endocrinol Metab* 46:317-325
  27. Helfand M, Redfern CC 1998 Clinical guideline, part 2. Screening for thyroid disease: an update. American College of Physicians. *Ann Intern Med* 129:144-158
  28. Ladenson PW, Singer PA, Ain KB, et al. 2000 American Thyroid Association guidelines for detection of thyroid dysfunction. *Arch Intern Med* 160:1573-1575
  29. Danese MD, Ladenson PW, Meinert CL, Powe NR 2000 Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. *J Clin Endocrinol Metab* 85:2993-3001
  30. Muller B, Zulewski H, Huber P, Ratcliffe JG, Staub JJ 1995 Impaired action of thyroid hormone associated with smoking in women with hypothyroidism. *N Engl J Med* 333:964-969
  31. Althaus BU, Staub JJ, Ryff-De Leche A, Oberhansli A, Stahelin HB 1988 LDL/HDL-changes in subclinical hypothyroidism: possible risk factors for coronary heart disease. *Clin Endocrinol (Oxf)* 28:157-163
  32. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC 2000 The Colorado thyroid disease prevalence study. *Arch Intern Med* 160:526-534
  33. Caron F, Calafat C, Parra HJ, Haff M, Louvet JP 1990 Decreased HDL cholesterol in subclinical hypothyroidism: the effect of L-thyroxine therapy. *Clin Endocrinol (Oxf)* 33:519-523
  34. Tanis BC, Westendorp GJ, Smelt HM 1996 Effect of thyroid substitution on hypercholesterolemia in patients with subclinical hypothyroidism: a reanalysis of intervention studies. *Clin Endocrinol (Oxf)* 44:643-649
  35. Verschuren WM, Jacobs DR, Bloemberg BP, Kromhout D, Menotti A, Aravanis C, Blackburn H, Buzina R, Dontas AS, Fidanza F, et al. 1995 Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. *JAMA* 274:131-136
  36. Schulte H, Collen P, Assmann G 1999 Obesity, mortality and cardiovascular disease in the Munster Heart Study (PROCAM). *Atherosclerosis* 144:199-209
  37. Bastenie PA, Vanhaelst L, Boonyasri M, Neve P, Staquet M 1971 Preclinical hypothyroidism: a risk factor for coronary heart-disease. *Lancet* 1:203-204
  38. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC 2000 Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Ann Intern Med* 132:270-278
  39. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, Young E, Bird T, Smith PA 1977 Lipid profiles and cardiovascular disease in the Wickham area with particular reference to thyroid failure. *Clin Endocrinol (Oxf)* 7:495-508
  40. Heinonen OP, Gordin A, Aho K, Puskar S, Pyorala K, Puro K 1972 Symptomless autoimmune thyroiditis in coronary heart-disease. *Lancet* 1:785-786
  41. Muller B, Tsakiris DA, Roth CB, Guglielmetti M, Staub JJ, Marbet CA 2001 Haemostatic profile in hypothyroidism as potential risk factor for vascular or thrombotic disease. *Eur J Clin Invest* 31:131-137
  42. Sellitti DF, Dennison D, Akamizu T, Doi SQ, Kohn LD, Koshiyama H 2000 Thyrotropin regulation of cyclic adenosine monophosphate production in human coronary artery smooth muscle cells. *Thyroid* 10:219-225
  43. Vanderpump MF, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, Grimley Evans J, Hasan DM, Rodgers H, Tunbridge F, et al. 1995 The incidence of thyroid disorders in the community: a twenty-year follow-up of the Wickham Survey. *Clin Endocrinol (Oxf)* 43:55-68
  44. Singer PA, Cooper DS, Levy EG, Ladenson PW, Braverman LE, Daniels G, Greenspan FS, McDougall IR, Nikolai TF 1995 Treatment guidelines for patients with hyperthyroidism and hypothyroidism. Standards of Care Committee. American Thyroid Association. *JAMA* 273:808-812
  45. Cooper DS 1998 Subclinical thyroid disease: a clinician's perspective. *Ann Intern Med* 129:135-138
  46. Biondi B, Palmieri EA, Fazio S, Cosco C, Nocera M, Sacca L, Filetti S, Lombardi G, Perticone F 2000 Endogenous Subclinical Hyperthyroidism Affects Quality of Life and Cardiac Morphology and Function in Young and Middle-Aged Patients. *J Clin Endocrinol Metab* 85:4701-4705
  47. Sawin CT, Geller A, Wolf PA, Belanger AJ, Baker E, Sacharich P, Wilson PW, Benjamin EJ, D'Agostino RB 1994 Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. *N Engl J Med* 331:1249-1252
  48. Kalmijn S, Mehta KM, Pols HA, Hofman A, Drexhage HA, Breteler MM 2000 Subclinical hyperthyroidism and the risk of dementia. The Rotterdam study. *Clin Endocrinol (Oxf)* 53:733-737

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## Changes in cystatin C during the treatment of subclinical hypothyroidism

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**Background:** Serum cystatin C is a novel marker for kidney function that has been claimed to be superior to serum creatinine. Cystatin C concentrations increased in the hyperthyroid patients and decreased in the hypothyroid patients. The cystatin C test detects kidney disease at earlier stages, before symptoms appear and creatinine levels rise. Another advantage is that, unlike creatinine, blood levels of cystatin C are less influenced by age, gender, race, or lean muscle mass, which makes it a better indicator of kidney function. This study was performed to evaluate changes in cystatin C and creatinine during the treatment of subclinical hypothyroidism (SH).

**Methods:** Cystatin C, creatinine, CRP and lipids were determined at the time of diagnosis of SH (TSH > 4.2 mIU/ml with normal level of fT3 and fT4), and when TSH returned into the normal range after treatment with levothyroxine in 35 SH women ages 35.3 ± 9.5 years.

**Results:** TSH was 9.4 ± 4.3 mIU/l (reference 0.3–4.2) at diagnosis and decreased to 2.9 ± 1.2 mIU/l following treatment with levothyroxine. Cystatin C increased from 0.68 ± 0.19 mg/l (reference 0.5–0.96) in the hypothyroid state to 0.89 ± 0.16 mg/l when TSH normalized ( $P < 0.01$ ). Creatinine decreased from 98 ± 11 µmol/l (reference 45–115) in the hypothyroid state to 67 ± 14 µmol/l when TSH normalized ( $P < 0.05$ ). CRP levels also decreased when TSH normalized (5.2 ± 1.1 vs 2.5 ± 0.9 mg/l). Mean total and LDL-cholesterol levels decreased too, but not significantly.

**Conclusion:** Subclinical hypothyroidism has a substantial impact on cystatin C levels. In contrast to creatinine concentrations, Cystatin C levels are lower in the hypothyroid state as compared with the euthyroid state. Therefore, thyroid function has to be considered when cystatin C is used as a marker of kidney function at many diseases like diabetes, hypertension, and cardiovascular diseases.

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ENDOCRINE CARE

## Endothelial Progenitor Cells in Subclinical Hypothyroidism: The Effect of Thyroid Hormone Replacement Therapy

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### Abstract

**Context:** Subclinical hypothyroidism (SCH) is associated with cardiovascular (CV) risk factors, and possibly CV disease. However, its management remains controversial. Endothelial progenitor cells (EPC), expressing both endothelial and stem cell markers, are known to offer a novel CV risk marker.

**Objective:** The aim of the study was to ascertain whether EPC count or function is reduced in SCH and whether it improves with  $T_4$  therapy.

**Design and Intervention:** EPC were studied in peripheral blood by fluorescence-activated cell sorter and following *in vitro* cultures before and after  $T_4$  together with CV risk factors in 20 SCH and healthy controls (HC).

**Main Outcome Measure:** EPC count was measured at baseline and after  $T_4$  replacement in SCH.

**Results:** EPC count was significantly reduced in SCH compared to HC: median (range)—CD133+VEGFR-2+, 0.09 (0.02–0.44) vs. 0.47 (0.17–2.12),  $P < 0.001$ ; CD34+VEGFR-2+, 0.10 (0.04–0.46) vs. 0.39 (0.11–2.13),  $P < 0.001$ ; whereas EPC function was similar. There was a significant positive correlation between CD133+VEGFR-2+ with free  $T_4$  levels ( $r = 0.38$ ;  $P = 0.02$ ); high-density lipoprotein cholesterol levels ( $r = 0.51$ ;  $P = 0.001$ ); and negative correlation with TSH concentrations ( $r = -0.64$ ;  $P < 0.001$ ). After adjustment for conventional CV risk factors, SCH predicted lower EPC count,  $\beta$  coefficient/ $P$  value: CD133+VEGFR-2+ ( $-0.77$ / $<0.001$ ), and CD34+VEGFR-2+ ( $-0.71$ / $<0.001$ ). In SCH participants, EPC count increased and was similar to HC after  $T_4$ : CD133+VEGFR-2+, 0.32 (0.03–0.94) vs. 0.09 (0.02–0.44),  $P < 0.001$ ; and CD34+VEGFR-2+, 0.26 (0.06–0.88) vs. 0.10 (0.04–0.46),  $P < 0.001$ .

**Conclusion:** SCH predicted lower EPC count, which improved with  $T_4$  treatment, independent of other CV risk factors, providing additional evidence that  $T_4$  replacement may improve CV risk in SCH.

Subclinical hypothyroidism (SCH) is a common disorder with a projected 3 million people affected in the United Kingdom and 15 million in the United States (1, 2). SCH has been associated with atherogenic lipid profile and endothelial dysfunction assessed by flow-mediated dilatation (FMD), which improved with thyroid hormone replacement therapy (3, 4). Few, but not all, studies have shown association of SCH and cardiovascular disease or mortality (5, 6, 7).

Lower number of circulating endothelial progenitor cells [EPC; expressing both endothelial vascular endothelial growth factor receptor (VEGFR)-2 and stem cell (CD34 and/or CD133) markers] and CD34+ cells have been associated with increased cardiovascular risk (8, 9, 10, 11, 12).

We hypothesize that SCH is associated with either an abnormal number or function of EPC. The aim of this study was to examine EPC count and function in SCH in comparison to healthy controls (HC) and to evaluate the effect of  $T_4$  replacement on these EPC parameters in these subjects.

### Subjects and Methods

#### Subjects

Twenty subjects with SCH (18 women) confirmed by TSH levels between 4.1 and 15.0 mU/Liter and normal free  $T_4$  (FT4) levels [9–25 pmol/Liter (0.7–1.9 ng/dl)] on two occasions at least 3 months apart were recruited from hospital endocrine clinic and family practices in the Gateshead (UK) area. Twenty HC (18 women; matched for age, body mass index (BMI), sex, and ethnic group) were recruited from friends, staff members, and by means of posters and local web pages (Gateshead Health National Health Service Foundation Trust and Newcastle University). Subjects with medical conditions or using drugs affecting EPC count or functions were excluded.

All subjects had anthropometric measurements [height, weight, BMI, blood pressure, FMD, fasting lipids, asymmetric dimethylarginine (ADMA)] and EPC analysis at baseline and after treatment (except controls).



SCH subjects were studied after 3 months on a stable dose of  $T_4$  therapy. The daily median  $T_4$  dose was 100  $\mu$ g. There was no addition of medications, which could affect EPC in SCH subjects.

All subjects gave their written informed consent, and the local ethics committee approved the study.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

#### Biochemical measurements

FT4 and TSH (reference range, 0.4–4.0 mU/liter) concentrations were measured by electrochemoluminescence immunoassay (Roche Diagnostics, Lewes, UK). Serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides were assayed using automated enzymatic methods (Roche Diagnostics). Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's equation. Plasma ADMA were measured by ELISA (DLD Diagnostika, Hamburg, Germany).

#### FMD of brachial artery

This was performed by high-resolution ultrasonography using the HDI 5000 system (Toshiba, Tokyo, Japan) and 12-MHz linear transducer as previously described by our group [4].

#### Flow cytometry

EPC in peripheral venous blood (100  $\mu$ l) were quantified by flow cytometry (LSRII; Becton Dickinson, San Jose, CA) after incubation in the dark with the following antibodies for 30 min: PE-Cy7 anti-CD14 (BD Pharmingen, San Jose, CA); Per CP-Cy5.5 anti-CD 34 (BD Pharmingen); APC anti-CD 133 (Miltenyi Biotec, Bergsch Gladbach, Germany); and PE-anti-VEGFR-2 (KDR) (R&D Systems, Minneapolis, MN). Isotype matching mouse anti-IgG was used as a control in Trucount tubes with beads. Cells were identified using BD FACSDiva software (Becton Dickinson, San Jose, CA) according to their forward and side scatter profile in the lymphocyte gate after acquiring at least 100,000 events. EPC count was calculated using the software-calculated percentage after subtracting nonspecific background staining for positive events in the control tube. CD34<sup>+</sup>/VEGFR-2<sup>+</sup> and CD133<sup>+</sup>/VEGFR-2<sup>+</sup> cells were identified as EPC. We have also studied progenitor cells, CD34<sup>+</sup> and CD133<sup>+</sup>.

#### EPC analysis after cultures

This was assessed in 11 SCH/HC and eight SCH subjects after  $T_4$  therapy. Mononuclear cells ( $1 \times 10^5$ ) were plated on fibronectin-coated 24-well plates enriched with endothelial medium [basal medium with supplement pack (Promocell, Heidelberg, Germany), supplemented with 20% fetal calf serum], and medium was changed after 72 and 120 h.

Counting was performed on d 5 in 15 randomly selected high-power fields (HPF  $\times$  400) by fluorescence microscopy after incubation with acetylated-LDL (Invitrogen, Carlsbad, CA; 5 mg/liter) and Ulex lectin (Sigma, St. Louis, MO; 10 mg/liter) for 4 h at 37 °C. EPC were identified as cells with combined uptake of acetylated-LDL and Ulex lectin binding.

#### EPC functions

EPC proliferation was assessed according to the manufacturer's instructions (MTT assay, 4, 5-dimethylthiazol-2-yl-2, 5-diphenyl tetrazolium bromide; Sigma) at d 5 after plating the mononuclear cells ( $1 \times 10^5$ ) in 96-well plates.

VEGF secretion and inducible nitric oxide synthase expression by the cultured cells were measured by ELISA (DVEDO and DNSO, respectively, R&D Systems).

#### Statistical analysis

The data were analyzed using the SPSS version 15 statistical package (SPSS, Inc., Chicago, IL). Normality of the samples was assessed by Shapiro-Wilk test. The difference between groups was analyzed using Student's *t* test or Mann-Whitney test (for not normally distributed data). Correlation between EPC and other measures was calculated by Spearman correlation analysis. Linear regression analysis was carried out using EPC (after log transformation) as the dependent variable after adjusting for age, blood pressure, BMI, lipids and patient group as categorical variables. The values are provided as mean  $\pm$  SD or median (range). Adjustment for multiple comparisons (2) was made using Bonferroni correction. Corrected *P* values have been reported for significant results (two-tailed significance,  $<0.05$ ).

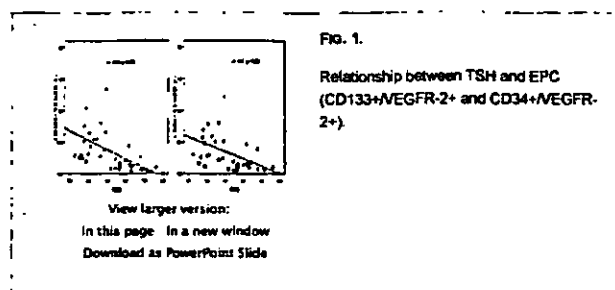
#### Results

EPC count and HDL-C levels were significantly lower in SCH compared with HC (Table 1).

<p>View this table: in this window    in a new window</p>	<p><b>TABLE 1.</b> Summary of difference in parameters in subject groups</p>
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The EPC function and other studied parameters were similar in both groups. There was a significant negative correlation (Spearman *rp*) between TSH and CD34<sup>+</sup> ( $-0.72 < 0.001$ ), CD133<sup>+</sup> ( $-0.59 < 0.001$ ), CD34<sup>+</sup>/VEGFR-2<sup>+</sup> ( $-0.47 < 0.004$ ), and CD133<sup>+</sup>/VEGFR-2<sup>+</sup> ( $-0.64 < 0.001$ ) (Fig. 1); there was positive correlation between FT4 and CD34<sup>+</sup> ( $0.33 < 0.04$ ), CD133<sup>+</sup>/VEGFR-2<sup>+</sup> ( $0.38 < 0.02$ ), positive correlation between HDL-C and CD34<sup>+</sup> ( $0.39 < 0.02$ ), CD34<sup>+</sup>/VEGFR-2<sup>+</sup>

(0.44/0.008), and CD133+VEGFR-2+ (0.51/0.001). There was no relationship between EPC and FMD or ADMA.



In multiple regression analysis, SCH significantly predicted lower EPC count after adjusting for age, BMI, blood pressure, TC, HDL-C, LDL-C (standardized  $\beta$  coefficient/P value): CD34+ (-0.91/-0.001), CD133+ (-0.83/-0.001), CD133+VEGFR-2+ (-0.77/-0.001), and CD34+VEGFR-2+ (-0.71/-0.001).

In SCH participants, EPC count increased and was similar to HC after  $T_4$  replacement (CD34+, CD133+, CD34+VEGFR-2+, and CD133+VEGFR-2+), with no significant difference in other parameters (Table 1g) including EPC count after culture and EPC functions.

### Discussion

We report, for the first time to our knowledge, lower circulating EPC count in SCH subjects, which increased significantly with  $T_4$  replacement. EPC showed significant negative and positive relations between serum TSH and FT4, respectively. SCH appears to be the single, most important factor determining lower EPC count when corrected for other cardiovascular risk factors studied, excluding the possibility that the reduction in EPC count could be secondary to prevailing risk factors.

The lack of difference between two groups in relation to EPC function may be related to the small effect of thyroid hormone on those functions, the small number of subjects studied, or both factors. Other functions of interest such as adhesion, migration, and capillary formation are worth studying in the future.

The pathogenesis behind lower EPC count in SCH needs to be explored. Reduced nitric oxide availability has been suggested to cause endothelial dysfunction in hypothyroidism and SCH contributing to reversible endothelial dysfunction (13). Nitric oxide is important for mobilization and differentiation of EPC (14). ADMA (endothelial nitric oxide synthetase inhibitor) correlated inversely with the circulating EPC count and reduced *in vitro* differentiation of EPC into endothelial tube-like structures in a dose-dependent manner in one study (15), whereas in another study it was found to be increased in SCH and significantly reduced after  $T_4$  therapy (16). This was not the case in our study, probably due to fewer subjects being studied. Furthermore, the relationship between ADMA and thyroid disease does not appear to be straightforward because higher ADMA levels were reported in both hyper- and hypothyroidism (17). The other possible mechanisms for reduced number of EPC include direct effects of thyroid hormone on EPC survival.

From the clinical perspective, we have shown reversible changes in EPC count with  $T_4$  replacement in subjects with a mild form of SCH (median TSH, 6.5 mU/Liter). Our subjects were younger (mean age, 44 yr), further supporting the evidence of higher cardiovascular risk in younger subjects with SCH in a recent meta-analysis (18), suggesting that  $T_4$  replacement should be considered in the younger patients with SCH. Further research is vital to explore whether  $T_4$  replacement therapy is translated into an improvement in cardiovascular outcomes in a double-blind, controlled study.

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### Footnotes

Trial registration: ISRCTN70334068 (<http://www.controlled-trials.com/iscrt/>).

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Abbreviations: ADMA, Asymmetric dimethylarginine; BMI, body mass index; EPC, endothelial progenitor cell(s); FMD, flow-mediated dilatation; FT4, free  $T_4$ ; HC, healthy controls; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SCH,

subclinical hypothyroidism; TC, total cholesterol; VEGFR, vascular endothelial growth factor receptor.

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## References

1. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, Young E, Bled T, Smith PA 1977 The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 7:481-493 [Medline](#)
2. Cooper DS, Ridgway EC 2002 Thoughts on prevention of thyroid disease in the United States. *Thyroid* 12:925-929 [CrossRef](#) [Medline](#)
3. Danese MD, Ladenson PW, Meinert CL, Powe NR 2000 Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. *J Clin Endocrinol Metab* 85:2993-3001 [Abstract/FREE Full Text](#)
4. Razvi S, Ingoe L, Keeka G, Oates C, McMillan C, Weaver JU 2007 The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. *J Clin Endocrinol Metab* 92:1715-1723 [Abstract/FREE Full Text](#)
5. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC 2000 Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Ann Intern Med* 132:270-278 [Abstract/FREE Full Text](#)
6. Walsh JP, Brenner AP, Bursara MK, O'Leary P, Leedman PJ, Faddema P, Michelangelo V 2005 Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. *Arch Intern Med* 165:2467-2472 [Abstract/FREE Full Text](#)
7. Imazumi M, Akashiwa M, Ichimaru S, Nakashima E, Hida A, Soda N, Usa T, Ashizawa K, Yokoyama N, Maeda R, Nagataki S, Eguchi K 2004 Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism. *J Clin Endocrinol Metab* 89:3365-3370
8. Vasa M, Fichtlscherer S, Aicher A, Adler K, Urbich C, Martin H, Zeiher AM, Dimmeler S 2001 Number and migratory activity of circulating endothelial progenitor cells inversely correlate with risk factors for coronary artery disease. *Circ Res* 89:E1-E7
9. Hill JM, Zalos G, Halcox JP, Schenke WH, Wactawski MA, Quyyum AA, Finkel T 2003 Circulating endothelial progenitor cells, vascular function, and cardiovascular risk. *N Engl J Med* 348:593-600 [CrossRef](#) [Medline](#)
10. Werner N, Kosiol S, Schlegl T, Ahlers P, Walenta K, Link A, Böhm M, Nickenig G 2005 Circulating endothelial progenitor cells and cardiovascular outcomes. *N Engl J Med* 353:999-1007 [CrossRef](#) [Medline](#)
11. Fadini GP, Miorin M, Facco M, Bonamico S, Baesso I, Grego F, Menegolo M, de Kreutzenberg SV, Tiengo A, Agostini C, Avogaro A 2005 Circulating endothelial progenitor cells are reduced in peripheral vascular complications of type 2 diabetes mellitus. *J Am Coll Cardiol* 45:1449-1457 [Abstract/FREE Full Text](#)
12. Fadini GP, de Kreutzenberg SV, Coracina A, Baesso I, Agostini C, Tiengo A, Avogaro A 2006 Circulating CD34+ cells, metabolic syndrome, and cardiovascular risk. *Eur Heart J* 27:2247-2255 [Abstract/FREE Full Text](#)
13. Taddei S, Caraccio N, Virdis A, Dardano A, Versari D, Ghiadoni L, Salvetti A, Ferrannini E, Montanari F 2003 Impaired endothelium-dependent vasodilation in subclinical hypothyroidism: beneficial effect of levothyroxine therapy. *J Clin Endocrinol Metab* 88:3731-3737 [Abstract/FREE Full Text](#)
14. Aicher A, Heeschen C, Mildner-Rilch C, Urbich C, Ihling C, Technau-Ihling K, Zeiher AM, Dimmeler S 2003 Essential role of endothelial nitric oxide synthase for mobilization of stem and progenitor cells. *Nat Med* 9:1370-1376 [CrossRef](#) [Medline](#)
15. Thum T, Tschöke D, Stein S, Schütthaus M, Eigenthaler M, Anker SD, Poole-Wilson PA, Erdi G, Bauernachs J 2005 Suppression of endothelial progenitor cells in human coronary artery disease by the endogenous nitric oxide synthase inhibitor asymmetric dimethylarginine. *J Am Coll Cardiol* 46:1693-1701 [Abstract/FREE Full Text](#)
16. Özcan O, Cakir E, Yaman H, Akgul EO, Erturk K, Bayhan Z, Bilgi C, Erbil MK 2005 The effects of thyroxine replacement on the levels of serum asymmetric dimethylarginine (ADMA) and other biochemical cardiovascular risk markers in patients with subclinical hypothyroidism. *Clin Endocrinol (Oxf)* 63:203-206 [CrossRef](#) [Medline](#)
17. Arkan E, Karadag CH, Gulduken S 2007 Asymmetric dimethylarginine levels in thyroid diseases. *J Endocrinol Invest* 30:186-191 [Medline](#)
18. Razvi S, Shakoor A, Vanderpump M, Weaver JU, Pearce SH 2008 The influence of age on the relationship between subclinical hypothyroidism and ischemic heart disease: a meta-analysis. *J Clin Endocrinol Metab* 93:2998-3007 [Abstract/FREE Full Text](#)

## Increased Prevalence of Subclinical Hypothyroidism in Common Bile Duct Stone Patients

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**Context:** Earlier, we have shown an increased prevalence of previously diagnosed hypothyroidism in common bile duct (CBD) stone patients and a delayed emptying of the biliary tract in hypothyroidism, explained partly by the missing prorelaxing effect of  $T_4$  on the sphincter of Oddi contractility.

**Objective:** In this study, the prevalence of previously undiagnosed subclinical hypothyroidism in CBD stone patients was compared with nongallstone controls.

**Patients:** All patients were clinically euthyretic and without a history of thyroid function abnormalities. CBD stones were diagnosed at endoscopic retrograde cholangiopancreatography (group I;  $n = 303$ ) or ruled out by previous medical history, liver function tests, and ultrasonography (control group II;  $n = 142$ ).

**Main Outcome Measures:** Serum free  $FT_4$  and TSH (S-TSH) were analyzed; S-TSH above the normal range ( $>6.0$  mU/liter) was con-

sidered as subclinical and S-TSH 5.0–6.0 mU/liter as borderline-subclinical hypothyroidism.

**Results:** A total of 5.3 and 5.0% (total 10.2%; 31 of 303) of the CBD stone patients were diagnosed to have subclinical and borderline-subclinical hypothyroidism, compared with 1.4% ( $P = 0.05$ ) and 1.4% (total 2.8%, four of 142;  $P = 0.026$ ) in the control group, respectively. In women older than 60 yr, the prevalence of subclinical hypothyroidism was 11.4% in CBD stone and 1.8% in control patients ( $P = 0.032$ ) and subclinical plus borderline-subclinical hypothyroidism 23.8% in CBD stone and 1.8% in control patients ( $P = 0.012$ ).

**Conclusion:** Subclinical hypothyroidism is more common in the CBD stone patients, compared with nongallstone controls, supporting our hypothesis that hypothyroidism might play a role in the forming of CBD stones. At minimum, women older than 60 yr with CBD stones should be screened for borderline or overt subclinical hypothyroidism. (*J Clin Endocrinol Metab* 92: 4260–4264, 2007)

IN WESTERN COUNTRIES, 10–12% of adults develop gallstones (1–3). The prevalence of common bile duct (CBD) stones in patients with gallbladder stones varies from 8 to 16% (4, 5). The pathogenesis of gallstones is a complex process involving factors affecting bile content and bile flow. A crucial factor in the forming of bile duct stones is biliary stasis (6), which may be caused for example by sphincter of Oddi (SO) stenosis, SO dyskinesia, or bile duct strictures (7–9).

Previously it has been shown that CBD stone patients have significantly more often diagnosed hypothyroidism, compared with gallbladder stone patients or controls (10, 11). The higher prevalence of previously diagnosed hypothyroidism in CBD stone patients, compared with gallbladder stone patients, suggests that factors other than merely changes in the cholesterol metabolism or bile excretion rate, particularly changes in the function of the SO, also may be behind the association between CBD stones and hypothyroidism. *Ex vivo* experiments with both the pig and human SO have

shown that thyroxine has a direct, prorelaxing effect on the SO motility at physiological concentrations, possibly mediated via thyroid hormone receptors- $\beta_1$  and  $\beta_2$ , and the absence of  $T_4$  may thus result in an increased tension in the SO (12, 13). In the rat the net bile flow to the duodenum is reduced in hypothyroidism and enhanced in hyperthyroidism (14), and in human cholecystigraphy the hepatic clearance of  $^{99m}Tc$  diethylenetriaminepentaacetic acid is decreased, and the hilum duodenum transit time tends to be increased in hypothyroidism (15).

The reduced prorelaxing effect of  $T_4$  on the SO in hypothyroidism shown in the experimental investigations may thus result in delayed emptying of the biliary tract, and, together with the possible cholesterol load in the bile and decreased hepatocytic excretion rate, may compose an important explanation for the increased association of CBD stones and hypothyroidism.

The prevalence of previously undiagnosed thyroid function abnormalities has never been studied in CBD stone patients before. If an increased prevalence of subclinical hypothyroidism will be found, it might have an effect on the diagnostic and therapeutic work-up of patients with CBD stones. Subclinical hypothyroidism is a prevalent condition among adult population; however, it is frequently overlooked. The previous studies about the prevalence of subclinical hypothyroidism among health subjects are few in number. There are no reported studies from Finland. In a

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Abbreviations: CBD, Common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; S-Bil, serum bilirubin; S- $FT_4$ , serum free  $T_4$ ; SO, sphincter of Oddi; S-TSH, serum TSH.

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recent study from the United Kingdom (16), the prevalence of subclinical hypothyroidism among healthy subjects was 2.6%.

The aim of this study was to investigate the thyroid function, especially the prevalence of previously undiagnosed subclinical hypothyroidism, in CBD stone patients compared with nongallstone controls.

### Patients and Methods

Patients who were diagnosed in endoscopic retrograde cholangiopancreatography (ERCP), performed as clinically indicated, to have CBD stones and who did not have a history of treated or diagnosed thyroid function abnormalities (group I;  $n = 303$ ; median age 68 yr; range 20–98) were recruited into the study from three hospitals involved (Tampere and Helsinki University Hospitals, Finland, and Kaunas Medical University Hospital, Lithuania). The control patients (group II;  $n = 142$ ; median age 65 yr; range 22–93) were recruited at the wards of gastrointestinal surgery, the inclusion criteria being admission to the hospital because of various gastrointestinal symptoms or diseases, with no gallstones detected at ultrasonography or in the medical history, no cholecystectomy performed, and no history of treated or diagnosed thyroid function abnormalities. Patients with phenytoin or carbamazepine therapy as well as pregnant patients were excluded from both groups.

From morning blood samples, serum free  $T_4$  (S-FT $_4$ ; method: immunofluorometric; normal range 9.0–19.0 pmol/liter $^{-1}$ ), TSH (S-TSH; method: immunofluorometric; normal range 0.35–6.0 mU/liter $^{-1}$ ), and total bilirubin (S-Bil; method: diazo reaction, photometric reading; normal range 5–25  $\mu$ mol/liter $^{-1}$ ) were analyzed in one laboratory (the laboratory center of Tampere University Hospital), and the results were compared between the two study groups. The symptom-free patients with S-TSH concentrations above the upper limit of the normal range ( $>6.0$  mU/liter $^{-1}$ ) were considered as subclinically hypothyroid (17), and with S-TSH close to the upper limit of the normal range (5.0–6.0 mU/liter $^{-1}$ ) as borderline subclinically hypothyroid. To be able to analyze further the

thyroid function in these patients, the levels of subclinical and borderline subclinical hypothyroidism were graded according to the S-TSH and S-FT $_4$  concentrations (see Table 1 for definitions). The blood tests were taken in the morning, before the ERCP procedure and thus not after given the patient oral cholecystographic contrast material or after endoscopic manipulation of the gastrointestinal tract. Only the samples from patients included into the study based on ERCP findings were later analyzed.

The data are shown as median and range. To calculate the statistical significance of the differences between the groups, Mann-Whitney  $U$  test was used for linear nonparametric variables and  $\chi^2$  test for cross-tabulated variables. Differences of  $P \leq 0.05$  were considered significant.

The study was conducted in accordance with the Helsinki Declaration. The study protocol was approved by the Ethical Councils of Tampere University Hospital and Helsinki University Hospital, Finland, and Kaunas Medical University Hospital, Lithuania.

### Results

Age and gender of the patients were similarly distributed in groups I (CBD stone) and II (control). There were 109 men (40%) in the CBD stone and 54 (38%) in the control group. Median age was 68 (range 18–98) and 65 (22–93) yr at the time of hospitalization in the CBD stone and control patients, respectively. Differences were nonsignificant between the groups. None of the patients included in the study were septic, and no weight loss was recorded.

S-Bil values were significantly higher in the CBD stone patients, compared with control patients ([56.6 (2.0–852.5) vs. 9.2 (2.7–18.2)  $\mu$ mol/liter $^{-1}$ ,  $P < 0.001$ ; median and range]). All control patients had a normal S-Bil level (2.0–20.0  $\mu$ mol/liter $^{-1}$ ).

None of the patients recruited into the study had symp-

**TABLE 1.** The prevalence of borderline subclinical and subclinical hypothyroidism graded (grades I–IV) according to the S-TSH and S-FT $_4$  levels in the group I (CBD stone) and group II (control) patients in different age groups and in total

Age (yr)	Total		Borderline subclinical hypothyroidism				Subclinical hypothyroidism				Total	
			Grade I S-TSH 5-6 mU/liter S-FT4 < 10 pmol/liter		Grade II S-TSH 5-6 mU/liter S-FT4 9-10 pmol/liter		Grade III S-TSH < 6 mU/liter, S-FT4 9-10 pmol/liter		Grade IV S-TSH < 6 mU/liter S-FT4 > 9 pmol/liter		Grades I-IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Group I												
21-30	11	3.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
31-40	21	6.9	1	0.3	0	0.0	0	0.0	0	0.0	1	0.3
41-50	26	8.6	1	0.3	1	0.3	1	0.3	0	0.0	3	1.0
51-60	42	13.9	1	0.3	0	0.0	1	0.3	0	0.0	2	0.3
61-70	75	24.8	7	2.3	0	0.0	4	1.3	3	1.0	14	4.6
71-80	72	23.8	1	0.3	0	0.0	3	1.0	4	1.3	8	2.6
81-90	47	15.5	3	1.0	0	0.0	0	0.0	0	0.0	3	1.0
91-100	9	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Total	303	100.0	14 <sup>a</sup>	4.6	1 <sup>a</sup>	0.3	9 <sup>b</sup>	3.0	7 <sup>b</sup>	2.3	31 <sup>c</sup>	10.2
Group II												
21-30	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
31-40	7	4.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
41-50	18	12.7	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7
51-60	29	20.4	2	1.4	0	0.0	0	0.0	0	0.0	2	1.4
61-70	37	26.1	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7
71-80	32	22.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
81-90	12	8.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
91-100	3	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Total	142	100.0	2 <sup>a</sup>	1.4	0 <sup>a</sup>	0.0	1 <sup>b</sup>	0.7	1 <sup>b</sup>	0.7	4 <sup>c</sup>	2.8

<sup>a</sup> NS (grades borderline I–II subclinical hypothyroidism between groups I and II).

<sup>b</sup>  $P = 0.05$  (grades III–IV subclinical hypothyroidism between groups I and II).

<sup>c</sup>  $P = 0.026$  [total (grades I–IV) borderline subclinical plus subclinical hypothyroidism between groups I and II].

toms of hypothyroidism. There was no difference in the median values of S-TSH (1.5, range 0.42–20.40 vs. 1.2, range 0.28–7.40 mU·liter<sup>-1</sup>) and S-FT4 (14.1, range 7.4–21.0 vs. 14.0, range 8.8–19.6 pmol·liter<sup>-1</sup>) between the groups.

S-TSH was above the upper normal range (>6.0 mU·liter<sup>-1</sup>; subclinical hypothyroidism) in 16 CBD stone patients (5.3%), compared with two controls (1.4%;  $P = 0.05$ ).

Fifteen CBD stone patients (5.0%) had S-TSH close to the upper limit of normal range (5–6 mU·liter<sup>-1</sup>; borderline subclinical hypothyroidism), compared with two patients (1.4%) in the control group ( $P = 0.026$ ). Thus, 5.3 and 5.0% (in total 10.2%; 31 of 303) of CBD stone patients had subclinical or borderline subclinical hypothyroidism, compared with 1.4 and 1.4% (in total 2.8%, four of 142;  $P = 0.026$ ) in the control group, respectively. The thyroid function of the 31 CBD stone (10.2%) and four control patients (2.8%) with S-TSH levels above 5.0 mU·liter<sup>-1</sup> is shown as graded into subgroups of borderline subclinical and subclinical hypothyroidism (grades I–IV) (Table 1), by combining the S-TSH and S-FT4 data. In each grade the prevalence of subclinical or borderline subclinical hypothyroidism was three to four times higher in CBD stone patients than the control patients.

The prevalence of subclinical (S-TSH > 6.0 mU·liter<sup>-1</sup>; grades III–IV) and borderline subclinical (S-TSH 5.0–6.0 mU·liter<sup>-1</sup>; grades I–II) hypothyroidism in women was 6.7 and 6.2% (total 12.9%) in CBD stone group and 2.3 and 2.3% (total 4.6%; NS) in the control group and in men 2.8 and 2.8% (total 5.5%) in the CBD stone group and 0 and 0% (total 0%,  $P = NS$ ) in control group, respectively.

In the patients older than 50 yr in the CBD stone group, the prevalence of subclinical (S-TSH > 6.0 mU·liter<sup>-1</sup>; grades III–IV) and borderline subclinical (S-TSH 5.0–6.0 mU·liter<sup>-1</sup>; grades I–II) hypothyroidism was 7.4 and 5.9% (total 13.3%), compared with 0.9% ( $P = 0.026$ ) and 1.8% (total 2.6%;  $P = 0.033$ ) in the control group, respectively. In patients older than 60 yr, the prevalences of subclinical and borderline subclinical hypothyroidism were 6.9 and 5.4% (total 12.3%) in the CBD stone group and 1.2% ( $P = 0.048$ ) and 0% ( $P = 0.048$ ) (total 1.2%;  $P = 0.007$ ) in the control group, respectively.

Most of the cases (12 of 16; 75%) with S-TSH values over 6.0 mU·liter<sup>-1</sup> (subclinical hypothyroidism; grades III–IV) in the CBD stone group were found in women older than 60 yr; in this subgroup the prevalence was 11.4% (12 of 105) in the CBD stone and 1.8% (one of 56) in the control group ( $P = 0.032$ ). In women older than 60 yr in CBD stone patients, the prevalence of grades I–IV (S-TSH  $\geq$  5.0 mU·liter<sup>-1</sup>) subclinical plus borderline subclinical hypothyroidism was 25 of 105 (23.8%), compared with one of 56 (1.8%) in the control group ( $P = 0.012$ ).

There were two patients (1.4%) in the control group (none in CBD stone group) who were recognized to have S-TSH values below the lower normal limit (<0.4 mU·liter<sup>-1</sup>). Of these two patients, one had S-FT4 above the upper normal limit (>19.0 pmol·liter<sup>-1</sup>), and the other had S-FT4 within the normal range. In addition, one patient in group I with S-TSH within the normal range (0.3%) had S-FT4 above the upper normal range. There was no statistical difference between the two groups.

In the general linear model multivariate analysis, patient group, age, and gender were associated with the level (grades I–IV) of thyroid function.

## Discussion

Earlier, an association between CBD stones and diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism have been shown, explained at least partly by the lack of the prorelaxing effect of T<sub>4</sub> on the sphincter of Oddi contractility (11–15). In this study we further investigated the prevalence of previously undiagnosed thyroid function abnormalities in CBD stone patients. To our knowledge, this has not been studied before. It was found that in the CBD stone patients, subclinical and borderline subclinical hypothyroidism are significantly more common, compared with the nongallstone controls (10.2 vs. 2.8%;  $P = 0.026$ ), the prevalence in the subgroup of women older than 60 yr being as high as 23.8%, compared with 1.8% in the control patients.

The two study groups were well comparable for age and gender distribution. Because of the possible effects on the serum thyroid values, patients with phenytoin or carbamazepine therapy as well as pregnant patients were excluded from both of the groups. The group I patients were diagnosed at ERCP to have CBD stones at the time of the procedure; patients with a suspicion of passed CBD stones but no stones seen at ERCP were not accepted into the study. Based on a normal serum bilirubin level, none of the control patients had signs of biliary stasis. Neither did the control patients have a history of gallstone disease or stones at ultrasonography performed during the study. In general, at ultrasonography about 95% of the gallbladder stones can be diagnosed (17). In addition, contrary to CBD stones, dilatation of bile ducts, suggesting ductal obstruction, may be detected with high sensitivity. In fact, the sensitivity of ultrasound in detecting biliary obstruction is about 85% (17), with a negligible false-positive rate (5), but a negative result does not exclude CBD stones or obstruction. Because there was no suspicion of CBD stones in the control patients, no imaging techniques except for ultrasonography (e.g. magnetic resonance cholangiopancreatography) were used to confirm the absence of CBD stones.

The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting early thyroid failure is an increased S-TSH concentration. The S-FT4 level is decreased in clinical hypothyroidism (18). In the subclinical form, an increased S-TSH level is accompanied by a normal S-FT4 level, and the patient is asymptomatic (19). In the present study, none of the patients was clinically hypothyroid. It was recognized that in 5.3% of the patients with CBD stones, S-TSH levels were above the upper limit of the normal range (defined as subclinical hypothyroidism), compared with 1.4% in the control patients ( $P = 0.05$ ). Furthermore, as many as 31 patients (10.2%) in the CBD stone group had S-TSH levels above or close to the upper limit of the normal range (defined as subclinical or borderline subclinical hypothyroidism, respectively), compared with four patients (2.4%) in the control group ( $P = 0.026$ ). Thus, subclinical and borderline subclinical forms of hypothyroidism are significantly

more common in patients with diagnosed CBD stones, compared with nongallstone control patients. In this study setting, the thyroid function serum determinations were done only once in each individual, and the findings are thus not based on a recording of a persistent abnormality. However, the measuring of the thyroid values was done similarly in both of the groups, and presumably remeasurements would not have changed the greatly significant difference in the prevalence of subclinical and borderline subclinical hypothyroidism between the two groups. However, in clinical practice, recording of a persistent abnormality should be preferred.

Subclinical hypothyroidism is a prevalent condition among adult population; however, it is frequently overlooked. The previous studies about the prevalence of subclinical hypothyroidism among health subjects are few in number. There are no reported studies from Finland. Thus, in the Finnish population, at the moment we can compare the results of the study population only with the control population of the current study. In a recent study from the United Kingdom (16), the prevalence of subclinical hypothyroidism among healthy subjects was 2.6%, which is somewhat higher compared with the prevalence of hypothyroidism among the control patients in the present study (1.8%). The prevalence of hypothyroidism (clinical plus subclinical) among women older than 60 yr may be as high as 20% (20). In the present study, the prevalence of subclinical hypothyroidism in women older than 60 yr was 11.4% in the CBD stone patients, compared with 1.8% in the control patients ( $P = 0.032$ ). The currently diagnosed 23.8% prevalence of subclinical plus borderline subclinical hypothyroidism and the previously diagnosed 11% prevalence of hypothyroidism (11) in female CBD stone patients older than 60 yr support the findings of Dickey and Feld (20) and suggest that at least this subgroup of patients might need to be screened for current thyroid dysfunction. It is uncertain whether treatment will improve quality of life in healthy, symptom-free patients who have abnormal TSH levels and normal FT4 levels (21, 22). Treatment of subclinical hypothyroidism is recommended if it is associated with changes in the cholesterol level, cardiovascular effects, or neuromuscular symptoms. Short-term studies have demonstrated that a positive effect on these symptoms may be achieved with early replacement treatment with L-thyroxine (23, 24). Thus, also patients with subclinical hypothyroidism and CBD stones might benefit from the  $T_4$  replacement therapy in general. The role of such therapy in preventing recurrent stone formation has not yet been studied.

The pathogenesis of gallstones is a complex process involving factors affecting bile content and bile flow. Brown pigment stones are formed secondary to biliary stasis (6), which is the major factor leading to anaerobic bacterial degradation and precipitation of biliary lipids (25, 26). Mechanical obstruction of the biliary tract leading to biliary stasis may be caused by bile duct strictures, SO stenosis, or SO dyskinesia (6, 8, 9). Brown pigment stones may also occur around a nidus of black or cholesterol stones or foreign material, which partially obstruct the CBD. Once initiated, the pathogenetic mechanism of stasis and bacterial overgrowth is difficult to reverse. The incidence of brown stones

increases with age, the phenomenon of which may be associated with deterioration of the SO function (6). In the current study, we did not analyze the composition of the diagnosed CBD stones, which is why the association of hypothyroidism with certain type of gallstones remains unverified.

Thyroid hormones are known to have a number of effects on cholesterol metabolism (27). When serum cholesterol values rise in hypothyroidism, bile may also become supersaturated with cholesterol, leading to gallbladder hypomotility (26), depressed contractility (28), and impaired filling (29), giving rise to a prolonged residence of bile in the gallbladder. This may contribute to the retention of cholesterol crystals, thereby allowing sufficient time for nucleation and continual growth into mature gallstones (26). In addition, the rate of bile secretion may be decreased (30), physically impairing clearance of precipitates from the bile ducts and gallbladder.

In the present study, we did not study the thyroid values in gallbladder stone patients without CBD stones. If the effect of  $T_4$  or the absence of  $T_4$  affected only the cholesterol metabolism and the hepatic bile secretion, the patients with gallbladder and CBD stones would presumably evince an equally increased prevalence of diagnosed or subclinical hypothyroidism. In a previous study, it was, however, noted the CBD stone patients had two times more previously diagnosed hypothyroidism than the gallbladder stone patients (11). This might be due to the previously shown reduced prorelaxing effect of  $T_4$  on the SO in hypothyroidism (12, 13), resulting in delayed emptying of the bile duct into the duodenum (14, 15), favoring the formation or retention of CBD stones.

Thyroid hormones are known to have an enterohepatic circulation (31, 32). Thus, at least theoretically, it might be possible that impaired bile acid secretion in a patient could interfere with the enterohepatic circulation of  $T_4$ , increase thyroid hormone clearance, and provoke hypothyroidism in an individual with decreased thyroid reserve, e.g. due to autoimmune thyroiditis. However, this would not explain the phenomena, that hypothyroidism is associated more with CBD stones than gallbladder stones (11), which we assume might be due to the lacking (prorelaxing) effect of  $T_4$  on SO (12, 13). It can also be further speculated whether the diminished biliary  $T_4$  concentration would have a direct effect on the SO contractility: we have reported that  $T_4$  has a prorelaxing effect on SO in *in vitro* experiments (12, 13), but it is not known whether, in a patient, in addition to the diminished serum  $T_4$  concentration, a potentially lower biliary  $T_4$  concentration would also play a role in this, having a direct, relaxation-impairing effect on the SO.

In a previous study (11), the CBD stone patients with diagnosed hypothyroidism were already receiving  $T_4$  replacement therapy and were already euthyretic in clinical and laboratory evaluation at the time of the diagnosis of CBD stones. Thus, CBD stone formation may already begin during the period of undiagnosed or subclinical hypothyroidism, later  $T_4$  replacement therapy not having enough effect on clearance of stones already formed. The findings of the present study are not in contrast with this hypothesis. There is only one case report that describes gallstone disappearance after treatment with  $T_4$  (33). There are currently no data to

suggest whether therapeutic doses of  $T_4$  could prevent gallstone formation.

In conclusion, subclinical hypothyroidism is more common in the CBD stone patients, compared with the nongallstone controls, which supports our previous hypothesis that hypothyroidism might play a role in the forming of CBD stones. Further studies are needed to investigate whether early treatment of subclinical or clinical hypothyroidism could prevent the CBD stones in these patients. At least a subgroup of CBD stone patients, i.e. women older than 60 yr, with the highest prevalence of subclinical hypothyroidism should be screened for thyroid function and offered replacement therapy, a positive effect on the symptoms associated with subclinical hypothyroidism as a possible achievement.

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### References

- Diehl AK 1991 Epidemiology and natural history of gallstone disease. *Gastroenterol Clin North Am* 20:1–19
- Heaton KW, Braddon FE, Mountford RA, Hughes AO, Emmett PM 1991 Symptomatic and silent gall stones in the community. *Gut* 32:316–320
- Kratzer W, Mason RA, Kachele V 1999 Prevalence of gallstones in sonographic surveys worldwide. *J Clin Ultrasound* 27:1–7
- Applemann RM, Priestley JT, Gate RP 1964 Cholelithiasis and choledocholithiasis: factors that influence relative incidence. *Mayo Clin Proc* 39:473–479
- Jordan Jr GL 1982 Choledocholithiasis. *Curr Probl Surg* 19:722–798
- Thistle JL 1998 Pathophysiology of bile duct stones. *World J Surg* 22:1114–1118
- Geenen JE, Hogan WJ, Dodds WJ, Stewart ET, Amadorer RC 1980 Intraluminal pressure recording from the human sphincter of Oddi. *Gastroenterology* 78:317–324
- Osnes M, Looftveit T, Larsen S, Aune S 1981 Duodenal diverticula and their relationship to age, sex, and biliary calculi. *Scand J Gastroenterol* 16:103–107
- Sandstad O, Osnes T, Skar V, Urdal P, Osnes M 1994 Common bile duct stones are mainly brown and associated with duodenal diverticula. *Gut* 35:1464–1467
- Honore LH 1981 A significant association between symptomatic cholesterol cholelithiasis and treated hypothyroidism in women. *J Med* 12:199–203
- Inkinen J, Sand J, Nordback I 2000 Association between common bile duct stones and treated hypothyroidism. *Hepatogastroenterology* 47:919–921
- Inkinen J, Sand J, Arvola P, Pörsi I, Nordback I 2001 Direct effect of thyroxine on pig sphincter of Oddi contractility. *Dig Dis Sci* 46:182–186
- Laukkanen J, Sand J, Aittomäki S, Pörsi I, Kööbi P, Kalliovalkama J, Silvennoinen O, Nordback I 2002 Mechanism of the prorelaxing effect of thyroxine on the sphincter of Oddi. *Scand J Gastroenterol* 37:667–673
- Laukkanen J, Kööbi P, Kalliovalkama J, Sand J, Mattila J, Turjanmaa V, Pörsi I, Nordback I 2002 Bile flow to duodenum is reduced in hypothyroidism and enhanced in hyperthyroidism. *Neurogastroenterol Motil* 14:183–188
- Laukkanen J, Sand J, Saaristo R, Salmi J, Turjanmaa V, Vehkalahti P, Nordback I 2003 Is bile flow reduced in patients with hypothyroidism? *Surgery* 133:288–293
- Wilson S, Parle JV, Roberts LM, Roalke AK, Hobbs FD, Clark P, Sheppard MC, Gammage MD, Pattison HM, Franklin JA, Birmingham Elderly Thyroid Study Team 2006 Prevalence of subclinical thyroid dysfunction and its relation to socioeconomic deprivation in the elderly: a community-based cross-sectional survey. *J Clin Endocrinol Metab* 91:4809–4816
- Way LW, Sleisenger MH 1989 Biliary obstruction, cholangitis and cholelithiasis. In: Sleisenger MH, Fordtran JS, eds. *Gastrointestinal disease*. Philadelphia: W. B. Saunders Co.; 1714–1729
- Woebber KA 2000 Update on the management of hyperthyroidism and hypothyroidism. *Arch Intern Med* 160:1067–1071
- Woebber KA 1997 Subclinical thyroid dysfunction. *Arch Intern Med* 157:1065–1068
- Dickey RA, Feld S 2000 The thyroid-cholesterol connection: an association between varying degrees of hypothyroidism and hypercholesterolemia in women. *J Womens Health Gen Based Med* 9:333–336
- U.S. Preventive Services Task Force 2004 Screening for thyroid disease: recommendation statement. *Ann Intern Med* 140:125–127
- Helfand M 2004 Screening for subclinical thyroid dysfunction in nonpregnant adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 140:128–141
- Gartner R 2004 Subclinical hyperthyroidism—does it have to be treated? *MMW Fortschr Med* 146:37–39
- Biondi B, Klein I 2004 Hypothyroidism as a risk factor for cardiovascular disease. *Endocrine* 24:1–13
- Carey MC 1993 Pathogenesis of gallstones. *Am J Surg* 165:410–419
- Donovan JM 1999 Physical and metabolic factors in gallstone pathogenesis. *Gastroenterol Clin North Am* 28:75–97
- Andreini JP, Prigge WF, Ma C, Gebbard RL 1994 Vesicles and mixed micelles in hypothyroid rat bile before and after thyroid hormone treatment: evidence for a vesicle transport system for biliary cholesterol secretion. *J Lipid Res* 35:1405–1412
- Behar J, Lee KY, Thompson WR, Biancani P 1989 Gallbladder contraction in patients with pigment and cholesterol stones. *Gastroenterology* 97:1479–1484
- Jazrawi RP, Pazzi P, Petroni ML, Prandini N, Paul C, Adam JA, Gullini S, Northfield TC 1995 Postprandial gallbladder motor function: refilling and turnover of bile in health and in cholelithiasis. *Gastroenterology* 109:582–591
- Field FJ, Albright E, Mathur SN 1986 Effect of dietary cholesterol on biliary cholesterol content and bile flow in the hypothyroid rat. *Gastroenterology* 91:297–304
- DiStefano 3rd JJ, Nguyen TT, Yen YM 1993 Transfer kinetics of 3,5,3'-triiodothyronine and thyroxine from rat blood to large and small intestines, liver, and kidneys *in vivo*. *Endocrinology* 132:1735–1744
- Rutgers M, Heusdens FA, Bonthuis F, de Herder WW, Hazenberg MP, Visser TJ 1989 Enterohepatic circulation of triiodothyronine (T3) in rats: importance of the microflora for the liberation and reabsorption of T3 from biliary T3 conjugates. *Endocrinology* 125:2822–2830
- Vassilakis JS, Nicolopoulos N 1981 Dissolution of gallstones following thyroxine administration. A case report. *Hepatogastroenterology* 28:60–61

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## Clinical Case Report: Ultrastructural Evidence of Skeletal Muscle Mitochondrial Dysfunction in Patients With Subclinical Hypothyroidism

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**Abstract. Objective:** The lack of overt signs and symptoms and controversies surrounding the thyroid stimulating hormone (TSH) reference range variability make the management of subclinical hypothyroidism (sHT) a challenge. Because muscle cramps and weakness have been noted in sHT, histological skeletal muscle examination may be of diagnostic significance as the presence of abnormalities would substantiate a significant consequence of the mild thyroid failure presumed to be present in the individual with sHT. The objective of this study was to investigate the ultrastructural and histological changes of skeletal muscle associated with sHT.

**Design:** Skeletal muscle biopsies from the vastus lateralis were obtained from four subjects with sHT. Samples were fixed, sectioned, and stained for quantitative and qualitative electron and light microscopic analysis.

**Main Outcome:** Analyses revealed characterizable morphological and ultrastructural alterations and quantitative mitochondrial variations between subjects, indicative of skeletal muscle mitochondrial dysfunction in sHT patients. For the 4 subjects, mean mitochondrial perimeter (MP) was  $1.09 \pm 0.312 \mu$ , mean mitochondrial area (MA) was  $0.10 \pm 0.05 \mu^2$ , and mean mitochondrial volume density was  $1.92 \pm 0.95$ .

**Conclusions:** The observed and quantified mitochondrial alterations and the noted morphological and ultrastructural alterations identify previously undocumented pathological skeletal muscle alterations associated with sHT. The observed morphological and ultrastructural alterations lend support to a trend of progression of sHT into overt hypothyroidism as a result of mitochondrial dysfunction and associated metabolic shift. The identification of these skeletal muscle alterations as sequelae of sHT may lend convincing objective evidence of a pathophysiologically significant abnormality in patients with sHT. If so, this should diminish the substantial resistance to treatment of these patients at an early stage of disease and attenuate the progression to overt hypothyroidism.

**Keywords.** Subclinical hypothyroidism • Mitochondria • Morphology • Skeletal muscle • Ultrastructure

### Introduction

Thyroid dysfunction affects more than 21 million Americans.<sup>[1]</sup> Untreated thyroid dysfunction has negative health consequences, including coronary heart disease, osteoporosis, atrial fibrillation, cognitive impairment, and depression. When analyzed as a whole, these negative health consequences resulting directly from untreated thyroid dysfunction are among the nation's largest causes of morbidity, mor-

talidity, and diminished quality of daily life in older adults.<sup>[1]</sup> The incidence of diagnosed hypothyroidism ranges from 4% to 8.5%.<sup>[2]</sup> Subclinical hypothyroidism is more common in women over the age of 60, (20%)<sup>[2]</sup> and males  $\geq 65$  years.<sup>[2,3]</sup>

Subclinical hypothyroidism represents the earliest stage of thyroid hypofunction.<sup>[4]</sup> It is diagnosed by an elevation of serum thyroid-stimulating hor-

ference range serum free  $T_4$  ( $FT_4$ ) level of 0.8-2.3 ng/dL.<sup>[4]</sup> The rate of progression from subclinical hypothyroidism to overt hypothyroidism directly correlates with the patient's initial TSH value,<sup>[2]</sup> and most experts recommend treatment of subclinical hypothyroidism when TSH values exceed 10 mIU/L. However, 75% of those diagnosed with subclinical hypothyroidism have TSH values in the 5-10 mIU/L range,<sup>[5]</sup> thereby creating an imprecise barometer regarding the need to and recommendations for the initiation of thyroid hormone treatment.

Typical signs and symptoms of overt hypothyroidism include cold intolerance, dry skin, constipation, depression, myalgia, arthralgia, cramps, and weakness as well as altered metabolic parameters including increased total and LDL cholesterol.<sup>[1]</sup> Adding to the difficulty in diagnosis, subclinical hypothyroid patients may not present with consistent symptoms. Since myalgia, muscle cramps, and weakness have been reported in subclinical hypothyroidism,<sup>[6]</sup> a histological examination of skeletal muscle in patients with subclinical hypothyroidism would be important in confirming a physical consequence of subclinical hypothyroidism. However, no literature exists describing the ultrastructural morphological characteristics of skeletal muscle in subclinical hypothyroid patients.

The purpose of this study was to examine biopsied skeletal muscle of 4 clinically diagnosed subclinical hypothyroid patients and identify ultrastructural and morphological characteristics, specifically mitochondrial alterations, found in the subclinical hypothyroid patients.

#### Materials and Methods

**Subjects.** Four patients served as study subjects. Each patient's informed consent for these procedures was obtained as part of the Institutional Review Board (Lifespan Academic Medical Center) approval process. A comprehensive physical examination and medical history review were included in the patients screening. Patients were included if they were ages 21-80 years, had no prior history of hormone supplements in the preceding six months, and had elevated TSH levels with  $FT_4$  levels within reference range.

**Patient 1.** A 34 year old female weighing 76.7 kg (169.1 lbs) with no family history of thyroid dysfunction presented with a TSH level of 14.33 mIU/L and a  $FT_4$  level of 0.84 ng/dL (Table 1). The patient presented with a weight gain  $\geq 6.8$  kg (14.99

lbs) over the course of the previous year, cold intolerance and low energy levels characterized by muscle weakness, myalgia, and muscle spasms exacerbated by cold exposure and alopecia. Her sleep pattern and bowel function were normal. At the time of her presentation, she was treated only with an oral contraceptive.

**Table 1.** TSH,  $FT_4$  Levels and Clinical Symptoms of 4 Patients with Subclinical Hypothyroidism.

Patient	TSH (mIU/L)	$FT_4$ (ng/dL)	Clinical Symptoms*
1	14.3	0.84	E, W, MW, P, MP, MS, CI, H
2	15.2	0.86	
3	5.5	1.03	E, P
4	11	0.8	E, S, W, MW, P, MP, MS, H

\*Decreased energy level (E), abnormal sleep pattern (S), increased weight (W), muscle weakness (MW), decreased physical performance (P), muscle pain (MP), muscle spasm (MS), cold intolerance (CI), and hair loss (H).

**Patient 2.** A 46 year old male weighing 78.0 kg (172.0 lbs) with no family history of thyroid dysfunction, presented with a TSH level of 15.2 mIU/L and a  $FT_4$  level of 0.86 ng/dL (Table 1). He was not on medication at the time of evaluation. Review of systems revealed no decrease in energy level as measured by physical performance, normal sleeping patterns, no weight change within the last year, no reported muscle weakness, spasm or myalgia and no perceptible intolerance to cold. Bowel movements were normal and there was no evidence of alopecia.

**Patient 3.** A 49 year old male weighing 83.5 kg (184.1 lbs) with a positive family history of thyroid dysfunction presented with a TSH of 5.5 mIU/L and  $FT_4$  level of 1.03 ng/dL (Table 1). His medications at presentation included Lovastatin, niacin, Metoprolol, Clopidogrel, ASA, and Ramipril. He reported a severe lack of energy characterized by a decrease in physical performance. He reported no weight gain, no muscle weakness, spasm or pain, and no perceptible increase in cold intolerance. His bowel function was normal and no alopecia was noted.

**Patient 4.** A 44 year old male weighing 70.8 kg (156.1 lbs) with a history of Graves' Disease. He was not on medication and presented with a TSH level of 11.01 mIU/L and a  $FT_4$  level of 0.80 ng/dL (Table 1). He reported a loss of energy, a significant weight

**Table 2.** Mitochondrial morphometric data of 4 subclinical hypothyroidism patients.

Patient	Mitochondria perimeter (MP) size range (l)	Mean MP (l) $\pm$ SD	Mitochondrial area (MA) ( $\mu^2$ )	Mitochondrial volume density (MVD)(%)
1	0.40-0.97	0.65 $\pm$ 0.14	0.03	1.95
2	0.56-2.25	1.25 $\pm$ 0.44	0.12	0.57
3	0.57-3.34	1.11 $\pm$ 0.36	0.10	2.55
4	0.53-4.57	1.36 $\pm$ 0.52	0.15	2.6

\*Mean Patient MP = 1.09  $\pm$  0.312 $\mu$ ; Mean Patient MA = 0.10  $\pm$  0.05  $\mu^2$ ; Mean Patient MVD = 1.92  $\pm$  0.95%.

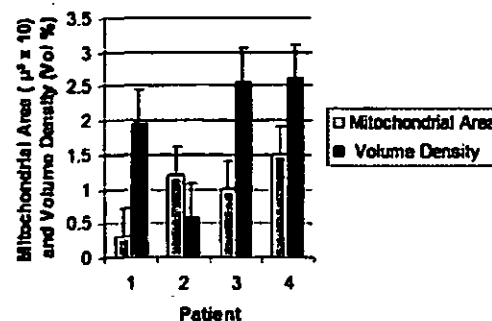
gain of  $\geq 6.8$  kg (15 lbs) within the previous year, alopecia, and generalized muscular weakness in his arms, legs, and back. He also complained of recurrent and localized back pain.

**Blood Measurements.** Blood samples were then taken to identify TSH and FT<sub>4</sub> levels to confirm the presence of subclinical hypothyroidism (Table 1). Patients were instructed to refrain from nonsteroidal anti-inflammatory drugs (NSAIDS) for 5 days prior to biopsy.

**Muscle Biopsy Procedure.** Biopsied samples were taken from the vastus lateralis muscle, 25 cm proximal to the tibial tuberosity and 5 cm lateral to the midline of the femur from each of the 4 patients.<sup>(7)</sup> The tissue was immediately placed in cold (4°C [39.2°F]) paraformaldehyde and 1.4% glutaraldehyde in 0.1M sodium cacodylate buffer. The tissue was cubed for light and electron microscopic evaluation and post fixed in osmium tetroxide in sodium cacodylate buffer. Following buffer rinses and dehydration in ethanol and propylene oxide, the tissues were flat embedded in Epon 812 and placed in a 70°C (158°F) oven to polymerize for 48-hours. Thick and ultrathin sections were cut using a Dupont Sorval MT2B ultramicrotome and prepared for light and electron microscopic analysis using standard procedures.<sup>(8)</sup>

**Morphological Analyses.** Qualitative light microscopy was performed using an Olympus BX51 light microscope with an Olympus DP11 digital camera. Digital images were analyzed using Image J and NIH Image analysis software. Electron microscopic examination was performed using a Philips 301 transmission electron microscope (TEM) equipped with an Advanced Microscopy Techniques image capturing system at magnifications from 4,500x to 45,000x, allowing for a more expansive examination of the muscle fiber.

Quantitative mitochondrial analysis was performed using Media Cybernetics, Inc. (Silver Springs, MD) Image-Pro Express image analysis software. Digital images were captured using a 1024 x 768 capture resolution setting using the Lumenera Scientific Infinity 2 side-column mounted digital camera. Each digital micrograph was then analyzed using the Image-Pro Express software.

**Figure 1.** Comparison of mitochondrial area and volume density of four subclinical hypothyroid patients.

A grating replica calibration grid (Electron Microscopy Services, Hatfield, PA) in conjunction with a Photomicrographic Scale Marker (Dunn and Reidman, Pacific Palisades, CA) were used to calibrate the determined perimeter of each mitochondrion and to convert measurements from pixels to micrometers ( $\mu$ ). Ten captured electron micrographs per subject, each taken from different fibers, were analyzed to determine mitochondrial perimeter (MP). Mitochondrial area (MA) was calculated as a function of perimeter. Mitochondrial volume density was

Mitochondrial area (MA) was calculated as a function of perimeter. Mitochondrial volume density was measured using a 110 point lattice grid and applying the stereological procedures of Weibel.<sup>[9]</sup>

## Results

**Morphological Analysis.** Microscopic analysis of skeletal muscle from these patients revealed focal areas of marked fiber size variation and atrophy, regions of myofibrillar disarray, and degeneration as well as widened intermyofibrillar regions. Areas of sarcolemmal blebbing, indicating a loss in membrane integrity, thickening, and lamination of the basement membrane were observed. Regions with occluded capillaries and areas with distended perivascular spaces filled with material of low electron density containing an infiltrate of red blood cells, macrophages, and lymphocytes were observed. Pyknotic nuclei as well as central nuclear migration, particularly in type II atrophic fibers, as well as Z-band streaming and disintegration, and areas devoid of myofilaments were observed. An increased concentration of glycogen aggregates and lipid deposits was obvious, particularly in type II fibers. Reduced numbers of mitochondria, many with disorganized membranes and cristae of unusual configurations, were observed (Figure 2). Vesicular structures adjacent to Z bands, intracytoplasmic inclusions, and lipofuscin granules were observed throughout but predominantly within subsarcolemmal and perinuclear regions.

**Clinical and Morphometric Analyses.** TSH, FT<sub>4</sub>, and clinical symptoms of the 4 patients are shown in Table 1. Patients 1 and 2 had higher blood TSH values when compared to patients 3 and 4. Also, the skeletal muscle mitochondrial densities of patients 1 and 2 (Table 2) were lower when compared with patients 3 and 4.

Mitochondrial mass per unit of muscle fiber area is a morphological indicator of muscle oxidative capacity and can be expressed by measuring mitochondrial area and mitochondrial density in the same micrograph. Figure 1 shows graphic illustrations of mitochondrial mass per unit area of skeletal muscle mass. This was determined by measuring mitochondrial volume density in combination with mean mitochondrial area for the 4 patients. Patients 3 and 4 had a greater mitochondrial mass per unit area of muscle mass than did patients 1 and 2. Smaller sized mitochondria were evident in the skeletal muscle of patient 1 in comparison to the other three.

## Discussion

The relationship between TSH levels and clinical symptoms in patients with subclinical hypothyroidism is variable and is thus of restricted diagnostic utility. This is illustrated by the cases reported in this study. For example, patient 2 had the highest TSH level (15.2 m IU/L) but did not complain of myalgia and reported no other hypothyroid symptoms (Table 1). In contrast, patient 4 complained of myalgia, reported symptoms compatible with overt hypothyroidism (Table 1), but had a lower TSH level (11.01 m IU/L). This represents an example where morphological analysis offers a more objective measurement of disease progression.

Myalgia is a consistent clinical hypothyroid symptom and often is a precursor to a decline in physical activity and exercise tolerance.<sup>[10,11,12]</sup> An early investigation of hypothyroid skeletal muscle identified areas of normal muscle that were interrupted by segments of complete structural disorganization characterized by myofilament loss.<sup>[13]</sup> Subsequent studies confirmed these results and thus established a relationship between myalgia due to overt hypothyroidism and skeletal muscle morphological changes.

Recognizing that specific skeletal muscle alterations are typical of hypothyroid patients, we examined skeletal muscle for histological changes that occur during subclinical hypothyroidism prior to its progression to overt hypothyroidism. We propose that the appearance of characteristic skeletal muscle "markers" would provide support for earlier intervention and perhaps a more efficacious treatment regimen.

Table 2 indicates that the mitochondrial mass (mitochondrial area or mitochondrial volume density) in 2 of our 4 patients is smaller compared to normal skeletal muscle (mitochondrial area = 0.11  $\mu^2$ ).<sup>[14]</sup> The number, size, and volume fraction of mitochondria closely reflect the metabolic capacity of the organism. Therefore, our data suggest that altered skeletal muscle metabolism is a prominent feature in the subclinical hypothyroid patient.

It is interesting to note that the 2 patients with elevated TSH levels (1 and 2) exhibited a low mitochondrial area per muscle fiber area (Figure 1) due to either an unusually low mean mitochondrial area (Patient 1 in Table 2) or a low mitochondrial volume density (Patient 2 in Table 2). In contrast, the 2 patients with lower TSH levels had mean mitochondrial

**Figure 2. Ultrastructural comparison of a control (a) and a subclinical hypothyroid patient (sHT) (b).**



a. Control Patient 25,000X



b. sHT Patient 4 25,000X

**Fig. 2a.** Control biopsy taken from an earlier unpublished study. Z bands (Z), mitochondria (M) and myofilaments (Mf) show good integrity. Small black dots are glycogen (I) particles.

**Fig. 2b.** Skeletal muscle taken from patient 4. Note the damaged sarcomere (DS) displaying sparse myofilaments (Mf) with elongated mitochondria (M) spanning across the sarcomere space, once occupied by Z bands.

areas and densities closer to those for healthy adults (range is  $0.088 \text{ i}^2$ – $0.155 \text{ i}^2$ ).<sup>[13]</sup>

In an earlier study, we measured mitochondrial area in patients with heart failure prior to (mitochondrial area  $\approx 0.036 \text{ i}^2$ ) and following (mitochondrial area  $\approx 0.046 \text{ i}^2$ ) combined aerobic and resistance training.<sup>[14]</sup> We also measured mitochondrial area in postmenopausal women at baseline ( $0.039 \text{ i}^2$ ) (un-

published data). Other authors reported a mitochondrial area of  $0.076 \text{ i}^2$  (obese),  $0.063 \text{ i}^2$  (diabetic), and  $0.114 \text{ i}^2$  (lean adults) in muscle biopsies.<sup>[17]</sup> The mean mitochondrial area from the subclinical hypothyroid patients in this study ( $0.10 \pm 0.05 \text{ i}^2$ ) was within a range of  $0.03 \text{ i}^2$  to  $0.15 \text{ i}^2$  (Table 2). This indicates that although mitochondrial area in subclinical hypothyroid patients did not differ greatly

from healthy adults, it did demonstrate a tendency to decrease as TSH levels increased. The larger than expected mean mitochondrial area in our patients may be due to the high frequency of enlarged and distorted mitochondria (Figure 2 and Figure 3) often referred to as megamitochondria.<sup>[16,17]</sup> These very large mitochondria with low inner membrane density may be undergoing apoptosis. However, mitochondrial area in the subclinical hypothyroid patients did demonstrate a tendency to decrease as TSH levels increased (Table 1 and Table 2), suggesting that specific mitochondrial changes in skeletal muscle are reflective of increased TSH levels. These data are in contrast to another investigation that reported the presence of mitochondrial alterations only in prolonged clinical cases.<sup>[18]</sup>

The skeletal muscle histological profile of subclinical hypothyroidism was found to include focal areas of marked fiber variation and atrophy, regions of myofibrillar disarray, degeneration, and central nuclear migration, predominantly in type II fibers, regions devoid of myofilaments, Z band streaming and disintegration. Other studies involving overt hypothyroid patients reported "cores" of myofibrillar

thyroidism.<sup>[19,20,21]</sup> Increased concentrations of glycogen aggregates was observed in type II fibers occupying up to  $\frac{1}{5}^{\text{th}}$  of the cross-sectional area.<sup>[20]</sup> The aggregates are thought to result from derangements of glycogen metabolism and to be related to the severity of subclinical hypothyroidism.<sup>[22]</sup> These observations are consistent with other reported findings.<sup>[20,22]</sup> The skeletal muscle changes that characterize subclinical hypothyroidism in our report are consistent with a previous study reporting a disease-related metabolic shift toward anaerobic ATP production in subclinical hypothyroidism.<sup>[24]</sup>

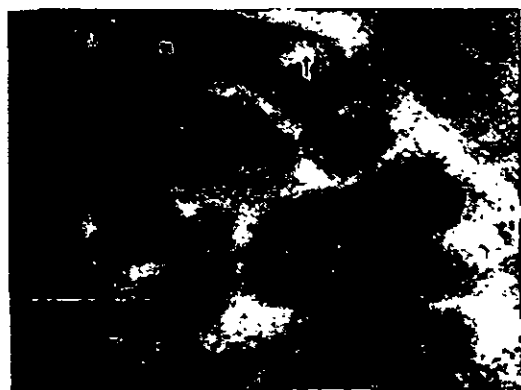
Mitochondrial plasticity is a response to changing metabolic conditions.<sup>[3,23,24]</sup> We observed reduced numbers of mitochondria, many with loss of membrane integrity, containing dense lipid inclusions and cristae of unusual configurations. These observations are consistent with previous studies of hypothyroid patients<sup>[10,19,22]</sup> and lead further support to the theory that thyroid hormones have a profound effect on mitochondrial energy expenditure.<sup>[25]</sup>

We also found areas containing pyknotic nuclei and central nuclear migration, consistent with severe hypothyroid myopathy,<sup>[26]</sup> as well as regions demonstrating a loss in sarcolemmal integrity and blebbing,<sup>[18,27,28]</sup> along with inflammatory cell infiltration into necrotic fiber areas. This contrasts with other studies where necrotic muscle fibers were found in the absence of interstitial inflammatory cells.<sup>[13]</sup>

In patients with severe hypothyroidism, selective type II fiber atrophy was reported to be due to impaired glycogen utilization and accompanied by an increased type I fiber area which gives the muscle a "bulky" appearance.<sup>[27,29]</sup> A link between the severity of myopathic symptoms, the degree of type II fiber atrophy and loss, and increased central nuclear displacement has been recognized.<sup>[22]</sup> A correlation between clinical severity of hypothyroidism and the degree of myofibrillar loss and abnormal glycogen accumulation has been established.<sup>[18]</sup> These observations are consistent with our report.

This report identifies specific skeletal muscle morphological changes that are characteristic of subclinical hypothyroidism. Establishing consistent morphological markers of subclinical hypothyroidism prior to disease progression could justify an earlier, more efficacious treatment with thyroid hormone. This treatment strategy may diminish morbidity by preventing disease progression from subclinical to overt hypothyroidism. Earlier initiation of

Figure 3. Subclinical hypothyroid patient 4.



Skeletal muscle taken from patient 4. Several mitochondria (M) have moved from their normal position between myofibrils (see Fig. 2) to within a sarcomere. They appear large, elongated and irregular in shape with a lower density of inner membranes. The curved mitochondrion has lost some internal membrane structure (1), suggesting that apoptosis may be taking place.

disarray in type I fibers, and this was observed to correlate with the severity and duration of hypo-

this therapy may ultimately translate into an improvement in patients' lifestyle. Further research to establish reproducibility and clinical effectiveness appears to be warranted from these case studies.

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#### References

- Legrys, V.A., Hartman, K., and Walsh, J.F.: The clinical consequences and diagnosis of hypothyroidism. *Clin. Lab. Sci.*, 4:203-208, 2004.
- Surks, M.I., Ortiz, E., and Daniels, G.H., et al.: Subclinical thyroid disease. *JAMA*, 291:228-238, 2004.
- Monzani, F., Caraccio, N., Del Guerra, P., et al.: Neuromuscular symptoms and dysfunction in subclinical hypothyroid patients: beneficial effect of L-T<sub>4</sub> replacement therapy. *Clin. Endo.*, 51:237-242, 1999.
- Col, N.F., Surks, M.I., and Daniels, G.H.: Subclinical thyroid disease. *JAMA*, 291:239-243, 2005.
- Wilson, G.R., and Whit Curry, R.: Subclinical thyroid disease. *Amer. Fam. Phys.*, 72:1517-1524, 2005.
- Cooper, D.S.: Thyroid disease in the oldest old. *JAMA*, 292:2651-2654, 2004.
- Hennessey, J.V., Chromiak, J.A., Della Ventura, S., et al.: Increase in percutaneous muscle biopsy yield with a suction-enhancement technique. *J. Appl. Physiol.*, 82:1739-1742, 1997.
- Cosmas, A.C., Monteiro, M., Levesque, S., et al.: Ultrastructural changes in skeletal muscle of postmenopausal women following twelve months of aerobic exercise and progressive resistance training. Proceedings of the 31st. annual American Aging Association/16th. Annual meeting of American College of Clinical Gerontology, 18, 2002.
- Weibel, E.R.: Stereological principles for morphometry in electron microscopic cytology. *Int. Rev. Cytol.*, 26:235-302, 1969.
- Jiskra, J.: Myopathy syndrome in undiagnosed hypothyroidism. *Vnitř. Lek.*, 47:642-646, 2001.
- Lochmuller, H., Reimers, C.D., Fischer, P., et al.: Exercise-induced myalgia in hypothyroidism. *Clin. Invest.*, 12:999-1001, 1993.
- Rodolico, R.A., Toscano, S., Benvenega, A., et al.: Myopathy as the persistently isolated symptomatology of primary autoimmune hypothyroidism. *Thyroid*, 8:1033-1038, 1998.
- Norris, F.H., and Panner, J.: Hypothyroid Myopathy. *Arch. Neurol.*, 11:574-589, 1961.
- Jerusalem, F., Engel, A.G., and Peterson, H.A.: Human muscle fiber fine structure: Morphometric data on controls. *Neurol.*, 25:127-134, 1975.
- Jerusalem, F., Engel, A.G., and Peterson, H.A.: Human muscle fiber fine structure: Morphometric data on controls. *Neurol.*, 25:127-134, 1975.
- Santoro, C., Cosmas, A., Forman, D., et al.: Exercise training alters skeletal muscle mitochondrial morphology in heart failure patients. *J. Cardiovas. Risk*, 9:377-381, 2002.
- Kelley, D.E., Jing, H., Menshikova, E.V., et al.: Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. *Diabetes*, 51:2944-2950, 2002.
- Lin, R.T., Liu, C., Tai, C., et al.: Hypothyroid myopathy: histopathological and ultrastructural study. *Kaohsiung J. Med. Sci.*, 16:68-75, 2000.
- Modi, G.: Cores in hypothyroid myopathy: a clinical, histological and immunofluorescence study. *J. Neuro. Sci.*, 175:28-32, 2000.
- Ono, S., Inouye, K., and Mannen, T.: Myopathology of hypothyroid myopathy: Some new observations. *J. Neurol. Sci.*, 77:237-248, 1987.
- Rodolico, C., Toscano, A., Benvenega, S., et al.: Myopathy as the persistently isolated symptomatology of primary autoimmune hypothyroidism. *Thyroid*, 8:1033-1038, 1998.
- Agostinucci, K., Manfredi, T.G., Cosmas, A., et al.: Vitamin E and liver mitochondrial morphometry. *Age*, 36:2393, 1999.
- Caraccio, N., Natali, A., Sironi, A., et al.: Muscle metabolism and exercise tolerance in subclinical hypothyroidism: A controlled trial of L-thyroxine. *J. Clin. Endocrinol. Metab.*, 90:4057-4062, 2005.
- Bertoni-Freddari, C., Fattoretti, P., Casoli, T., et al.: Morphological plasticity of synaptic mitochondria during aging. *Brain Research*, 628:193-200, 1993.
- Evans, R.M., Watanabe, I., and Singer, P.A.: Central changes in hypothyroid myopathy: A case report. *Muscle & Nerve*, 13:952-956, 1999.
- Harper, M., and Seifert, E.L.: Thyroid hormone effects on mitochondrial energetics. *Thyroid*, 18:145-156, 2008.
- Khalceeli, A.A., Gohil, K., McPhail, G., et al.: Muscle morphology and metabolism in hypothyroid myopathy: effect of treatment. *J. Clin. Pathol.*, 36:519-526, 1983.
- Staub, J.J., Althaus, B.U., Engler, H., et al.: Spectrum of subclinical and overt hypothyroidism: effect on

8 Dunn, M.E., et al.: Muscle Mitochondrial Dysfunction . . . Subclinical Hypothyroidism. *Thyroid Science* 4(5):CR1-8, 2009

thyrotropin, prolactin and thyroid reserve, and metabolic impact on peripheral target tissues. *Am. J. Med.*, 92:631-642, 1992.

29. Khalceeli, A.A., Griffith, D.G., and Edwards, R.H.T.:

The clinical presentation of hypothyroid myopathy and its relationship to abnormalities in structure and function of skeletal muscle. *Clin. Endocrin.*, 19:365376, 1983.





## Pre-eclampsia, soluble fms-like tyrosine kinase 1, and the risk of reduced thyroid function: nested case-control and population based study

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### Abstract

**Objective** To determine if pre-eclampsia is associated with reduced thyroid function during and after pregnancy.

**Design** Nested case-control study during pregnancy and population based follow-up study after pregnancy.

**Setting** Calcium for Pre-eclampsia Prevention trial of healthy pregnant nulliparous women in the United States during 1992-5, and a Norwegian population based study (Nord-Trondelag Health Study or HUNT-2) during 1995-7 with linkage to the medical birth registry of Norway.

**Participants** All 141 women (cases) in the Calcium for Pre-eclampsia Prevention trial with serum measurements before 21 weeks' gestation (baseline) and after onset of pre-eclampsia (before delivery), 141 normotensive controls with serum measurements at similar gestational ages, and 7121 women in the Nord-Trondelag Health Study whose first birth had occurred in 1967 or later and in whom serum levels of thyroid stimulating hormone had been subsequently measured.

**Main outcome measures** Thyroid function tests and human chorionic gonadotrophin and soluble fms-like tyrosine kinase 1 concentrations in the Calcium for Pre-eclampsia Prevention cohort and odds ratios for levels of thyroid stimulating hormone above the reference range, according to pre-eclampsia status in singleton pregnancies before the Nord-Trondelag Health Study.

**Results** In predelivery specimens of the Calcium for Pre-eclampsia Prevention cohort after the onset of pre-eclampsia, thyroid stimulating hormone levels increased 2.42 times above baseline compared with a 1.48 times increase in controls. The ratio of the predelivery to baseline ratio of cases to that of the controls was 1.64 (95% confidence interval 1.29 to 2.08). Free triiodothyronine decreased more in the women with pre-eclampsia than in the controls (case ratio to control ratio 0.96, 95% confidence interval 0.92 to 0.99). The predelivery specimens but not baseline samples from women with pre-eclampsia were significantly more likely than those from controls to have concentrations of thyroid stimulating hormone above the reference range (adjusted odds ratio 2.2, 95% confidence interval 1.1 to 4.4). Both in women who developed pre-eclampsia and in normotensive controls the increase in thyroid stimulating hormone concentration between baseline and predelivery specimens was strongly associated with increasing quarters of predelivery soluble fms-like tyrosine kinase 1 (P for trend 0.002 and <0.001, respectively). In the Nord-Trøndelag Health Study, women with a history of pre-eclampsia in their first pregnancy were more likely than other women (adjusted odds ratio 1.7, 95% confidence interval 1.1 to 2.5) to have concentrations of thyroid stimulating hormone above the reference range (>3.5 mIU/l). In particular, they were more likely to have high concentrations of thyroid stimulating hormone without thyroid peroxidase antibodies (adjusted odds ratio 2.6, 95% confidence interval 1.3 to 5.0), suggesting hypothyroid function in the absence of an autoimmune process. This association was especially strong (5.8, 1.3 to 25.5) if pre-eclampsia had occurred in both the first and the second pregnancies.

**Conclusion** Increased serum concentration of soluble fms-like tyrosine kinase 1 during pre-eclampsia is associated with subclinical hypothyroidism during pregnancy. Pre-eclampsia may also predispose to reduced thyroid function in later years.

## Introduction

Pre-eclampsia, a pregnancy specific syndrome characterised by new onset hypertension and proteinuria, causes substantial morbidity and mortality in mothers and infants.<sup>1 2</sup> Women with a history of pre-eclampsia have an increased risk of dyslipidaemia, hypertension, and cardiovascular and renal disease.<sup>3 4 5 6</sup>

Although the cause of pre-eclampsia is still unclear, studies in both humans and animals suggest that excess circulating antiangiogenic factors such as soluble fms-like tyrosine kinase 1 (sFlt-1 or sVEGFR1) may be responsible for the clinical phenotype of pre-eclampsia.<sup>7 8 9</sup> Blood concentrations of soluble fms-like tyrosine kinase 1 increase during the last two months of normal pregnancy and increase to much greater levels in women with pre-eclampsia. Soluble fms-like tyrosine kinase 1 acts by inhibiting vascular endothelial growth factor and placental growth factor signalling. Indeed, the use of vascular endothelial growth factor inhibitors for the treatment of cancer related angiogenesis has been associated with hypertension, proteinuria, glomerular endothelial damage, increased concentrations of circulating liver enzymes, cerebral oedema, and reversible posterior leucoencephalopathy—a constellation of conditions resembling those found in women with pre-eclampsia or eclampsia.<sup>10 11</sup>

More recently, patients with cancer who had received prolonged therapy with vascular endothelial growth factor inhibitors were found to be at greater risk of hypothyroidism.<sup>12 13 14</sup> Furthermore, studies in mice using vascular endothelial growth factor inhibitors such as soluble fms-like tyrosine kinase 1 have shown substantial thyroid capillary regression and increased concentrations of thyroid stimulating hormone.<sup>11 15</sup> We therefore hypothesised that the excess soluble fms-like tyrosine kinase 1 accompanying pre-eclampsia might be associated with reduced thyroid function during pregnancy and that women who have experienced pre-eclampsia would have an increased risk of hypothyroid function later in life.

To compare thyroid function in women who developed pre-eclampsia with those who remained normotensive during pregnancy, we carried out a nested case-control study within the Calcium for Pre-eclampsia Prevention (CPEP) trial cohort. We hypothesised that women with pre-eclampsia would experience a greater increase in thyroid stimulating hormone concentration during pregnancy than normotensive controls and that the extent of the increase would correlate with the magnitude of the soluble fms-like tyrosine kinase 1 concentration during pre-eclampsia. In addition, we used a Norwegian population based cohort study (the Nord-Trøndelag Health Study or HUNT-2) to test whether pre-eclampsia in a previous pregnancy is associated with risk of reduced thyroid function in later life.

### **Calcium for Pre-eclampsia Prevention trial**

#### *Participants and specimens*

The Calcium for Pre-eclampsia Prevention trial was a randomised, double blind clinical trial carried out during 1992-5 in healthy nulliparous women with singleton pregnancies to evaluate the effects of daily supplementation with calcium or placebo on the incidence and severity of pre-eclampsia.<sup>16 17</sup> Calcium supplementation did not reduce the incidence or severity of pre-eclampsia or delay its onset.

Of the 4589 women enrolled in the trial we excluded 300 with incomplete information on outcomes or whose pregnancy ended before 21 weeks. Of 326 women who developed pre-eclampsia, 141 had at least one serum specimen collected before 21 weeks' gestation (baseline specimen) and one collected after the onset of pre-eclampsia (predelivery specimen). If a woman had more than one specimen collected within each of these intervals, we selected the earliest before 21 weeks and the latest after the onset of pre-eclampsia. Soluble fms-like tyrosine kinase 1 had previously been analysed in all serum specimens of a random sample of 2200 women and in all women with pre-eclampsia.<sup>18</sup> After excluding women with pre-eclampsia, gestational hypertension, or gestational proteinuria, 1649 women remained who had been normotensive and without proteinuria during their pregnancies (controls). Each case of pre-eclampsia was matched to the control with two serum specimens that were closest in gestation to the two case specimens. Two case specimens—one baseline, one predelivery—were not located in the specimen repository.

Women with active dysfunction of the thyroid that required drugs were excluded from the Calcium for Pre-eclampsia Prevention trial except those with hypothyroidism who were stable while receiving thyroid replacement therapy. A check of drugs reported by the participants of this study showed that only one woman (who later developed pre-eclampsia) had received thyroxine. This woman had subclinical hypothyroidism at baseline, but concentrations of thyroid stimulating hormone and free thyroxine in her predelivery specimen were within clinical reference ranges.

Pre-eclampsia was defined as hypertension—that is, a diastolic blood pressure of at least 90 mm Hg on two occasions four to 168 hours apart—and proteinuria, characterised as one of the following: urine dipstick results of at least + (30 mg/dl) on two occasions four to 168 hours apart; a protein to creatinine ratio of at least 0.35; urine dipstick results of at least ++ (100 mg/dl), or a 24 hour urine specimen containing at least 300 mg of protein. Detailed definitions have been published previously.<sup>16 17</sup>

#### *Procedures*

We randomly ordered archived serum specimens, which had been stored at -70°C, for analysis. Assays were carried out by staff who were unaware of the outcome of the pregnancy. Enzyme linked immunosorbent assays for human soluble fms-like tyrosine kinase 1 had previously been done in duplicate by R&D Systems Analytical Testing Services (Minneapolis, MN, USA).<sup>18</sup> Thyroid function tests (thyroid stimulating hormone, free thyroxine, free triiodothyronine, thyroid peroxidase antibodies) were carried out and human chorionic gonadotrophin measured using a Roche Diagnostics Modular

Analytics E170 analyzer (Roche Diagnostics, Indianapolis, IN, USA). Human chorionic gonadotrophin was measured because it is known to stimulate the thyroid gland and to decrease concentrations of thyroid stimulating hormone.<sup>19</sup> The Roche human chorionic gonadotrophin assay shows no cross reactivity with thyroid stimulating hormone. Coefficients of variation in normal serum in mid-pregnancy were less than 5%. Reference ranges for thyroid stimulating hormone (mIU/l) provided by the manufacturer were 0.33-4.60, 0.35-4.10, and 0.21-3.15 in sera from the first, second, and third trimester, respectively. The upper limits of the reference ranges for thyroid peroxidase antibodies (IU/ml) provided by the manufacturer were 119, 91, and 171 in sera from the first, second, and third trimester, respectively.<sup>20</sup> Women with values above the reference range were considered to have tested positive for thyroid peroxidase antibodies.

### Statistical analysis

We compared categorical variables using the  $\chi^2$  test and continuous variables using *t* tests. The geometric means of thyroid stimulating hormone, free thyroxine, free triiodothyronine, and human chorionic gonadotrophin and their standard deviations are reported for baseline and predelivery specimens for both cases and controls. Comparisons of cases and controls are presented as two tailed *P* values. Statistical comparisons of specimens from cases and controls were carried out using linear models, adjusting for age, body mass index, race or ethnicity (black people v others), smoking status (current smoker or quit during pregnancy v never smoker or quit before pregnancy), human chorionic gonadotrophin concentration, and presence of thyroid peroxidase antibodies above the reference range. The levels of change from baseline to predelivery are presented as ratios. Geometric means of the ratios and their standard deviations are given. We present the comparison statistic between case and control, which is the ratio of their geometric means, with its 95% confidence interval.

## Results

### Characteristics of the women

Of the 141 women with pre-eclampsia, 63 (42%) had severe pre-eclampsia and in 47 (33%) pre-eclampsia began before 37 weeks' gestation (table 1). Compared with the controls, women with pre-eclampsia had a greater body mass index and higher blood pressure at the time of enrolment in the Calcium for Pre-eclampsia Prevention trial. Moreover, a larger proportion of their current pregnancies had been complicated by preterm delivery or had resulted in the delivery of small for gestational age infants (table 1). The difference in gestational age between baseline and predelivery specimens in cases and controls did not differ significantly (154 v 148 days, *P*=0.08).

Table 1  
Characteristics of women with pre-eclampsia and controls at enrolment in Calcium for Pre-eclampsia Prevention trial and characteristics of their infants and specimens\*  
Values are numbers (percentages) unless stated otherwise

Characteristic	Cases (n=141)	Controls (n=185)	<i>P</i> value
Maternal			
Mean (SD) age (years)	28.9 (4.2)	28.1 (3.2)	0.55
Mean (SD) height (cm)	161 (7)	162 (6)	0.88
Mean (SD) weight (kg)	77.0 (19.2)	66.2 (15.4)	0.002
Mean (SD) body mass index	27.1 (4.9)	24.7 (4.7)	<0.001
Mean (SD) systolic blood pressure (mm Hg)	111 (16)	107 (9)	<0.001
Mean (SD) diastolic blood pressure (mm Hg)	67 (10)	66 (6)	0.001
Mean (SD) gestational age at enrolment (weeks)	17.4 (2.6)	17.5 (2.3)	0.91
Current smoker	11 (8%)	22 (12%)	0.83

Table 1

Characteristics of women with pre-eclampsia and controls at enrolment in Calcium for Pre-eclampsia Prevention trial and characteristics of their infants and specimens\*. Values are numbers (percentages) unless stated otherwise

With one exception the characteristics of the 141 women with pre-eclampsia and their infants from the Calcium for Pre-eclampsia Prevention trial included in this study (table 1) did not differ significantly from those of the 185 women with pre-eclampsia and their infants who had not been included owing to lack of specimens: infants of the women who had been included were more often delivered preterm (28% v 16%, *P*=0.006).

*Thyroid function tests and pre-eclampsia*

The mean values of thyroid function tests at baseline were not significantly different (table 2). However, after the onset of pre-eclampsia, concentrations of thyroid stimulating hormone and human chorionic gonadotrophin were higher in cases than in controls. The magnitude of the increase in thyroid stimulating hormone concentration from baseline to predelivery (predelivery to baseline ratio) was greater in cases than in controls (table 2); case ratio to control ratio 1.64 (95% confidence interval 1.29 to 2.08). Compared with baseline specimens, levels of free triiodothyronine were lower in predelivery specimens, and the magnitude of the decrease was significantly greater in cases than in controls (predelivery to baseline ratio 0.85 v 0.89, case ratio to control ratio 0.96, 0.92 to 0.99). Although free thyroxine concentrations were also lower in predelivery specimens than in baseline specimens, the decrease was similar between cases and controls.

Table 2  
Results of thyroid function test in baseline and predelivery specimens and predelivery to baseline ratio in cases and controls. Values are geometric means (standard deviations) unless stated otherwise

	Baseline		Predelivery		Ratio	
Variable	Controls	Cases	Controls	Cases	Controls	Cases
No. of women	140	140	140	140		
Thyroid stimulating hormone (mIU/l)	1.12 (0.55)	1.17 (0.60)	2.00 (1.14)	2.52 (1.55)	1.78 (1.29)	2.14 (1.64)
Free triiodothyronine (pmol/l)	3.20 (0.50)	3.15 (0.48)	2.85 (0.45)	2.75 (0.42)	0.89 (0.92)	0.85 (0.96)
Free thyroxine (pmol/l)	12.5 (2.5)	12.2 (2.4)	11.5 (2.2)	11.0 (2.1)	0.92 (0.98)	0.88 (0.94)

**Table 2**

Results of thyroid function test in baseline and predelivery specimens and predelivery to baseline ratio in cases and controls. Values are geometric means (standard deviations) unless stated otherwise

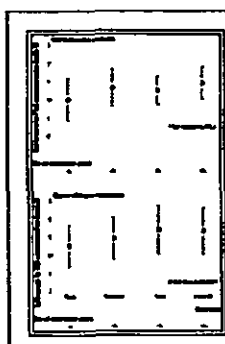
The distribution of test results for thyroid function among cases and controls at baseline and before delivery was examined in relation to the gestational age specific reference ranges for pregnant women. This was done to determine whether subgroups of the women who developed pre-eclampsia might have concentrations of thyroid hormones indicating the potential for clinically significant thyroid malfunction. Only the distributions of thyroid stimulating hormone concentration were significantly different between cases and controls. At baseline the proportion of women with thyroid stimulating hormone concentrations above the reference range did not differ between women who would later develop pre-eclampsia and controls (2% and 3%, respectively,  $P=0.28$  after adjustment for age, body mass index, race, smoking, logarithmically transformed human chorionic gonadotrophin concentration, and the presence or absence of thyroid peroxidase antibodies). However, before delivery the proportion with thyroid stimulating hormone concentrations above the reference range was greater in the women with pre-eclampsia than in the controls: 24% of cases and 14% of controls (arithmetic means 4.47 mIU/l and 4.26 mIU/l) had thyroid stimulating hormone concentrations above the reference range (adjusted  $P=0.03$ ). In predelivery specimens, but not at baseline, women with pre-eclampsia were significantly more likely than controls to have concentrations of thyroid stimulating hormone above the reference range (adjusted odds ratio 2.2, 95% confidence interval 1.1 to 4.4).

Of the 140 women with subsequent pre-eclampsia and 140 controls tested for thyroid peroxidase antibodies at baseline, six (4%) in each group had positive results—that is, had levels above the reference range. In predelivery specimens, seven (5%) cases and four (3%) controls had positive results. The distributions of women with thyroid peroxidase antibodies above the upper limit of the reference range did not differ significantly between the women who developed pre-eclampsia and the normotensive controls.

At baseline none of the women had clinical hypothyroidism as defined by thyroid stimulating hormone concentration above the reference range and free thyroxine below. However, in predelivery specimens two women had developed clinical hypothyroidism (thyroid stimulating hormone 5.46 and 7.33 mIU/l and free thyroxine 8.0 and 8.2 pmol/l), both after the onset of pre-eclampsia.

### *Differences in thyroid stimulating hormone concentrations across quarters of soluble fms-like tyrosine kinase 1 concentrations*

To investigate mechanisms by which pre-eclampsia may be associated with the development of hypothyroidism, the differences between predelivery and baseline values of thyroid function tests were examined according to quarters of soluble fms-like tyrosine kinase 1 concentrations in the predelivery specimens. Cases and controls were analysed separately. Among controls the increase in thyroid stimulating hormone concentration between baseline and predelivery specimens was strongly associated ( $P$  for trend  $<0.001$ ) with increasing quarters of predelivery soluble fms-like tyrosine kinase 1 concentration: arithmetic means 0.01 (SD 1.14) mIU/l, 0.66 (1.04), 0.52 (0.75), and 0.92 (0.91), respectively (figure). The arithmetic mean of the difference in free thyroxine concentration between predelivery and baseline specimens was greater in the fourth quarter than in the first quarter ( $-2.70$  v  $-1.67$  pmol/l,  $P=0.03$ ); but the test for trend was not significant. None of the other differences in thyroid function test results or the differences in human chorionic gonadotrophin concentration were associated with quarters of soluble fms-like tyrosine kinase 1 in predelivery specimens.



Comparisons of differences in thyroid stimulating hormone (TSH) concentration between predelivery and baseline specimens across quarters of predelivery soluble fms-like tyrosine kinase 1 concentrations in normotensive controls and cases with pre-eclampsia (more ...)

Among the cases with pre-eclampsia, the increase in thyroid stimulating hormone concentration between baseline and predelivery specimens was also strongly associated ( $P$  for trend 0.002) with increasing quarters of predelivery soluble fms-like tyrosine kinase: arithmetic means, respectively, 0.51 (SD 1.12) mIU/l, 0.94 (1.13) mIU/l, 1.41 (1.32) mIU/l, and 1.33 (1.29) mIU/l. Compared with controls, the increase in the pre-eclampsia group was consistently greater in each corresponding quarter. Differences between predelivery and baseline specimens for the other thyroid function tests and for human chorionic gonadotrophin were not associated with quarters of soluble fms-like tyrosine kinase 1 concentration in predelivery specimens.

### **Nord-Trøndelag Health Study**

#### *Participants and specimens*

Between 1995 and 1997 all inhabitants 20 years and older in Nord-Trøndelag county in Norway were invited to participate in the Nord-Trøndelag Health Study (HUNT-2).<sup>22</sup> Nord-Trøndelag county is characterised by a stable and ethnically homogeneous population, which is generally considered to have adequate iodine intake. A total of 92 936 adults were eligible for the study, and 66 140 (71.2%) participated. The study has been described in detail elsewhere.<sup>22 23</sup> A non-fasting venous blood sample was requested from each participant. Thyroid stimulating hormone concentrations were determined in samples of the study population and included all women older than 40 years and a 5% random sample of women aged 20–40.

#### *Linkage to medical birth registry of Norway*

The unique 11 digit identification number of every Norwegian citizen enabled linkage of parous women to information in the medical birth registry of Norway. This nationwide registry has recorded data on all

births in Norway since 1967. We therefore restricted the analysis to women who had had their first birth registered during the period from 1967 until participation in the Nord-Trøndelag Health Study. Among women with a measurement for thyroid stimulating hormone concentration, 7933 had had their first birth in 1967 or later. We excluded women with known thyroid disease ( $n=695$ ), twin or triplet first pregnancies ( $n=74$ ), pregnancy at the time thyroid stimulating hormone concentration was determined ( $n=33$ ), and women without information on smoking habits ( $n=10$ ), leaving 7121 women for analysis. Thyroid peroxidase antibodies were also measured in women with a thyroid stimulating hormone concentration greater than 4 mIU/l.

Criteria for pre-eclampsia used by the reporting midwives and obstetricians have been in accordance with the 1972 recommendations of the American College of Obstetrics and Gynecologists.<sup>24</sup> These criteria include increased blood pressure after 20 weeks' gestation ( $\geq 140/90$  mm Hg, or an increase in systolic blood pressure of  $\geq 30$  mm Hg or in diastolic blood pressure of  $\geq 15$  mm Hg), from measurements made before 20 weeks' gestation, and proteinuria ( $\geq 0.3$  g in a 24 hour urine specimen or a urine dipstick result of  $\geq +$ ).

### Procedures

Serum concentrations of thyroid stimulating hormone were measured at the Hormone Laboratory, Aker University Hospital, Oslo, using DELFIA hTSH Ultra (Wallac Oy, Turku, Finland). The coefficient of variation was less than 5%. The clinical reference range for thyroid stimulating hormone in this population was defined as 0.50–3.50 mIU/l.<sup>25</sup> Thyroid peroxidase antibodies were also measured in people with concentrations of thyroid stimulating hormone greater than 4 mIU/l (BRAHMS Diagnostica, Berlin, Germany). Those with levels greater than 200 IU/ml were considered to have tested positive for thyroid peroxidase antibodies.

### Statistical analysis

We used multiple logistic regression analysis to determine odds ratios and 95% confidence intervals. All analyses were adjusted for age and smoking status (current, former, or never).

### Results

Analyses were carried out among 7121 women with thyroid stimulating hormone measurements who had delivered their first child during or after 1967, when the medical birth registry of Norway was established (table 3). Among women who had experienced pre-eclampsia in their first pregnancy the probability of having serum thyroid stimulating hormone concentrations greater than the clinical reference range ( $>3.5$  mIU/l) was higher than for women who did not develop pre-eclampsia in their first pregnancy (adjusted odds ratio 1.7, 95% confidence interval 1.1 to 2.5). The mean number of years elapsed from delivery of the first pregnancy to the date of the thyroid stimulating hormone measurement was 20.4 among the women with pre-eclampsia in that pregnancy and 21.8 years among the women without pre-eclampsia in that pregnancy.

Table 3

Odds ratios for thyroid stimulating hormone (TSH) concentrations above the reference range ( $>3.5$  mIU/l) and for high TSH concentrations ( $\geq 4.0$  mIU/l) with positive ( $>200$  IU/ml) or negative ( $\leq 200$  IU/ml) results for thyroid peroxidase antibodies (TPA) in women who had experienced pre-eclampsia in their first pregnancy.

Variables	TSH concentration $>3.5$ mIU/l		TSH concentration $\geq 4.0$ mIU/l		TSH $\geq 4.0$ mIU/l with positive TPA
	Number	Odds ratio (95% CI)	Number	Odds ratio (95% CI)	
Pre-eclampsia	10	1.7 (1.1 to 2.5)	10	1.7 (1.1 to 2.5)	10
No pre-eclampsia	10	1.0	10	1.0	10

Table 3

Odds ratios for thyroid stimulating hormone (TSH) concentrations above the reference range ( $>3.5$  mIU/l), and for high TSH concentrations ( $\geq 4.0$  mIU/l) with positive ( $>200$  IU/ml) or negative ( $\leq 200$  IU/ml) results (more ...)

Thyroid peroxidase antibodies were also measured in women with thyroid stimulating hormone concentrations greater than 4.0 mIU/l. The association of pre-eclampsia with subsequent hypothyroid function (thyroid stimulating hormone >4.0 mIU/l) was slightly stronger in the absence of thyroid peroxidase antibodies (adjusted odds ratio 2.6, 95% confidence interval 1.3 to 5.0) than for hypothyroid function with thyroid peroxidase antibodies (1.8, 1.0 to 3.1; table 3). Among women who had experienced pre-eclampsia in two pregnancies, the association with hypothyroid function in the absence of thyroid peroxidase antibodies was particularly strong (5.8, 1.3 to 25.5).

### Discussion

This study found that pre-eclampsia among nulliparous women is associated with a greater subsequent risk of subclinical hypothyroidism in pregnancy and that women with a history of pre-eclampsia are at greater risk of hypothyroid function many years after pre-eclampsia.

The findings during pregnancy are consistent with the results of previous studies<sup>26 27 28</sup> and indicate that the increases in thyroid stimulating hormone concentration during pre-eclampsia are not related to changes in circulating human chorionic gonadotrophin concentrations, a protein that stimulates the thyroid gland and suppresses thyroid stimulating hormone.<sup>19</sup> In women with pre-eclampsia, but also in normotensive controls, the extent of increase in thyroid stimulating hormone during pregnancy was directly related to the magnitude of circulating soluble fms-like tyrosine kinase 1 concentrations before delivery. This increase was substantially greater in the pre-eclampsia group, consistent with the suggestion that the effect of pre-eclampsia on thyroid function may be mediated by soluble fms-like tyrosine kinase 1.

Norwegian women who had experienced pre-eclampsia in their first pregnancy were more likely than other women to have concentrations of thyroid stimulating hormone above the clinical reference range many years after the pregnancy. The association was stronger if the high concentration of thyroid stimulating hormone was combined with absence of thyroid peroxidase antibodies, and particularly strong if pre-eclampsia had occurred in two pregnancies. This suggests that the hypothyroid function associated with increased circulating concentrations of thyroid stimulating hormone in pre-eclampsia may occur independent of the autoimmune mechanisms that are generally accepted as the most likely cause of subclinical and overt hypothyroidism in iodine replete women.<sup>29 30</sup>

The clinical syndrome of pre-eclampsia has been hypothesised to result from excessive release of antiangiogenic proteins—most notably soluble fms-like tyrosine kinase 1—from the placenta into maternal blood, resulting in an antiangiogenic state with low levels of free placental growth factor and free vascular endothelial growth factor.<sup>6 31</sup> Administration of vascular endothelial growth factor inhibitors such as soluble fms-like tyrosine kinase 1 to rodents induces hypertension, proteinuria, and glomerular endotheliosis, the hallmarks of pre-eclampsia. The particular sensitivity of glomerular capillaries to reduced levels of vascular endothelial growth factor may be attributed to their fenestrated endothelium, which requires the constitutive expression of vascular endothelial growth factor by renal podocytes for health and function.<sup>32</sup> Thyroid capillaries also have a fenestrated endothelium.<sup>15</sup> In mice, two weeks' exposure to exogenous soluble fms-like tyrosine kinase 1 or to other vascular endothelial growth factor inhibitors resulted in a reduction of thyroid tissue capillary density by two thirds and increased thyroid stimulating hormone concentration. Stopping soluble fms-like tyrosine kinase 1 from being administered led to a nearly complete recovery after three weeks.<sup>15</sup> This seems to be analogous to the recovery from hypertension and proteinuria in experimental animals after stopping inhibition of vascular endothelial growth factor and in women with pre-eclampsia after delivery of the placenta.<sup>7 10</sup> Together with reports of hypothyroidism in patients with cancer treated with vascular endothelial growth factor receptor inhibitors,<sup>11 12 13 14 15</sup> the evidence suggests that high levels of exposure to soluble fms-like tyrosine



kinase 1 as in pre-eclampsia may be associated with increased risk for reduced thyroid function during and after pregnancy.

As women with subclinical thyroid dysfunction are at greater risk of progression to overt hypothyroidism,<sup>33</sup> our findings could have important implications for the subsequent care of women with pre-eclampsia. Not only should they be followed closely for the development of cardiovascular and renal disease and the amelioration of predisposing risk factors, but consideration should also be given to monitoring for the development of reduced thyroid function and clinically important hypothyroidism. Although the absolute risk for reduced thyroid function and the future development of hypothyroidism in these women seems to be low, the availability of low cost thyroxine replacement therapy makes early treatment of hypothyroidism an attractive option that may substantially reduce the associated morbidity and improve quality of life. Moreover, untreated hypothyroidism may be a modifiable risk factor for cardiovascular disease; and its treatment might prevent early cardiovascular disease in women with a history of pre-eclampsia.<sup>23</sup>

Our study raises several questions: Is there a contribution of hypothyroid function to the excess of cardiovascular disease in women with a history of pre-eclampsia? Does subclinical hypothyroidism in women with pre-eclampsia have adverse effects on the long term health of the children?<sup>34 35</sup> Does the risk of subclinical and overt hypothyroidism in women with pre-eclampsia increase with time elapsed after pregnancy? Are women who have had multiple normal pregnancies or pregnancies with multiple fetuses at greater risk of hypothyroidism because of the increased levels of soluble fms-like tyrosine kinase 1 in pregnancies with multiple fetuses and in normal pregnancies at term? The latter possibility is supported by our finding that soluble fms-like tyrosine kinase 1 concentration is positively associated with thyroid stimulating hormone concentration in normotensive pregnancies as well.

In summary, increased circulating concentrations of soluble fms-like tyrosine kinase 1, most notably after onset of pre-eclampsia, were associated with subtle abnormalities of the thyroid during pregnancy. These in turn may predispose to the development of reduced thyroid function and possibly overt hypothyroidism in later life.

#### **What is already known on this topic**

Limited data suggest that pre-eclampsia may be associated with hypothyroid function during pregnancy

Women with a history of pre-eclampsia are at increased risk of future cardiovascular and renal disease

#### **What this study adds**

Hypothyroid function during pre-eclampsia may result from the antiangiogenic state

Women with a history of pre-eclampsia may be at increased risk of future hypothyroid function

#### **Notes**

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Ethical approval: Because the study used specimens that had been collected as part of the Calcium for Pre-eclampsia trial and could not be linked to identifiable women, the Office of Human Subjects Research of the National Institutes of Health granted an exemption from the requirement for review and approval by the institutional review board. Use of the Nord-Trøndelag Health Study and Norwegian birth registry was approved by the Norwegian regional committee for medical research ethics and by the Norwegian Data Inspectorate.

## Notes

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## References

1. Redman CW, Sargent IL. Latest advances in understanding preeclampsia. *Science* 2005;308:1592-4. [PubMed]
2. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. *Lancet* 2005;365:785-99. [PubMed]
3. Hubel CA, Snaedal S, Ness RB, Weissfeld LA, Geirsson RT, Roberts JM, et al. Dyslipoproteinaemia in postmenopausal women with a history of eclampsia. *Br J Obstet Gynaecol* 2000;107:776-84.
4. Sibai BM, el-Nazer A, Gonzalez-Ruiz A. Severe preeclampsia-eclampsia in young primigravid women: subsequent pregnancy outcome and remote prognosis. *Am J Obstet Gynecol* 1986;155:1011-6. [PubMed]
5. Irgens HU, Reisaeter L, Irgens LM, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. *BMJ* 2001;323:1213-7. [PMC free article] [PubMed]
6. Vikse BE, Irgens LM, Leivestad T, Skjaerven R, Iversen BM. Preeclampsia and the risk of end-stage renal disease. *N Engl J Med* 2008;359:800-9. [PubMed]

7. Maynard SE, Min JY, Merchan J, Lim KH, Li J, Mondal S, et al. Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. *J Clin Invest* 2003;111:649-58. [PMC free article] [PubMed]
8. Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, et al. Circulating angiogenic factors and the risk of preeclampsia. *N Engl J Med* 2004;350:672-83. [PubMed]
9. Chaiworapongsa T, Romero R, Espinoza J, Bujold E, Mee Kim Y, Goncalves LF, et al. Evidence supporting a role for blockade of the vascular endothelial growth factor system in the pathophysiology of preeclampsia. Young investigator award. *Am J Obstet Gynecol* 2004;190:1541-7. [PubMed]
10. Eremina V, Jefferson JA, Kowalewska J, Hochster H, Haas M, Weisstuch J, et al. VEGF inhibition and renal thrombotic microangiopathy. *N Engl J Med* 2008;358:1129-36. [PMC free article] [PubMed]
11. Kamba T, McDonald DM. Mechanisms of adverse effects of anti-VEGF therapy for cancer. *Br J Cancer* 2007;96:1788-95. [PMC free article] [PubMed]
12. Desai J, Yassa L, Marqusee E, George S, Frates MC, Chen MH, et al. Hypothyroidism after sunitinib treatment for patients with gastrointestinal stromal tumors. *Ann Intern Med* 2006;145:660-4. [PubMed]
13. Wolter P, Stefan C, Decallonne B, Dumez H, Bex M, Carmeliet P, et al. The clinical implications of sunitinib-induced hypothyroidism: a prospective evaluation. *Br J Cancer* 2008;99:448-54. [PMC free article] [PubMed]
14. Feldman DR, Baum MS, Ginsberg MS, Hassoun H, Flombaum CD, Velasco S, et al. Phase I trial of bevacizumab plus escalated doses of sunitinib in patients with metastatic renal cell carcinoma. *J Clin Oncol* 2009;27:1432-9. [PubMed]
15. Kamba T, Tam BY, Hashizume H, Haskell A, Sennino B, Mancuso MR, et al. VEGF-dependent plasticity of fenestrated capillaries in the normal adult microvasculature. *Am J Physiol Heart Circ Physiol* 2006;290:H560-76. [PubMed]
16. Levine RJ, Esterlitz JR, Raymond EG, DerSimonian R, Hauth JC, Curet LB, et al. Trial of calcium for preeclampsia prevention (CPEP): rationale, design, and methods. *Control Clin Trials* 1996;17:442-69. [PubMed]
17. Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, et al. Trial of calcium to prevent preeclampsia. *N Engl J Med* 1997;337:69-76. [PubMed]
18. Holston AM, Qian C, Karumanchi SA, Yu KF, Levine RJ. Circulating angiogenic factors in gestational proteinuria without hypertension. *Am J Obstet Gynecol* 2009;200:392e1-10. [PMC free article] [PubMed]
19. Burrow GN, Fisher DA, Larsen PR. Maternal and fetal thyroid function. *N Engl J Med* 1994;331:1072-8. [PubMed]
20. Roche Diagnostics. Reference intervals for children and adults. In: *Elecsys thyroid tests* Mannheim, Germany: Roche Diagnostics, 2004:5.
21. Zhang J, Bowes WA Jr. Birth-weight-for-gestational-age patterns by race, sex, and parity in the United States population. *Obstet Gynecol* 1995;86:200-8. [PubMed]
22. Holmen J, Midtjell K, Kruger O, Langhammer A, Holmen TL, Bratberg GH, et al. The Nord-Trøndelag Health Study 1995-97 (HUNT 2): objectives, contents, methods and participation. *Norsk Epidemiol* 2003;13:19-32.
23. Asvold BO, Bjoro T, Nilsen TI, Gunnell D, Vatten LJ. Thyrotropin levels and risk of fatal coronary heart disease: the HUNT study. *Arch Intern Med* 2008;168:855-60. [PubMed]
24. National High Blood Pressure Education Program Working Group. Report on high blood pressure in pregnancy. *Am J Obstet Gynecol* 1990;163:1691-712. [PubMed]
25. Bjoro T, Holmen J, Kruger O, Midtjell K, Hunstad K, Schreiner T, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population: the Health Study of Nord-Trøndelag (HUNT). *Eur J Endocrinol* 2000;143:639-47. [PubMed]
26. Larijani B, Marsoosi V, Aghakhani S, Moradi A, Hashemipour S. Thyroid hormone alteration in pre-eclamptic women. *Gynecol Endocrinol* 2004;18:97-100. [PubMed]
27. Lao TT, Chin RK, Swaminathan R, Lam YM. Maternal thyroid hormones and outcome of pre-eclamptic pregnancies. *Br J Obstet Gynaecol* 1990;97:71-4. [PubMed]

28. Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, et al. Maternal thyroid hypofunction and pregnancy outcome. *Obstet Gynecol* 2008;112:85-92. [PubMed]
29. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2002;87:489-89. [PubMed]
30. Roberts CG, Ladenson PW. Hypothyroidism. *Lancet* 2004;363:793-803. [PubMed]
31. Maynard S, Epstein FH, Kanumanchi SA. Preeclampsia and angiogenic imbalance. *Annu Rev Med* 2008;59:61-78. [PubMed]
32. Risau W. Development and differentiation of endothelium. *Kidney Int* 1998;67:S3-6.
33. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocr Rev* 2008;29:76-131. [PubMed]
34. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, et al. Subclinical hypothyroidism and pregnancy outcomes. *Obstet Gynecol* 2005;105:239-45. [PubMed]
35. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 1999;341:549-55. [PubMed]

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### Subclinical hypothyroidism and the risk of coronary heart disease and mortality.

Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, Asvold BO, Iervasi G, Imaizumi M, Collet TH, Bremner A, Maisonneuve P, Sgarbi JA, Khaw KT, Vanderpump MP, Newman AB, Comuz J, Franklyn JA, Westendorp RG, Vittinghoff E, Gussekloo J; Thyroid Studies Collaboration.

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#### Abstract

**CONTEXT:** Data regarding the association between subclinical hypothyroidism and cardiovascular disease outcomes are conflicting among large prospective cohort studies. This might reflect differences in participants' age, sex, thyroid-stimulating hormone (TSH) levels, or preexisting cardiovascular disease.

**OBJECTIVE:** To assess the risks of coronary heart disease (CHD) and total mortality for adults with subclinical hypothyroidism.

**DATA SOURCES AND STUDY SELECTION:** The databases of MEDLINE and EMBASE (1950 to May 31, 2010) were searched without language restrictions for prospective cohort studies with baseline thyroid function and subsequent CHD events, CHD mortality, and total mortality. The reference lists of retrieved articles also were searched.

**DATA EXTRACTION:** Individual data on 55,287 participants with 542,494 person-years of follow-up between 1972 and 2007 were supplied from 11 prospective cohorts in the United States, Europe, Australia, Brazil, and Japan. The risk of CHD events was examined in 25,977 participants from 7 cohorts with available data. Euthyroidism was defined as a TSH level of 0.50 to 4.49 mIU/L. Subclinical hypothyroidism was defined as a TSH level of 4.5 to 19.9 mIU/L with normal thyroxine concentrations.

**RESULTS:** Among 55,287 adults, 3450 had subclinical hypothyroidism (6.2%) and 51,837 had euthyroidism. During follow-up, 9664 participants died (2168 of CHD), and 4470 participants had CHD events (among 7 studies). The risk of CHD events and CHD mortality increased with higher TSH concentrations. In age- and sex-adjusted analyses, the hazard ratio (HR) for CHD events was 1.00 (95% confidence interval [CI], 0.86-1.18) for a TSH level of 4.5 to 6.9 mIU/L (20.3 vs 20.3/1000 person-years for participants with euthyroidism), 1.17 (95% CI, 0.96-1.43) for a TSH level of 7.0 to 9.9 mIU/L (23.8/1000 person-years), and 1.89 (95% CI, 1.28-2.80) for a TSH level of 10 to 19.9 mIU/L (n = 70 events/235; 38.4/1000 person-years;  $P < .001$  for trend). The corresponding HRs for CHD mortality were 1.09 (95% CI, 0.91-1.30; 5.3 vs 4.9/1000 person-years for participants with euthyroidism), 1.42 (95% CI, 1.03-1.95; 6.9/1000 person-years), and 1.58 (95% CI, 1.10-2.27, n = 28 deaths/333; 7.7/1000 person-years;  $P = .005$  for trend). Total mortality was not increased among participants with subclinical hypothyroidism. Results were similar after further adjustment for traditional cardiovascular risk factors. Risks did not significantly differ by age, sex, or preexisting cardiovascular disease.

**CONCLUSIONS:** Subclinical hypothyroidism is associated with an increased risk of CHD events and CHD mortality in those with higher TSH levels, particularly in those with a TSH concentration of 10 mIU/L or greater.

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### **Cardiovascular consequences of subclinical hyper- and hypothyroidism**

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#### **Introduction**

Subclinical thyroid dysfunctions are defined by normal free-triiodothyronine (FT3) and free-thyroxine (FT4) concentrations in the presence of abnormal TSH, which is low-undetectable in subclinical hyperthyroidism (SH) and increased in subclinical hypothyroidism (Sh).

The clinical significance of subclinical thyroid dysfunction is much debated (1-3). The presence of tissue effects, symptoms and signs of mild thyroid hormone excess or deficiency and the management and treatment of these conditions are controversial issues. Similarly, the TSH cut-off point that determines the effects of subclinical thyroid dysfunction remains to be established.

The cardiovascular system, which is a major target of thyroid hormone, is sensitive to the effects of thyroid hormone excess or deficiency at the tissue level. Many symptoms and signs in patients with overt hypo- or hyperthyroidism are related to the reduced or increased action of thyroid hormone on cardiac function. Triiodothyronine (T3) affects the heart and vascular system through genomic and non-genomic mechanisms; it influences heart rate, systolic and diastolic function and systemic vascular resistance, and hence cardiac performance (4,5).

In human overt hyperthyroidism, the increase in left ventricular performance is predominantly sustained by the increased preload that results in enhanced left ventricular diastolic function (6,7). The reduced systemic vascular resistance, coupled with increased venous return and preload, enhances cardiac output (6,7). The decreased cardiac output in hypothyroid patients at rest depends largely on altered diastolic relaxation and hemodynamic loading (5,8). The reduced cardiac preload, combined with bradycardia and slightly depressed myocardial contractility, accounts for a subnormal cardiac output in overt hypothyroidism, whereas peripheral vascular resistance is remarkably increased (4,5,8). Moreover, cardiovascular alterations have been found in individuals with subclinical thyroid disease (9). This review covers the data about the progression of subclinical thyroid dysfunctions and cardiovascular risk. It also deals with the cardiovascular risk and the need for treatment as estimated from epidemiological data on cardiovascular morbidity and mortality.

#### **Subclinical hyperthyroidism**

##### **Causes, prevalence and progression**

The reported overall prevalence of SH ranges between 0.5 and 6.3%, the prevalence being higher in patients over 65 years. The prevalence can differ in relation to iodine intake and the TSH cut-off point used for diagnosis (10,11).

Subclinical hyperthyroidism may be caused by exogenous or endogenous factors. The exogenous form is usually related to TSH-suppressive therapy with L-thyroxine for the treatment of benign thyroid disease and differentiated thyroid carcinoma. The endogenous form is usually related to the same causes as overt thyrotoxicosis subsequent to autonomously functioning thyroid adenomas, and multinodular goitre. TSH suppressive or unintentional over-replacement L-thyroxine therapy was the most common form of SH (20.7%) among subjects taking L-thyroxine in the Colorado study (11), whereas endogenous factors accounted for a minority of cases and prevailed in areas of iodine insufficiency (12). Endogenous SH is usually a slowly progressive disorder and may last several years before developing into overt thyrotoxicosis. The risk of SH

progressing to overt hyperthyroidism varies between 2% and 7% per year in patients with undetectable TSH (12). Unfortunately, there are no data on the progression of SH in patients with TSH between 0.1-0.5 mU/L.

#### **Cardiovascular risk**

Exogenous and endogenous SH may lead to signs and symptoms of thyroid hormone excess thereby mimicking adrenergic overactivity and impairing quality of life (12, 13). Subclinical hyperthyroidism affects the cardiovascular system in various ways, and its increased cardiovascular risk is well documented in the elderly (14,15). *The cardiovascular abnormalities are similar in stable endogenous and exogenous SH (12)*

**Table 1**

#### **Potential cardiac effects of subclinical hyperthyroidism**

- Increased heart rate
- Increased prevalence of atrial arrhythmias
- Increased systolic function at rest
- Increased left ventricular mass
- Impaired diastolic function
- Systolic dysfunction during effort

The major cardiovascular findings in patients with SH coupled with undetectable TSH are a higher heart rate and a higher risk of supraventricular arrhythmias (15-17). The most consistent cardiac abnormality is a significant increase in left ventricular mass with unchanged or increased at-rest systolic function and, usually, impaired diastolic function (16,18-20). Moreover, reduced systolic performance on effort and decreased exercise tolerance has been reported in patients with SH who had a greater increase in left ventricular mass (21). Thyroid hormone-induced hypertrophy in SH is due primarily to the cardiac response induced by the increased cardiac workload. This is accordance with cardiac hypertrophy induced in rats by thyroid hormone excess (22). Moreover, the significant increase in left ventricular mass with a tendency towards LV concentric remodelling reported in patients with long-standing SH (16,18,19) may counteract the favourable effect acutely exerted by thyroid hormone on diastolic performance, and so lead to impaired ventricular relaxation and systolic dysfunction during effort (20,21). The altered passive elasticity of the ventricle (chamber stiffness) determined by the presence of myocardial hypertrophy is the major determinant of diastolic dysfunction in patients with SH.

The prognostic significance of these cardiovascular alterations in patients with SH remains to be clarified especially in young and middle-aged patients with low TSH. Unfortunately, there is no study of the effects on cardiovascular system of minimally suppressed TSH (i.e., TSH between 0.1-0.4 mU/L). However, the increase in heart rate and in left ventricular mass usually precedes the onset of more severe cardiovascular disease, and is an independent risk factor for increased cardiovascular morbidity and mortality in the general population (23).

The detrimental effects of SH are well documented in the elderly and atrial fibrillation represents an important cardiovascular risk. The Framingham study evaluated the risk of atrial fibrillation during the 10-year follow-up in 2007 people aged 60 years or older with endogenous or exogenous SH (15). The adjusted relative risk for

atrial fibrillation was 3.1 times higher in the group with serum TSH  $\geq 0.1$  mU/L compared with those with normal TSH concentrations ( $>0.4$ – $5.0$  mU/L). The relative risk of atrial fibrillation was 1.6 times higher in the group with slightly low TSH concentrations ( $0.1$ – $0.4$  mU/L) ( $p=0.04$ ) with an incidence of atrial fibrillation in 16/1000 patients person-years ( $p=0.11$ ) (15). Similarly, in a large retrospective study on hospitalized consecutive older subjects, the relative risk of atrial fibrillation was 5.2 ( $p<0.01$ ) in patients affected by SH with TSH  $<0.4$  mU/L (17). The combination of subclinical hyperthyroidism and age may have deleterious effects on the heart (12,23). Furthermore, the possible onset of overt hyperthyroidism in hearts previously exposed to longstanding untreated SH may further increase the cardiovascular risk (9). This body of data is in agreement with the increased cardiovascular mortality reported in a community-based review of subjects aged 60 years or older with endogenous SH and TSH values  $<0.5$  mU/L monitored for 10 years (14).

In patients with benign thyroid disease and in low-risk patients with differentiated thyroid cancer, cardiovascular parameters and quality of life can be improved by reducing L-T4 dosage to keep TSH at the lower limit of normal range (24). A cardioselective  $\beta$ -blocking drug, in addition to L-thyroxine, can be used in high-risk thyroid cancer patients to attenuate symptoms caused by mild thyroid hormone excess, and to reduce the risk of atrial arrhythmias and an increase in left ventricular mass (12). Methimazole administration and radioiodine therapy may restore euthyroidism and so improve the cardiovascular risk in patients with endogenous SH (25,26).

A panel of experts recently recommended that treatment of endogenous SH should be considered in case of TSH  $<0.1$  mU/L especially when patients are older than 60 years, and if there are symptoms or risk of heart disease (3). The routine treatment of SH if TSH is between 0.1 and 0.4 mU/L is not recommended (3). In fact, despite increased mortality in the elderly, it remains to be established if a subnormal TSH concentration induces the same adverse effects as suppressed TSH on the heart of young and middle-aged patients. However, it is important to stress that the clinical manifestations of 'subclinical' hyperthyroidism may be related to an individual's sensitivity to thyroid hormone excess, which depends on the patient's thyroid function set-point (12), and may be triggered by individual predisposing conditions (12,27).

### **Subclinical hypothyroidism**

#### *Causes, prevalence and progression*

Subclinical hypothyroidism reflects an early and mild form of thyroid failure. Most patients with Sh have chronic autoimmune thyroiditis and test positive for serum antithyroid peroxidase (anti-TPO) antibodies; in these patients, the risk of progression to overt disease is particularly increased. Poor compliance with L-T4 therapy or suboptimal treatment, may also result in Sh. Medications (e.g., lithium, iodine, interferon, etc.), 131I therapy or thyroidectomy and external irradiation of the neck can also cause Sh. The epidemiologic data from three large population-based screening studies (the Whickham Survey, the Colorado Thyroid Disease Prevalence Study and the National Health and Nutrition Examination Survey III) (10,11,28) show that the prevalence of Sh is 4–10% and that this condition increases significantly with age, so that by the ninth decade of life the prevalence is 15%–20%.

A mild TSH increase (between 4–10 mU/L) is present in about 74% of Sh patients, and whether to treat Sh associated with this TSH range is hotly debated. The progression to overt hypothyroidism occurs at a rate of 2–5% per year and it is increased in patients with TSH  $>6$  mU/L and positive thyroid antibodies.

The reasons for treating Sh are: to prevent progression to overt disease, to attenuate symptoms, and to correct lipid profile and cardiovascular abnormalities and so reduce the cardiovascular risk. However, the TSH cut-off at which to start replacement therapy with L-thyroxine is still debated (1–3).

#### *Cardiovascular risk*

The cardiovascular risk in patients with Sh results from changes in cardiovascular function and from



accelerated atherosclerosis (8,9)

**Table 2**

**Subclinical hypothyroidism and cardiovascular risk**

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**Increased risk for functional cardiovascular changes**

- Normal/depressed systolic function at rest
- Left ventricular diastolic dysfunction at rest and during exercise
- Impaired left ventricular systolic function on exercise
- Increased systemic vascular resistance
- Increased prevalence of diastolic heart failure in the elderly

**Increased risk for atherosclerosis**

- Increased prevalence of hypertension
- Endothelial dysfunction
- Atherogenic lipid profile
- Hypofibrinolytic and hypercoagulable state
- Elevated C-reactive protein levels

The most consistent cardiac abnormality in patients with Sh is impaired left ventricular diastolic function, which is characterized by slowed myocardial relaxation and impaired early ventricular filling (9,29). Impaired left ventricular relaxation was identified in patients with Sh by echocardiography and radionuclide ventriculography (30-33). All studies of young and middle-aged patients with a mild and persistent TSH increase (4-10 mU/L) due to Hashimoto thyroiditis show that diastolic dysfunction of the left ventricle is a common finding in patients with persistent Sh (30-33). Diastolic function is impaired both at rest and during exercise (33). Slowed left ventricle relaxation is in accordance with the finding that thyroid hormone affects the calcium-regulating proteins SERCA and PLB thereby slowing down calcium re-uptake into the sarcoplasmic reticulum during diastole (29). Altered diastolic function can be reversed by L-thyroxine replacement therapy (8,9,29-33).

Conflicting results on systolic function are reported in patients with overt and Sh (8). Impaired left ventricular systolic function on effort was documented in patients with Sh by using radionuclide ventriculography, Doppler echocardiography and cardiopulmonary exercise testing (29, 34). The negative effect induced by Sh on systolic function at rest and during effort is reverted by restoring euthyroidism with L-T4 therapy (29-34). Ultrasonic myocardial textural analysis indicates that myocardial composition is altered in patients with Sh (35). Many Sh patients are elderly and the onset or progression of the disease in these vulnerable subjects may precipitate cardiac decompensation and promote congestive diastolic heart failure (5,8).

Overt hypothyroidism is associated with premature atherosclerosis and coronary artery disease. Epidemiological studies of the link between Sh and atherosclerosis have yielded conflicting results (36,37). Compelling evidence of a higher prevalence of atherosclerotic cardiovascular disease in patients with Sh (defined as TSH >4.0 mU/L) emerges from a recent large cross-sectional survey of 1,149 women aged 55 years or more, living in Rotterdam (37). It was shown that Sh patients had a significantly increased age-adjusted prevalence of aortic atherosclerosis on chest radiographs and myocardial infarction compared with

controls. The attributable risk percentage for Sh associated with myocardial infarction was within the range of the traditionally recognized risk factors for coronary artery disease, including hypercholesterolemia, hypertension, smoking and diabetes mellitus. Moreover, in a cross-sectional analysis, Sh was associated with ischemic heart disease independent of age, systolic blood pressure, body mass index, cholesterol, smoking, or presence of diabetes mellitus (38).

The mechanisms responsible for atherosclerosis and coronary artery disease in patients with Sh are controversial (8,39). Diastolic hypertension (40,41), dyslipidemia (42-45), endothelial dysfunction (46), elevated C reactive protein levels (47) and coagulation abnormalities (48) are atherosclerotic risk factors associated with Sh and may be reversed after L-T4-induced euthyroidism.

In a recent review of guidelines, treatment of Sh was recommended when serum TSH is  $>10$  mU/L so as to prevent progression to overt disease (3). Treatment of subclinical hypothyroidism based on cardiovascular risk was not recommended because the data available were considered insufficient and unconvincing (3). Furthermore, routine levo-thyroxine treatment was not recommended when TSH is between 4.5 and 10 mU/L (3).

However, mild hypothyroidism (TSH  $<10$  mU/L) can negatively affect the cardiovascular system, especially diastolic function, endothelial function and systemic vascular resistance. Treatment of this mild form of hypothyroidism may improve cardiovascular function (8, 49) and it may prevent atherosclerosis and coronary artery disease (50) thereby reducing the cardiovascular risk.

## REFERENCES

1. Cooper DS. Clinical practice. Subclinical hypothyroidism. *N Engl J Med* 345: 260-265,2001.
2. McDermott MT, Ridgway EC. Subclinical hypothyroidism is mild thyroid failure and should be treated. *J Clin Endocrinol Metab* 86: 4585-4590,2001.
3. Surks M, Ortiz E, Daniels GH et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA* 291: 228-238,2004.
4. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med* 344:501-509,2001.
5. Fazio S, Palmieri EA, Lombardi G et al. Effects of thyroid hormone on the cardiovascular system. *Recent Prog Horm Res* 59:31-50,2004.
6. Biondi B, Palmieri EA, Lombardi G et al. Effects of thyroid hormone on cardiac function: the relative importance of heart rate, loading conditions, and myocardial contractility in the regulation of cardiac performance in human hyperthyroidism. *J Clin Endocrinol Metab* 87: 968-974,2002.
7. Palmieri EA, Fazio S, Palmieri V et al. Myocardial contractility and total arterial stiffness in patients with overt hyperthyroidism: acute effects of beta1-adrenergic blockade. *Eur J Endocrinol* 150: 757-762,2004.
8. Biondi B, Klein I. Hypothyroidism as a risk factor for cardiovascular disease. *Endocrine* 24: 1-13,2004.
9. Biondi B, Palmieri EA, Lombardi G et al. Effects of subclinical thyroid dysfunction on the heart. *Ann Intern Med* 137: 904-914,2002.
10. Hollowell JG, Staehling NW, Flanders WD et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 87: 489-499,2002.
11. Canaris GJ, Manowitz NR, Mayor G et al. The Colorado thyroid disease prevalence study. *Arch Intern Med* 160: 526-534,2000.
12. Biondi B, Palmieri EA, Klain M et al. Subclinical hyperthyroidism: clinical features and treatment options. *Eur J Endocrinol* in press.
13. Biondi B, Fazio S, Carella C et al. Control of adrenergic overactivity by  $\beta$ -blockade improves quality of life in patients receiving long term suppressive therapy with levothyroxine. *J Clin Endocrinol Metab* 78: 1028-1033,1994.
14. Parle JV, Maisonneuve P, Sheppard MC et al. Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. *Lancet* 358: 861-865,2001.
15. Sawin CT, Geller A, Wolf PA et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. *N Engl J Med* 331:1249-1252,1994.
16. Biondi B, Fazio S, Carella C et al. Cardiac effects of long-term thyrotropin-suppressive therapy with levothyroxine. *J Clin Endocrinol Metab* 77: 334-338,1993.
17. Auer J, Scheibner P, Mische T et al. Subclinical hyperthyroidism as a risk factor for atrial fibrillation. *Am Heart J* 142: 838-842,2001.
18. Biondi B, Fazio S, Palmieri EA et al. Effects of chronic subclinical hyperthyroidism on cardiac morphology

- and function. *Cardiologia* 44: 443-449,1999.
19. Ching GW, Franklyn JA, Stallard TJ et al. Cardiac hypertrophy as a result of long-term thyroxine therapy and thyrotoxicosis. *Heart* 75:363-368,1996.
  20. Fazio S, Biondi B, Carella C et al. Diastolic dysfunction in patients on thyroid-stimulating-hormone suppressive therapy with levothyroxine: beneficial effect of  $\beta$  blockade. *J Clin Endocrinol Metab* 80: 2222-2226,1995.
  21. Biondi B, Fazio S, Cuocolo A et al. Impaired cardiac reserve and exercise capacity in patients receiving long-term thyrotropin suppressive therapy with levothyroxine. *J Clin Endocrinol Metab* 81: 4224-4228,1996.
  22. Klein I, Ojama K, Samarel AM et al. Hemodynamic regulation of myosin heavy chain gene expression. Studies in the transplanted rat heart. *J Clin Invest* 89: 68-73,1992.
  23. Biondi B, Fazio S, Palmieri EA et al. Mortality in elderly patients with subclinical hyperthyroidism. *Lancet* 359: 799-800,2002.
  24. Mercuro G, Panzuto MG, Bina A et al. Cardiac function, physical exercise capacity, and quality of life during long-term thyrotropin-suppressive therapy with levothyroxine: effect of individual dose tailoring. *J Clin Endocrinol Metab* 85:159-164, 2000.
  25. Biondi B, Palmieri EA, Fazio S et al. Endogenous subclinical hyperthyroidism affects quality of life and cardiac morphology and function in young and middle-aged patients. *J Clin Endocrinol Metab* 85: 4701-4705,2000.
  26. Sgarbi JA, Villaca F, Garbeline B et al. The effects of early antithyroid therapy for endogenous subclinical hyperthyroidism on clinical and heart abnormalities. *J Clin Endocrinol Metab* 88: 1672-1677,2003.
  27. Biondi B, Fazio S, Coltorti F et al. Clinical case seminar: Reentrant atrioventricular nodal tachycardia induced by levothyroxine. *J Clin Endocrinol Metab* 83: 2643-2645,1998.
  28. Vanderpump MP, Tunbridge WM, French JM et al. The incidence of thyroid disease in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol(Oxf)* 43: 55-68, 1995.
  29. Biondi B, Palmieri EA, Lombardi G et al. Subclinical hypothyroidism and cardiac function. *Thyroid* 12: 505-510,2002.
  30. Biondi B, Fazio S, Palmieri EA et al. Left ventricular diastolic dysfunction in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab* 84: 2064-2067,1999.
  31. Monzani F, Di Bello V, Caraccio N et al. Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. *J Clin Endocrinol Metab* 86: 1110-1115,2001.
  32. Vitale G, Galderisi M, Lupoli GA et al. Left ventricular myocardial impairment in subclinical hypothyroidism assessed by a new ultrasound tool: pulsed tissue Doppler. *J Clin Endocrinol Metab* 87: 4350-4355,2002.
  33. Brenta G, Mutti LA, Schnitman M et al. Assessment of left ventricular diastolic function by radionuclide ventriculography at rest and exercise in subclinical hypothyroidism, and its response to L-thyroxine therapy. *Am J Cardiol* 91: 1327-1330,2003.
  34. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. *Thyroid* 10: 665-679,2000.
  35. Di Bello V, Monzani F, Giorgi D et al. Ultrasonic myocardial textural analysis in subclinical hypothyroidism. *J Am Soc Echocardiogr* 13: 832-840,2000.
  36. Vanderpump MP, Tunbridge WM, French JM et al. The development of ischemic heart disease in relation to autoimmune thyroid disease in a 20-year follow-up study of an English community. *Thyroid* 6: 155-160, 1996.
  37. Hak AE, Pols HAP, Visser TJ et al. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Ann Intern Med* 132: 270-278, 2000.
  38. Imaizumi M, Akahoshi M, Ichimaru S et al. Risk of ischemic heart disease and all-cause mortality in subclinical hypothyroidism. *J Clin Endocrinol* 89: 3365-3370,2004.
  39. Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. *J Clin Endocrinol Metab* 88: 2438-2444,2003.
  40. Luboshitzky R, Aviv A, Herer P et al. Risk factors for cardiovascular disease in women with subclinical hypothyroidism. *Thyroid* 12: 421-425,2002.
  41. Faber J, Petersen L, Winberg N et al. Hemodynamic changes after levothyroxine treatment in subclinical hypothyroidism. *Thyroid* 12: 319-324,2002.
  42. Duntas LH. Thyroid disease and lipids. *Thyroid* 12: 287-293,2002.
  43. Danese MD, Ladenson PW, Meinert CL et al. Effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. *J Clin Endocrinol Metab* 85: 2993-3001,2000.
  44. Palmieri EA, Fazio S, Lombardi G et al. Subclinical hypothyroidism and cardiovascular risk. A reason to treat? *Treat Endocrinol* 3:233,2004.
  45. Biondi B, Palmieri EA, Lombardi G et al. The importance of using strict inclusion criteria in subclinical hypothyroid studies. *Am J Med* 114:76, 2002.
  46. Taddei S, Caraccio N, Virdis A et al. Impaired endothelium-dependent vasodilatation in subclinical hypothyroidism: beneficial effect of levothyroxine therapy. *J Clin Endocrinol Metab* 88: 3731-3737,2003.
  47. Kvetny J, Heldgaard PE, Bladbjerg EM et al. Subclinical hypothyroidism is associated with a low-grade

inflammation, increased trygliceride levels and predicts cardiovascular disease in males below 50 years. Clin Endocrinol 61: 232-238,2004

48. Christ-Crain M, Meier C, Guglielmetti M et al. Elevated C-reactive protein and homocysteine values: cardiovascular risk factors in hypothyroidism? A cross-sectional and a double-blind, placebo-controlled trial. Atherosclerosis 166: 379-386,2003.
  49. Biondi B, Lombardi G, Palmieri EA. Screening and treatment for subclinical thyroid disease. JAMA 291: 1562-1563, 2004.
  50. Perk M, O'Neill BJ. The effect of thyroid hormone therapy on angiographic coronary artery disease progression. Can J Cardiol 13: 273-276,1997.
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# Prevalence of Subclinical Hypothyroidism in Patients with Chronic Kidney Disease

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**Background and objectives:** Subclinical primary hypothyroidism is highly prevalent in the general population, especially in the elderly. However, the prevalence of subclinical primary hypothyroidism in persons with chronic kidney disease (CKD) not requiring chronic dialysis is not well defined.

**Design, setting, participants, and measurements:** Cross-sectional data from 3089 adult outpatients, who were consecutively referred by general practitioners for routine blood testing over the last two years, were analyzed. Glomerular filtration rate (GFR) was estimated by the abbreviated Modification of Diet in Renal Disease equation. Multivariable logistic regression was used to evaluate the independent association between prevalent subclinical primary hypothyroidism and estimated GFR.

**Results:** Among 3089 adult participants, 293 (9.5%) had subclinical primary hypothyroidism and 277 (9%) had an estimated GFR <60 ml/min per 1.73 m<sup>2</sup>. The prevalence of subclinical primary hypothyroidism increased from 7% at an estimated GFR ≥90 ml/min per 1.73 m<sup>2</sup> to 17.9% at an estimated GFR <60 ml/min per 1.73 m<sup>2</sup> ( $P < 0.0001$  for trend). Compared with participants with an estimated GFR ≥60 ml/min per 1.73 m<sup>2</sup>, those with estimated GFR <60 ml/min per 1.73 m<sup>2</sup> had an increased odds of subclinical primary hypothyroidism after adjusting for age, gender, fasting plasma glucose, total cholesterol, and triglyceride concentrations.

**Conclusions:** These findings suggest that subclinical primary hypothyroidism is a relatively common condition (~18%) among persons with CKD not requiring chronic dialysis, and it is independently associated with progressively lower estimated GFR in a large cohort of unselected outpatient adults.

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The concept of subclinical primary hypothyroidism has emerged over the past several decades, as our ability to detect subtle changes in thyroid function tests is progressively improved (1,2). Although it is recognized that patients with subclinical primary hypothyroidism may have subtle symptoms of thyroid dysfunction, the definition is purely a biochemical one, defined as elevated serum thyrotropin (TSH) levels but normal free thyroxine (FT<sub>4</sub>) levels (3).

Subclinical primary hypothyroidism has been recognized in several studies to be associated with markers of cardiovascular risk and cardiac impairment (4–7). Even minor deviations from serum TSH normal range might accelerate the development of atherosclerosis and have adverse effects on cardiovascular performance in the general population (4–7). Moreover, subclinical primary hypothyroidism has been identified as a strong predictor of all-cause mortality in chronic dialysis patients and as a risk factor for nephropathy and cardiovascular events in type 2 diabetic patients (8,9). There is, however, limited quantitative

evidence regarding the prevalence of subclinical primary hypothyroidism in large samples of individuals, including large non-U.S. cohorts at different levels of estimated glomerular filtration rate (GFR) (10).

To explore this question, we have performed a cross-sectional analysis using a large database from a Clinical Chemistry Laboratory, with the purpose of estimating the prevalence of subclinical primary hypothyroidism at different levels of kidney function.

## Materials and Methods

We performed a cross-sectional analysis on the database of the Laboratory Information System of the Clinical Chemistry Laboratory at the Verona University Hospital to retrieve results of serum creatinine, glucose, lipids, and thyroid function tests, which have been performed on 3233 outpatient adults (≥18 yr of age) consecutively referred by general practitioners for routine blood testing over the last 2 yr (from December 2005 to December 2007). For these analyses, we excluded participants who had abnormal serum FT<sub>4</sub> concentrations ( $n = 144$ ); thus, a sample of 3089 adult participants was included in the final analysis (Figure 1). If a subject had more than one blood test ordered over the 2 yr, only the first result was included in analysis. All participants gave their informed consent. The local ethics committee approved the study protocol.

Venous blood from all outpatients was routinely collected in the morning on fasting subjects, and serum creatinine, glucose, total cho-

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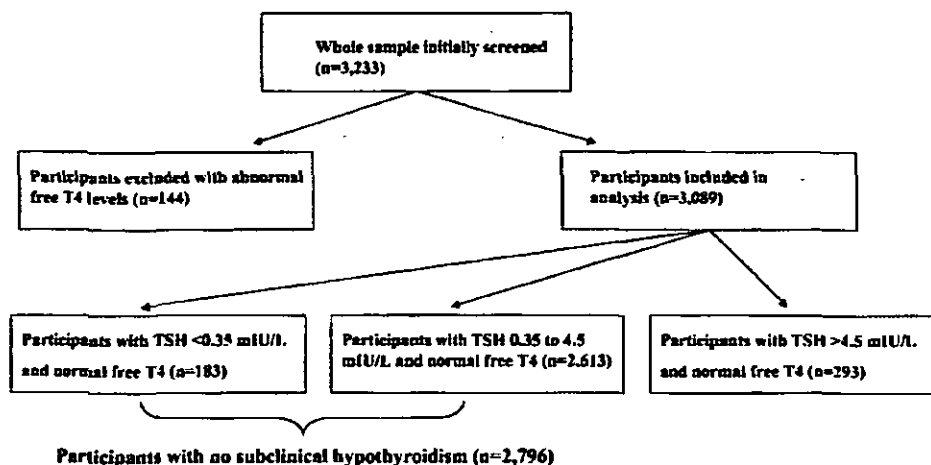


Figure 1. Details of the study design.

lesterol, and triglyceride concentrations were assayed by enzymatic procedures on Roche/Hitachi Modular System (Roche Diagnostics GmbH, Milan, Italy), according to manufacturer's specifications and employing proprietary reagents. Serum TSH and FT<sub>4</sub> concentrations were quantified by two-site, chemiluminescent, immunometric assays on the IMMULITE-2000 analyzer (Diagnostics Products, Los Angeles, CA). Functional sensitivity for TSH and FT<sub>4</sub> was quoted by the manufacturer as 0.004 mIU/L and 0.3 ng/dl, respectively. Reference values in our laboratory were 0.35 to 4.5 mIU/L for TSH and 0.8 to 1.8 ng/dl for FT<sub>4</sub>, respectively. No serum thyroid peroxidase antibody measurements were available.

Kidney function was calculated by using the formula developed and validated in the Modification of Diet in Renal Disease study. The Modification of Diet in Renal Disease formula was as follows: estimated GFR =  $175.0 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \times 1.212$  (if black)  $\times 0.742$  (if female) (11).

### Statistical Analysis

Data are expressed as mean  $\pm$  SD or proportions. Statistical analyses included the unpaired *t* test (for continuous measures) and the  $\chi^2$  test with Yates' correction for continuity (for categorical variables). Skewed variables (triglycerides) were logarithmically transformed to improve normality before analysis. The independent relationship between subclinical primary hypothyroidism (as defined as TSH >4.5 mIU/L with FT<sub>4</sub> levels within the reference range) and chronic kidney disease (CKD) (categorized as estimated GFR <60 ml/min per 1.73 m<sup>2</sup>) was tested by multivariable logistic regression analysis. All known potential confounders (age, gender, plasma glucose, total cholesterol, and triglycerides) were entered in the multivariable model to ensure giving an unbiased estimate for the relation between subclinical hypothyroidism and CKD. *P* values <0.05 were considered to be statistically significant.

### Results

Details of the study design are summarized in Figure 1. After excluding participants with abnormal serum FT<sub>4</sub> concentrations (i.e., those with FT<sub>4</sub> <0.8 or >1.8 ng/dl), cumulative results for main demographic variables, and serum TSH, FT<sub>4</sub>, lipids, creatinine, and glucose concentrations were retrieved for 3089 adults (78.4% female) with a broad spectrum of age (mean age,  $54.9 \pm 16.2$  yr; range, 18 to 94 yr).

In the whole sample, the mean values of estimated GFR, serum TSH, and FT<sub>4</sub> concentrations were  $83.3 \pm 19.5$  ml/min per 1.73 m<sup>2</sup> (range, 8 to 195 ml/min per 1.73 m<sup>2</sup>),  $2.30 \pm 2.79$  mIU/L (range, 0.001 to 47.6 mIU/L), and  $1.3 \pm 0.2$  ng/dl (range, 0.8 to 1.8 ng/dl), respectively. Most participants (*n* = 2613, 84.6%) had serum thyroid function test results within the reference range (i.e., TSH values ranging from 0.35 to 4.5 mIU/L with normal FT<sub>4</sub> levels), whereas 9.5% (*n* = 293) had subclinical biochemical hypothyroidism (i.e., TSH >4.5 mIU/L with normal FT<sub>4</sub> levels), and 5.9% (*n* = 183) had subclinical biochemical hyperthyroidism (i.e., TSH <0.35 mIU/L with normal FT<sub>4</sub> levels). Overall, 277 (9%) subjects had estimated GFR <60 ml/min per 1.73 m<sup>2</sup>, 265 of whom had estimated GFR between 30 and 59 ml/min per 1.73 m<sup>2</sup> and 12 subjects had estimated GFR <30 ml/min per 1.73 m<sup>2</sup>; none of them required chronic dialytic therapy. Most participants (*n* = 1741, 56.4%) had an estimated GFR of 60 to 89 ml/min per 1.73 m<sup>2</sup>, and 34.6% (*n* = 1071) had an estimated GFR >90 ml/min per 1.73 m<sup>2</sup>.

As shown in Table 1, participants with subclinical primary hypothyroidism were likely to be older and had higher values of fasting plasma glucose, total cholesterol, and triglycerides, and lower estimated GFR levels than their counterparts with no subclinical hypothyroidism. As expected, serum TSH levels were higher and FT<sub>4</sub> levels were lower in the hypothyroid group. No significant difference was found in gender distribution between the groups. The prevalence of participants with estimated GFR <60 ml/min per 1.73 m<sup>2</sup> was remarkably greater among those with subclinical hypothyroidism than among those with no hypothyroidism. Almost identical results were observed when participants with low TSH and normal FT<sub>4</sub> levels (*n* = 183) were excluded from the nonhypothyroid group (data not shown).

Conversely, as shown in Figure 2, the prevalence of subclinical primary hypothyroidism was increased in persons with progressively lower kidney function, ranging from 7% for persons with estimated GFR  $\geq 90$  ml/min per 1.73 m<sup>2</sup> to 17.9% in persons with estimated GFR below 60 ml/min per 1.73 m<sup>2</sup>.

Table 1. Characteristics of participants with and without prevalent subclinical hypothyroidism ( $n = 3089$ )

	Subclinical Hypothyroidism ( $n = 293$ )	No Hypothyroidism ( $n = 2796$ )	P
Age (yr)	$57.9 \pm 17.3$	$53.2 \pm 17.5$	$<0.0001$
Women [N (%)]	228 (77.8%)	2179 (77.9%)	0.90
TSH (mIU/L)	$8.19 \pm 5.72$	$1.69 \pm 1.01$	$<0.0001$
Free $T_4$ (ng/dl)	$1.2 \pm 0.2$	$1.3 \pm 0.2$	$<0.0001$
Fasting glucose (mg/dl)	$105 \pm 20$	$92 \pm 16$	$<0.0001$
Total cholesterol (mg/dl)	$209 \pm 50$	$189 \pm 43$	$<0.0001$
Triglycerides (mg/dl)	$124 \pm 89$	$108 \pm 53$	$<0.0001$
Estimated GFR (ml/min per $1.73 \text{ m}^2$ )	$79.7 \pm 40.7$	$86.6 \pm 32.2$	$<0.001$
$\geq 90$	76 (25.9%)	995 (35.6%)	$<0.0001$
60-89	169 (57.8%)	1572 (56.2%)	
30-59	47 (16.0%)	218 (7.8%)	
$<30$	1 (0.3%)	11 (0.4%)	

Values are mean  $\pm$  SD or number or proportions. Differences between groups are assessed by the unpaired  $t$  test (for continuous variables) and the  $\chi^2$  test (for categorical variables). TSH, thyrotropin;  $T_4$ , thyroxine; GFR, glomerular filtration rate.

Notably, when estimated GFR was subdivided into deciles instead of widely accepted diagnostic categories for CKD stages (Figure 3), the prevalence of subclinical primary hypothyroidism was markedly increased among those in the first decile of estimated GFR (mean estimated GFR,  $50.4 \pm 10$  ml/min per  $1.73 \text{ m}^2$ ) compared with those in the highest estimated GFR decile (mean estimated GFR,  $121 \pm 13$  ml/min per  $1.73 \text{ m}^2$ ), *i.e.*, 17.1% and 4.0% in the lowest *versus* highest estimated GFR decile, respectively ( $P < 0.0001$  for trend by the  $\chi^2$  test). Similarly, there was a graded significant decrease in mean serum TSH levels across estimated GFR deciles (range, 2.92 to 1.84 mIU/L;  $P < 0.0001$ ) in the whole population (Figure 3).

In logistic regression analysis (Table 2), the presence of CKD (included as categorical measure and defined as estimated GFR  $<60$  ml/min per  $1.73 \text{ m}^2$ ) was independently associated with prevalent subclinical primary hypothyroidism after adjustment for age, gender, total cholesterol, triglyceride, and glucose concentrations (adjusted odds ratio = 1.73; 95% confidence interval, 1.20 to 2.48;  $P = 0.003$ ). Of note, older age was also independently associated with prevalent subclinical hypo-

thyroidism, whereas sex, fasting plasma glucose, and lipid levels were not.

The results remained essentially unchanged even when estimated GFR was included as a continuous variable in the above regression model (adjusted odds ratio = 1.19, 95% confidence interval, 1.10 to 1.28 per unit decrease in estimated GFR;  $P < 0.001$ ) or when the association between estimated GFR and prevalent subclinical hypothyroidism was examined in subgroups stratified by gender and age ( $<70$  *versus*  $\geq 70$  yr; data not shown).

## Discussion

In this large cohort of unselected adult outpatients, we found an increased prevalence of subclinical primary hypothyroidism in persons with reduced estimated GFR independent of age, gender, fasting plasma glucose, total cholesterol, and triglyceride concentrations. Moreover, with progressively lower estimated GFR, there was a graded increased likelihood of subclin-

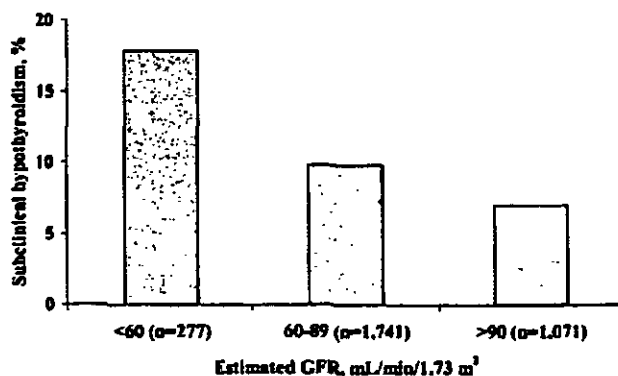


Figure 2. Prevalence of subclinical primary hypothyroidism by level of estimated GFR ( $P < 0.0001$  for trend by the  $\chi^2$  test).

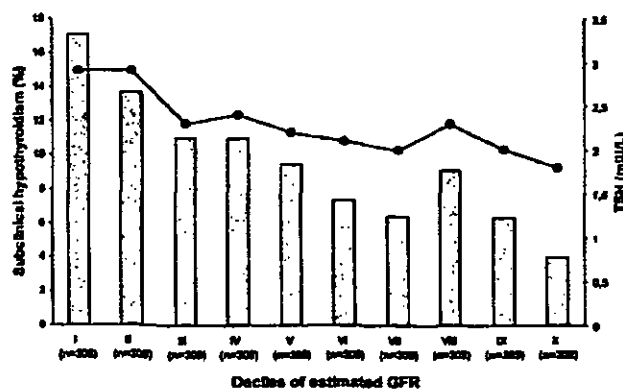


Figure 3. Prevalence of subclinical primary hypothyroidism (columns) and serum thyrotropin levels (line) by deciles of estimated GFR ( $P < 0.0001$  for both trends). Persons in the lowest decile are those with lower values of estimated GFR.

Table 2. Determinants of subclinical hypothyroidism in the whole population as evaluated by multiple logistic regression analysis ( $n = 3089$ )

Independent Variables	Odds Ratio ( $\pm$ 95% CI)	P
Age (per 10 yr)	1.16 (1.06-1.23)	0.001
Gender (male versus female)	0.96 (0.71-1.30)	0.871
Fasting glucose (per unit increase)	1.08 (0.96-1.18)	0.602
Triglycerides (per unit increase)	1.14 (0.97-1.24)	0.297
Total cholesterol (per unit increase)	1.05 (0.98-1.10)	0.549
Estimated GFR ( $<60$ versus $\geq 60$ ml/min per 1.73 m <sup>2</sup> )	1.73 (1.20-2.48)	0.003

CI, confidence interval; GFR, glomerular filtration rate.

ical primary hypothyroidism. Accordingly, there was a significant inverse association between estimated GFR and TSH levels throughout the normal and high TSH ranges.

It has been estimated that the prevalence of subclinical primary hypothyroidism ranges between 4% and 10% in the general population (12-14) and between 7% and 26% in the elderly (15-17). Previous studies have reported a higher prevalence of goiter and/or thyroid hormone abnormalities in persons with end-stage renal disease (18-22). In addition, some of these studies suggest that abnormal thyroid hormone levels (*i.e.*, low plasma free triiodothyronine with normal TSH levels as typically seen in the low T<sub>3</sub> syndrome) in patients requiring chronic dialysis are independent predictors of all-cause and cardiovascular mortality (20-22), likely because of an association with underlying chronic inflammation (19,22). Although numerous contributing factors have been hypothesized, including altered iodine metabolism, decreased peripheral sensitivity to hormones, and autoimmune thyroiditis, the exact underlying mechanisms linking advanced CKD and primary thyroid dysfunction remain unclear. Conversely, in clinically overt primary hypothyroidism (myxedema), the most significant manifestation of changes in renal function is hyponatremia, which results from an impairment in renal diluting capacity leading to water retention (23). Moreover, clinically overt hypothyroidism may also cause renal hemodynamic alterations produced by a decreased cardiac output, which lead to a progressive decline in GFR.

Currently, little is known regarding the epidemiology of thyroid function abnormalities in persons with less severe kidney dysfunction. Lo *et al.* recently noticed that the prevalence of subclinical and clinical primary hypothyroidism increased with progressively lower levels of kidney function in a nationally representative cohort of U.S. adults (10). Among these participants, more than 20% of those with an estimated GFR  $<60$  ml/min per 1.73 m<sup>2</sup> had clinical or subclinical primary hypothyroidism after controlling for age, gender, and race/ethnicity (10). Their study differed from ours in that their multiethnic U.S. cohort was younger (mean age, 48.7 versus 54.9 yr), had a greater prevalence of males, only 56% of hypothyroid cases were considered subclinical, and total T<sub>4</sub> and not FT<sub>4</sub> concentrations were assessed. Thus, our study extends these previous observations by demonstrating a high prevalence of subclinical primary hypothyroidism (~18%) in a large non-U.S. cohort of

persons with CKD not requiring chronic dialysis that is independent of important confounding factors.

Subclinical primary hypothyroidism is most commonly caused by chronic autoimmune thyroiditis, which is typically characterized by a mild asymptomatic goiter with diffuse hypoechogenicity on thyroid ultrasound and by the presence of a high titer of serum thyroid autoantibodies (24). Other less common causes of transient or permanent primary hypothyroidism include drug-induced hypothyroidism, subacute thyroiditis, radiation thyroiditis, and postpartum thyroiditis (25). However, independent of its specific etiology, several studies have shown that subclinical primary hypothyroidism may affect both diastolic and systolic cardiac function, worsen traditional risk factors for cardiovascular disease, including blood pressure, plasma lipid profile, and endothelial function (5-8,26).

This study has several limitations that should be noted. First, because this study is cross-sectional, the present analysis is limited in its ability to establish causal or temporal relationships between subclinical primary hypothyroidism and kidney disease. Second, the definition of kidney function was based on estimated GFR rather than on more precise measurement of kidney function, such as iothalamate clearance. Third, nonthyroidal (*e.g.*, low T<sub>3</sub> syndrome, which is typically seen in some ill patients, including those with end-stage renal disease) and thyroidal (as reported above) causes of subclinical hypothyroidism were not identified. Finally, because our analysis depended on automated databases to establish the presence of subclinical hypothyroidism and kidney disease, it may have led to some misclassification; in particular, we do not have any information on coexisting medical conditions and current use of thyroid medications (thyroid replacement therapy or anti-thyroid drugs). Moreover, thyroid function tests could be requested when there was a (clinical) suspicion of altered thyroid function, thus tending to inflate the magnitude of the estimate of the relation. However, in this study we excluded all patients with low or high FT<sub>4</sub> levels, who are those likely to have clinical symptoms of hypothyroidism or hyperthyroidism, respectively.

Notwithstanding these possible limitations, this analysis has several strengths. First, our clinical laboratory used uniform methods to collect data on serum TSH and FT<sub>4</sub> concentrations. Second, subclinical primary hypothyroidism was diagnosed according to widely accepted diagnostic criteria (*i.e.*, high TSH



**From:** Heather Cook (0161 923 6472)

**Sent:** 20 July 2011 16:31

**To:** [REDACTED]

**Subject:** FW: URGENT: FAO Heather Cook, Investigation Officer RE: Gordon Skinner

Dear [REDACTED]

Thank you for your email. I will ensure it is included in the papers to be considered at the review Fitness to Practise Panel hearing.

Regards

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
DDL: 0161 923 6472  
Fax: 0161 923 6401  
Email: HCook@gmc-uk.org

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**From:** [REDACTED]  
**Sent:** 19 July 2011 13:48  
**To:** GMC Fitness to Practise  
**Subject:** URGENT: FAO Heather Cook, Investigation Officer

Re: Dr Gordon R B Skinner GMC No. 0726922

Dear Ms Cook,

I was, this morning, astonished and alarmed to discover that Dr Skinner is being called to a Fitness to Practise Hearing. Therefore, it is with great urgency that I implore you to read my email to fully understand how he has helped me and to understand my very grave fear of again losing my health should he be prevented from practising.

I had been very unwell for several years until I reached the point where I could no longer function and began to believe that I may even die. My symptoms were diverse and too many to list

[REDACTED]  
[REDACTED] I visited different GPs who advised there was nothing wrong with me and that I was most likely [REDACTED]. I continued to offer. [REDACTED]

my job through my inability to function [REDACTED] Life was a struggle and still all blood tests came back normal. Finally I got my GP to do a Thyroid Test which indicated I was slightly out of range. "Slightly", [REDACTED]

[REDACTED] After so long, I received Levothyroxine from my GP which took the edge off [REDACTED] but little else. I feared I must live the rest of my life like an invalid. [REDACTED]

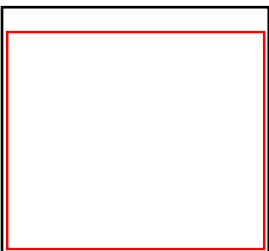
Finally, I requested my GP (who had tried her best but lacked the expertise or indeed the time to fully help me) to refer me to Dr Skinner. Thank God she did, I shudder to think of the state I would be in had she not. I saw Dr Skinner who had both the knowledge and the time to fully assess me. I explained how unwell I felt on Levothyroxine and fortunately he agreed to prescribe Armour Thyroid.

I have not felt as well as I currently do for many years. I am again beginning to enjoy life again, [REDACTED] I feel as if I have a second chance of life. People are remarking as to my health, only now saying how ill I looked before.

Therefore, I beg of you to continue to allow Dr Skinner to help people like myself. I am extremely fearful that I shall again lose my health if you do not. It may appear somewhat dramatic but my health quite literally lies in your hands. Please, please allow me to continue feeling this well.

Please be so very kind as to acknowledge my email, so I know you have had the opportunity to see it.

Kindest Regards



tel.

0

Re; Dr. J. Skinner MD, D.Sc. FRCOG, FRC Path.

Dear Mrs. Cook,

I write as a current patient of Dr. Skinner.  
I am appalled that Dr. Skinner, one  
of very few experts on hypothyroidism in this  
country, is to be examined for his fitness to  
practise.

After all the errors and misjudgements  
- of which I can show you documentary evidence -  
of my Doctors in the past it was such a relief  
to find, in Doctor Skinner, one who knew thoroughly  
what he was talking about.

I have the fullest confidence in  
Dr. Skinner and would appreciate your comments  
upon what this case is based and how it  
is progressing.

Yours faithfully,

c.c.

Mr. Ralph Shipway.

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19<sup>th</sup> July 2011

**Heather Cook**  
**Investigation Officer**  
**Fitness to Practise Directorate**  
**General Medical Council**  
**3 Hardman Street**  
**Manchester**  
**M3 3AW**

Dear Ms Cook,

**RE: Dr G. Skinner MD DSc FRCPath, FRCG;**

I am writing this letter in support of Dr G Skinner. Although not a patient of Dr Skinner I have read with great interest his publications on the subject of hypothyroidism. Having endured, in my view, poor and inadequate treatment under the NHS, I find his insight into the symptoms and treatment of hypothyroidism excellent information for myself as a patient. Also from my experience as a patient I cannot help but agree with him.

Since thyroid hormones are vital for every organ and process in the body it is surprising that more doctors from other specialities do not in follow in Dr Skinner's footsteps and take as much interest in the treatment and diagnosis of this condition. Perhaps medical schools have a part to play here and I believe he would be an excellent teacher in this important subject. Dr Skinner is therefore to be admired as being a very well qualified doctor, but not an endocrinologist; who can however bring another perspective in analysing the symptoms endured by the patient. He must also be admired for providing adequate treatment which is acceptable to the patient. This is not something I have received under the NHS. I therefore consider his patients are extremely fortunate to have him as their doctor.

Dr Skinner has been described as "*a caring and compassionate doctor whose overwhelming concern is the care and wellbeing of your patients*". He should therefore be applauded for behaving in this fashion. In my experience I have discovered that the health risks of untreated hypothyroidism can be extremely serious. A doctor, like Dr Skinner, who looks closely at symptoms as well as blood tests, is therefore I believe behaving in an extremely responsible fashion towards his patients.

I conclude in saying that Dr Skinner should be allowed to continue his important work in helping patients to regain their health. I am very sad that I was not referred to him a number of years ago as I am sure he could have saved me considerable suffering.

Dr Skinner has my full unqualified support.

Yours faithfully

Copies

R Skinner 2854

Ms Heather Cook  
Investigations Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

19<sup>th</sup> July 2011

Dear Ms Cook

**Re: Dr G Skinner Review Hearing**

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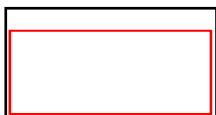
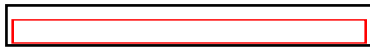
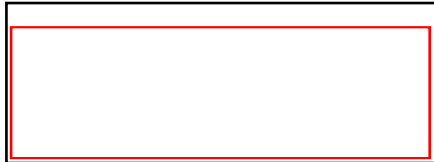
I would like to politely ask a question of the GMC: *Why do members of the Board think members of the public with access to the NHS are prepared to travel long distances and pay to see Dr Skinner privately?*

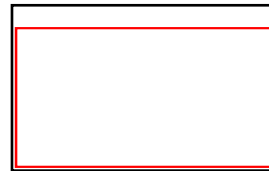
For those of us with a thyroid condition it is certainly not a question of vanity or queue jumping or of having more money than we know what to do with. It has been our experience of the NHS over a substantial number of years that it becomes a matter of the uppermost necessity in our daily lives to pay to see Dr Skinner privately. After years of GP's who, as you are not about to drop dead do not appear to view the symptoms of a thyroid problem as warranting a referral to an Endocrinologist, of GP's who do not interpret the blood results correctly, and of GP's whose approach to an undiagnosed thyroid problem is to essentially 'blame the patient' with endless lectures about how if you adopt a better diet, loose weight and do more exercise i.e. so if you give up your one remaining pleasure of sitting curled up on the sofa reading a book and drinking a glass of wine then your health and well being will definitely improve; it is your fault your life feels like you are trudging through a thick bed of treacle every day. Dr Skinner, with his wealth of specialist knowledge, his caring attitude, his empathy and understanding of how the symptoms of Myxoedema can adversely impact on multiple areas of daily life is therefore, for us, a positive oasis after years in a totally demoralising wilderness that is unfortunately all too commonly encountered by patients with a thyroid condition under the 'care' of the NHS.

With the greatest respect I would therefore request the GMC board to think very carefully about potentially interrupting this vital, life affirming and life altering service for patients with a thyroid problem because, for us, Dr Skinner is an absolute God send. Our quality of life would quite literally not be the same without the extremely knowledgeable service and outstanding support offered by Dr Skinner. Therefore, as a member of the general public served by the GMC, my vote is that the GMC Board should on the contrary now be meeting to consider the award of a well deserved honour to Dr Skinner for his outstanding service to thyroid medicine. In my opinion it is the doctors *who do nothing* to help their patients with a thyroid problem who should be called to stand before the GMC Board.

If you have any questions or if I can be of further assistance then please do not hesitate to contact me.

Yours sincerely





18<sup>th</sup> July 2011

Heather Cook  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

General Medical Council	
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Dear Ms Cook

Re: Testimonial for Dr G Skinner

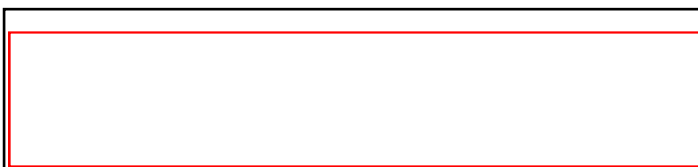
*I have been treated by Dr Skinner for a long time and it is a joy to be treated as an individual rather than someone who fits into a neat little box.*

Dr Skinner takes time to discuss my symptoms and is alert to any changes in my condition.

It would be a shame if it was decided at this review that Dr Skinner is not fit to practice as he has brought relief and hope to so many patients.

Thank you for taking the time to read this testimonial and I am praying that you will allow Dr Skinner to continue as a much needed Doctor.

Yours sincerely



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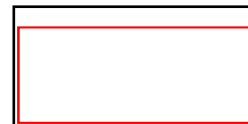
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Copies to 

--

 and Mr Ralph Shipway.

To Ms. H. Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester M3 3AW



20<sup>th</sup> July 2011

Dear Ms. Cook,

REF: DR. GORDON SKINNER

I have been a patient of Dr. Skinner for approximately  years.

For the next  years I had many symptoms of low thyroid function with realizing it.

In the late 's I approached my then GP who ordered blood tests for thyroid function.

I was advised that the results showed my thyroid to be "in the normal range" and it was concluded that despite a partial thyroidectomy and no replacement thyroxine for almost  years, my symptoms could not be attributed to hypothyroidism.

Enter Dr. Skinner.

After feeling let down by the treatment or lack of it from the NHS, I became a patient of Dr. Skinner's. I was particularly encouraged by his approach: i.e. that he did not simply diagnose solely on blood test results, but he also took into account the patient's myriad and often seemingly unrelated symptoms.

I have found Dr. Skinner to be thorough, thoughtful, and measured throughout my many consultations with him over the years. He has a quiet, professional manner.

I'm aware that he has been criticized because his views on the treatment of hypothyroidism fall outside current mainstream thinking in this country.

However, I have appreciated Dr. Skinner's approach of taking all my symptoms into account, in addition to blood test results, and "partnering" with me to find the optimum dosages I require.

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As his patient of the last [redacted] years, I have always been completely satisfied in my dealings with Dr. Skinner and his administration team [redacted].

I am deeply saddened to hear that he is facing a review hearing with the GMC.

I hope you can appreciate that without Dr. Skinner's help my life would be so different. It's most likely that I would still not be treated or at best be undertreated for hypothyroidism with little or no relief of my symptoms.

I wish him well.

Yours sincerely, [redacted]

[redacted]

[redacted]

Cc Mr. Ralph Shipway,  
RadcliffesleBrasseur (Solicitors)  
5 Great College Street,  
Westminster,  
London, SW1P 3SJ

Cc

[redacted]

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

General Medical Council	
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Friday 8<sup>th</sup> July 2011

Dear Ms Cook,

RE: DR GORDON SKINNER

I am writing to express my gratitude, respect, thanks and appreciation of the work that Dr Gordon Skinner does.

[redacted]  
[redacted] I am completely indebted to Dr Skinner. If I had not been referred to Dr Skinner by my GP I would without doubt no longer be [redacted] and the lives of my husband and children would be in a very sad state. [redacted] my health had deteriorated to such a point that I was becoming incapable [redacted]

[redacted]  
I have been in Dr Skinner's care since [redacted] as the NHS have completely refused to acknowledge that my ill health is caused by hypothyroidism despite having a multitude of clinical symptoms, a family and personal history of thyroid problems [redacted]

[redacted]  
[redacted] This disbelief by the NHS has continued despite a virtually complete recovery and a massive improvement in mine and my family's quality of life since starting medication under Dr Skinner.

I feel completely and utterly let down by the NHS in regard to the treatment of my hypothyroidism. The NHS Endocrinology department at [redacted] [redacted] have failed to show me any level of care and have made me feel that I am completely in the wrong no matter how much evidence they are given or how much better they can see my health is. I have asked them to provide an explanation as to how my health could possibly have improved as a result of the treatment for hypothyroidism if the problem is not my thyroid. They have been completely unable or willing to do this to date. Dr Skinner has restored my faith in the medical profession.

As a result of the appalling manner in which I was treated by the NHS I asked to be referred to Dr Skinner in [redacted]. He could see immediately that the problem was my thyroid from my clinical features and he took the time to listen to my concerns and background information in a caring and professional manner. During the past year I have found Dr Skinner to be diligent, thorough and a highly caring professional. Dr Skinner has kept my GP informed of every step of my treatment in a professional, polite and pleasant manner, ensuring that he (GP) is kept completely up to date with my treatment and the reasons for my treatment. Dr Skinner has my complete trust and total respect, which is more than can be said for many of the professionals I have come across in the NHS. Dr Skinner is devoted to ensuring that the patients in his care are listened to and treated with respect and he has provided a treatment that is working successfully where my GP and the [redacted] have failed. Indeed my GP and [redacted] would have left me untreated, with no quality of life and no profession as I would have been dismissed due to ill health, while they were/are still trying to discover what my mysterious illness is and wasting NHS funds on pointless visits to different clinics and consultants.

Dr Skinner is an old school doctor, who was well trained in a time where the patient was put first and doctors did not rely upon blood tests to confirm/tell them what they could see with their own eyes. Dr Skinner is very much like my old doctors, all of whom have now retired, none of these well trained and wise doctors would agree with doctoring by numbers, ignoring the patient's actual symptoms. I would suggest that rather than questioning and making these professionals practice outside of the NHS, doctors like Dr Skinner should be encouraged to train the other doctors who think that a blood test will give them all the answers they need.

I do not have enough superlatives to express how wonderful Dr Skinner is and how much he has helped me and my family. How anyone could even question his fitness to practise is completely beyond me. The only reason I can see for this is entirely political, which is a disgraceful reason to persecute someone who is making so many people well and giving them a quality of life that the NHS would take away from them. Dr Skinner is providing a much needed service that the NHS refuses to even acknowledge.

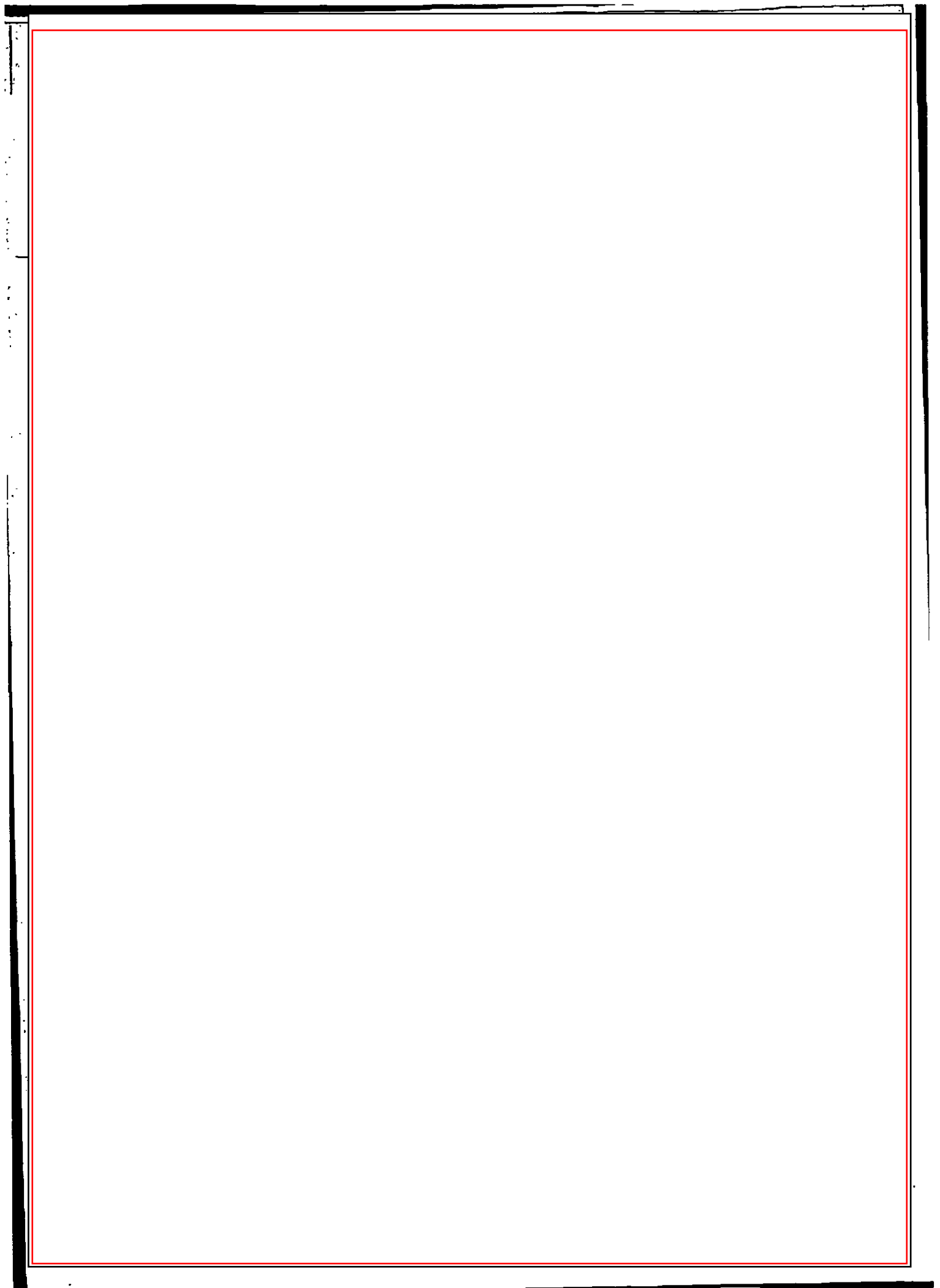
I would be more than happy to appear as a witness for Dr Skinner and I can be contacted at the above address.

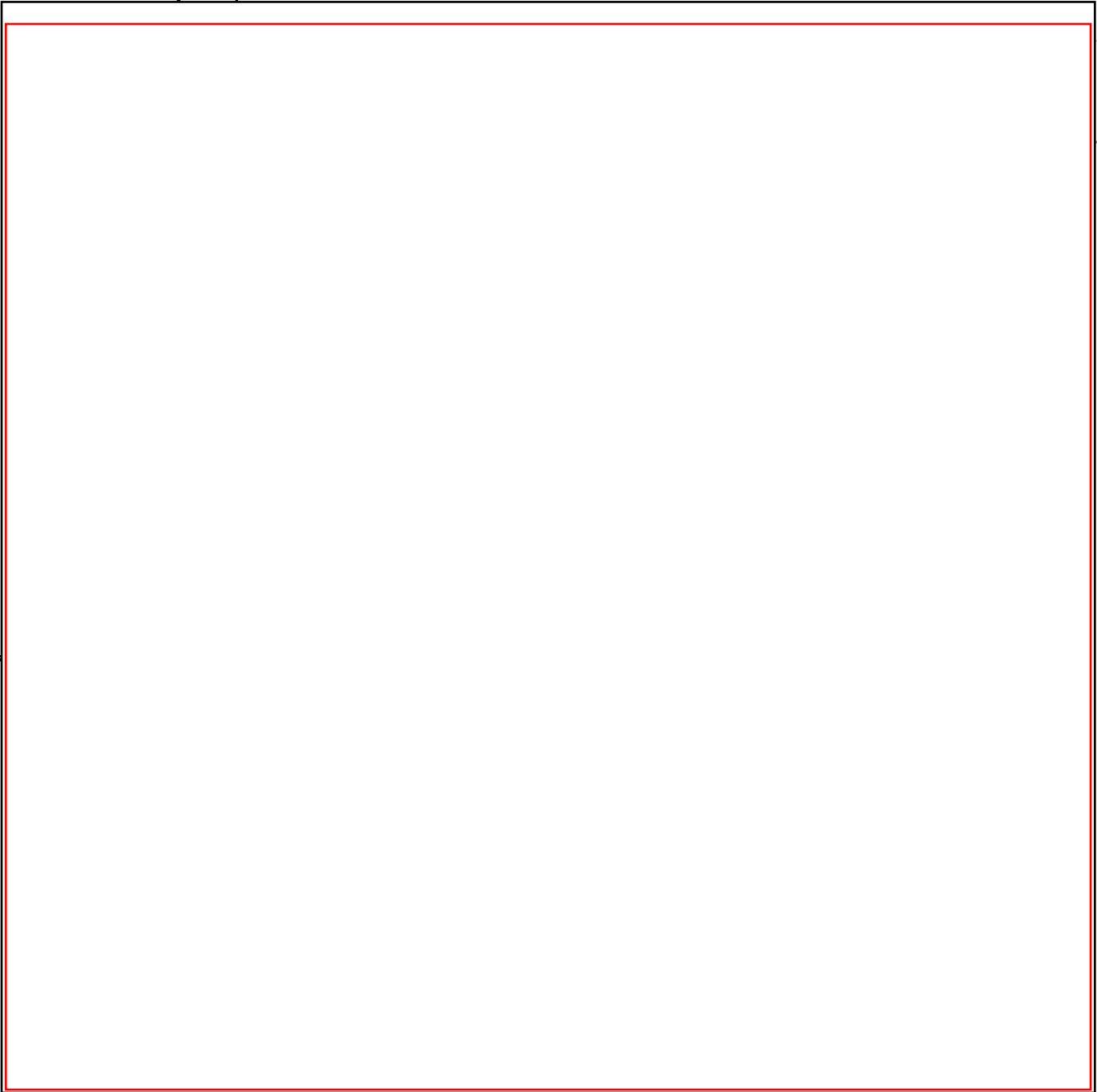
Yours sincerely

[redacted]

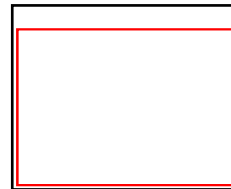
CC: Mr Ralph Shipway

[redacted]





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20<sup>th</sup> July, 2011.

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Ms Cook,

**Dr. Gordon Skinner** .

I am writing to express my concern over Dr. Skinner being asked to attend a Fitness to Practise Hearing on 28th July.

I have been disabled for many years and am under the care of [redacted] at the [redacted]. I was diagnosed with [redacted]. One of the doctors there realised that I was hypothyroid despite a FT4 level just within the reference range. I went to an endocrinologist privately but was told that because my blood test was normal, nothing could be done for me. [redacted] made me an appointment with an N.H.S. endocrinologist. When that was postponed, I went to see Dr. Skinner.

It is painful now to remember how serious my illness was at that time. I was in a severely weakened state, unable to look after myself, work or take part in any kind of normal life. I was struggling with incapacitating symptoms including extreme [redacted]. I was steadily growing worse.

Since Dr. Skinner began treating me my health has improved greatly [redacted] and his team have followed my progress and never suggested that any change be made to Dr. Skinner's choice of prescribing [redacted].

One of the neurologists explained the need to diagnose hypothyroidism by a combination of symptoms and blood tests in this way: [redacted]

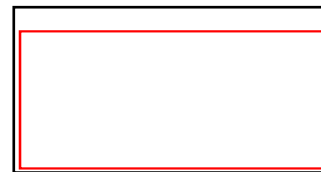
Dr. [redacted] of the [redacted] has said that being hypothyroid "is a disease where it is crucial that the doctor treats the patient and not the

blood test result ." I have endured years of unnecessary illness because this is so often forgotten .

I am one of many thousands of patients who have recovered our health because Dr. Skinner has considered our symptoms . He has made my life worth living again . I hope that he will be allowed to continue to help others.

Yours sincerely ,

Cc Dr. Skinner .



20<sup>th</sup> July, 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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Dear Ms. Cook,

**Dr. Gordon R.B. Skinner**  
**FTP Review Hearing**  
**28<sup>th</sup> July – 3<sup>rd</sup> August, 2011**

**A mother's perspective**

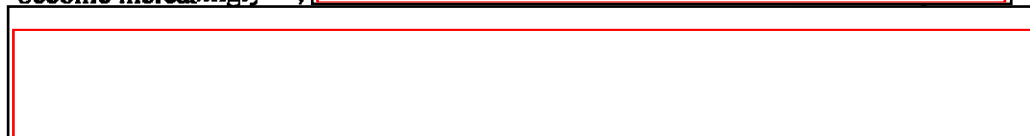
I have sent in a testimonial for Dr. Skinner regarding my own health, but would now like to give a mother's perspective on treatment given to my daughters by Dr. Skinner.

I have two daughters who mean the world to me and it broke my heart to see them so ill. It was like seeing a carbon copy of myself and I couldn't bear to see them suffer as I had for so many years.

If only there more Dr. Skinner's in this world to help patients as he has. He is an exceptional doctor with an in-depth understanding of hypothyroidism; a doctor who cares for his patients' as was evident at his Fitness to Practise Hearing in 2007 where members of the public (seated in the public gallery) were reduced to tears by the heart-rending stories told by many of his patients.



Around  years ago, my daughter  had become increasingly ill,



We found out about Dr. Skinner through someone who had written an article in a magazine.



At the first consultation with Dr. Skinner, he said she was so ill that she shouldn't [redacted] but once on medication, she improved rapidly. She still had some symptoms, so was changed to Armour Thyroid and her recovery was amazing. [redacted]

[redacted]

Thanks to Dr. Skinner, he changed all that and at the age of [redacted], she blossomed as a young lady.

[redacted]

[redacted]

Dr. Skinner prescribed thyroxine and again, the difference in her health was wonderful. [redacted]

[redacted]

Again, thanks to Dr. Skinner, my younger daughter has returned to good health.

Thank you Dr. Skinner for helping my daughters recover from this dreadful illness. Without you, I can't even begin to imagine how ill they would be by now.

Hopefully one day, sooner rather than later, the medical world will wake up to the fact that patients lives have been ruined purely because of thyroid blood tests and therefore doctors unwillingness to treat when the results are within range. Also, there has to be a choice of thyroid medication and not just to prescribe Thyroxine.

I trust this letter will be put onto Dr. Skinner's file.

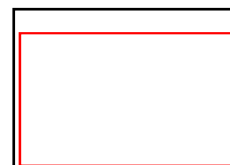
Yours sincerely,

[redacted]

cc Mr. R. Shipway

[redacted]

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20.07.2011

Ms. Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Ms. Cook

I am writing to you to show my support for Dr. Gordon Skinner. I have been a patient of his since [redacted] and I wanted to share my story.

I was born hypothyroid and I lost [redacted] years of my life to this awful disease. I didn't have a childhood; I missed out on my teenage years due to my crippling illness. [redacted]

My GP was happy to give me [redacted] but refused to consider my thyroid, despite me having many hypothyroid symptoms and an extremely strong family history. It took years of battling to get a referral to an NHS endocrinologist. When I finally saw one I was told it was all in my head. 5 other NHS endocrinologists said the same. Have you any idea how that makes you feel? A final trip to the local hospital and a new endocrinologist decided to trial me on thyroxine [redacted]

In [redacted] I discovered Dr. Skinner. I finally convinced a GP to refer me and I saw Dr Skinner in [redacted]. He was nothing but courteous, professional, caring and understanding. After blood tests and an examination I was finally diagnosed as being hypothyroid. At this stage I'd been kept on [redacted]mcg of thyroxine prescribed by an NHS endocrinologist for [redacted], with no

improvement to my health at all. Gradually Dr Skinner increased my dose and suddenly I felt as if I was coming alive. I was scared, I was feeling 'normal' and this was a concept so alien to me it was terrifying at first. After more visits to his clinic [redacted] my dose was increased and eventually Armour Thyroid was added as I was improving but was still not 100%. Pretty much immediately I felt fantastic, I felt re-born. I felt like 'me'.

[redacted] years on and I am in extremely good health. I don't even think about my thyroid disease, [redacted]

[redacted] If, [redacted] years ago someone would have told me I would one day be 'normal' I would have laughed at them.

I will not consider having a family myself as I am petrified of passing on this disease to my children. I do not want anyone to ever have to go through what I have been through. I am so angry that I have been robbed of what I should have had in my early years. I am so angry that Dr Skinner, the most fantastic doctor I have ever met and the man that well and truly saved me, may not be given the opportunity to save other people the way that he did me. I am angry that I had to go privately to get treated; many people aren't as fortunate as me and cannot afford to pay.

If Dr. Skinner is struck off I will have to be treated by the NHS. I do not want to have to be treated by NHS endocrinologists again, who, from my previous experiences, failed appallingly in diagnosing and treating my illness accordingly. I lost [redacted] years of my life; I will never get those years back. My Armour Thyroid will be stopped and my thyroxine dose will be almost halved, just to fit in with the current clinical 'guidelines'. This will be totally devastating to my health and is not a situation that I am prepared to be put in. The NHS should be making people well, not killing them off.

I would implore you and the panel to listen to Dr Skinner and his patients and please, please do not let any other human being ever go through what I had to go through. Dr Skinner should be praised – not persecuted.

Yours sincerely

[redacted]



Ms Heather Cook,  
Investigation Officer,  
Fitness to Practice Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

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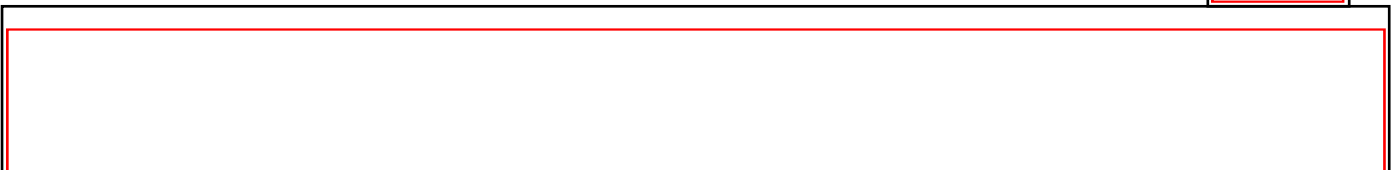
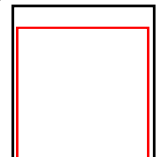
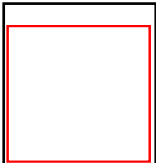
Dear Ms Cook,

Ref: Doctor G. Skinner Review Hearing

I am concerned to learn that Doctor Skinner is to be the subject of a General Medical Council review.

In approx [redacted] my daughter, [redacted] was diagnosed by her G.P. and subsequent consultant at [redacted]. It was decided by the consultant that my daughter should be subject of remedial treatment in order to assist in curing the condition. Whilst I have no medical knowledge I considered that the treatment recommended was extreme and therefore unacceptable. I decided to seek an additional opinion in order to ensure that such a remedial treatment was necessary. For that purpose it was recommended to me that Doctor Skinner was an expert with regard to the subject and that it would be prudent to seek his assistance.

My Daughter and I attended the initial consultation with Doctor Skinner. I was impressed by his knowledge of the subject, thoroughness of his investigations into [redacted]'s condition and subsequent care and attention she received. His diagnosis was carefully considered and subsequent on going medication requirements and treatment monitored at regular intervals. My Daughter soon and successfully responded to the medication provided.



The on going treatment was carefully supported by Doctor Skinner, monitoring regular independent blood test analysis together with further consultations. My daughters condition remains stable, thanks to the efforts of Doctor Skinner and without the necessity of the recommended original extreme treatment. My daughter is restored to a good, very active, stable health and I trust will continue to receive the benefit of Doctor Skinners valuable expertise.

Yours sincerely,

[Redacted signature block]

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

21<sup>st</sup> July 2011

Dear Heather

Re Dr GRB Skinner

Please find the enclosed letter from my GP regarding the medication that is recommended by Dr Skinner that has improved my health tremendously.

Yours sincerely

[Redacted Signature]

[Redacted Stamp]

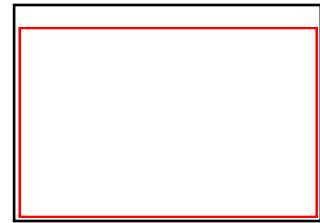
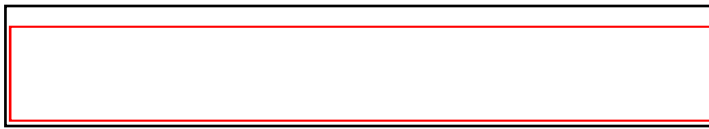
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Copies to

[Redacted Name]

Mr Ralph Shipway

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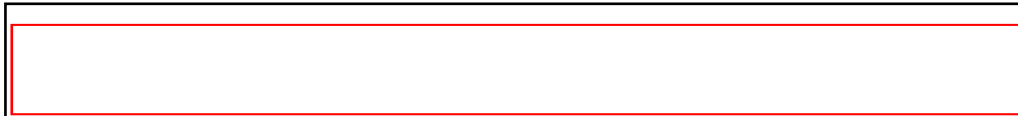
21<sup>st</sup> July 2011

FAO Heather Cook  
Investigation Office  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Heather

[redacted] has been one of my patients since [redacted] she suffers with Hypothyroidism.

I have witnessed this lady when she is taking T3 and also when she is not. T3 tablets alongside Thyroxin have made a tremendous difference to her wellbeing.



As soon as [redacted] resumed T3 she was a different woman and therefore I feel this currently unaccepted treatment pathway must be looked at and re-valued as to whether it can be adapted on the NHS as this is likely to improve quality of life for patients and will also be of benefit to employers who suffer employee absenteeism due staff suffering with this condition.



General Practitioner

**RE: TESTIMONIAL FOR DR. G.R.B. SKINNER**

Dear Sir/Madam,

Dr Gordon Skinner saved my life!...he certainly saved me from a life that felt like "living death" [redacted] [redacted]

[redacted] "Dr Skinner switched the light back on at the end of my tunnel.... Finding him seemed like the miracle that was the answer to my prayers. He gave me hope and a reason to live, then he gave me back the most precious gift of all...my health.

Maybe that sounds a little dramatic, but it only begins to hint at how grateful I am to him for restoring me to good health. My life was devastated for [redacted] years by an illness, diagnosed as [redacted] which deprived me of everything in my world that was dear to me. [redacted]

From the beginning of my illness I suspected it was caused by a problem with my thyroid gland. As I had more than 50 physical symptoms it was clear to me that my metabolism was severely challenged. For me, the most obvious culprit was the gland which regulated it. My GP assured me on six occasions, after my blood was taken, that the results of my TSH tests were "well within normal limits" and that there was, therefore, no problem with my thyroid function. For [redacted] years I doubted my diagnosis but accepted their opinion that my thyroid was OK. Doctors and specialists advised me that my illness was incurable...the best I could do was treat it symptomatically and learn to manage it, to minimize the impact on my life.

Not satisfied to accept this "less than half-life" I drew upon my knowledge of Biochemistry and Human Biology to research my illness, starting with CFS/ME and, by a circuitous route, finally returned to the thyroid gland. Disappointed and frustrated by the lack of enthusiasm shown by my GP in pursuing this line of enquiry again, I decided to help myself. It was when looking on the internet for an Endocrinologist with a specialism in thyroid illnesses, that I first came across.... Dr Gordon R.B. Skinner.

There was a lot of open and honest information available about him, including his CV, medical experience and extracts from his book on the Management and Treatment of Hypothyroidism, which chimed with me and quickly convinced me that he was exactly the man I needed to see. On request, my GP referred me and I visited him privately at his surgery in [redacted]. On my first visit, I found in him my ideal of a professional and outstandingly caring, old-fashioned MD. (Such a refreshing change from my experience of seeing my GP, who sees me for just ten minutes and only allows discussion of one symptom at each appointment. A GP who is dismissive and condescending, does not look at me or listen properly to me and frequently looks at her watch. Half of my appointment is spent typing my notes into the computer and if my problem cannot be fixed with a prescription drug the MD



acts as if I have wasted her time).

In contrast, Dr Skinner put me at ease straightaway. He listened patiently while, due to my cognitive difficulties, I waffled on incoherently about my numerous symptoms and my anger at the devastation of my life, caused by the illness. Looking back, I must have seemed very rude and distrusting when I railed against the appalling treatment I had received from various people in the medical profession, before finding him. All this he accepted calmly and graciously, he was not judgemental or critical, he just re-assured me that he believed me, I was not going mad, I was *extremely ill* and he would do his best to support and help me. He treated me with great kindness and made me feel appreciated as an intelligent, knowledgeable woman who had a great knowledge and understanding of her illness and the way her body worked. Of course, I know now that he had heard it all before!....and thousands of times, at that!....but he made me feel special, that I was the sole focus of his attention. Finally, [redacted] years of misery and battling alone, I had found a champion who would let nothing stand in his way to restore me to full health.

In [redacted] years of illness, Dr Skinner was the first to do a thorough physical exam. In preparation for the appointment I sent him a full medical history and it was obvious that he had studied this very carefully before seeing me. He had also studied the referral from my GP which detailed the results of my blood tests. After careful consideration of all the facts and his observations, he gave me a diagnosis based on history, signs and symptoms as well as blood results. By correcting my diagnosis to hypothyroidism and starting me on a course of treatment with synthetic thyroxine, this man literally gave me my life back. He was able to explain all my symptoms and put my mind at peace that a cure was possible with appropriate medication. [redacted]

[redacted]

When I left his surgery after that first visit, I felt euphoric, light-headed and slightly dazed. Such was the effect of Dr Skinner's caring attitude and optimism, that while resting in the car before attempting to drive home, I burst into uncharacteristic tears... of relief! ....and yes!.... happiness! something that I thought I would never experience again.

In the [redacted] months since I first met Dr Skinner he has seen me three times, monitored my progress and shown genuine delight in seeing me gradually return to good health. He wrote to my GPs regularly to update them and ask them to participate in my care. Since my GP practice refused to accept my new diagnosis or to prescribe thyroxine for me and do monitoring blood tests, Dr Skinner continued to prescribe for me privately. He started my medication at a very low dose, increased and adjusted my daily dosage very gradually over a period of [redacted] months and carefully monitored my progress until, with a combination of T4 and T3 equivalent to [redacted] mcg of synthetic thyroxine, my health has been stabilised and is returning to normal. He was also very careful to explain to me what symptoms would be experienced if at any time I started to overdose on the medication, and what the consequences could be, so I knew immediately when I slightly over-reached my optimal dosage.

Having made a series of complaints to my new GP about the lack of support and unhelpful attitude of other GPs in the practice, I wrote a review of my treatment at the practice over the past [redacted] years. It was not my intention to apportion blame but my hope that my experience of the illness would be better understood and other patients presenting with [redacted] would not go through the same torturous experience again. As a result my GP offered to refer me to a local NHS Endocrinologist for a second opinion. Dr Skinner, as always, supported me and wrote to the Endocrinologist. The outcome was, finally, that my hypothyroidism (and it's severity) were acknowledged. Now my medication and blood monitoring tests are being handled by the NHS and I am treated, at last!... as a intelligent partner in my own care. Dr Skinner continues to see me periodically to support me and ensure that my GP continues to care for my best interests.

(I would also like to mention a dear friend of mine, [redacted] who has also gone through a very similar distressing experience as my own, being ill for [redacted] years and finally diagnosed with [redacted]. Her GP was also reluctant to investigate further than TSH but referred her to an Endocrinologist for further blood tests who insisted there was nothing wrong with her thyroid. Having exhausted the "normal channels" with no satisfaction, she went to Dr Skinner on my recommendation. I am delighted to report she is now a new woman, and I am delighted to see my dear friend well on the road to recovery.... thanks to him).

In summary, I would describe Dr Gordon Skinner as a consummate professional with an amazing depth of understanding, knowledge and experience in his chosen field of specialism. His practical application of this knowledge in clinical observation, diagnosis and treatment is outstanding and, sad to say, in my experience of consultants, very rare. On a personal level with his patients he is warm, patient, understanding and compassionate. He really *cares* about people and you can tell that his whole world revolves around his desire to restore people to optimal health. He is also a courageous man who stands up for what he believes in and will challenge and overcome all obstacles that stand in the way of his patients regaining their health. He has my greatest admiration and undying gratitude for having the courage of his convictions and helping so many people back to health.

It is incredible to me that someone should lodge a complaint about Dr Skinner and oblige him to prove his fitness to practice in this field. The only scandal here is, that there are not more doctors like him. The world is a far better place for having Dr Skinner in it, as thousands of people have cause to be grateful to him for being a thorough, old-fashioned, caring doctor. In my experience, the modern medical world is forcing practitioners to be so time-poor, shackled by costs and budgets, and frightened of litigation that they are starting to lose sight of their vocation and indeed the Hippocratic oath...to put the care and health of their patients first and above all other considerations.

If called, I shall be honoured to appear as a witness for the character and professionalism of this very caring doctor. For myself, before being incapacitated by my illness, I had a very successful and fulfilling career [redacted]

[redacted]



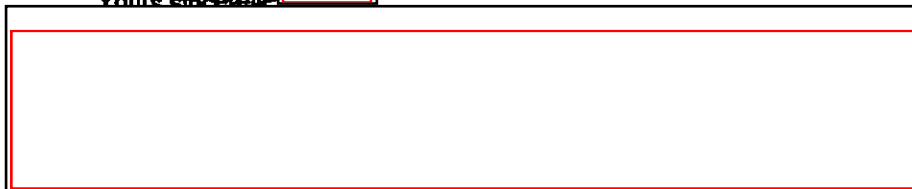
**Dr Skinner's whole life has been dedicated to these (sadly) "old-fashioned" principles and his selfless desire to help others. His life is fulfilled by his success in two areas of medicine:**

**1) the invention of important vaccines which are saving so many lives around the world and**

**2) re-storing his thyroid patients to full health**

**Everything that made my life worth living was taken away by my illness and my life was re-stored to me by Dr Gordon Skinner. My debt of honour and eternal gratitude compels me to stand up for him in his time of need and help to save his life right back!**

**Yours sincerely**

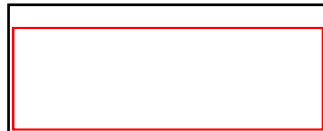


### TESTIMONIAL FOR DR SKINNER'S HEARING.

'Patient - [redacted] Testimonial.18-7-2011.'

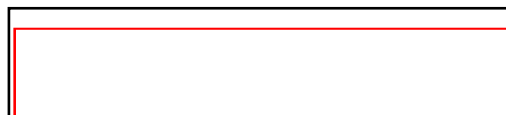
In [redacted], at the age of [redacted] years, I became very ill [redacted]  
[redacted] This was unusual as I had always been very fit and healthy. After [redacted] of  
deterioration, I was tested for viruses and [redacted] The NHS could only  
give me the advice to give up all activities and take a little [redacted] to help me  
sleep. [redacted] the illness became worse.

In [redacted] a friend contacted me and recommended Dr Skinner who had  
successfully treated M E patients. By this time I had tried various treatments privately  
and none had been successful. My parents took me to meet Dr Skinner in  
[redacted] and after a very thorough check up, he recommended that I start to take  
Sodium Thyroxine. Thankfully after a couple of months I regained energy and many  
ailments connected to the [redacted] improved significantly. I therefore continued to be  
treated by Dr Skinner [redacted]. I am very grateful to Dr  
Skinner who over the past few years has helped me to improve and am not sure  
what I would have done without his care.

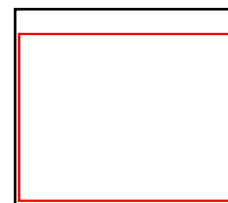


'Parents of [redacted] Testimonial.18 -7-2011.'

Our previously fit, Sporty son [redacted] was diagnosed [redacted]. He became  
desperately ill, constantly in pain and had lost all quality of life until he met Dr  
Skinner In [redacted] Dr Skinner was the first person who took the time to treat our  
son as an individual and we believe the Thyroxine gave him a much needed boost.  
[redacted]'s GP is unable to prescribe Thyroxine because his blood test results only come  
within the normal range. However, she admits that if her own child was suffering in  
the way [redacted] is she would do what we have done and she apologised for not being  
allowed to help him! Consequently, we travel to [redacted] and pay vast sums of  
money for thyroxine as this gives him the opportunity to study and carry out some  
activities. [redacted] is still limited [redacted]  
[redacted] but we fear without Dr Skinner he would be in a wheelchair  
or bed ridden. We are very grateful to Dr Skinner for his kindness and care which  
others have failed to give him. We hope that fellow sufferers will continue to benefit  
from Dr Skinner's expertise in the future.



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Heather Cook,

General Medical Council

Manchester.

Dear Ms. Cook,

I am writing to you as a patient of Dr. Skinner in the support of his practice. I feel very strongly that the act of trying to vilify a man who works both with and for his patient is both grossly unfair and against all the ethics of the practice of medicine, which is to return a patient to health.

I have been suffering with thyroid issues for years. The last  years I have spent in  and have run the gamut of doctors who ..in the fact place didn't even detect I was underactive until a year after the initial blood test and then lowered or tried to take me off completely once I was on replacement. Eventually I found a doctor knowledgeable in thyroid issues who put me on Armour thyroid and himself believed in increasing amounts of replacement until the patient was well. (Incidentally he is currently treating my brother and sister-in-law this way and they are both feeling markedly better). I, however, thanks to my own ignorance would take as little as possible under the misconceived idea that I would be better on less(!).

I returned to the UK in  went to a doctor complaining of   
 The doctor was kindness itself and listened attentively. Blood tests were taken. Nothing showed up but I was advised (by the by) to decrease my thyroid intake. My T4 level was  if I remember correctly.

When my years supply of Armour started to run out (and also feeling desperate with the way I was feeling) I searched the internet for a doctor who could supply it. It was here I learned about Dr. Skinner. I went to see him in . I can honestly say that I have never spent time in a doctor's office with someone who was actually prepared to listen to what I had to say in the same way as with Dr. Skinner. I was not told that I was over-reacting or imagining my symptoms. I was treated as some-one with a modicum of intelligence, able to discuss and actually understand what was going on in my body .....an attitude that can be sadly lacking with some GP's.

I have since been to see Dr. Skinner as a follow up. I am now taking a dose that I suppose would be thought excessive  .....however...I begin to feel like a person again, the dial-tone world is

changing for the better. Very importantly ..to me...

Taking all this into consideration I question how generally GP's are trained to go by bloodtests only....a fact that in any case is being hotly disputed and views as out-dated by a core of specialists in the US. My GP told me that Dr. Skinner approach was 'not scientific'. Therefore, presumably, I must suffer, and the fact that I feel better with Dr. Skinner's regimen no proof that it's right.....!!!! Were not doctor's years ago trained on symptomology? Isn't it important to address symptoms the patient is exhibiting rather than a few numbers on a page. Does a blind belief in a blood test along with a hide-bound attitude of 'it's what we were taught' make it right?

I would finish, whilst apologising for taking your time, by adding that I have many times over the years been offered [redacted] for symptoms that have turned out to be simply that I was not getting enough thyroid replacement. I have been told that Dr. Skinner's approach is unsafe and that I could end up in hospital if I was overdosed. Paradoxically I was also told that I probably wouldn't die if I took the whole bottle of thyroxine.....however, by the same GP I was offered an [redacted]

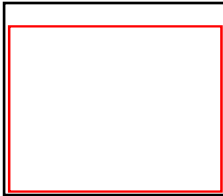
Please really consider that in any condemnation of Dr. Skinner you are doing us, the patients, the ones who suffer a disservice. Doctors of Dr. Skinner's calibre are not easy to come by.

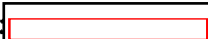
Yours sincerely

[redacted]

FOR THE IMMEDIATE ATTENTION OF HEATHER COOK, INVESTIGATION  
OFFICER OF THE FITNESS TO PRACTISE DIRECTORATE OF THE GMC

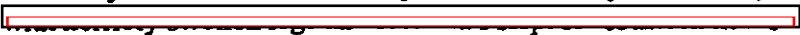
RE: DR GORDON SKINNER.

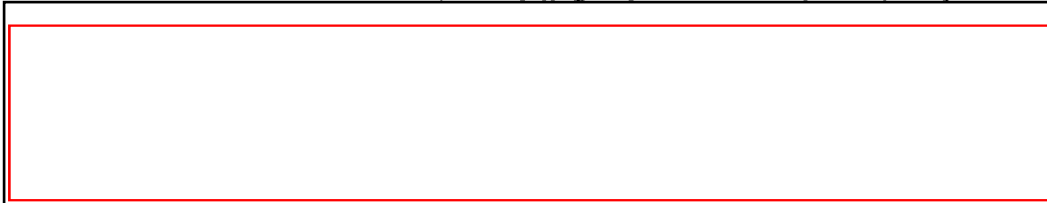



Tel: 

19<sup>th</sup> July 2011.

Dear Madam,

Prior to consulting with Dr Gordon Skinner I had been suffering from Hypothyroidism for several years. I had reached the point in which my whole body was a mass of pain 

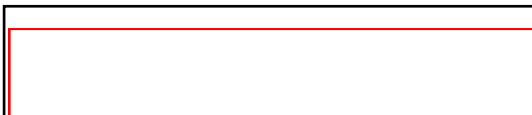


My condition is responding well to Dr Skinner's method of treatment (gradual introduction of Levothyroxine in my case). It is wonderful to be able to feel "wide awake" after years of utter weariness. 

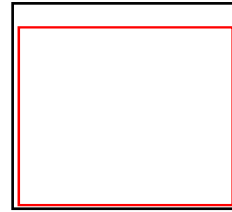


I dread to think of the consequences if I had not been able to consult Dr Skinner. I wonder how much more my tired and pain-racked body could have taken. Those who suffer from Thyroid Disease cannot afford to lose the expertise and experience of Dr Skinner, to say nothing of his compassion. For he listens patiently and examines thoroughly which is not always the case in the modern medical profession as you, as an Investigating Officer, will be all too aware of.

Yours Faithfully,



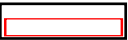
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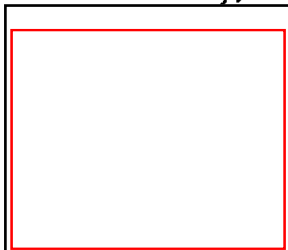
22 July 2011.

Heather Cook,  
General Medical Council,  
Manchester.

To whom it may concern,

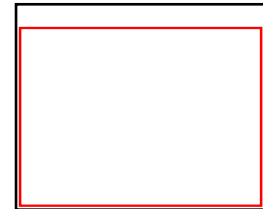
My wife was recommended to Dr. Skinner and contacted him after unsuccessful diagnoses of her many symptoms. She has been treated for hypothyroidism for  to date by Dr. Skinner and appears to, and is, doing very much better and the symptoms that have been distressing her reduced.

Yours faithfully,



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22<sup>nd</sup> July 2011

General Medical Council,  
Manchester.

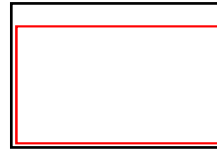
To whom it may concern,

I have been seeing Dr. Skinner since [redacted] for hypothyroidism (borderline) and have been taking the tablets he has prescribed. I am feeling much better and am sure that he has located the source of the problem that has given me many distressing symptoms. I have been diagnosed (supposedly) with other problems from various GP's but have felt little benefit.

Yours faithfully,

[redacted]

[redacted]



22nd July 2011

F.A.O.  
Heather Cook,  
Investigating Officer,  
*Fitness to Practise Directorate*,  
General Medical Council,  
3, Hardman Street,  
MANCHESTER,  
M3 3AW.

Testimonial for Dr. Gordon R B Skinner MD, DSc, FRCOG, FRC Path,

[Redacted]

Dear General Medical Council,

As the NHS refused to support and help me, my thyroid condition was left to deteriorate untreated. Hence, I was left hanging in an awful horrible way.

Having lost complete and utter trust with the NHS, Thank heavens for me that I eventually met Dr. Skinner. Genuinely and sincerely, without him, it deeply concerns me, as to how my present and future health lies within the hand of the NHS.

In my experience, as I believe, see and feel it, my neglected thyroid disorder caused other symptoms. These symptoms with NHS, became misdiagnosed for other health conditions.

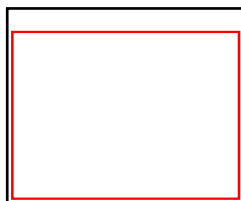
These other symptoms that I endured are now less of a problem than they were, or are now completely gone, thanks to the guidance, support and treatment from Dr Skinner.

Yours sincerely,

[Redacted]

[Redacted]

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21<sup>st</sup> July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

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Dear Ms Cook

Re: Dr Skinner

In advance of the hearing arranged for Dr Skinner I would like to make you aware of the fact that he diagnosed and treated me when the NHS failed. [redacted]

[redacted] My general health was under  
par and [redacted]

[redacted]

I saw my general practitioner several times and asked for thyroid function tests as I recognised the symptoms from my studies and also remembered my grandmother having similar problems. Even when my TSH level came back at [redacted] I was told I was borderline hypothyroid as my FT4 was deemed to be within the normal range at [redacted]. May I point out that there was absolutely nothing normal about the way I was feeling! It was suggested I return for a repeat blood test the following year. I actually returned to the surgery a week later and requested a private referral to Dr Skinner after receiving help from Thyroid UK. Although reluctant to refer me my general practitioner did agree to do this and a week later I saw Dr Skinner who diagnosed me to be clinically hypothyroid. I was commenced on Armour immediately and gradually got better. He didn't just interpret the blood test results (although they were clearly sub-optimal) but also looked at my clinical picture. I was ill and on reflection more ill than I realised at the time.

Over [redacted] years down the line I am completely stable and Euthyroid. I take [redacted] grain of Armour and [redacted] mg of Thyroxine each day and have my levels checked by my general practitioner annually. Blood tests show that I have been stable for the last [redacted] years.

Dr Skinner listened to me and provided me with a route to recovery. I was a [redacted] year old mother of two young children, I wanted to be energetic and well and if I had not sought Dr Skinner's professional opinion I am under no doubt that my health would have declined and I may never have been diagnosed. Happily, I enjoyed my children's younger years and now have two fabulous teenagers who I can keep up with. [redacted]

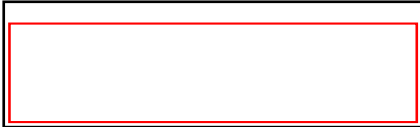
[redacted]

The care I received from Dr Skinner has allowed me to live a very rewarding and busy life and more importantly my children had what all children deserve - a well mother to take care of them. My care on the NHS would have compromised this and I will be eternally grateful to Dr Skinner for treating me.

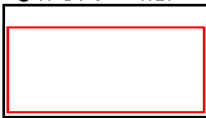
I do hope you take my comments into consideration and I would be happy to answer any questions you may have.

Best wishes

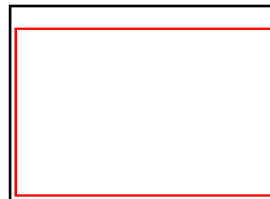
Yours sincerely



CC: Dr Skinner



Mr R Shipway  
Radcliffes le Brasseur  
Solicitors  
5 Great College Street  
Westminster  
London SW1P 3SJ



Testimonial in support of Dr Skinner:

I am the sister of a patient of Dr Skinner, [redacted]

My sister was very unwell [redacted]

[redacted] She was referred to the local hospital [redacted] but felt she was not received sympathetically and that she was being told that her symptoms were 'all in her mind'. My sister has always been a very capable and strong person but I saw her deteriorate even further and she didn't feel that anyone was listening to her.

She began to research her condition in a hope of finding someone who could help her. She found articles relating to Dr Skinner and her GP referred her to him. The contrast with the approach from her hospital couldn't have been greater. I accompanied her to all her sessions with Dr Skinner as moral support as she was so accustomed to being told how she should feel and her confidence had been undermined. Dr Skinner put her at ease and listened and undertook her treatment.

From that point on I have seen her improve greatly and regain her quality of life, [redacted]. The contrast with [redacted] years ago is wonderful and her grandchildren have their Gran back.

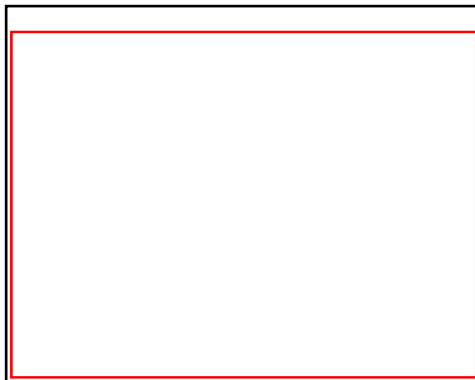
I and the whole family are immensely grateful to Dr Skinner and his staff for the care and treatment they are giving to my sister.

Yours Sincerely

[redacted]

[redacted]

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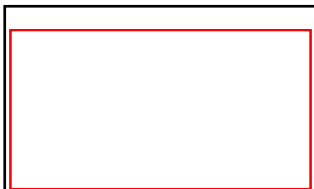
18/07/2011

Dear Ms. Cook,

I am writing in support of Dr. Gordon Skinner whom I understand is due to attend a hearing of the General Medical Council starting on 28<sup>th</sup> July 2011. I have been a patient of Dr. Skinner's for over [redacted] years as I suffer from [redacted]. I consulted Dr. Skinner after [redacted] years of misdiagnoses and ineffective treatment administered by over 30 different doctors, both in the UK and abroad. It was therefore a great relief to finally find a doctor who is sufficiently advanced in his research and experience to understand that my extremely debilitating symptoms were being caused by my thyroid condition. Without Dr. Skinner's help I would never have stood a chance of getting well as every other specialist I had seen before him had dismissed the possibility that my thyroid could be the cause of my extremely poor health. As a result I was not receiving the sufficient thyroid hormone replacement that I so desperately needed.

I am very grateful to Dr. Skinner for his help and I believe that the medical world desperately needs more doctors like him. One only has to look on online thyroid support forums to realise that there are so many undiagnosed and under-treated thyroid patients out there who could benefit from the help of Dr. Skinner. It appears that a lot of doctors and specialists seem to be failing their thyroid patients and I would therefore recommend Dr. Skinner to any fellow sufferers who are not getting the help they need to recover elsewhere. He truly is a pioneer in this field.

Yours sincerely,



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[Redacted]

22.07.11

Dear Heather Cook

My name is [Redacted] and I am writing in support of Dr Skinner. I am a patient whose life has been transformed by having my clinical symptoms and my blood tests very carefully and thoroughly considered and treated by Dr Skinner. After only [Redacted] weeks I began to improve and to feel normal again for the first time in [Redacted] years. Since then I have enjoyed [Redacted] years of good health and productive work.

[Redacted]

My GP was conscientious in ordering a battery of blood and memory tests. He agreed that I had classic hypothyroid symptoms but because my tests remained in the 'normal' range was unable to prescribe.

I have a strong family history of thyroid disease and all my children have been diagnosed. However, both my daughters were ill for [Redacted] years before blood tests confirmed diagnosis. During this time they suffered enormously, the eldest unable to work or look after herself.

By discounting clinical symptoms and focusing entirely on blood tests as 'evidence based medicine' patients are left to suffer, become disabled, unable to function in a job or at home. At the time I felt completely let down by this system and I continue to feel that there will be many other patients who are still being let down by this narrow focus.

[Redacted] I am committed to the NHS and to high clinical standards. The modern NHS aspires to be patient focused. Professionals are asked to listen to us. I would like the GMC to listen to us and believe us when we say that we have become healthy with Dr Skinner's treatment. I would like the GMC to become engaged in an open attempt to understand why blood tests are not always a reliable indicator of dysfunction and why Dr Skinner's approach is of such immense value to his patients.

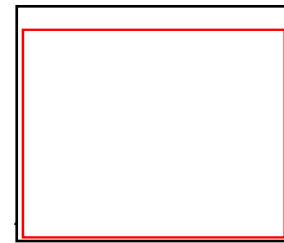
Yours sincerely

[Redacted]

[Redacted]

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19<sup>th</sup> July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

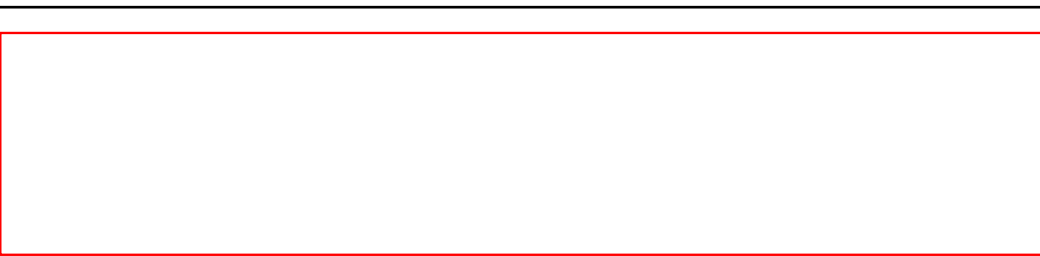
Dear Heather

Re Dr GRB Skinner

I am a patient of the above doctor and owe my life to him after I was 'diagnosed' with  by my then GPs and the NHS Endocrinologist in  as my Thyroid Stimulating Hormone (TSH) returned within mid range which is within the blood reference range that I understand is widely used by the medical profession.

When I finally found Dr Skinner I was at my wits end as my life was not worth living

". Dr Skinner went on to take full bloods to test for Hypothyroidism finding that my T4 blood level was very low. Therefore, started to treat me for Hypothyroidism over a period of  years until I slowly regained my health on Levothyroxin, but only later gaining optimum health after including Armour Thyroid medication.



I had not had any reason to see Dr Skinner regarding my health over the past few years as I am now treated for Hypothyroidism by my GP and the  Endocrinologist who prescribed me  mgs of Thyroxin for life at Dr Skinner's suggestion and the resulting outcome. However, on my noticing the low T3 blood results I made an appointment to see Dr Skinner in  where he suggested a starting dose of  mgs of T3 due to my body not converting the Levothyroxin, T4 into T3 and reducing the Thyroxin accordingly. It is now July and I am feeling so well on T3 that it is unbelievable. My GP cannot comprehend the



--

[redacted] Dr Skinner's treatment of my thyroid condition and his diagnosis of Hypothyroidism from [redacted] onwards has never been disputed by the [redacted] Endocrinologist, who prescribed [redacted] mgs of Thyroxin on the NHS as previously prescribed privately by Dr Skinner.

a correct diagnosis.

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[redacted] it was by reading an earlier publication of 'Understanding Thyroid Disorders' available in any chemist together with a book called 'Tears Behind Closed Doors' that I realised that I might not have [redacted] but a Hypothyroid condition and therefore consider myself very fortunate in locating Dr Skinner in time.

If Dr Skinner is found 'against' at this GMC hearing it would be an injustice to him and to his existing patients that I understand travel to him from all over the UK and abroad to seek treatment. Also for all those patients still out there somewhere that are still being misdiagnosed with CFS and ME who are told "TO LIVE WITH IT". This is a modern day tragedy, and we CANNOT LIVE WITH IT! Would you like to loose your job, your home, and have your relationships fail due to having to put up with poor health making it impossible to work to earn a living? When there is a SIMPLE solution out there in Dr Skinner and his treatment of this condition that is not being utilised by others doctors due to ignorance, misguidance or more likely the fear of loosing face by being proved wrong in their facts. This is a tragedy to the nth degree that requires education from the GMC to prevent this wrongdoing to a large number of humanity.

Dr Skinner has not harmed anyone; he's made them well. I have not complained to the GMC about him. He has taken the Hippocratic oath and performed it admirably affirming his obligations and proper conduct to his patients. I recommend him highly and he should be praised not penalised for finding treatments that work. I have sought out Dr Skinner twice in the past [redacted] years where he has prevented me becoming an invalid on both occasions.

Yours sincerely

[redacted]

[redacted]

Encs.

[redacted]

Copies to

[redacted]

Mr Ralph Shipway









July 2011-07-21

Testimonial for Dr. Skinner (copy to Dr. Afshan Ahmad)  
To whom it may concern.

I was prescribed 'natural desiccated thyroid' medication over [redacted] years ago by Dr. Gordon Skinner. I had been suffering from chronic ill health for a number of years and was a member of the M.E. association who put me in touch with Dr. Skinner. After a diagnostic meeting and the taking of blood for testing Dr. Skinner subsequently diagnosed 'Border Line Hypothyroidism'. Initially I was prescribed low doses of Levothyroxine but was later transferred to Armour Thyroid as I was told that this contained a combination of T3 and T4 which had been found to benefit those with [redacted] symptoms. It did indeed help me. Slowly I returned to good health. I very gradually, under Dr. Skinner's supervision, increased my dosage until I was eventually taking [redacted] grains. I was taking this maintenance dose until approx [redacted] years ago when it was increased to [redacted] grains. During this time we had difficulty in obtaining Armour due to manufacturing difficulties and I transferred to Erfa Thyroid.

Throughout my time under Dr. Skinner I saw my GP and he took regular blood tests and he was perfectly happy to prescribe the drug. At the moment I have [redacted] monthly blood tests and they are consistently 'normal'. I have and do find Dr. Skinner to be most ethical and helpful. At a time when I had exhausted all known channels he was the only Doctor that helped me and moreover believed me when I told him my symptoms. Some years after being on this medication I was asked by a GP for details of my medication and history as he had found that he could offer no hope to his ME patients and was keen to hear of how, my now stable health had been achieved by a Doctor that was willing to believe that, for some individuals, border line results can mean a limbo land of chronic ill health and years of frustrating surgery and hospital visits.

I had no hesitation in putting my name forward to speak at the hearing or write the above testimonial.

[redacted]

[redacted]

[redacted]

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22nd July 2011

Ms Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook

**Re: Review Hearing of Dr Gordon Skinner**

I am dismayed to hear that this wonderful doctor is still the subject of an investigation. I would like to offer my wholehearted support of Dr Skinner.

I have been one of Dr Skinner's patients since [redacted]. When I first asked my GP to refer me to him I was very ill indeed, with all the classic clinical signs of hypothyroidism. My TSH was at the 'upper end of the reference range', and although my GP had prescribed a low dose of thyroxine, I was still unwell and deteriorating fast. On a scale of one to ten I would put my quality of life at no more than two as I became increasingly disabled by my illness. [redacted]

[redacted] I was [redacted] left with no alternative but to seek some treatment myself.

Dr Skinner's name was recommended to me via two different sources, and since becoming a patient I have never looked back. Under his fantastic, solicitous care my health has steadily been restored to me - to the point where I can work again and have a very good quality of life.

I have at all times found Dr Skinner totally professional, compassionate, completely committed, and very thorough - and what's more, he actually makes ill people better! What more could anyone want from a doctor?

I have been very carefully monitored as his patient. At each of my appointments Dr Skinner carries out a full clinical appraisal, he takes blood samples where necessary, and, most importantly, takes account of how I actually feel. Any change in medication has been closely monitored, and I have always known that I could phone him for advice if I had any concerns. He has kept my GP fully informed by letters.



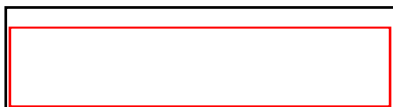
I believe that there are concerns about Dr Skinner 'prescribing outside recommended guidelines'. Perhaps it is time for the GMC to look at the guidelines instead of the doctor.

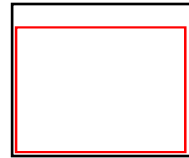
It is abundantly clear to me (as it is to the many patients with thyroid problems and other doctors who support Dr Skinner's work) that it is the guidelines which are putting patients' health in jeopardy, not the doctor. Thyroid testing and treatment is flawed: my GP's reliance on a blood test to tell her whether I was hypothyroid or not rendered me practically bedridden! Before tests like TSH existed, I believe doctors prescribed medication based on a clinical appraisal and how a patient felt - which is exactly what Dr Skinner is doing now with great success. And thank heavens that we have courageous doctors like Dr Skinner who treat their patients and not their blood tests, or there would be very many more people, quite unnecessarily, condemned to a miserable life with untreated hypothyroidism.

It would be a retrograde step for the medical profession if the GMC took action to restrict the work of this enlightened doctor.

I ask that you would please take my comments into account when considering your Review.

Yours sincerely

A rectangular box with a red border, used to redact the signature of the author.



23 JUL 2011

23 July 2011

Ms Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street

Manchester M15 6FQ

Dear Ms Cook

**Dr Skinner - letter of testimonial and support**

I write in support and huge thanks of Dr Skinner.

Quite simply, he has made my life a whole lot better.

When I was first referred to him, no other doctors or consultants had come close to correctly diagnosing my symptoms. All "conventional" diagnosis and methods had failed me. All of your conventional doctors and consultants had failed me. Dr Skinner helped me. He is a brilliant man and should be encouraged and supported to help as many people as possible in the same way.

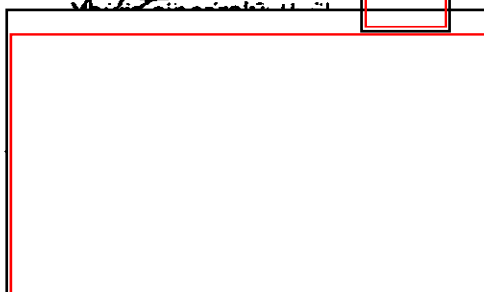
I was at my wit's end and Dr Skinner was almost my last hope. I had tried everything that had been wrongly prescribed and it had failed.

This man gave me (and hundreds like me) hope. He correctly diagnosed my symptoms and I immediately improved. I had my life back.

Patients such as me don't need hundreds of medical professionals who continue to do everything according to procedure and get it wrong. We need experienced, gifted consultants like Dr Skinner whose focus is on helping people, nothing else, and may sometimes go slightly off convention to do so.

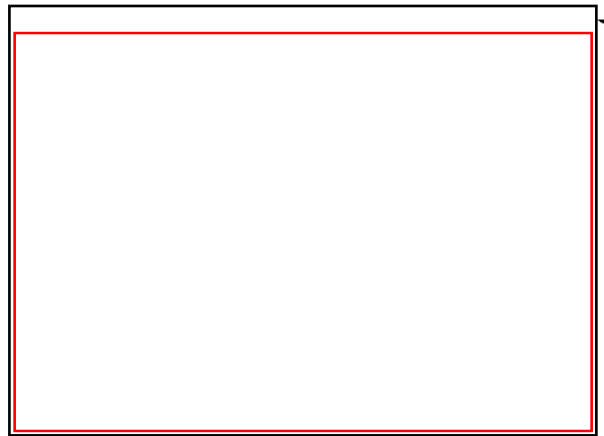
I will be eternally grateful to him and hope sincerely that pen-pushers and administrators are not allowed to deny others the treatment I received.

Thank you Doctor Skinner.



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Ref. GRB SKINNER.  
FITNESS TO PRACTICE  
28th July - 3rd Aug.



Dear MS Cook,

21st July 2011

I wish to register my whole-hearted support for Dr Gordon Skinner whose case will be reviewed by the GMC panel commencing 28th July.

That Dr Skinner should have been subjected to the allegations of impairment by reason of misconduct and deficient professional performance in the first place, is in itself appalling.

Dr Skinner works tirelessly for his PATIENTS and puts their needs above his own, often to his detriment (GMC hearings)

② My own family has been devastated by thyroid disease going through several generations, yet these facts were ignored by my own GP who would rather spend time consulting blood tests on a computer than actually observing & listening to the patient.

How is it possible that my own GP has no case to answer (by virtue of doing nothing) and yet Dr Skinner, who has restored the health of thousands of patients is made a Scapegoat by the GMC. This undoubtedly discourages any forward thinking GPs who believe their patients are Hypothyroid despite blood tests, from even trialling thyroid hormone for fear of retribution, by colleagues or the GMC.

There is plenty of academic <sup>3</sup> research to show that current thyroid testing may be flawed especially with regard to what is happening at cellular level, & in the cases of autoimmune thyroid disease

Blood tests are just that - they show the hormone that is circulating in the blood they DO NOT show how it is working at cellular level.

As a member of a patient led thyroid support group I read on a daily basis of the terrible impact hypothyroidism has on patients & their families. Groups like these ~~exist~~ only because patients are not getting back to good health on Levothyroxine alone, or even worse are not getting any treatment at all despite <sup>336</sup> a myriad of classic thyroid symptoms

4 For years patients have been told that their blood tests are 'Normal' So any symptoms/residual symptoms with treatment, are not thyroid related.

Patients may have believed this in the past, but with the advent of internet access these THOUSANDS of patients are finding that they are not alone in their concerns & are not the 'only' cases who are finding their current treatment by their GPs / Endocrinologists unsatisfactory.

The situation in this country is truly appalling when a patient can be diagnosed & treated in another country, but when they arrive in the UK told that they 'do not' have a thyroid problem, because of their blood tests!

Are doctors in these other countries

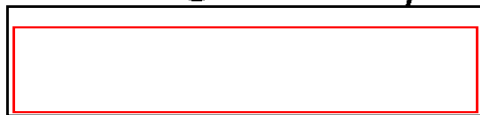
totally incompetent, or could it <sup>⑤</sup>  
be that the UK has the widest  
ranges in the world and is leaving  
thousands of patients untreated!

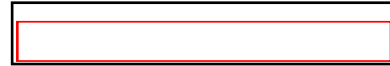
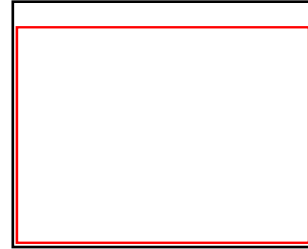
It would seem to me that  
the diagnosis & management of  
hypothyroidism in this country is  
so lacking as to amount to  
negligence.

Please listen to the PATIENTS  
that are being brought back to  
health by Dr SKINNER & not the  
uninformed GPs who complain  
about his work.

If in doubt there are plenty  
of papers on thyroid disease  
available on the internet to support  
Dr Skinner's findings.

Yours sincerely





July 25, 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practice Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester, M3 3AW.

Dear Ms Cook,

I write concerning the review hearing of Dr Gordon Skinner beginning on Thursday, July 28.

I do not know Dr Skinner personally but I am familiar with two of his patients, one my daughter and the other a friend, both of whom have been patients of Dr Skinner and treated by him for hypothyroidism, who both have subsequently shown marked improvements in their health.

Before her treatment by Dr Skinner, my daughter, [REDACTED] [REDACTED] had been tested for hypothyroidism by blood analysis that had shown her reading to be within the normal range. [REDACTED]

[REDACTED] Since her treatment she [REDACTED] returned to her former self. It is no coincidence that, with the co-operation of her husband, she has returned to normal life. She now plays her full part within the family and successfully works full time in a demanding professional role.

My knowledge of the medical condition of the friend who contacted Dr Skinner on [REDACTED]'s advice is more limited but she has told me that her health has greatly improved as a result of his treatment.



I also experience some of the symptoms of hypothyroidism, and hope shortly to be referred to Dr Skinner. If he were not allowed to continue to practice medicine, many patients and potential patients such as myself would be denied treatment for a condition that can severely reduce their enjoyment and effectiveness in life.

I might add that, because of my own symptoms, I have had to labour to produce this letter. I sincerely hope to learn that Dr Skinner will be allowed to continue to practice until he chooses to retire.

Yours sincerely,

cc. Ralph Shipway

re: DR GORDON R B SKINNER

20JUL2011

Dear [redacted]

I have severe thyroid impairment and consider myself most fortunate in having been referred to Dr. Skinner by my excellent GP when it became clear that her very best efforts were falling to restore my health. With Dr. Skinner's kind and diligent guidance, she has been enabled to relieve my hypothyroid misery with benefits beyond all measure.

When first I saw Dr. Skinner I was very ill, [redacted] hope of recovery had begun to fade. I now realise that he is all too well accustomed to receiving referrals in such sorry state, and is at great pains to put such patients at their ease from the outset (with consummate success). Most impressive was his meticulous care and patience in eliciting an accurate history from a patient who was [redacted]

In subsequent consultations as my health and awareness have improved, I have noticed the same care and patience being applied without fail - some responses to questions were being subtly double-checked by an obliquely equivalent question a few minutes later to ensure an unerringly accurate report to my GP. No less impressive was his constant concern to detect and identify any coexistent pathology and his very careful scrutiny of the numerous test results with which I have been able to supply him.

Dr. Skinner has not prescribed for me any medication, preferring to work in collaboration with my GP, in which he has engendered excellent results. I have noted that he is unwilling to suggest any course of treatment which is not supported by clear evidence before him.

In consulting Dr. Skinner I feel privileged to have met one of the world's few remaining gentlemen, and a physician *sans pareil* whose courtesy and professional diligence should stand as a shining example to those who may attempt to follow him. I believe that his experience in dealing with problematic hypothyroid patients such as myself is now quite unrivalled in the UK, and probably well beyond; I am appalled that the GMC should yet again seek to pillory him to the detriment of patients in grave need of his expert help. In my opinion, such action serves not the interest of the medical profession nor that of the public, but only that of a now mainly self-serving echelon of bureaucracy trying to justify its own continuing, but unworthy, existence.

Yours sincerely,

⇒ c. [redacted]

c. Radcliffe de Brasseur

Whether or not data which have been stripped of all personal identifiers are personal data in the hands of a person to whom they are disclosed, will depend upon that person being in possession of, or likely to come into the possession of, other information which would enable that person to identify a living individual.

It should be noted that the disclosure of personal data by a data controller amounts to processing under the Act.

For example:

The obtaining of clinical information linked to a National Health Service number by a person having access to the National Health Service Central Register will amount to processing of personal data by that person because that person will have access to information enabling him to identify the individuals concerned.

It will be incumbent upon anyone processing data to take such technical and organisational measures as are necessary to ensure that the data cannot be reconstituted to become personal data and to be prepared to justify any decision they make with regard to the processing of the data.

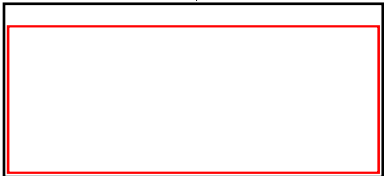
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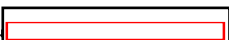
In the case of data collected by the Office of National Statistics, where there is a disclosure of samples of anonymised data, it is conceivable that a combination of information in a particular geographic area may be unique to an individual or family who could therefore be identifiable from that information. In recognition of this fact, disclosures of information are done in such a way that any obvious identifiers are removed and the data presented so as to avoid particular individuals being distinguished.

If data have been stripped of all personal identifiers such that the data controller is no longer able to single out an individual and treat that individual differently, the data cease to be personal data. Whether this has been achieved may be open to challenge. Data controllers may therefore be required to justify the grounds for their view that the data are no longer personal data.

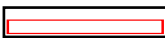
When a subject access request is received, a data controller must be able to identify the data relating to the data subject making the request, to enable him to provide information specific to that data subject. In making a subject access request, a data subject might provide the data controller with sufficient information to enable his data to be distinguished from data relating to other individuals, in a situation where the data controller would not otherwise be able to do so from the information in his possession, which he may have stripped of all personal identifiers. In this case the data relating to the individual making the request become personal data but the information provided by the data subject does not render the other data being held personal data unless the data controller believes that it is likely that the information will come into his possession to render the other data personal data.

If there are any doubts as to whether data are personal data the Commissioner's advice would be to treat the data as personal data, having particular regard to whether those

  
14/7/11

Dear 

I am writing to support Dr Skinner's case, as he is appearing again at another hearing in August.

I have been treated by him  with Armour thyroid, without which I would not be able to function. This is with my GP's consent. My late father was also helped by Dr Skinner many years ago.

I feel that Dr Skinner's work for his thyroid patients is highly commendable! Hypothyroidism does not seem to be addressed properly by many doctors and Dr Skinner has brought many people peace of mind and understanding. Several people in my family have this disease, which is very debilitating and often goes undiagnosed for many years, leaving us suffering and without fulfilling our potential.

My blood tests proved from the start without doubt, that I was hypothyroid. However, Dr Skinner taught myself and my GP that I need to have a T4 test at the top of the normal range, or a little over in order to feel well.

Also that I was a non-convertor and needed T3 as well as thyroxine. Dr Skinner prescribes Armour thyroid for me, which is not available on the NHS and should be.

I know that some people have many debilitating symptoms of hypothyroidism, but a 'normal' blood test result and that Dr Skinner has been able to help them too by listening to symptoms and by their appearance.

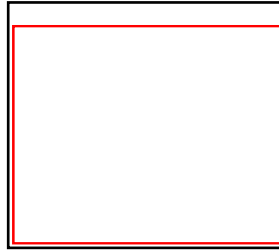
I fully support Dr Skinner's work and expertise and without him, myself and many people would continue to suffer from hypothyroidism, which ruins lives and can lead to premature death. I could not survive without Armour thyroid.

I hope this letter will help him.


Yours sincerely,

[Redacted signature]

[Redacted address]

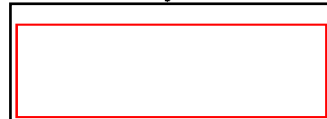


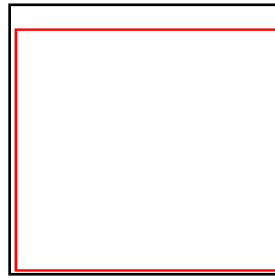
Dear Ms Cook,

I have two friends who have been treated by Dr Skinner for about  years. One of them was suffering very badly from hypothyroidism and was repeatedly wrongly diagnosed. Eventually she went to Dr Skinner who recognised her problems and his treatment improved her health amazingly. So from years of unnecessary suffering and a shortening of her career, she regained a good quality of life. The other friend was not severely hypothyroid but had a similar return to good health.

It is essential that Doctors are able to treat patients according to their knowledge and judgment without being constrained by a professional body with a rather blinkered approach. It appears that some endocrinologists are more concerned about upholding their views than improving their patients health.

Yours truly





Testimonial in support of Dr Skinner:

I was referred by my GP to the [redacted] in [redacted] years ago with thyroid problems. I was unable to work for 6 months and spent most of the time

[redacted]

I did not feel any better on the treatment from the hospital but the consultant said he would do no more; I would 'just have to live with it' and discharged me. I felt there had to be more that could be done as my quality of life was so poor there was no prospect of my returning to work. I felt I was at 'rock bottom' and no one was listening. Life had no meaning if it was to carry on like this.

I contacted Thyroid UK and learnt there was other treatment available. I asked to be referred to Dr Skinner who listened to me and believed I would get better with his help, and I have.

I have continued to see Dr Skinner and my condition has improved greatly and I have been able to return to work and pursue my hobbies as I did prior to my illness.

I now have my life back thanks to the care and treatment provided by Dr Skinner.

Yours Sincerely

[redacted]

[redacted]

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[REDACTED]

25 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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Re: Letter in support of -  
Dr Gordon R B Skinner MD (Hons) DSc FRCPath FRCOG

I wish to pledge my support for Dr Skinner for the improvement he has achieved in my health and lifestyle over the past two years.

I am a ☐ year old woman who suffered very badly over many years with what I now know was Hypothyroidism.

General Practitioners and Endocrinologists I had consulted, at no time took any personal history or performed any physical examination, just merely stated that "my blood tests were 'normal'" [REDACTED]

[REDACTED] Following this advice avidly - did nothing to relieve any of my obvious and numerous signs and symptoms, other than to make things worse?

Subsequent treatment by Dr Skinner has resulted in a marked reduction of my previous clinical signs and symptoms.

Dr Skinner has also treated my daughter who has suffered similarly, and her condition has likewise also improved.

[REDACTED]

Dr Skinner has helped both my daughter and me by giving us back our lives, and the opportunity for a healthier and happier future.

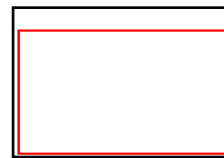
Yours sincerely

[REDACTED]

Cc: ☐  
Mr Ralph Shipway



Heather Cook  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester  
M3 3BE



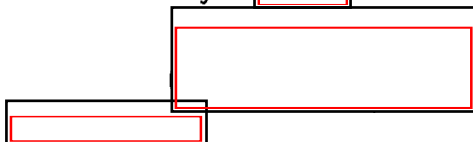
July 24<sup>th</sup> 2011

Dear Heather Cook.

My name is [redacted] and I'm aged [redacted] and for the past [redacted] years, I have been a private patient of Dr. Gordon Skinner, I feel so positive regarding the treatment that I received I can honestly say thanks to this my life has been turned round. I have had a long history of illnesses for many years, because my own GP's had ignored all my symptoms and told me [redacted]. thanks to Dr Skinner this did not prove to be true, although I really did not feel the benefit on only T4 I came to optimum health once I started taking Armour thyroid. As T4 was not converting for me.

I have nothing but praise for Dr Skinner and long may he be able to carry on his great work

Yours Sincerely [redacted]



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Ms. Heather Cook  
Investigating Officer, Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester, M3 3AW

Dear Ms Cook,

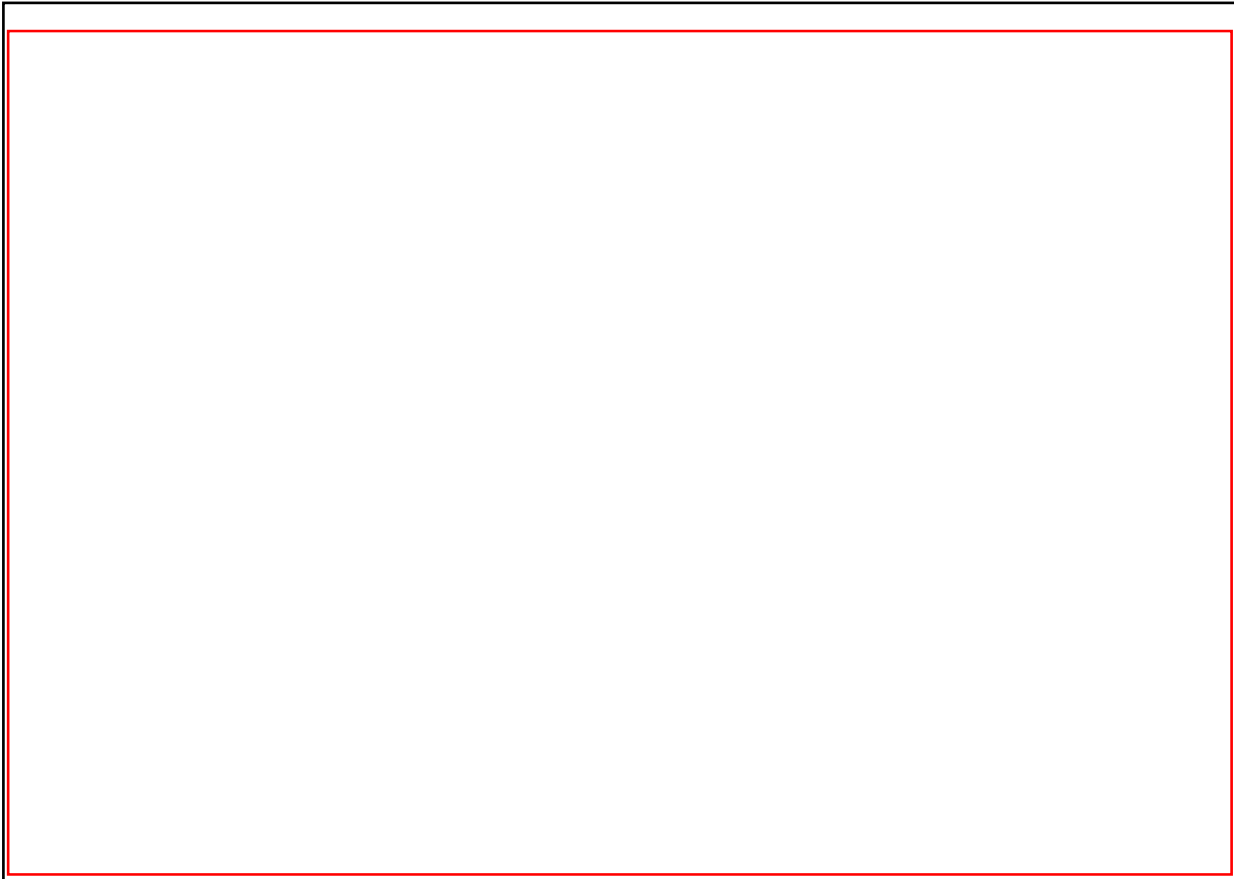
**Re: Dr Gordon Skinner / Fitness to Practice**

General Medical Council 25 July 2011	
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It has come to my attention that Dr Gordon Skinner is being reviewed under his Fitness to Practice order, and I would like to add my statement of support for Dr Skinner, following the excellent treatment he has provided me.

When I was [ ] years old, I developed [ ] and never fully regained my energy levels until my consultation with Dr Skinner [ ] years later. For those [ ] years, I reluctantly accepted that this was just the way I will be and that maybe my days of being alert and active were over. My Mother, however, was determined that she had seen too drastic a change in me and was constantly appealing to our GP that I needed further testing to get to the bottom of my behavioural change. It was only when my Mother was diagnosed and correctly treated by Doctor Skinner for hypothyroidism that she could see for herself the fundamental impact thyroid illness has on one's life. She realised how many people in our family had suffered mis-diagnosis, once she became aware of the illness and all its manifestations. We finally managed to convince our family GP to refer me to Dr Skinner, and my life has been transformed as a result. Dr Skinner gradually, cautiously, built up my medication to a dosage where I felt that I had my life back. This may sound dramatic, but it is only once one is correctly medicated that one realises quite how dormant one has become. I had energy, could concentrate, my physical conditions improved [ ]

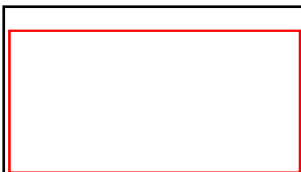
Having finally been correctly diagnosed, I was also lucky in finding an incredibly supportive, intelligent GP in [ ] where I was living at the time, who supported Dr Skinner's recommended prescription for me of levothyroxine at the strength I needed. I got my life back on track, my then fiancé was getting to know the woman he always knew I had the potential to be and nothing felt too great an obstacle at work; I was finally myself again.



I can only hope that you will read the testaments of Dr Skinner's patients, and listen, with understanding to his patients when they testify. Dr Skinner has himself had the courage to listen to his patients and has shown the ability to turn around their lives. It is vital that patients are properly diagnosed and treated with the backup of blood tests following diagnosis. Because trust me, once you have lived with the condition untreated and then lived knowing that you can reach your full potential again, you would move heaven and earth to prevent one further misdiagnosis. Please, don't let this continue. I for one am terrified of returning to a life with the dimmer switch turned down low, terrified and overwhelmed. And I speak from the strength of once having had correct treatment, who's been through far greater challenges in life than a new job and pregnancy.

Thank you for your time.

Yours sincerely,



Copies to: Mr Ralph Shipman  
Dr Gordon Skinner

[redacted]  
Ms Heather Cook  
Investigating Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

24 July, 2011

Dear Ms Cook,

Dr Gordon Skinner

I understand there is to be a review of Dr Skinner's fitness to practise, and I wish to write further to appearing in his defence as a witness at his Fitness to Practise in November 2007.

[redacted]  
[redacted]. However, during these two years I remain grateful to Dr Skinner for having diagnosed my hypothyroid condition correctly and setting me up with the correct balance of treatment, and to my GP for having recognised his skills and prescribed the balance of levothyroxine and liothyronine he recommended. I am confident that this has been paramount in helping me to maintain good health.

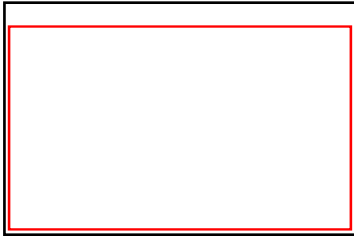
However I am concerned about my hypothyroid daughter [redacted] who has been under two GPs in the last [redacted] years, having moved. Her more recent doctor has been governed by blood test results rather than her well being. This has resulted in wanting to cut back on her levothyroxine dosage after blood tests with the effects of hypothyroid symptoms. How can it be that GPs are nervous of treating patients correctly, could it be the threat of litigation?

[redacted]  
[redacted] Further to the threat to her health, this has of course also affected her ability to perform well at work, where she has been struggling to work effectively on reduced medication. If her correct treatment is not forthcoming, and we sincerely hope it will, we need to be confident that Dr Skinner will be available to advise her. Without him and the way he carefully monitors the physical and mental state of his patients, how can the situation for hypothyroid patients in the British Isles improve?

Yours sincerely,

[redacted]  
Copies to: Mr Ralph Shipman  
Dr Gordon Skinner

General Medical Council	
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23<sup>rd</sup> July 2011

Dear Ms. Cook

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Once again I am writing to support Dr. Skinner in his work. It seems beyond belief that he now has to face a review hearing regarding his fitness to practise as a doctor when he is a man of such integrity and works to the highest standards.

I enclose a copy of my 2007 letter to reiterate my history. I would like to add that there have been times over the last few years when Armour Thyroid has not been readily available in this country which forced me to reduce my dosage for a period. This caused my symptoms to start to return, which was very frightening, [REDACTED]

[REDACTED] Proving, I feel, Dr. Skinner's clinical assessment of me that I didn't have [REDACTED] but hypothyroidism and [REDACTED].

It is quite clear to me that without Dr. Skinner's intervention and treatment of my thyroid and adrenal glands I would still be either chronically ill, unable to have any sort of normal life with my husband and family, or in all honesty I would probably no longer be alive. Thanks to Dr Skinner I am able to lead a full life, [REDACTED]

[REDACTED]

I cannot speak highly enough of Dr Skinner and my hope is that after this review hearing the GMC will allow him to continue with his valuable and important work unhindered.

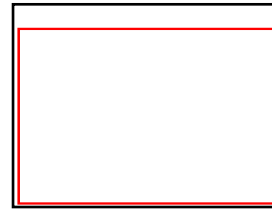
Yours sincerely [REDACTED]

[REDACTED]

Copies to:

[REDACTED] and Mr Ralph Shipway at

[REDACTED]



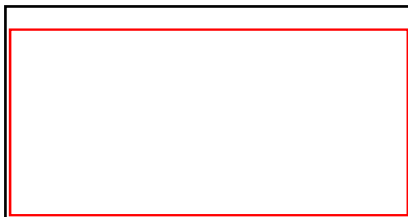
23<sup>rd</sup> July 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

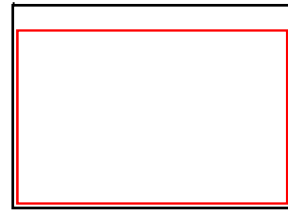
Dear Ms Cook

I wish to register in the strongest possible terms my support for Dr Skinner.

Yours sincerely



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23<sup>rd</sup> July 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Ms Cook

I wish to register in the strongest possible terms my support for Dr Skinner. My life has been utterly transformed since being diagnosed and treated for hypothyroidism.

Yours sincerely

A rectangular box with a red border, likely used to redact a signature or name.

A rectangular box with a red border, likely used to redact information from the document.




23<sup>rd</sup> July 2011

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M3 3AW

Dear Ms Cook

I wish to register in the strongest possible terms my support for Dr Skinner.

Yours sincerely





21<sup>st</sup> July 2011

F.A.O. Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester.  
M3 3AW.

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Dear Ms Cook,

I understand that the General Medical Council are, once again, investigating a complaint from someone wholly ignorant of the huge number of patients who owe their life and ongoing health to Dr Gordon Skinner. I am one of the many patients left untreated for years with severely declining health, exhibiting every clinical symptom of hypothyroidism. I am fully reliant on Dr Skinner to receive prescriptions as my thyroid function tests narrowly fail to qualify me to gain NHS treatment in the arbitrary, financially motivated lottery system existing in Britain. I have experienced excellent health thanks to Dr Skinner's sound judgement and support for the last [redacted] years. I will give a short outline of my medical history.

I experienced increasing levels of tiredness from [redacted] onwards and approached a number of doctors over a [redacted] year period, receiving no diagnosis or treatment. During this time my thyroid function tests were either fractionally within 'normal range', or, as I have later found out, just outside reference range. [redacted]

[redacted]

[redacted]

My father was fortunately given Dr Skinner's details. Within a few [redacted] of treatment with thyroxine my health improved. Dr Skinner returned me to complete health and has given me excellent levels of care to date. He has supported me through [redacted] that I know would not have been possible without his sensible, clinical judgement.

I have found out from my childhood hospital records that my thyroid function has been tested as low since I was . I was therefore left untreated for over  years before Dr Skinner's intervention.

Yours Sincerely

[Redacted]  
Ms Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
G M C  
3 Hardman Street  
Manchester M3 3AW

21 July 2011

Dear Ms Cook,

DR G R B SKINNER

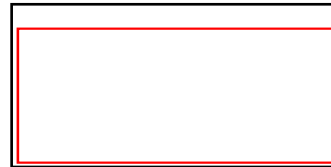
As a patient at Dr Skinner's thyroid clinic for over ☐ years, I would like to state that I have found Dr Skinner a very fine doctor who puts the health of patients before any personal gain and who inspires trust and confidence. He listens and keeps meticulous records and seems to actually care what happens to patients. I do not know how I would have managed all these years without the help and care I receive from Dr Skinner and his clinic.

Yours sincerely

[Redacted Signature]

CC:   
Mr Ralph Shipway

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


23 July 2011

Dear Heather Cook;

I write in total support of Dr G Skinner.

Several specialists misdiagnosed my Thyroid illness. It seemed their in word at the time was "stress". I am a normal balanced person and certainly was not and presently am not under any stress.

Fortunately I heard about Dr Skinner and attended in  His consultation was different in that he had a full discussion and took note of my symptoms.

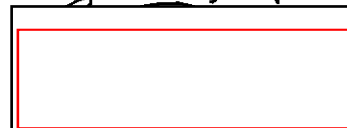
Since then, I continue to consult Dr Skinner but have to get prescriptions from our local GP, which is a ludicrous situation.

He is the only Doctor who has helped me maintain a balanced healthy life.

I cannot understand why the GMC continue to hound a Doctor who actually cures people.

I request the Council to fully reinstate and not further curtail Dr Skinner.

Yours faithfully



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[REDACTED]

22 July 2011

Ms Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

Dear Ms Cook,

TESTIMONIAL FOR DR G.R.B. SKINNER

I am pleased to write for [REDACTED] a Testimonial on behalf of Dr Skinner. I must point out that I have never met Dr Skinner so my support for him is because of the effect his regime of care has had on my friend (and I hope for countless others too).

I have known [REDACTED] for many years and have been aware of the wide range of her interests and curiosity in life around her. She was active and involved in a variety of pursuits: [REDACTED]

[REDACTED]

It was only when [REDACTED] began to get better under Dr Skinner's care that I realised just how much of her life had been lost. [REDACTED]

[REDACTED] The deterioration had been so gradual but it had gone on for years. [REDACTED]

[REDACTED]

The marked improvement following Dr Skinner's intervention brought [REDACTED] back into focus; slowly she emerged as a real person again. She's more engaged, interested again in life around her, and other people. She has more energy and is alert, talks more freely, laughs easily and sings again (still off-key), and joins in sometimes. Her appearance has also changed: [REDACTED]

[REDACTED] The years without sufficient thyroid medication have had a profound effect on [REDACTED] and I don't think she will ever really come back.

I thank God that there are still doctors like Dr Skinner who are committed to their patients' care, put them first, and honour their "do no harm" assertion. [REDACTED] has a whole string of GPs whose Fitness to Practise should be examined.

Yours sincerely,

[REDACTED]

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[redacted]

22 July 2011

Miss Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

Dear Miss Cook,

DR GRB SKINNER

[redacted] has asked me to write a Testimonial for Dr Skinner, whom I have never met. However, by the end of [redacted] I saw [redacted] come back to life, so I feel qualified to comment on the Dr Skinner effect, compared to the effect which several GPs (including my own) had had upon her health. In fact their lack of competence has undermined my own confidence in my GP. I have done some considerable reading on this subject.

The problems with hypothyroidism may be that this incompetence stems from the teaching of medical students who fail to understand the complexities of this condition. At one level thyroid deficiency is serious enough to warrant free medication (a status which cancer patients have only recently achieved) or the patient is treated as neurotic by the average GP, even after s/he has managed to diagnose the condition. Then there is the management of this condition.

I will quote Peter Bourdillon, Head of Specialist Clinical, NHS Executive in the Department of Health who wrote in April 1995 that:

"there are two reasons why there is a medico-scientific problem. The first is that the normal range of thyroid function tests is based on the measurements from a healthy population; by definition 2% of the healthy population have measurements below the normal range and 2% have measurements above the normal range. Thus 2% are, by definition, hypothyroid. The second problem relates to the intra-individual day-to-day variability in thyroid function tests. The normal range of TSH, for instance, is roughly 0.5 to 5 mU per mL. A change of greater than 0.8 mU per mL in an individual's measurement, assuming no intercurrent illness, is a significant change. Consequently, a person having a TSH of 1.5 on one occasion and subsequently a TSH of 3.5 has had a significant rise in his/her TSH, yet both are within the normal range..."

with the regrettable result that the average GP (by definition, most are average) would reach the all-too-common diagnosis of neurotic depression.

Peter Bourdillon goes on to say:

" I suggested that there were two ways of handling the issue of day-to-day variability in thyroid function tests: one is to stimulate some research and the other is to make patients with treated hypothyroidism aware that they may benefit from a further increase in their thyroxine therapy even if their thyroid function tests are within the normal range ..."

This made me LOL! It is the GP who is unaware, or affects to be so, which is even more disgraceful! *No GP would risk this approach despite having a duty of care for their patients.* Only Dr Skinner, and his like-minded colleagues, are willing to try this approach to effect a beneficial improvement in their patients' health for which he stands before your panel. Two per-cent of the population is equal to well over a million people, most at the mercy of their GP. This figure should frighten you. One day this lack of care of GPs will really hit the fan. Only Dr Skinner (and colleagues) will be left standing with their moral integrity intact.

One last comment: are the members of the Fitness to Practise panel the same people who fail to teach medical students to treat their patients and not the blood test result. I suspect it is these teachers who have a vested interest in maintaining the status quo.

Yours sincerely,

[redacted]

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

#### TESTIMONIAL FOR DR G R B SKINNER

Dr Skinner began treating my hypothyroidism in the Spring of [redacted]. The previous [redacted] years had seen a gradual diminution of my life and I attach a copy of my symptom list current on my first visit to Dr Skinner. He questioned me closely going over the detail of my symptoms, wanting to know how different this was. He took a family history and established that this is an condition inherited from my mother. [redacted]

A condensed version of this list had previously been given to an NHS GP (Dr [redacted]) who agreed there was clearly something wrong but stated categorically that it was not thyroid-related. She was just one of several NHS GPs who were either unable to diagnose, or then to treat my hypothyroidism adequately. My current NHS GP joined this group, after a consultation of less than 10 minutes in which he failed to look at me, failed to ask about progress or otherwise, checked my blood test results and declared a reduction in my thyroxine meds would be appropriate. I thought that hypothyroidism was a condition where it was crucial that NHS GPs treat the patient and not the blood test result.

Dr Skinner treats me with respect, answers questions I may have, consults me about how I think I am managing and questions my responses. He discussed with me a possible way forward. At all times he maintains a most professional approach. I regularly receive a copy of "Possible side-effects of thyroid replacement" in which he makes clear the problems of over-medication. I have *a priori* knowledge of under-medication. He treats the patient and their symptoms, not the blood test result.

Dr Skinner gave me back my life. I can now laugh again and sing; I can go out without negotiating with myself all the reasons for staying at home; I can just do things without endlessly thinking about doing them. [redacted]

[redacted] Living, in other words. [redacted]

In [redacted] under Dr Skinner's care my life began again. He gave me back the freedom to be myself and to live. Had there been no Dr Skinner I would have arranged my funeral whilst I was still able.

20 July 2011

Hypo symptoms *still outstanding on 100ug throxine.*





**To whom it may concern**

I have had an under-active thyroid for [ ] years. My late husband would have said longer as he had spent several years urging me to have it checked but blood samples confirmed it was "within normal range". [ ]

About this time I saw another doctor in the practice that would only go by the guidelines given by the laboratory so I started a downward spiral going back to the early years before I was diagnosed

[ ] My quality of life was greatly diminished but all my GP was prepared to do was to treat the symptoms not the cause. During this period I was not examined at all other than by a hospital doctor when I

I started to look for an alternative and found Dr Skinner praised a Newsletter online. He was very well recommended but I was horrified to see he was due to be questioned by the GMC. I put contacting him on hold but read many testimonials as to his expertise, his knowledge and his thoroughness. The point that was mentioned time and time again was that he listens. Once the hearing was over I contacted my then GP and asked if I could be referred. I was honest and told her all I knew and although she voiced caution she did refer me. With Dr Skinner's help I feel very much better than I have been for many years. He gives me a thorough examination, both physically and by probing questions which is so refreshing. He also keeps me informed when I visit of what the national trends seem to be. It is not a bias conversation that precludes the thoughts of others but it does give me the chance to ask questions and also ask and comment on his views. My GP is reluctant though to let me follow his advice and at times it is a battle but would I spend a day travelling down to [ ] and paying for a consultation if I didn't think it was in my own interest? I think not.

CC Dr G Skinner; Mr Ralf Shipway

25<sup>th</sup> July 2011

24.07.11

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman St.  
Manchester  
M3 3AW

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Dear Ms Cook,

**REVIEW HEARING – DR G R B SKINNER**

I am writing in support of Dr Skinner who has treated my wife, [REDACTED], for the past [REDACTED] years.

During the [REDACTED] years prior to seeing Dr Skinner in [REDACTED] my wife's health had been extremely poor. This resulted in a very different lifestyle to that of our previous [REDACTED] years of married life when we both led busy professional and social lives.

My wife experienced many debilitating symptoms, [REDACTED]

[REDACTED]'s parents, relatives, friends and myself were all very concerned about her health and frustrated that no treatment or support seemed to be offered by her GP. I don't know how Susan did not suffer depression during this time as the reduction in her ability to lead a normal life was so profound.

The difference after [redacted] saw Dr Skinner, was diagnosed with an under active thyroid and commenced medication was amazing. Her symptoms gradually reduced and her quality of life improved to the point where she was able to resume work properly again and return to social activities she had stopped. I know how very grateful she has been to Dr Skinner not only for diagnosing her condition after years of poor health but also for the care and understanding shown in treating her symptoms, something she had not experienced prior to this. I also feel very thankful that my wife heard of Dr Skinner and as a result obtained the treatment that she obviously needed.

I find it very disturbing that someone who has helped so many people including many who have suffered thyroid problems for many years without getting treatment should be called before the General Medical Council in this way.

Yours Sincerely,

[redacted]  
[redacted]  
[redacted]

23.07.11

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman St.  
Manchester  
M3 3AW

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Dear Ms Cook,

REVIEW HEARING 28.07.11-03.08.11 – DR G R B SKINNER

I am writing in support of the diagnosis, treatment and care given by Dr Skinner in respect of my thyroid condition.

I was unwell for  years from

On a number of occasions I asked my GP if I could have my blood tested for low thyroid function as I felt my symptoms fitted this condition. On each occasion my GP informed me that the results indicated that my thyroid was functioning normally.

I arranged to see Dr Skinner following an article in "InterAction" (ME/Chronic fatigue publication) regarding his work with patients whose chronic fatigue may have been the result of undiagnosed hormonal conditions. I first saw Dr Skinner in [redacted]. [redacted] I was very impressed by the very thorough medical history and examination undertaken. I was also overwhelmed by the concern and understanding shown as well as the explanation of the signs and symptoms I had been experiencing during the previous few years. The combination of the signs and symptoms and blood tests resulted in a diagnosis of an underactive thyroid being made. A small dose of Armour thyroid was prescribed, gradually increased during the following year. I have been regularly reviewed by Dr Skinner [redacted] to monitor my condition. I have blood tests every [redacted] months.

On commencement of medication my symptoms diminished over the coming months so that [redacted] later I was almost back to my previous state of good health. My strength and stamina continued to improve and I became able to increase physical activity. I now lead a busy and fulfilling life again and am working part time once more.

I feel extremely fortunate to have been able to receive excellent medical treatment from Dr Skinner. By taking a detailed medical history as well as the consideration of my thyroid blood results, a diagnosis of an underactive thyroid was made and appropriate treatment given. Without this diagnosis and treatment I feel sure that my health including my cardiac problems and lifestyle would have deteriorated further with, I am convinced, very serious consequence.

I appreciate and understand that blood investigations are important in reaching a diagnosis but to make that diagnosis solely on blood results without taking into account the patient's often very serious signs and symptoms (indeed often dismissing them as insignificant) would seem wrong and negligent. Despite having many classic signs and symptoms of the condition, my TSH level being slightly raised and my FT4 being near the lower end of the range I was seen as not having

**this condition. This situation has resulted in very many people remaining undiagnosed or on inadequate doses of thyroid medication causing severe ill health, inability to work and NHS finances being wasted on unnecessary investigations and treatment. Since my diagnosis and treatment many people with similar medical histories have contacted me for support and advice in trying to obtain diagnosis and treatment.**

**I have been shocked and upset that Dr Skinner's medical expertise has been questioned and investigated during recent years. Myself, along with so many others have had their health and lives transformed as a result of his diagnostic skills, treatment and his desire to ensure patients achieve their optimal health. Surely the focus must be on changing policy on the diagnosis and treatment of the many people whom the NHS has neglected for so long.**

**Yours Sincerely,**

[Redacted signature]

[Redacted name]

[Redacted address]

Dear *Reather Cook*

Dr G.R.B.SKINNER

My Wife and Daughter suffer thyroid problems. We attended various specialists but achieved nothing.

We heard of Dr Skinner and visited him. His consultation and examinations were more thorough than the visits to others.

For [redacted] years my Wife and Daughter continue to consult Dr Skinner and they remain in good health.

Why the GMC attack a Doctor who actually cures patients or succeeds in reducing their health problems is beyond me. It is as bad as the present phone hacking scandal.

We have only praise for and great confidence in Dr Skinner and hope common sense prevails at this hearing. I am assuming the GMC is interested in restoring people to health.

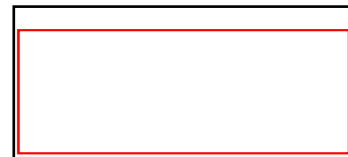
His work in this field should be applauded by the GMC even though it may be against their entrenched principles from the days of the arc.

Yours sincerely [redacted]

[redacted]

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
23 July 2011

Dear Heather Cook,

I write in support of Dr G Skinner.

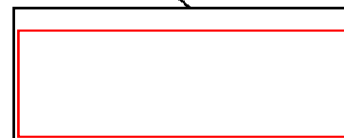
After visiting other medical people, who did not seem to know what my problem was and therefore could not offer treatment, I visited Dr Skinner.

Dr Skinner was more thorough in his consultations and examinations than the previous specialists. He diagnosed a thyroid deficiency and prescribed medicine.

With his help and expertise, during the last  years I have been much healthier and virtually symptom free.

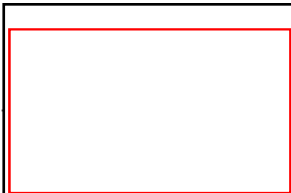
The GMC should support him in his work and recognise his ability.

Yours sincerely



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Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW



25<sup>th</sup> July 2011

General Medical Council	
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Date: 26 JUL 2011	
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Dear Ms Cook

**RE: Dr Skinner's Hearing in Manchester.**

I am a patient of Dr Skinner and I live in the [redacted] area.

[redacted]

I have been suffering with extreme symptoms due to an underactive thyroid (Hypothyroidism) for many years and have been unable to get any satisfactory treatment through my own GP. It is only since I went to see Dr Skinner for both myself and my daughter [redacted] that I have had any success in achieving much greater health.

[redacted]

It is only since I have been receiving treatment from Dr Skinner that I have started to improve in health. I have been misdiagnosed with many things; [redacted]

[redacted]

I have been unable to work for seven years due to [redacted]  
[redacted] offered Thyroid blood tests in the past by my GP but from those tests have been told that I had no need for thyroid supplementation and that my thyroid is the 'normal range'.

However, since speaking extensively with Dr Skinner and being treated with Levothyroxine, I am for the first time in many years of suffering starting to feel much better with gradual improvements in many of the symptoms that I have been suffering for such a long time.

Dr Skinner has never mislead me or told me to expect quick results, he has informed me extensively about my symptoms and has really reassured me that my symptoms (such as memory loss) are all part of the underactive thyroid condition. He put me on a very low dose of Levothyroxine to begin with and has slowly and safely ramped up the dose to the point that I am now beginning to feel the benefit in many ways.

Dr Skinner is the first person I have had faith in for a long time. I won't say that I was not a little sceptical when I first read about him and decided to make an appointment, as I was not able to work out how yet another doctor could have a different opinion on my symptoms than all the others I had spoken with. I was at the point of giving up. I was quite desperate to find someone who would believe I was suffering. [REDACTED]

I consider myself to be a level headed person who is capable of making an informed decision and that is why after extensive reading and checking of Dr Skinners credentials, I decided to make an appointment for a consultation with him.

It was most certainly the best decision I have made in many years. I can honestly say that for the first time since my late [REDACTED] [REDACTED], I have started to feel relieved of some very extreme symptoms.

Dr Skinner is thorough, informative and very considerate of long term health problems. I believe that more doctors should be aware of the problems with the current blood tests for low thyroid and that they should not be so afraid to 'think outside of the box' when it comes to treating hypothyroidism. If I hadn't met Dr Skinner I would be facing yet another miserable year of suffering and emotional heartache. During my illness I have lost thousands of pounds on lost income from lack of employment, I have spent thousands of pounds on natural health remedies, seen doctor after doctor, hospital after hospital, had blood tests, one after another and have never had any satisfaction or proper explanation of my symptoms.

When I approached Dr Skinner for a consultation he was my last resort. I was at the end of my rope. I also went to see him with no great hope that he could do anything for me as I had been disappointed so many times in the past. I am really assured that he did not have any kind of 'placebo' effect on me as I was so used to not getting any improvements from taking tablets recommended by doctors in the past that I thought, well, I will just take the medication and see. You could say I was rather sceptical due to past experience.

I needn't have been, I noticed a very subtle change at first and now as time has gone on and the dosage has been adjusted by Dr Skinner, I have started to find great improvement for the first time in  years.

I am now facing a positive future with every day improvements in my health and the reassurance that I have found a 'sensible doctor' who is willing to really listen to me and help me to get my life back on track. My daughter has only just started to see him for treatment as we discovered she has the same condition.

When I read about hypothyroidism and how the test results are evaluated, I was rather shocked that so many people are being overlooked and not treated due to the poor reasoning behind the way the tests are interpreted. It was through this that I found information on Dr Skinner and it was this reason that led me to him. I had been convinced for many years that the thyroid was at the route of my problem but blood tests done by own GP kept disputing that anything was wrong as it was explained to me that I was in the so called 'normal range'. If my endless list of symptoms had also been taken into account as well as the blood test I feel that I would have been treated a long time ago for this condition.

that would have saved me not only physical pain but emotional heartache, loss of a job, the disruption it caused to my husband and my family and the loss of confidence, self esteem, friendships etc etc. I feel very strongly that more doctors should have the same attitude as Doctor Skinner when assessing patients for the possibility of hypothyroidism. The so called 'normal range scale' that the blood test indicates cannot be the ultimate decision maker in diagnosing this illness.

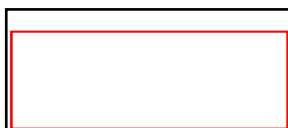
Dr Skinner does not deserve to have to be reviewed for his fitness to practice. I just wish more doctors would have the strength to dispute the way that this illness is assessed and be willing to come forward to dispute that that the blood test is not the cumulative answer when making a decision for diagnosing this illness.

Dr Skinner should be admired and applauded for administering some good old fashioned 'bedside manner' in the way that he really listens to and evaluates a patients symptoms and looks at the whole picture rather than relying solely on a very inaccurate blood test.

I certainly hope that my daughter  is destined to get similar results and some relief after suffering all through her teenage years with this awful condition.

I hope that this assists in your review hearing. If I can be of any further assistance please do not hesitate to contact me.

Yours sincerely



22 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW


General Medical Council	
Original Written Proceedings	
Original Written Proceedings	
Date recd for review	26 JUL 2011
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Dear Ms Cook

**Dr G R B Skinner MD, DSc, FRCOG, FRCPath**

I write in support of the above doctor.

With a family history of thyroid conditions, I know from personal experience that the strict adherence of diagnosing by blood results alone leaves many undiagnosed and living a very incomplete life.

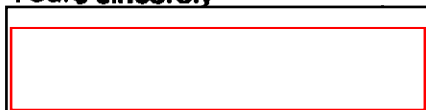
Having been an endocrinology patient then outpatient for a considerable number of years I think the outlook for many NHS thyroid patients appears increasingly unsatisfactory. I have witnessed a change in view from my first consultant, 

  
who initially prescribed a combination thyroid replacement until he reluctantly had to stop ('my hands are tied') through to the current thinking of 'one size fits all' with only one medication offered and at a dosage that takes little regard of anything but blood tests within a perceived 'normal' reference range that is applicable to all.

Doctor Skinner is able to look outside this narrow way of thinking and take account of individuals and their clinical presentation and history, both when making a diagnosis and with subsequent treatment.

I know that Dr Skinner gives invaluable advice and that he has given hope and health back to so many and I fully support him.

Yours sincerely



Cc: Mr Ralph Shipway 

23<sup>rd</sup> July, 2011,

Ms Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester,  
M3 3AW.

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Dear Ms Cook,

**Review Hearing Dr Gordon Skinner – 28<sup>th</sup>/29<sup>th</sup> July, 1<sup>st</sup>/2<sup>nd</sup>/3<sup>rd</sup> August, 2011.**

In [redacted], I first consulted Dr Gordon Skinner.

For years I had suffered from [redacted] general debilitation and as my mother had a thyroid problem I wondered if I could possibly have the same condition as these things do tend sometimes to run in families. Every few months over a number of years I visited my G.P. for tests on the Thyroid Gland. Every time I was told that the readings were "within the range".

I became quite desperate about my condition and eventually sought the advice of a nutritionist in [redacted] recommended by a friend. This lady felt that my Thyroid could be the problem and told me about Dr Skinner. I then asked my G.P. to write a referral letter to Dr Skinner, although he was not very happy doing this, but I was very insistent, as I had a right to be and armed with all my Thyroid test results, I saw Dr Skinner in [redacted]. He felt that my results showed a deficiency and put me on a programme of Thyroxine.

I started taking it straight away – first of all in a low dose and then gradually increasing over [redacted] months. During that spring and summer I very slowly started to feel better. By [redacted] I was feeling significantly better and was feeling very hopeful that I was on the right track. Since then I have improved enormously and have considerably more energy and general wellbeing than I have had for many years. Some days before taking Thyroxine I could hardly rise off the sofa.

I need to be able to continue consulting Dr Skinner. The thought of not being able to take Thyroxine any more is unbearable and while my G.P. is unable or unwilling, for whatever reason to prescribe this for me, that is what would happen. What would happen to my health if I were suddenly unable to obtain the prescription, and actually have to stop taking Thyroxine? I dread to think!

I feel that Dr Skinner has saved me from a miserable and wretched time and he has my total support in what he is doing.

Yours sincerely,

[redacted]

cc

Mr Ralph Shipway

23<sup>rd</sup> July, 2011,

Ms Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3, Hardman Street,  
Manchester,  
M3 3AW.

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Dear Ms Cook,

**Review hearing Dr G. Skinner – 28<sup>th</sup>/29<sup>th</sup> July 1<sup>st</sup>/2<sup>nd</sup>/3<sup>rd</sup> August**

You will have received my wife's letter of the same date as this.

I would like to confirm all that she writes. In the early days our lives, and particularly hers, were a miserable experience, chiefly due to the intransigent stand of her G.P. Thank goodness for the understanding attitude of the nutritionist in [redacted] the guidance she gave my wife and later, particularly, the support and counselling she received from Dr Skinner.

We made, and were happy to make four round trips to Dr. Skinner's consulting rooms in [redacted] A small price to pay for the medical and moral support that my wife experienced.

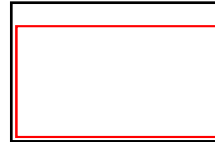
Should Dr Skinner not be able to continue practising, I don't know what would happen to my wife's mental and physical health. It is very worrying to think about. To return to the early days of this experience would be a disaster which I feel quite desperate about.

In view of our experiences I wish to add my support for Dr Skinner and his work for his patients which I consider to be invaluable.

Yours sincerely,

[redacted]

cc [redacted]  
Mr Ralph Shipway



25th July 2011

**F.A.O. Heather Cook,  
Investigating Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3, Hardman Street,  
MANCHESTER,  
M3 3AW.**

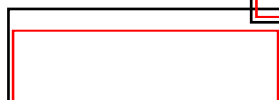
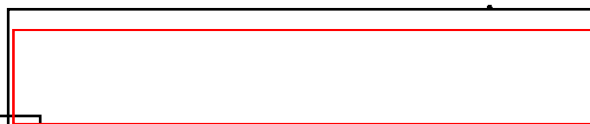
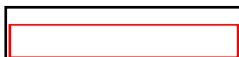
**Copies x 2 Foreword to:** Mr Ralf Shipway, Raddcliffes le Brasseur (Solicitors), WESTMINSTER, SW1P 3SJ

**Testimonial Part 2 For:** Dr. Gordon R B Skinner MD, DSc, FRCOG, FRC Path,

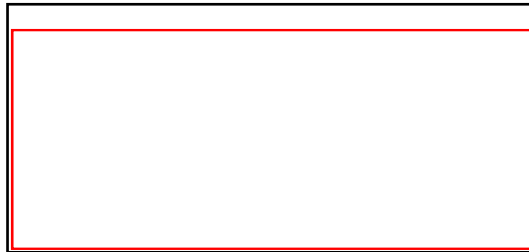
Dear General Medical Council,

- \* **Dr Skinner, Listened to me, He Heard Me, Understood, Helped and Supported Me.**
- \* **Dr Skinner saw me as a person, a human being that counts, as an individual.**
- \* **Dr Skinner was and still is my sanctuary.**
- \* **Dr Skinner gave me back my life.**
- \* As I see it based on my own personal experiences'. NHS 'pretended' to listen to me, fobbed me off, dismissed and rejected me my voice, and my words.
- \* For years, I was ill; I was in an awful state. My health was deteriorating, I was deteriorating, my life was deteriorating, and my life has been terrible, horrible and awful, frustrating and distressing.
- \* As I see it, Heaven knows the state I would be in if it wasn't for Dr Skinner.
- \* **GOD KNOWS the good Dr Skinner has done. He is a medical Angel.**
- \* It's my believe, the unpleasant, distressing, neglected, abandonment I experienced, that was inflicted upon me by the NHS; - Is Just The TIP of a Major load of Massive ICE BURG'S'.
- \* There's no reason at all why the GMC and NHS could not learn the good from Dr Skinner.
- \* **With Thanks, the GMC and NHS should take heed, embrace and utilise Dr Skinner's wisdom.**
- \* As I see it, based on my own personal experiences; - Life without Dr Skinner would be scary where the only other option being, is the out of touch NHS at the helm.
- \* **Thank you Dr. Skinner for having courage and self belief.**
- \* **Thank you Dr. Skinner for being you and the person you are.**
- \* **Thank you Dr. Skinner for taking an interest in, and giving your devotion to Thyroid.**
- \* **Thank you Dr. Skinner for VALUING the Thyroid SUFFERING person.**

Yours sincerely,







Ms Heather Cook  
Investigating Officer  
Fitness to Practice Directorate  
General Medical Council  
3, Hardman Street  
Manchester M3 3AW

25<sup>th</sup> July 2011

Dear Ms Cook

General Medical Council	
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#### TESTIMONIAL

Further to letters of support in favour of Dr Gordon R.B. Skinner (for both current and previous investigations), by my mother, [REDACTED], a patient under his care, I hereby give testimony to the transformation I have seen in my mother, since receiving treatment and prescriptions from Dr Skinner.

Following a period of prolonged ill-health in the early [REDACTED]  
[REDACTED], my mother struggled for many years with [REDACTED]  
[REDACTED]. We feared that she was in a gradual process of decline. She was subsequently diagnosed with poor thyroid function and was prescribed a variety of chemical thyroid substitutes. Unfortunately, the side-effects of these prescriptions by far outweighed any benefit, so there was no tangible improvement to her quality of life.

Then, in [REDACTED], she consulted with, and came under the care of Dr Skinner. Within a few months the transformation was almost miraculous. [REDACTED]  
[REDACTED]

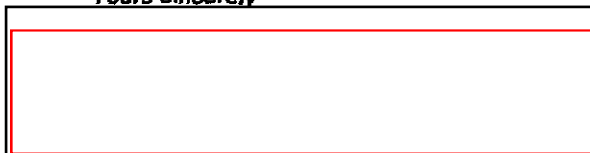
[REDACTED] I would say, as a lady in her early [REDACTED]'s she has at least as much get up and go as peers of her age, if not more so, and I can only put this down to the good offices of Dr Skinner.

It is right and proper for the GMC to actively vet the medical community to ensure that any rogue elements and bad practices are weeded out. By the same token medical science would not be what it is today without there being pioneers, and sometimes to be a pioneer you have to depart from convention. The travesty arises when convention suppresses true and good pioneering spirit.

My own belief is that any questioning of Dr Skinner's activities as being unacceptable is misguided. The results speak for themselves, and I am sure you must be in receipt of many testimonials to this effect.

My personal fear is that if the GMC find against Dr Skinner such that he is unable to continue his practice, that it will effectively be a slow-death sentence for my mother.

Yours sincerely



24<sup>th</sup> July 2011

Ms Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

General Medical Council	
Fitness to Practise Directorate	
Received by: [redacted]	
Date: 26 JUL 2011	Time: [redacted]
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Dear Ms Cook

Re: Review Hearing for Dr Skinner

In [redacted], my sister discovered she had an underactive thyroid gland, and on the advice of her GP, she insisted that the whole family went for tests to find out if anyone else had the condition. She was especially concerned about me, [redacted]

[redacted] Whilst I understood her concern, I was very reluctant to take a test, as at that time, I was more than happy with the way I felt. I was reasonably fit and active, and I felt very healthy. [redacted]

However, to reassure my sister, I finally agreed to take a test and was stunned to learn that I did have the same condition, although mine was described as a "borderline" case. Despite being borderline, my GP strongly advised that I commence treatment immediately, assuring me that in the long run, this would be the best option for me, and it was stressed that there would be no side-effects, as this was hormone replacement, rather than medication. Other than that, he believed that I would feel the benefits almost immediately, and would end up "feeling even better". I considered his recommendation carefully before agreeing to it, and I regret to say that I did no actual research on the subject, before I agreed to it, but I couldn't fault his logic. With hindsight, this was the worst decision of my life, and I have regretted it ever since.

As more and more information became available on the internet, I discovered "I was not alone" and that other people suffered side effects with T4. I also discovered that there was "at least one alternative treatment available" that I could try: T3. After a great deal of effort, I did eventually persuade one doctor to let me try it. Although I improved a little initially, I encountered problems as soon as I tried to increase my dose, but I had to admit that my symptoms were not quite so severe. It was only a subtle difference but any improvement was welcome, so I stayed on T3. However, my overall condition continued to deteriorate and I became so ill that at the end of [redacted], I gave up my job.

[REDACTED]

I promised myself that I would use every last drop of energy I had, and immediately started to scour the internet. I was surprised at how quickly I found the help I needed. Several brands of natural desiccated thyroid tablet existed, that had helped many others, but I also quickly learned that they were not licensed in the UK.

Armed with this information and lots of corroborating evidence, I sought help from my GP again, and was flatly refused any support, other than a referral to another endocrinologist. My GP would not even investigate the matter or consider trying the treatment. The endocrinologist also refused to help, and I went away disgusted by their apathy and intransigence. I then discovered Dr Skinner, who came highly recommended, but I needed a referral, and this proved to be just as difficult to obtain. [REDACTED]

When I saw Dr Skinner, I was immediately impressed by his professionalism and caring nature. He was the first person to truly listen to me and he immediately tried to piece together my medical and life history, wanting to know how I had ended up in such a poor state. He examined and questioned me, and I had to fill in forms, giving details of all my symptoms. I ticked almost every box on the symptom list and it was a very extensive list. I hadn't even realised that some of the symptoms I had were "directly attributable to hypothyroidism". I was even taken aback at his genuine anger and disgust at how I had been treated up until then.

He realised that I had a good understanding of my situation and had come to him with a plan in mind, and he asked me how I wanted to proceed. When I told him that I wanted to try Armour Thyroid, and why, he talked me through what would be involved, and agreed that it could indeed be the right way forward for me. He was quick to stress that it might not work, but that he felt it was well worth trying, and he reassured me that "if it did not work, he would never give up on me". It was clear that he was genuinely prepared to investigate and try anything and everything that might help me. He was the first doctor to care what happened to me and he instilled a sense of trust and gave me hope.

Within days I began to take Armour Thyroid, and enjoyed the benefits almost immediately. [REDACTED]

[REDACTED]

Since then, I have gone from strength to strength and I am sure I will continue to do so. [REDACTED]

[REDACTED] There are only a few symptoms left, and I know that I may have to live with some of those for the rest of my life. After all, many of them are the result of other symptoms not being treated, [REDACTED]. However, I am optimistic about the future now and I am living life again. I am able to work for a living, be a good wife and enjoy social pursuits and hobbies again. I have enough of my life back to want to live it. [REDACTED]

Considering my case and how appallingly I have been treated, I do not know how you can even remotely consider removing Dr Skinner's right to practise. If he is not allowed to practise any longer, then the very least you can do, is to also investigate every single doctor and endocrinologist I have ever seen, and strike them off too, for they have not just failed me, they willingly condemned me to a life of suffering and distress.

In short, Dr Skinner saved my life and I will always be indebted to him.

Yours faithfully

[REDACTED]

CC

[REDACTED]  
Mr R Shipway

Ref ARB/Soc/Skinner GMC 1301.doc

25 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

General Medical Council	
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Dear Ms Cook,

Re: Dr Skinner Review Hearing

If you've never been in love, you don't know what it's like!

Some people, out of a subconscious desire to appear intelligent and knowledgeable, often use glib phrases, such as the above, having heard others use them. Another example would be the ridiculous and inaccurate saying "It's too cold to snow".

I am NOT one of those people. The things that I say and the opinions that I hold are born of my innate ability to observe, digest and judge things on their own merits. So if I were to say, "If you've never been in love, you don't know what it's like." I would be saying it because I knew what I was talking about. I used to THINK I was in love with my first wife, and my second, but when I met she who was to become my third (and final) wife, I KNEW! It was instinctive.

I only mention this in order to emphasise that this letter is the product of my own observations and NOT a rehashed version of someone else's.

So, I DO know what it's like to be in love. However, if there is something that you have not experienced for yourself then the next best thing is to live with someone who has.

My wife was diagnosed with hypothyroidism shortly after we first met. When we met, she was lively, attentive, bright and sharp witted, a bit like me which was why we hit it off! She was then prescribed Thyroxin tablets (T4) which she dutifully began to take and I observed, over the following months, the bright and sharp witted love of my life descend into a state of apathetic torpor. She became a zombie but retained enough wit to search the Internet for alternatives to the tablets that were taking away her livelihood.

As the years rolled by she was allowed to try Triiodothyronine (T3), which suited her better but still had unpleasant side-effects; [REDACTED]

[REDACTED]

These are NOT the things that a woman in the prime of her life should have to put up with. In short, the NHS recommended treatment took away her life!

Eventually my wife discovered that there were "natural" alternatives to the drug companies' synthetic, chemical "cash cow" tablets and lobbied medical practitioners to prescribe one for her. THEY REFUSED! It seemed that in spite of these products being the preferred course of treatment in the USA, they are not licensed in this country. My wife saw alternative GPs and two endocrinologists who, it has to be said, were less than sympathetic and appeared to be ignorant of the symptoms and implications of hypothyroidism, preferring to hold the untenable view that the symptoms were all 'in the patient's head' - complete BUNKUM!

As these consultations led nowhere and it became clear that the NHS didn't care, my wife

managed to obtain a referral to Dr. Skinner. I accompanied my wife to many of the consultations she had had through the zombie years and was less than impressed with her treatment at the hands of the NHS. However, when I sat in on her first consultation with Dr. Skinner I observed a sympathetic, caring and VERY professional person at work. Not only did he bother to actually LISTEN to his patient, he was at pains to carefully outline all of the implications of the alternative medication my wife wished to make trial of.

The first thing my wife was given was a sheet of paper containing a list symptoms. She was asked to tick all that she felt she had experienced since being diagnosed. Many of those that she ticked (in excess of 50%) were ones she had not even realised were symptoms of hypothyroidism, unquestionably due to the fact that none of the NHS people she had consulted had mentioned them. Surely this indicates a serious failing among NHS staff (INCLUDING the endocrinologists!!!)?

Dr Skinner carried out an extensive and sympathetic examination, both physically and verbally, and agreed to prescribe the "natural" product the NHS had refused, to see how my wife coped with it. The transformation was astonishing!

Within a very short space of time the depression and headaches disappeared. Palpitations faded away and I observed the vitality return to my wife's day to day demeanour. Her sense of humour returned to full strength, she once more had enthusiasm for domestic projects and leisure activities [REDACTED] In short, Dr Skinner gave her back her life!

In conclusion, I have to observe that if the GMC seek to prevent Dr. Skinner from practicing then it will be a VERY, VERY sad day for British Medicine. If Dr Skinner has to go then surely, indubitably, all the NHS staff who FAILED my wife must also go, otherwise the only conclusion will be that the GMC will have left the path of wisdom!

I DO hope, not only for my wife's sake, but for all of the many patients Dr. Skinner has successfully treated that the GMC continues to allow the good work practiced by this paragon of medical science.

Yours Sincerely

[REDACTED]

cc:

[REDACTED]

Mr Ralph Shipway

[REDACTED]

[REDACTED]

Mrs Heather Cook  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

23 July 2011

Dear Mrs Cook

**RE: GORDON R B SKINNER MD (Hons), DSc, FRCPath, FRCOG.**

My wife [REDACTED] has been a patient of Doctor Skinner for several years during this period he has treated her for an underlying Thyroid Condition. We sought his help as we discovered that her treatment elsewhere was mostly dependent upon laboratory test results, if considered to be "within range" was either given no help or a course of medication which did not work for her, despite her symptoms, in what appears to be a one size fits all remedy. I understand that there is some dispute with established medical practise in this particular field and with some patients and other more open minded Practitioners who are willing to challenge the established protocols in treating their patients. That said the purpose of this letter is not to debate this issue but to offer support for Dr Skinner for his review hearing.

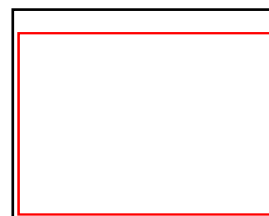
In the time I have known Dr Skinner he has always conducted himself in a most correct and professional manner. He has acted with integrity, explained issues thoroughly and conferred with [REDACTED]'s GP at all the relevant times of her treatment. Her GP being well aware of the ineffective response to conventional remedy was willing to seek a solution for debilitating symptoms and very much like Doctor Skinner wants to treat the whole person as an individual avoiding the stereotypical approach to treatment by numbers.

[REDACTED]

[REDACTED] Dr Skinner was very supportive with regular telephone consultations with [REDACTED]. He [REDACTED] remains very much part of Susan's overall "Care Plan". [REDACTED] is far from well but has confidence in Dr Skinner as a caring, experienced and knowledgeable professional who has been willing to push at the boundaries of convention to seek a solution for her illness which he should be applauded for rather than pilloried. [REDACTED]

Yours sincerely

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23 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate, General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook

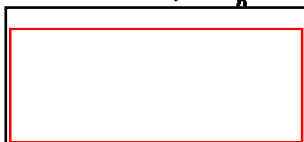
Hearing: Dr Skinner

[redacted] my wife of [redacted] years, became increasingly ill following a hugely stressful, prolonged external event during the [redacted]s to early [redacted]. [redacted]  
[redacted] Aside from many of those standard and well documented hypothyroid symptoms, she increasingly became more [redacted]  
[redacted]

From [redacted] life became more and more difficult for her and our relationship. Not one doctor or endocrinologist she consulted really took any of the [redacted] difficulties seriously. There seems to be a general consensus and/or intimation that [redacted] requires lifestyle changes, when in fact [redacted] could not possibly have done any more than she had already done.

Finally my wife visited Dr Skinner during [redacted]. I now understand that the T4 she was initially taking was only helpful to her in a minor way. Following her taking Armour Thyroid there has been a considerable improvement in her [redacted]  
[redacted] In my view my wife is now two-thirds plus improved to those dark days, when hypothyroidism had really 'taken hold'. Improvement is purely down to her seeing Dr Skinner. I also know my wife is very concerned and I am too when considering the inevitable day that Dr Skinner retires. The prospect of going back to those days without Armour is unthinkable and incomprehensible when the role of doctors is not to disregard, seemingly out of hand, the health of their patients by castigating a medication that is long tried and tested.

Yours faithfully



Cc Mr Ralph Shipway, RadcliffesleBrasseur [Solicitors], [redacted]

23 July 2011

Heather Cook, Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

Dear Heather Cook

**Dr Gordon Skinner - Hearing**

Since [redacted] I suffered a range of [redacted] symptoms, [redacted]  
[redacted]. I was progressively  
ignored by doctors over three decades. More latterly, and at my insistence to be tested ([redacted]  
[redacted]), endocrinologists declared me not to be hypothyroid [redacted], over  
the long run, my displaying increasingly debilitating signs/symptoms including pre-syncope,  
[redacted]

My first contact with Dr Skinner was [redacted]. Dr Skinner took my medical history,  
examined me and stated that I had hypothyroidism (something I had come to realise in my  
own long search to try to feel well again). He prescribed Levothyroxine and wrote to my GP.  
Minor success was achieved with this medication but as soon as I progressed beyond [redacted]mg, I  
became 'toxic' (feeling weird, simply 'not right') and so sensibly reduced this back down.

I read sufficient to grasp that T4 alone may not be a successful treatment for all patients.  
Given the duration of my other (not listed here) multi-faceted symptoms, I considered buying  
Armour Thyroid online but was too wary to do so. On my next visit to Dr Skinner I asked  
him if he could prescribe Armour Thyroid for me. Dr Skinner did so and this led to a more  
significant improvement than with T4 alone. My progress on a combination of [redacted]mg of T4  
and Armour (commencing with [redacted] Grain each day, increasing in [redacted]  
[redacted] Grains) has significantly improved my overall health [redacted]

Certain US research indicates that people in my circumstances (long term untreated  
hypothyroidism, also the genetic variant of Hypothyroidism Type II proposed by Dr Mark  
Starr) can have T3 conversion difficulties. I have familiarised myself with the work of many,  
including Dr Hertoghe, Broda Barnes, Barry Peatfield, John Lowe and Dr Skinner.



With my own scientific background and knowledge (including my own self knowledge) I feel adequately equipped to be able to decipher wheat from chaff and monitor my own perceived sense of illness and of well being. [redacted]

[redacted]  
[redacted] It is my belief that I know when I am taking too much or too little thyroid hormones, be these artificial or natural. I believe anyone taking such medication will quickly work out whether or not such preparations are needed!

Without the help of Dr Skinner in [redacted] I simply do not know where I would be now. My condition had become so dreadful that I 'lost' several years of my life dragging myself in and out of bed, barely able to function. There are no words sufficient to express my gratitude to Dr Skinner. His professionalism is so refreshing against the dismissive and disgraceful treatment to which I have been repeatedly subjected over decades.

I heard that T3 is difficult to come by but a reliable source (not Dr Skinner) told me where I could purchase it abroad. Use of Cynomel (Cytomel in UK) has further improved my health. I use T3 with some trepidation but, in the absence of a sustained release formula in the UK (I could have this made up by a compounding chemist in the US city where my family lives but a prescription is required), I manage by using [redacted]

My health is constantly improving and, save for my one attempt to purchase Armour Thyroid abroad to save some money [redacted]

[redacted], I shall continue to use T3. I will sensibly monitor my own health until statutory health authorities recognise their folly and begin to implement the exacting knowledge acquired over one hundred years ago. As someone with hypothyroidism it is my believe that current UK treatment is akin to Middle Age 'dooking stool' mentality.

From all accounts it would seem that the calm, cool, compassionate approach of Dr Skinner gives many people a light at the end of a terribly frightening dark hole. I am interested to know what will happen to patients when Dr Skinner retires? Are we to be informed of the provision of proposed alternatives for those who do not 'satisfy' the blatantly flawed [for a significant number] TSH test and for those who also do not respond to Levothyroxine in any meaningful way?

Yours sincerely

[redacted]

cc Mr Ralph Shipway, RadcliffesLeBrasseur [Solicitors],  
[redacted]

[Redacted]

Investigating Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

[Redacted]

22<sup>nd</sup> July 2011

Dear Heather Cook

**DR GORDON SKINNER MD. BSC FRCPATH FRCOG  
GMC HEARING 28<sup>th</sup> July to 3<sup>rd</sup> August 2011**

I have recently returned from an extended holiday to hear, with deep concern, of yet another GMC Hearing for Dr Skinner regarding his fitness to practise.

[Redacted]  
[Redacted] am very aware of the excellent work done by Dr Skinner in helping our members and many others regarding their thyroid/adrenal dysfunction.

Dr Skinner is caring, well qualified and very experienced and knowledgeable in this field. Without his expertise I do not believe I would have achieved full recovery [Redacted]  
[Redacted]

My NHS Consultant and local GP's all failed to diagnose or treat my T3 dysfunction, which was a major factor in my illness. Like many others I did not respond well to synthetic medication and the long proven Armour Thyroid has been essential to my recovery and the maintenance of my now healthy and productive life.

Many people have expressed the very strong feeling that the GMC is unfairly persecuting Dr Skinner, who has a long, excellent and safe track record in this specialist field.

Why does the GMC not focus it's attention on the reasons for the major tragedy in the UK of so much undiagnosed hypothyroidism and the lack of effective treatment by GPs and Consultants?

Yours sincerely

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[REDACTED]

Ms Heather Cook  
Investigating Officer  
Fitness to Practice Directorate  
General Medical Council  
3, Hardman Street  
Manchester M3 3AW

RE: Dr.Gordon R.B. Skinner review

21st July 2011

Dear Madam,

My first contact with Dr.Skinner was in [REDACTED]. There was the initial consultation to which I had to bring a letter of referral from my GP with names, addresses, postcodes of any specialist I had seen in recent years. In addition copies of any thyroid or other blood tests which would be helpful i.e FT4 TSH FT3 cortisol B12 and fasting blood glucose. Which I did. I also knew that a diary of pre-rising morning body temperature over a 3 week period would be helpful. There was a lengthy examination, a long questionnaire had to be filled in. He gave me ten pages of printed matter on his work, clinical research, and professional qualifications. He explained, that I would be obliged to provide regular 3-4 monthly thyroidfunction tests, monitor and report my body's reaction to the medication.

I have been under Dr.Skinner's care for more than [REDACTED]. Apart from fulfilling the above requirements, I write to him about changes. [REDACTED]

[REDACTED] I like to physically consult him at least once annually, making the journey to [REDACTED]. With every prescription he sends, there is much paperwork i.e.new prescription request form, up-dates of information etc. I believe every last aspect of state of health and treatment follow-up must be covered.

I am delighted to have Dr.Skinner looking after my health, he has my complete trust and I cannot possibly imagine anyone more qualified, caring and good.

May I refer to my letter of 17.06.07, addressed to Ms P Collins for Dr.Skinners first hearing.(copy attached) in which I gave a brief history. I need to expand on this, to properly explain the devastation of my life by my thyroidmalfunction.



At last I found Dr.Gordon B.Skinner. No doubt, he has saved my life. His care and the correct treatment made me well

At  I have become slow, life is sedate and apart from creaky bones and other nuisances that befall one with age, I am well. There are a few friends left, hobbies to enjoy, the pleasure of my two grand-children of  I am delighted that I am still usefull and needed.

In conclusion I would like to say, I have been through hell and back twice and I will not be able to do it a third time. If you find against Dr.Skinner --- you will condemn me.

Yours faithfully



**From:** [REDACTED]

**Sent:** 26 July 2011 12:47

**To:** Heather Cook (0161 923 6472)

**Subject:** FW: Testimonial for Dr Gordon R B Skinner, F.A.O Heather Cook.

Dear Ms Cook,

This patient has sent his testimonial to us directly and I wonder if you could include this in your bundle to the Panel please.

Kind regards,

Gordon Skinner MD, DSc, FRCOG, FRCPath

---

**From:** [REDACTED]

**Sent:** 26 July 2011 11:55

**To:** [REDACTED]

**Subject:** Testimonial for Dr Gordon R B Skinner, F.A.O Heather Cook.

For the attention of Heather Cook, Investigation Officer, General Medical Council, 3 Hardman Street, Manchester M3 3AW.

I first came under the care of Dr Gordon Skinner over [REDACTED] years ago, i presented him with symptoms i was experiencing, [REDACTED]

[REDACTED] i had lost all drive and motivation, i had no zest for life at all, in fact i was at my wits end, i had travelled the length and breadth of England seeing supposed specialist's to try and identify exactly what was wrong with me, a number of physicians had identified a low thyroid reading with blood test's but were not prepared to issue me with thyroid medication because although my reading's were low i was still within NHS guidelines and range.

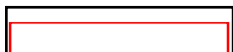
I eventually came across Dr Skinner, after a lengthy and very thorough consultation he organised for me to have a set of blood tests after which i went back to see him for a further consultation, again, lengthy and thorough, he explained in great detail and depth about the fact that he thought i was in fact suffering with hypothyroidism and that there is so much more to the condition than just attempting to determine whether someone is suffering with it or not by a simple blood test and whether they are within the NHS prescribed range of results.

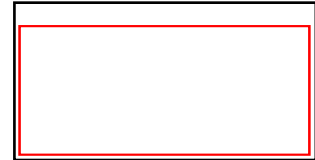
I started on the prescribed thyroid medication and within a week i noticed a distinct improvement and after approx a month i was positively euphoric, the difference was night and day, chalk and cheese, life was worth living once again, Dr Skinner is a consummate professional and has made a colossal difference to the quality of my life, i will never be able to thank him enough!

yours sincerely

[REDACTED]

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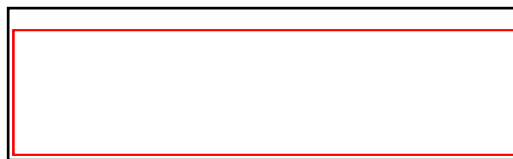
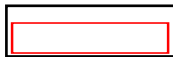


22 July 2011

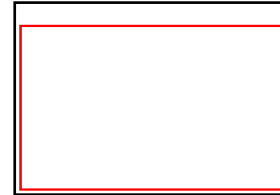
Dear Heather Cook

I am writing in support of Dr Gordon Skinner. I have an under-active thyroid condition diagnosed by my G.P. when I was ☐ I have been very unwell with my condition and have a much better quality of life since being treated by Dr Skinner. My progress would be threatened if I was no longer able to access this treatment. My G.P. is supportive but does not have the specialised knowledge and experience to help me.

Yours sincerely



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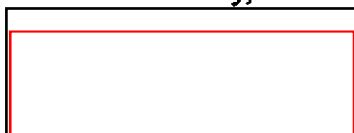
23<sup>rd</sup> July 2011.

Heather Cook,  
Investigating Officer,  
Fitness To Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester, M3 3AW.

Dear Ms. Cook,

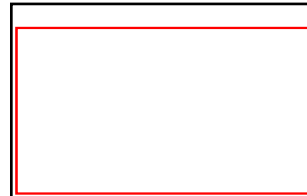
My daughter  has been a patient of Doctor Skinner for about  years. Prior to this her GP. at the time did not take her condition seriously and she was very unwell with all the symptoms of an under active thyroid. Dr. Skinner's treatment changed her life for the better and he continues to be a very knowledgeable and sympathetic doctor. I dread to think what will happen if he can no longer treat my daughter.

Yours Sincerely,



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24/07/11

Heather Cook  
Investigating Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester. M3 3AW

Dear Ms Cook,

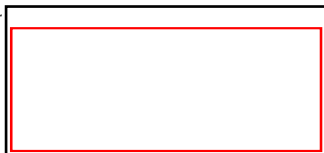
I write in support of Dr Gordon Skinner MD Dsc FRCOG, who has treated me for Hypothyroidism for the last  years. It is my understanding that Dr Skinner is awaiting a hearing with the GMC as part of the review process for the case brought against him in 2007. I submitted a letter at that time, addressed to Ms Patricia Collins (24/08/07 ) outlining my experience as an undiagnosed Hypothyroid patient, subsequently returned to health through excellent professional care from Dr Skinner.

As a patient of Dr Skinners for many years, I sincerely hope for a favorable outcome from this process, and must reiterate that he plays a vital role in the lives of his patients. Indeed, I am concerned that there is heightened anxiety among these patients, who like me have the utmost respect and concern for Dr Skinner, who finds himself yet again under scrutiny.

Please accept my total support for Dr Skinner, and that of my husband, who appreciates and enjoys my good health as a result of Dr Skinner's unequalled care and attention.

We wish him well, and pray for his continued success.

Yours sincerely,



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In reference to the Fitness To Practice Hearing in respect of Dr. Gordon Skinner to be held in Manchester on 29/07/11-05/08/11.

I wish to be made known my wholehearted support for Dr. Skinner, who has restored me to full health in the last few years. When I first became ill with [redacted], my Thyroid blood test results were within the "normal" range. After struggling for almost a year and finally confined to bed, I was told of Dr. Skinner's approach to the treatment of the Thyroid. Since I was suffering from almost all of the symptoms of Hypothyroidism [redacted]

[redacted] I decided to make an appointment with him immediately in [redacted]. I had by this stage attended a variety of doctors, including a consultant Endocrinologist Dr. [redacted] in [redacted] [redacted] who said I most likely had a "Syndrome" of some kind and prescribed me

It was, therefore, with some hope in my heart that I attended Dr. Skinner's clinic in [redacted]. After careful examination of my clinical symptoms and taking into account my family's history of Thyroid problems, he prescribed [redacted]ug of Throxine with further increases as my health improved. Over the next few years I was restored to now full health, and I am now taking [redacted]ug of Thyroxine and [redacted]ug of Liothyronine daily along with [redacted]ug of Vitamin B12.

My GP, Dr. [redacted] of [redacted], is supportive of Dr. Skinner and has been a witness over these last few years to my returning health. She has happily supported his guidance in prescribing me such a high dosage of Thyroid medication.

I cannot praise DR. Skinner highly enough. It is not too much of an exaggeration to say that I owe him my quality of life today. It is appalling that his work to improve the lives of so many clinically Hypothyroid patients has gone unrecognised by the GMC. Surely the Hippocratic oath taken by all doctors <sup>contains</sup> ~~starts with~~ the words "First do no harm". By failing to recognise the fact that current Thyroid blood tests are flawed, the GMC are guilty indeed of doing harm to many poor Hypothyroid souls who suffer on needlessly.

It is, therefore, not Dr. Skinner who should be tried for misconduct, but those who support the current method of diagnosis of Hypothyroidism. Too many people are being treated needlessly with

expensive anti-depressants and confined to a life in bed, when they could well be suffering from an underactive Thyroid.

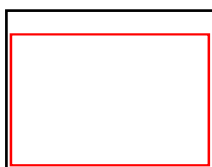
My daughter , [redacted] has since also been successfully treated by the good Dr. Skinner and is now too restored to full health.

I hope this letter reaches you in time and I bitterly regret not being able to attend this hearing.

Your most sincerely

[redacted]

[redacted]



July 25<sup>th</sup> 2011.

General Practitioner Council	
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Sir,

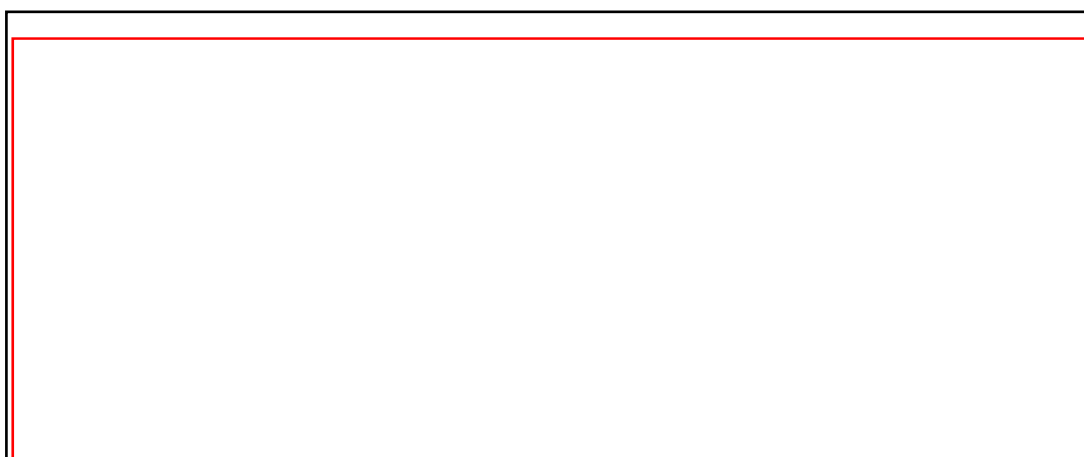
I am a sufferer who could and should have been returned to full health more than  years ago but for the current stance of the GMC.

Following the birth of twin daughters  years ago, I was, I believe, wrongly diagnosed with  and given  which I took for several years, during which time my health deteriorated further. Inadequate "partial" TSH-only blood tests during this period failed to pick up a worsening thyroid problem.

It was not until I had a full tests done privately, which included the TSH, FT3 and FT4 tests and went to see Dr Gordon Skinner, who diagnosed myxoedema, that my condition was finally acknowledged by my own GP. He then prescribed for me as directed by Dr Skinner.

Unlike all the other GPs and endocrinologists I have seen in the intervening years, Dr Skinner is the only one to take time to assess my blood results in conjunction with signs and symptoms, taking more notice of the symptoms and how the patient feels, considering how these impact on their quality of life in preference to a single blood result number.

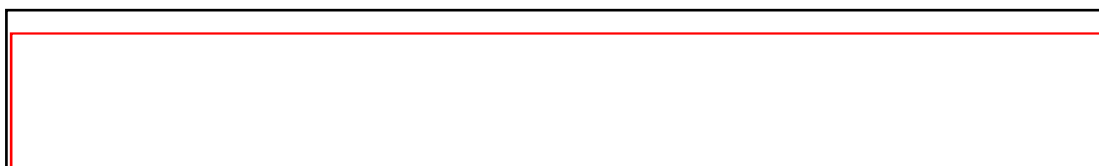
Dr Skinner started me on T4 treatment and recognising that it was not working changed me firstly onto T4 with T3, and when that did not alleviate my symptoms, onto T3 with Armour. The T3/Armour suited me and my health began to improve significantly.





What took Dr Skinner 12 months to rectify was destroyed in a matter of weeks by the NHS. It has taken over [ ] years to restore my health to the point that he had got me to. Partially with my own input as the endocrinologist was quite adamant in [ ] that the [ ]  $\mu$ g T4 and [ ]  $\mu$ g T3 were sufficient by merely looking at the TSH figure and not taking my signs [ ] and symptoms into consideration.

I genuinely feel that the NHS has failed in its duty of care, subjecting me to years of unnecessary suffering, through the persistent prescription of incorrect medication when others are available and known, through experience, to work more satisfactorily.



Consider utilising Dr Gordon Skinners experience and expertise, putting them to good use treating people like me, restoring us to health economically in months rather than consigning us to years of suffering. Like Dr Skinner *listen* to what the patient is saying about their quality of life and symptoms, do not dismiss them out of hand as irrelevant, suggesting the symptoms are "all in their minds" or "due to their age, diet or lifestyle" in favour of an inaccurate single blood test result, the TSH.

Having seen Dr Skinner at the start of my thyroid journey I knew what the "gold standard" was. This has enabled me to persevere through the years of neglect I was subjected to by the NHS. Had I not had his input initially I fear I would not have had the strength to fight for what I knew was the right medication for me.

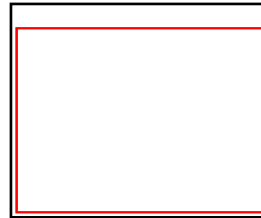
Please, stop pillorying a doctor who has the best interest of his patients at heart and look closer to home at the so-called professionals, who fail on a daily basis to diagnose and adequately treat thousands of thyroid sufferers nationwide, consigning them to years of unnecessary pain, suffering and in numerous cases poverty because they are too unwell to work.

Yours faithfully

[Redacted]

[Redacted]

[Redacted]



25<sup>th</sup> July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

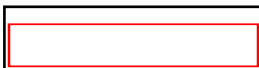
Dear Mrs Cook

Re: Dr Gordon Robert Bruce Skinner

Please find enclosed my testimonial in support of Dr Skinner.

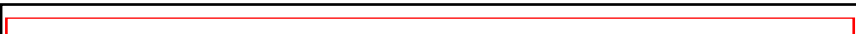
Kind regards

Yours sincerely



Encs.

c.c.

  
Mr Ralph Shipway

General Medical Council	
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Dr Gordon Robert Bruce Skinner  
GMC Ref No. 0726922

I,  of   
 state as follows:-

It has been  years since my initial visit to Dr Skinner's Clinic in  in   
 and I have to say with great conviction that I have never looked back.

Dr Skinner's whole demeanour is patient and caring, having seen so many doctors during my time as a very unwell lady, this came as an extremely pleasant change.

After Dr Skinner's examination and blood tests in  for FT4 and TSH, he started me on thyroid replacement. Dr Skinner thought that this was the right treatment and of course he was right.

Dr Skinner has always strived to be professional in that he asked me as a new patient for a referral letter from my doctor together with a complete history. He carried out a medical examination, for example, blood pressure, pulse rate, temperature, examination of thyroid gland and tongue. He also asked me if I would like a chaperone during my medical examination.

During the consultation with Dr Skinner, he explained what he had found, his diagnosis, further investigations required and suggested a treatment plan that I should follow. Dr Skinner answered any of my questions that I had regarding all aspects of the diagnosis and treatment.

Dr Skinner wrote a full letter to my GP and copied in any other medical carers and he explained his findings and treatment plan. No new treatments or modifications of previous treatments would be carried out without prior agreement from my GP.

I was provided with explanatory sheets regarding thyroid replacement.



If a follow up appointment was required, then Dr Skinner would advise of the appropriate interval and I would then be required to make a further appointment through Dr Skinner's secretary.

My recovery since [ ] has been remarkable. I was so poorly at the time [ ]  
[ ] I thought that there was no hope until I saw Dr Skinner. In fact, I made such a remarkable recovery that  
[ ]

I feel it a great privilege to support Dr Skinner. My own doctor, Dr [ ] has often said that Dr Skinner truly is a marvellous man as he has seen such a significant difference in my health that he decided to take over my care and now prescribes my Thyroxine. Dr [ ] has also referred other patients to Dr Skinner including my husband, [ ] who also has hypothyroidism. Thanks to Dr Skinner, my husband is also now well after two years of poor health.

A very dear friend, [ ] also found herself battling with ill health many years ago. She was also treated by Dr Skinner and is now back to optimum health. I cannot thank Dr Skinner enough for his dedication to his patients. I truly believe that without his intervention, I would not be here today.

26-7-2011  
Date

25<sup>th</sup> July 2011

Heather Cook,  
Investigating Officer,  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street,  
Manchester  
M3 3AW

General Medical Council	
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Dear Ms Cook

Re: Dr Gordon Skinner

I write in repeated support and in the hope that Dr Skinner may be allowed to continue his good work, because without his help many of us would suffer greatly.

For myself, his knowledge and understanding of thyroid symptom's and wise prescribing allows me to continue with a much better quality of life.

Prior to having met Dr Skinner (he was recommended to me, and referred to by my G.P.) I struggled with a system with such narrow bands of recognition, by blood tests and G.P.s that ignored the many symptoms of thyroid problems.

My symptoms included, [redacted]  
[redacted] Which with Dr Skinner's help have been much improved, and some symptoms have disappeared altogether.

I now have the quality of life I thought I would never see again.

I have complete trust in Dr Skinner and find he is very professional in all regards.

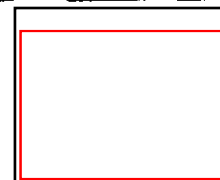
Yours faithfully

[redacted]

26<sup>th</sup> July 2011

General Medical Council	
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Date recd for exam	27 JUL 2011
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Ms. Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester, M3 3AW



Dear Ms. Cook,

I am writing in support of Dr. Gordon Skinner's review hearing by the GMC.

My thyroid illness all began in [redacted] I suffered [redacted]  
[redacted]

I went to see my local GP concerning these symptoms (Dr [redacted]  
[redacted]), he ordered some blood tests to be undertaken for my thyroid.  
Following the results of the blood tests, Dr [redacted] made the decision that my thyroid was not an  
issue and advised me to "take a tonic". - my husband was present at this appointment as I was  
feeling so unwell.

Still suffering with the symptoms I was visiting family in [redacted] when I decided I must undergo a  
second opinion as Dr [redacted]'s prognosis was risible. I visited [redacted]  
[redacted]. They immediately took blood  
tests and diagnosed, based on the results, that I had hypothyroidism. The practice referred me to Dr  
Gordon Skinner for further treatment.

On my first visit, Dr. Skinner examined me and asked me lots of questions about my symptoms and  
looked through the results of my blood tests taken in [redacted] Dr Skinner initially prescribed Thyroxin  
but after a couple of months, it was clear it wasn't producing the required results. Dr. Skinner  
suggested taking Armour Thyroid; I accepted and within a short space of time my general health  
improved dramatically and my symptoms started to dissipate. I have been taking Armour Thyroid  
now for the past [redacted] years and my quality of life is far improved.

--

Dr Skinner is fantastic. When I have visited Dr Skinner for any appointment, he has been so understanding and always checks to see how you are feeling as an individual. I can't tell you how seeing Dr. Skinner and taking Armour Thyroid medication has changed my health. I now have three young children and know for a fact I could not cope without this medication and knowing I had the support of Dr. Skinner.

I would personally be devastated if I thought I could not attend Dr. Skinner as I have complete trust in him. I can only say that I just accepted the advice of the NHS doctors that had treated me I would have had a far lower quality of life. There is a lot to say about listening to a patient, this is what Dr Skinner is about.

Yours sincerely,

[Redacted signature]

[Redacted name]

Cc:

[Redacted email address]

Mr. Ralph Shipway, [Redacted email address]

Heather Cook, Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester, M3 3AW.

26 July 2011

General Medical Council	
Original was a Photocopy	
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Date recd for scan	27 JUL 2011
It has been Photocopied to improve quality	
and physical objects referred	

Review Hearing for Dr. Gordon Skinner (28th July – 3rd August 2011)

Dear Ms. Cook,

I became a patient of Dr. Skinner in

At that time  
my GP told me that tests (including a thyroid test) indicated nothing wrong

years later I was recommended to Dr. Skinner. After a blood test and examination he suggested I try thyroid replacement. Starting with  armour thyroid daily we progressed slowly to a higher dosage, eventually two  grain. It was NEVER increased without a further examination and frequent further blood tests. For the first time in years I experienced an improvement in my condition. I understood that, given normal reference levels, thyroid replacement was considered inappropriate and I was warned of the dangers and symptoms of hyperthyroidism if I took too high a dosage.

I would like to make the following points.

- 1) Dr. Skinner always discussed his proposed course of action with me and maintained a consistently cautious approach to treatment by thyroid replacement, advising me if he thought there could be other

possible causes for my problems. My GP later confirmed that the dosage prescribed by Dr. Skinner left me within normal reference levels in accordance with blood test results.

- 2) His concern for his patients' well-being was self-evident. It was also seen in the low fees he charged in comparison with other colleagues in specialist medical fields [redacted] I noticed that Dr. Skinner was charging no more for imported armour thyroid than it would have cost to buy it direct in the USA.
- 3) I am aware from his publications that Dr. Skinner would welcome larger trials and deeper scientific investigation of the issues surrounding thyroid replacement but has been unable to obtain the necessary support.

Blind adherence to blood test results appears to leave thousands of people, who could potentially be helped, suffering needlessly. Knowing Dr. Skinner's work at first hand I see a doctor who has transformed the lives of untold numbers of his patients. In my case his diagnosis of many years ago has proved correct. I am now kept stable by taking Levothyroxine and Liothyronine as prescribed by my GP in accordance with regular blood tests. But my need for this medication was first picked up by Dr. Skinner. He alone has enabled me to continue working as a concert pianist. You will understand my strong desire to support his work.

Yours sincerely,

[redacted]

[redacted]

Copies to

Mr Ralph Spivway

26.7.2011

Dear Ms. Cook,

I am writing in support of Dr. Gordon Skinner who has treated me for my hypothyroidism following a total thyroidectomy in [redacted]. Initially, following my thyroidectomy, I was prescribed thyroxine but I had a very severe reaction to this drug. I requested an appointment with Dr. Skinner on the advice of my friend who is a G.P. Dr. Skinner assessed my condition and has assisted me in returning to health. After trying a mix of thyroxine and natural thyroid, Dr. Skinner decided I was better on the natural thyroid and that I am unable to tolerate thyroxine. Dr. Skinner has been professional, considerate and supportive in returning me to health. He has

worked with my G.P to give me  
excellent care.

I can affirm that Dr  
Skinner is a clinician of the  
highest calibre and is prepared to  
stand up for what he believes  
will help his patients.

Yours faithfully,



28th July, 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER M3 3AW

General Medical Council	
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Date Recd.	27 JUL 2011
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Dear Ms Cook,

I have been a patient of Dr. Skinner's for the past ☐ years.

The problem then, as it is now, the reliance of GPs basing a diagnosis on the use of the blood test and the absolute limit applied to its use. Even though the GP thinks there is a thyroid problem, because the reading on the blood test is high in regard to thyroid function, the patient's illness is thought to have some other cause.

Whilst many GPs nowadays let the blood test result dictate their patients treatment, certain people - and there are many of us - fail the thyroid blood test as our reading is high although we still have a thyroid problem.

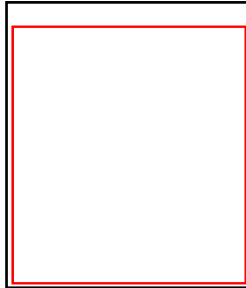
People like myself spent years being misdiagnosed, and in my case, having to give up work prematurely because of the failure to recognise that there are those of us outside this scale.

Doctor Skinner has brought treatment and hope to many, many patients which has been truly dramatic. Surely these results speak for themselves

Doctor Skinner is a man of the greatest integrity and in all his work his patients come first with him.

I just wish that some of you who are bringing this action against Dr Skinner would have to spend years in our shoes, denied treatment for thyroid illness, turned away at GPs, labelled time wasters at hospitals, and left to suffer as we have been, until Dr Skinner shone the light of understanding and compassion on us...

Yours truly



Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

26 July 2011

Dear Ms Cook

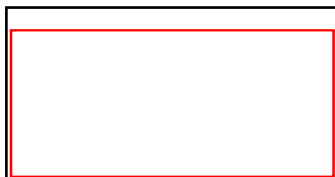
**Re: Letter in support of Dr Gordon R B Skinner MD (Hons) DSc FRCPath FRCOG**

I wish to pledge my support for Dr Skinner for the improvement he has achieved in my health and lifestyle over the past  years.

I am  years old and have suffered from  etc. for years and years. Since being treated by Dr Skinner I feel that all the symptoms that I have had for years have disappeared and I have my life back at last.

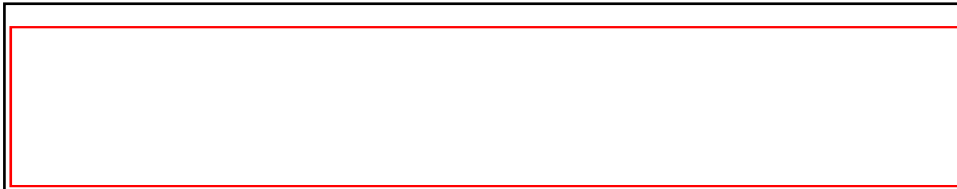
Dr Skinner is also treating my cousin  (who has written to you as well) and her daughter and they are so much better now as well.

Yours sincerely



Cc:   
Mr Ralph Shipway

General Medical Council	
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Original was Poor Quality	
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Original has been Photocopied to Improve Quality	
Content had physical objects re	



27 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

General Medical Council	
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#### HEARING REVIEW OF DOCTOR GORDON SKINNER

Dear Madam,

I understand that a practice review of Dr Gordon Skinner is about to take place and I should wish to make the following points concerning this doctor and the treatment that I received.

I first consulted Dr Skinner in [redacted] as a result of my having been, reluctantly, diagnosed with 'sub clinical' Hypothyroidism in [redacted] and consequently, inadequately treated by the GP and Endocrinologist, to the extent that I was still suffering considerable symptoms of the condition, although my blood test results were shown to be in the 'normal' range. My symptoms included [redacted]

[redacted]

I always found Dr Skinner to be entirely professional, compassionate and careful in his treatment of me. He always checked my vital signs and examined me at each and every consultation (this has never happened when I have visited my GP) and he also took a careful record of my symptoms and physical condition.

Doctor Skinner's treatment involved prescribing both Levothyroxine and Liothyronine and there has been a dramatic improvement in my condition, particularly after my taking the Liothyronine alone.

Dr Skinner has, undoubtedly, allowed me to regain a quality of life, which, as a result of the debilitating symptoms of Hypothyroidism, I have not experienced for many years. I, therefore, cannot speak more highly of his professionalism and dedication to his patients.

I can only say, that I wish more of our GPs and Endocrinologists expressed the knowledge, attention to detail and dedication to their patients that his doctor has shown.

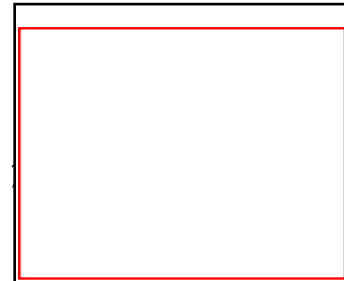
I trust that you will take this information into account when considering this Doctor's fitness to practice

Yours faithfully,

cc:

Mr Ralph Shipway, Solicitor, RadcliffesLeBrasseur

Heather Cook  
Investigation Officer,  
Fitness to Practice Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester,  
M33AW



27<sup>th</sup> July 2011

Dear Madam,

Ref: Doctor Skinner Review Hearing

When diagnosed with [redacted] in the [redacted]s, following a long severe viral illness from which I seemed unable to recover (main symptoms: [redacted])

[redacted]

[redacted] I consulted Doctor Skinner whose slow and careful treatment, and regular monitoring with blood tests for under active thyroid, helped to restore me to normal life.

At the age of [redacted], still take [redacted] grains of Armour Thyroid daily, which for me means my body works well, [redacted]

[redacted]

Doctor Skinner has looked after me for many years with kindness, humour and sensitivity for which I have been very grateful.

I wish him well.

Yours sincerely,

[redacted]

General Medical Council	
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26th July 2011

Dear Sirs,

I write with regard to Dr Skinner who has been treating my partner [redacted] since [redacted].

[redacted] began suffering from [redacted] in [redacted], and she became increasingly unable to lead a normal active life.

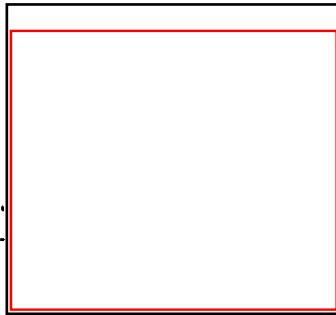
We sought treatment initially from her GP and then from a general consultant, and an consultant endocrinologist consultant. The GP ordered thyroid tests and was pleased to learn that the results were within normal parameters and therefore advised that the problem lay elsewhere but was unable to be more specific. [redacted]

[redacted] became increasing fatigued and frustrated that conventional medicine could neither diagnose the problem nor offer any solution. Our impression was that they practised "diagnosis by text book" in that they tested and measured and when they found the results to be in accordance with text book parameters they appeared both cynical and helpless.

[redacted] in increasing desperation, trawled through web pages looking for people who had experienced similar symptoms, and eventually found Dr Skinner to whom she was referred by her GP. Our initial impression at the first meeting was that Dr Skinner had time to listen to the problem, understood the effect that the symptoms were having on her life, and was prepared to consider a diagnosis that was unconventional, based not upon laboratory tests but on how she felt. The meeting with Dr Skinner and subsequent prescriptions of thyroxin and armour thyroid, have enabled [redacted] to almost return to a normal life, where she used to have the odd "good" day, she now has the odd "bad" day.

I believe that Dr Skinner has researched and specialised in this elusive illness, and offers his patients a lifeline that no-one else that we consulted had any enthusiasm to discover. In my opinion this illness is one of the "too difficult" variety that confound doctors who have only Laboratory tests and text books to support them. Dr Skinner however, has had the courage to challenge conventional thinking and has given [redacted] and many other patients a quality of life that they had despaired of ever experiencing again.

Yours sincerely



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Tuesday 26th July 2011

For the attention of :- Heather Cook

Dear Heather,

I am writing to support Dr Gordon Skinner who transformed my life having been greatly let down by the NHS and Bupa.

From [redacted] until [redacted], I experienced [redacted] which went undiagnosed by two different Doctor's practices. [redacted]

[redacted]

During the [redacted] years, my thyroid levels were tested by my local GPs and since the results fell in what the NHS deem to be the normal range, I was told that it was not a thyroid problem. I tried many alternative options to try and improve the quality of my life, all paid for by myself, these included, [redacted]

[redacted]

[redacted]

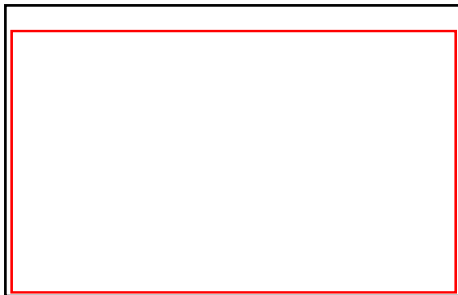
[redacted]

Since the NHS thought that my thyroid was fine, I researched which private consultant to be referred to and thought Dr Skinner to be the most suitable for my situation.

Following my consultation with Dr Skinner, I began treatment with Thyroxine and later with a combination of Thyroxine and Armour thyroid. Under Dr Skinner's supervision, the medication was adjusted until I became stable, my health and well being greatly improved.

I can only thank Dr Skinner for the care and treatment that I have received from him so that I can now lead a normal life. I do not know what I would have done had he not been there and I had to rely on the NHS who rely on outdated blood tests.

Your Sincerely,





26.7.2011

Dear Heather Cook,

I am writing to inform you about my experience of Dr Skinner.

Since seeing Doctor Skinner I feel so very much better.

I felt and was very ill when I was first referred to him even though I had been diagnosed and treated by my GP previously.

Dr Skinner listened to me, took me and my specific hypothyroid symptoms seriously from the start.

He was actually the only Doctor to observe and make a note of my specific symptoms.

After seeing Doctor Skinner my quality of life has and continues to improve remarkably. Prior to seeing Dr Skinner I had experienced numerous hospital admissions related to my hypothyroidism and felt 'untreated' by GP's and hospital Doctors I saw.

Since seeing Dr Skinner I have had no hospital admissions.

Dr Skinner is diligent, switched on, thorough and always ensures my condition is monitored regularly and encourages me to monitor myself. I have learned a lot about certain aspects of the condition I wasn't even aware of.

He has always behaved professionally and with the utmost integrity towards me. I am sure, from my experience, that my quality of life would have remained absolutely unbearable had I not been treated by him.

Thanks for your kind attention

Yours sincerely,

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General Medical Council	
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26<sup>th</sup> July 2011

Dear Ms Cook,

I am writing in support of Dr Skinner, I have been a patient of his for [redacted] and when he prescribed Armour natural thyroid medication for me. Prior to this I had been prescribed Thyroxine for [redacted] years by various consultant endocrinologists'. I sought out Dr Skinner after finding a book on alternative treatment of hypothyroidism on Amazon. I was quite intrigued by what I read as it explained reasons for so many of the problems I had experienced over the years.

The period during my life when I experienced the most intense and disturbing symptoms was just prior to my [redacted]<sup>th</sup> Birthday when I felt like I was starting to go insane. [redacted]

Since starting Armour (after a few initial hiccups due to my over treatment) I have started to understand and appreciate 'to feel normal' actually feels like. [redacted]

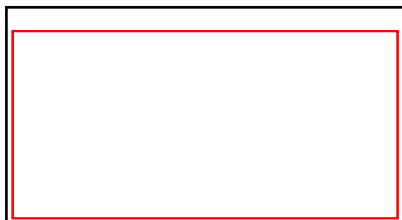
[redacted] I feel that so much of my life has been stolen from me due to inadequate treatment.

Dr Skinner has been a saviour for me. I am now [redacted] years old and I want to enjoy as fully as possible for my remaining years. I feel I need to make up for lost time, in fact [redacted] years of lost time. I am happy to pay for my medication as I would much prefer a full life rather than to revert back to the half life zombie state I existed in prior to receiving treatment from Dr Skinner. If Dr Skinner is struck off, which would be an absolute tragedy; I along with many others will be forced to seek expensive treatment abroad. Those who can't afford this will have to revert to living a half life once again.

I do not understand what the issue is? Dr Skinner is doing his absolute best to treat his patients with the medication that best suits us, why is it possible to receive this treatment in other countries but you are trying to deny us patients this treatment in this country? My wish is that you could live for just one month in the manner I was forced to exist in for [redacted] years. I feel that you would be assisting Dr Skinner and not trying to destroy him if you could only live in my shoes for just one month.

**Please allow Dr Skinner to continue his valiant work – surely it is not a lot to ask to be able to live like a human being rather than a zombie!**

**Yours sincerely**



[redacted]  
24/7/2011.

[redacted]  
Dear Dr. [redacted]

I writing in support  
of Dr. Skinner who is still treating  
my wife privately, for an under active  
thyriod.

My wife [redacted] has for many  
years suffered from an underactive  
thyriod, together with many of the  
symtons, [redacted]  
[redacted]

[redacted] [redacted]'s first visit to Dr. Skinner  
was in [redacted] She has visited  
him twice more since then, [redacted]  
and [redacted]. Since her medi-  
cation has been upped and properly  
balanced, she is a changed person.

[redacted]  
[redacted] in short she  
has got her life back,! all her friends  
and family, have noticed a big difference.  
The both of us can't thank Dr. Skinner  
enough,! also we are recommending  
him to as many people as possible.  
We would greatly appreciate if this  
letter could be circulated to the review  
panel, in his support, for it would be  
a tremendous <sup>loss</sup> to thousands of people,

3

who have been helped by him, or those  
looking for help. if he is told by the  
review panel, he can no longer practice.

Yours Sincerely,



23-7-2011

1

I first saw Dr Skinner in

I had heard how People had improved with adjustments to medication, having had Blood tests and any other Medication considered first.

Dr Skinner Has Helped me, THE Pain I had before has gone!

You name it! if I had it before

, I haven't got it now! my life is mine again now. I look better, sound Better, and feel Better. I've had lots of comments on the way I Tackle things Now

23-7-2011

2

AND How much Better I look,

I THOUGHT ABOUT THE <sup>cost</sup> OF GOING TO  
Doctor Skinner For About 5 seconds  
and knew, I had to go somehow.

I Had Read Diana Holmes Tragic Tale  
'TEARS BEHIND CLOSED DOORS' covering  
Her 23 yrs of Frustration and misdiagnosis  
it said, so much of How I felt!

Before Reading 'Tears Behind closed Doors'  
I Had Bought a Book called 'THE THYROID  
SOLUTION' By RIDHA AREM MD. I WAS  
ALREADY Searching for a Solution!  
So then Made my first Appointment with  
DR Skinner.

You See there are no Standard Human beings.  
We are all individuals, so should have  
a wider Range of Testings, what suits one  
does not suit another, DR Skinner has this  
skill, and uses it with care for each Person.  
We don't get Ten Minutes consultation  
we get "30" I have never Heard one word  
of complaint By a Patient of his, everyone is  
Happy and smiling even though we Pay<sup>482</sup>.



23-7-2011

3

In spite of very Good Help from my GP  
I was only given the Maximum dose of Thyroxine  
Allowed under NHS.

My Health.

It is possible, as Dr Skinner has  
proved to 'Balance' an under Active  
Thyroid we, the Patients, are living  
Proof of this!

I look forward to seeing Dr Skinner  
again soon. When I hope, I can  
take my Son who is in dire need  
of Dr Skinners Help!

And Help is what He does, tirelessly!

I would like to see a Hundred Dr  
Skinners, changing the lives of Thousands  
more people, like me, through every  
Available channel possible.

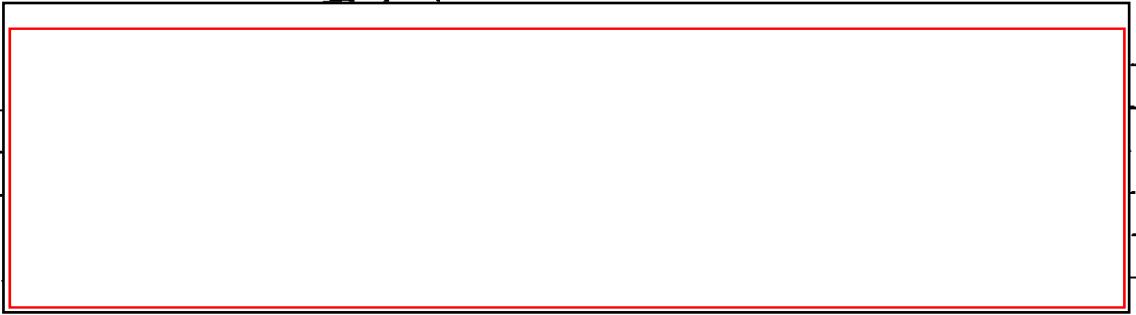
I am fed up with People telling us  
what we can or cannot do these days, what  
we can spend our money on!

Well THANK you Dr Skinner  
you are worth every Penny!!!

483

23-7-2011

4

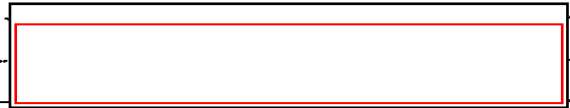


Long Live

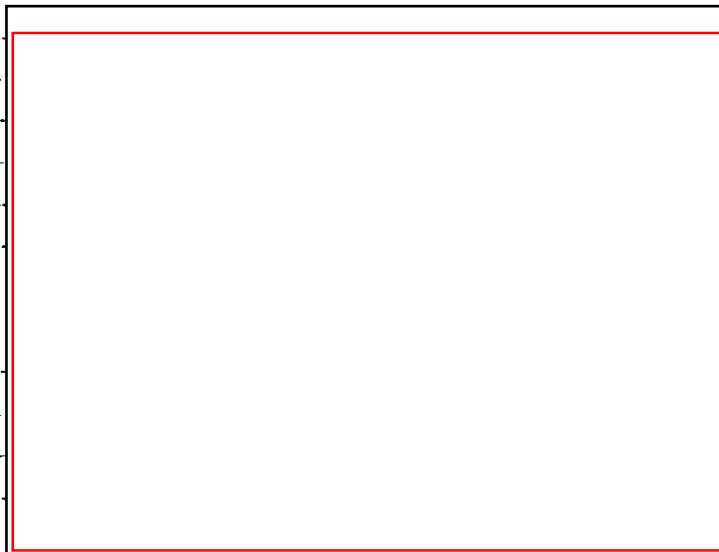
DR Skinner !!

With Love

from

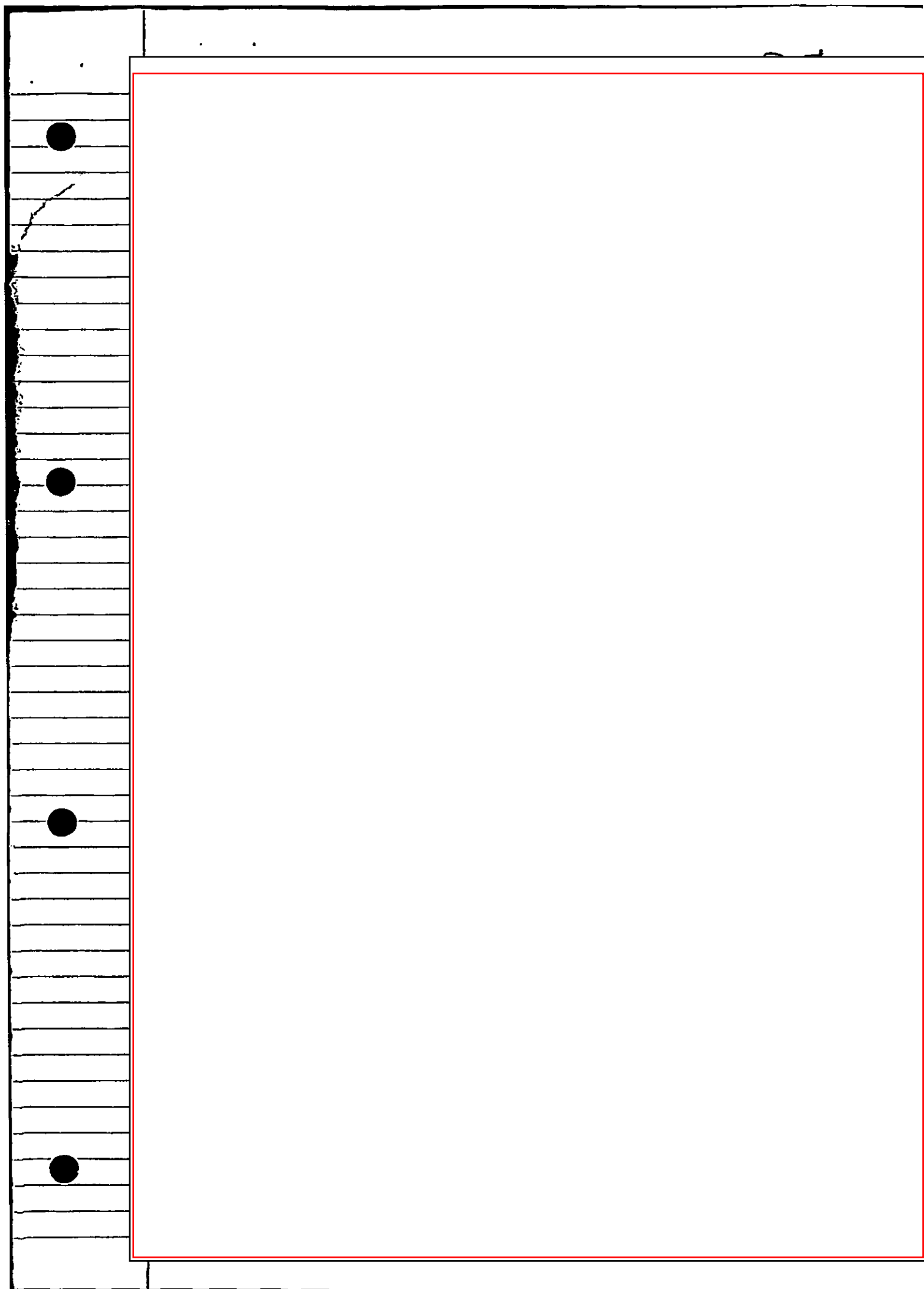


& family



23-7-2011

THYROID SYMPTOMS' 1-B



THE THYROID CONTROLS THE ENTIRE BODY  
ALONG WITH THE HEART

WHY IS IT NOT GIVEN AS MUCH IMPORTANCE?

# 'THYROID SYMPTOMS'

4-4

SOME PEOPLE GET A LOT OF THEM

SOME A FEW

THERE IS NO ORDER TO THEM

THEY COME & GO ALL THE TIME

NOT EVERYONE GETS THE SAME ONES

IMAGINE THE MENTAL FRUSTRATION

~~ESPECIALLY~~ ESPECIALLY, WHEN YOUR DOCTOR

DOESNT HELP, OR SAYS YOU ARE WITHIN

'THE GUIDE LINES'

BUT THESE ARE ONLY GUIDE LINES

WE ARE NOT ALL THE SAME

WHEN THE THYROID IS BALANCED

ALL THE SYMPTOMS GO AWAY

PLEASE HELP US

NOT HINDER

STOP TREATING SYMPTOMS

INDIVIDUALLY

TREAT US INDIVIDUALLY

Heather Cook  
Investigation Officer  
General Medical Council  
7th Floor  
St James's Buildings  
79 Oxford Street  
Manchester  
M1 6FQ

27.7.11

General Medical Council	
Mr Gordon Skinner	
29 JUL 2011	
Physician Objector ref:	

Dear Ms Cook

I happened to notice on the internet that Dr Gordon Skinner is yet again being examined at a hearing by the GMC. I would like to ask (under the Freedom of Information Act) why this hearing is taking place. I would also like to ask why he originally came under the scrutiny of the GMC in the first place.

I believe I read somewhere that there was a complaint made by 'one patient'. I sure you will enlighten me as to the veracity of this fact. When I think of the incompetence of some medical personnel that I have encountered in my experiences within the NHS, I find it farcical that a clinician of Dr Skinner's calibre should be treated in such a manner. Quite honestly, it smacks of the Salem Witch trials!

I have always found Dr Skinner to be well informed and helpful and to have his patients best interests at heart. His enlightened view on the treatment of hypothyroidism has helped his many patients (myself included).

Medicine claims to be a 'science'. Science and human knowledge in general is an ever expanding and developing field. The truths held so dearly at one time can subsequently be proven to be, at least inaccurate or sometimes downright wrong.

Current endocrinologists appear to think that the TSH standard testing for thyroid disorders was handed down from Mount Sinai on tablets of stone. Do none of them take time to keep abreast of research and changing views. There is a wealth of information on the internet from eminent and educated medical personnel who agree with Dr Skinner's views on the subject of hypothyroidism.

They say 'if it aint broke, don't fix it.' Unfortunately endocrinology in the UK is broken and requires a thorough overhaul to make it fit for purpose. How many NHS endocrinologists would have happy and satisfied patients willing to go out of their way to show support and gratitude to them. Not many, I fancy.

The worthies of the medieval church (who felt that they were the keepers of all knowledge) were quick to deride Copernicus and Galileo for their advances in the science of astronomy. Who looks stupid now?

I would hope that the persons involved in this hearing prove themselves to be the enlightened and educated people that they are. Do what you are supposed to do and help patients.

I thought the Hippocratic oath was 'First do no harm.' You are harming patients if you remove the one source of support and effective treatment that they have managed to find.

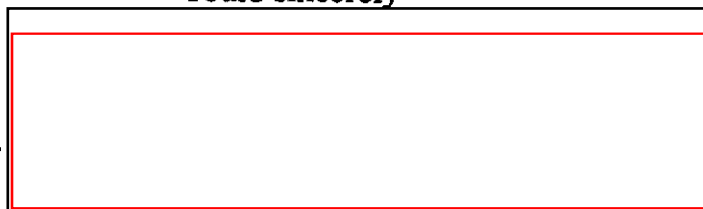
You can take it that this letter is to state my very strong support for Dr Gordon Skinner and my disappointment that the GMC is acting like a group of school bullies.

In this time of financial restraint why is a five day hearing being scheduled into this matter?

Another freedom of information request, How much is it costing for this hearing and where is the money coming from to pay for it?

I am sure that common sense will prevail and that the GMC will make the correct decision and completely exonerate Dr Skinner, allowing him to do what he does best, help people!

Yours sincerely



ps. I apologise for the lateness of this letter but only noticed that this hearing was taking place on the 27th. Thus the reason for sending it to where the hearing is taking place.



8 July 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook

Ref. Dr Gordon Skinner

I write in support of Dr Gordon Skinner who I understand is to undergo a hearing to review the conditions placed on his Practice by the General Medical Council commencing on 28<sup>th</sup> July 2011.

I have been a patient of Dr Skinner since 2001.

I first became ill when I was  years old in . Over the following two years I sought medical help from my General Practitioner for a wide variety of symptoms which included:

I saw many GPs within the Practice I attended at the time in an effort to get help but was repeatedly told that I was suffering post viral syndrome.

I was referred to several specialist practitioners, including a Dermatologist, Gastroenterologist and a General Physician.

These practitioners all refused to link my symptoms which I was convinced were connected and I explained had occurred at the same time. The investigations and consultations they conducted were paid for by my private insurance but I consider that they were all unnecessary when I could have been treated easily and cheaply by my own GP with thyroxin, had they recognised my symptoms. I know that many patients have had similar experiences and these consultations and tests cost the NHS thousands of pounds unnecessarily.

It was only on visiting Dr Skinner, who thoroughly examined me, investigated my full medical history and assessed my symptoms as well as blood tests results, that I got an accurate diagnosis after three years of life changing suffering.

During my treatment by Dr Skinner, I have always found him extremely professional, I consider him to be an excellent and empathetic doctor with unrivalled knowledge of his area of specialisation. He has taken time to fully investigate, explain and record my symptoms as no other doctor I have seen since the beginning of my illness has done. My GP takes blood tests every  months, the results of which are sent to Dr Skinner and held on file. During our consultations we discuss these blood test results and go through medication and dosage, which is adjusted as appropriate. I do not consider that Dr Skinner has ever inappropriately prescribed medication for me, quite the opposite, without the Armour thyroid medication Dr Skinner prescribes for me I would not be well. Dr Skinner has always ensured that I fully understand my treatment plan and he has written to my GP, Dr  following every appointment to keep her fully informed. She is happy with my care and the medication prescribed.

As a result of Dr Skinner's care I have regained my full health, I am able to lead a normal busy life, [REDACTED]. Without his treatment I fear that I would be unable to keep regular employment due to poor health and would become a burden to the NHS and have to consequently claim social benefits. This is obviously a situation that I wish to completely avoid.

I believe that Dr Skinner has been wrongly pursued and persecuted as he prescribes natural thyroxin and T3 in order to help his patients become well as many of us do not respond to conventional synthetic T4 medication alone. I also believe that without doctors like Dr Skinner who have entered medicine with a genuine desire to help people and who are open minded and willing to challenge normal protocol, there would be no strides made in medicine. It is not right that what has become 'normal' procedure is considered the only accepted treatment method, all patients are individuals and react in different ways. In a recent article in the Mail on Sunday, Dr Mark Vanderpump of the Royal Free Hospital states that "five percent of patients do not respond to conventional T4 therapy and that there is active research being carried out to find out why these people react differently to their medication". Surely whilst this research is going on we must not ignore the suffering of these patients and refuse to treat them with medication that improves their condition cheaply and effectively, nor persecute the doctors that help them when others refuse.

[REDACTED]  
[REDACTED] I feel very strongly that Dr Skinner must now be allowed to continue to practice without restriction and to consequently help his many patients to regain and maintain their full health.

I sincerely hope that the proceeding in Manchester will follow the course of natural justice and will be conducted in a far more professional manner than was encountered during the initial Fitness to Practice hearing in London, where it was both an eye-opener and terrible shock to encounter how the GMC handles complaints and conducts hearings, with emphasis being given to immaterial facts such as the use of Post It notes and with Dr Skinner being refused opportunity to speak in his defence.

Should you require any further information in support of Dr Skinner please do not hesitate to contact me.

Kind regards

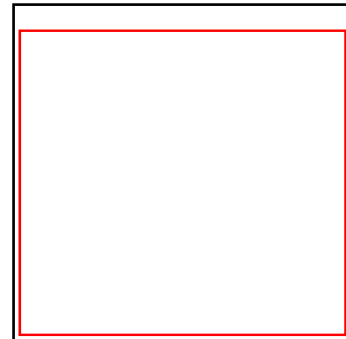
[REDACTED]

cc

[REDACTED]

Mr Ralph Shipway, Radcliffe House, 5 Great College Street, Westminster, London, SW1P 3SJ

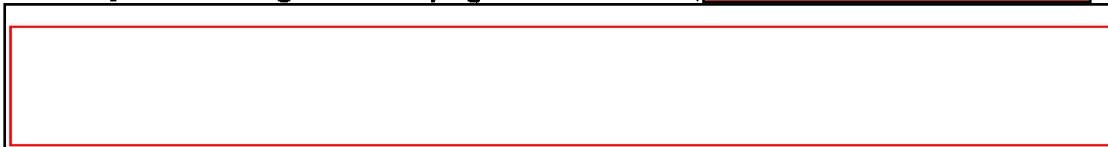
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Dear Ms Cook,

I am writing in sheer disbelief at the news I have heard recently regarding Dr Gordon Skinner and the GMC, and the hearing that is going ahead this week.

I was treated by Dr Skinner back in [redacted]. I was a [redacted] year old [redacted] at the time. My life was living hell. I was plagued with ill health; [redacted]

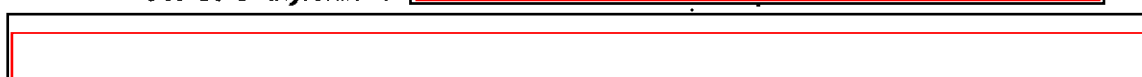


A student [redacted] one day commented on how similar our symptoms were, and informed me that after years of ill health and no support at all from her GP, she was seeing a wonderful practitioner in [redacted]. I immediately asked for his contact details. It transpired she had an underactive thyroid.

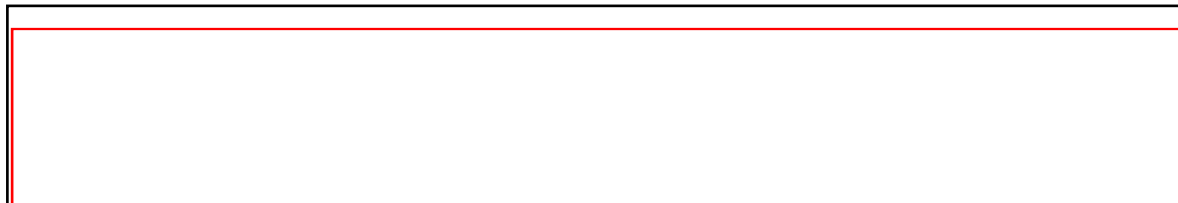
My GP had queried my thyroid results previously [redacted] but admitted he didn't know what to do about it as it wasn't really 'that bad'.

I took my results to Dr Skinner, who acknowledged the clinical proof but actually listened to what I was saying, and how I felt, which my own GP had not done. My GP had convinced himself that my profession was the problem.

I started a course of thyroxin and [redacted]



I returned to my GP who admitted that the change was immense, only to be told that 'now you are better, we'll start reducing your tablets'. What a ludicrous statement when all the journals state that Thyroxin is for life. I was eventually taken off it.



I was once again prescribed Thyroxin, and thankfully am still on it. Oh and did I mention ..... I now have a beautiful, healthy two year old daughter, conceived naturally.

Where I would be today without Dr Skinner I do not know. The action taken against him is criminal and I am prepared to make my story public.

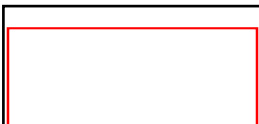
However, that aside, I would like you answer some simple questions for me please.

1. An organ is an organ, whether it is a heart, kidney, liver etc and tests to prove if any of the above are malfunctioning are indeed pretty established and consistent, as indeed are blood pressure guidelines, diabetes scales etc; how then do so many General Practitioners up and down the country have their own take on what a normal thyroid result is?
2. Why, with a TSH of  was I told – it's not too bad
3. Why has America dropped its TSH scale to 3 and state that a thyroid works best at under 3?

This is total inconsistency, and I wonder if it has something to do with the fact that Thyroxin actually works, after all, we know that almost every tablet prescribed these days has a side effect which causes as many, if not more problems than the original complaint, due to their high level of toxicity.

I also discovered recently that Britain is the only nation who remove iodine from their salt. Surely doesn't this prove that the British people no longer have the required amount of this vital element.

I look forward to hearing from you,



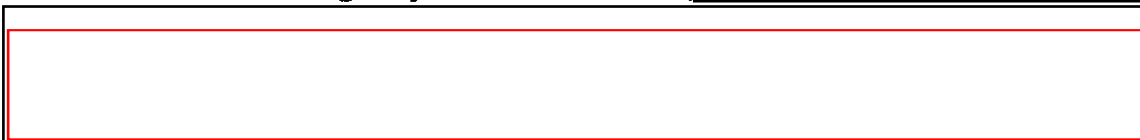
[Redacted]

30th July 2011

Dear Dr Skinner/ Heather Cook. (Arts Please)

I have just received my Thyroid UK - Spring Issue today 30th July 2011 and seen the article regarding a further investigation by the GMC I hope my letter gets to you in time.

I came to see you in [Redacted] after meeting another lady you had helped. After [Redacted] years of chronic ill health [Redacted] and had a borderline thyroid test result. My GP would only give me [Redacted] mgs thyroxine and that did absolutely nothing for me. I now take [Redacted] mgs. My life was a shambles. [Redacted]



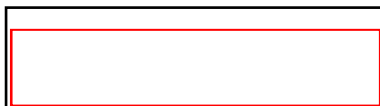
[Redacted] I lost my life as I had known it and my job, which I loved.

I came to see you and after a "thorough hour and half assessment" you sent me for blood tests via my GP and I then embarked on slow improvement and got an acceptable quality of life. Without your help and subsequent hour long sessions with you and discussions with GP, I improved over time and have a reasonable quality of life. I am [Redacted] years of age so have other medical problems associated with age and temperament.

I am appalled at the GMC hounding such Doctors as yourself and others, who help people like myself, who do not fit into the "medical criteria and framework" You spent far more time with me going over all aspects of my problems, than I have never received from any GP or Consultant in the NHS.

Please feel free if there is anything else I can do to assist in your case. I cannot travel at the moment but would be willing to speak or write on your behalf as I firmly believe that you helped me tremendously to improve my life. I used to see you at the [Redacted] Clinic and met others there who had received your help and had a better quality of life because of your professional advice.

Yours sincerely



Copy to Heather Cook

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Ms Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

31<sup>st</sup> July 2011

Dear Ms Cook

Dr. G R B Skinner MD(Hons) DSc FRCPATH FRCOG  
Fitness to Practice Hearing

I understand that the Fitness to Practice hearing involving Dr G R B Skinner is happening now in August 2011.

I wish to add my voice to those of Dr Skinner's patients who have already expressed their support for him, and who would not enjoy good health without his successful treatment for hypothyroidism.

When I was first told about the "borderline hypothyroidism", I looked up information about the condition, and was amazed to find that I had had many of the symptoms for a period of about  years:

My GP would not discuss my symptoms, and would only go by the blood test results.

I heard about Dr Skinner, and asked my GP if she would refer me to him, which she duly did in . Dr. Skinner considered my blood test results and my symptoms, and prescribed thyroxine at a low level, subsequently building up as he monitored my condition. What I have to report

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Ms Heather Cook

-2-

is that from then onwards my energy levels picked up and I enjoyed improvements of other symptoms, and over several months of treatment I knew I could consider returning to my job.

[redacted]  
[redacted] I absolutely believe that Dr Skinner's treatment for hypothyroidism has enabled me to return to a full and demanding life – something I could not have contemplated back in [redacted] when I was told I had [redacted]

As the senior partners of my local surgery advise my GP not to prescribe me thyroxine because of the difference of academic opinion and an unwillingness to acknowledge Dr Skinner's repeated success in treating hypothyroidism – then, if Dr Skinner were found "not fit to practice", I am greatly concerned that I should no longer be able to obtain a prescription for the thyroid replacement medication I need, and my health will be impaired.

Dr Skinner has always monitored my progress and written to my GP after each consultation. I know he has undertaken research, and I have read his book. I considered very carefully all aspects of the situation before agreeing to his treatment, but I believe that without his treatment I would not enjoy my current good state of health.

The outcome of this hearing is of huge importance and great consequence to me – and many, many people like me.

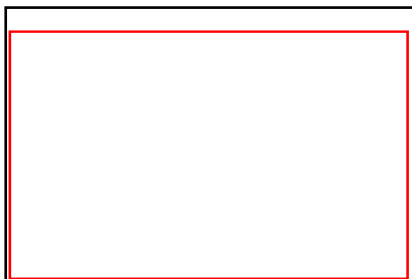
Yours sincerely

[redacted]

Copies to:

Mr R Shipway, RadcliffesLeBrasseur, 5 Great College Street, Westminster,  
London SW1P 3SJ;

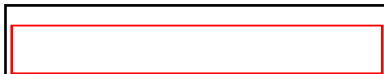
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In respect of Dr Skinners hearing with the GMC.

I am writing this letter in respect of the high regard and esteem that his patients hold for him and my gratitude for the excellent care I personally received from him in my hour of need . He gave me the time to talk and gave me the treatment I so desperately needed. I have no hesitation in recommending him to anyone who has symptoms of a metabolic or thyroid nature, as no stone will be left unturned in his quest for answers to your symptoms, causes and for an appropriate treatment .

Yours sincerely



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[REDACTED]

Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Re: Fitness to Practise Hearing:  
Dr Gordon R B Skinner MD (Hons) DSc FRCPath FRCOG

Dear Ms Cook,

Over a period of [REDACTED] years, from [REDACTED] to [REDACTED], I became increasingly ill, unable to live a normal life and I lost my career as a result. I had been perfectly healthy before [REDACTED]

My GP believed she understood my symptoms and tested my thyroid levels every 6 months but because my TSH was always in the low end of the normal range, she constantly told me that there was nothing wrong with me.

Finally, in [REDACTED] after [REDACTED] years of suffering, I obtained all my thyroid test results, put them into a chart, showed the chart to my GP and asked for an explanation of my steadily declining Free T4 and Free T3 (on the odd occasions when they had been tested) despite my steadfastly low TSH result. My GP explained that she did not understand thyroid test results and that she always acted solely on the laboratory technicians' comments, but she suggested that a doctor she knew of in [REDACTED] may be able to understand them and help me.

She referred me to Dr Skinner who recognized my condition as hypothyroidism, [REDACTED]

[REDACTED], and he began my treatment. I had been left untreated for so long that it took some time for me to recover but I have now retrieved (most) of my life, if not my original career. I am very lucky that my family believed me during all the years of illness, many husbands and children stop believing and an entire family can also be ruined in these circumstances.

[REDACTED] I discovered that different countries approach the diagnosis and treatment of hypothyroidism in very different ways. Patients in Greece with test results which are anomalous are sent, very quickly, to knowledgeable endocrinologists for diagnosis. From my own enquires, the endocrinologists then treat their hypothyroid patients until symptoms are alleviated, not just until their blood test results are back in the normal range. They also prescribe T3 routinely for thyroid nodules, whether benign or malignant, until suppression of TSH is achieved and they also prescribe T3 in any other case where it is deemed helpful. This is in marked contrast to the UK where T3 seems to have been designated a dangerous drug. Greek doctors then educate their patients in the workings of the thyroid, what has gone wrong, why, what is being done to remedy it and what their patients can

expect from treatment. Their patients in turn, can discuss thyroid health with more knowledge and understanding than most British GPs I've had similar conversations with!

This treatment to alleviate symptoms rather than to achieve a blood test result in the normal range, and the regular use of T3 are the two major differences which I have found.

I have also found the normal prescribing of a combined synthetic T3 and T4 hormone called "Euthyrox", at a cost of €2.35 for 50 tablets of 100mcg, and marketed by Merck. The package insert has a section showing its name in various European countries – Austria, Belgium, Denmark, Germany, Greece, Iceland, Italy, Norway, Portugal, Spain and Sweden, but, tellingly, there is no name given for it in the UK.

Why different countries have such different standards is itself amazing, but why a country cannot liaise with another to compare and adopt the best practice for the patient is astonishing. That doctors in the UK are bound by guidelines which do not include the treatment of a significant group of patients whose blood test results are questionable or who do not respond to treatment with thyroxine alone, is disgraceful.

My NHS GP and others in her practice - despite seeing how I have now recovered - still refuse to either treat me (for medico-legal reasons) or to mention in my medical notes that I am being treated for hypothyroidism, I believe my notes simply state 'being treated for a thyroid condition'. All this is because my TSH test over ☐ years did not show what it was expected to. The fact that I could, by now, be seriously incapacitated had Dr Skinner not treated me, does not seem to enter my GP's medico-legal argument, which is curious.

Dr Skinner has been prepared to treat his patients to best help them, rather than to satisfy the narrow current British guidelines which are so lacking in any form of consideration or compassion for some patients. His treatment is similar to that given in other countries, and no doubt similar to that given here prior to the introduction of the blood tests and the prevailing approach taken by the Royal College of Endocrinologists.

I sincerely hope that the GMC Panel will take note of the wonderful work which Dr Skinner does in helping his patients, and that it will not be waylaid by the idea that, in putting the patient's health first, he is in any way working outside his remit as a doctor. He alone has done more to help a significant group of hypothyroid patients in the UK than any other doctor. Please do not stop him continuing to do so. It would also be helpful if someone could take note of how effectively to treat hypothyroid patients and make such treatment the norm throughout the UK.

Yours sincerely,

Heather Cook,  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

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Copies to:

Mr Ralph Shipway, 3 Hardman Street, Manchester, M3 3AW

I was diagnosed with hypothyroidism, [redacted] years ago. I was treated with thyroxine on the national health. It was always my opinion that I was very undertreated, because I continued to feel [redacted] symptoms of thyroid disease.

Trips to doctors and hospital endocrinologist were a waste of time as I was told my thyroid was being properly treated. [redacted] This was far from acceptable to me, my goal being to have my thyroid properly treated.

I researched the condition. The doctors name that kept coming up as helping people like me was doctor Skinner.

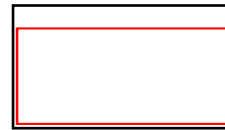
I made an appointment with Dr Skinner and it was decided that as well as my daily thyroxine I was prescribed a small dose of liothyronine [redacted] mcg. Also know as T3.

On this treatment I now feel well again. For the first time in years I have a feeling of well being back. It is recognised among doctors who properly understand thyroid conditions that not everyones body can tolerate thyroxine only. There can be a failure to convert T4 thyroxine to T3. If this fails to happen the thyroid patient continues to feel unwell. Unfortunately doctors in general are poorly informed about this condition and continue to treat it with a very blinkered approach.

I would recommend Dr Skinner to anyone who continues to feel unwell under national health guidelines for this condition. I know of a lot of people just like me that continue not feeling well. If it was not for Dr Skinner I would have no choice but to purchase thyroid drugs from the internet and self medicate. I think you will agree that this would be a lot more dangerous to my health than having my condition monitored with Dr Skinner. Also my doctor has been informed by letter from Dr Skinner what medication I'm taking.

Your Truly,

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7th August 2011

Dear Ms Cook

I am writing in support of Dr. Skinner.

About  years ago I accompanied a friend who had an appointment with Dr. Skinner. At the time she had various symptoms but as her TSH came within normal reference interval, her doctor was not concerned.

She was referred to Dr. Skinner who examined her thoroughly and prescribed thyroid medication for her. Within  months of taking the medication she became pregnant and I am glad to say she had a wonderful little boy who is now  years old. That was a very satisfactory and lovely outcome.

My story is different. My then GP refused to give me a reference to Dr. Skinner. I had at that time been on thyroxine for about  years, but I was gradually getting all kinds of things wrong with me, culminating in so many tests (not on thyroid I would mention), even an operation because of all my symptoms. Each symptom being taken separately not as a whole. However TSH was about 1.6 so obviously thyroid was automatically ruled out.

After the appointment with my friend Dr. Skinner looked at me and told me that I was hypothyroid. I said that I knew because I was taking thyroxine. He said 'well you are not taking sufficient' He said as I was sitting in the waiting room he thought I was going to be his patient not my friend.

*If the GP had only done a full thyroid test for me, including T3, if the labs had done the T3 test if it had been requested, if they took notice of T3, the NHS would have been thousands of pounds better off, and so would I.*

*I can only say thank you to Dr. Skinner for a passing remark and being so aware and thereby being instrumental in me being alive today, and I am not exaggerating, my life was slowly being eroded, and I would have spent the last years of my life in a wheelchair, housebound, very miserable and possibly if I didn't die of a heart attack because of lack of the proper hormone treatment, I might have done something I cannot bear to think about now.*

*Dr. Skinner who is up for a fitness to practice case compared to that one who is not - Dr. Skinner who is only concerned with keeping his patients well, whereas that GP was not concerned that his patient was slowly getting worse. I am*

wondering if you have your priorities right.

*This is my own personal experience, but I have read on various support groups of how Dr. Skinner has caused so many to get a life back and I do so believe this.*

*To deprive Dr. Skinner of practicing would be a travesty of justice and it would be the GMC who would be guilty of causing gross abuse of all the patients he would no longer be able to treat.*

*If I come across as being angry I am. I am angry at the waste of time and public money and the GMC spending even more public money trying to find some way to justify bringing this case.*

Yours faithfully,

[Redacted signature box]

Ms. Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

cc.  
Mr. Ralph Shipway  
5 Great College Street  
Westminster  
London SW1P 3SJ

[Redacted signature box]

10/08/2011

To:

Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman St.  
Manchester  
M3 3AW

CC:

Mr. R. Shipway – RadcliffesLeBrasseur, 5 Great College St, Westminster, London, SW1P 3SJ

RE: Hearing regarding the Fitness to Practise of Dr. R. B. Skinner MD (Hons) in August 2011

Dear Ms Cook,

I am writing to you in support of Dr. Skinner regarding the above-mentioned hearing. I will keep this letter as brief as possible while making my position clear.

I have been a patient of Dr. Skinner for over ☐ years now and I consider him to have helped me achieve a complete recovery from my long-term illness, a recovery which I have now sustained for several years. ☐

☐ Prior to this period I suffered with very bad health for ☐ years during which time I attempted to find a solution via the NHS but was completely unsuccessful ☐

☐ I have a clear understanding of the medication prescribed to me by Dr. Skinner, which is not a drug and am perfectly satisfied with the concept of its interaction with my endocrine system. In my opinion Dr. Skinner has always shown the highest level of professionalism, medical knowledge and caring with regard to myself while under his medical supervision.

I consider this matter to be of a very serious nature, as I believe any impediment of Dr. Skinner in his role of providing myself with medical treatment & supervision would put the health of myself in serious jeopardy; I do NOT consider the NHS system as a viable alternative to this as they have already had ☐ years of my time in which they failed to make a correct diagnosis or provide effective treatment.

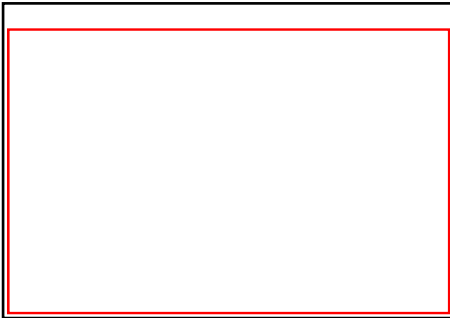
Furthermore, if you are successful in impeding Dr. Skinner of his ability to practise and depriving me of the medical care, I will hold you personally responsible for any illness or degradation in health which I suffer as a result. In such a situation I will not hesitate to take all available legal action against you and the GMC, going as far as the European Court if necessary. I will also bring this matter, including the effect on other patients of Dr. Skinner, to the public attention by all possible means.

I trust I have made my position clear on this matter and I thank you for your time.

Yours truly,

☐

☐



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4<sup>th</sup> August 2011

Dear Heather Cook,

Although I have not been a patient of DR SKINNERS, in turn I have not heard of him causing any of his patients any harm, but from what I have been told that the GMC are supposed to have kept an eye on DR SKINNERS patients, and have kept records, which they had not done, then surely had any harm come to them the GMC themselves would have been to blame.

I also feel that the TPA have helped many patients, and even knowing that others have suffered from remarks made by NHS DOCTORS such as being deluded and hypochondriacs, and in turn damaged by the drugs that they have been prescribed, has helped me to know that we are not Hypochondriacs or deluded.

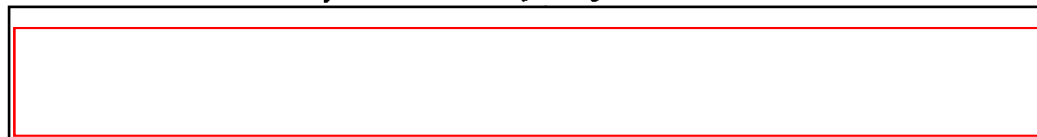
The TPA have in fact saved lives.

DR SKINNER has not harmed patients in this way, but many NHS DOCTORS are getting away with the harm that they have done, even murder.

What does anyone fear most "their mental status", and to be told that they are deluded, hypochondriacs and mental can cause more harm and cause them to take an overdose.

I have been a member of the TPA for several years now, and have heard no complaints against DR SKINNER, only good remarks on how their health has improved.

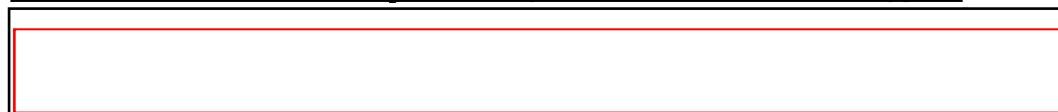
Most people will also turn to Charities for help due to how they are being treated by the NHS; and I too have faced this very bad lack of care and nasty remarks by NHS. Doctors working in the NHS who are in fact using drugs that in turn shorten ones life and are not the correct way to treat ones thyroid problems.



If DR SKINNERS fitness to practise is in doubt, what about the many Doctors who's fitness to practise is in doubt by causing grievous harm to patients and get away with it.

I wish that the Internet and the TPA were around quite a few years ago, as to know that there are others who suffer the same symptoms and that we are not mental as the NHS dictate and that there are Doctors like DR SKINNER there to help.

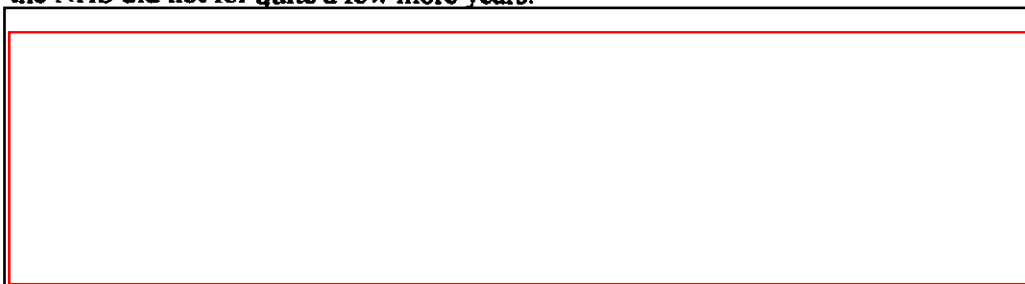
I have consulted [redacted] and he too knows far more than an NHS Doctor would, and no nasty remarks.




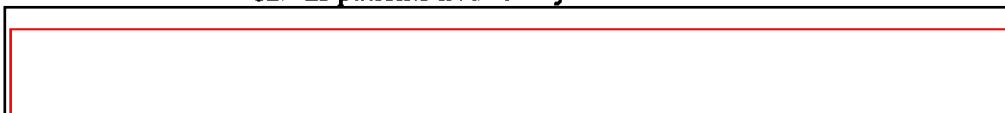




I think DR SKINNER would have diagnosed Hypothyroidism before this point, but the NHS did not for quite a few more years.



 On this occasion left until too weak to stand and in a lot of pain before being admitted to hospital, and I doubt if DR SKINNER would treat his patients in this way.



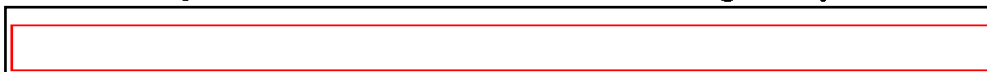


Although I still have problems, hospital will not be on the agenda for me until they learn to control and protect patients from infection, and stop the illicit practices that are going on.

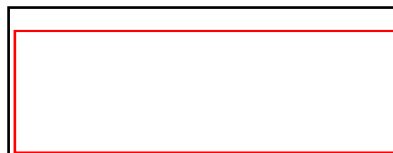
How can you say that DR SKINNER is guilty of anything when the NHS are guilty, yet how many of these Doctors or Nurses appear before the GMC.

I also think DR SKINNER would have enough sense to treat the adrenal glands before prescribing Thyroxin, as no amount of thyroxin will treat the adrenal glands, but do Doctors in the NHS know this or even test ones adrenal glands. The way NHS doctors treat patients cause the adrenal glands to get worse, in fact they get away with murder. I offer my full support for DR SKINNER as I did for  although she too was not my Doctor, but these Doctors who are there to help those that the NHS are not helping is it fair to hound them in this way.

There are also other members in my family with thyroid related problems, but not all have been diagnosed, so tests are not accurate that are being used by the NHS.



Yours sincerely



[Redacted]

[Redacted]

11 August 2011

Ms Heather Cook,  
General Medical Council,  
St James's Buildings,  
79 Oxford Street,  
Manchester, M1 6FQ

General Medical Council

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Date rec for scan	16 AUG 2011
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*Dear Mrs Cook,*

Dr Gordon Skinner

I understand that the General Medical Council is to consider the case of Dr Skinner shortly and I write to recount how my experience of treatment by him compares extremely favourably with that given by other doctors.

For decades I suffered a variety of symptoms that several doctors pronounced were unconnected and for which they offered no treatment. The symptoms seriously affected my quality of life with, among other recurrent symptoms, [Redacted]

[Redacted]

Eventually a GP fed my symptoms into a diagnostic computer programme and showed surprise when advised to test thyroid activity. He prescribed increasing doses of Levothyroxine; however when the symptoms failed to reduce he stated that he could do no more and suggested that I seek private treatment. (This area appears to be without an NHS consultant specialising in thyroid medicine.) I was left with my previous symptoms plus the worry of a newly diagnosed illness that was described to me as serious, but without medical support.

I read up about hypothyroidism and Dr Skinner agreed to my referral to him. He showed a full understanding of thyroid problems and their effects and was able to confirm my diagnosis by examination. He provided valuable advice on my illness, advised on supplementing my diet and replied to my GP with his diagnosis and prescription recommendation. Getting an appointment was quick and his charges were clear and reasonable. I had two consultations and corresponded with him subsequently receiving free, practical advice and support (not available from my GP) that exceeded my expectations.

My health has since improved to the point where I have felt able to take on active roles in organisations again as well as pursuing an active life and, [Redacted]

[Redacted] I owe this to Dr Skinner's intervention.

I have an illness that, I understand, is quite common and easily treatable. However I suffered unnecessarily due the apparent inability or reluctance of several doctors to diagnose and treat it, and their seeming lack of appreciation of the effects on a patient of its symptoms. In contrast, Dr Skinner's treatment has been open, practical, straightforward and effective.

From a patient's point of view, it seems strange that the GMC, a body charged with protecting patients, should concern itself with a respected practitioner who achieves excellent outcomes for his thyroid patients while apparently not addressing the conduct of the other doctors who, perhaps through professional failings, do not achieve a satisfactory outcome for a sector of their thyroid patients. This could give the impression that the GMC is actually more concerned with politics than probity, protocol than patient benefits and conformity than promoting good practice.

I do hope his peers will support Dr Skinner and accord him the recognition as a knowledgeable and effective practitioner in his field that his great dedication and excellent results deserve.

Yours sincerely,

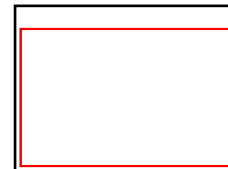
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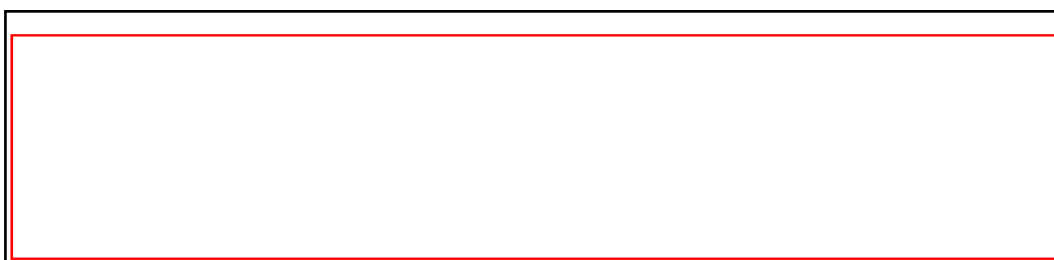


19<sup>th</sup> August, 2011

To Heather Cook, GMC

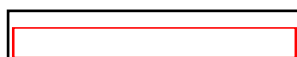
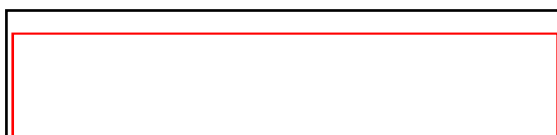
This is a letter in support of Dr Gordon Skinner

I first went to see Dr. Skinner [redacted] years ago having exhausted the systems available to me on the NHS. At the time I was quiet ill due to the fact that having taken levothyroxine for many years for my Hypothyroidism I had developed an allergy to the medication. I had been put on T3 but this alone was not helping and with my symptoms.



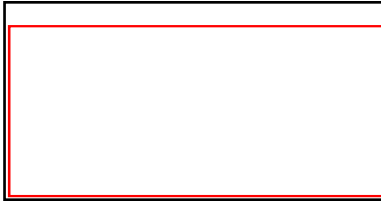
Now thanks to Dr Skinner [redacted]  
[redacted] I no longer suffer [redacted]  
[redacted] due to my thyroid. My health in regards to my hypothyroidism is much improved and I now only see Dr Skinner [redacted] with regular blood test results sent to him during the year and always prior to my appointment.

Yours sincerely,



Copy to Mr. Ralph Shipway, Westminster.  
Dr. Gordon Skinner, [redacted]

General Medical Council	
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[redacted] had physical organs, etc.	



23 August 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW  
U.K.

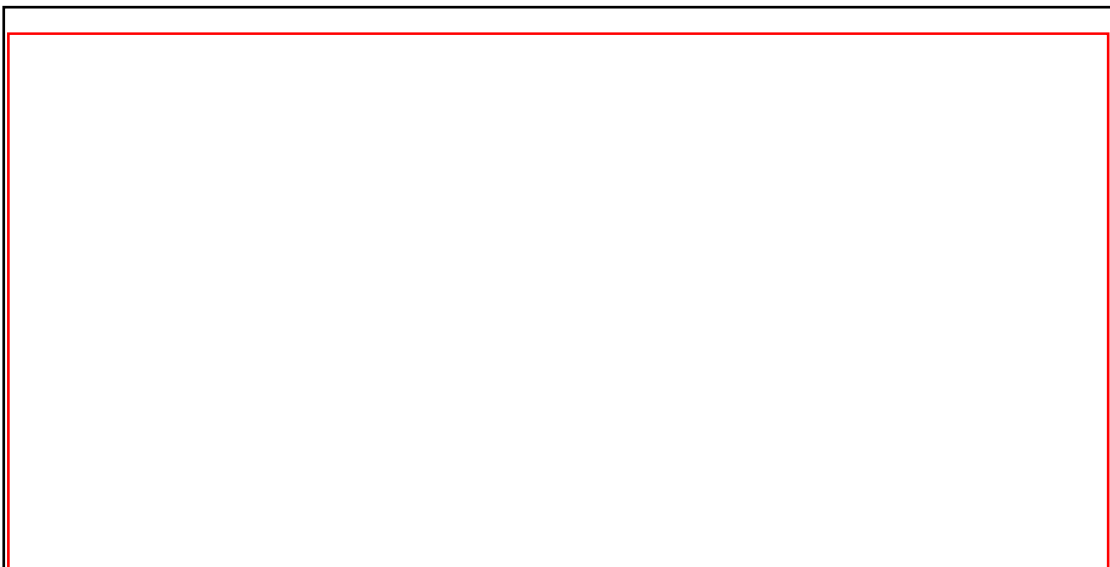
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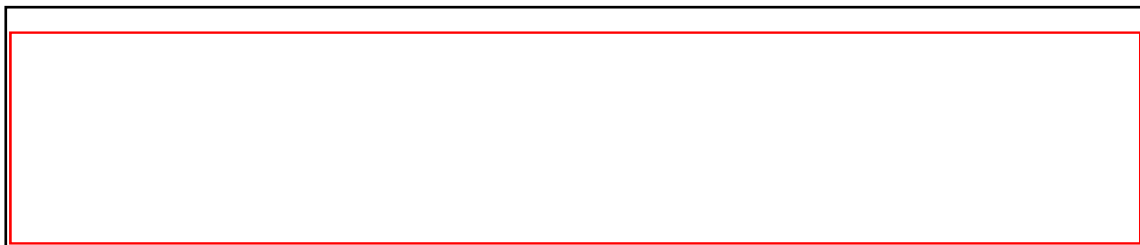
Re: G.M.C. Hearing November 2011 - Dr Gordon Skinner

Dear Ms Cook

I have been a patient of Dr. Skinner for nearly ☐ years. In all this time he has been the most caring and supportive doctor. During the consultation he listens to what I have to say and I feel that my overall health is his prime consideration. He is extremely professional in his approach to me and treats me as an individual. He is happy to talk to me about my illness with no thought to time constraints.

We need practitioners like Dr Skinner as patients like me are constantly being let down by the N.H.S.





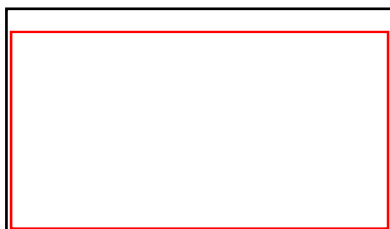
Not long after, I read an article about thyroid problems and realized I had 95% of the symptoms listed. I should point out that I did not make my symptoms fit the list in case you are wondering. I was able to see a private practitioner who "took one look" at me and stated that indeed, I had a thyroid problem. The relief was overwhelming. After all the years of beating myself up I was being told that no, it wasn't all in the mind. It took about a year before I started to feel really well and have now got my life back on track. Naturally my thyroid medication has needed adjustment over the years which is not unusual. In fact medicine prescribed by my G.P. for other ailments had to be discontinued due to unwanted side effects.

Do I feel bitter? Yes I do. **VERY BITTER**. The N.H.S. has failed me as a patient and wasted  years of my life but I can only now pick up the pieces and get on with what is left. This is why the percentage of people like me who do not fit into the N.H.S. guidelines need practitioners like Dr. Skinner, a doctor who is prepared to look at the patient as an individual and to use all the available methods of deciding who is hypothyroid in his evaluation. Besides, the old methods were acceptable once. Who is to say that just because the blood test is the latest diagnostic tool it is the best? Why can't all strategies be used in conjunction?

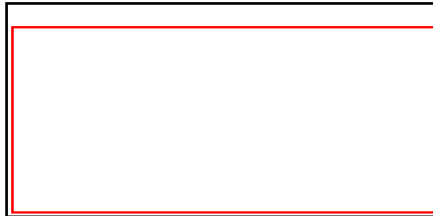
The N.H.S. must accept that there are groups of the human race who have illnesses unique to them, such as sickle cell anemia, so why can't they accept that not all the human race will conform to the parameters they have set for the thyroid blood test.

Dr. Skinner must be allowed to carry on treating patients as I feel that he is the only doctor considering my overall health. I am immensely grateful to him for his care. He is an asset to the medical profession.

Yours sincerely



cc:   
cc: Mr Ralph Shipway



23 August 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW  
U.K.

General Medical Council	
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Date rec for scan	31 AUG 2011
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Re: G.M.C. Hearing November 2011 - Dr Gordon Skinner

Dear Ms Cook

I am writing to you regarding the above hearing as the husband of Thyroid patient and one who you could say has suffered the condition by proxy.

From very early on in our marriage it was apparent that my wife had some sort of medical condition which caused her to be . She made numerous visits to our G.P. and underwent many blood tests to establish a possible cause. I accompanied her whenever possible because of my concerns for her health and, as someone who relied upon hard facts in my work, was unable to understand how all of her results could return as "normal".



Fortunately, after some considerable time, we read an article concerning Hypothyroidism and the conflict in diagnosis caused by the blood test being used as the standard method. The symptoms in the article read like a shopping list and I could recognize something in the region of 95% of them being mentioned by my wife in the preceding years. She is not someone who will complain without good reason.



My wife has been receiving treatment for Hypothyroidism from Dr Skinner for approximately  years and I have the following comments to make:-

He has an *unimpeachable manner* during the consultation. He is informative and will take the time to listen intently to her whilst making notes. I have watched him as he studies her throughout the consultation and I have seen that little, if anything, escapes his notice. His doctor/patient relationship is such that he is one of the few who can take her blood pressure without the reading being affected by the stress of the consultation. I have the opinion that he treats my wife as an individual and not as member of a group who should conform to an arbitrary list of parameters. I am totally confident that he has her health and welfare as the driving force for any treatment he prescribes.

Once my wife was able to begin her medication for Hypothyroidism I notice changes in her which proved to me that she was, at last, feeling like a human being once again. We went to our G.P. with copies of information regarding this condition (and particularly the role of the blood test currently used for diagnosis) in the hope that she would take the time to give it consideration in the light of how my wife now felt. Sadly she showed no interest in what we had to say nor did she accept the copies. She did admit though that she had many other patients who presented with the same symptoms. I feel sorry for them if they have been dismissed in the same manner. Despite this she was not prepared to consider an alternative viewpoint on the subject. I feel that this closed minded attitude is indicative of the N.H.S. and is causing it to lose sight of the most important person in the equation, namely the patient. Surely this is a failing in the "Duty of Care" responsibility that we hear so much about. In these enlightened times the medical profession must be prepared to accept that a patient cannot be "pigeon holed" and therefore may benefit from treatment despite test results to the contrary.

I have nothing but gratitude to Dr Skinner for his continued support and the fact that I have my wife back.

Yours sincerely

cc:

cc: Mr Ralph Shipway

**From:**

**Sent:** 31 August 2011 03:00

**To:** Heather Cook (0161 923 6472)

**Subject:** Dr Skinner

Dear Ms Cook

The Medical profession is supposed to be one of care and concern for the patient - in fact its primary concern. However in number of cases that I have observed, particularly those concerned with the treatment and diagnosis of Hypothyroidism, this is certainly not the case.

You and your Committee have no idea, or care nothing for, the suffering experienced by those who have a sub acute level of Hypothyroidism.

In spite of all my indicative symptoms, and because of the dictats of the (somewhat bigoted) medical profession I am not hypothyroid and therefore not worthy of treatment with thyroxine, due to an arbitrary limit that has been set by a "so called" expert endocrinologist. And this condemning decision is decided by a single blood test! How crass! If a single blood test is not considered sufficient in diagnosing other conditions why is this not the case for hypothyroidism? The fact that you and your Committee support this rigid concept over the needs of patients, and that you never cease to hound those doctors *caring enough* to try and help people like me, demonstrates totally that you, your Committee, the GMC and your whole profession is definitely NOT worthy to be called caring. You would rather adhere to your rigid rules than listen to the chorus of cries of help from those who suffer this condition!

SHAME ON YOU!

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
GMC  
Manchester M3 3AW

General Medical Council	
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27 August 2010

Dear Ms Cook

I am writing in support of Dr Gordon Skinner, as I did in June 2005.

I suffered at least  years of ill health with the difficult to diagnose and insidious symptoms of hypothyroidism, and I think it was much longer than that. My problem was that all my TSH blood tests came back as normal over the decade and my doctors treated me for other things with other drugs. I attach the hypothyroid questionnaire that I completed at the start of my treatment by Dr Skinner from which you will see the many often niggling, debilitating symptoms which add up to misery. (Now I only have about 13 of the symptoms, probably caused by other things.)

When I finally got to see Dr Skinner in  he tested my FT4 as well as my TSH. This test came back at .

But still the NHS insisted that the  test was the correct one and there was nothing wrong with me. All this was decided just on the blood test. The endocrinologist did not examine me, did not take my blood pressure, hardly even looked at me. Although looking back I think it was obvious that I was suffering from hypothyroidism

My doctor referred me back to Dr Skinner and he has been in charge of my treatment ever since. My life has been completely turned round and I am far healthier at  than I was at ; fit, active and so glad that I had the good fortune to be treated by Dr Skinner. I regard him as an expert in his field who takes the time to examine his patients properly and does not just rely on blood tests for a diagnosis.

After such a long time getting a diagnosis I was very lucky to be referred to Dr Skinner and I offer my full support.

Yours sincerely

## ***HYPOTHYROID QUESTIONNAIRE***



29 August 2011

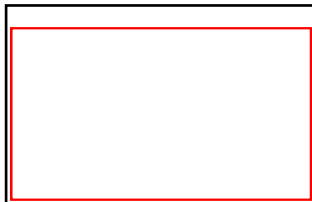
Dear Heather

I would like to express my anger at the way the GMC has treated Dr Skinner and would like the case against him dropped.

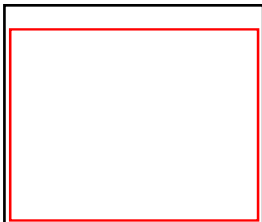
I am a patient of Dr Skinners and before I found him I was at rock bottom as my NHS practice would not take me seriously. Dr Skinner diagnosed me with an Underactive thyroid and started me on Thyroxine, slowly with small doses until I started to feel better. I have been seeing him now for over  years and have received support, reassurance and good medical judgement from him. If I had stayed with the NHS I am sure I would still be in bed and diagnosed with

I am willing to stand up in court and tell the panel my positive experience and how well I feel now. I believe the case recently of  should be used as a precedent and stop trying to strike off doctors who make their patients well.

Regards



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30 th August 2011

**Re Testimonial**

To whom it may concern

General Medical Council	
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I have been a patient of Dr Skinner s for approximately  years; during this time my health has improved greatly. Thanks to Dr Skinner I was finally diagnosed with an under active thyroid and through patience and good communication have now received the correct treatment for my condition. The years before my diagnosis my GPs blatantly refused to acknowledge I had a medical condition  often suggesting my symptoms were all in my head. I believe that without Dr Skinners help I would not be alive now. I have researched my complaint thoroughly and have found that there are thousands of people suffering the way I had without diagnosis due to the blatant ignorance of their GPs refusing to recognize the symptoms and comparing of thyroid tests to previous thyroid tests. I give my permission to Dr Skinner to use my medical records in any way he finds necessary to assist in the resolve of the current issues to help other patients who suffer with this complaint.

Sig



[REDACTED]

9<sup>th</sup> Sept 11

Dear Heather Cook,

I understand that  
Dr Skinner is to attend a  
hearing for 14<sup>th</sup> - 18<sup>th</sup> Nov 11 at  
the GMC offices M/c.

I have been attending his  
clinic for thyroxine for [REDACTED] yrs.  
because my own doctor would  
not give it me even though

I [REDACTED]

[redacted] had symptoms but was in the "Normal range" just. My TSH was [redacted] and was not well at all. Dr Skinner Saved my Life because he could see by my symptoms

[redacted] that he started me on medication straight away. I had been bad with symptoms for [redacted] yrs and I have improved so much. It is only through Dr Skinner that I am so much better. There should be more doctors like Dr Skinner and <sup>541</sup>G P's



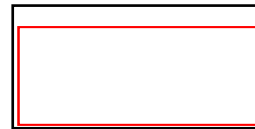
Should not keep rigidly to the  
reference range, which the

Practice and

hospital does. Dr Skinner is  
a caring man and he is trying  
hard to treat the symptoms that  
other doctors dismiss, saying  
they can't help.

I hope that what I have  
said will be of help

Yours sincerely



7th September 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

Dear Madam,

I cannot believe that the GMC are wasting so much time and money investigating Dr Gordon Skinner, without him my life would have been non-existent.

I was diagnosed with Hypothyroidism in [redacted] and I was put on a dose of [redacted] mg until [redacted]

[redacted]  
In early [redacted] I started to feel absolutely dreadful, [redacted]

[redacted]  
I went to my GP who sent me for blood tests, only to be told I was "normal" and to go away, and come back if I was still unwell and he would send me for more tests. What a total waste of NHS money, when all I needed was my Thyroxin dose increased. The guidelines are ridiculous, surely you should be treating the symptoms and getting the patient well, and not totally relying on the blood tests.

I changed my GP and I am now with a brilliant practice who agreed to refer me to Dr Skinner. What a lifesaver he is. I saw him in [redacted] for the first time and I have now got my life back.

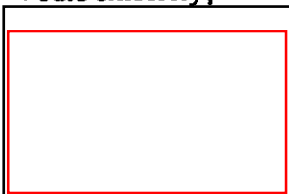
Dr Skinner is obviously a very thorough practitioner who knows and understands his subject exceedingly well.

It is scandalous that hundreds of thousands of people are battling with Hypothyroidism when they can so easily be treated without the exorbitant cost of seeking unnecessary further medical investigations.

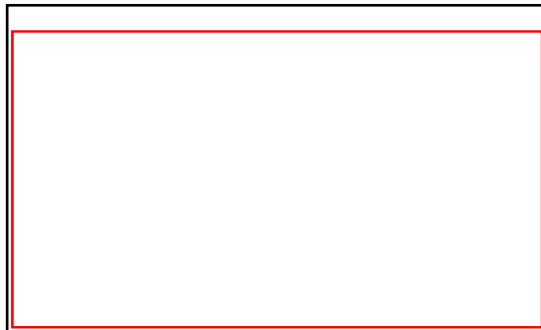
We need more practitioners like Dr Skinner who take notice of patient's symptoms rather than purely depending on an unreliable blood test.

Dr Skinner has changed my life.

Yours sincerely,



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09 September 2011

Heather Cook

Investigating officer

Fitness to Practise Directorate

General Medical Council

3 Hardman Street

Manchester M3 3AW

General Medical Council	
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Date rec for scan	13 SEP 2011
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Dear Ms Cook

I am not a patient of Dr Skinner but [redacted]  
[redacted] I recognize [redacted] that many people  
have achieved full recovery under his care and dedication so I wish to fully  
support his practice. He is doing great work.

I am trying to pursue effective treatment through the NHS at this stage but I have  
encountered bewilderment and a lack of understanding of the issues amongst  
GPs. There is a reluctance to move beyond the 'infallibility' of the TSH and to  
focus on the signs and symptoms presented. There is also a reliance on  
regarding anywhere within the reference range as 'normal' when signs and  
symptoms are present and often obvious. There is also the perceived supremacy  
of T4 when other treatments have been shown to work and are backed by the  
science.

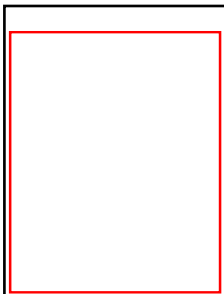
I have numerous symptoms which have all been investigated separately over the  
last [redacted] years and earlier. They have never been knowledgeably  
recognized in a group as thyroid-related. These separate investigations have  
been expensive for the NHS, frustrating and time consuming for me. My  
symptoms have been disregarded when no obvious cause could be found. I also  
have family history of hypothyroidism. I feel very let down that GPs often do not  
recognize a problem exists when the blood test result is returned as 'normal' - it  
is an unfair and one-dimensional approach.

My wish is that all GPs in the NHS should be positively encouraged to equip  
themselves with the current information about the greater thyroid system, to  
read the many medical and endocrinological articles which support Dr Skinner's  
methods, with Type 2 hypothyroidism, particularly resistance to T4 at the cellular  
level.

They could not do better than to learn from Dr Skinner.

Yours faithfully

cc  and R Shipway



11<sup>th</sup> September 2011

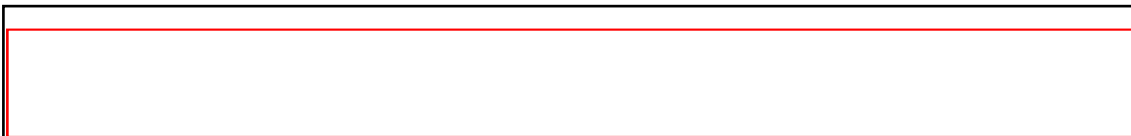
Ms Heather Cook, Investigation Officer

General Medical Council

Dear Ms Cook,

I am writing in support of Dr Skinner regarding the forthcoming GMC hearing in November. I have been a patient of Dr Skinner for  years. Dr Skinner diagnosed me with hypothyroidism  years ago and gave me back my life when he prescribed thyroid medication. Prior to this diagnosis, I was

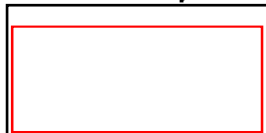
Dr Skinner certainly saved my life.



Dr Skinner is an excellent doctor. He is one of the best doctors I have ever met as he actually listens to his patients.

Dr Skinner does not deserve to be up before the GMC: he should instead be highly commended for his work.

Yours sincerely



Cc.



Ralph Shipway of RadcliffesLeBrasseur (Solicitors)

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10 Sept 11

Dear Ms Cook

Please find enclosed my testimonial  
for Dr Skinner's case in November.

If you require any other information,  
please feel free to contact me.

All best

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10 Sept 2011

Testimonial for Gordon Skinner from Pamela Booth for hearing from Mon 14 -> Fri 18 Nov 11

Since receiving treatment for hypothyroidism from Dr Skinner, the quality of my physical, mental and emotional health has significantly improved.

Before seeing Dr Skinner, I:

Since being treated by Dr Skinner, these symptoms have not only dramatically improved, but most have been eliminated and I find I have a lease of life back. I remember the day I looked at my busy diary for the week ahead and felt excited by it, rather than scared, anxious and overwhelmed: this was a totally new feeling for me. I have been able to exercise, work, sleep and socialise normally and look forward to the future. I do not think it is coincidence that since seeing Dr Skinner, I have been able to further my personal life and career in a way I wasn't able to do before.

The symptoms that I listed above are classically indicative of hypothyroidism, despite this, because my test results for TSH came back just within the "normal range" at my GPs, my symptoms were ignored

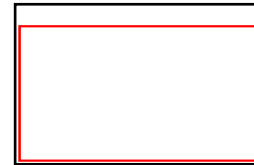
they did not attempt to investigate answers, happy to ignore them because the test results on the paper in front of them came back in the "normal range". If I wasn't a well-informed individual with a great deal of health knowledge and the ability to research and analyse information independently, this fixation on test results over the symptoms I was presenting with may have led me to accept the GPs offer of

If I had gone down this route, I would not have worked to deal with the root cause of my problems, and would perhaps be in an even worse situation with my thyroid, not to mention dealing with possible complications of anti-depressants.

It is also worth noting that the "normal range" for TSH changed during my visits to the doctors and made a previous test result I had come in the hypothyroid range, however, this was not considered in the hypothyroid range because of a difference in time. The "normal range" in the USA, with a respectable and established medical system, would also have meant my tests showed I was hypothyroid all along. That my diagnosis and health was resting on these test results dependant on space and time meant that I suffered from many symptoms for far longer than I should have done.

Visits to the GPs involved little, if any discussion of my symptoms and focussed on test results. My visits to Dr Skinner involved thorough discussion of symptoms and physical examination and also an assessment of my test results. Through this approach, I was accurately diagnosed and treated and I am deeply grateful to Dr Skinner for this.

To Heather Cook  
General Medical Council  
Saint James's Buildings  
79 Oxford Street  
Manchester  
M1 6FQ



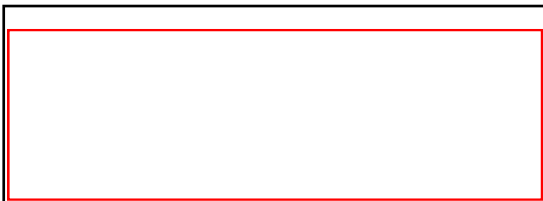
16/09/2011

Dear Heather Cook

Re hearing

Doctor Skinner is light years ahead when it comes to the understand of the thyroid gland and its treatment. I can only wish that the GMC recognises his contribution and does not waste the talents of this doctor.

Your Faithfully



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Tel: [REDACTED]  
15<sup>th</sup> September 2011

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### Symptoms Before Dr Skinner Treated Me:-



**How I survived I do not know.**

**The NHS doctors who failed to diagnose my hypothyroidism and left me for dead were:**

**At one time I was prescribed 26 different types of medication.**

**What Happened After I was Assessed Diagnosed and Treated by Dr Skinner?**

**I got better.**

**I was able to stop all the unnecessary medication which was being prescribed to me.**

I now take armour thyroid and occasional paracetamol when I get the occasional flu. I still cannot tolerate levothyroxine or synthetic T3.

I recovered and I returned to work and I now work full time [redacted]

Also interestingly, my cousin became very ill after a [redacted] and her blood test results were 'normal'. Her symptoms were the same as mine. She was diagnosed as hypothyroid using her signs and symptoms and now she takes armour thyroid and has completely recovered.

I am extremely grateful to Dr Skinner for saving my life and giving me my life back.

I know from harsh experience that thyroid blood test results give false results and are open to misinterpretation.

I feel that NHS medics need to have the clinical skills to be able to diagnose hypothyroidism using signs and symptoms so that more people do not become as ill as me.

I hope that my experience and this information is useful to the GMC. I hate to think of other people suffering the way I did. Sadly, I am very much aware that they are.

Yours sincerely,

[redacted]

c.c. Dr. Skinner, [redacted]  
Mr. Ralph Shipway, Radcliffe Le Brasseur, 5, Great College St, Westminster,  
London SW1P 3SJ

**29<sup>th</sup> September 2011**

**Heather Cook,  
Investigating Officer,  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street,  
Manchester  
M3 3AW**

**Dear Ms Cook**

**Re: Dr Gordon Skinner**

**I write in repeated support and in the hope that Dr Skinner may be allowed to continue his good work, because without his help many of us would suffer greatly.**

**For myself, his knowledge and understanding of thyroid symptom's and wise prescribing allows me to continue with a much better quality of life.**

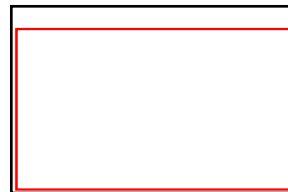
**Prior to having met Dr Skinner (he was recommended to me, and referred to by my G.P. : I struggled with a system with such narrow bands of recognition, by blood tests and G.P.s that ignored the many symptoms of thyroid problems.**

**Which with Dr Skinner's help have been much improved, and some symptoms have disappeared altogether.**

**I now have the quality of life I thought I would never see again.**

**I have complete trust in Dr Skinner and find he is very professional in all regards.**

**Yours faithfully**



3 / 10 / 11

Dear Heather,

As [redacted]'s daughter-in-law, my memories of [redacted] years ago [redacted]  
[redacted] was her [redacted]  
[redacted] always complaining  
of not feeling well and that even though she was under the doctor, they didn't seem to  
be able to find out why.

[redacted]  
[redacted] she stumbled upon a magazine article about women relating their thyroid  
problems and unrecognised symptoms; there was a reference to Dr Skinner. She  
relayed to us how relieved she was to finally have her problems reaffirmed in writing.  
She had no hesitation in booking her first consultation and that step changed her life.

Since that time, I watched [redacted] gradually gain energy, be able to get warm and  
become fit and healthy; so much so that she carried on working well into her [redacted]s. She  
is living proof in herself that she is still fit and healthy and energetic enough to amuse  
her great granddaughters at [redacted]

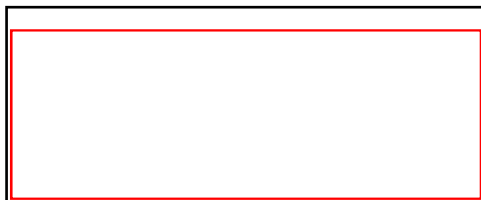
I have seen the difference in her, first hand, over those [redacted] years and it is remarkable. I  
think it is ludicrous that consultants and doctors spend their time arguing the  
principal/point of whether medications are correct or should be prescribed but actually  
spend no time listening to /observing the patient as to their state of health; isn't this  
why so many serious illnesses get overlooked and not referred?

Yours sincerely

[redacted]

Cc: [redacted]  
Mr Ralph Shipway.

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4<sup>th</sup> October 2011.

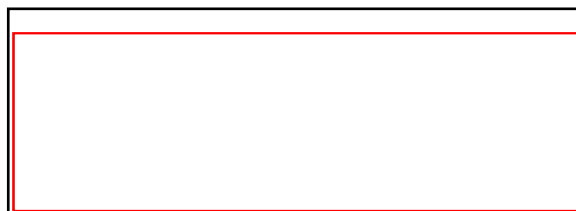
Testimonial for Dr Gordon Skinner

Dr Skinner has been treating my underactive thyroid since [redacted], and it resolved the [redacted] I suffered from until then. My NHS GP consistently refused to treat it for several years on the grounds that my blood tests, which I had every year regularly, showed as normal.

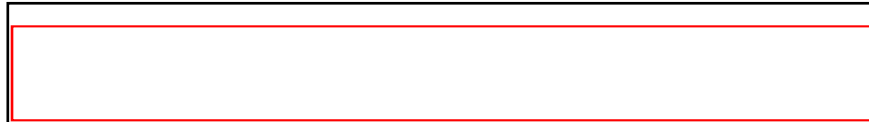
After my blood test in [redacted] however, [redacted] years after starting treatment with Dr Skinner,) she informed me that it was now showing as underactive, and so I underwent a trial period of treatment with her on the NHS, which included being referred to an endocrinologist at my local hospital. [redacted]

[redacted] Despite this, both she and my GP after her refused to prescribe me any higher a dose of thyroxine than [redacted] mcg per day, even though I had by now established that my symptom [redacted] only disappeared at 150 mcg. I was forced therefore to return to private treatment with Dr Skinner for the sake of just [redacted] mcg extra.

Dr Skinner has been consistently helpful and informative at every consultation and I feel that he respects my symptom in a way that my NHS GP does not.



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29 September 2011

Heather Cook, Investigating Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW  
United Kingdom

General Medical Council	
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**Regarding:**                    **Personal testimonial in favour of Dr. Gordon Skinner**

Dear Ms. Cook,

I am writing to you to testify for Dr. Gordon Skinner. I will mention my own symptoms and treatment but also how my first marriage was severely affected by my former wife suffering undiagnosed hypothyroidism for  years, and furthermore my present wife. I will account for this in chronological order.

I certify that everything said in the present testimonial are my own personal and real experiences and thoughts and that nobody has told me to write anything specific.





[REDACTED]

In the surgery of a British GP, one quickly gets the impression that any illness that cannot be diagnosed and treated with a prescription in the ten minutes allocated for each patient isn't worthy of diagnosis and treatment, although I admit a certain exaggeration to make the point. But [REDACTED]'s hypothyroidism was left undiagnosed from late [REDACTED] to early [REDACTED] when she started suspecting it herself, after months of research, and she had heard about Dr. Skinner. She had recalled that a doctor at a public US hospital had mentioned that she might want to get her thyroid checked. Dr. [REDACTED] claimed there was nothing wrong with her thyroid, as she was in the "normal" range, but he offered no other explanation for her miserable condition.

According to my diaries and account files, [REDACTED] consulted Dr. Skinner first time on [REDACTED]. He performed a thorough clinical examination of her and evaluated that together with her blood tests showing TSH, T3 and T4. He concluded that she most probably was hypothyroid and prescribed thyroxin treatment, later supplemented with armour thyroid.

[REDACTED] consulted Dr. Skinner again on [REDACTED] and [REDACTED]. During each nearly hour-long consultation, Dr. Skinner very carefully made a clinical examination that included questions about her mental health and general well-being. Although her condition gradually improved, her body had been so deprived of thyroid hormones for so long time that it took most of a year before she started becoming herself again. [REDACTED]

[REDACTED] Thanks to Dr. Skinner, and Dr. Skinner alone out of the many medical professionals [REDACTED] had seen, [REDACTED] fully recovered.

[REDACTED]



I thought that it would be too much of a coincidence if I were to suffer the same illness as [redacted], but I decided nevertheless to ask Dr. [redacted] for a referral to Dr. Skinner, as [redacted] had originally done too. My first consultation with Dr. Skinner was on the [redacted]. He examined me as carefully as he had always examined [redacted] and he concluded that I should try thyroxin, suspecting that I did

indeed suffer hypothyroidism too.

Over the following months, I too fully recovered my health, thanks to Dr. Skinner, and thanks to [redacted] who had worked tirelessly for years to try to find the reason for her own problems, faced with one incompetent doctor after another. [redacted]

What angers me is the nonsensical way doctors treat statistics and blood tests. [redacted]

[redacted] Again and again, we hear doctors falsely concluding that if a blood test result is within some more or less arbitrary "normal" range, then

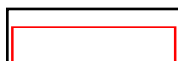
there is nothing wrong with the patient, regardless of how miserable that patient is feeling or how many clinical symptoms he presents. We even hear that if the TSH is not high, then there is nothing wrong, and we don't even need to measure T4. Because of this almost religious belief in a simple blood test being able to diagnose a patient, thousands of hypothyroid patients are left undiagnosed.

May I remind the reader that the purpose of the medical profession is to treat patients, not numbers or blood tests.

If for example 95% of people who are well are within the "normal" range, it means that 5% of people who are well are NOT within the "normal" range. If hypothyroid patients who should naturally belong to this 5% group are persistently refused treatment simply because of their blood tests, without any clinical examination to help determine their condition, then there is clearly something wrong with that conclusion.

Furthermore, the fact that one can measure a "normal" range for 95% of people who are well doesn't mean that any value within that range is suitable for everybody. It is a logical error to conclude that. One only has to use another example such as tyre pressures for vehicles to illustrate how incorrect and unintelligent that conclusion is. Let us consider the hypothesis that car manufacturers don't inform the car buyers of the correct tyre pressures, just as our Maker doesn't provide us with a fact sheet of correct thyroxin levels. Some smart guy in a garage then gets the idea that to figure out how much air to stuff into the tyres, we'll go out on the roads and measure the tyre pressures in all the cars that look to be ok, then define a 'normal' range corresponding to 95% of the tyre pressures measured. If a driver worried that his tyres are under-inflated asks, we'll simply measure his tyre pressures and compare them with our 'normal' range, without even as much as examining the car or how it is driving. If his existing tyre pressure is within our 'normal' range, then we'll tell him there is nothing to worry about and that if he feels the car is behaving funny or that the vehicle doesn't seem to be turning according to the steering wheel, it is just his imagination. Using these principles, we'll end up with buses and trucks driving around with tyre pressures intended for a Mini, every single of them being a danger to everyone around them. Most readers will understand that this way of treating tyre pressures is quite obviously pure nonsense. Yet, this is precisely how doctors are treating hypothyroid patients. A patient who naturally requires a high level of thyroxin to function well will automatically be refused treatment because he happens to have a thyroid level that corresponds to someone else's needs.

Many doctors have an almost religious respect for these numbers, as if numbers alone could tell them how the patient is feeling. They forget that medicine is not an exact science as mathematics or IT and that the 'normal' ranges are empirical knowledge and estimations. They forget that it is uncertain if all those measured to define the 'normal' range were 100% euthyroid. They also seem to presume that the only possible cause of hypothyroidism can be an underactive thyroid gland. But the TSH is produced by the anterior pituitary gland, and how do these doctors know that the hypothyroidism is always caused by an underactive thyroid gland and never because the anterior pituitary gland is not functioning correctly, producing insufficient TSH, thus not stimulating the thyroid gland correctly? And to quote Wikipedia, "TSH production is controlled by thyrotropin-releasing hormone (TRH), which is manufactured in the hypothalamus and transported to the anterior pituitary gland via the hypothalamo-hypophyseal portal system". How do we know that the hypothalamus and the hypothalamo-hypophyseal portal system are functioning correctly? As some computer programs, the endocrine system is very complex, and failures can appear at many different levels. It is simply not credible to claim that the sole level of TSH can be used to determine whether or not a patient is potentially hypothyroid, even before measuring T4. Has medicine become so obsessed with numbers and blood tests that the primary purpose – how the patient is feeling – has been completely forgotten? Patients are not robots or computer programs.



The accusation of Dr. Skinner claims that the fact that Dr. Skinner diagnoses hypothyroid patients as hypothyroid risks overlooking other illnesses.

- First of all, why is it of no concern at all that so many doctors overlook hypothyroidism and in many cases make people's lives miserable, leaving ill people ill, with ruined jobs and broken down marriages, despite the fact that this illness can be completely cured?

- Secondly, if there is some mysterious other illness that needs to be diagnosed and which is causing all these symptoms and illnesses instead of hypothyroidism, then why is it that none of the many doctors people consult diagnose such a mysterious illness and then cure people? The fact is the vast majority of doctors involved simply do nothing, diagnose nothing, treat nothing. They just give the ill patients some general comments, and then leave them ill.

- Thirdly, Dr. Skinner has never explicitly nor implicitly told us that the only thing that is wrong with us should be hypothyroidism. He has diagnosed that we do have hypothyroidism, and then treated it, in both [ ]'s and my case with entirely satisfactory result, to the extent that we considered ourselves cured, feeling completely well. What, then, does the accusation expect Dr. Skinner to do? Keep on hunting for other illnesses despite the fact that the patient is feeling well, simply because the accusation has religiously decided that it must not be possible that the only illness in a person is hypothyroidism? In my opinion, chasing phantom illnesses would be medical malpractice.

The ultimate insult to hypothyroid patients is to find in the accusations by the medical establishment against Dr. Skinner: all these patients have just made up their symptoms and illnesses. They are all feeling very well, it is claimed, they just felt some Monty Python'ish need to imagine they were hypothyroid so they could behave silly and spend a lot of money on medical fees and medication. Neither I nor [ ] had ever heard about hypothyroidism during the first years she was ill. How on earth could she make up being hypothyroid before even knowing about the illness? For which perverse reason should she invent being ill and behave as someone who is ill for many years, just to ruin our marriage?

What happened to common sense in the medical establishment?

What happened to the humility before science, admitting that medicine is not an exact science but an empiric science that has continuously developed over centuries thanks to dedicated researchers committed to making people's lives better, not being fossilised in a table of numbers, as the Establishment now insist?

What happened to the respect for the patient when he informs his doctor he is feeling miserable and is showing clear clinical signs that something is wrong, just to be fobbed off with a list of 'normal' ranges?

In its arrogance, the medical establishment seem to have started behaving as the Vatican church in the Middle Ages: if anyone dared contradict the official view that the Earth is the centre of the universe, then off with his head.

As a patient having lived through the nightmare of undiagnosed hypothyroidism, I revolt against this state of affairs in the medical establishment. Some doctors seem to have forgotten what their vocation is about, falsely believing medicine can be defined as absolute truth, as if it were mathematics.

It is thanks to Dr. Skinner that [ ], I, and countless other former patients have a life to live today.

If it had been up to the medical establishment, we would have been like vegetables, with lost careers, broken marriages, personal bankruptcies, out in the street in many cases, and in the worst cases dead because of suicide.

It is a total, utter, and outrageous scandal that the medical establishment has started a witch hunt on Dr. Skinner, a hunt lasting several years. I am frightened just thinking about the risk of Dr. Skinner no longer being able to prescribe the armour thyroid I need to function, the synthetic thyroxin alone not having been able to heal my concentration problems.

I wonder what exactly is motivating the establishment in this witch hunt. In any case, it is not the well-being of patients.

Yours sincerely,

CC:

Mr. Ralph Shipway, RadcliffesleBrasseur Solicitors, 5 Great College Street, Westminster, London SW1P 3SJ, UK

TO WHOM IT MAY CONCERN

Re: DR. GORDON R. B. SKINNER MD, DSc, FRCOG, FRCPath

Testimonial

My name is [ ] and I am [ ]. I have been a patient of Dr. Skinner since [ ] and his treatment has been crucial in changing my life for the better.

I was an athletic boy who achieved good academic results until the age of [ ] when I started lacking energy and concentration.

[ ] My doctor tried to help but the possibility of thyroid dysfunction was ignored because my blood profile tested just inside the 'normal' range on the NHS scale. I was so lucky to eventually be referred to Dr. Skinner.

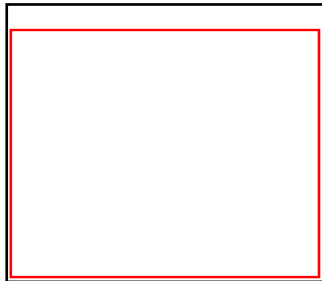
Dr. Skinner helped me when no one else in the medical establishment could, or would. I wasn't very communicative at first, [ ] for treatment which was always traumatic. However he listened to me, understood my problems and persevered. Over the [ ] years he has been treating me, my symptoms have improved enough for me to start living my

life again.

Dr. Skinner transforms the lives of many patients like me by observing and listening to them, and then treating them accordingly until they feel better. Isn't this the whole purpose of being referred to a consultant who is an expert in their field, after other practitioners have found no answer to one's problem?

The GMC should be recognising the dedication and extraordinary successes of Doctor Skinner. Instead of impeding him in his work, why not agree that his techniques could be adopted by more consultants to offer desperate patients hope where none lay before? Thus redressing the faults in a system which refuses to admit that each individual can have a hugely different optimum thyroid level.

Yours,





TO WHOM IT MAY CONCERN

Re: DR. GORDON R. B. SKINNER MD, DSc, FRCOG, FRCPath

Testimonial

Our son [ ] is [ ]. [ ]

[ ]'s mental and physical health slowly became a cause for concern from the age of [ ], [ ]

[ ] Despite a caring and very professional doctor, thyroid dysfunction was discounted for several years because Tom's blood profile tested just inside the 'normal' range on the NHS scale. By the age of [ ], no doctor, counsellor or psychiatrist had been able to help him. [ ]

[ ] We as parents were at our wits' end. Then we found Dr. Skinner.

To say that Dr. Skinner has made a hugely beneficial change in our family circumstances is an understatement. He helped us when no one else in the medical establishment could, or would. He listened to [ ], paid attention to how he felt, to his symptoms. He then treated him until his symptoms improved, and after [ ] years [ ] was able to slowly start functioning again in the 'real world'.

The benefits of this to us as a family cannot be overstated. The last [ ] years have been a huge strain on us all, including [ ]'s younger brother. To see [ ] with a girlfriend this year was truly like a miracle. Being treated for hypo-thyroidism has given [ ] his life back; [ ]

Dr. Skinner clearly transforms his patients' lives by observing and listening to them, and then treating them accordingly. Patients whose blood profiles don't confirm to the exact expectations of the medical profession, and would otherwise, like our son, remain ill and untreated and risk eventually falling through the cracks of society into non-functioning limbo. Doctor Skinner's dedication in putting his patients' wellbeing first shows courage and conviction. It reflects years of experience and observation. He represents to many patients the only lifeline available to them. Literally. There should be more doctors like him and they should be functioning within the NHS system. Why did it take so long for us to find a way of helping our son, despite an excellent and caring GP? Because she felt unable to even explore the possibilities of treating his symptoms with thyroxin, even bearing in mind that hypo-thyroidism is known to be familial and his grandmother had a history of thyroid malfunction. Crazy.

Please, celebrate the dedication and extraordinary successes of Doctor Skinner. Instead of impeding him in his work, why not admit that his techniques could be adopted by more consultants to offer desperate patients hope where none lay before? Thus redressing the faults in a system which refuses to admit that each individual can have a hugely different optimum thyroid level.

Yours, [ ]

[ ]

TO WHOM IT MAY CONCERN

Re: DR. GORDON R. B. SKINNER MD, DSc, FRCOG, FRCPath

Testimonial

Our son Tom is [redacted]

[redacted]'s mental and physical health slowly became a cause for concern from the age of [redacted]

[redacted] Despite a caring and very professional doctor, thyroid dysfunction was discounted for several years because Tom's blood profile tested just inside the 'normal' range on the NHS scale. By the age of [redacted] no doctor, counsellor or psychiatrist had been able to help him. [redacted]

[redacted] We as parents were at our wits' end. Then we found Dr. Skinner.

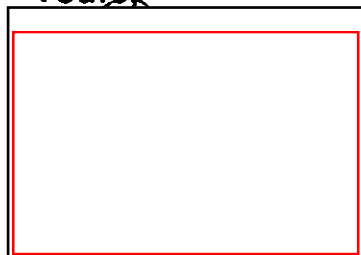
To say that Dr. Skinner has made a hugely beneficial change in our family circumstances is an understatement. He helped us when no one else in the medical establishment could, or would. He listened to [redacted], paid attention to how he felt, to his symptoms. He then treated him until his symptoms improved, and after [redacted] years [redacted] was able to slowly start functioning again in the 'real world'.

The benefits of this to us as a family cannot be overstated. The last [ ] years have been a huge strain on us all, including [ ]s younger brother. To see [ ] with a girlfriend this year was truly like a miracle. Being treated for hypo-thyroidism has given [ ] his life back; [ ]

Dr. Skinner clearly transforms his patients' lives by observing and listening to them, and then treating them accordingly. Patients whose blood profiles don't confirm to the exact expectations of the medical profession, and would otherwise, like our son, remain ill and untreated and risk eventually falling through the cracks of society into non-functioning limbo. Doctor Skinner's dedication in putting his patients' wellbeing first shows courage and conviction. It reflects years of experience and observation. He represents to many patients the only lifeline available to them. Literally. There should be more doctors like him and they should be functioning within the NHS system. Why did it take so long for us to find a way of helping our son, despite an excellent and caring GP? Because she felt unable to even explore the possibilities of treating his symptoms with thyroxin, even bearing in mind that hypo-thyroidism is known to be familial and his grandmother had a history of thyroid malfunction. Crazy.

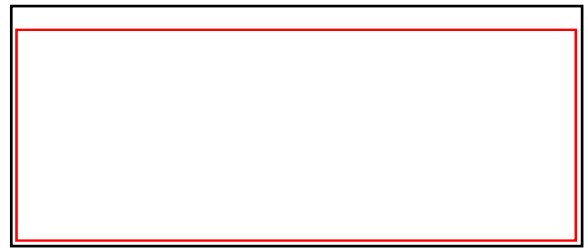
Please, celebrate the dedication and extraordinary successes of Doctor Skinner. Instead of impeding him in his work, why not admit that his techniques could be adopted by more consultants to offer desperate patients hope where none lay before? Thus redressing the faults in a system which refuses to admit that each individual can have a hugely different optimum thyroid level.

Yours,



30.9.11

PS. We know of so many people in a similar situation to ourselves. Surely Dr. Skinner's patients' loyalty speaks much more than words.



5.10.2011.

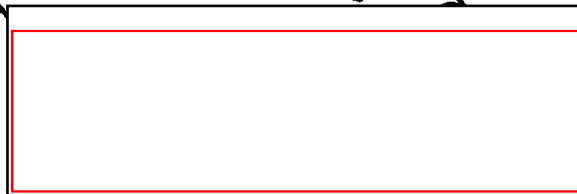
Dear Heather Cook.

I would like to support Dr. Skinner with my testimonial. I have been a patient of Dr. Skinner for  years

Dr. Skinner has always been extremely professional, thorough, patient and understanding, requesting a thyroid blood test to monitor my thyroid, every  months

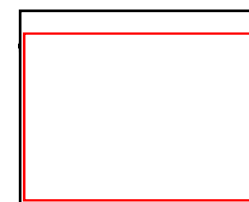
Dr. Skinner took my illness seriously so now am able to live a full life.

Yours Sincerely



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Ms. Heather Cook,  
Investigation Officer,  
Fitness to Practise Directorate,  
General Medical Council,  
3 Hardman Street,  
Manchester  
M3 3AW



8<sup>th</sup> October 2011

Dear Ms. Cook,

In support of Dr.G.R.B.Skinner

I have been referred to Dr. Skinner as a result of long-standing health problems that my G.P. has been unable to address. So far I have had ☐ consultations with Dr. Skinner and am showing signs of improvement.

I am writing to express my complete confidence in his diagnosis and treatment. I also feel that it is imperative that patients can, if necessary, access physicians such as Dr. Skinner who have the breadth of knowledge and experience to give a true 'second opinion'.

Thank you for your attention.

Yours sincerely



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[Redacted]

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER  
M3 3AW

17 October 2011

Dear Ms Cook

Re: Dr Gordon Skinner – Review Hearing 14 November 2011

I see no reason to write again to you on this subject, having already written to you in more than adequate terms in the letter I sent dated 2 July 2011, the contents of which are here below. I have altered the dates accordingly for this Hearing. All our family are anxious that the Hearing are aware of our correspondence.

I am writing to you – once more – in support of Dr Skinner. I have been writing to you to express my admiration of his technical skill, medical judgment and straightforward commonsense since 2006! Why is his outstanding capability and service to countless hypothyroid sufferers still in any question whatsoever?

My wife suffered with hypothyroidism for [Redacted] years until Dr Skinner gave her appropriate doses of Thyroxine, which restored her to full health in a matter of months. Read that sentence again, and ask yourself how YOU would feel if that were a member of YOUR family.

[Redacted] years of 'half life' for want of being prescribed adequate doses of Thyroxine! Recovery within months! Does this not shout out as skilled treatment by a professional who has specialised in the area of hypothyroidism? Someone whose close understanding of this disease should be made known widely rather than be called into question for incomprehensible reasons?

Do you want even one more person to be deprived of the prime of their life because a blood test result falls within arbitrary limits despite the countless symptoms of acute hypothyroidism?

Dr Skinner has restored full and active life to thousands of people who, without his considered treatment, would have continued in the 'half life' to which they were condemned by GPs who slavishly adhered to the Blood Test Guidelines for individuals suffering from hypothyroidism, ignoring the obvious symptoms displayed by their patients simply because the Guidelines said they were 'well'.

Both my wife and I are totally indebted to Dr Skinner. And our daughter too, whose health has improved immeasurably since becoming his patient. And other members of our family. And several friends and acquaintances. That is just our immediate experience. This is repeated countless times across the country.

Please stop reviewing or in any way questioning the medical capability of Dr Skinner. Rather, recognise the huge positive contribution he has made to the well-being of so many hypothyroid sufferers and leave him free to carry on his good work.

Yours sincerely,

[Redacted Signature]

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[redacted]  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER M3 3AW

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16 October 2011

Dear Ms Cook

Re: Dr Gordon Skinner – Hearing 14 November 2011

I wrote to the GMC voicing my views in support of Dr Skinner in 2007, in July this year and now I am shocked to find myself having to do it all over again. I am nearly [redacted] now and dictating this as my writing these days is very difficult to read.

[redacted] In our day we always believed the disgrace of appearing before the GMC was reserved for doctors who harmed their patients. Nothing could be further from the truth in the case of Dr Skinner who is a wonderful man.

Both my daughter, [redacted] and her daughter [redacted], have been recipients of his excellent care. Indeed, I myself became hypothyroid some years ago and on the strength of their treatment regimes my GP treated me in the same way and I too recovered. You could say I am now a patient of Dr Skinner's by proxy! Anyway I'm very grateful to have had 'his' treatment.

We are a 'thyroid family' and I could never understand why this was not taken into account when family members became ill and could not get treatment. It took eighteen years for my daughter, [redacted] despite it being apparent even to me that she had all the signs and symptoms in the book. She was very unwell for a long time but the blood tests always said she was normal. Rubbish. Normal she was not. [redacted] Fortunately, once treated by Dr Skinner, [redacted] was able to see clearly for the first time that my granddaughter [redacted] was also desperately in need of treatment. [redacted] was lucky. Her blood tests showed her to be very unwell and she rapidly became a patient of Dr Skinner – with excellent effect. [redacted]

[redacted]

There is clearly something wrong with the test for hypothyroidism. In my day it was clearly apparent from the signs and symptoms if a patient had the condition. These days they can have them till they are blue in the face but if the test says they are alright, no treatment. I think relying just on a blood test is a very poor medicine. Indeed, I think it is a scandalous state of affairs. Thank goodness for Dr Skinner.

My son-in-law recounts with utter relief the first consultation my daughter had with him. It lasted over an hour and during that time the most thorough history, test evaluation, examination and discussion took place. This was a complete contrast to the useless consultations [redacted] had had with endocrinologists and doctors over the [redacted] long years. Thanks to Dr Skinner, [redacted] made a brilliant recovery and has been well ever since.

In conclusion I can only say that I think there is something very badly wrong with endocrinologists today and with their teaching of thyroid medicine. NHS doctors are terrified of coming before you if they ignore the diagnostic blood test and consequently fail to treat their patients. Endocrinologists go on to diagnose them with ME and the endocrinology gravy train is then guaranteed. SHAMEFUL. What is the GMC doing about it?

Yours sincerely, [redacted]



[redacted]  
Miss Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
MANCHESTER M3 3AW

Dear Miss Cook

Re: Dr Gordon Skinner

General Medical Council	
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16 October 2011

My sister [redacted] has told me that her doctor, Dr Skinner, has got to appear before the GMC again. I'm very sorry to hear this as it upset our family a lot when it happened last time, fearing he would no longer be able to treat his patients.

By all accounts from [redacted] and my niece, [redacted] who is also his patient, he is a wonderful doctor who transformed their lives when he gave them the correct treatment. [redacted] in particular had a dreadful experience, being unable to get any treatment at all for her hypothyroidism over an [redacted] year period.

For our family there was a terrible realisation when [redacted] got better. [redacted]

[redacted]  
This is how bad it gets for patients without hope when they cannot get any treatment, or even the right treatment, for such a common condition. I gather that with both [redacted] and [redacted] they fell foul of some blood test or other which decreed they didn't qualify for treatment. It blows your mind when you see people so ill being turned away by the medical profession for something as stupid as THAT. It is cruel and unnecessary. It makes you want to scream with frustration.

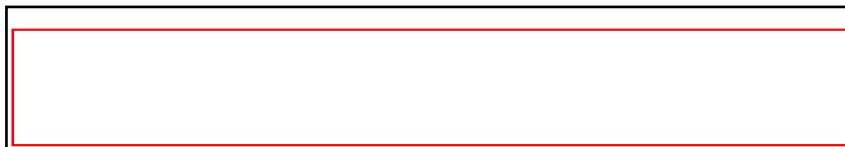
We are a medical family and also a thyroid family – but even that is no use, it would appear, when things are really bad. [redacted]

[redacted] Getting treatment is like getting blood out of a stone.

Is the GMC in a position to do something about all this?? If [redacted] went from being so ill, SO quickly, what about all the others in this world in the same position? Surely the GMC are perfectly placed to look into this situation. It is all so hushed up. You wonder what is going on.

Clearly the one person who must be saved to continue his amazingly successful work is Dr Skinner. Our family love him and we haven't even met him! Please ensure that nothing happens to prevent him continuing to treat his patients. He is a wonderful doctor. You need someone out there who gets his patients better.

Yours sincerely,



16 October 2011

Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
Manchester M3 3AW

General Medical Council	
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Dear Ms Cook

**Re: Dr Gordon Skinner – appearing @ the GMC 14-18 November 2011**

I cannot quite believe that the letter I wrote dated 10 July 2011 will not be considered at the further Hearing of Dr Skinner on 14 November. For some unknown reason we are all expected to write again. I therefore submit my original letter with appropriate date changes. It does bear out my views that this whole procedure is a charade. It grieves me that all this time and public expense is being wasted on humiliating an excellent doctor who should be left to get on with his work, curing sick people, without all this harassment.

For many years my mother had been suffering an 'unknown' illness that was making her so very unwell that we, as a family, were actually surprised she could live from day to day.

They had lasted [redacted] years. She felt this was her life. To all those who knew her this was quite unacceptable.

What I/we didn't know at the time, and what her doctors never picked up (quite shamefully in my opinion), was that she suffered from hypothyroidism. She was left untreated by every doctor she approached.

One evening I was discussing my mother's plight with a friend of mine, [redacted]. Describing her symptoms she instantly recognised them as her own and told me of Dr Skinner and how he had transformed her life, having herself suffered from similar debilitating symptoms.

**Quite simply: Dr Skinner saved my mother's life.**

Armed with her test results, Dr Skinner listened to my mother, questioned, queried, evaluated and only then diagnosed and prescribed. She spent a long time with him, and was impressed by his thoroughness. My mother did not fall into the 'you have hypothyroidism' blood test results. There are many, many of us that do not. This is not unusual for hypothyroid patients (if anyone would study the clinical evidence thoroughly). However doctors in the UK will not treat patients if they do not fall into the "normal" categories.

I also have hypothyroidism. I too did not pass the infamous blood tests. However I am very lucky and have a broad minded doctor who saw the results of Dr Skinner's treatment (initially obtained privately) positively. She continues to treat me, even though I do not fall into the "NHS rules and regulations".

I would very much like you to take into account that thyroid medicine is NOT an exact science. CLINICAL diagnosis is by far the most important than any statutory blood test. Doctors need to look at the patient and diagnose his or her symptoms, NOT whether or not they fit into a, to be frank, quite ridiculous set of 'rules' set out by people (yes, they are actually doctors) who do not really understand the condition.

Hypothyroid conditions are not ME. It may be easy for a doctor to put this simple label on something they do not understand or cannot spend the funds on to get to the bottom of, but this leaves too many patients untreated, with quite unacceptable lives. Hypothyroidism is treatable, very successfully as my mother and I can attest to.

Please do not allow the medical profession to 'bully' Dr Skinner simply because they do not have the knowledge, clinical experience and expertise that he has gained studying this very debilitating illness. It exists. Recognise it. Allow diligent, intelligent doctors, such as Dr Skinner, to treat it the way it can be treated.

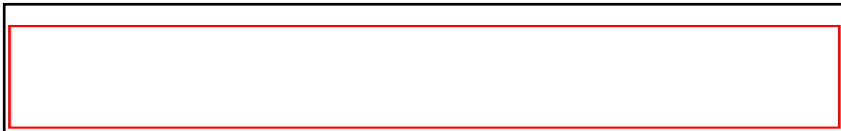
Dr Skinner should be recognised for the value he is to people such as me and my mother. His treatment methods should be evaluated and adopted for the wider good.

That I have to write again to support such an excellent doctor and clinician renders me speechless.

Dr Skinner has my full and wholehearted support. Without him not only would I not have my mother but I too would be very ill.

Please remember the patients' lives he has changed for the better, indeed saved, when you are discussing these quite ridiculous charges at the GMC.

Yours sincerely



Investigation Officer  
Heather Cook  
Fitness to Practice Directorate  
General Medical Council  
MANCHESTER M3 3AW

15 October 2011

Dear Ms Cook

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**Re: Hearing for Dr Gordon Skinner - 14-18 November**

This is the same letter I sent to you dated 3<sup>rd</sup> July this year, altered appropriately. I see no reason to alter my original comments which I would like the Hearing in November to be aware of.

I am the son of [redacted], the brother of [redacted] and the good friend of [redacted] all of whom are patients of Dr Skinner.

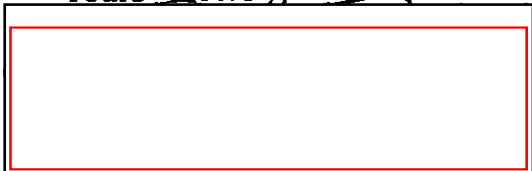
I would like to testify to the Hearing of the excellent treatment they all received from Dr Skinner. My mother tried consistently over [redacted] years to get treatment for her under-active thyroid. Again and again she was prevented from receiving it by the blood test, taken repeatedly, which always indicated that her health was normal, when it most certainly wasn't. As a consequence she could get not treatment. As a family we were mystified because she was clearly so very unwell and struggling. Eventually she was diagnosed with [redacted], which outraged her as they told her then there was no further treatment she could have. She knew it was her thyroid and the whole awful thing ruined her life for [redacted] years.

In [redacted] she heard about Dr Skinner and was referred to him. In a remarkably short time he restored her to normal again. All it took was a drug called Thyroxine which he gave to her in appropriate doses - which apparently the NHS are barred from doing above a certain level. All I can say is that it was like watching her coming back to life.

Our family holds Dr Skinner in the highest esteem. He treated my sister [redacted] with the same success. When my then girlfriend, [redacted] was diagnosed with [redacted] she was devastated. Fortunately I was able to get my mother to talk to her about her experiences and she too then went on to see Dr Skinner with excellent results. It seems so simple if you know what you're doing, as Dr Skinner clearly does. What on earth is wrong with a system that condemns so many people to a life of misery, without treatment, all for want of passing the great blood test?

I can only ask why a man who has such success treating patients, is in danger of losing his livelihood by appearing before the GMC? What about all the doctors who failed my family? Will you be holding them to account for withholding treatment? I find the whole thing baffling. Dr Skinner is a remarkable man for whom I have the utmost respect.

Yours sincerely,



[redacted]  
Heather Cook, Investigating Officer,  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester M3 3AW

18<sup>th</sup> October 2011

Dear Ms Cook,

Dr Gordon Skinner

I understand there is to be a review of Dr Skinner's Fitness to Practise on 16<sup>th</sup> November and whether he has complied with the restrictions placed upon him. I wish to write further to appearing in his defence as a witness at his Fitness to Practise and to the letter I wrote to the previous Panel when his case was postponed earlier this year until now. I feel it is relevant that the current Panel should read what I said before. I enclose my previous letter.

Firstly, I find it quite extraordinary that a medical practitioner of the calibre of Dr Gordon Skinner should be inconvenienced as he has this year when it is clear to those who have been treated by him that there should be no question that he is more than 'Fit to Practise' and are appalled that he has been expected to take time away from his work for a second time after he was invited to appear before a previous Panel this Summer through no fault of his own.

As I said in my previous letter, since [redacted] there have been some stressful periods in my life, the [redacted]

[redacted] However, during those [redacted] years I remain grateful to Dr Skinner for having diagnosed my hypothyroid condition correctly and setting me up with the correct balance of treatment, and to both my past GP and present GP for having recognised his skills and prescribing the balance of levothyroxine and liothyronine he recommended. I am confident that this has been paramount in helping me to maintain good health. As in my previous letter, my major concern is for my daughter [redacted] and the experience of medical care she has undergone during her pregnancy. I have noticed a widespread lack of common sense amongst the medical profession when recognising hypothyroid symptoms in her pregnancy when her thyroid has clearly been affected. We have noticed an obsession with blood test results and an unwillingness to regard her symptoms thereby ignoring a clinical picture. Fortunately her new GP recognizes her symptoms foremost alongside her blood test results.

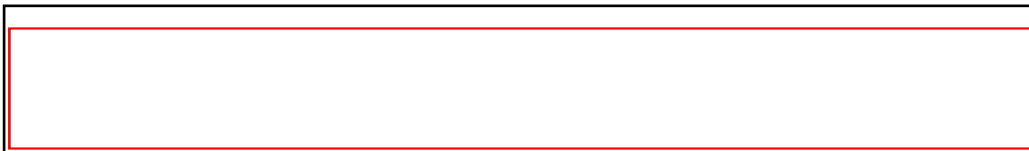
In describing my daughter's predicament, I appeal to you as a Panel to appreciate my hope that Dr Skinner will continue to practise so that he, as a FRCOG and with his expertise with the hypothyroid condition, will be one of the few experts who can help my daughter in the later stage of her pregnancy.

Yours sincerely,

[redacted]

Copies to: Mr Ralph Shipman and Dr Gordon Skinner

600



Ms Heather Cook  
Investigation Officer  
Fitness to Practice Directorate  
General Medical Council  
3 Hardman Street  
MANCHESTER M3 3AW

17 October 2011

Dear Ms Cook

**Re: Dr Gordon Skinner – GMC Hearing 14-18 November**

I enclose my Testimonial on behalf of Dr Skinner.

Yours sincerely



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## TESTIMONIAL: DR GORDON SKINNER – GMC HEARING 14-18 NOVEMBER 2011

The essentials to grasp in my commendation of the Dr Skinner's excellence are these. I bullet point them for ease of assimilation.

- In the prime of my life, at the age of [redacted] from which I failed to recover, instead, becoming ever more ill. Appended is a simplified account. Please read it and see what happened to me. It mirrors the experiences of so many people cast into similar nightmares. Mine was to last [redacted] years.
- It was rapidly apparent that I had become Hypothyroid [I had been Hyperthyroid in my [redacted] with all the readily identifiable signs and symptoms. Five members of my family are hypothyroid. [redacted]
- I ran a gamut of platitudes from [redacted]
- The adherence to diagnostic blood tests and the Reference Interval was my nemesis. All the classical signs and symptoms of hypothyroidism were ignored. GPs trained in the same [redacted] hospital, sharing with me the same professor of endocrinology, ignored his teachings in favour of these instant diagnostic tests.
- Again and again I was told my test results were 'within normal limits.' Years passed with my being repeatedly treated for conditions arising *from* my dysfunctional thyroid state, but not *for* that state itself. No matter how hard I tried I could get no help and my health deteriorated. These good years of my life were slipping helplessly by.
- All this time, resting in the middle of the Reference Interval, and therefore 'not eligible for treatment,' my requests for Thyroxine fell on deaf ears. This terrible reliance on the Full Thyroid Function Test/Reference Interval, does not take into consideration the fact that human beings VARY. Not everyone ticks this limited box – sadly to their detriment.
- This intractable, inflexible system of diagnosis denies treatment to a great many people
- One day, after seeing my GP yet again, with yet another problem, and being sent for yet another blood test, I wrote him a hand delivered note: "How ill do I have to be before you take notice of me?"
- The response was astonishing. Within 24 hours I was prescribed Thyroxine.
- I was now [redacted] It had taken me [redacted] to get the medication I needed.
- It worked! I started returning to life, my thyroid greedily sucking in sustenance. Then my progress stopped. I had reached the [redacted]mcg limit imposed on patients within the NHS. I needed more. None was forthcoming.
- Instead I was referred to an endocrinologist – *no examination* – just the stabbing of my GP's letter with his pen and the words [redacted]
- In my view, *that diagnosis* is the official mark of indifference which *that* professional body bestows upon its patients. It is shameful.
- [redacted] more years passed during which I barely held my own on insufficient Thyroxine.
- At the age of [redacted], despondent and desperate, when things couldn't be worse, I heard of Dr Skinner and was referred to him. He had long waiting lists but eventually I saw him. Then my life began to change.

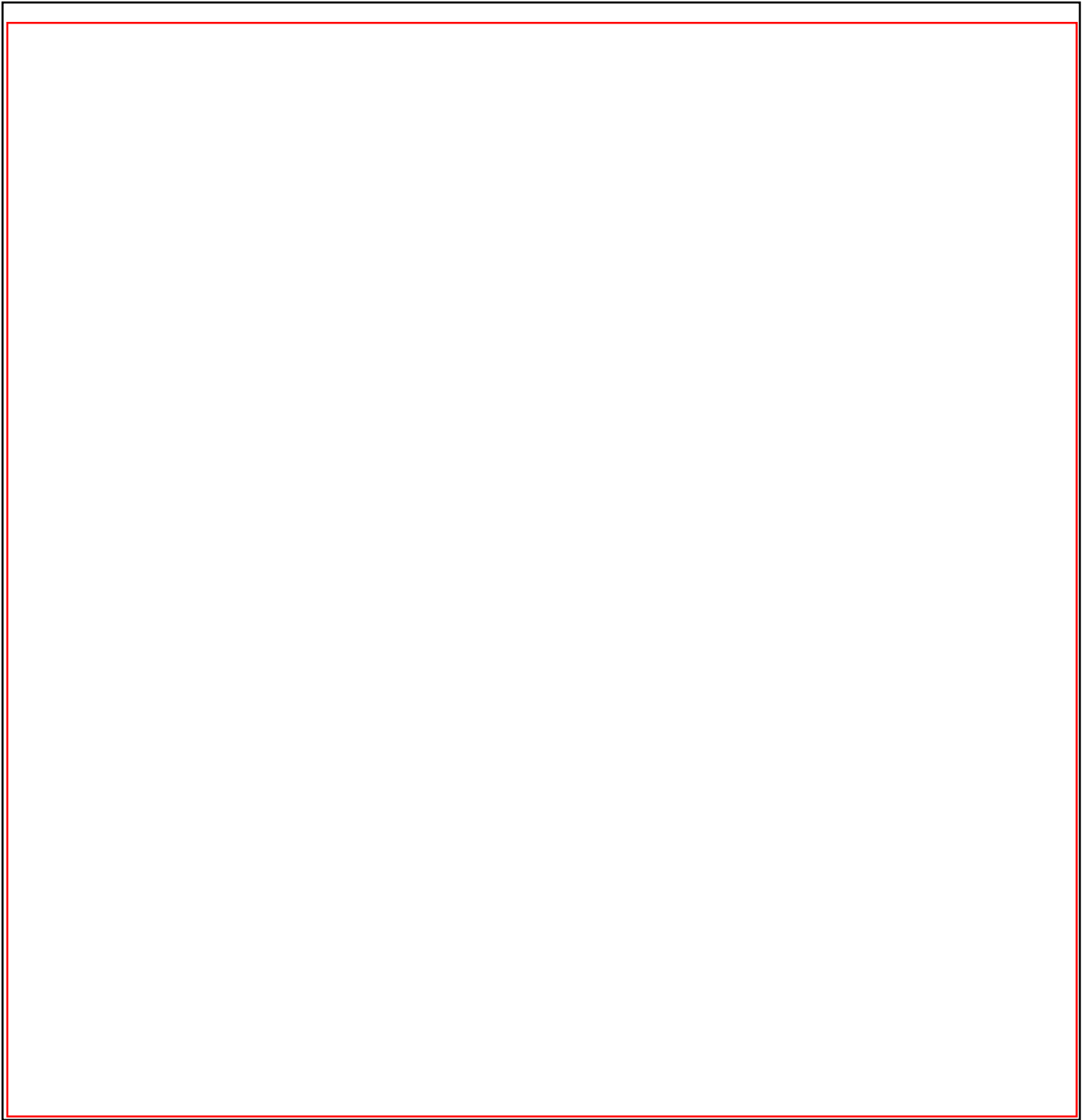
Dr Skinner is a physician of the old school; a man of calibre and excellence. He has a gentle manner and warm sense of humour. He is observant and misses nothing. He examined me thoroughly, painstakingly questioning and evaluating everything I said. He actually *believed* me – an entirely novel experience.

My husband accompanied me and we were both struck by his professionalism and integrity. It was apparent he had a total grasp of his subject. He was a man who listened, evaluated, diagnosed – and – crucially, interpreted my blood tests with a sureness of touch. He clearly had vast experience. His professionalism outshone that of any doctor I had seen since the onset of my condition and continues to this day. No doctor had ever examined me before, let alone listened to what I had to say, so you can imagine the impact Dr Skinner had on me, and indeed, my husband. We trusted him completely. In his hands I felt safe. On his treatment regime of adequate, escalating doses of Thyroxine he predicted I would feel better quite quickly and be stable within [redacted] months. He was right. Under his supervision I then reduced my Thyroxine to a level at which I remained so. I was well again! Dr Skinner had given me back my life.

Can you imagine the depth of my/our gratitude?







2004 - New referral to consultant in  Dr Gordon Skinner

This doctor's *rigorous* and in depth examination, and crucially different interpretation of my thyroid function tests, resulted in my being **formally diagnosed for the first time ever** as having **Hypothyroidism, with a long neglected thyroid**. He treated me with an effective, escalating regime of Thyroxine which I took under his close supervision.

Eventually, at mcg of Thyroxine, my thyroid kicked back to life and I felt normal for the first time in  years.

Once I was stable the dose was gradually reduced until such time as I remained that way.

**It only took 6 months for me to become normal in every way and 9 months for my stability to be maintained.**

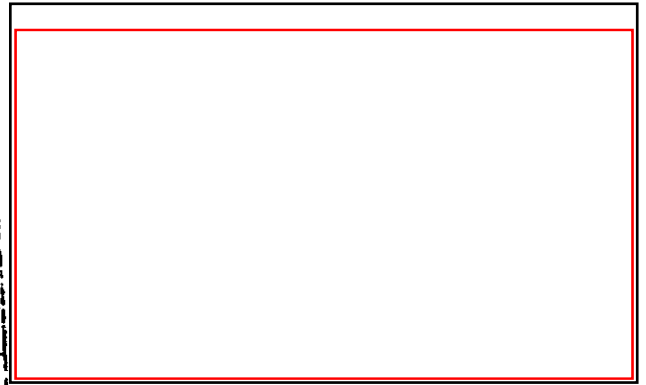
NB: When I say I was normal, I was just that.

ALL my health difficulties disappeared.

I felt FANTASTIC. It felt like a miracle!

After  long, unhealthy years in the prime of my life, I remain forever indebted to the excellent Dr Skinner, who, after all that time, competently and caringly returned me to life.

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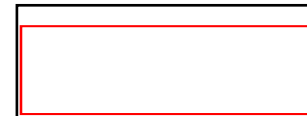
To whom it may concern,

After being diagnosed with hypothyroidism and struggling to return to health for  years with so many symptoms to list! I finally found Dr. Skinner who in my opinion has helped me beyond all recognition. No other doctor has been able to do this even a consultant in this field.

I have always found Dr. Skinner to be encouraging, understanding and professional at all times, his advice has proved that my condition can get better. My condition under Dr Skinner's care and guidance has improved immensely.

I would not hesitate to recommend Dr Skinner to any other sufferer - in fact I already have.

Yours Sincerely



19.10.2011

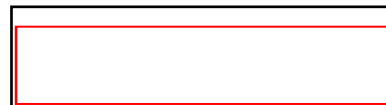
Dr Skinner's Hearing: November 2011

Dear Sir

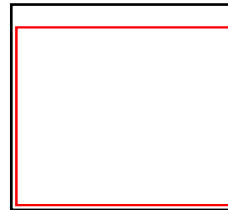
Dr Skinner has treated two of my friends and they have been most appreciative of his care. They had been misdiagnosed by other doctors and consultants and had been given their health back by this exceptional doctor.

He should be allowed to work without conditions on his practice and his patients should be able to go to the who helps them the most..

Yours truly,



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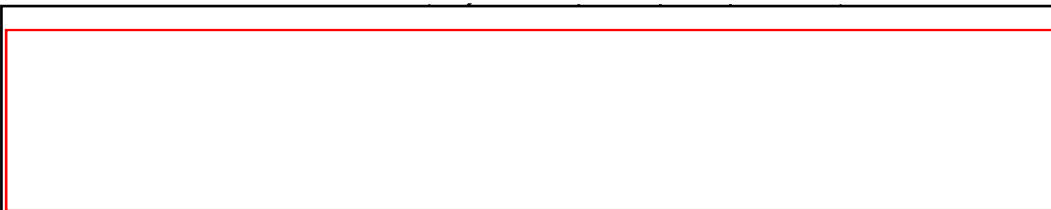
17th October 2011

Heather Cook  
Investigation Officer  
Fitness to Practise Directorate  
General Medical Council  
3 Hardman Street  
Manchester  
M3 3AW

Dear Ms Cook

I write this letter in support of Dr Gordon Skinner who is to appear before the GMC at a review hearing from Monday 14th November to Friday 18th November 2011.

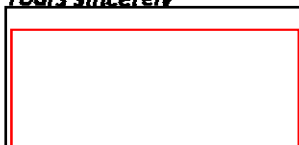
I am a patient of Dr Skinner and can only say that he has helped me where others in the medical profession would not. I have hypothyroidism, which I suspected for [redacted] years that I might have, as thyroid disease runs in my family. My mother, grandmother, several aunts and cousins had the disease also, but I was always told that my thyroid function tests were in the "NORMAL" range. I did not feel particularly "NORMAL" [redacted]



Dr Skinner listened to symptoms and checked my signs and he concluded that I had hypothyroidism and I now take Levothyroxine. I cannot believe the difference this has made to my health and wellbeing. I can never go back to the way I felt before I consulted Dr Skinner therefore I write this letter of support as he has the courage and experience to look beyond a set of blood tests, which are not the gold standard that they are claimed to be, and treat the patient.

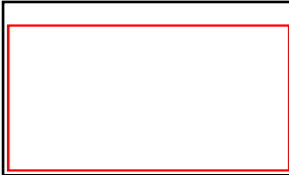
I want to let the panel members know that if I cannot be monitored and treated by Dr Skinner then I will be looking at all avenues available to me and will, if necessary, use the Human Rights Act as I am capable of making decisions and accepting the consequences of my actions in using thyroid hormones which are currently prescribed by Dr Skinner.

Yours sincerely



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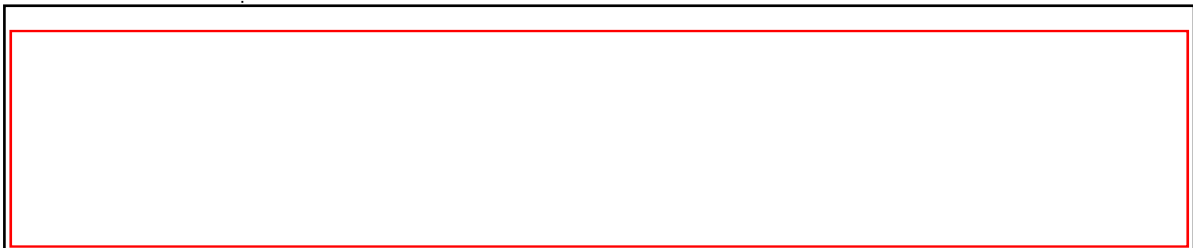


Dr Gordon Skinner's hearing at G.M.C 15, 16, 17, and 18 November 2011 at GMC offices, Oxford Street, Manchester.

To: Ms Heather Cook, Investigation Officer, Fitness to Practice Directorate, GMC

Dear Ms Cook,

With regard to the above case, I am writing to you to support Dr Skinner, who has treated me for underactive thyroid for the last [redacted] years, since [redacted] [redacted]



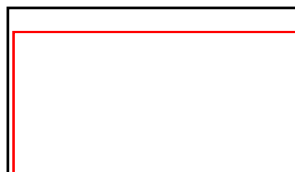
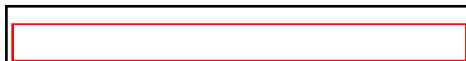
I struggled on for the next few years until [redacted] when through a friend who had had treatment with Dr Skinner and consequently lost a lot of weight in six months, put me in touch with him. He discovered that I had an extremely underactive remnant t of a thyroid gland and prescribed levothyroxine gradually increasing the dose to [redacted] mg a day.

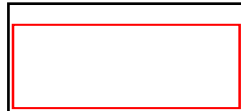
I can say that Dr Skinner literally gave me my life back- I was able to return to paid work and [redacted]  
[redacted]

Personally, I feel that the NHS neglected my condition with a) no follow up appointments at the [redacted] Hospital following [redacted] and b) lack of perception by my doctors (GPs) that my [redacted] might be due to underactive thyroid.

The treatment with Dr Skinner has always been careful and considerate of my general state of health and well being. It would be a great loss to this area of medicine should he be forced to retire from practice, as he must have greatly improved the health of many people through the correct thyroid treatment.

Yours sincerely





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Dear Sir

I am writing to support Dr Skinner who is due to attend a Hearing in mid- November.

I know him to be an excellent doctor who has cared for some friends of mine and returned them to health. They found him to be a very caring doctor. He was very thorough in consultations in the questions he put and the tests he gave. He had obviously prepared himself well on their previous history.

No-one can understand why he is under investigation.

Yours truly,

