GENERAL MEDICAL COUNCIL

FITNESS TO PRACTISE PANEL (MISCONDUCT/PERFORMANCE)

On:

Thursady, 12th July 2007

Held at:
St James's Buildings
79 Oxford Street
Manchester M1 6FQ

Case of:

GORDON ROBERT BRUCE SKINNER MB ChB 1965 Glasg SR
Registration No: 0726922
(Day 9)

Panel Members:
Mrs S Sturdy (Chairman)
Dr M Elliot
Mr W Payne
Mrs K Whitehill
Mr P Gribble (Legal Assessor)

MR A JENKINS, Counsel, instructed by RadcliffesLeBrasseur, Solicitors, appeared on behalf of the doctor, who was present.
MR T KARK, Counsel, instructed by Eversheds, Solicitors, appeared on behalf of the General Medical Council.

Thursday, 12th July 2007

(9.30 am)

(Panel in camera)

(9.40 am)

THE CHAIRMAN: Good morning, everyone. Good morning, Dr Skinner.

A. Good morning, ma'am.

THE CHAIRMAN: I just want to remind everyone, in order to maintain the anonymity of the patients involved in the case should their names be mentioned in error, please do not refer to them outside ever outside of the room. Mobile phones to be turned off and if you do have any discussions, please have them outside.

We are now still hearing questions from the Panel, which is where we finished last evening, and Dr Elliot has one more question for Dr Skinner, and then we will proceed with the barristers' questions.

We will finish the days at 5 o'clock, unless there's prior notice from now on.

MR JENKINS: Can I just apologise for being slightly late?

THE CHAIRMAN: That is all right, thank you.

DR GORDON SKINNER (continued)

Questions from THE PANEL (continued)

DR ELLIOT: Good morning, Dr Skinner. Sorry, this is an area I had forgotten to ask you about yesterday. It's

in connection with one of the charges, charge 10b, if you have the charge sheet there. I will just speak as you're looking for that.

This is Patient B that we are talking about who is a lady from Scotland.

Charge 10b says:

"Between 20th March 2003 and 21st January 2004 you failed to monitor Miss B adequately or at all."

That's the area I want to ask you about.

If you look at the large file, C1, tab 4, those are your notes pertaining to Patient B. On page 6 is your letter to her GP after you saw her on 20th March 2003.

A. I'm sorry, Dr Elliot, something has gone astray here. Can you, please, remind me of the page again?

Q. Yes, it's tab 4, page 6.

This is your letter to Dr Blair, the patient's GP. It's the last paragraph in which you say:

"I perhaps just need to see her once more in about eight weeks' time."

Was it your intention to see Patient B in eight weeks' time after her first visit?

A. Yes, indeed.

Q. It was?

A. Yes.

Q. Do you know why that didn't happen?

A. Yes. She told me Dr Blair was looking after her and was very happy with the situation. That is what I strive for anyway.

Q. Yes. So were you in touch with her then, after that first visit, before the eight week point, at which you had intended to review her? Because you said that as a rule the patients made their follow-up visit when they left after their --

A. Yes, that's quite right. She was in fact, as I said to the Panel before, a friend of the practice manager, so in fact I would see her informally almost every time I went to the rooms in Glasgow. I hope I'm answering your question. I was very happy that Dr Blair was -- who saw her many times, very diligently -- looking after her.

Q. As far as you actually recall, the patient said Dr Blair was looking after her?

A. Oh, absolutely, yes.

Q. And then on page 7 of the same file, this is a form which I think your practice sent out to patients.

A. We wouldn't normally send this out. That form would normally be filled in by the patient at a visit.

Q. Right. This form says that the last checkup was on 15th May 2003. That coincides with a checkup that the patient had with her own doctor, Dr Blair.

A. Yes, that's right.
Q. So that information was information that you had, in your practice, that you had this evidence, if you like, completed by the patient that she had seen a doctor on 15th May 2003, approximately two months after your first visit?
A. Yes, indeed.
Q. That would normally be completed by the patient at the surgery, it wasn't posted out to them?
A. No, we wouldn't post that out.
Q. And you don't recall at what point this was --
A. I can't recall when this was filled in precisely.
Q. Because it must have been after 15th May?
A. Yes, it must been, yes.
Q. Probably from the sound of it, before 17th June, because it says 100 micrograms of thyroxine, until 17th June. But that's speculation.
A. That is speculation.
Q. But this is some evidence that the patient had been seen by a doctor on 15th May?
A. Yes, and these are Dr Blair's notes, of course, as well.
DR ELLIOT: Thank you very much.
THE CHAIRMAN: That concludes the Panel's questions. Now further the questions from Mr Kark.
Further cross-examination by MR KARK

MR KARK: Just in relation to those questions you were just asked, you are saying that this patient was telling you that Dr Blair was happy, when we know, of course, that Dr Blair was not. Is that what you're telling the Panel?

A. I don't recall saying that, Mr Kark. I said that I was aware, and the patient said she was seeing Dr Blair.

Q. Yes, but we know that Dr Blair wasn't happy at all, don't we, because he was telling his patient --

A. We know it now.

Q. Do we have to go through that again?

We know that he was telling her not to take thyroxine. If you want to have a reference to it again, have a look at tab 3, page 28, if you've forgotten what Dr Blair was telling his patient.

He told her repeatedly to stop taking thyroxine, didn't he?

A. Dr Blair told the patient?

Q. Yes.

A. Why did Dr Blair not tell me?

Q. Well, that wasn't the question.

A. It is relevant.

Q. Dr Skinner, what I asked you was whether the patient -- you said the patient was telling you one thing. We know the patient was being told by her GP something quite

different, don't we? Do you accept that?
A. I accept that the patient --
Q. Right.
A. I didn't finish what I said.
Q. Go on then.
A. May I finish, please?
Q. Yes, please.
A. My memory of three years ago and this patient was -- I think she did indicate that Dr Blair wasn't overjoyed about her. I don't remember any communication to me to the level which seems to retrospectively be displayed.
Q. Well, if the patient was telling you that Dr Blair was not overjoyed about it, presumably not overjoyed about you prescribing thyroxine?
A. If a colleague was not overjoyed, I would have thought the colleague would make contact with me.
Q. Sorry, can I just remind you of evidence you gave to the Panel a few minutes ago. Dr Blair was very happy with the situation. Which one is it, please? Was Dr Blair very happy with the situation, according to the patient, or was the patient telling you that Dr Blair wasn't happy? Which is it?
A. I don't remember saying that the patient said Dr Blair was happy.
Q. Well, that's the note I've got. I don't know if the

Panel members --

A. Is that correct? It seems very incongruous.

Q. Perhaps I could ask for a transcript.

THE CHAIRMAN: Yes. I have: patient said Blair was looking after her absolutely. I don't know that I have the words "happy". Do you have the word "happy"?

MR KARK: I would be happy if we could ask for the transcript.

I thought you said -- let me just make it clear, because if I've got my note wrong, which it is quite possible: she had told me that Dr Blair was very happy with the situation, I would see her informally.

Can I just ask, if I've got that wrong, I should correct my note, and I will obviously withdraw my note straight away.

(Record read)

MR KARK: So the patient was very happy that Dr --

THE CHAIRMAN: No.

MR JENKINS: Dr Skinner was happy --

A. That's the first person singular, Mr Kark. I was happy that she was being so competently monitored.

MR JENKINS: Everybody was happy except Dr Blair.

MR KARK: You never realised then, is that what you're saying, that Dr -- let me start again. Did you realise that Dr Blair was advising the patient that she should

stop taking thyroxine?
A. I -- was never presented to me in such strong terms.
Q. Well, then, how did you understand the situation in relation to what Dr Blair was telling his patient?
A. Right, well, my memory of it some years ago, and it's quite hard to remember your every thought every day, my feeling of the matter was Dr Blair was not particularly in favour of it. I'm sorry to be reiterative, but I've always rather assumed that you wouldn't receive an active communication in this way from a patient. You would expect the practitioner to advise you accordingly, not a vague sort of feeble he was perhaps feeling a little unhappy about it. I feel I behaved quite correctly there.
Q. Yesterday you were asked by Mrs Sturdy about your experience of whether the thyroid would recover after a period of treatment with thyroxine. Do you remember that?
A. I do.
Q. Is it right that your evidence is that, in your experience, the thyroid would recover and would even recover a long time after the use of thyroxine?
A. Yes. My experience is that if a patient stops the medication, they don't go into a severely hypothyroid state because the thyroid's been irrevocably damaged.

It seems to me the patients I've seen, they just return to their previously parlous state. There isn't a permanent damage to the thyroid gland.

Q. Your experience of dealing with these complaints dates back to, what, 97 at the earliest?

A. Which complaints are these?

Q. Thyroid complaints.

A. Oh, seeing patients? Yes, about that. In a significant way from about then.

Q. What I'm going to suggest based on the evidence that was given, I think it was by Mr Lynn, was that the thyroid would shrivel and atrophy, and it would not recover, if the patient had been using thyroxine for a long period of time. Do you accept that or not?

A. I've just provided evidence which I think gainsays that contention.

Q. Can you just help us: what is that based upon? Which of your patients had you stopped giving thyroxine to whose thyroid has been recovered after, say, a ten-year period?

A. Do you mean -- I'm not absolutely sure what you mean.

Q. You're telling the Panel --

A. You mean the patients -- can I identify the patient for the Panel this morning?

Q. You're telling the Panel that your experience is that

the thyroid will recover after a long period of use by the patient of thyroxine. I want to know what that's based on. When have you stopped giving a patient thyroxine and then you found that the thyroid recovered?

A. On quite a number of occasions the medication has been stopped and the patient has returned to where the patient was before. Now, commensurate -- if the experience of a clinical outcome had been that the thyroid had shrivelled and was unable to recover, which Mr Lynn suggested, the patient would continue or would be in a seriously hypothyroid state. My experience is the patient just goes back to where they were.

Q. Sorry, how long ago did this happen? What was the last occasion on which you stopped a patient taking thyroxine and the thyroid recovered?

A. Do you mean at what point in time?

Q. Yes.

A. That's quite a difficult question. I've got to scan my practice at the drop of a hat. But I can try.

I wonder if we could get an example, not a perfect example, from Patient C. Now, this of course, would be in the caveat that neither Mr Lynn nor Professor Weetman feel the patient was ever hypothyroid. But working on the operative belief that I thought she was, yet when she was stopped, and indeed Patient B -- they are not

worse than they were. Patient B is as hypothyroid as I think she was when we started.

Q. But, Dr Skinner, I don't want to spend too long on this. Patient B, you put onto thyroxine in March of 2003 and she came off thyroxine in October of 2004. Patient C, you put onto thyroxine in March of 2004, she was off it by October of 2004. Those aren't long periods of use of thyroxine, are they?

A. No, obviously they're not prolonged periods.

Q. Let me turn to another part of your evidence to Dr Elliot when she was asking questions. You were asked a question, I think I might have asked: why do blood tests at all?

You said:

"I do take cognisance of it."

Can we take it that that answer is really in relation to taking cognisance of blood tests prior to starting thyroxine treatment as opposed to once you have started it, or does it apply to both?

A. It would apply to both.

Q. Well, I don't want to flog a dead horse for too long, but once you started thyroxine, I thought your evidence was that there was no level of TSH with which you would be uncomfortable?

A. I think we were talk there in terms of a patient under

treatment. I think I've said quite a few times to the Panel that there is value in blood tests, and I outlined four or five examples.

I think we were talking specifically -- I hope I'm correct -- in monitoring a patient whose TSH can shoot down quite early on in treatment. I think the evidence is very clear, indeed Professor Toft in Edinburgh, who's worked in this field for many years, I think he is now coming round to this view, that a TSH level may often need to be zero for a patient to return to wellbeing. I think he's very clear on this point.

Q. I'm sorry, the question was: when you gave that reply to Dr Elliot about taking cognisance of blood tests, are you saying that prior to starting treatment, or during treatment, or both?

A. I think I said both.

Q. So your answer that you gave us, I think at least a day ago, about that there was no TSH level with which you were uncomfortable, that still stands, does it?

A. I thought I had explained that that was patients under treatment. I'm very uncomfortable if a patient has a TSH level of 66.

Q. Again asked by Dr Elliot, you mentioned your experience of nurses who used to take thyroxine so that they would be, as you put it, "jollier at the dance". Their

experience appeared to be, did it, that they get a buzz out of it?

A. I don't think I asserted that. I said they said they would do that because it would make them more of the belle of the ball. Indeed -- I think they realised very soon that it didn't, and I don't think people do such a foolish thing really now. I think there's no question that people become -- they do not become euphoric or -- if they take thyroxine.

Q. But that was their perception, was it, that they got a buzz out of it? In the same way as somebody perhaps taking amphetamine, they got a buzz out of it? Is that their perception?

A. I can't remember their perception when I was a house officer. It's more years ago than I care to remember, Mr Kark.

Q. Yes, it's 1969.

A. It's indeed more years ago than I care to ...

Q. In answer to a question from Mr Payne, just two matters I think I want to ask you about. You said you see about 1,000 patients a year, about 100 to 150 new patients a year. Yes?

A. Yes, about.

Q. The majority fall within -- I think you said, about 66 per cent fall within the reference range?

A. Yes, I took that figure off the top of my head. Remember that's patients, not on medication. More than half the patients I see are already taking thyroxine from the family practitioner or consultant colleague.

Q. Let me just ask you about the 30 [sic] per cent outside the limit. Are you talking about those who are on thyroxine and are therefore outside the limit on thyroxine, or are you saying that they were not being medicated and still outside the limit? Can you help us?

A. I thought your question was driven at new patients who were not on anything. I was trying to clarify that issue.

Q. So it was patients who were not on anything at all?

A. I think that's what you're addressing your forthcoming remarks towards.

Q. I'm asking you about the answers you gave to Mr Payne. I am just trying to clarify them.

When you spoke about the majority, 66 per cent fall within the reference range, and 33 per cent outside it, are those patients being treated or not being treated?

A. That totality I think are not being -- we're talking about patients not being treated who come to me and not taking thyroid replacement, just to be clear what we're talking about.

Right, now in answer to your question -- I've

forgotten your question.

Q. I think that is the answer to my question.

A. Is it?

Q. You're saying that those patients were not being treated when they came to see you, yes?

A. A proportion, yes.

Q. Right. Of the patients, the 33 per cent who are outside the reference range when they come to you, can you help us why they come to you as opposed to their GPs?

A. Do you mean why did the family practitioner refer them?

Q. Well, either really --

A. I don't see patients directly.

Q. -- whether it's on a referral --

A. Well, I don't see patients without referrals. That's manifestly clear to the Panel by now.

Q. Why couldn't their GPs prescribe them thyroxine if they're outside the reference range?

A. The GP could prescribe anything that the family practitioner feels is indicated. You must remember here there are two hormones, one may be, one may not be. The family practitioner may not -- maybe "timid" is not the word I'm looking for. Maybe "frightened", to call a spade a spade, to prescribe for a patient if one of the thyroid hormones are outside the range and the other one isn't. And essentially I think most of the

referrals in this circumstance would be if the patient's still not feeling well and the family practitioner wishes an opinion from me.

Q. Of that 100 per cent total, 66 per cent within the reference range and 33 per cent outside it, does your figure stand that 95 per cent of patients who walk through the door "I will treat with thyroxine"?

A. That would be 95 per cent of those who come on no treatment whatsoever. I won't personally treat them. About a third of these I will put on thyroxine and about two-thirds I will write back -- well, I always write back, but I will flag the thing up and give my opinion of whether the patient should be treated with thyroid replacement or not.

Q. But 95 per cent you would either treat yourself or recommend treatment, is that fair?

A. I would say that would be about the figure, yes.

Q. Finally, this: you were asked by Mrs Whitehill about why you were reluctant to undergo the performance assessment, and the answer you gave was that you didn't know who the complainants were.

A. That was part of my answer, Mr Kark.

Q. Tell us what the rest of the reason was again. Forgive me if I missed it.

A. I thought -- and I would stand by this view, that if I'm

being asked to have a performance re-evaluation, whatever it was called, and I'm not told who is the complainant in some of the case or who is the patient even, and indeed what is the nature of the complaint in some precision, I think very few practitioners would accept that this was a reasonable way forward.

Q. I'm sorry, but you knew about Liz Jordan's complaint and you knew about Dr Blair's complaint, and you agreed to a performance assessment.

A. I certainly agreed initially.

Q. What happened was that you went through the process of filling in your portfolio for the assessment to take place, but then you decided you didn't want to go through the process. What caused you then to decide you didn't want to go through the process having filled in a portfolio?

A. I felt the lack of communication from the General Medical Council was not such that I was -- it was a reasonable thing, and my understanding is that cases were cancelled, which were making up the necessity for re-evaluation.

Q. Is the reality that you realised you faced a choice between being tested as a GP, which you were not, of course, and being treated as an endocrinologist, or being tested as a endocrinologist, which you were not,

of course? What did you think you were going to be tested against, what standard?

A. That's part of the problem. I did try to find out what was the nature of the examination, who was marking it and what were the marking standards.

I think it was a little -- I think it's a little cavalier to a practitioner. I know I'm in the hallowed halls of the General Medical Council, but I do feel that.

And the answer to your question is: no, I wasn't concerned I was purporting to be a practitioner, an endocrinologist, and this would discriminate between the two.

Q. So by which standard would you have wanted to be tested? Against what standard would you wish to be tested?

A. I made that very clear, I actually wrote, it didn't evoke any response. The way to test this is not to have somebody who may have polarised view, I don't know, construct an examination.

What I suggested, and I would stand by this, we need to do a comparative audit of the results of management and diagnosis of hypothyroidism at randomly selected clinics, including my own, in the United Kingdom. That will give you a clear answer of competence of the practitioner.

Q. But you wanted your competence to be tested by effectively putting a number of your patients before the Performance Assessment Panel, is that right?
A. No. I wanted a group of competent people, fair-minded and reasonable people, to examine the results of my clinic and compare it to perhaps a colleague. Mr Lynn would agree that would be the only really fair way to examine if there was a shortfall in care and the wellbeing of patients having been in my care.
Q. I'll finish this topic, but I just want to ask you: against whose standards were you asked to be compared?
A. Was I asked to be compared?
Q. No, were you asking to be compared, would it be -- you see, the people you normally treat these thyroid problems are those who purport to specialise in this area, which you agree, are endocrinologists?
A. Yes, I agree with that.
Q. Then there are GPs who occasionally treat these problems, yes?
A. I think quite frequently.
Q. I just want to know where you place yourself. You're not a GP, are you?
A. No, I think that's been established. I place it exactly where you're saying. The answer is: let's compare the

results in these different settings; it seems very fair and I can't say anyone would really oppose such sensible suggestion.

MR KARK: Thank you, Dr Skinner.

Re-examination by MR JENKINS

MR JENKINS: Can I ask questions about that last matter, Dr Skinner. I'm going to ask you to turn to bundle 2, please, tab 4, page 141, if you would, please. It's very near the back, three pages in from the back.

THE CHAIRMAN: I think, Mr Jenkins, we decided that we don't have 141.

MR JENKINS: I'm sorry. I think it might be helpful if it's included. Perhaps we can get it copied and look at it in a minute.

If I give that to somebody else it may be that someone could copy it.

MR KARK: I'm getting it copied.

MR JENKINS: Can I turn to another document which perhaps we should have seen earlier and the fault is probably mine. I want to give you a patient information leaflet for treatment and ask about it. I'm going to ask that it be circulated.

In that same tab the Panel have seen a number of guidelines and protocols that attach to your practice.

THE CHAIRMAN: This will be D11.

MR JENKINS: Thank you very much.

We looked yesterday in the same tab, tab 4 of bundle 2, at page 9, which is headed "A patient's guide".

I'm going to go through the patient information leaflet in a moment, and we'll look at it in detail. But we saw page 92 yesterday, A Patient's Guide, which is expressed as available to any patient or party attending the clinic. It sets out the aim and objective of the clinic, and then talks about the policies, that patients should be treated in a polite, friendly and welcoming way. You go on to introduce the staff. You talk about the majority of patients are hypothyroid and will receive thyroid replacement. It goes on to say a little bit about that treatment.

Over the page, page 93, you say how patients are referred, and you give information about the workings of the service, fees, and matters of that nature, if patients want to cancel a consultation.

You then talk about confidentiality in the consulting room and if there's a need for examination. There's a couch and the possibility of a chaperone. You then talk about charges, and then go on to the need for feedback and a complaint, and how that process should be dealt with.

You don't really give any information about treatment, and I want to ask about this leaflet, D11. If I take you back to page 77 in tab 4, we see a document, which is part of the protocols, and I'm looking at the bottom of that protocol, version number 1, review date 7th June 2004, author or Dr Gordon RB Skinner.

It's exactly the same way this document, D11, is finished. Yes? Version number 1, same date, 7th June, and you're the author.

A. Yes, thank you, sir.

Q. If you turn to page 103, we have the same. Version number 1, review date 7th June 2004. Author: Dr Gordon RB Skinner. This isn't included, D11, in the bundle of material that you sent to the GMC as part of your protocols and --

A. Was it not? That's an omission.

Q. There we are.

A. I don't know why.

Q. What happens to this document, D11, the one you have just been handed, Patient Information Leaflet for Treatment?

A. It's one of the documents that are out for the patients to read when they come.

Q. I understand. Can we go through it, please.

I recognise that there may well be questions arising from this document:

"If Dr Skinner considers that you're hypothyroid according to evidence and guidelines for this diagnosis in various publications, he will normally suggest that you have thyroid replacement using Sodium Thyroxine. There are other preparations for certain indications or for introduction later in your treatment schedule which Dr Skinner will discuss with you in detail at your initial consultation or follow-up appointment. Dr Skinner will generally try to return your care to your family practitioner, who referred you to Dr Skinner, but it is perfectly acceptable if you wish to continue for follow-up to attend the clinic and Dr Skinner will work in close co-operation with your family practitioner.

"Treatment is usually begun at a lowish level ..."

The Panel will read the rest of the sentence:

"It has to be emphasised that there will be some considerable variation in your treatment plan depending on feedback from you by letter, fax, or telephone, or by a follow-up consultation which will usually be in two months from your original visit. It may also be necessary to modify your dose level or introduce other preparations ..."

You go on to name them. One is Tertroxin:

"In some patients the natural thyroid preparation Armour Thyroid."

You say:

"It's unusual to experience adverse effects from thyroid replacement but if your dose becomes too high you may experience feelings of being somewhat 'driven' with difficulty in settling down to a given task and in some patients there is increased heart rate, bowel upset with diarrhoea, slight tremor of the hands, headaches, and in some patients palpitations. It should be remembered that many of these features are also features of an underactive thyroid before treatment and it is important that you contact Dr Skinner by letter or telephone or fax to seek advice if you are at all concerned.

"It is also important to emphasise that while some of these adverse features can be uncomfortable they will not have any permanent or long-term effects and will be quite easily reversible by a reduction of your dosage following consultation by any of these methods with Dr Skinner."

You go on to talk about a family practitioner, if he agrees with the diagnoses and management strategy, will prescribe thyroxine and Tertroxin through the National

Health Service, and you talk about Armour Thyroid and how that may be prescribed.

Do patients see that information when they come to see you?

A. Yes. Oh yes.

Q. Can I ask about one other matter. You were asked about repeat blood tests and it was suggested that you take the view that they are of no use, and you don't do them. Can I ask you to turn to the other bundle, please, if it still works, tab 8, please, Patient D.

A. Page?

Q. 31.

The Panel will recall that Patient D was a lady you first saw in August 2004. Your note for August 2005 on page 31 ends with a prescription, an indication "see in three months time and do blood test".

What did you mean by "do blood test", writing it at that point in your note?

A. That's what Mr Lynn called an aide memoire to remind me when the patient came back again.

Q. You were telling yourself that you should do a blood test when the patient came back?

A. Yes.

Q. That was something that happened with patients, that you would take blood tests during treatment?

A. Yes, I do it quite frequently.
Q. Thank you. That is all I wanted to ask about, but I do want to ask about the letter at page 141. I'm afraid I have to wait for that to come back.

Perhaps I can take you a little earlier in tab 4. It's back to the other file I'm afraid. Page 2. This was the letter sent to you by the GMC after you had agreed to undergo an assessment, and they said to you:

"I confirm we are now making the arrangements for your performance assessment. We are aware that your speciality is general practice."

Do you regard yourself as a general practitioner?
A. Oh no.
Q. No.
A. I don't know why they said that.
Q. Well, if you had been assessed as an endocrinologist, who would have been undertaking the assessment so far as you were aware?
A. I don't know. That's information I was unable to glean. I was given no further information.
Q. You say you wrote. Wrote to who?
A. I can't remember who I wrote to. I think I phoned. I don't remember who I phoned because there's a myriad of people.
Q. I've got to pause, I'm afraid, for a moment. I'm

waiting for the letter to come through. (Pause).

THE CHAIRMAN: This will be D12.

MR JENKINS: Thank you.

MR KARK: Well, I would have thought it could just go at the back of the bundle.

THE CHAIRMAN: Yes.

MR JENKINS: We know that Mr Prentice, Malcolm Prentice, from the Mayday Hospital, who was a witness before the Panel, was responding when asked by Dr Ince about Patient C. Dr Prentice found himself writing a letter to say that you'd started a patient on 150 micrograms of thyroxine and also that you had not communicated with the GP. We know that that was wrong.

A. Yes, that was wrong.

Q. So that's part of the background, I think, before we come to this letter at page 141. This is you writing to the president of the General Medical Council asking for a few minutes of his time to consider this note, which expresses grave concern.

You say:

"I have been in practice for some forty years and am not ashamed to proclaim that I have never had a litigious action and have only had one complaint from a patient."

Is that Patient A?

A. Yes.

Q. You say:

"I have been 'invited' to undergo a performance assessment by the General Medical Council to which I have reluctantly agreed. There is however an important point of principle contained herein. In essence I have been obliged to take a decision on whether or not to agree to a performance assessment but have not been permitted to know the precise allegations nor the name of any patients involved in these allegations nor in most cases the allegations. Thus one is not allowed the opportunity to make any reasonably informed comments to the screener ..."

You then go on to say:

"... the following assertions have been made wherein it beggars briefly that the GMC would not redispatch such nonsense to its progenitors."

You mention Dr Toft.

The Panel have seen earlier in bundle 4 a reference to Dr Toft, and I think he wrote to the GMC saying that you had rendered a patient clinically hyperthyroid, and you say what you do: the patient felt well, no evidence of that contention.

There were other matters raised with the GMC by the British Thyroid Association, and you had been given no

details of those patients.

A. It was an anonymised little bundle.

Q. The Panel haven't heard anything about those allegations.

A. Not to my knowledge, I don't think. I don't know the process really, what the Panel receive.

Q. There's then mention of Dr Jordan. Well, the Panel have heard about Dr Jordan, they have seen the letter with regard to Patient B.

There's then your point number 4, a suggestion that -- talk of bovine thyroid extract, which you say you didn't know existed, and you're saying that this is something which is simply not true, point number 4.

A. I had never seen or talked to this patient in my life.

Q. You say it was suggested that you were a member of Thyroid UK, of which you are not a member. Lastly, you're saying it was suggested to the GMC that you're not registered to provide medical services. You go on to say that those last three points are fatuous.

There's then another allegation dating from 1990, which you dismiss.

A. That's beyond belief, basically.

Q. Yes. You say over the page, page 143:

"... it is on the basis of these assertions that I have been invited to a performance assessment without

being permitted the courtesy of reviewing the evidence on which this assessment is presently to be based."

Well, is that the true basis of your rejection of -- or your refusal to undergo a performance assessment?

A. Yes. I think this is an expansion and gives a flavour of my concerns, to be invited to do something on evidence that was wildly flawed and not available to me, in fact, what the evidence was.

MR JENKINS: Thank you. Again, I recognise that the documents I've handed in may give rise to further questions.

MR KARK: There are fresh matters. I don't want to restart all my cross-examination, just on two points. May I ask further questions?

THE CHAIRMAN: Yes.

Further further cross-examination by MR KARK

MR KARK: The document that you put in, Patient Information Leaflet for Treatment, you say that this was given to your patients. Was it given to them pre June of 2004? Was there a similar document prior to June of 2004 or was it only from June of 2004?

A. It was prepared essentially on the advice of the Commission of Healthcare. I can't, off the top of my head, remember what was the first day it appeared in the clinic. I simply can't remember that.

It would be about two or three years ago. I know that's not answering your question, but I can find the answer from the clinic.

Q. Are you saying there might not have been one before this date?

A. Before which date?

Q. The document is dated 7th June 2004, and I just want to know if there was a prior version of it.

A. I wouldn't have thought so. I think I prepared it then.

Q. Secondly, this: the first line to your patient is:

"If Dr Skinner considers that you are hypothyroid according to evidence and guidelines for this diagnosis in various publications ..."

Now, the reader of that might think that you're in line with current standard medical thinking. You would possibly agree that you're not.

A. No, I wouldn't try and reintroduce my survey, you didn't allow that. I think Dr Hertoghe will demonstrate very clearly that I am.

Q. I see.

A. Certainly in an international basis.

Q. So a patient who reads the words "according to evidence and guidelines for this diagnosis in various publications", you don't think is being misled in any way?

A. I'm absolutely sure it's not misleading. I wouldn't do that.

MR KARK: Thank you.

THE CHAIRMAN: Does this conclude the process for Dr Skinner?

Further examination by MR JENKINS

MR JENKINS: Just one question arising out of that, if I may.

What would patients be told about the information contained in this leaflet before this leaflet existed? Do you know what I mean?

A. I know what you mean.

Q. This document has a lot of information about it, about side effects and the need to contact you if there are any, and that sort of matter. Before this document was in existence would patients receive any of that information in a documentary form --

A. No.

Q. -- or in the other way?

A. That would be part -- and I think, as I said to Dr Elliot yesterday, I slightly baulked at this. I felt that that should be part and parcel of a medical consultation, and that's how this information was imparted. I prefer to do that face to face with the

patient rather than give out a series of documents. I know that's the trend, and the Commission of Healthcare are quite document oriented, if you like.

Q. So for any patient who saw you, let's say in May 2004, would anything be said to them, or any document be given to them, which encouraged them, if they had any adverse effects, to contact you by letter, telephone or fax?

A. Absolutely so.

Q. How would they be told that?

A. At the consultation.

MR JENKINS: I'm grateful, thank you very much.

THE CHAIRMAN: Thank you, Dr Skinner. Thank you very much. You can return to the side.

Mr Jenkins, I believe you now want to call your expert witness.

MR JENKINS: I do. I think it may take a couple of minutes to set up his computer, so I am going to invite you to rise, as it were, for perhaps five minutes so that we can do that.

THE CHAIRMAN: Fine. We will return at 10.55. Mr Gribble has something he wants to comment on.

THE LEGAL ASSESSOR: I think Dr Skinner needs to return to his place in fact.

In relation to a document that has just been produced by Mr Jenkins, which is page 141 -- and it is

the letter to Sir Graeme -- on reading that letter, Dr Elliot, quite rightly and properly, sent a note to the Chairman saying, "I know Dr Toft. He was in my year at uni". That is page 142, at the top of that page, where it refers to an allegation made by a Dr Toft, which I think has not been followed up in any way insofar as these proceedings are concerned.

I took the view, of course, that we had better wait until Dr Skinner had completed his evidence so that Mr Jenkins could have an opportunity of speaking to him. That's the practical reason why I waited until now, until this matter was raised. I also took the opportunity of finding out from Dr Elliot what knowledge she had of Dr Toft. She last spoke to him four or five years ago. I don't think, under those circumstances, there's any suggestion that there has been any conversation or any knowledge of this particular case.

It's a matter which I felt had to be put before you for information, really.

MR JENKINS: I'm grateful, there's no problem at all. I'm very grateful to Dr Elliot for raising it.

I think if you look at tab 3, page 31, Dr Toft's name is already on the document. You won't have perhaps seen it already, but his name is already in the papers. I don't have any difficulty at all.

MR KARK: I agree, and can I just mention that the reason is perhaps obvious as to why those pages were not included in the bundle, because they contained information that could conceivably have been thought to have been prejudicial to the doctor.

THE CHAIRMAN: Thank you. So 10.55, please.

(10.32 am)

(A short break)

(10.55 am)

THE CHAIRMAN: Dr Hertoghe, are you ready to begin?

A. I am ready.

DR THIERRY HERTOGHE (Affirmed)

Examination-in-chief by MR JENKINS

MR JENKINS: Have a seat, Dr Hertoghe, because I'm going to ask that your CV is handed round. Whilst that is happening, I wonder if you could tell us your full name.

A. My full name is Thierry Hertoghe.

Q. You are Belgian?

A. Yes, I'm Belgian.

Q. I think you qualified, as the CV tells us, in 1986 at the University of Louvain in Belgium, and you then got a specialisation degree in general medicine in Brussels in 1989.

A. That is correct.

Q. You talk about a certificate in Anti-Ageing Medical

Therapeutics at the University Centre of Charleroi, is that in France or is that Belgium?

A. No, that's in Belgium.

Q. Sorry. A diploma again, in the same topic, anti-ageing medicine at the European Institute of Scientific Anti-Ageing Medicine in Paris.

You mention various responsibilities that you have. You are presently -- I'm looking at 2004 -- a co-founder of the International Hormone Society, and you indicate where that is based, and president of the World Society of Anti-ageing Medicine, which is based in Rome.

You say that you're a member of the directory of the Board of the European Organisation of Scientific Anti-Ageing Medicine, and founder and member of the editing staff of the Journal of European Anti-Ageing Medicine, which I think is based in London.

A. Yes.

Q. You are presently president of the International Hormone Society I know you'll tell us a bit more about that as the morning wears on, but tell us now what is the International Hormone Society?

A. The International Hormone Society is probably the third in the world in membership, in physician membership, endocrine society in the world, it's extremely fast growing, so I think it will be probably in two years'

time we're the most important one, and contrary to most of endocrine societies, we're open to all specialities because we are of the opinion that hormone therapies are applicable in almost all the medical specialities where it could be helpful, and so every physician should have more training in hormone therapies.

Q. How many members do you have at the moment?

A. At the moment we over a thousand members which are real numbers because the numbers are a little changed by societies, but these are real numbers.

Q. Are those all directors or can lay people join?

A. They are all doctors. We do have two subsections in the society for patient organisation. One is the International Thyroid Patient Organisation, and the other one is the International Hormone Society Organisation, but they are not of the same importance for the moment in numbers of members as the International Hormone Society for physicians.

Q. I think, as you indicate on the first page of your CV, you come from a family of doctors and doctors interested in hormone problems.

A. Yes, and I think it will be very interesting for the audience to know that my great grandfather actually learned from Murray, who is an Englishman here, how to treat hormone therapies in the very beginning, in 1892,

and each generation we continued doing hormone therapy and mainly thyroid therapy.

Q. You then set out your previous medical posts. I don't know that I need go through them.

You've given lectures, as we see over the page, over many years in various parts of the world. Again, perhaps I needn't take you through, but a lot of lectures in America and many in Europe, but also other parts of the world as well.

A. Yes. In the seminars you see, I didn't put all the lectures, but I do lecture extensively, and also on the thyroid therapy. I think every year I train around 600 physicians, at least for two days of training. This year will be much more. Something like 1,000 physicians.

Q. On page 5 you have listed seminars that you've given, I think.

A. Yes.

Q. Again, for medically qualified individuals.

A. Yes, either I give them totally myself for two or three days, either I do them as a combination with other physicians.

Q. You then go on on page 6 to list articles that you have been involved in writing. I think you've written papers on thyroid function.

A. Yes, and I think specifically on what is here, the centre of the debate, comparing T3 and T4 medications to T4, and the problems of diagnosis of the TSH test, and also all the conditions where there's a reduced conversion of the prohormone T4 to the active T3 hormone.

Q. I think you've conducted research as well.

A. Well, most of my research is -- I did some smaller research, but most of my research is to review the literature, and usually when I review a topic, it is the last 30 years of the studies I can find on Medline.

Q. Right. On page 7, there are more reports that you list, that you have written.

On page 8 I think you list some books that you have written as well, a couple of which have been translated into a number of languages.

A. Yes.

Q. I think you are published in Chinese as well.

A. In Chinese also as well, yes.

Q. You have written The Hormone Handbook, and you're in the process, I think, of writing other books on hormone therapy.

A. Yes. Well, actually they're already written, I just have to put the references in.

Q. All right. I think you were asked to look at the papers

in the case, to look at the reports of Professor Weetman and Mr Lynn. You've seen the medical records of the various patients A to D that this Panel have, and I think you have written a report, which I am going to ask to be distributed now, please, and marked D13.

A. In this report I've always focused to give the evidence, so not to say a thing without proofs of the evidence.

Q. I understand. Well, we'll come back to your report. I was going to distribute it now just so that the Panel have it. We will go through it, but I think before we do that, you've -- D13, please.

Before we do that, I think you've prepared a slide show for us, as it were, just to take us through --

A. I think it's much more understandable with a slide show. I think it's worth to review of the words, but I think it will be much easier to understand.

Q. Madam, we have reduced the slide show to quite a large number of pages, which I think will be helpful. Some of the images are not going to be clearly visible on the screen, so we put that into paper form in an attempt to assist you. I wonder if we can distribute that as well. This is D14, please.

This falls into two parts, and I'm just giving you the first part now.

A. I have added some other slides because I thought it was

important, so I will pack them together, and you'll get a copy of them later.

Q. What I have not asked you, Dr Hertoghe, is your treatment of patients. Tell us about you treating patients.

A. Well, I work with a team of six doctors under my supervision, and we get patients from all over the world, and I see mostly the patients coming from other continents because there's a little too much. I have reduced my activity recently, since January, in order to face all the activities of organising international congresses and writing books and reviewing the literature.

But before January I worked three days a week in practice. The other days were for a seminar preparation, and we see quite extensively the patient takes about an hour, see the patients for an hour.

We do look up much more endocrine deficiencies than Dr Skinner. We look up also for lack male hormones, lack of female hormones and other hormones, and also much about the nutrients, and we do extensive lab testing and clinical examination. So we take about 15 to 20 minutes of clinical examination. It's very important, as I will show you, hand we do also more extensive lab tests because that's helpful.

Q. For how many years have you been treating patients who may have thyroid or --

A. It's a little more than 20 years, and I did a lot of training with my father, who was a quite successful endocrinologist.

Q. To what extent is the treatment of thyroid patients part of your practice?

A. I would say it's the major hormone actually we look up. So it's the majority of the patients are screened for thyroid function and treated when they have a deficiency.

Q. You told us from January you see patients two days a week.

A. No, it's one day. It was two days a week, now it's going to be one day a week active from July on.

Q. Is that because of your other commitments?

A. Yes, yes. I organise a lot of quite important international congresses, and also I supervise two -- well, there's going to be a second one, two educational programmes that are very evidence-based for physicians, two years to three years of diploma or masters of anti-ageing medicine, which is recognised for the moment as by far the best education for physicians in the world.

We have had more than 75 different nationalities

trained there and more than 700 physicians in the last years. So it's quite important. We're also starting, and I will talk about that, 400 hour training in endocrinology and hormone therapies because there's some major problems in the actual educational programme.

Q. Right. Take us through the slides as we need to see them. I think the first few slides cover information that we've already dealt with. The international --

A. Yes, I will go quite quickly on this.

This is the logo of the International Hormone Society, and it's going to start a new course. And I have other commitments, I'm also a member Of the Endocrine Society. In order to be a member of this big, important society, you have to have written articles and you have to be accepted.

I also will supervise the new information. These are general public books also in Russian, German and other languages.

This is the book that has had the best success among physicians. It has 300 pages of quite solid references; it took me quite a time. It talks of physician, how to do the therapy, and when there are problems, how to solve the problems.

There's a lot of different hormones. These are reports for societies. For instance, melatonin

treatment. We had obtained a cancellation of the law. Thanks to this text, we had a law forbidding melatonin as a hormone. We showed it's beneficial and it's beneficial effects, and I'm working on this textbook.

This is my great grandfather, and you will see it has an importance in the text.

Q. Can I ask you to slow down a little bit because we are flicking through pages at the same time. That is your great grandfather.

A. That's my great grandfather. He doesn't look like me, probably a skinhead in that time.

He was very famous in the world. He went teaching in the United States at that moment, so you can find in very old textbooks pictures of his patients before and after therapy, and I will show some of those pictures.

He was also its vice president of the Royal Academy of Medicine of Belgium. We have a lot of books of him.

Q. You list under your photograph both your great grandfather and other members of the family.

A. Yes, my grandfather Luke and my father Jack were endocrinologists.

Q. Do you have siblings, brothers or sisters working --

A. I have a sister who is an internist endocrinologist.

Q. Do go on.

A. So here, this is a quite an important society. The

World Society of Anti-ageing Medicine. It's also extremely fast growing. We also get here 100 to 200 new members every month, so it's very, very quick.

I have taken away the congresses that I supervised. There are four important ones, which are in Asia and Europe.

Q. I should say that --

A. The World Congress of Anti-ageing Medicine, for instance, more than 3,000 physicians are participating. The Bangkok congress is about 1,000, and the European congress is about 2,000 physicians, and it's very evidence-based. We do not allow non-evidence-based medicine.

Q. Can you just explain to us, and the medical member will certainly know, but just remind us what evidence-based medicine means.

A. Evidence-based medicine means that when you come forward with an argument you have scientific studies to support and you can bring the evidence. This evidence forward. It's in a way that it's balanced. You don't select your scientific evidence to support your personal opinion, but you try to find the truth and to give the truth.

So I was also wanting to review a little bit, very shortly, why we are here, and I have an extensive, I would say, experience as an expert. I was also

a medical board member during seven years in Belgium. I had even the highest vote, because in Belgium it's a voting of Brussels for that post.

It's to protect the patient, I think, ensure that the patient has welfare, and it's -- I don't think -- in Belgium at least it's like this, you're not here to decide between two schools of medicine, you just have to see that the therapy of Dr Skinner is not a wrong therapy. You don't have to say it's a good therapy, or the best, but that it's not an incorrect therapy that can put in danger the welfare of the patient.

Then: what's it all about? It's all about the thyroid gland, that you know already, and that the thyroid gland that is situated here in the neck (indicating) produces hormones thyroid hormones.

It produces, as you know, T4, thyroxine alone, mostly T4. And accessory T3, I would say the most important hormone, is the active hormone in the cells.

What is important to know is that the T3 is much more distributed, we have much more T3 everywhere in our body than T4. T4 is located to blood and eventually intracellular fluid, but in the cells, where it has to be active, it's mainly T3 that is there.

Why is it important? Well, the thyroid has major actions, and you are going to see some pictures of

patients that will make you understand how important it is, what you're doing now.

Q. Can we go through that gradually. You talk about mental and physical quickness, mood and energy.

A. Yes. So we'll see this with a picture, but if you don't have any thyroid hormones, you become a human plant, you have no emotions and no thought. You're in a coma and you will die in the coma after several weeks.

So it's extremely important to have enough, and if you have a lack, it will impair your body quite a lot. This is why it's so important that you make the right judgment.

Q. Can we just stay there. You have on the right-hand side "elimination of waste products".

A. Yes, so many of the people who have a low thyroid are swollen up. They are swollen up but it's not fat that they have. It could be a little fat but mostly it's sort of waste products that are situated between the cells. So we don't have no -- everything is piling up with waste products called mucopolysaccherides.

Q. You have mentioned myxoedema.

A. Myxoedema, that's a sort of oedema.

Q. Swelling oedema.

A. A swelling oedema. It will be all over, and on some places more than others. For instance, the (inaudible

word) will be much thicker, and the face will be much more swollen, but even the muscles will be swollen. So a person like that could like look he or she has muscles, but it's mainly myxoedema.

Q. And are there other --

A. So thyroid hormones stimulate the process to take that away. Also the heat production, if you don't have enough thyroid you become very, very cold because it heats up your body, you get more temperature. So people have to put a lot of clothes on, because they have it always too cold, are suspected of having low thyroid function.

Q. Before we move on, tell us about the immune system as well because you've suggested --

A. It's to my experience probably the most immune stimulating hormone. So when children have a lot of infections you have to check the thyroid function, because one of the reasons I myself was put on thyroid hormones, it's a long time ago, is I had so much infections. It was actually my grandfather made the diagnosis, and when I was on thyroid hormones it got all a way. I didn't have any problems any more.

Another important thing is the blood supply. The blood supply goes much quicker. When you don't have enough thyroid hormone, the blood supply to the brain is

slower and there's less blood. So you will think slower, it will give more difficulties. And you will have to move all the time in order to stimulate your bloodstream to feel better. But as soon as you sit down or you lie down at a certain time, you'll feel tired or not good.

Q. Could I just raise the question of constipation as well.

A. That's a fundamental sign of, I would say, low thyroid function. Probably of more severe form.

Q. Should we regard that as relevant for the elimination of waste products, is that part --

A. No. That is different. When there's a low thyroid function, the muscles of the intestines are surrounded by muscles, that muscle structure is much slower, it not very active, hypotonic, not tonic enough, and you get constipated because it doesn't go quick enough at --

Q. I understand.

A. So thyroid hormones quicken most of the metabolic reactions. Everything goes quicker, and when it's too much, you heat up too much, and you get excess thyroid hormones, you are too warm, the temperature's too high.

Q. Let's go to the next slide.

A. Thyroid hormones are essential will life, but not only life. Like I said, if you have no thyroid activity you are a human plant. Before some of those people died as

human plants.

But when you have a lack, you do have a decrease in quality of life and of your health, and probably your lifespan will also be impaired. So a poor thyroid activity is a measure of life. That is why you have so many thyroid patient websites that's usually done by patients who recovered of their ill health or their miserable life by getting thyroid hormones, that is why there's so much passion around the topic.

Q. Yes.

A. What I will try to remember you several times at the lecture is that a healthy thyroid is in the cells that it has to be healthy, not necessarily in the blood. If you have already good thyroid hormones in the blood, you're likely to have a better thyroid function in the cells but you have some circumstances where this may not be the case.

It has to be enough thyroid hormones in the bones, the heart, the muscles, the brain, digestive system, everywhere; this is fundamental.

In order to have that you have to have specifically not sufficient T4, but sufficient T3 in the target cells, and not only enough of that T3 hormone, but it has to be active in the cells and you have to have enough receptors. Receptors are molecules, compounds,

that when the thyroid hormone goes on it, the action will start, the action of thyroid hormone.

You need also to have -- even if you have enough receptors -- good food and good nutrients. You need some vitamins to be able to have full effects of the thyroid function. So it's not only enough to give thyroid hormones to have an optimal function.

When you have a poor and low thyroid activity it's actually inside of the target cells that there's not enough thyroid hormones. That is called cellular hypothyroidism.

Hypothyroidism means low thyroid function. Cellular, that inside of the cells where it has to be active. So it's very important that the physician, when he treats a patient, there's enough thyroid activity in the cells.

So what is maybe also an important question, it's always good to have a picture: how does a person look like when he has a low thyroid function? This is a hypothyroid patient.

Q. Is this taken from one of the books of your grandfather?

A. My great grandfather. In that time they didn't have lab tests, they did clinical follow-up, they looked at patients.

You have a lot of symptoms, and I'm not going to

list all, but I'll going to list some that you just have an impression, and you can see: you see those swollen eyelids? Those are more swollen in the morning with low thyroid function and that will go away with an adequate treatment. So a person who has swollen eyelids in the morning is suspected of having low thyroid function.

The hair is dry, it does not blink [sic] so much, and you see the person looks swollen and even fat, even the hands look swollen, and she looks a little sad.

This is a typical pre myxoedematous or myxoedematous face, that means the face is swollen up with waste products between the cells. You'll see that also the lips are swollen. We will see the difference when that person is treated later on. So these are pictures more than a hundred years ago.

When a person has a low thyroid function the blood supply is not enough and the hands are cold. The feet are also much more cold, because there's between 5 and 20 per cent less blood flow. There's led blood, so it doesn't go all over, and the blood supply is slower, the blood circulation goes slower. The heart rate is slower, so it will pump the blood on a slower rate.

Q. What are re-seeing there, clearly some feet but what should we be noting?

A. Those are feet, they are actually cold and a little

reddish. It is called achrocyanosis, not enough oxygen going to the feet and they're cold.

You see here also when a person has a high risk of having also other family members having it, you see this person is swollen up with the typical lower swollen eyelids, and look what happens with treatment. Very bizarre, actually this should be 14 months later, you see that the person looks younger than this. Why is this so?

Because thyroid hormones at the beginning will take out the myxoedema so you get thinner, but once after a certain while it will also stimulate other endocrine glands. The male hormones of this man have -- the testicles have worked better, and so he has better muscles and he looks younger, I would say a year later, than he looked in the beginning.

This person is his sister. You see also the sort of swelling of the face, typical of low thyroid function.

In order to understand the complaints a patient has, you have to look at how the blood is supplied in the brain. If there's not enough thyroid hormones, you will see that there's less blood flow in the brain, and it will not go to all the cells as easily as it went in a normal thyroid situation. So you will have a lot of mental complaints and emotional complaints when there's

a low thyroid function.

Q. Could you tell us, are we looking at a --

A. This is a skull of a person.

Q. Is that a scanning of a patient?

A. This is actually a sort of visualisation of the blood flow in the brain, of the arteries. These are all arteries of the brain. There will be less blood going in those arteries and at a slower speed because of the lack of thyroid hormones.

So what sort of complaints does a patient have when he has low thyroid? I will not go all over those, but I'll mention that there's a lot.

There will be two types of person. The patient who is too slow, who is depressed, who is -- everything's too heavy for that person, doesn't think very clearly and thinks too slowly, and will have memory loss and concentration problems.

Some people get hyper active because they have understood that as long as they stay active or they take a lot of coffee that kicks them, they feel better, so they will be either coffee drinkers or people who keep on moving in order to feel better.

Q. You've listed a series of signs there or attributes, apathy, sleepiness.

A. Those are adapted from the thyroid textbook.

Q. The Panel will note that. You refer to headaches as well.
A. Yes. Headaches is very common. I will show also information on that, that there are a lot of references, because it seems that one of the experts said that headaches was not a symptoms of low thyroid function. It's very frequent.
Q. Professor Weetman said he had never seen it in any textbook, the suggestion that any headaches might be a sign or symptom of hypothyroidism.
A. I will show several slides that show that many of his interventions, when he talks about clinical symptoms, are not adequate, they have don't have adequate information. He doesn't seem to be well-informed.
Q. Can I break off at this point and deal with the question of headaches and ask to you look at two other documents, please. One is from the University of Maryland Medical Centre in the United States.
THE CHAIRMAN: Is this then D15 and 16?
MR JENKINS: It should be, yes.
Can I say that the University of Maryland document -- you will see it was printed off from the Internet a couple of days ago, the date's at the bottom right-hand corner. You will see as well -- I have only given you page 3 of 4, I can produce page 4 of 4, but it

contains nothing of any relevance whatsoever.

If you go to the bottom of page 3 you will see the sort of thing you often get on an Internet document:

"Please rate the quality of the article.

"Do you find this article to be helpful/informative?"

It then invites comments from the reader.

There's slightly more of that on page 4. I can give it to you if you want it, but it will not help.

THE CHAIRMAN: I'm sure that's fine. This is D15, and the other D16.

MR JENKINS: Can I just ask you about it, Dr Hertoghe, if you would. This is a medical centre in the United States, the University Hospital in Maryland, and their website. This is their web page for hypothyroidism.

They go on to give a description and talk about hypothyroidism in various ways. I'm going to take you to the second page, if I may.

Under the heading "Other health effects of hypothyroidism", they refer to headache:

"The following medical conditions have been associated with hypothyroidism. Often the causal relationship is not clear in such cases:

"Headache. (Hypothyroidism made worse in headaches

in people predisposed to them.)"

Yes?

A. The headache is due to piling up of the myxoedema in the head, and that makes it that everything's compressed. The skull cannot expand so there's a sort of compression. That is why thyroid hormones in people who have low thyroid function will take away the headaches in most of the patients.

Q. I'm going to ask you to look at another document as well. It is the International Headache Society's book on headaches. D16.

Have the Panel received that?

THE CHAIRMAN: Yes.

MR JENKINS: Thank you.

This is several pages long. I only want to look at one small entry. The top left-hand corner, we have chapter 10, "Headache attributed to disorder of homoeostasis".

10.4, the Panel will see there's a heading for "Headache attributed to hypothyroidism". If I could, please, take you on to page 111.

At the bottom of left-hand column, "Headache attributed to hypothyroidism", various diagnostic criteria are listed, which I don't read. There's then a comment:

"It has been estimated that approximately 30 per cent of patients with hypothyroidism suffer from headache."

Is that within your experience? Headaches are fairly common.

A. Yes. I haven't done a review, but about 30/40 per cent of my patients before treatment with thyroid hormones, and that have thyroid deficiency, have headaches. It's very common, and I would say it's usually 9 on 10 will get rid of their headaches. 8 to 9 on 10, completely rid of their headaches with thyroid hormones.

Q. Thank you.

Let's go on to the next slide, if we may. You have dealt with mental signs or symptoms of --

A. There are some because there's a lot, some of the physical symptoms. One of the most characteristic is the coldness, cold hands and cold feet that will improve with treat, and you could have sometimes people are very warmly dressed so they don't suffer from the cold, but then they are too warmly dressed. And they have also easier -- dry skin, very typical. It's called follicular keratosis. I won't go into the details but it is linked also with vitamin A deficiency, a person produces much less precursor when there's a low thyroid function.

As everything is swollen up the voice may be hoarse in the morning and will clear up during the day, and they will not sweat so much, their sweat glands are not stimulated enough.

If they lose their hair, they loss all over their hair, it's a diffuse hair loss, just not on the upper part, it's all over, and we'll see a picture like that.

You see the menstruations are not so good because other endocrine glands will not work well with thyroid hormone therapy. Why are doctors often enthusiastic when they give thyroid hormones? It just seems to clear up so many problems because it stimulates other endocrine glands to work better, also the ovaries.

If they have pain in the joints because of the myxoedema in the joints or in the muscles, it will be all over, it's diffuse. That is how you can recognise between, let's say, an adrenal deficiency that causes joint pains, or a deficiency -- problems caused in joints by low thyroid function.

They will also be stiff in the morning, will feel better during the rest of the day when part of the myxoedema is cleared up, and they many have other problems, I will not go into in detail in order not to overload you with too much information.

Q. Let's go on.

A. So what is one of the main cause of thyroid deficiency? I was not really surprised, but I was a little deceived that in the expert reports they didn't talk about that, is that one of the main causes of thyroid deficiency is just ageing, and we all age.

I'm 50 years, I already age. People can be -- you can start ageing at 30, 35, 40 years. And I will show you with evidence, because I will repeat, I will not give you information if it does not come out of strong evidence or out of my personal practice, but mostly it will come from strong evidence.

You see in order for the thyroid gland -- and here again I show you the thyroid gland is situated here, on the base of the neck, in order for that to work in the cells there's a lot of stages that have to be fulfilled. Everything starts in the brain and the brain will stimulate -- another part of the brain will stimulate factors, thyroid releasing hormone, to stimulate in the pituitary gland -- it's a little gland under the base of the skull here -- this little gland that you see here (indicating).

Q. TRH is thyroid releasing hormone.

A. Thyroid releasing hormone, and the TSH is thyroid stimulating hormone, that will go through the blood, to the endocrine glands, stimulate the endocrine gland,

which makes mostly a precursor hormone, T4 is poorly active, it's mainly T3, and that T4 will go mostly in the liver, and (inaudible word) in the kidneys, and in the liver it will be converted to the active T3 for the cells.

Every cell can make its -- most of the cells can make their own T3 but mostly of the T3 is made in the liver for the rest of the body. The brain has a separate system.

In order for that to work, if one of the steps of the stages there's a problem, there may be a thyroid deficiency at the end. So when you have some schools of thinking like you seem to have here in the UK, quite extremist, I would say, and I will show you with evidence that it's quite extremist, is that only you check the blood. It's not in the blood that the hormones work, it's in the tissues. You need to have enough thyroid hormones in the tissues, and I will show you studies that show there might be a problem -- even if blood level are okay, there might be a problem.

Q. Can we just go back to the start. The hypothalamus, a part of the brain.

A. Is here.

Q. Is that releasing thyroid releasing hormone?

A. TRH, thyroid releasing hormone.

Q. Does that go to the pituitary?
A. That goes to the pituitary, they thyroid releasing hormone.
Q. Which will then produce thyroid stimulating hormone.
A. Mm-hm.
Q. Which goes round in the blood. If that reaches the thyroid, as it would do, the thyroid is then provoked into --
A. T4 and T3.
Q. Which is what the thyroid produces.
A. Yes.
Q. There's then a conversion of T4 to T3.
A. In the liver.
Q. And that is then circulated around the body.
A. To the muscles, et cetera.
Q. -- it goes to the various parts of the body.
A. Yes.
Q. -- that are supplied by blood.
A. But you need in the target tissues to have enough T3 receptors, mainly T3 receptors. There are some T4 but mainly T3 receptors for everything to work.
Q. Let me ask you this question: is the level of T4 and T3 in the blood an indication of how the tissues are responding?
A. Not directly, because it's just a preliminary stage. So

it is assumed often in medicine that if blood levels are okay, it should be okay in the cells, which is not always the case.

Q. I understand. Let's move on. You're talking about ageing.

A. Or it's not enough to take blood test.

So ages on all the places, and I will show you studies that show that every step ages. Every.

In the brain, for instance, with age, our brain volume decreases 20 per cent in 90 year olds. So 90 year olds have the brain of a person between 3 and 6 years, and it shrinks, and there's a decrease in neurones, there's a decrease in blood flow. That means also less oxygen, et cetera. And in the brain there's also a decrease in dendritic connections.

So even if you have enough neurones the connections between neurones are less, and thyroid hormones can stimulate all the connections between the cells. So you need to have enough thyroid hormones --

Q. Forgive me, dendritic connections --

A. That is connections between the nerve cells, if you want, of the brain cells. Also the number of neurotransmitters decreases, and you have also a decreased responsiveness to receptors. So even if there are enough receptors, the affinity, the way that

the hormone binds to the receptors, is also in the brain decreased, not only in the other target tissues, as we will see.

Again, I will not go too much in detail, but TRH has been shown to be decreased. There are scientific studies to show --

Q. You're citing papers each time, I think.

A. Yes. Each times it's a paper I'm citing.

Q. The neurotransmitters are chemicals.

A. Are chemicals that go from one brain cell to the other, from one nerve cell to the other. The ones, they tend either to increase like somatostatin who inhibits TSH(?). So some neurotransmitters increase and they decrease thyroid function.

Q. Before we move on, for each of those you have an arrow going up in some cases at the bottom or mostly down.

A. Here an inhibiting factor of the thyroid function somatostatin increases.

Q. I understand. So for the first two under the heading "Neurons" there's a decrease in the number of ventral medial and arcuate nuclei, a decrease in the next thing that you mentioned.

A. Yes.

Q. And as the brain ages, there's a decrease --

A. Decrease of all sorts of --

Q. -- in thyroid releasing hormone.
A. It's one of the results of the other stages that we saw as a decrease.
Q. Thank you.
A. This is a neuron. Just to show you, there's a lot of those little tentacles, they are connections, they will make connections with other neurones and those connections decrease with --
Q. I should ask, the neuron has been hugely magnified, hasn't it? That's not real size.
A. Yes. No, it's extremely small.

You see this is the pituitary gland. Nobody can have a good thyroid function if the pituitary gland is not healthy. But you see that with age there's much less TSH secretion when it should be. We should make more when it was cold. It makes much less. So the more we age, the more likely it is that there's a problem with the thyroid activity.

In all stages, even the -- to give an idea, this pituitary gland with age will fibrose for 40 per cent. That means 40 per cent of the material of the pituitary gland will disappear and be replaced by non-active cells, fibrous tissue, but the remaining cells that should stimulate the thyroid function and make TSH -- not all of those make TSH, but many of those -- they

will also be let active, less able to produce TSH. So on older person will not necessarily be able to make high levels of TSH later. So he may be thyroid deficient, even though the TSH is normal because it ages.

Q. I should ask, where we have two down arrows, does that mean significantly --

A. Remarkable decrease. So at night we make a sort of peak of TSH that is significant, everything flattens. There's a lot, I'm not going to mention everything in order not to overload you too much.

Even in blood things are not so well. Inevitably the levels of thyroid hormones decrease with age.

T4 has not always been shown to decrease, but T3, the active hormone, does, about 25 to 30 per cent. And it's not as simple as that is that in the blood there's also sort of anti-thyroid hormone called reverse T3 and that increases with age.

So you have the blockers increase, the active hormones you need decreased, and that is not shown in classical texts the reverse T3 that is sort of blocker.

Q. You have mentioned as well --

A. There are also more antibodies.

Q. -- antibodies at the bottom. Are those increased with age?

A. They increase with age, yes.
Q. Right.
A. So they will aggress more the thyroid glands.
So it is inevitably you see that the levels of T3 -- this is a study that shows the levels of T3 to decrease by 25 per cent with age and 20 per cent for the T4. So we won't remain optimally healthy for the thyroid gland our whole life. The one who succeeds in that must have, I would say, the elixir of long living, and I would like to take it, but for the moment I don't think it exists.
You see it's not only that. When you look at the blood level in an older person, it's not the same as a younger person even if the hormone levels are the same, it's not the same. When you look here, the metabolic clearance decreases by age in 50 per cent in men. What does this mean? This means --
Q. Remind us what clearance is.
A. The clearance means when the hormone gets inside of the cells it's cleared away from the blood. So the decrease of metabolic clearance we see is that the hormones remain in the blood longer and don't go in the cells so easily. So even if you have an optimal level in blood, if the person is older, and if there's a 50 per cent decrease, then it will be taken by the cells. So it might be two times less thyroid hormone in the cells.

This is very important. This happens with all the hormones -- well, with most of the hormones. But it is detrimental, very detrimental, when there are problems with thyroid hormones. You see the half-life increases, that means it remains longer in blood, et cetera.

Also the arteries get a little ager [sic] and they will bring blood a little bit easy because they have a certain atherosclerosis and that will also decrease. So there are studies that show the weight and volume of the thyroid gland decreases, it atrophies, but it has more with age abnormal nodules, or goitres, and I think in one study one of the people died. More than 90 per cent had nodules.

Q. Tell us what a nodule is.

A. A nodule is a sort of tumour. It is mainly of the thyroid gland tries to make more, thyroid hormones, and it increased its size but, after a certain time it will do this irregularly, and you get a nodule.

Q. A growth?

A. It's a growth, and one of the treatments -- because it has been assumed here that endocrinologists never treat biochemical euthyroid patients but that's normally not true. Most of the good endocrinologists they treat -- when a person has a nodule, even if the thyroid levels of normal they give the thyroid hormones to reduce the

volume.

Q. Reduce the volume?

A. The volume of the nodules, and that goes often away. I have often people with nodules when you give thyroid hormones after a year, if it's just appeared since half a year or one year, it can go away.

Q. Remind us, what is goitre?

A. A goitre is a very large increase of the thyroid gland, and it has been seen in many countries where there's not enough iodine. In order to be able to make thyroid hormones, you need to have iodine. If there's not enough iodine, the thyroid gland will try to increase its size, even very heavily, in order to absorb as much iodine as possible, and to make the necessary thyroid hormones. So you can block goitre formation often by giving thyroid hormones.

Q. Right.

A. So people with goitre, even if they have normal lab tests, will get often from the endocrinologist thyroid hormones.

Q. Let's move on to the next slide, please. I'm on page 24 just to check with the Panel.

A. Even the nerves that go to the thyroid gland will decrease. So they will be less active thyroid gland with ageing. Inside of the cells there's accumulation

of waste products, so even if there are enough receptors, it's not always as easy with age for the thyroid hormones to go on to the receptors.

Q. Again, it's under the general topic as the patient ages --

A. With age in the target cells there's an accumulation of waste products, and levothryoxine(?) is sort of oxidation products.

So even the cells of the thyroid glands will -- and that's in all the organs, so in those cells will less easily work because there's a little bit too much waste inside. Levothyroxine deposits.

Q. Let's go to the next slide, please.

A. We see that when we look at the thyroid gland, the production decreases with age, around 25 per cent. So inevitably everybody, although the body stays the same size, will have less and less thyroid hormone production.

So the body has been built up for a certain amount of thyroid hormones, so if you stay big and tall, and you have less thyroid hormones, you will suffer. Not only mentally, but also it will be physically seen.

All sorts of process in order to bring the thyroid hormones into the bloodstream decrease. The iodine uptake decreases, so they are not able to make enough

thyroid hormones because the cells who are a little bit aging do not take the iodine from the bloodstream as good. So everything's made for having a deficiency sooner or later.

Even the liver, the liver has a fundamental role to activate the thyroid hormones. So the T4 that is mainly produced by thyroid gland has to be converted but the liver ages. So it will make this conversion less and less. When I hear that one of the experts said there's nothing like a poor conversion, or it almost never exists, it doesn't match the data. That's all I can say. I'm not going to put any judgment on the reports, I'm just going to say it doesn't match the data.

So it has been shown here in the study for instance that the liver cell responsiveness to T3 decreases, so even they are not as active because there are probably less receptors.

Q. Again, it's the T3 that is active on the cells.

A. It really the active one. The conversion of T4 into T3 it has decreased. It has been shown over and over with aging. So only young adults are generally optimally able to convert if they have enough hormones.

This is very important. When do you think that middle age starts? We have young page, middle age, old age; when does this start?

Q. Depressingly early by the look of your graph.
A. You look at age 31 here, people are considered being middle aged. So there's not so many who are escaping. I think you escape, but I'm not sure the rest does.
Q. Can you just explain to us --
A. I'm going to show. You see for thyroxine the receptors inside of the cells -- and this is on humans, this is not on rats -- the receptors on blood cells like the white blood cells for thyroxine do not decrease with middle age, but decrease by 42 per cent in an elderly person. An elderly person is considered 61 or more.

But the T3 that is so fundamental that you feel good -- I have heard about the feel good feeling -- at middle age is decreased by 41 per cent. That means that even if your blood level is okay, it is absolutely not guaranteed, it's probably that it is not so, that there's enough thyroid hormone in the cells. That is why the frequency in thyroid deficiency is much more than suspected by official guidelines that are based on laboratory tests that may have inadequate reference ranges.

Q. Can we just explore what you have told us, because it may be very important. If you have a certain level of T4 and T3 in a patient aged 25, and have the same level in a patient aged 55 --

A. It's not the same because there's less receptors for the thyroid hormones in the person of age 65. So a person might need higher levels, because one of the ways to overcome this low receptors is to increase availability of the hormones, and you can do that generally also by staying inside of the reference ranges of the hormones. You see that middle age decrease of the very and crucially important T3. But that is not the only problem.

Like I told already before, the receptors are less likely to bind, even if there are enough receptors, the binding is decreased by 54 per cent here. So everything's made to sooner other later create thyroid deficiency.

Now, we see even that the cell -- there's a study for instance that shows that when the thyroid hormones are in the blood they are not transported inside the cells easily. We will go on over this.

You see this also, that the effect finally, it is like Dr Skinner assumed, it is not only the complaints of a patient that can give us an idea of this cellular thyroid activity, it is also we have certain number of markers, enzymes, that are less produced when the effect of the thyroid hormones are less present in the cells, when there's less thyroid activity.

So a lot of enzymes that we can check also in blood that are inside of the cells are decreased, because of this lower thyroid activity. So they are markers that there's a lower thyroid activity inside the cells.

Even the muscles will contract less but part of the reason is that there's no enough thyroid hormones on those target cells. So it's very important to have this in mind that just one of the factors that can cause hypothyroidism is overwhelming in a population, it's very present after a certain age. I'm not going to put here a limit but you saw that already after age 31 there's a receptors can be decreased.

So now, what can a thyroid treatment do? Because the doctors who work with thyroid treatment, like Dr Lynn and Dr Skinner, see the patient before and they see the patient after, and why are they so enthusiastic when they correctly give the thyroid hormones is that the patient is not only feeling better, but looks better.

This is before, and this is after two months. See the difference. She looks much more, I would say, beautiful and smarter. This patient stopped her treatment and she came back to this sort of outlook. When she took back the treatment, she was there again.

See how the swollenness has disappeared practically,

the swelling of the face also has disappeared. You see that her hair seems to shine better, they are more lively, they grow also quicker, and the hands even look thinner and the global outlook looks much better.

This is before and after. See the complete change of the person. It's not only outer that changes. Inside the patient feels much better.

So when you do not treat a person like this who has low thyroid function, not only does she feel less well but you see a persistence of changes that aren't favourable to health.

It looks a completely different person, but this is just two or three months of treatment.

Now, what I would say here, this person might still have thyroid hormones inside of the blood levels. Low, normal or something.

This person will probably definitely -- much more swollen, will probably definitely have really outside of the ranges of thyroid hormones. So there are two sorts of groups of patients when you define them by a laboratory test.

Look at the difference. You see, this person has also low thyroid function, swollen here, and see how the hair comes back almost completely, just by giving thyroid hormones. It's just to mark how important

it is, what you're doing now.

You have decisions to take and do that in consciousness, but this is what it's all about.

Just to give you an idea, this is a study where 1,569 thyroid patients were treated -- and I bet a lot of them were biochemically euthyroid -- they were followed for up to 20 years, but the mean follow-up was 5.2 years, and there was almost no appearance of new ischaemic heart disease, so it was protective, and there are other studies like that on a smaller scale.

Q. That was the Framingham study?

A. No, that's compared to the Framingham, this is what Framingham has as a percentage of new heart disease and this is the percentage that was in those people who were treated with thyroid hormones. Because we are always talking it is bad for the heart to give thyroid hormones, but we have not had some of the good data. I'm not saying there has been a selection, but there has been an omission of data.

Q. Just explain that to us?

A. The graphic? So normally in a population in five years' time if the Framingham is sort of representative population of the United States that were used to screen cholesterol and heart problems, so that village or that city where those people had a sort of free check up

regularly, they saw in those people who were not the treated you had a 4.6 per cent of new heart disease.

The patients who were treated with thyroid hormones by -- it was actually Dr Barnes actually who published in The Lancet in 1959, had only four patients, that means 0.25 per cent had new heart disease. I have done a similar study in my patient, I didn't go get those good figures, I got 25 per cent decrease in new ischaemic heart disease.

Q. 25 pere cent decrease --

A. Decrease in what was expected after follow up of six years in a smaller sample of 281 patients, and 20 per cent less high blood pressure.

Q. Forgive me. What should we understand from --

A. What we should understand is it's protective against the heart to correct a thyroid deficiency, if there was a thyroid deficiency.

Q. So hypothyroid patients who are given thyroid treatment --

A. Right.

Q. -- there is a reduced risk of heart disease?

A. Here was 16 to 18 times reduction of the risk.

These patients did not all receive lab tests. They were treated at that time based on the temperature test, on a clinical evaluation, which does not mean the lab

tests are bad, it means at that time they did it differently and they had good results for the heart.

Q. We've been told that there have been lab tests for about 20 or 30 years.

A. That was in 1959.

Q. That was, yes.

A. So ...

Q. Do you agree that the lab tests have been around for up to 30 years?

A. At that time the lab tests came around, it's more than 40 to 50 years that you have lab tests, but the lab tests for T3 and T4 were specifically more around since the 1970s, that's true.

Q. I understand.

A. But they had iodine binding or something, a test that was used in that time, but they used a much more clinical evaluation. This is to show you that the people who had high blood pressure, the dangerous form, the diastolic, the lower blood pressure is higher, they almost all improved with thyroid treatment.

But these are all studies -- just to give you an idea, in that time they were beginning to have a certain form of lab test and they had good results, even though they were probably not screened. They were clinically screened.

This is to show you that a person to lose weight, for instance, I don't say you have to get tired not to lose weight, but it comes from the old thyroid, 1986, and it showed -- I found up [sic] this study -- they had doubling of the loss of weight when they receive additionally not T4 but T3, because when you're on a weight reducing diet, it increases the conversion of T4 to T3. They improved because weight reduction diet makes you T3 deficient, it decreased the conversion, it makes lower T3 level.

So by giving the adequate T3, without overdosing, they were not overdosed, they were doubling of the weight loss.

So you understand that several aspects make the patients enthusiastic and physicians. That doesn't mean that they can do whatever, but that means that there's a big importance of what we're doing now.

This is just to show you what happens with a kid when he has not enough thyroid -- also of the collection of my great grandfather.

Q. Do you mean 14 years old or --

A. He's 14 years old and he's only 74 centimetres. He almost didn't grow. That is real excess.

But just to show you how important it is, this child almost had no thyroid hormones, he had some, otherwise

he wouldn't be conscious, but you see -- I saw much more, I saw a baby of 8 years not able to walk, and in one year's time he could walk, grow much better, but he has for life a definite mental deficiency when this happens.

You see how different, the change. How the thyroid hormones change, it's not just something that people give additionally, it's things that have to be given when it's necessary.

Now, I'm going to the allegations, because just a preview, and I think it's important to stay to the facts, why we are here.

So of what I understood when reading the reports, and I have adapted a little the presentation to what I hear here, the allegation is Dr Skinner would make the wrong diagnoses of hypothyroidism, he would give to everybody thyroid hormones. So he makes a wrong diagnosis because he sticks to the thing that it is hypothyroidism he's treating, he does not give additional.

The arguments that are given that he would give wrong diagnoses of hypothyroidism should only based on thyroid lab test, outside the reference range.

Dr Lynn, that we have here, I think he repeated also here. It has exclusively to be based -- because the

hypothyroid syndromes are unreliable, but I showed you how typical the outlook is, it's typical, you can typically see signs.

You have to have a very high TSH, some say about 5 or above 10, which is even much higher than the upper reference range actually, and very low T4 levels, so you have to be under the reference in fact, which is very low, which none of the four patients have. That is certain. They didn't have those abnormal results.

There are other arguments that will see one or the other. Arguments 2 and 3 are actually the same, is -- and Dr Lynn confirmed this here -- patients are healthy within the thyroid lab test. They are healthy. There's no scientific evidence that shows that they would be unhealthy, except one study showed that they might make easier a full-blown, clear cut thyroid deficiency if they have a TSH in the upper part of the reference range.

Q. Can I remind you of something Professor Weetman said. I put it to him that there will be patients whose chemistry is within the reference range but who may still show signs and symptoms of hypothyroidism. He told us that was not within his experience. He had never seen it.

A. It's very strange because he wrote an editorial that

says the contrary, and I'll show that later.

Q. All right. Let's keep going. The third argument for the prosecution you are putting down?

A. So there's no evidence of disease when thyroid test levels are within the reference range of thyroid tests, except the fact that you might develop an overt, a very severe form of hypothyroidism if the TSH is above 2.5. That is the only -- in the report.

Let's look at the first argument. Is it true that hypothyroidism should only be based on thyroid lab tests?

Let's look at history, and we already actually went to history. The diagnosis of hypothyroidism was only clinical before because they didn't have lab tests.

What it means clinical, is that you interview the patient and you mark the typical complaints because the are complaints that are much more common when you have a low thyroid function, and there are physical signs, they are very typical. It's not true that there's no typical clinical sign. So it all started clinically.

What are actually complaints, the physical signs, they're the reflection of what happens in the cells.

When you're used to -- it's also even more for other endocrine deficiencies, it's a little less for thyroid hormones because the lab tests are not as perfect. But

usually when I examine a patient I can almost know exactly the level I will have in blood with a 10 per cent change because the more physical signs you see, the more complaints there are, the lower the levels are used(?). It's a little bit less accurate with the thyroid test, but for other hormones it's very clear.

These are the books written by my great grandfather and I'm going to show you this picture later. It has a reason. It's not just showing that the family does this, et cetera. You see here a book in English, a famous article.

When he talked, he asked people of the audience to come up and show the clinical signs of hypothyroidism, because it's not so uncommon that you don't find a person in the public who has typical signs. Not so many people are being treated.

You see the myxoedema before and after. They only looked at the person interviewed, typical group. One complaint by itself is not sufficient. Constipation alone is not sufficient. But if you have constipation, coldness, stiffness in the morning, diffuse hair loss, drier skin, you have more and more reason to suspect thyroid deficiency. One is not enough, just headaches, no.

Before and after, see the difference. So it was clinical, before and after. You see how the person improves. Still doesn't look good, probably has other hormone deficiencies. At that time they didn't know about that.

See, look at this person. This person looks stupid, in a sense, and how smart she looks after.

Q. Do you see similar changes in your patients?

A. Yes, because that is what makes a physician enthusiastic, and the patients also. They say: everybody says I look much younger, I look better. But we treat also other hormone deficiencies so there's a combination. That's why you even have more chances of having success.

Look at, for example, this child. No hair, and look just at thyroid hormone, how it goes because thyroid hormones are essential to make hair grow. Again, it's not the male pattern baldness that is caused by thyroid deficiency, that's another hormone problem. This is the typical one of low thyroid function. When you have a child who has that, he is slow to wake up in the morning, he's cold, he's a lot of infections. So this is just the tip of the iceberg, you see.

Before and after. This is a person who developed thyroid deficiency in adulthood, so everything was

clinical before. And she's a little bit more obese, but not extremely obese, and swollen up. Typical, these flat feet, because ligaments are not very strong, and you see also this group of symptoms. I'm not going to go into detail there. But when I look at a patient I can know if there was a lower thyroid function in childhood than in an adult because they're a little shorter of build often when they had severe thyroid deficiency and they're smaller.

Q. I don't think we need to spend much time on children because we're not dealing with them in this case.

A. No. Now, how valuable are thyroid lab tests? There are shortcomings and advantages. So I always propose to my students: do lab tests always. Also in the follow-up.

Let's go back. 1940, 1950 they began to start to be able to detect molecules and in the 1950s, 1960s, the tests became available. Then a bright or a non-bright idea was to make reference values because that's a bright idea. Values, because the option of the reference value was values where people are healthy, and outside of it will be unhealthy. When the reference values were easy some doctors said, "How fantastic, I have less work to do, I don't have to do the physical examination, I just do lab tests, I can see more patients and help more patients", because doctors are

not really, I don't think, for money, they're there to help people, so if they can help more people it's also good.

So lab tests are useful, but they are not sufficient on their own as well I'm going to show, and they do not replace clinical examination. That is a part of diagnosis, it's not enough or exclusive, I think, you need to have lab tests but you need the whole picture.

One of the problems with lab tests is the daily fluctuations, it's not all stable, it doesn't stay at the same level. How is it done with the thyroid lab test? Maybe they are more stable than the others.

Here's the fluctuations you will have with TSH in a whole group. That is for a whole group, the average for a whole group, so in a morning they're about half of what they are in the evening or at night. But actually the personal fluctuation curve fluctuates much more when you just take a person. This is the average of the whole group.

This gives an idea of the fluctuation of the T4, the thyroxine. You see the difference. This is something like 8 and here it's 4. The levels can double during the day. So it depends on which moment you are.

We will see later what happens with the graph, what happens when you gave thyroid hormones, how it changes.

But you see a lot of fluctuations and this is for almost all tests in blood for the hormones, it fluctuates.

There are many conditions that change the thyroid lab test and may mask hypothyroidism. This is a summary of some, not all, some of the conditions that change the TSH. Many people go fasting in the morning and when you fast, you decrease your TSH. So if you would be with a high TSH, you might have a normal TSH. Ageing, we saw, decreases the TSH, so even if you should normally have a high TSH you might be normal.

There are a lot of situations, you have trauma or whatever, but just think, the stress can change, can even increase it, and the fasting in the morning, and the ageing, it already changes.

We saw that there are several fluctuations. Again, age is one of the major factors that the test, TSH test, is not sufficient any more and never was, actually, for thyroid diagnosis. If you have a very high, you're almost sure to have a low thyroid function, but if it's normal the older the person gets, the less efficient it is. But some people are already old at 30, 40 years. They have gone through so much stress, infections or whatever, they can have premature ageing, so you see the decrease of TSH is 50 per cent with age. 50 per cent.

So if you had a TSH of 6, for instance, which is

clearly accepted as being too high, it might be 3 on an older person, but the body suffers the same. We saw blood ageing, et cetera. The metabolic clearance, that is decreased, et cetera.

So the tests on their own are not sufficient. Now they have a problem with the reference values. So first what are reference values of lab tests? How are they determined? Well, first there's an obligation of every laboratory to have its own reference ranges for the tests they do because they work maybe with different machines. And on who are they going to base their reference ranges that they are making?

Q. Can I ask you just to look at the first tick and look across. What are you meaning to say?

A. This is "too large". They are too large.

So they are based on the people who go to the laboratory. How many people will take a blood test and are perfectly healthy? Not much. So it's mainly based on sick people. The laboratories do one thing. They do one terrific thing: when a lab test is completely abnormal, they will not use it to determine their reference ranges. But when it's slightly high, slightly low, they incorporate it.

So the lab tests are based on actual sick people. It's mainly based on sick persons, those who go to the

laboratory. It's actually not healthy values. It was never meant to be healthy values. When one of the experts said, "It's healthy values or normal values", it's absolutely incorrect. Absolutely not correct.

Q. Can I ask you to go back to the previous screen?

A. The previous one I think is not --

Q. You're saying that the reference range is too large.

A. Yes.

Q. What we know is that there are moves in America significantly to reduce the reference range?

A. For the TSH.

Q. Yes. Way below 5 or 5.5?

A. Yes.

Q. And --

A. But this is in the normal population, most of the people will be between the reference range; if they are sick or not sick, they will be between it.

Q. And Professor Weetman had looked at some documents that you had produced from German laboratories?

A. Yes.

Q. Where the upper limit of the TSH range was 2 or 2.5?

A. 2.5, yes.

Q. A long way from the 5 or 5.5 that we have here?

A. Yes. They have already followed the guidelines or propositions of the most important society for that, the

National Academy of Clinical Biochemistry.

Q. So the reference range that we're dealing with in this case, you say is too large?

A. Yes, the one you have in the UK is really quite conservative, I would say.

Q. I understand. The second point that you made is that the reference range is not related to the age of the patient.

A. For thyroid tests they usually are valid for most of the patients. This is why I wanted to go over -- this is a slide I should have taken away because I have better slides to explain it. For other hormones it's adapted to age, which is a wrong thing, but for the thyroid hormones it's usually between 50, 70, or 80 years so they do not adapt it so easily.

What is meant here is that the reference range should be based on the reference range of young adults. Everybody's incorporated so we know with age, it decreases with age, and they make then reference ranges where for instance the lower limit of the T4 and the T3 is quite low because they incorporate also a lot of old people.

Reference ranges, to be optimally healthy, should be done on young people who are absolutely sure they have no thyroid disease and no other disease, which is not

the case because the laboratory doesn't know who goes to do the blood test. They are generally don't know whether they're very sick or not. And it's not like Professor Weetman said, 300 patients. Normally a laboratory needs 3,000 samples before it makes reference ranges, and they pick everybody except the most abnormal results, which is not sufficient for good reference ranges.

Just to show you, it is also a little different and has been shown for the TSH, is that the reference ranges for one person, optimal reference range, is different for another person. I may need a reference range that is very shortly around 1 and another may need around 2 or 1.5 or something. Individuals are different and the reference range given by the laboratory is based on 3,000 patients so it's always larger because it incorporates the maximum number of people. But if you have to have your own personal reference range, it is more narrow, it's narrower. So it's not health values and it never was meant actually to be so. It's just statistical ranges. 95 per cent of the population between the reference range, and the 2.5, under 2.5 above.

It was so evident that for the cholesterol they changed the ranges, they didn't base it any more. They

based it on a consensus, they asked main medical authorities, those people, "What do you think would be a good reference range?" and that's why it's lower. But this has not happened for the thyroid function. It was happening because there's much recent data, but it's still not the case.

So normally if you take very healthy persons, for instance for the TSH without thyroid abnormalities, this is a (inaudible word) curve, so the more people you have in the middle, the more levels you have, the higher the curve is. If we take only healthy people, they are much closer in the values and for instance for the TSH they might be lower and for the thyroid hormones they will be higher. So this should be a more healthy way of determining the reference ranges and for the TSH that will be lower.

I was quite surprised when one of the experts said that, "Three out of four studies I have checked in healthy and non-healthy persons, that reference ranges were the same". I have seen so much the report of that expert, I have very great doubts that whatever he says is correct. I'm a little ashamed to be able to say that, but I was so surprised; either the level is not good or there is a problem there. This is a scientific evidence problem.

I come back here. So it's too large, for each individual the reference range is narrower and it's wrongly adapted to regional changes. Because there is one change, and Dr Lynn pointed out very well, that for instance in Sweden or in other countries there could be iodine deficiency or iodine excess and, as a result, the reference range is even higher; you can go to a TSH of 11. But a person who has a TSH of 11 here has the same sort of hypothyroidism, as a severe form, so these reference ranges that are even larger are actually inadequate, even more.

So how can we check for diagnosis of thyroid deficiency? Well, what is historically the case, and I think is accepted even by the main endocrine societies -- I don't know why the British Thyroid Association wants to be a different group -- is to do a medical history, complaints, physical signs, lab tests. Where there's some controversy is: do you do also a therapeutic test or not?

Q. What is a therapeutic test?

A. A therapeutic test is: you suspect somebody to have a problem and, if you're not 100 per cent sure, you will give the therapy and, if he responds well, that means it was adequate.

Q. Do you mean a trial?

A. It's a trial, yes. It's a trial of treatment. Now, just to give you an idea that there have been a lot of critics of hypothyroid complaints and that it's not adequate enough -- but let's investigate what the critics were doing.

Q. By "W", do you mean Professor Weetman?

A. Yes, I wanted not to name the name. Yes, Professor Weetman.

Remember to have health, you need to have health inside of the target cells. Essential. Essential. How can we check for the intracellular thyroid activity inside of the cells? By several means. You could check for a hormone. It's classical, you check the metabolites. When the hormone has been used as a hormone, it goes on the receptors, has its effect, it's changed. It becomes for thyroid hormones T2, diiodothyronine, and then T1, one iodine atom, et cetera. Then T0, it has no iodine atoms.

We can trace those results and have an idea of the metabolic activity, only the tests are not available commonly in laboratory tests so we cannot do it. But that would be a good way, one of the good ways. We can do it for other hormones.

We can check -- and that is more possible -- for the results on the cells of thyroid hormones, like making

more enzymes, and they will also become more available inside of the blood. We can, for instance, check alkaline phosphatase. It's a marker, it's an enzyme that is there for new bone formation. The more new bone you make, the more it is present in the blood.

When you give thyroid hormone, it increases, because thyroid hormones increase the new bone formation. We have talked about thyroid hormones, that it may decrease bone density. But without thyroid hormones, you're not able to make new bone formation. So too much is not good, too low is not good. So we can do that. Also markers, proteins like SHBG, sex hormone, it transports the sex hormones to the target cells from the endocrine gland --

THE CHAIRMAN: Excuse me, Dr Hertoghe, I wonder are you speaking a bit too quickly for the --

A. Am I?

THE COURT REPORTER: Yes.

THE CHAIRMAN: If you could slow down for all of us.

A. So you can check the results on the cells of the thyroid hormones by what we call blood markers. Markers are usually enzymes or proteins; they are proteins, products, compounds that you find in the blood.

One of the ways to check is also the TSH, but I'll show you it's a poor way to check because TSH is

secreted by tissue that is very different from other tissues, the pituitary gland. You can also check by the clinical signs and symptoms, that's the less expensive way, and one of the most, if not the most, efficient.

Then one of the experts -- because I don't like to make it a personal affair, I'm not against that expert, I just show the flaws in his report. He gives a study where he states that the study concludes by saying that checking hypothyroid symptoms are not useful. So what is my work as an expert? To check the information. Go on the Internet, get the abstract.

And what does the abstract conclude? The abstract concludes: evaluation of symptoms and signs of hypothyroidism with this new score in addition to thyroid function testing is very useful; it's not adequate, it's very useful for the individual assessment of thyroid failure and the monitoring of treatment. I don't know why he changed the information.

MR JENKINS: That's a paper from 1997?

A. 1997, about ten years. He says headaches does not exist. And you take The Thyroid and it's page 698, this an old version. It's written, "Headaches". And it's also written, "Visual impairment." You just have to open the textbook, we have good equipment here. But this is an old edition, two or three years behind,

but I think you still have it.

Again you have the symptoms and headaches. This is a series of references where headaches are a symptom of hypothyroidism. And this is just a small check. I'm almost sure I could find 30 references on this, or more. So it's acceptable to be criticised by people who know what they are talking about.

But this is one of the major complaints of thyroid deficiency, it's not one of the smaller ones, and this is a study I did by switching over patients that were on thyroxine alone and they had headaches and were switched over by T3 and T4 combinations. I used synthetic and dessicated thyroid. 62 per cent of the patients, I would say almost all patients improved on their headaches. Some had a total disappearance of headaches and a third here had a great improvement.

So headaches are a symptom of hypothyroidism, and then I had some strange information that last week the expert had said patients who have too much thyroid hormone, they get euphoric. I never heard about this from my father, I never saw it mentioned in the books of my great grandfather. I think in our familial tradition we never saw euphoria happen in a person with too much thyroid hormone.

So as I don't know everything, my brain is not big

enough for that, I have to look it up. I look it up, euphoria in hypothyroidism on the Medline. The Medline is on the Internet, a sort of information centre where you can get all the information on the articles or the most important articles. And I find no items. No items were found on euphoria.

But this is not enough. I was curious, I said, "Maybe by giving thyroid hormones, you provoke euphoria", so I had to do a new search. And what did I find? A study that shows that thyroid hormones decrease euphoria. It's actually TRH, thyroid releasing hormone increases euphoria. So you can give separately TRH and be more euphoric. It's one of the stimulating steps. When you give thyroid hormones, you decrease TSH as you decrease the euphoria given by TRH.

Q. Slow down.

A. This is in agreement with what I see with the patients, they get much better focused. What happens in a person who has overdosed -- I'm taking thyroid hormones, I know it myself. You don't get euphoric, you get anxious; anxious and anxious, without any reason. It's very uncomfortable when you're overdosed. I didn't see a patient who liked to be overdosed. You get a lot of other complaints, but anxiety is the dominating mental symptom.

Visual side perceptions as a hypothyroid complaint. When I read about that by reading the papers of Dr Skinner, I said I never heard about it before.

Q. Professor Weetman hadn't heard of it, nor had you?

A. Nor had I. So it's possible, but I'm critical. So I went to look on the Internet and I saw another study that said: visual hallucinations or side hallucinations. That I didn't see. But in 71 per cent of patients with primary hypothyroidism you find visual field defects, which is very close to what has been said.

As I'm curious, I like to go and look further, I like to see what could be the causes. The causes in the literature of having vision defects in hypothyroidism is a compression of the nerves that go from the eyes to the rest of the brain by myxoedema, by the waste products that pile up in the head.

Also, the nerves work slower, and that is one of the reasons that is also put forward because of those vision defects. Also there's a reduction of the blood supply, there's less blood supply to the visual nerves, the nerves of the vision.

Q. I'm going to interrupt you. I know that we need to understand the reasons why there may be visual defects, but you have researched it.

A. It does inform that there's information that may support what has been said.
Q. I understand.
A. And there's also information to support visual hallucinations in hypothyroidism being more often. I'm just showing that it exists. You see the references there.
Q. Can you tell us about the bottom part of that?
A. The bottom is: when you give thyroid hormones, like for the euphoria, it decreases those wrong symptoms and you do perceive more accurately.
Q. Visual perception is improved for --
A. Yes, so they did see better and better. So that doesn't mean that those visual side perceptions are exactly the same as this, but the chances are it's likely. And we saw that The Thyroid textbook put "visual impairment", and very strangely in the new edition they put it when there's a sort of tumour that causes low thyroid function, but in the old edition that wasn't there.
Anyway, the myxoedema, the waste products that accumulate in the head are enough to cause that. You see here the thyroid visual impairment.
Q. We've seen that. Thank you.
A. A little info on types of hypothyroidism may be necessary because one of the experts talked about

subclinical hypothyroidism. So what is clinical hypothyroidism and subclinical? Well, when you look at the terms it means that the person who has subclinical hypothyroidism does not have any complaints or physical signs, it's only the lab tests that are abnormal. So actually we're not talking about subclinical hypothyroidism because all the patients here had clinical hypothyroid complaints or suggestive of hypothyroidism.

So we are talking about two forms. Overt hypothyroidism that any doctor will treat, it's the one who has clinical signs and symptoms, and lab tests that are outside the reference range. And what we're mainly talking about is patients who have the same sort of symptoms, but their lab test looks normal.

Then you have other sorts of syndromes that we're not going to talk much about, where people can be with clinical symptoms, a normal lab test -- euthyroid sick syndrome, they have normally low T3. But as physicians look only at the T4 and the TSH, the physician can be misled because he doesn't look at the T3.

Q. Slow down.

A. Okay. But all the others, like euthyroid sick syndrome, autoimmune thyroidism, goitre and thyroid nodules can have normal lab tests, but have clinical -- because

having a goitre is already a sign of hypothyroidism, can have signs of hypothyroidism.

So I'm just going to stress that I'm not going to talk too much on subclinical hypothyroidism, but I'm going to show you some of the information. We are talking about patients who suffer and who have complaints, we're not talking of patients who do not suffer. In subclinical hypothyroidism, normally the patients do not suffer.

So this was to end up the part of the chapter on hypothyroid complaints and we go back to the TSH test. When we saw all the problems with the TSH, why do some physicians rely so importantly on the TSH? Well, because the believers in the quality of the TSH test -- and I'm partially a believer so I don't reject the believers -- say that the serum TSH, the blood test, reflects how good the thyroid hormones work in the cells. Because in order to decrease the secretion of TSH, the thyroid hormones have to go inside of the cells that secrete TSH to suppress its secretion. So the belief is that this is representative for the whole body. The more thyroid hormones, the lower the TSH is. But this is not always true. The cells that secrete TSH are very different cells from the rest of the body and they react differently. For instance --

Q. Can you take this slowly? I'm thinking of the Panel as well as the stenographer.

A. Yes. Well, let's say what you have to remember, because I'm not going into all the details, is that it's not representative for the target tissues because it's enzyme systems. In order for a cell to work, it does reactions, and it bases its reactions on enzymes; its enzymatic equipment is different.

For instance, if you have a high or a low T3, one of the enzyme systems does not react while it does react in other tissues. This means that a patient can be euthyroid in his or her pituitary gland, but in the target tissues, other target tissues can be low thyroid or vice versa. But usually the body reacts so that in problems, it will preserve the pituitary function more than other functions, like for the muscles.

Q. Does that mean that a patient may have a TSH within the reference range, but the target tissues are not getting enough --

A. Are not getting enough.

Q. -- hormone?

A. Exactly. So here are the different kinetics between the different enzyme systems, and it's in the pituitary gland. You have mixing of type I and type II, but you mainly have type II. The liver, for instance, has

mainly type I and they react differently. For instance, the hypothyroidism, one of the enzymes systems --

Q. Slow down.

A. The enzyme system of the liver will decrease while it increases in the pituitary gland.

Q. Right.

A. So the serum TSH does reflect intracellular thyroid activity in the pituitary gland, but not in the rest of the target cells. So the pituitary gland ages also, it makes the test less reliable. The hypothalamus that should stimulate the pituitary gland also ages, so a normal TSH in an elderly person is not necessarily normal. It doesn't mean that there's adequate thyroid function in the other target cells than the pituitary gland.

So less and less age will be good, and so many people, I would say, prematurely age with all the toxins we have; the pesticides can also have an adverse influence. So in many people the serum TSH alone does not well reflect thyroid function in target cells.

So the conclusion is that clinical signs and symptoms remain an inherent part of the diagnosis of thyroid hormone deficiency. The physician disagreed, they underestimate the usefulness of clinical signs and symptoms. Like we saw, Professor Weetman -- where does

he publish his articles? One of the articles that I saw of him was in Annals of Clinical Biochemistry or something. This is where the experts in lab tests publish. So I agree, but you have to take this into account, that it's clinical knowledge -- well, he probably does underestimate very much the importance of those clinical signs.

I personally cannot follow up a patient without seeing him. I have to examine him or I cannot know if the dose is too much or too low. It's not enough on the blood test to know if it's ultimately good. So I would say that allegation number 1 is not true for Dr Skinner. The diagnosis of hypothyroidism should not only rely on thyroid lab tests.

Do you want to make a pause? Is it okay? I can continue. I don't know how okay it is for you.

THE CHAIRMAN: I thought we would break around 1 o'clock.

MR JENKINS: Are you able to go on for 15 minutes?

A. Sure. Let me take a glass of water.

Q. That's the first proposition that you've dealt with.

A. Now I'm going to talk on the evidence. Within the reference ranges there are proven problems and it concerns everybody, and more when you're sick or you're a patient. These are the reference ranges given, so here, if you see the graph --

Q. We cannot quite see the bottom figures, but the Panel have the range clearly shown on page 65 of their bundle.

A. You see here the reference ranges are between -- I've taken the one we have here, 5.5, to 0.4, 0.2. So it's very large. A person who has 5.5 has about 25 times a higher value than a person who has 0.2 or 0.3.

Is this normal? This is not found normal any more by big endocrine societies. So the old TSH reference range, 5.5, has been reduced actually, and that is more internationally accepted, up 4.2, 0.2 to 4.2.

That is the actual TSH reference range of the world's most important institute for those guidelines, the National Academy of Clinical Biochemistry.

Q. That's the American organisation?

A. That's the American organisation but it has been re-evaluated by physicians from all over the world who are experts. We had even Belgians and French people, et cetera, and even Professor Weetman has been taking in those as reviewer(?)

The new reference range of the American Association of Clinical Endocrinologists is this reference range, 0.3 to 3, and the proposed better TSH reference range now by the NACB is from 0.2 to 2.5, so these will probably be the internationally accepted reference ranges in the next years that come. The TSH reference

range of the International Hormone Society is smaller, it's 0.2 to 2. But this is a proposition.

The target TSH reference range on the thyroid therapy of most important endocrine societies is even smaller. It's 0.5 to 1.5 or up to 2. It depends, but it's very stricter.

Q. That's the National Academy of Clinical Biochemistry?

A. And the Endocrine Society and the American Association of Clinical Endocrinologists. When you're under therapy you should be under 1.5 or 2.

Q. Slow down, if you would.

A. 2.0. The target for thyroid cancer, when you have thyroid cancer you have to be under 0.4 or you have an increased risk of recurrence.

Q. Can I remind you of the range which most of the patients, A to D, were judged by. It was the reference range of 0.4 to 5.5.

A. But that's a outdated reference range, so that means that it's not that easy. And there are problems around the reference range that have been accepted also by the experts, I think; at least by Professor Weetman.

I don't think that you, Dr Lynn, had proposed that those reference ranges ... I think there was a comment like that.

Now let's look a little bit at the TSH reference

ranges. These are two studies that show that within the reference range in the upper 25th percentile of TSH there are already abnormalities. People who take anti-depressants do not respond well if they're in the upper 25th percentile of TSH. Upper 25th means the upper 25 per cent of the reference range is already not so normal. If you give an anti-depressant to the person, he will not respond so well. This is why there's a number of studies on patients who have a normal thyroid, but they receive anti-depressants in combination with T3 therapy, and then it works much better.

Another study shows here also that there's an increased risk of severe depression, suicide attempts, and somatic disease if you're in the upper 25 per cent of the values of the TSH reference range. So if you're above something around 2.5, 3, you're not normal any more.

Here are two other studies: in the upper 25th percentile of TSH you are fatter. You have a higher body mass index, you're fatter. You have more fat.

Here another study shows that your waist circumference -- it is better than your weight to check the waist circumference because the bad fat is the fat that accumulates around your belly. Who cares about

your weight? What is important is not to have a fat belly, I would say. And not only is the waist circumference higher, the body mass index higher, but the sugar level is high in the blood, the triglycerides are higher and your systolic blood pressure is higher, significantly, so that part of the reference range is not a good part.

Here is another study that shows in the upper 25th percentile, so upper 25 per cent, you probably also can be suspected of having a mild thyroid failure, in normal people, because the blood pressure is generally higher, not very much, but slightly.

In order to be accurate, because I'm not only taking information in one direction, if you're in the lower 20th percentile of TSH for a woman you can have a risk, an increased risk of lower bone mineral density. Generally this is only seen in post menopausal women, so women who don't have their menstruations any more and they don't get any treatment, they might have a problem if they have a low TSH. But these are not people who are treated. That's the big difference. They are not treated with thyroid hormone.

Also if you have a tendency to be depressed or manic, to be euphoric excessively, the risk increases if you have a lower TSH. So there are studies that show

you shouldn't be too low.

Q. Those are patients within the reference range?

A. Those are people within the reference range. But this is just the beginning, because ... There are studies that are very precise. They check: what if a person is above 3? Well, if a person is above 3 and they have also antibodies against their thyroid, they will have more heart abnormalities when you check by ultrasound, so the heart is not normal any more.

Q. Doppler is the ultrasound?

A. Yes. If the TSH is above 3, it's the same information, so I'm going to get over. If it's above 2.5, women who are pregnant have an increased risk of having antibodies against their thyroid, which will at the end generally destroy the thyroid gland sufficiently to create hypothyroidism in many cases.

If it is above 2.5 of TSH, women who have in vitro fertilisation, who have test tube babies, they will have smaller babies who will be born too soon and who will have lower birth weight, which is not good. So pregnant women should be under 2.5, not above.

Remember the TSH range here goes up to 5. If you're above 2.1, and you're a patient who has a heart problem, you will have more stenosis of the coronary arteries. So the heart receives its blood supply by arteries that

are called coronary arteries and other arteries and there will be more plaques in those arteries, in other arteries. If you're above 2.01, so above 2, and you're a normal person -- let's say that we're all normal here -- the arterial wall of your arteries is already stiffer.

Q. Thicker?

A. Thicker and stiffer. Normally an artery should open up when the bloodstream goes through and it gets stiff like an old person, so you have a significant mild increase of arterial stiffness. If you're above 2, a pregnant woman in the third trimester, there's doubling of the risk of having a low birth weight, which is not good.

If you're above 0.9 and you have a thyroid abnormality, a thyroid nodule, a little tumour here, that normally is benign, you have a significant risk of having thyroid cancer. So people who have nodules should be under 0.9. I think one of the patients had nodules.

If you're above 0.4, or have at least an increased size of the thyroid gland, 0.4, there's another study that shows the same but there the limit is 0.4. So you have to be at the lower reference range there to be safe. He has other studies.

Q. Can we summarise those?

A. Yes. Cholesterol also is a problem, above 2.0. You can have also other markers of atherosclerosis, aging of the arteries is increased when you're above 2. You have up to 71 times more risk when you're 2 to develop an overt hypothyroidism compared to people with a TSH under 2, et cetera.

Here is also greatly increased risk. For people with diabetes the limit is 1.53. It may not be higher or you have an increased risk of developing overt hypothyroidism. Here is a study that shows that when it's too low, less than 0.3, there could be an increased risk in post menopausal women of having bone loss. Again, women who are not treated, all those studies are done with non-treated people.

THE CHAIRMAN: Is this a good place to stop for lunch?

A. Yes, I think so, because I have to go also in details and it might take too much time.

THE CHAIRMAN: We will meet again at 2.00. Thank you.

(1.00 pm)

(Lunch Adjournment)

(2.00 pm)

MR JENKINS: We dealt with TSH range and your analysis of a number of papers, and we turn to the T4 reference range.

A. So now it's about the T4 reference range, and we have

about the same, we don't have at much studies as for the TSH, but all those studies are quite recent, and recent means the last ten years. Some may be older but most of them are recent.

Here we have a study, this is the reference range, I don't know if you see on the bottom, but on the bottom and certainly on your papers, you have numbers that are more or less the British T4 reference range in picamols per litre.

Q. Take it nice and slowly, please.

A. Yes. You see here, this is a study, and in the reference range from here to there (indicating), there's increased scores for depression in patients with Alzheimers disease. If they are situated in the lower half of the reference range, just the lower half, they have the two quartiles -- they have increased scores of depression, but everything is not as clear cut. They have at the same time also less memory loss, so there's an advantage and a disadvantage.

Here in the reference range in the lower tertile, that means the lower 33 per cent of the reference range, there's increased insulin resistance in normal people.

Q. What does that mean?

A. That means that they have tendency to get on fat and to develop in a later stage diabetes. So if we're in the

lower tertile, we're probably at huge risk of insulin resistance, and many people who are obese have insulin resistance. Insulin does not work well enough. The body's resistant to insulin. So the lower tertile of the serum T4 is not a good tertile.

Here is a study where patients who had lipid problems in their blood had also -- if they were in the lower tertile of the free T4, the reference range, had a higher CRP, that's a substance that is increased when there's premature atherosclerosis. So people in that range, if they have high lipids they also -- in that range of the T4 are increased risk of atherosclerosis. That is aging the arteries.

Here is a study in women. Normal woman. If they are in the lower tertile of serum T4, they score lower for the many mental states, so they have an increased risk of having great memory problems and dementia. That's not a safe range following that study for a woman.

Q. Right.

A. Here is a study when you're in the lower quartile, normal people as we. You are at an increased risk of dying. So it's not only disease, mortality is also increased.

If you're under the low reference range, the

mortality increases very quickly and, if you are just in a very, very low level of T4, 80 per cent mortality.

Q. Remind us, are these patients being treated?

A. None of these patients are treated.

Here is another study, when you're in the lower quartile, that means the lower 25 per cent of the reference interval, so some studies consider that when you're in the lower part they include also all the lab tests that go up to zero.

This is a study which includes the interval itself, the 95 per cent. When you're in the lower third of that interval you have a twofold incidence in metabolic syndrome. Metabolic syndrome is related to obesity, high lipids in blood, high blood pressure, et cetera. So all risk factors for increased mortality and lower wellbeing.

Here is another study, when you lower 25 per cent of the thyroxine, the free thyroxine, but that means also all the values up to zero.

Q. Slow down, please.

A. In children that have been prematurely born, there's white matter damage. So children being in lower quartile, if they are born too early, they have damage in their brain at those levels, and not if it's higher.

Here is a study where under the 10th percentile,

that means in the lower 10 per cent of the population, one in ten of us is indicated here. If they were infants, because this is in infants, when they are just born, they need ventilation assistance, they cannot breathe correctly. So they need to be helped at the beginning of their life.

Q. I don't know that we need to talk about infants.

A. Here's another one in pregnant mothers. Still it's important to see because some of those women could have still babies, the four patients we're talking about.

If a woman is in the free T4, in the lower 10 per cent, so 7.5 percent of that 10 per cent is still within the reference range.

If pregnant mothers have that, there's lower levels of -- there's impaired psychomotor development, so the children have intelligence problems and problems of behaviour and also of coordinating their movements more if the mother during the pregnancy was in the lower 10 per cent of the values.

Q. Right.

A. Also it shows that the lower the T4 is in a pregnant mother, at age 15 years, so much later, the children have psychomotoric problems and also behaviour problems.

What about the T3? We have just seen one or two tests on the T3. I will still go over, there's some

information.

Women who have values, who still can be within the reference range but quite low, women who have been obese have usually lower values than a woman who has never been obese. That means that probably the fact that they have low values of the T3 give them a tendency to get obese, and they keep this tendency even though they have lost weight.

Here's another value, if you're in the lower tertile, the lower 33 per cent of the population, up to the values of zero, if there's chronic heart failure, people with heart problems, there's increased risk of worsening of this disease, adverse cardiac diseases.

Also here, a study that shows that also values within the reference range can predict -- of the serum T3 -- mental disability. So if you're in the lower part and you're and you're aging you will probably have more mental problems, memory loss and others.

Here are studies that are no so well-defined on the values but still in women who have breast cancer. In several studies they usually have lower T3 levels so it's not so interesting to be in these reference ranges in the lower part.

Here is another study that in patients who have multiple trauma, if they have a low T3, they have

increased mortality, but that's usually values under the reference range which is very low but you see the lower it is, there more risk there is to die.

If you are under 1 picamol, which is a very low value of the serum T3, it's five times lower than it should be, you have 17 times more risk of dying.

So there is evidence, it is not true there is no evidence.

Now there was some talking about alternative diagnoses. Dr Lynn's talked about depression, for instance.

Just to show you, when there's low thyroid function, one study showed there's eight times more risk of being depressed, and even more subtle forms, like subclinical hypothyroidism, where the patients don't really seem to complain and they just have a high TSH, so one of the lab tests is normal.

They have three times more risk of being depressed.

Q. Compared with normal subjects?

A. With normal subjects. In my impression, when I started medicine actually I wanted to go as much away from the hormones as possible, so I decided to do psychiatry.

So I was admitted as an assistant of psychiatry but I saw so many cases I would say with hormone deficiencies, not only thyroid deficiency, that

I preferred to go into endocrinology, and I had much more success in treating low thyroid function with thyroid hormones in people who had also depression at the same time, for depression than with the medications we gave. It was actually treating the cause rather than the symptoms.

You see that even when you have a disease of the thyroid gland that is linked with autoantibodies so you make molecules that attack your own thyroid gland. You have also three times more risk of being depressed probably because those patients already have a mild form of thyroid failure. Thyroid insufficiency.

So we could treat the depression, but are we treating the consequence or the cause?

Then it was said maybe the cause is constipation. In one of the reports, it's constipation, it's an excellent symptom of thyroid deficiency.

So we can do two sorts of medicine. We take a patient who's hypothyroid, and we declare because his blood tests are maybe not 100 per cent convincing that he's not hypothyroid and we will treat the depression, we'll give antidepressants, we'll treat the sleep problems, because sleep problems are also impaired, there's less deep sleep, the deep phases, the most important phases of sleep is less in hypothyroidism so

we give sleep indications.

Q. Slow down.

A. There's constipation, we will give laxatives and we'll end up maybe by giving 5 to 20 different products in the place of treating the cause.

It's two types of medicine. Treating cause or treating the consequences. For the pharmaceutical industry it's much more interesting to treat the consequences.

Now, what about the controversy? This is taken out of the British Medical Journal, I believe.

Q. Yes. That's Dr Skinner's letter from 1997.

A. What about treating clinical hypothyroid patients but biochemical euthyroid? Is there data, is there information that would justify it? Is there information that it works?

THE CHAIRMAN: Is there a page number that you're up to?

A. I think I added this and I'll give you all those slides later. I'm sorry, some of the slides I've added.

MR JENKINS: I think you were told at the start madam, and it will be apparent as we go through, that some of the slides are not reflected in slides that we have on photocopies. But that is an extract from a document that the Panel have seen before.

A. Yes.

Q. It's Dr Skinner's letter and it's at the back of bundle 2, tab 4.

A. It's a study on 80 patients that were considered hypothyroid, are based on clinical signs but not on biochemical.

Q. Bundle 2, tab 4, page 138.

A. Dr Skinner published something many physicians were doing.

Is it possible that there would be a lack of thyroid hormones although the blood tests are normal? This is the debate between two schools of thinking.

When there's a debate in order to get out of the controversy, we have to go back to science. We have to look up the data. We cannot just rely on our belief.

This is to give you an idea of what happens when there are deficiencies. This is based actually on the scheme that a Czech doctor wrote about decreasing levels.

Before you get a severe deficiency and irreversible damage there are moderate degrees or intimate degrees of deficiencies, and the lower the levels are, the more problems you can get or the more signs you can have also in lab tests.

Conventional endocrinology treats when it's severe deficiencies under the lower reference range, and then

even outside of the range, then even in certain conditions. Because we heard that some endocrinologists would only treat the TSH above 10, although the outdated reference range we have here is 5.5.

I will explain also later what the problem is in endocrinology, it's diebetology, it's not really endocrinology that most endocrinologists have educational specialisation during their training before they have a speciality.

Optimal medicine may start here, treating also moderate (inaudible) deficiencies. In order to avoid arterial stiffness you have in your arteries, we saw this when you were already in inside the reference range, you have already arterial stiffness with higher TSH in the reference range.

You have to start treating early. Again, conventional medicine treats severe deficiencies when they're under, but often the levels of hormones are 25 per cent to 30 per cent of optimal before you are under the lower reference range.

Q. Can we go back to the previous slide?

A. This one?

Q. Next one. Where are you suggesting treatment should be considered to start?

A. Treatment should start when there's already a mild

deficiency. Because a mild deficiency will already have traces, you will have marks on the body, and if you wait too long, it will be irreversible. It's much easier to prevent than to reverse.

We saw some, in a certain sense, miracles when you saw how the patients changed with thyroid therapy, but if you saw very well the most elderly patients that changed, they didn't have so much beautiful change than when people were young, because there's already some irreversible damage when you wait too long.

So there are several authors that have given names to all those intimate degrees, preliminary, biochemical, physiological, clinical, anatomical, following the stage, but those are just from moderate to severe. It's just names and the importance is to treat early enough to you don't have -- but don't overtreat. I'm not a proponent of doping the whole proposition. As soon as there's real identified deficiency documented, treatment is necessary. For this concept of borderline deficiencies means that there's much more deficiencies than actually are treated in conventional endocrinology.

Remember receptors are already much lower, are really from age 31 on.

Q. Yes.

A. To give you an idea, almost all of the patients, three

of the four patient, did not have T3 testing. There's a special syndrome called low T3 syndrome where T4 could be normal, TSH could be normal, and T3 is low.

Q. T3 is the active --

A. Is the active hormone.

Q. For acting on cells.

A. And there has been quite a lot of debate in endocrinology, should we treat or not, because the T4 is good and the TSH is fantastic, normal. I haven't put all the literature here, I have a whole slide show, but that shows increased mortality with a low T3 syndrome, at least two studies and I think there's a lot of other studies, but I probably didn't collect it all.

Just to show you, in red are the levels in the tissues when there's a low T3 syndrome. They have been examined in people who died. They examined two sorts of people who died, people who had the normal T3 and people who had the low T3.

The people who had the low T3 had on the average about 50 to 60 per cent lower T3 levels. So there is in the tissues less of the active hormone.

Q. Can I pause you there. Should we see each pair of cylinders as resulting to a different part of the body?

A. Yes. So this is for instance the pituitary gland. This is the hypothalamus in the brain, the cortex in the

brain, 45 per cent less T3.

Kidney, much less, 71 per cent.

Liver also much less, 76 per cent less.

Lungs much less.

And here most patients had lower in the heart and skeletal muscle but some had fantastically high levels and we do not know why. But in most of the tissues the results are not good.

This is one of the proofs that they can exist although T4 and TSH are normal, much too low levels in the target cells.

Now, also in those diseases you have also reduced binding, diabetes is one disease with lower T3. There is the receptors inside of the cells, they don't bind easily, the T3, so there's also less activity although the T4 and TSH are normal.

Here also around in the brain, in diabetes, in glycocells(?), one type of brain cell, there's less binding of the important hormone, T3.

Here is people who have adrenal deficiency. They stop their medication for two days and in two days' time in the cells there was 50 per cent less receptors for T3. So if you have another endocrine deficiency like cortisol deficiency, you can have a too low T3 inside of the cells, although blood tests are normal. There could

be not enough thyroid hormones in the cells.

Q. Right.

A. When you take back the medication you normalise the situation.

There are several studies that show reduced binding, also in obesity. Obese persons have lower T4 neuroreceptors I don't think they checked here the T3, but they had lower T4 neuroreceptors.

Also these persons can have thyroid insufficiency although the lab test may be normal.

Here is another person, that older persons tend to accumulate the blocker of T3, reverse T3. It's another hormone that is also produced from T4, and that is more present when you have a disease or when you are aging; and who is not aging at one way or another. Even if you have normal lab tests in the cells, there can be an excess of reverse T3 and that can block inside of the cells the function.

So also if you fast, you go on a low calorie diet, for instance, you have more reverse T3 that will block -- even though you might have normal thyroid test, will block the remaining T3.

The crucial question here is -- it's actually the question I think here: may physicians treat clinically hypothyroid patients but apparently biochemical

euthyroid within the large reference ranges we have here? And may they do what is called a trial, a therapy trial.

The International Hormone Society has made a consensus on this on which conditions this could be done. Clinical symptoms, accurate dating, you have to do tests also, eventually repeat tests, but it could be done if it's done on smaller doses and very slowly increased.

Q. This is your society, the society of which you are president?

A. Yes. That's one of the -- we have 11 consensuses. The consensus number 1 is on thyroid therapy, exists already since for two years and we have something like 1,245 signatures. Physicians from all over the world.

We won't go into details because there's a little too much information. I'm going to show you that Dr Weetman himself now in a recent editorial gave another version of what he gave here as information.

Dr Weetman says he falls into the camp which believes that a trial of thyroxine is granted in any symptomatic patient -- any symptomatic patient -- with sustained subclinical hypothyroidism, but a real subclinical hypothyroidism you don't have any complaints because it's subclinical, it's under the clinical,

irrespective of the TSH concentration.

Q. Subclinical hypothyroidism?

A. American Journal of Clinical Biochemistry.

Q. Does subclinical hypothyroidism mean that the TSH falls outside a reference range?

A. Normally it means that the TSH is above the reference range. But he says here irrespective of the TSH concentration, so I think he really means biochemical euthyroid patients.

He also says that when talking about TSH guidelines, the danger in simplification is obvious in that it fails to take the patient as an individual into account.

Dr Weetman says he has also justification for flexibility in deciding on treatment in an individual patient. There's a lack of understanding still that reference ranges are not normal ranges.

This is clearly much still to do to refine TSH as says and their interpretation, there never will be a single simple test for thyroid disease. I fully agree with him.

I do not know, I absolutely do not know why he had a different version here; and it's not my task to judge that.

Now, you have to know that the majority, if not all, endocrinologists treat regularly biochemical euthyroid

patients. The ones with thyroid nodules. It's a safety measure against cancer, but it can also reduce the size of nodules if it's recent appearance.

So endocrinologists are all regularly treating biochemical euthyroid patients, and here they have no problems with that. I have no problems with that. No conscious problems. They want to talk about arterial fibrillations, I've written "not very much".

Since how long are endocrinologists treating clinical hypothyroid but apparently biochemical euthyroid patients with thyroid hormones? Since the beginning.

Look at this picture again my great grandfather. Look at the title of one of his books "Myxoedeme Fruste", that means mild myxoedema. Mild myxoedema would probably fit into the category today of biochemical euthyroid clinical hypothyroid patients.

They were treating patients, not lab tests at that moment. Lab tests are good but they have to have their place where their place is, part of the team, not solely reliable. We see that in the latest editions or editorials of Dr Weetman that he also changes position.

So Dr Skinner is not the only one who treats clinical hypothyroid biochemical euthyroid patients. All UK endocrinologists treat euthyroid patients with

thyroid hormones if they have nodules, goitre or thyroid cancer. I don't think they treat all the patients with nodules but many of those.

There's about 200 physicians who have already signed the very recent, just two or three months ago, written consensus. There seems to be the study that Dr Skinner did --

Q. I'm going to ask you to ignore that because that is Dr Skinner's study, and it has found its way into your report. The Panel will ignore that.

But we come on to your society.

A. So the International Hormone Society has made that contents, more than a thousand members, and can say you when we asked them to sign that sort of paper, they signed, because it's reasonable and you can look up the high number of references that references this on the International Hormone Society website, you don't even have to give the address, you just type International Hormone Society on the website.

So many patients also support the approach of Dr Skinner. I have signers of the -- there's a patient petition, that I didn't do, that the other doctors of the hormone society didn't do, but that they did, they have signed also a paper putting up the importance of being treated. But I didn't do any part, I didn't even

correct it. So it's really written in patient words.

At least 80 scientific studies back up the treatment of many patients and we'll see those 80 studies -- well, we have seen actually most of these studies, I just have to mention that there are other studies that we will see where in other conditions than thyroid nodules also patients are treated. So it's not true that there's just one study on treatment of biochemical hypothyroid -- no, clinical hypothyroid biochemical euthyroid patients.

So this is the third biggest endocrine society in the world, and it will grow very quickly, I think now, because there's a doubling of the number of congresses and they will also increase in size and it's mainly other congresses that doctors sign those papers.

The opponents of thyroid treatment of clinical hypothyroid and apparently biochemical euthyroid patients say there's no evidence, there's one study and it is seen in double blind placebo control say it does not work.

Q. Is that the Stobhill, the Pollock study?

A. Yes, the Pollock study. I think published in the British Medical Journal.

Q. The Panel have heard about that study.

A. Is this true? There's no evidence.

So studies that show that it has no effect, that's one study, the Pollock study. You have heard about that.

But it only -- well, it checked the cognitive function and psychological wellbeing. It doesn't seem to have -- but there's other things you can check, it maybe it would have improvement.

And then the big problem of this study: was it made with the right medication? Thyroxine alone, the precursor. Why not give also active hormone?

Here are a series of studies, generally double blind placebo controlled, where it has beneficial effects, and this is known by psychiatrists, treating patients who are resistant to antidepressant, they give some T3 and then it works. Probably because those patients have depression, partially or totally because of hypothyroidism but it works, the combination.

So those studies, this is very known, sometimes you have old studies, 1990, but there's 1984, but also 2002, et cetera. It's still a practice going on.

Also there's a study that showed that within the reference ranges, when you give thyroid hormone to people with high cholesterol, if -- and the only condition -- their TSH is above 2, you reduce their cholesterol with thyroid medication. If it's under the

2, they probably have enough thyroid hormones, you cannot reduce the cholesterol at a small dose of 50 micrograms. Usually that's a small dose for a patient.

Here are studies where thyroid hormones are given in euthyroid patients but who have nodules and goitres, so there's literature enough. I don't mean enough, it's never enough. It's always good to do other studies and bigger studies, et cetera. So we get more data. But is this a reason that there's only maybe 20 or 15 smaller studies that you may not treat? That you have to wait until there are 200 studies?

I will let you yourself evaluate that situation.

Opponents of thyroid treatment reinforce their arguments by saying: look at what happens with subclinical thyroid diseases. The subclinical patients have no pathology, they have high TSH, and when you give a treatment it does not work. Is this true? This is not true.

Q. Can we just go back to the previous slide because I don't think we have it in the photocopies that we have. Give the Panel a chance to read it again.

A. It says that the two arguments reinforce that you should not treat patients with clinical hypothyroidism but no lab test that confirmed that, because subclinical

hypothyroidism, which is normally a more severe form of laboratory thyroid dysfunction, it does not work, it's not associated with disease parameters and it would not help to give thyroid hormones because there are studies that show it doesn't work. Okay?

They are right, there are some studies that show no relationship between disease and that treatment doesn't work, but it's a minority of studies, a small minority, not a big minority. Small.

So the facts there are many, I would say several studies, but still quite a number, that show that there's an association if you already have a high TSH, you already have disease parameters that can be checked and when you give the treatment, you improve these disease markers.

So what the expert who is not here said is not true. And you see that these studies tend to confirm that there's arguments against treatment. You would overtreat the patients. But then in the same studies, it says both results you could minimise by educating well your patient, by saying: look, if you have those symptoms, you should decrease the dose, and try to get a TSH that is not necessarily suppressed, but we will see there are some exceptions to that.

Here is a test that shows there's no improvement and

here are controlled trials, two, no relevant improvement, so that would tend to reinforce what has been said.

Q. Can you pause so that the Panel can read them because I don't think it has been photocopied?

THE CHAIRMAN: I don't know about anyone else but I find it slightly difficult to read. If you want us to absorb it, you will have a to read it.

A. What is written here is, one of the titles is, "T4 treatment does not improve clinically hypothyroid patients who have normal tests". That's the Pollock study, I took it again here.

It's not subclinical hypothyroidism disease but I would like to reinforce the arguments of the others just to show that there is a disproportionate (inaudible word).

Controlled trials, it's normally placebo controlled, that means that some patients get a treatment, the others do not, they get a sort of fake treatment. So they don't know that they are having a fake treatment.

So there is also no relevant improvement in those who have hight TSH and the rest of the lab tests are normal. It does not improve. So there are two studies.

But when you look at the dose, the target, they try to get the TSH, in those who had a TSH of 8 under 5.

The outdated reference range. Upper limit.

They did not try to get it under 3 or 2, and that is essential. To get improvement with thyroid treatment at least that sort of type, you need to get under the 3.

MR JENKINS: Could you go back one page? I think we have moved on.

A. This is the information, the target is under the 5, that's a too high target, you should go on the lower to get improvement, and there are studies to show that.

So this is just arguments that it's necessary to treat because when you have subclinical thyroid disease you will probably get an aggravation of the problem and really get a clear hypothyroidism later on. There's 5 per cent per year who will at least be getting to overt -- 50 per cent of the patients who have a high TSH will get a overt hypothyroid with low thyroid hormones in ten years later.

Q. Slow down, if you would.

A. Here are all studies that show, and it's too small to read, of course.

Q. What you're showing us are authors, papers?

A. There are 19 studies here that show when you have a high TSH, there are abnormal factors, you have a high cholesterol, you have aging of the coronary arteries, so the arteries that supply blood. You have abnormal

clinical reflexes, et cetera. So there are other abnormalities linked to the high TSH. If you don't have a high TSH it's normal, you don't have those abnormalities.

There are studies that show that there's little benefit of T4 therapy if the TSH is only put into only the range of 3 to 3.5. You have to be under 3 to get improvement. That means everything that above 3 is probably not a good range, also not for a person who is not treated with thyroid hormones.

You improve lipid, cholesterol abnormalities and triglycerides and cardiovascular function. The heart pumps better when you get under the 3 of TSH.

If you don't do it under, it's above, it doesn't work.

Here's a number of studies that show adverse psychological effects. I think we saw it in another slide. You have adverse physical and psychological effects if you get this sort of high TSH. So it's not normal to have a high TSH.

Here are controlled trials, that means double blind placebo controlled, the best quality studies, that show there were, I believe two control studies that showed no effect, but no effect on the parameters that were checked. That doesn't mean it would have no effect or

nothing.

And here they say it has effect. Your heart pumps better when you give thyroid hormones to those who have subclinical hypothyroidism because the heart functions less well in that situation. Lipids are better, here it was mostly -- and even ... Well, on the skin some collagen -- content of the skin was better.

Here again, improvement. So there are studies, it's not true what has been said. It is partially true, but for a minority of the studies, and I don't know why only that evidence was given.

I have no judgment to give. I know there's a sort of hot debate between some physicians here and the British Thyroid Association, but I think we should always be balanced in our expertise.

How did Dr Skinner apply his diagnosis of hypothyroidism to the patients A and D?

Q. You go on to analyse each of the patients I think.

A. Yes. We are here on the diagnostic procedure to see if he does wrong diagnosis.

MR KARK: Sorry to interrupt, but before we move onto another topic, the screens we have here, we went do here I don't think.

MR JENKINS: We will copy them. But I think they're still on Dr Hertoghe's computer.

MR KARK: If we could have them today.
MR JENKINS: I'm sure we could arrange that.
Dr Hertoghe, I know you have analysed Dr Skinner's treatment of these patients in the report that we've already given to the Panel?
A. But that's later. It's only diagnosis here.
Q. I'm just wondering if we need to do it twice. Do we have the same information in your report?
A. The information is in the report, yes. It's like you want. We can do it now, but because I give the explanation it's maybe interesting at least so see one patient case. I don't know what the Panel wants.
Q. Let's keep going with what we're doing.
THE CHAIRMAN: Mr Jenkins, I think we need to be as time efficient as we can, so whatever you think is best.
MR JENKINS: I agree, and it may be helpful for the Panel to look at the same time at the back of Dr Hertoghe's report. I'm starting at page 26.
A. It's exactly the same as in the report.
Q. Because you have more information on the page than you have on the slides.
If you turn to D13, it's headed medical legal report. Page 26 takes us to Patient A where we presently stand.
THE CHAIRMAN: This is D13, page 26?

MR JENKINS: It is.

I think in the slides and in your photocopies you should be at page 89.

A. So we have here a patient of 43 years, and when analysing the files and medical records, I found the following symptoms that were written down, are typed, that can make you think that there's probably hypothyroidism in the past.

Rheumatic fever, there's easier [sic] rheumatic fever and other forms of infection in the immune deficiency of thyroid deficiency.

Postnatal depression, I saw a certain number of patients having postnatal depression improve when they went on thyroid therapy.

Long, heavy irregular periods. We have seen that in the beginning with the symptoms, that you can have the ovaries not working well. Also heavy periods is due to the fact that in low thyroid deficiency there's a lack of coagulation factors, and thyroid hormones improve.

No family history of thyroid disease. So it's not typical, there's no person treated, no goitre.

There's depression, fatigue, can be linked directly -- not on its own but with constipation you have to think. Constipation since her teens, recurrent

sore throats, dyspepsia. Recurrent infections is really a symptom to think about.

Medical history, was suggestive of hypothyroidism, and this is also integral part of diagnosis. Because it is already since long you have this sort of problem, it's a more severe thyroid deficiency problem because it will only aggravate in time.

Then there's the clinical exam, but that clinical exam includes the fact that you take a listing of all the complaints.

There's six years of extreme fatigue, tired all the time.

Constipation with predominant irritable bowel syndrome. It's more the constipation than irritable bowel syndrome due to low thyroid function.

And the joint pains. Arthralgia is joint pains, but a special sort of joint pains, it's diffused all over because it's myxoedema in all the joints.

Then the physical signs that were noted in the examination were: hoarse voice, loss of external third of the eyebrows, it's also called in the French language the sign of Dr Eugene Hertoghe, my great grandfather because he was the first to see that. And you find that still in the French medical dictionaries.

Also the syndrome of mild thyroid deficiency is

called Syndrome of Dr Eugene Hertoghe. So I had no choice but to do another profession.

The pulse rate is slow, the heart rate is slow, that is typical for low thyroid function, and it's also a special form, you don't here it so much. I don't know if it was this case, but probably will, bradycardia is very typical. Cracked heels, fissures in the heals -- heals very well with giving the thyroid hormone.

Q. Fissures?

A. Likes cracks.

Yellow tint of the skin, why? Because in low thyroid function it's yellow on the hand palms, at least in severe cases, certainly at the foot soles, much easier, because the keratin that we eat in the food that is the provitamin A does not convert to vitamin A easily, so they have vitamin A deficiency and excess of keratin, and you see that in physical examination with yellow foot soles, yellow hand palms.

Fibrocystic diseases often due to a sort of progesterone deficiency, deficiency in one of the female who were hormones. Women who are thyroid deficient they can not ovulate well, they will not make enough progesterone that is protective against fibrocystic disease. So cyst in the breast.

So these were all conclusive for hypothyroid

symptoms. Let's look at the lab test. TSH was in the reference range, if she has no thyroid nodule, it's acceptable. But the T4 is 12.2 in the lower quartile, where you have increased risk of memory loss, of mental disability, and lower intellectual development in children.

Metabolic syndrome features, like fasting, high sugar level in blood, blood pressure is higher, obesity, et cetera, so a patient with this sort of T4 is more likely to have disease.

Also lipid abnormalities, abnormal cardiovascular risk markers means that the CRP can be higher, so you can have signs of premature atherosclerosis, and coronary heart disease is more frequent in this case, chronic heart failure.

Patients have usually lower levels so there's associations with it. Breast cancer can be more, et cetera, mortality, et cetera. So also if there was pregnancy but she's getting a little old to get pregnant, not totally, but 43 gets a little bit limit. But if there's a pregnancy it is a problem for the baby.

So this is not a healthy value. So in this case because you had the four different approaches for diagnosis, were all tending to suggest hypothyroidism, I think a therapy trial, a trial with thyroid hormones

was justified on one condition, of course, it's done very, very slowly. On small doses, increased.

It's justified because of the medical history, the signs and symptoms, the lab test, T4 lower quartile, and also it was justified after, we will see later when we talk about the treatment, the patient -- it made a huge difference for the patient. Remember this euphoria that is said by Dr Weetman, it's not caused by thyroid hormones, it's just that the patient is finally relieved of her symptoms.

What do hormones give? Hormones do not change your personality. They don't make you different. If you're adequately dosed, they do not. But they free you from parasite emotions and feelings. If you feel always tired, they take that away. If you feel always depressed, they can take that away, if it's the adequate treatment, of course. If not, then the therapy trial doesn't work, it doesn't confirm the diagnosis.

Here it rather confirms. I would say very much. And although the patient was not very positive to Dr Skinner -- and even Professor Franklyn saw some things had improved, the better bowel movements and when she checked the patient on the therapy, she did not find a sign of hypothyroidism, so it was probably an adequate treatment.

Q. Before we go to Patient B, can I take you to your report.
A. Yes.
Q. We have taken the Panel to it. Page 26. If we stay with Patient A and look at your views. We will return to the main body of your report soon, but if we can deal with this patient and conclude your observations on her.
A. What I had propose assisted I had see the treatment -- after there are slides -- after on the treatment and I grouped the treatment together. It might be more interesting, otherwise it might be too much.
Q. Can I suggest this then, that we move beyond Patient B, C and D in your slides, and come back to do each patient just once?
A. Okay. I'll do Patient A now.
Q. Well, I was going to say, if you want to do treatment after looking at the rest of your slides.
A. I think it's wiser to do so, because otherwise it will get a little complicated. You need some information to understand the conclusions.
Q. Let's not do the patients in your slides, but come on to treatment in your slides. Then we'll do the patients once each, rather than doing them twice each.
A. Is that good for you?
Q. It's what I'm suggesting, so it's good.

A. All right. What I'm suggesting is that Dr Skinner had an acceptable approach in his diagnosis of hypothyroidism and this is a neutral position, it is based on the way I teach, and the way I have learned.

Apparently, at least for Patient A I have shown this.

Q. We will come back to B, C and D and the approach that Dr Skinner took. We'll come back to that when we look at your report.

A. What is clear is that there is solid evidence. It is never enough, but it's already interesting and very important evidence, and that these reference ranges are not necessarily the healthy ones. We have to have narrower reference ranges, and even then we still have to be careful because some patients could have in the cells a lower function that is expressed in the clinical symptoms.

Q. So just dealing with what you've said at the bottom of that slide, there is solid evidence --

A. Yes.

Q. -- meaning there is solid evidence the patients may have disease even though their thyroid test levels are within the reference range?

A. Yes. And I'm ready to challenge that at any moment. I'm a little bit deceived [sic] Dr Weetman is not here,

but I don't think there is any evidence to counter it for the moment.

Q. Let's move on.

A. Allegation 2.

THE CHAIRMAN: Can you just get us back on what document you are on and what page.

MR JENKINS: Back on the slides, we have just looked at page 95 at the bottom of that page, and we're now going to page 96.

THE CHAIRMAN: Thank you.

MR JENKINS: Again, we will ensure you get the outstanding slides or certainly Mr Kark does within the day. It may be that we do not get much beyond examination-in-chief of Dr Hertoghe today. Mr Kark will certainly have them overnight, which I think is his concern.

Allegation 2, Dr Skinner provides the wrong treatments for hypothyroidism. That's the suggestion that you're analysing.

A. Yes, and two arguments, that only thyroxine alone is needed, there's no need for another one, and that T3 and T4 combination or dessicated Armour Thyroid are not good products.

So actually you have to go to another.

Q. You have another document, I know.

A. And has it been distributed or not?

Q. It's just about to be.
THE CHAIRMAN: This will be D17.
MR JENKINS: Thank you very much.
I'm going to suggest a summary of what this contains and invite you to agree it. Your view is that thyroxine, T4, may be suitable for a large number of patients, but that there are other preparations which are better for some patients, including giving T3 and T4, or giving the dessicated natural version --
A. Yes.
Q. -- armour Thyroid.
A. That's it.
Q. And --
A. What I can suggest, for instance, is to show maybe a fourth of the slides and give additional information to them. What do you think?
Q. I don't know that it's right at the heart of the matters the Panel have to consider and there was clearly a lot of material that the Panel may need to consider if they do need to go into the detail of it, but if there's a way of short circuiting it, I think given Mr Lynn's answers to me the other day, it may be that we don't have to get too deeply embedded into arguments about T4 as against T3 and T4 as against Armour Thyroid. But you say there are arguments for adjusting treatment?

A. Yes.
Q. Depending on patient response?
THE CHAIRMAN: Can I just suggest -- am I right that this is your expert witness opinion about the T3 and T4.
A. Yes.
THE CHAIRMAN: And Armour Thyroid. It can be used as alternative and very valuable treatments.
A. Yes.
THE CHAIRMAN: So that's a summation of what's in --
A. There should be a lot of possibilities for patients and the different treatments should be available, and possible to treat following the experience of the physician.
THE CHAIRMAN: Right. That's good. So shall we take Mr Jenkins's suggestion and agree this, if Mr Kark is in favour of that?
MR JENKINS: It is an issue, madam, if I can address the Panel directly. Mr Lynn said to me the other day that if it was appropriate to treat patients for hypothyroidism he was less concerned about the mode of treatment, whether it was T4 or T3 and T4 or Armour Thyroid. That's the thrust of the answers he gave.
In those circumstances, I don't know that we need to get heavily involved in which form of treatment might be appropriate once you have got over the stage of agreeing

that it is appropriate to treat patients. The two central questions, as I seem them in this case, are: what is appropriate for Dr Skinner to treat any or all of the patients, A to D? And if it was appropriate for him to treat them, how did he manage them?

I don't think we are involved greatly in discussions whether Armour Thyroid as against T4 or T3 and T4 were relevant.

But I think Mr Kark does persist in concerns about the use of Tertroxin, amongst others, or the prescription or suggestion for some that Armour Thyroid might be appropriate. So I think I do need to go into this in some detail, but I hope to reduce it as much as I can.

THE CHAIRMAN: Mr Kark, do you have comment?

MR KARK: Not specifically with that. I think the focus is more on the change of dosage without there being adequate monitoring, and adding T3 into the system without adequate monitoring or blood tests. I think that's more the focus of the charge.

MR JENKINS: I'm grateful.

THE CHAIRMAN: Thank you.

MR JENKINS: Do you want to take us through some of the slides? You said look at about a quarter of them.

A. I propose to go to some of the slides because they'll

give an idea that apparently it's quite safe to do and it's even safer because the patient improves more.

THE CHAIRMAN: We will break around 3.15, if that will work into your slides. Thank you.

A. So just showing you that there's also a problem with T4 that has not been talked about here, is that the absorption of T4 is irregular.

THE CHAIRMAN: Just remind us where you are.

A. I think it's page 7.

MR JENKINS: 6.

THE CHAIRMAN: Thank you.

A. So these are studies where the absorption varies between 41 per cent and 46 per cent, and 73.5 per cent. That means that you're not 100 per cent sure when you take T4 if it's going to be totally or partially associated. That depends on -- so one of the reasons is to take it before breakfast, try without eating. But this you do not have with T3.

So patients who take a preparation that contains T4 and T3 are more sure to have thyroid hormones in their blood and in their cells than the ones who take T4 where the absorption could be irregular.

MR JENKINS: Could I stop you there. T4 is taken as an oral preparation, it's a tablet.

A. Yes.

Q. It's swallowed and absorbed through the intestine.
A. Irregular. 50 per cent across the model to three-quarters of it is absorbed.
Q. What that studies shows and what you're showing us on that slide is that the absorption rate of T4, when taken as a tablet, may be unpredictable?
A. May be unpredictable, which is not the case with T3, for instance, where you have a 95 per cent absorption. So almost everything of T3 is absorbed but not of T4.

The other study showed -- and this is only one of the factors that can influence -- in what sort of tablet it is put in. If there's lactose or other fillings, it will change the whole absorption.

Q. We remember again that if you take T4 or if it's secreted by the thyroid, it's then converted into T3 which is the active chemical acting on the tissues.
A. What we'll see also but very briefly is that a person cannot convert T4 to T3 if they do not have enough T3, and this may explain why patients who take T3 feel so much better because finally their own T4 they produce is better converted into T3.

There's legal problems with T4. The firm that made the most -- sold T4 had to pay a lot of fine because it didn't do its work very good.

This is an important slide because it not been

tested by any other study.

Q. Let's find it for a moment. Are we on page 11?

A. It's page 12 and 11, yes. So here the rats had their thyroid function was blocked, so it could not produce any more by high anti-thyroid medication. So they could not produce any more thyroid hormones, and they had this sort of levels in the tissues, T3 and T4. It's too low. You have to be in this range, the blue range that you see here.

So when T4 alone was given, never in the tissues, in the spleen, adrenal glands, or the ovaries or in other tissues could they have enough T3. So only supplying T4 permits not to have enough T3 in the cells which is fundamental to have a thyroidism.

So if a patient would not make any thyroid hormones, T4 would never be adequate enough or you'll have to give very high doses.

Q. Can I stop you again.

A. So you see here, in red. Here in yellow those are levels of T4 at 0.80 micrograms per kilo or something like that and -- per 100 grams I think, and here he had 0.90, so he had a higher dose of T4, that's okay. They always had enough T4 in the tissues but never had enough T3 in the tissues that's in red, it's too low, the value. So the higher the columns are, the more thyroid

hormones they have.

T3 here is in red, it's always too low when T4 alone is given. In the spleen is the adrenal gland. So we can take the spleen away and you can still live on.

If the take the adrenal glands away, they don't work because there are not enough thyroid hormones, the person will not be able to survive.

So adrenal glands are essential for survival. So having not enough thyroid hormones there, will make that they do not work enough.

Ovaries, you can take the ovaries away, the woman can still continue living but not a fantastic quality of life.

As soon as you give a small dose of T3 added, you do get adequate levels here in the blue levels, of T3, depending on how high you are, but usually you get adequate levels and always the same. A small dose can already be sufficient.

Q. Can I stop you. If we look at the top graph to the left, extreme left. We're looking at --

A. Total thyroid deficiency.

Q. An animal that is given no therapy at all.

A. But also a therapy that blocks the secretion of thyroid hormones.

Q. Right. And the little yellow column that we see is the

T4 level in the blood.

A. Yes. And in green and in red are T3 levels. I put them in green when they were adequate, I put them in red when they were not adequate.

Q. I understand. So we can see for the various charts, staying with the top one --

A. Even if you increase the does of T4, you do not get adequate levels of T3, never in the study.

Q. So when you increase the levels of T3 and T4 --

A. You add a little T3 to the preparation, you do get adequate levels. This explains why endocrinologists say: no, I just looked at T4 and TSH and those patients with thyroxine are good, they feel good, and the patient says: doctor, I don't feel good; you see that on the Internet. You see testaments: I have never felt good a thyroxine, now I'm on a T3/T4 combination I finally feel better.

It is possible because they are not able to have enough T3 in the cells.

Q. I think your next chart shows --

A. It's a bit the same.

Q. -- heart, muscle and lungs.

A. Same in the heart, same in the muscle, same in the lungs. Without a heart, if it does not work well, you cannot live. Without the muscles you cannot move.

Without the lungs you cannot breathe. So in essential organs you need to have enough thyroid hormones.

This is one of the studies that show that when you add a small dose of T3, you decrease the T4, but add a little T3 you have better results. The patients had less fatigue, less depression, less hostility. There are not many studies like this, because this is a double blind placebo controlled study, but this study does exist.

THE CHAIRMAN: Do we have this in our papers?

A. You should have that normally, yes. Sorry, I should explain this to you.

MR JENKINS: Page 19.

A. Also patient's sadness was decreased, even irritability was decreased, angriness and tenseness.

Q. Can we go back to the previous study so that we know what we're looking at? These are measures of patients' moods.

A. Yes.

Q. Looking at measures of patients' moods --

A. Yes.

Q. -- looking at various --

A. And energy levels.

Q. -- aspects of mood.

A. Yes.

Q. And they are less marked when you give T3 as well as T4.
A. Yes.
Q. And we are looking --
A. You see the fatigue, for instance, is decreased.
Q. Indeed.
A. And depression is decreased.
Q. Anger and hostility --
A. By a small change. So normally the total dose equivalent is the same, but they improved.
Q. The next chart that you showed us were other aspects of the same thing: sad, tense, irritable and angry, patients given combined therapy, thyroxine and the T3 preparation. They are less sad, less tense, less irritable --
A. Even less fearful, less confused.
Q. And less angry.
A. Small change.
Q. Thank you.
A. 12.5 micrograms of T3. Very, very small dose. Sleepiness was decreased, et cetera.

Many of the studies that have not worked might not have given a sufficient dose of T3.

And study 2 is a study I did myself. I'll just show two or three things. But I switched 91 patients from thyroxine treatment alone, which came to my

consultation, they said: I don't feel good on this thyroxine.

Although many of those patients had -- if they increased the dose, they could not tolerate it, so they couldn't go on a higher dose. So it was not the dose that was the problem.

Most of those patients were overt hypothyroidism. They had thyroid taken away, had radioactive iodine or something like that. So they were treated with thyroxine by other physicians before they came to me. So another person made the diagnosis.

For fatigue, for instance, by switching them over to an equivalent preparation that they tolerated better, so the doses were also slightly higher, they became either symptom free, they didn't have the fatigue any more, or they improved, and -- it's not put here -- mainly very much.

Q. So what we can see is that 98 per cent of those patients of the 91 that changed from T4, 98 per cent improved or became symptom free?

A. Yes.

Q. And you've shown us that about 20 per cent became symptom free looking at fatigue.

A. Fatigue is the symptom that is best relieved with thyroid hormones, at least the mental symptoms.

Depression is also 90 per cent were improved. So you can imagine my surprise, when I started treating patients, how much depression was much less of a problem when I started to treat hypothyroidism in patients who were depressed.

MR JENKINS: Madam, it is quarter past. I will stop whenever you would wish.

THE CHAIRMAN: I think if that is appropriate --

MR JENKINS: It isn't quite --

A. Maybe I'll just finish this study. If it's okay for you.

THE CHAIRMAN: Finish the study.

A. So also for coldness, swelling of face, physical symptoms were improved.

Slowness, 79 per cent had improvement, 21 per cent no effect, but nobody was worse.

Constipation, 75 per cent improved, just by switching the type of medication.

Joint pains, 70 per cent had joint pains -- no this is the person's age, so 35 per cent had joint pains, and they improved with the T4 and T3 treatment.

Dry skin, nocturnal cramps, is the symptom that improves the most as a physical symptom. Cramps in the legs because the blood circulation is not good in hypothyroidism.

So overall improvement, 86 per cent improvement of the symptoms and only 2 per cent worsening. 1 or 2 per cent.

Thank you.

THE CHAIRMAN: We'll break until 3.35.

(3.18 pm)

(A short break)

(3.35 pm)

THE CHAIRMAN: Ready when you are.

MR JENKINS: We've dealt with two studies. Coming to the third one.

A. I am just going to show some slides because there's so much. This is not the most beautiful slide, but it shows that when you compare preparations with T4 or Cytomel that has only T3, Tertroxin here, you can lower the cholesterol more with Tertroxin, with a competitive dose than with preparations having synthetic T3 and T4 with too small dose of T3 than with thyroxine. So thyroxine does not work well to decrease the cholesterol.

The dessicated Armour Thyroid works quite will compared to synthetic T3 and T4 preparation.

Also compared in other -- that I don't have here -- slide, it decreases more the cholesterol. One of the reasons is that the dessicated thyroid actually has --

T3 is bound to bigger protein, named thyroglobulin, and it's likely that the absorption is slower because it's more, and so to separate the T3, the body separates the T3 from this bigger molecule, thyroglobulin, it does the slowly, so there is a 24-hour provision of the treatment. And this is maybe one of the explanations why dessicated thyroid may work better than T4 alone or T3 and T4 synthetic preparations.

Q. We are on page 29, I think, of the slides.

A. If we go a little bit forward, I wanted to show you this slide. In patients with rheumatoid arthritis, for instance, they are more likely to have thyroid dysfunction and hypothyroidism.

Q. Page 35.

A. The next slide I wanted to show you it was a review of all the studies where thyroid hormones were used in patients who had rheumatism. Rheumatoid diseases. You see that generally in all the studies, they there were older studies, they had a complete or almost complete efficacy, almost all patients improved with thyroid medication on joint pains.

Then suddenly recent studies have then less and less effects, but actually the recent studies are done with thyroxine, and the others were done with T3, T3/T4 or dessicated thyroid preparations. Just one more clue

that there might be a necessity to have preparations with T3 included.

For cancer, T3 is very important, I'm going to skip that.

Just to show you that patients who have a low free T3 --

Q. Page 39.

A. And all patient who is take only thyroxine have a severe deficiency in thyroid hormones and take thyroxine only may have a low free T3.

If cardiac patients have that, they die easier, there is less survival, and the mortality is increased by about four or five times more mortality if your T3 is too low.

You don't find many studies with a low T4 linked to mortality as much as studies that show a link between a low free T3 and mortality, so it seems to be the critical factor for survival.

Q. I'm going to ask you to slow down, because your talking too fast for some of us to take it in. I don't mean the stenographer, I mean those who are listening and trying to understand.

A. Okay. If I show here you have heart patients. One-third of heart patients have a low free T3, and those who have a low free T3, so it's under the low

reference range, will have four to five times increased risk of dying because of their low free T3.

Dying by heart disease it's about five times more.

Q. It's five times, isn't it?

A. Yes. So that means that we probably have to pay attention to T3 much more and specifically in the medications.

Q. Right.

A. To imagine how important it is, we know all that is important to have good lipids in our blood, and if the lipids are too high, it's a critical factor, you might get more death in cardiac patients, but the T3 is even much more important for cardiac patients because when the T3 is too low, this is a more important risk factor than the lipids.

Q. Take us on to conversion, if you would.

A. So here's a number of studies that show that the conversion's lower when there's iron deficiency, for instance. On the average when a woman is iron deficient, she has a 22 per cent lower T3. Selenium deficiency, iodine deficiency, all can give a slow conversion.

How many women are not iron deficient? Iron deficiency is one of the most frequent deficiencies, it's much more than the 2.5 per cent of the reference

ranges for iron.

Zinc also, zinc deficiency gives us slower conversion. Also a number of toxins can -- if you have too much cadmium -- you could find that in the foods sometimes -- you slow down the conversion and many other hormone deficiencies. Male hormone deficiencies, men who age, for instance, they have a slower conversion of T4 to T3 because they have less male hormone.

Q. Again, remind us. If there is poor conversion of T4 to T3, what's the consequence of that?

A. If there's a poor conversion, the consequence is that there's a lower levels of T3, also in the tissues, in the cells.

Q. But if we measure T4 in the blood or TSH --

A. You cannot see that there's a poor conversion. A person can have a high T4 and still be thyroid deficient because there's not enough T3, and this is much more frequent than Dr Weetman or the other expert thought.

If you're in an stress situation, for instance, you can decrease your conversion of T4 to T3, because express makes a lot of cortisol and that decreases the conversion.

Q. We know that Dr Skinner was writing to one or more GPs, with patients A to D, suggesting that there may be poor conversion from T4 to T3, and saying that he still

believed that the patient was hypothyroid.

A. That's a plausible and credible explanation. It's a frequent explanation also.

Q. Frequent explanation?

A. When we give, for instance, iron to a woman who is iron deficient and has a poor conversion she gets warmer hands, warmer feet because her T3 goes up, but sometimes it's not sufficient to give the iron that corrects the iron deficiency, corrects this conversion, because there are a lot of other factors.

You see a lot of hormone factors. When there's lower growth hormone, at the age of 30 years we decrease much in our growth hormone and that gives a sort of more important aging, collapsing of the body, and growth hormone is the most potent hormone to increase the conversion, and adults need growth hormone. So when they become growth hormone deficient, they have a poor conversion.

What is very important, and it's not well written, so I'll have to correct it here because it's too important, is that the T3 itself increases the conversion of T4 to T3, since you need the minimum amount of T3 to increase the conversion.

We saw this in a previous slide, where we saw that the tissue levels of T3 were too low if the rats there

did not receive some T3. If you get a small dose of T3, all the levels of T3, if it was higher or lower, the amount of T3 you give were about the same because the conversion was improved by the small dose of T3.

Women who take a birth control pill, they slow down the conversion. The hormone causes to slow down most the conversion. That is why women who take the pill often get colder hands and colder feet, and drier skin, and have more weight problems.

Q. Right. Take us on, if you would, to the next slide.

A. That's the study I did that was published.

Q. This is an article you wrote in a book.

A. Yes. Many conditions relate to attributes(?), the conversion of thyroxine to three other -- so there's a lot of conditions where there's decreased conversion. It is, I would say, difficult for a person not to have at least once in his life, during a certain period, this decrease in conversion. If you don't do enough physical exercise, it's decreased, the conversion. So sedentary persons can have a poor conversion.

Q. Right.

A. If you eat too much proteins, you decrease conversion, and patients where we have to ask them to increase the protein intake, and they take thyroid hormones, we have to increase the thyroid hormones. Just to give you that

it's frequent and there are more than 200 studies, that was an article I did years ago.

This is just an overview of the daily production of thyroid hormones we make.

Q. Page 45, for those who have the bundle.

A. And what we see is that there's thyroxine made, but it's only one-third of what we daily make in thyroid hormones. Our body makes T3 out of T4 in the liver. Reverse T3, diiodothyronine, monoiodothyronine was one iodine atom, this is two, and this is zero iodine atoms. And it's possible because it has not been extensively investigated that those other hormones had a role. This may explain why dessicated thyroid also works better in a lot of patients.

Q. We heard concerns from Professor Weetman about the ratio of T4 to T3 in dessicated --

A. But it's a ratio that works better because the problem of a person who is deficient in thyroid hormones, that person often has, because of the deficiency in thyroid hormones and in T3, a deficiency in conversion of T4 to T3. So when you take the thyroid hormones with more T3, they react better, and they are generally well tolerated if it is dessicated thyroid.

I agree with Dr Weetman that if you take T3 and T4 synthetic, once a day, because normally you should take

the T3 three or four times a day, you do have a risk of being, at the end of the morning, a little hypothyroid, but the problem is because the T3 is quickly absorbed, quickly in action, it quickly disappears, but you have the risk that in the evening there's not enough T3, and so they feel a little lethargic. So in those patients that T3 and T4, I tend, if they are not responding enough, to separate in two the doses, most in the morning and a little bit at lunch so you spread the effect.

Q. I understand.

A. But with dessicated thyroid you don't have the problem in most of the patients. It's slowly absorbed, so there's a sort of 24-hour prolonged effect, and it's not too concentrated an as an action. So it's safer.

In a person who is adrenal deficiency, for instance, they have easy palpitations with thyroid hormones, because they convert too quickly the T4 to T3. Dessicated thyroid is slower absorbed, they tolerate it better.

Q. If you go to your next three slides, are those the points that you make?

A. Yes, better 24-hour, and 24-hour action.

Q. Go back one. Dessicated thyroid works better --

A. It works better, especially pork. I don't have the data

here, but I remember seeing very old studies where the pork type was considered of the best because it had a higher T3, and the patients responded better, they felt better, the clinical signs disappeared better, the cholesterol was more decreased.

Q. Right. Next one.

A. It has also a stronger anti-goitre action. So one of the ways to see if a treatment works well is, in rats, to block the thyroid gland and then they have goitres, but you can block the formation of goitres easier with dessicated thyroid or T3 but you almost cannot block it with T4 only in those studies.

Those are all the points.

Q. Thank you. Can we go back to the other set of slides that we were looking at. The Panel have the larger bundle, D14, and I think we're still on page 96.

We have just dealt, I think, with allegation 2. As you put it, Dr Skinner provides the wrong treatment for hypothyroidism.

A. What I propose is to another, I would say, upsetting information, I found in the report of Dr Weetman, is he said that there's no study to show that T4/T3 works better than T4 alone -- or almost no study. There's this study of Bunevicius. And what was strange was there's about 10/11 studies where they compared the

effect of patients treated with T3 and T4, and T4 only. And only in one study they see a significant effect.

But in all the other studies, in the rare studies with other patients they did, the tests were not better. In other patients where they asked: do you feel better? They felt better. In the four studies where they asked the patient: do you feel better with the medication? Just a simple question; they felt better, although they couldn't know which medication they were taking, because it was double blind placebo controlled, so they had either the T4, either the T3 and T4, and then they switched. They were all on a period of one of the products successively. So they didn't ask the right questions to see how it worked better.

Also another problem is when you give T3, with T4 it's quickly absorbed, the action disappears quickly. So if you give this dessicated thyroid, you have more 24 hour, and 24-hour effect, and they probably would have better results if they get a product where the T3 was more constantly present, and not only for six hours or four hours.

Here is another slide where near significant effects are almost clearly significant. So here, for instance, 18 out of 24 patients felt better with T3/T4 combinations, and they couldn't know which product they

were taking. They said: this product I took first, the first weeks, was the best; because that was maybe the week where they took it.

So most patients prefer it. So when you increase the ratio of T3, you had 52 per cent that preferred that medication. The higher the T3 was in the preparation, the more it was preferred by the patients.

Q. Right.

A. So evidence is rather pointing in the direction of T3 and T4 is okay, but what I think is not interesting here to know, which is superior, that's not our business for none of us here, but just so show you next to T4, T3 and T4 preparation and dessicated thyroid have an interesting place.

Q. Right, thank you.

A. That's not in your slides that you're going to get at 4 o'clock. They're going to bring the papers, I heard. About the allegation of iodine B12, I don't say it's futile, but it's a safe therapy. Dr Skinner didn't do a blood test, but as I heard, he relied on the GP. I think, it's an acceptable practice to do so. I would, of course, have asked myself to test if I suspect it had, but here you have more relationship with the GP, so I can understand that he could do it. And I heard that some expert had said that vitamin B12 does not work

orally.
Q. It was one of the GPs said that.
A. Well, I give regularly vitamin B12 orally. It takes two to four months, we give it sub-lingual, and it does work, you put it on the tongue and part of it is absorbed through the mucus, part by the stomach, but generally the preparations we give -- there's an interesting factor joint, so in order to absorb vitamin B12, you need another compound that the stomach makes. Generally, when it's added it also improves the absorption. But we have good results but, of course, we do not have the high levels we have with injections, but we have acceptable levels after two to four months of treatment with 2,000, 3,000 microgram per day.
THE CHAIRMAN: Mr Jenkins, do we have that?
MR JENKINS: No.
A. I'm sorry for that.
MR JENKINS: We'll make sure you do have it.
A. I tried to be complete, and so I added some slides.
Q. Let's go on to your allegation 3, as you have analysed it. The suggestion that Dr Skinner's --
A. It's not only that it shouldn't be treated, but that also potentially in the dangerous. You're giving to people who don't need thyroid hormones, you are giving thyroid hormones. Is it then dangerous --

because normally, if they don't need it, you're overtreating, you're overdosing them.

Let's look at the doses.

Q. We're on page 98.

A. Before the doses, I wanted to show you how does person with too much thyroid hormone look like. This is not enough, that we know, but when you have too much, you don't only lose the swelling, but you get a thinner face, in extreme forms at least.

Q. So the patient on the right there --

A. This is a person with hyperthyroid. You see the eyes bulging and things like that. This is typical, and they look very anxious, because you're anxious when you have too much thyroid hormones. You're not euphoric, you're anxious, and nervous, very nervous, you're trembling, even when you hold a glass, you tremble.

When you have spontaneous excessive thyroid hormones, because atrial fibrillation, bone density problems are often based on real hyperthyroid patients, patients not receiving medication, patients having too much thyroid hormones, those patients have an incredible high level of production of thyroid hormones. It's not 50 per cent more, it's 400 per cent more.

Q. So patients who are hyperthyroid, who have an overactive thyroid --

A. They make incredibly high doses that you cannot reach with 200 or 300 microgram. You need to give 500 microgram, or 600 in classical hyperthyroid, full-blown hyperthyroid.

Q. So we're not looking at a patient who has been rendered --

A. No.

Q. -- have been made --

A. No. If a patient would be end rendered, they would be something like 20 per cent more than normal but not 400 per cent more -- or 50 per cent more maybe, but certainly not more. Or they have to have those high doses of 500/600 micrograms. So we are talking about different diseases or different grades of disease.

So here the suggestion was 200 or 225 micrograms, would that be too much? Dr Lynn said for that patient he didn't think it was too much, but you never know. Well, when we read the BNF, what I read there was that the usual maintenance dose to relieve hypothyroidism 100 to 200 micrograms per day.

Q. That's what the Panel have seen before.

A. Yes, so we're still in those safe ranges, because that person had a high BMI or something.

Now, I wanted to show you if we follow the suggestion of Dr Lynn, what happens in coronary

heart patients. What Dr Lynn said is to stay on safe doses. For him safe doses is 100 micrograms or a little best. That was 1.6 micrograms per kilo.

What happens to cardiac patients when you do that and they have hypothyroidism? This is coronary atherosclerosis. Some patients have that and need treatment by the cardiologist. But it's easier also to have coronary atherosclerosis when you have low thyroid function.

If we follow the suggestion that most patients should remain on 100, it's not valid for patients with coronary atherosclerosis, because if you remain on doses of 100 micrograms or less, the coronary atherosclerosis that is already there, that means the arteries that supply the blood to the heart have obstructions, there are plaques of atheromas. So the blood cannot circulate well and the heart doesn't receive enough blood. You may not be stressed, otherwise you don't get enough blood in those stressful situations, and you can have a heart attack.

If they receive 100 micrograms or less, the next year they will aggravate their coronary arteries, it will get worse. If they receive a dose of 150 micrograms or higher, 200 -- but you may not give too much in those patients, you have to be -- I would

stay at optimal dose, but you need to give higher doses than 100, if they tolerate it correctly.

Well, only 28 per cent, one-third, a little less than one-third will aggravate the coronary atherosclerosis. The other will have a blocking of it. So we need to have the optimal dose.

This is one study. There are probably others. This is the one I could produce quickly.

Q. It's a study from 1997.

A. Yes, but it remains that you need to have an adequate dose in order to have a good heart condition.

100 micrograms may be for a cardiac patient not enough.

What about the low TSH that we've seen during treatment in clinically not hyperthyroid patients? Were these patients overdosed? Because it has been said over and over that these patients might be overdosed while they didn't have clinical symptoms.

Q. I think this is a new slide.

A. Yes, I'm sorry.

I would say if I have a little problem with the experts here and with the information that's been given, it's here that I have the problem. Even with Dr Skinner I have a problem here.

When you have a patient with low TSH and high T4 the most evident cause, almost -- I will not say

100 per cent but at least 80/90 per cent of the cases is just that the patient took the thyroid hormones before the blood test. This is a fundamental thing in all textbooks.

When you give a thyroid treatment do not ask the follow-up test after the intake of thyroid hormones.

Q. When are people told to take thyroid hormones, particularly T4, thyroxine?

A. They should take that day not the thyroid hormones, they should take it after the blood test.

Q. People are told to take it before breakfast, aren't they?

A. Yes, usually they take it always in the morning, and the have to chew on it. If they don't chew on it, there's less absorptions.

So if they take it in the morning and then they go to the GP or Dr Skinner or whoever, they will have higher levels of T4 normally, if they are well treated, and I'll show you also why, and a lower TSH easier.

When I looked at those results, for me if they were really clinically hypothyroid or euthyroid, normal or low, it's almost sure that they took. I have no hesitation and I don't even understand why a doctor here doesn't even do it and say to his patient: please don't take the thyroid hormones that day before the blood

test.

It's in the NACB guideline. Nine hours after intake of T4 you may not ask for the blood test.

Q. So if a patient took their medication in the morning and then went to the doctor, let's say to see Dr Blair or Dr Cundy, and a blood sample was taken from them during the working day --

A. If they were well treated with thyroid hormones, they have a high T4 and a low TSH.

Q. Right.

A. I will show you why. Again, with evidence, not my belief, but with evidence.

Q. There aren't many patients who go to their doctor before breakfast.

A. No.

Q. You talk about age-related decline in the pituitary gland as well.

A. Yes. This is what happens when you give thyroxine in the morning to the TSH. If you look here -- you don't have that on your slides, you'll get it -- you see here in green they get it between 6 and 7 o'clock in the morning, you get up early, and then go about an hour after the TSH starts declining and declining. It declines about 2 milliunits per litre, and it declines -- about 11 hours, it will be lower, so go to

your GP after 6.30 or 6.00 pm.

Q. Forgive me, is this a patient on treatment or --

A. This is a patient who receives the treatment, he has a high TSH, it's a real low -- high TSH patient with thyroid insufficiency, he gets thyroid hormones and then the lower levels, when they take it later -- they took several blood samples every hour, and you see the blood levels continue declining, and he took it at 6.30 in the morning, the lowest level will be around 1 o'clock.

Now, this is an average. Some patients will have a more severe depression, some less, of the TSH, and it's only around 6 o'clock, 6.30, that you should go to the GP to take a blood test.

But we see that this patient does not receive thyroxine. So if the patient came here to the GP, the GP will say: I'm happy if he or she would come after 6 o'clock, it would be still hypothyroid. So they are only better balanced during certain time and not after.

Now, the point I was going to make is: what do you do when you treat a patient with a normal TSH of around 2, for instance? What happens? About the same happens.

So what happens is the following: you get a suppressed TSH, some hours, and then it gets better and better. So I just lowered that from 2. So you will have, depending on when you come, a suppressed TSH

during the test.

What happens when a patient has a TSH of 1? Clinical hypo, but you treat her because she has too many symptoms and this treatment it probably will work. Then it's suppressed all the time.

All the time of the day, from 9 o'clock you get it suppressed to 6 o'clock, exactly the time they go to the doctor. So physicians should not take blood after the patient took the medication, but before.

Two solutions. Either the doctor goes to see the patient at 5 o'clock in the morning, which he probably won't want to do, or just ask the patient very simply not to take the medication before the blood test.

When I have a patient who has a high T4 and a low TSH, and maybe a high T3, I'm almost sure that the patient took the -- because if the patient is clinical normal, I'm almost sure the patient took the medication before.

What I do is on re-do a blood test later in good circumstance and then it's normal. If it is not, I reduce the dose, or maybe that patient is one of those patients who has a resistance because of low receptors, but the most classical, 80/90 per cent is that. Never do a blood test before.

In elderly patients you get probably more, this is

more in young people, but imagine you have an elderly person, you'll probably get a greater suppression of the TSH, because the TSH has already declined.

Q. Do you mean a greater variation during the day?

A. No -- yes, I think a greater decline. A greater decline of TSH because of treatment, because there's a weakness.

There are other studies that have been done on those tests, and conclude that the tests do have major flaws in the follow-up. For diagnosis without thyroid treatment it's okay, but with thyroid treatment it's a problem, but I think the problem relies often also on the fact that they the did blood test without warning the patient not to take the medication before.

Q. The first author we see there is Professor Jane Franklyn of Birmingham.

A. Yes. She found in the patients she treated, on 77 patients, that means 75 per cent, who were receiving T4 undetectable TSH, probably somewhat overdosed, but others were probably normally dosed and need to have a dose.

But again, no discrimination perhaps. She didn't ask not to take the thyroid hormones before. But that means that there's a very high ratio in, let's say ... Here is another study where the 71 per cent actually had an undetectable TSH.

Q. I think the third author there is a name we've seen before, Toft.

A. Yes. Is that the same doctor?

Q. I think it is Dr Toft we've heard mentioned, Anthony Toft.

A. Here is Custro.

Q. I don't need to ask you about names now.

A. No, but measurements of serum concentrations, the free T4 -- the free T3, the TSH, they found that it didn't permit to distinguish the patients between gross abnormalities, they didn't know if the patients were adequately treated from excessive replacement. They couldn't see the difference. So they had to rely on physical examination.

Their conclusion was here, what they said a biochemical test of thyroid function of any value -- that is Fraser actually, it's a Sottish doctor. He said those measurements are little, if any value, in monitoring patients. So it's golden standard to do the test before.

During treatment I really advise to do the test, but not to rely only on the test to the conclusion how you are going to adapt the treatment or not. You have to have an confirmation. If the person is clinically nervous and hyper, et cetera, plus those suppression of

TSH and high T4, you have to lower the hormones and not to increase them or to let the same dose.

So to stop doing thyroid function tests in this case would result in considerable savings nationally in the costs of reagents(?) in laboratories. I do not totally agree, because I still I think it's helpful when I see a patient who has a low TSH and a high T4, and she did not take, or he didn't take it before, I do look at physical examination much more, and I interview the patient much more, and there are a certain number of cases where really the dose is too high.

Q. Let's move on?

A. What about the high free T4? What does happen when you take T4?

Q. This is also a new slide, I think.

A. Remember it is not --

THE CHAIRMAN: Is this a new slide and therefore --

A. Yes, it is a new slide, and the slides that come also will be new slides what is important to have in the cells enough T3, the dominating hormone for action.

At what level of T4 will you have in the blood and a sufficient level of T3 and a sufficient level, let's say, when we saw that it's not in the lower tertile, it's, let's say, average level between the two, the higher level and the lower level. The middle level

would be more or less an acceptable level, but how much T4 do you have to have in blood to have an acceptable level of T3?

Q. In the tissues?

A. Probably with you not certainly in the tissues. You have to have a very high level of T4 at the upper limit of the reference.

A little complicated slide, but it shows here, this an average level of T3. So you are just between the two reference limits in the middle. To be in the limit you never have this with free T4 that is low or free T4 that is average or high/normal.

You actually have it when it's above or at the upper reference range then only will you have a sufficient free T3, and this in the average person. So that's why the UK guidelines for thyroid action was said that you have to have a high or average level of free T4 because they knew about this study.

Q. That's the 1996 guidelines that we've heard of.

A. Yes. This is a study of 1984. We know this already since long. It has been forgotten.

So in order to have sufficient level of T3 in blood and not necessarily in the cells, but your likelihood is higher, you need to be on the high level. If not above the reference range.

I'm open to critics of this, but I don't think there will be another study to come from this.

High free T4 during treatment in clinical non-hyperthyroid. I think here in this case for me it's evident. It's probably not evident for Dr Skinner or for the other doctor, but for me it is evident this is, and this I say truthfully. It's generally caused by blood intake just after -- not the test after taking the thyroid hormones.

Q. Taking blood after the patient has taken the medication?

A. Is incorrect, and then you get always a high free T4.

Q. Right.

A. But even if you don't take it, the free T4 must always be high enough to get enough T3 if you only rely on thyroxine. So a patient only on thyroxine should certainly have a high T4 all the time.

But you can also have a poor conversion, and I'm going to show you what happens in a person with a poor conversion in the blood levels of intake. You also can have a high absorption. The patient can exceptionally highly absorb the T4 much better than others. In the place of 50 per cent it will be 75 or 80 per cent. Of course blood levels will be higher.

This is what happens with the T4 in the same study of the TSH. In other studies it's more evident, there's

a higher increase. You increase the -- it's not the TSH. I have to change that, sorry.

On the slide you will have to change it also because the one that are being printed there is some wrong information.

So the person takes the thyroxine and there's an increase in level during between 9 and 14 hours, after intake the level is increased.

Q. Can I stop you. On your chart --

A. This is 2007 study.

Q. We see time, and the patient takes the medication at about 7 o'clock in the morning.

A. Yes. 6/7 o'clock. You see it here, and then the level increases very quickly. Half an hour later, already increases, and will remain increased during up to nine hours, 10 o'clock in the evening with T4. This is an average. Some patients will have higher increases, others lower.

Because remember, T4 is not so easy to absorb as T3.

Q. You have told us there may be unpredictable absorption rates when the patient has swallowed the tablet.

A. Yes. For instance, patients who take wholegrain bread, the cellulose of the wholegrain bread will glue the thyroxine taken, and a lot will get in the stools and the TSH, for instance, will be much higher, so there

will be much less absorption. So you may not take the thyroid hormones with wholegrain bread, for instance.

Q. Don't take thyroid with wholegrain bread because it binds to the --

A. There are other reasons no to the take it anyway, you lose also sex hormones, but that's another subject.

If a patient is, for instance at 13 and she gets thyroid hormones, and she has a poor conversion of T4, she will not quickly convert the T4 to T3. That's one of the causes -- or high absorption -- and you can have a high level, but an inactive level, not very active because there's a poor conversion, because remember it must be enough T3 in the cells.

Q. And your blue dotted line across the chart --

A. That's the upper limit --

Q. -- shows the upper limit of the reference range for some of the ranges that we've seen?

A. This is the result of the study. This is what I have put personally. It's not in the study. It's just for explanation. The same for here. However, when we saw this slide, when I put -- this is in the study. This I put --

Q. The green line.

A. I added this myself just to make the point clear. Now,

another point I want to stress, the danger of absence of treatment of clinical hypothyroid --

Q. This is another new slide, I think.

A. Is it? No, I think you have at least this slide.

THE CHAIRMAN: I think it's page 102.

MR JENKINS: I'll very grateful. That is, yes.

A. So the absence of treatment is potentially dangerous. There's a reduced quality of life. And as we will see a little later there's an increased risk of atrial fibrillation.

Q. If you don't treat?

A. If you don't treat.

At least in cardiac patients who are being operated [sic].

There remains an increased risk of bone loss with thyroid hormones in post-menopausal women.

I'm going to answer to the arguments that -- we don't have to forget it's potentially does, but let me see if I ... I'm going also to answer to the arguments that it's potentially dangerous for thyroid treatment. Keep in mind we have seen that absence of thyroid treatment may be deleterious. Apparently it is.

The approach is not to treat -- that you can have heart problems, bone loss, and some patients may become addicted et cetera. So we're going to talk about that.

There are two schools in treatment. This is a repetition actually. One will say your normal lab tests do not treat. Let's say this is one extreme. Only lab test counts and the actual reference ranges stick to it. It's wholly a religion. The dogma not to oversee. Not to exceed.

This is an extremist attitude because even in the States they are, let's say, a little more open, and in Germany much more open, et cetera. Why should the UK be so extremist?

The other attitude is: do a safe therapeutic trial so there are certain conditions to do a safe one. You have to start with small doses, you have to do a good evaluation before, and a whole medical history, complaints, physical examination, lab tests and under therapy trial. This is the position of the International Hormone Society. I don't think it's an extremist. It is just that we are here to help the patient and not to help the lab test.

The difference is, and I talked about it, so I'm not going to talk too much it, but if you have depression, we give antidepressant, but why not look the underlying causes. It may be thyroid deficiency or other hormone deficiencies.

So if you don't treat the hypothyroidism, you will

have to give maybe antidepressants, do psychotherapy, takes laxatives against constipation --

Q. You have said maybe 20 medicines for various conditions?

A. Maybe 20 medicines, and it's almost the same. Slower school and work results, easier job you have to find, et cetera, antibiotics because of the infection. It's too much.

So therapeutic trial may be the solution if it takes all the symptoms away. If it doesn't, stop the therapeutic trial and give all the laxatives and antidepressants you want, but why not the therapy trial? Which attitude is really safer?

Because we know that people are depressed, they have an increased mortality, cardiovascular mortality, maybe.

Let's look at the potential dangers of the treatment of Dr Skinner and of comparable doctors. We will do the same.

Q. Page 104, I think?

A. What about atrial fibrillation. I'm very happy that the risks have been cited because these are eventually risk, and possible risks, I don't deny that. But let's look at the data.

The data that shows a relationship between a low TSH and atrial fibrillation is based on -- to my knowledge, not on a study with thyroid hormones.

Anecdotally there are some publications, but they're very anecdotal, it was not sure it was caused by the thyroid hormones.

But the studies are based on people who have hypothyroidism. Overt hypothyroidism, you remember the huge amounts they make you. Too much of something good is too much, and will give a problem. But they make very big amounts of thyroid hormones. Huge amounts.

There's some disease, subclinical hypothyroidism, low TSH, where there's increased risk of atrial fibrillation. But some patients with a low TSH have a central hypothyroidism.

Q. Central?

A. Central, that means that the brain is not able to make enough TSH. When I look at the studies, I don't find really that they discriminate correctly.

So I am not always sure the study has well distinguished real patients who might have too much thyroid hormones, but those studies show a certain relationship. They come to the conclusion that the risk of developing atrial fibrillation is only really greater in patients who have 0.1 or lower levels of TSH.

But again, not patients who are treated. It has not been shown to my knowledge -- maybe there's a study and I am interested to know about it. Really interested.

Here's a study that shows that actually, when you look at patients who have had atrial fibrillation, there's ... When you have too low levels of TSH or too high, you only have certain hypothyroidism or hyperthyroidism, you have about the same risk of atrial fibrillation, so not enough thyroid hormones are too much -- are not good, and you increase of the risk of atrial fibrillation.

So when you have a low free -- because the risk of atrial fibrillation seemed, when I looked at the report, to be related more to the T3, giving T3 additionally might be a greater risk and it seems no true. In patients who get a bypass operation because the coronary arteries of the heart are obstructed by plaques, atheroma plaques, those patients have an increased risk of atrial fibrillation if they have a low T3, and actually this is evident, of course.

What is a symptom of low thyroid function of hypothyroidism. Irregular heart beat is a symptom. It's a slow irregular heart beat is a symptom of low -- they make more extra systoles, and when you give thyroid hormones, it normalises the pulse and the heart rate.

Usually when you have too much thyroid hormones you don't get irregular heart beat, you get a too fast heart and too strong. It contracts too strongly.

You see also there's a high frequency of hypothyroidism in dogs who have atrial fibrillation, and in patients with irregular heart beat there's a low T3 and a high T4. So poor converters of T4 to T3 have easier arrhythmia because their hypothyroid in their heart.

Here is a study that shows when you give T3 therapy you decrease the incidence of atrial fibrillation after heart operations, so there is surgery for the heart, you have less risks.

And I was not looking at such a study, I was looking to find a study that showed -- that really proved that you had increased risk of atrial fibrillation. I found the contrary.

I didn't look it up for this case, it's a long time ago. The reports where they talked about T4 causing atrial fibrillation were only review articles where they suggested that it could increase the risk, but maybe there's a study that is really solid but I didn't find it.

Q. So just looking at the question of atrial fibrillation, the study that has there have been with patients who are hyperthyroid suggest that they are at greater risk of atrial fibrillation.

A. Yes.

Q. Those are patients who are not on treatment.
A. But they made huge amounts of thyroid hormones for most of those people.
Q. And you've shown us the graph --
A. Not comparable --
Q. -- where we saw an enormous amount of T4 being produced by those patients.
A. Yes.
Q. As to patients who are being treated for hypothyroidism, is there any study to suggest that those patients, even if the T4 levels or the TSH are high, outside the reference range, or the TSH levels below the reference range, is there any study to suggest --
A. I did find a study --
Q. -- that those patients are at increased risk of --
A. I didn't really find a study. But I was searching for it. But maybe there is a study, so I'm interested, because still too much thyroid hormones is related to atrial fibrillation, but too low thyroid hormones apparently also. So we have to be in the safe margin where people have a normal thyroid function, healthy thyroid function.
Q. As judged by?
A. Certainly the clinical examination would be certainly when you have thoughts, you have to rely on that, but

the best would be to have a TSH, let's say, above 0.1, and probably under the 2, but again, there are exceptions.

Q. I understand. Let's come on to bones and bone density. page 107.

A. What about the bones? It has been repeatedly said by Dr Lynn said that the problem has been overemphasised.

Let's look at the data. This is one of the data that shows that people with subclinical hyperthyroidism have a lower bone density.

So people who have a low TSH you give them block of thyroid function. So they have too much thyroid hormones, and you block that and you see indeed that the bone density was the product increased. There's more in the forearm, more bone density.

Why are we always talking about bone density, what is important? Well, when you don't have enough bone density, you break your bones easier. And if it happens in your back, you collapse and you get smaller and smaller, with a bending back. Imagine how you live with a bending back all the time. So it's important indeed to correct any abnormality. And you see that indeed people who spontaneously have a low TSH because of too much thyroid hormone they do improve.

Here are studies that show that actually the bone

loss has only really been evidenced in patients who had spontaneously hyperthyroidism, or those huge amounts of thyroid hormones, or a woman in the post menopause. This is a review. Everything I show you normally comes out of a review of the 30 years of studies.

So we know that women who are not taking female hormones after having menopause, they don't have -- they get osteoporosis and bone loss, and that is aggravated when they take thyroid hormones, so you need to treat those patients with female hormones, but with the safe ones, not the oral oestrogens, but that is another debate.

The bone loss, when it is identified, it is mainly transitory only the first year, because how is the bone when a person has hypothyroidism. It's swollen. It also swells. And it probably has a thicker density thanks to the swelling, maybe there's more calcium, I don't know, accumulated. So after the first year you clean up the face, the bone gets less swollen, it's probably a reason. I don't know.

But after it doesn't seem to have an effect even if a woman is in the post menopause, the first years at risk.

But there are several studies with no adverse effect of thyroid therapy on bone density. There are two

studies that show that there's no increased fracture incidence in women with low TSH and one of those studies was given by Mr Kark. I think I have it here. It's the Bauer study, I believe.

So you don't have an increase risk of fractures. What is important mostly do you have an increase. Actually the bone is maybe even in better health because to have new bone formation, for the bone to be in health, must have a good new bone formation, and the thyroid hormones are an essential tool for that.

Here another study that shows there's no bone loss in women in the post menopause if they get the female hormones. So oestrogens therapy neutralises that risk.

Here is a whole series of studies, one of those is by Professor Franklyn, that is studies with patients on the therapy did not have any significant bone loss. So there are much more studies that are reassuring, although I do find that the last years -- and I didn't take all that literature because this information, I have put it together about a year and a half -- but the latest study or some other studies show you have to watch out with women in the post menopause: please provide hormones or watch out.

Don't get the TSH too suppressed in women after the menopause, but women before the menopause, even if it's

suppressed it doesn't seem to be a problem. That's on the lower part. It's a study where thyroid therapy improves bone formation, stimulates new bone formation.

So I think the studies are relatively showing this just in a small fraction of the population, post-menopausal women have to watch out, but that doesn't mean we may overdose our patients. They should be safely dosed on a correct dose.

So the allegation 3 in the report I say that is potentially dangerous. I think the experts who have concluded of those potentially dangerous, did not have the data. I think there's always a danger in any treatment, and no treatment should be overdosed. But we have seen that the blood tests are less than for other hormone deficiencies, useful for examination, although I think it should always be done, blood test and follow-up.

What about the addictive effect? I have shown that scientifically at least there's no study to show that their hormones provoke euphoria although there's -- well, there's no real study. But they do feel better the patients. When you get relief from your hypothyroid symptoms, of course you feel better. And why did they get enthusiastic? Because I showed you how important the thyroid hormones are. So they really changed the

life of a person.

If I wouldn't taken up my thyroid hormones, I would be here swollen up, probably be tired all day, and wouldn't be here even, and probably not have the intelligence to talk to you clearly. So it does change your whole life.

Q. Let's go on. The next slide we have is the danger of TSH suppression.

THE CHAIRMAN: Excuse me, could I just remind you we're going to finish at 5. Just to keep that in mind.

A. So if you suppress the TSH are you going to atrophy the thyroid glands? We are not giving here doping. What is doping? Doping is 100 -- let's say it's 10 times more than you daily need. We're giving a fraction of what is necessary. If a person needs maybe 120 micrograms per day of T4, we are giving -- not everything is absorbed so we probably have to give 200 micrograms, or 220, to replace in a person who has had total thyroid gland loss.

So we're giving a fraction and you, in my knowledge, rarely suppress totally the thyroid gland like this. The lab tests we saw, the evidence, I think, is that during certain time there was suppression, there was suppression of the TSH, but it was not 24-hour suppression. At least if the person is not clinically

hypothyroid, I would doubt, I really doubt.

But let's look at the studies. How many years a person would take thyroid hormones? 10, 20, 30? I didn't have by hand the study where it showed that patients that took since 32 years thyroid hormones had a test of stopping the thyroid hormones. But here is a study where patients were taking between five months and 22 years dessicated thyroid or synthetic T4 or thyroxine, et cetera.

On the average, even after 22 years, the T3 had a full recovery in three weeks. 22 days on the average. In order to have a normal free T4, it was full recovery on the average 19 days, even after 22 years. The plasma TSH response to TRH, that means that when you inject TRH if the pituitary gland is not atrophied by the treatment, it has good response. That response is recovered after 16 days, two weeks, a little more than two weeks. So two to three weeks on the average to recover everything. But we're not doing doping. You cannot do doping with thyroid hormones, it's unbearable. The person gets anxious and you certainly can't do that for 22 years.

The information that you get when you over-replace euphoric is not the right information. It's incorrect information, erroneous.

Q. Let's go to the next slide, if we may.
A. About the patients?
Q. I think we might want to start the other document and come back to the patients.
A. I have two documents. I have one document with evaluation of the patients of Dr Skinner and how they were treated and a document on the evaluation of the reports of the experts.
Q. Shall we start on the experts?
A. Yes.
Q. And then come back to the patients.
THE CHAIRMAN: Remind me where we are then.
MR JENKINS: We are going to Dr Hertoghe's report, which is document D13.
A. Part of my task was to evaluate the scientific --
THE CHAIRMAN: Do you have a page number?
A. These are the ones we should normally have. Maybe we can distribute them. Do you have them? Otherwise we do it tomorrow.
MR JENKINS: We had better get on. Do you have it? Do you want a written copy? Here is a printed copy.
A. That's the report. I have the report. The information I am giving is a sort of brief review of actually my report. It's mainly based on the report of Dr Weetman because he had, let's say, the most information and the

most erroneous information, if I may say.

THE CHAIRMAN: Is that in this?

A. It's all here. I will follow the same order, but you have more text and more explanations.

MR JENKINS: Why don't I take to you the text? We can leave that. I'm taking you to page 3 to start with.

A. Page 3 I have also on slides.

Q. I'm going to stop slides for a while. Stay with the typed document. You talk of, under paragraph 6, scientific divergence on thyroid treatment between two medical schools of thinking?

A. Yes. I think this is fundamental, that there is -- in order for a medicine to progress you need diversity, you need different therapies, you need different thoughts so that we can arrive to the best treatment. But there's apparently not one way of thinking who is the best, so it's never good to have just one way of thinking and everything.

I think here the centre of the debate and the centre of the troubles is that there are two schools of thinking in medicine. One who is, let's say, in a power position, at least in the UK, and one who goes forward with, let's say, more evidence. I try to show you the evidence, part of that.

Q. Paragraph 8.1.

A. So you have the school of endocrinologists, but what is an endocrinologist actually? When you look at his training, it's a half year to one year and a half. Maybe some things have changed in recent years, but before it was mainly internal medicine and additionally internal medicine has nothing to do with endocrinology.

Then additionally they had at the end of their formation a half year, or one year and a half, in a hospital in an endocrinology unit. And what do they learn there? They learn with the patients who come to the hospital. Who comes to the hospital? Diabetes patients. So they are very good experts in diabetes. But, like you see, Dr Weetman writes in textbooks of the thyroid, gives a lot of incorrect information, erroneous information. I don't think he had an adequate training.

He says himself, "My speciality is internal medicine, diabetology and endocrinology." He doesn't even say thyroidology, the science of thyroid diseases.

Then the school has formed the local GPs, and so they have the same approach. What I see each time I go in congresses and debates, it's always the same. They don't learn enough about scientific data and they don't pay attention enough to the patients -- more lab test endocrinology -- and that's because in diabetes that's what works, you need to know very well the lab

test for having diabetes well controlled.

So often there's poor scientific evidence and for thyroid pathology, it is like Dr Lynn said and Dr Weetman: you only treat outside of the reference range and even then -- so not only above TSH of 10. And the leading societies in the world, it's not the BTA, it's the Endocrine Society or the American Society of Clinical Endocrinologists who are getting much more diverse information, but most of them are diabetes specialists.

There's also the school of hormone therapists. That is all the doctors who -- don't consider them as endocrinologists, but use hormone therapies, including endocrinologists, official endocrinologists. So in our International Hormone Society we do have endocrinologists, but it's not the majority.

Q. You have doctors from all over the word?

A. All over the world.

Q. America?

A. America, Chinese, Europeans. All over the world, yes.

Q. Do go on. What's the approach?

A. The approach of those doctors of the International Hormone Society is: don't treat only the most severe deficiencies, but treat also the intimate degrees of deficiencies. So you can prevent or decrease the number

of pathologies or disease that come when the thyroid function is not sufficient, and we have seen when there is already disease, it was in the reference ranges.

So they suggest therapy trials, but also the reason is not only to decrease the incidence of disease and mortality, but also improve the quality of life of the patient. And it has been more and more recognised that for treating the quality of life of the patient, you can do certain therapies. For instance, for cancer therapies they can get injectable EPO, the one that sports people take; they can get it reimbursed, although the cost is high, when they have cancer. And the reason was not because it decreased the disease of cancer, but just because it corrects the quality of life.

So the leading society is the International Hormone Society and I'm very amazed how much enthusiasm it provokes, so I'm sure we're going to continue growing especially as we're making more congresses. What we try to do, in order to palliate, we don't think that the diabetologists are bad doctors, we think there's a need for much more training, evidence-based training, but also patient-oriented training.

When I was looking at the reports of the doctors, I think we all had the same concern, every one of you has the same concern: we want the patient's safety and

wellbeing. They had it also. But it was not as much focused, I think, as it could be. So we're doing this "trainingship" and I know, because of my experience with training, that it will have a lot of people following this trainingship.

Q. Let's move on to Professor Weetman's report. I take you on to your page 5.

A. And the one of Professor Weetman, point 4. He names all the causes of hypothyroidism, but he forgets aging, infections, and inadequate nutrition are probably very important. I can in one week decrease my thyroid function by eating a lot of meat, for instance, because I slow down the conversion of T4 and T3, so nutrition is also an important point.

Q. That's first point you have on the slide that we have.

A. The first. So it's incomplete.

Q. Right.

A. Important omissions that may have made a better understanding of what Dr Skinner does. Because if there's so much frequent causes of hypothyroidism, the incidents of hypothyroidism are higher than officially proposed by dogmatic institutions.

Q. You then deal with --

A. The symptoms and signs of hypothyroidism. So this was for me a hard point. I couldn't understand why a doctor

would give a different conclusion to a study than the authors themselves. So he said that the study that evaluated a sort of symptom list to see a global score of physical signs and symptoms to -- if that was possible to detect people with slow thyroid function, and he said it was not significant; it showed that it didn't work, et cetera. It's not true, it showed exactly the opposite. He said something like: you have healthy individuals that are inside the reference range who also have symptoms of low thyroid function.

So they have, I think it was 6 per cent in the place of 62, so people who have values of lab tests of thyroid function outside the reference range, 62 per cent had heavy complaints of low thyroid function. And 6 per cent of people inside the reference ranges, who were normal for him, had severe hypothyroid symptoms, so he concluded because there was no total separation that actually it was not reliable.

But what does that mean? That probably means that the people who were inside the reference range had some kind of low thyroid function. It may explain exactly the contrary. And with the experience I have, I think it is that. So I give the conclusion of the authors that was different than his conclusion and I do not understand why he changes the conclusion. Then he says

very rightly TSH can be misleading in central hypothyroidism.

Q. This is your paragraph 13 on page 6.

A. But incomplete, it forgets that central hypothyroidism -- that means the brain does not secrete enough TSH. The pituitary gland does not secrete enough.

Q. You talk about aging and that the majority of us will develop --

A. Yes. So for him it is a very rare exceptional pathology. And if it happens, you immediately have to send it to a super specialist, who has to search for a tumour. We all are developing a secondary, a central hypothyroid. Yes, we all are developing.

Q. You go on to comment on Professor Weetman's view that the goal of treatment should be to normalise the blood TSH level.

A. Yes. I had found a number of insurmountable inaccuracies. It's in contradiction with the UK consensus, so the consensus published in the British Medical Journal. The consensus of the BTA, the British Thyroid Association, his society, is actually, I don't think, published in a peer review journal.

Q. What we have in Professor Weetman's report at the bottom of his page 6 is the statement that a UK consensus

statement published in 1996 stated that the correct dose was one which relieved symptoms and would in most patients result in a normal or raised serum thyroxine concentration [i.e. T4] a normal Tri-iodothyronine concentration, T3, and a normal or below normal serum thyroid stimulating hormone concentration. And he gives a reference, the BMJ 1996. Do you have it?

A. Yes, I have also the article here. So I think this is a right definition for follow-up.

Q. To relieve symptoms?

A. To relieve symptoms should be the first of our targets. If the test could also be, let's say, more or less normal, it's okay except in some cases where probably there's in the cells a need for thyroid hormones, a lack of thyroid hormones.

Q. You go on to say that --

A. Dr Weetman seems to believe that the American Thyroid Association confronts [sic] this belief.

Q. Confirms his belief?

A. Confirms his belief, yes.

Q. Does it?

A. Actually on review of this guideline, because it's a very long guideline, it states that:

"We have to rely not only on lab tests but on association of laboratory measurements and clinical

evaluation."

And I think this in any endocrine pathology has to be, because the cellular deficiency will always be seen by good clinical examination, almost always. There are groups of symptoms that, when you put them together, are very typical to a deficiency. I work with a lot of different hormones, with complex patients, and I can say what I will have in the lab test I already almost know when I have done a good clinical evaluation.

MR JENKINS: I see the time, it is not quite 5 o'clock, but I know we've got some printing to do before we finish the day. Mr Kark is anxious to get documents. I don't know whether the Panel would like to have overnight any extra slides photocopied for them or whether you feel you can wait until the morning. I will follow your wishes on that.

THE CHAIRMAN: I think we can wait until the morning. We will meet tomorrow at 9.30 and Dr Hertoghe is obviously still under oath.

MR JENKINS: I'm told in fact that the slides have already been printed and, if you would like them now, we can give them to you now, but again you can wait until the morning if you wish.

MR KARK: Tomorrow, after this witness has finished, I think my learned friend may have one more witness that he

wishes to call and there may be some legal argument about that. Can I just indicate that given the length of this evidence and the amount of material that we are having to deal with, I doubt very much that I will be able to make a speech tomorrow and I would hope that you will not require me to do so. We are dealing with a huge amount of material and I can indicate straightaway I would very much prefer to make my speech on Monday.

THE CHAIRMAN: That's fine, Mr Kark. We are finished for the day, thank you.

(5.00 pm)

(The hearing adjourned until 9.30 am on Friday, 13th July 2007)

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