The Thyroid Trust briefing note for HoL T3 debate[1]

The Thyroid Trust says

- The plight of thyroid patients deserves to be better understood and addressed. A minority of patients need this drug, liothyronine/T3, (either on it’s own or in combination with levothyroxine/T4) and many of those people are experiencing considerable difficulty being able to access it. We believe this is due to budget pressures in the NHS and/or unclear prescribing guidance. The Department of Health and NHS England have the power to address both issues and must do so urgently.

- More generally however, inconsistent and often poor standards of care for thyroid disorders are causing significant hardship to many patients and fuelling what may be an unnaturally high demand for T3 as some desperate patients believe it is their only hope, when it may not be.

[1] This document was updated 18/6/18

- Hypothyroidism is a very finely tuned disorder and a significant minority of thyroid patients are not being treated as they should be, not only because of the issues around access to T3, but because
    - many GPs are not following treatment guidelines:
        - to fine tune the dose of the standard medication for this condition, levothyroxine, where patients still feel unwell when their blood tests are within a certain range and,
        - to refer patients to see a specialist, if wellbeing can't be restored in primary care.

- Both of these issues are likely causing many more people to be unnecessarily unwell and also fuelling demand for T3 from patients who are being led to believe, by campaigning organisations, that it is the best/only solution for them.

- Patients who are hypothyroid do not pay for their prescriptions. So it is in the government's interest to ensure those people are supported to be as well as possible, as the population deserves good health as far as possible - but also in order to minimise the amount of other medicines they may have to take – and associated costs of any such additional medication.

Dr Anthony Toft comments

Dr Anthony Toft, ex president of the British Thyroid Association, has kindly advised us on this document and says:

It is the exorbitant cost of Liothyronine tablets which is the basis for Health Authorities arguing against its use. If the hormone cost what it should there would be no argument about prescribing Liothyronine. Government should stop paying inflated prices from UK suppliers [2]and look to other suppliers overseas. Some patients undoubtedly benefit from taking Liothyronine in addition to Levothyroxine, despite the failure of underpowered studies to demonstrate an advantage.

1. It is likely that the 10-15% of patients with primary hypothyroidism who do benefit from taking both hormones have a faulty gene, encoding for the enzyme responsible for converting the inactive hormone, T4, to the active hormone, T3, in the body[3].
2. It is possible to identify whether a patient possesses the faulty gene, via private testing.
3. The normal thyroid gland secretes a small amount of T3 for a reason and it makes sense to replicate as far as possible normal physiology. It is an accident of history that we use Levothyroxine alone to treat hypothyroidism. If we were

[2] https://www.thetimes.co.uk/article/concordia-international-drugs-company-faces-huge-fine-after-overcharging-nhs-by-33m-8skqntg68

[3] Hershman JM. A deiodinase 2 polymorphism may lower serum T3 and tissue T3 in levothyroxine-treated patients. Clin Thyroidol 2017; 29: 338-40.

starting afresh we would be prescribing both hormones and I suspect that this will happen in the fullness of time.

I cannot emphasise enough that the primary fault for the current situation lies with Government and by proxy, NHS management, in failing to deal with escalating prices. It is quite wrong to take the easy route of placing Liothyronine on a prescription blacklist, disadvantaging a small but significant group of patients with what is a very common disorder. Manufacturers entering the UK market to produce Liothyronine in this country are doubtless attracted by the huge profits to be made here from patients so desperate to obtain Liothyronine that they self-fund the prescriptions, sometimes enduring hardship to do so.[4]

Stats and facts

- About one in 20 people in the UK have a thyroid condition (source: British Thyroid Foundation - BTF)
- 8% women over 50 and 8% men over 65 have underactive thyroids (source: Journal of Medical Screening 2011 - http://www.bbc.com/news/health-12252813)
- Thyroid disorders also affect children – it is standard procedure to perform a heel prick test around five days after birth
- It can be an important factor in successful pregnancy
- There are several different thyroid disorders including hypothyroidism (underactive thyroid), hyperthyroidism (overactive thyroid) and thyroid cancer.
- The most common is an underactive thyroid which is most commonly caused, in this country, by an autoimmune condition called Hashimoto's disease.
- Experts commonly accept that between 5-20% of hypothyroid patients do not thrive on the standard treatment - the research has not been done to quantify this more precisely.
    - These are the patients who may require T3 – or they may simply require their thyroxine dose to be fine tuned but in many cases this is not happening.
    - If just 5% of hypothyroid patients require T3 the number of affected patients is estimated at >50,000. This puts a tremendous and unnecessary financial burden on the health service if the cost issue is not satisfactorily dealt with.
    - There is anecdotal evidence that some patients are already self-medicating by obtaining T3 from abroad (e.g. Greece) where it is a fraction of the price currently charged in the UK. This 'under the radar' treatment may cause health problems later in life.
- Until 2017 the only manufacturer in the UK to hold a licence for manufacturing liothyronine - the generic T3 drug - was Concordia. The price to the NHS rose 6000% between 2007 and 2016, from £600,000 to £34million, despite falling volumes.
    - We are informed by Concordia[5] that the price rises were instigated to mitigate against costs arising in response to meeting MHRA requirements to improve the manufacturing process. Each price rise was approved by the DoH and at no point has the DoH challenged pricing although they could have done. Two

[4] Dr Toft's comments updated 18/6/18
[5] Information from Concordia has been included in the updated version of this document 18/6/18

new suppliers entered the market in 2017, Teva and Morningside and the price is now beginning to come down.

Brief explanation of the thyroid

- The thyroid is a gland in our neck and controls our metabolism - which is not just about our waistlines and energy levels but all of our physical and mental processes.
- If our metabolism is slowed or speeded up, we can experience debilitating apathy, brain fog, anxiety or even, in extreme cases, serious mental disorders up to and including psychosis and dementia like symptoms[6]. Everyone who has any kind of mental illness should have their thyroid function checked but how many people are aware of this? It appears that the mental health connection is often not well known even amongst mental health professionals. Contacts at Mind Charity and other mental health charity professionals have confirmed this to us anecdotally.

What is liothyronine/ T3 and why is it controversial?

- T3 is the active thyroid hormone, also known as liothyronine.
- Most patients who have an underactive thyroid gland are treated successfully with levothyroxine (T4, also known by the short name, thyroxine) but some may require T3, either in addition to T4 or as an alternative, on its own, in order to feel well.
- As many patients who take T3 get it on private prescription or buy it themselves online there are no definitive data to say how many patients take T3 in the UK.
- T3 has been used to support thyroid cancer patients who need to withdraw from levothyroxine before radioactive iodine treatment but the introduction of a new drug Thyrogen (recombinant human TSH) has largely (although not completely) replaced this practice.
- More research is needed into the efficacy and risks of T3 and this house should take steps to support such research.
    - (Professor Colin Dayan at Cardiff University is currently seeking funding for just such a study, analysing the dataset of deceased Dr Gordon Skinner who used T3 extensively[7].)
- This is a controversial area in thyroid treatment, with a very active patient lobby for T3 and natural desiccated thyroid (NDT) which is produced from pigs' thyroids and contains both T4 and T3.
    - Hillary Clinton is one high profile individual who is known to be prescribed NDT.
    - In the UK, NDT is not licensed, although patients can get it on a named patient basis on a GP prescription.

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[6] Thyromind.info

[7]Update: 14/5/18 The data from Dr Skinners patients will be linked anonymously to information held in the NHS Health and Social Care Information Centre (HSCIC). The researchers will then compare this data to similar data in individuals that have only received LT4, without knowing the identities of any of these patients. On this basis, individual patient consent is not required. http://www.btf-thyroid.org/professionals/research-award/358-2018-research-award

- In the UK, organisations who campaign for greater access to T3 are Thyroid UK, Thyroid Patient Advocacy and Improve Thyroid Treatment (ITT).

"Hard to treat patients"

- Experts commonly accept that 5-20% of patients with underactive thyroid may be classed as "hard to treat" - more research is needed in order to quantify this more accurately and understand more about how to help these patients, but in some cases it has been seen that treatment with T3 can be life changing – to the extent that people who were unable to live a full life have been able to 'get their mojo back', go back to work and so on, rather than languishing in a very poor state and having to claim benefits if they are otherwise unsupported.

NHS consultation in 2017 on T3 withdrawal results

- The NHS consulted last year on de-prescribing a number of drugs. Liothyronine was on the list ostensibly because of questions over how effective it is as a treatment, but perhaps more because of cost concerns, but the consultation received strong submissions from both patients and doctors[8], including a petition signed by over 31,000[9] patients, and concluded that the drug should continue to be available to those who need it.

NHS procurement issue, price increases and tax payers money

- It was reported in The Times[10] and elsewhere at the end of last year that the cost of liothyronine to the NHS has spiralled by 6000%. In November 2017 the CMA accused Canadian firm, Concordia, of overcharging by £100m, with price per pack rising from £4.46 to £258 in 10 years.
- EU prices of liothyronine are around 2p to 26p per tablet whereas the NHS pays over £9 per tablet.
- The CMA investigation will ascertain whether there is any wrongdoing.
- We believe the cost of this generic medicine should be managed by more robust procurement processes in the NHS.
- When liothyronine is looked at in isolation, it is clear that the cost of this drug has risen dramatically.

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[8] The Patients Association response to the NHS consultation on liothyronine from last year is here: https://www.patients-association.org.uk/Handlers/Download.ashx?IDMF=3692914d-fb56-4555-b88e-c775109e3ec7 .

The British Thyroid Association's response is here (BTA is the organisation for thyroid specialists) http://www.british-thyroid-association.org/sandbox/bta2016/bta_response_to_the_nhs_england_consultation_for_website.pdf

[9] ITT Petition for T3 (31,000+ signatures) https://www.change.org/p/itt-campaign-group-improve-thyroid-treatment-for-millions-of-people-stop-the-withdrawal-of-t3

[10] https://www.thetimes.co.uk/article/concordia-international-drugs-company-faces-huge-fine-after-overcharging-nhs-by-33m-8skqntg68

- However, pharma companies have responded that costs should be noted as a whole, and that when total cost and average cost per pack of all generic medicines is looked at, the UK generic medicines market, created and managed by the DoH, is recognised as being one of the most effective in the world. As the Under-Secretary of State for Health said in March 2018: "Recent research published in the Milbank Quarterly demonstrated that the United Kingdom pays considerably less for unbranded generic medicines than other countries with a comparable income level". Similar findings were made in the OECD report of 2016 on Healthcare in Europe.
- And it is notable that within the NHS budget for the UK of approximately £140bn in 2017/18, it is estimated that the total cost of the UK generic medicines prescribed in primary care was £3.5billion (just 2.5% of the total NHS budget) [11]which then created £13.5 billions of pounds of savings overall for the NHS. We are informed by Concordia that if wholesaling costs and a £800m contribution to pharmacy remuneration are factored in, then the total cost of UK generic medicines falls to approx. £1.5billion (just 1% of the total NHS budget).
- Pharma companies also state that the DoH has correctly taken a *macro approach* and focused its resources on maintaining billions of £ of savings for the NHS budget overall. This makes sense, and the macro numbers demonstrate it is cost-effective, to do so. It appears that the DoH recognises that this 'portfolio approach' allows generics manufacturers to recover more on profitable medicines so thereby continue to supply the DoH/NHS with a wide range of medicines, including loss-making and marginally profitable medicines. Concordia informs us that 25% of its UK medicines fall into this category.
- In general terms it appears that the free market should correct any imbalances. We are informed that costs are falling rapidly since 2 new suppliers of Liothyronine launched in 2017.
- The way that the NHS manages its budget is clearly complex, but **the key point is that the cost of this individual medicine appears not to be adversely impacting overall NHS costs and therefore should not affect continuity of supply for patients**. However, that is what is happening, as illustrated by the testimonials below, and that needs to change.
- While treatment for individuals is a matter between that individual and their doctor to agree, we receive many testimonials that
    - Patients believe that CCGs are restricting access to this vital medicine because of the high cost. We are concerned these decisions are being driven by cost concerns rather than by clinical need. NHS England have stated that Liothyronine has categorically not been black-listed. Yet the level of anxiety and ill health caused by preventing patients from accessing medication that they require is intolerable.
- It is important that the NHS receives value for money, from a robust and sustainable generic medicines industry and that patients have access to appropriate treatment.

[11] https://www.nao.org.uk/wp-content/uploads/2018/06/Investigation-into-NHS-spending-on-generic-medicines-in-primary-care.pdf

Recommendations

- NHS England needs to issue guidance to clarify the position for thyroid patients, in particular to inform them and health professionals that, contrary to what they may be hearing from GPs, individual CCGs or campaigning organisations**, liothyronine has not in fact been black-listed**. Any thyroid patients who have been using liothyronine **should continue to receive it whilst they may be assessed** for an alternative medicine. They certainly ought not to be taken off liothyronine pending such an assessment, which may not occur until many months later and it must be clearly acknowledged that for some patients this treatment is required and that the patient's own experience is not to be overlooked when they are assessed. These simple changes would make a dramatic and immediate difference to UK thyroid patients. The DoH is the expert regulatory authority for pricing issues and overall NHS spend on medicines. It has considerable knowledge of how the sector operates, how the NHS budget is allocated and the demands that are particular to it. The DoH has statutory and non-statutory powers to intervene in the pricing of generic medicines, when it wishes to do so. Therefore we recommend that it is charged with reviewing the price of Liothyronine and, if necessary, working with the three suppliers of Liothyronine to reduce the price. And that this discussion should not impact on prescribing for patients that need Liothyronine

The importance of fine tuning treatment and further testing

- The goal of treating an underactive thyroid – as the most common thyroid disorder – is to get blood test results within a 'normal' range AND to restore wellbeing. But doctors are often ignoring the second part of this goal. Too many patients are not listened to, if they find that they still feel unwell once their blood test results show that they are anywhere within that range of so called 'normal'.
- Doctors in general practice must be called upon to remember that hypothyroidism is an extremely fine tuned disorder and many patients once they are 'in range', if they still do not feel well, can benefit from their healthcare practitioner fine tuning their dose of levothyroxine within the parameters of that range.
- One person may feel much better if they are at the upper or lower end of the scale and it can take several months or more to get the balance right.
- Doctors ought also remember that, if a patient has symptoms which are unexplained and do not resolve, they should be tested for other possible disorders and, if wellbeing cannot be restored by a primary care practitioner, they should be referred to a specialist promptly for further investigations and the option of specialist treatment.[12]
- We know from talking to patients that in many cases these treatment guidelines are not being applied and so it is no wonder that so many patients are asking for T3 – when in fact a good proportion of them may not actually need it.

[12] http://www.british-thyroid-association.org/sandbox/bta2016/bta_statement_on_the_management_of_primary_hypothyroidism.pdf

The French experience

- In 2017 in France a change to the formulation of the Merck brand of levothyroxine the standard treatment for hypothyroidism, caused >17,000 reports of adverse side effects, which patients who had been stable on their previous medication attributed to this change - and most of which were ultimately resolved when they were returned to the original formulation.
- A petition of concerned individuals gained over 300,000 signatures,
- The cause of the reactions is still being investigated but indicates just how finely balanced the wellbeing of thyroid patients is and how important it is that they are treated consistently and listened to when they experience adverse symptoms.
- Significant patient reports of issues preceded media coverage. (source: BMJ report Feb 2018[13] and this matter was widely reported in the French press and in British Thyroid Foundation Newsletter, Autumn 2017)
- French patient associations have distributed a letter to patient organisations in other countries to help prevent what happened there happening elsewhere and we should take steps to learn from the French experience.
- The MHRA has been working with UK manufacturers over many years to improve quality and safety standards of UK supplied levothyroxine. This, along with the multi-source supply hopefully means that the chances of similar issues occurring here in the UK are substantially reduced. The NHS prescribes >50 million packs a year of Levothyroxine and benefits from very low prices (28 tablets = <£1)[14].

Testimonial: patient felt well on liothyronine for 10 years, told by her GP to buy it herself online, as NHS cannot afford it[15]

- One patient, Maureen Elliott from Kent was told last year her doctor could no longer prescribe Liothyronine due to the cost. This led to her firstly becoming extremely unwell and subsequently having to purchase the drug online from abroad, which raised lots of concerns and cost varied wildly from over £600 to £60 for a two month supply, when she is entitled to free prescriptions on the NHS.
- Maureen is keen to share her story in order to shine a light on the issue she and other patients who need liothyronine are facing. She says:
    - “I have been taking this medication for ten years now and my health deteriorates significantly if I stop taking it. I am very concerned that the NHS is being grossly overcharged, but as a patient I feel that I am stuck in the middle of a pricing war between Concordia and the NHS.
    - I was left with no other option than to buy it online from a supplier overseas. I was very unhappy with the quality of the medicine purchased online and negotiating to buy it is so complex and expensive that I am at a complete loss in trying to understand it…

[13] https://www.bmj.com/content/360/bmj.k714
[14] MHRA information added 18/6/18
[15] Maureen’s story added 18/6/18

- I am in my 60's and a full-time Carer for my mother. Paying for my medication is an additional financial burden. The situation I've been in has also been extremely stressful. Having to cope with the withdrawal of a medication that I need in order to maintain my health is completely unacceptable and stress causes a worsening of my hypothyroid symptoms which makes it very difficult to cope on a day to day basis."

- Maureen's local CCG (Thanet) have commented that the GP practice should not be withholding the drug for reasons of cost and have offered to intervene, so hopefully her case may be shortly resolved. However we know of many other patients facing the same issue who do not yet have any such reassurances

Example 'hard to treat' patient helped by best practice and not requiring T3

- The Director of The Thyroid Trust reports that when she first began taking levothyroxine she became first very much more unwell and amongst other disturbing symptoms was completely unable to think clearly for several months, despite her blood test results being brought into range.
- Thankfully her GP followed the best practice treatment guidance from the British Thyroid Association and after several dose adjustments and ongoing testing to optimise her dose, she is now functioning well without the need for T3.
- It is The Thyroid Trust's belief, from talking with many hundreds of patients about their care, that many patients are not receiving this basic standard of good treatment and some end up led to believe that they need T3, because of what they read on the internet, when they may not.

Large numbers of patients very concerned and some accessing the drug online

- Other thyroid patient organisations such as Thyroid UK and Thyroid Patient Advocacy, who campaign very actively for T3 to be made more available and are not in agreement with current treatment guidelines[16], have many thousands of followers on social media platforms – Thyroid UK have 70,000 on Health Unlocked and 17,000 on Facebook for example - and as mentioned above, over 31,000 number signed a petition in the recent NHS consultation.
- This strength of feeling - and in some cases desperation amongst patients - must be acknowledged.
- From observing social media posts and discussions with thyroid patients it seems that many are bypassing the NHS access issues and purchasing their medication unsupervised online from abroad, which is deeply troubling and we are sure none of them do that lightly.

[16] This sentence was updated 14/5/18 at the request of Thyroid UK..

T3 access vital for those who need it to be able to function

- It is clearly the case that many patients who require T3 will continue to require it as will new patients who are hard to treat and whose symptoms are not alleviated by adjusting their dose or finding and treating other disorders.
- If they and their doctor wish to trial and / or continue treatment with T3 it should be an option that is available to them without them having to fight tooth and nail for it – since it is in all our interests for people to have the opportunity to be as well as they can be and to be able to contribute to society.
- We should note that those who are most unwell at the point of need are the ones least likely to be able to fight the system and they should not have to.

Background to the T3 Debate

A debate on issues with availability of the thyroid drug, T3, has been called by Lord Hunt of Kings Heath, Labour's spokesperson on the NHS, Higher Education and Cabinet Office in the Lords.

We understand the debate has come about because Lyn Mynott (CEO of Thyroid UK) had a meeting with Lord Hunt on 22nd March. Representatives from ITT (see below) have also since met with Vince Cable who subsequently led a debate on hypothyroidism in the Commons on 21st May.[17]

Thyroid UK have produced a report[18], along with with other thyroid patient groups who are very pro T3 (Improving Thyroid Treatment, ITT, and Thyroid Patient Advocacy, TPA).

Thyroid UK are calling for their followers to contact their MPs and say:

- You have concerns that many local CCG prescribing policies for liothyronine (T3) are not consistent with NHS England policy and updated clinical guidance from the British Thyroid Association[19].
- the consequences of this are variations in patient treatment in local areas (postcode lottery) and extra costs caused by ineffective healthcare.
- Briefly explain your circumstances i.e. you have had your T3 withdrawn without referral or you have been refused T3 without referral
- you understand that there will be a members' debate on the cost and policy concerns, outlined in the report, and ask for their support

[17] This sentence was updated, 9th May 2018, it originally stated that Lyn Mynott had met with Vince Cable but this is not correct, the meeting was with ITT. With thanks to Lyn Mynott for the correction. Updated again on 13/6, to include the date of the Commons debate, the Hansard transcript video are both now available to view on our website.

[18] http://thyroiduk.org.uk/tuk/T3-Campaign/Improving%20T3%20Prescription%20in%20the%20UK%20for%20Submission%20to%20NHS%20%20England.pdf

[19] http://www.british-thyroid-association.org/sandbox/bta2016/bta_statement_on_the_management_of_primary_hypothyroidism.pdf

Further references

BTA position statement on T3 for endocrinologists http://www.british-thyroid-association.org/sandbox/bta2016/information_for_endocrinologists.pdf

NHS Consultation response document https://www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-precscribed-in-pc-ccg-guidance.pdf

Dr Toft article in Edinburgh Journal - on treating patients as individuals http://www.rcpe.ac.uk/sites/default/files/jrcpe_47_4_toft.pdf

The European Thyroid Association advises as follows: L-T4 + L-T3 combination therapy might be considered as an experimental approach in compliant L-T4-treated hypothyroid patients who have persistent complaints despite serum TSH values within the reference range, provided they have previously received support to deal with the chronic nature of their disease, and associated autoimmune diseases have been excluded. Treatment should only be instituted by accredited internists/endocrinologists, and discontinued if no improvement is experienced after 3 months. (source: ETA guidelines 2012 The Use of L-T4 + L-T3 in the Treatment of Hypothyroidism https://www.karger.com/Article/FullText/339444)