

Genetic haemochromatosis (GH) in the context of UK health service priorities

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It is difficult to imagine a clinical problem that represents lower-hanging fruit for the government and the NHS. As such, there is no time like the present to elevate the priority of genetic haemochromatosis on the UK health-care agenda.

The Lancet (Gastroenterology and Hepatology) January 2019 ¹

Summary

Genetic haemochromatosis (GH) is poorly diagnosed and managed in the UK. This leads to multiple chronic, expensive, debilitating and even fatal complications of toxic iron overload. The reasons for this are many, but key is a lack of consistent clinical guidelines. What protocols exist are often non-mandatory, owned by individual trusts, inconsistent, poorly adopted, and/or discipline-specific.

Introducing guidelines has the potential to increase diagnosis as much as ten-fold. In turn this will prevent many follow on conditions including cancers, heart failures, diabetes, joint disease, and some of the chronic conditions that are most demanding on our GP / primary care services.

Prevention of disease is at the heart of NHS, PHE and government health priorities. Addressing issues around the early diagnosis of GH can contribute significantly to these objectives.

Diagnosing and treating GH is inexpensive. Guidelines that apply existing knowledge and technologies are all that is required. Iron overload is treated by a process of bloodletting, thus in many cases diagnosis could also lead to a boosting of available blood supplies to NHSBT.

It sounds like a no-brainer to me ...

Julie Elliott MP, at recent meeting of the All Party Parliamentary Group for Genetic Haemochromatosis, on reducing the time taken to diagnose GH and so prevent organ damage

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Background

GH is the most common genetic condition in people of white European origin ². The mutations cause the body to absorb excess iron from the diet, which builds up to highly toxic, even fatal levels. This iron overload causes numerous health problems including chronic and debilitating issues:

Chronic fatigue	Joint pain and disease	Menstrual problems / early menopause
Skin conditions	Sexual health problems	Cardiomyopathy
Mental health concerns	Liver disease and cancer	Diabetes

Iron overload has also been tentatively linked with other health issues including other cancers, eye problems, dental disease and dementias, although these are currently unproven.

Despite being very common and known to be linked with some of our country's major health problems, GH is vastly underdiagnosed.

In the UK approximately 10% of our European and particularly Celtic populations (about 5,000,000) are genetic carriers with one mutated copy of the haemochromatosis gene (HFE). Approximately 0.5% (about 250,000) have 2 mutated copies of the HFE gene and are at risk of iron overload and related diseases. Yet for every patient diagnosed and at risk, there are some 8 to 10 who are undiagnosed and unaware of their risk.

Prof Edward Fitzsimons, Consultant Haematologist, University of Glasgow

Ironically, if GH is diagnosed before significant damage is done to tissues, treatment is effective, inexpensive and in addition could supply blood for NHSBT use.

There are no formal nationally adopted universal clinical guidelines or patient pathways for the diagnosis, treatment, monitoring and management of GH, despite the fact that to do these things more effectively would address several national healthcare priorities, at very little short term cost, while saving considerable resources, suffering and even lives in the longer term.

We know what causes GH; we know how to diagnose GH; we know how to treat GH and prevent the consequent serious health problems. We don't need massive financial investment in research or expensive treatments, we just need common sense protocols, and the application of the knowledge we already have, to diagnose and treat early.

David Head MBA, Chief Executive, Haemochromatosis UK
Speaking at the House of Commons in October 2018

Recent developments

Two recent developments make moving GH up the national healthcare agenda even more pressing.

- The new long term plan for our NHS which emphasises prevention of our major health problems, application of new technologies, and improving patient experiences (pathways).
- The publication of recent research into the impact of iron overload, which clearly shows (a) inconsistencies in patient experience and (b) that prevalence, penetrance and the effects of chronic symptoms resulting from non-diagnosis of GH is far more significant in the UK than was previously understood. ^{3, 4, 5}

Making GH the subject of wide ranging binding clinical guidelines will bring it to the attention of the healthcare professionals who should be diagnosing early. Early diagnosis in turn will address a number of UK healthcare priorities, as outlined below.

The NHS Long Term Plan ⁶

NHS priority: World class care for major health problems ... preventing 150,000 heart attacks ... preventing 14,000 premature deaths ... saving 55,000 more lives a year by diagnosing more cancers early helping 380,000 more people get therapy for depression and anxiety by 2023/24

Iron overload is known to lead to cardiomyopathy and heart failure. Prevention is through effective diagnosis of iron overload before damage is done, followed by de-ironing. Simple pathways for ensuring this happens will contribute to this NHS objective.

Iron overload is known to cause liver cancer (a cancer for which mortality is increasing in the UK). The UK has the overall highest liver cancer incidence, followed by the United States ⁷. Research published this year ⁴ found that 5.8% of all liver cancers occurred in those with two GH mutations. GH has also been linked with colorectal and other cancers. Prevention is by diagnosis of GH before liver damage occurs, followed by de-ironing. Clinical guidelines that ensure this happens will therefore contribute significantly to this NHS objective.

Over 80% of a 2017 survey of 2,000 GH patients report mental health difficulties ³. Whether this is attributed directly to iron or to the stress of dealing with chronic pain and complications, establishing GH patient pathways and protocols that take mental health into account will ensure that those needing therapy for depression and anxiety will receive it, thus addressing this NHS priority.

NHS priority: Support people to age well ... professionals to coordinate care better ... helping more people to live independently at home ... (preventing) unnecessary hospital spells.

Recent reports from The University of Exeter ^{4,5} highlight the significant impact of iron overload on our aging population. The two major biobank studies revealed that haemochromatosis, previously thought to be a low-level health risk, actually quadruples the risk of liver disease and doubles the risk of arthritis and frailty in older age groups. It also increases the risk of diabetes and chronic pain.

Over 80% of haemochromatosis patients report joint pain and or disease, notably arthritis in the hands, feet, knees and hips. Melzer found that in men, 1.6% of all the hip replacements occurred in those with the two haemochromatosis gene mutations. Haemochromatosis UK members report multiple and repeat joint replacements.

Guidelines that lead from patients presenting at a young age with joint pain to testing for iron overload and HFE mutations would be aligned with this NHS priority. Early diagnosis and de-ironing will result in a reduction in the requirement for joint replacements, thus improving independence and reducing the number of hospital spells.

NHS Implementation: 2. Preventing illness and tackling health inequalities: the NHS will increase its contribution to tackling some of the most *significant causes of ill health*, including new action to help people ... avoid Type 2 diabetes, with a particular focus on the communities and groups of people most affected by these problems.

Iron overload is now recognised as a “significant cause of ill health” ^{3,4,5} and should therefore be included as a specific issue to be addressed as part of the NHS long term plan. In particular in the context of this implementation point, iron overload is known to damage the pancreas and cause type 2 diabetes, a consequence that is usually reversed by de-ironing and is totally preventable in the

first place by early diagnosis of GH before the pancreas is affected. Guidelines for healthcare professionals working with diabetes patients and with GH patients should be consistent / integrated.

In terms of groups of people at risk, known GH families, Irish traveller communities and people of Irish and Northern Irish extraction are known to be at higher risk, as the main mutation (HFE C282Y) that causes iron overload originated in Ireland. Guidelines should include reference to these groups.

NHS Implementation: 4. Making better use of data and digital technology: we will provide more convenient access to services and health information for patients...

Clear guidelines have a role to play here in respect of GH. In particular, guidelines for appropriate use of radiology / imaging technology (notably MRI scanning of the liver and CT scanning of joints) as a diagnostic tool will serve to (a) speed diagnosis and therefore prevent further disease and damage, (b) improve efficiency, (c) reduce the need for invasive, expensive and low-accuracy biopsies (and hospital stays), and (d) allow for more efficient and accurate treatment planning.

NHS financial drivers: Test 1: The NHS (including providers) will return to financial balance

Test 2: The NHS will achieve cash-releasing productivity growth of at least 1.1% per year

Test 3: The NHS will reduce the growth in demand for care through better integration / prevention

Test 4: The NHS will reduce unjustified variation in performance

Test 5: The NHS will make better use of capital investment and assets to drive transformation

Patient pathways that lead to early diagnosis of GH will contribute to all 5 tests, on the simple premise that diagnosis need not be expensive and treatment is effective and (for the vast majority of patients) does not involve expensive procedures or drugs. The prevention of GH related liver disease, heart disease, diabetes, joint disease, and chronic conditions will save considerable sums.

Further, early diagnosis will reduce the demand on our primary care service from tens of thousands of chronically affected patients for whom the underlying cause of GH remains unidentified.

Test 4 would in particular be addressed by the introduction of clear clinical guidelines for the diagnosis, treatment, and monitoring of GH patients that are adopted by all disciplines in all trusts.

To summarise in respect of the NHS long term plan; this focuses on the prevention of ill-health so people live “longer, healthier lives”. There is a fundamental link between the early diagnosis and treatment of GH, and the top priorities of the NHS. Put simply, early diagnosis can result in the reversal and/or prevention of all of the health problems listed above. A GH patient who is identified and treated early, and then gives blood in the usual way every quarter, will live a normal healthy life.

“Prevention is better than cure” is a mantra that is no better illustrated by introducing processes and protocols to identify a common condition that is then easily and cheaply treated, and that otherwise leads to complications that impact significantly on NHS resources and on patients’ quality of life

NICE Centre for Guidelines (CfG)

The NICE CfG develops guidance for the handling of many conditions by our health services. These are evidence-based and developed by independent committees, including professionals and lay members, and consulted on by stakeholders. NICE CfG focus is on

- the promotion of good health
- the prevention of ill health
- appropriate treatment and care
- social care and service delivery

Currently however there are no NICE guidelines in respects of any aspect of the GH patient pathway, including for:

- Diagnosis (testing, screening, radiology, referral from primary care)
- Management (referrals, treatment, multidisciplinary care, mental health, radiology)
- Treatment (target measures, venesection protocols, re-referral, alternatives to venesection, donating blood to NHSBT, venesection in old age)
- Ownership (GPs, discharge, consultants, venesection teams, multidisciplinary care, NHSBT)

The development of best practice protocols and/or mandatory national guidelines for genetic haemochromatosis will therefore address all four of the NICE CfG's priority areas listed above.

It is of concern to patients and to Haemochromatosis UK as a patient organisation that there is nothing in NICE guidelines in respect of the UK's most common genetic disorder, one which in turn is known to cause some of our countries priority health problems.

Public Health England

We welcome (the Exeter GH) study and think the work will be clinically very important as the results could have implications for clinical practice and help us find people much earlier, before significant damage is done. This work shows the real benefit to the population of linking academic research to policy and clinical practice.

Professor Debra Laphorne, Director for the South West, Public Health England, January 2019

... for years we have known that prevention is better than cure. We need to help people to stay well and in work for longer, so they need the NHS less and later in life. And when people are unwell, we need to help them stay independent in their own home for longer ... we must seek a better balance between a system focused on detecting and treating illnesses, with one that also predicts and prevents poor health. To achieve this we must ensure prevention is invested in by the NHS.

Duncan Selbie, Chief Executive, Public Health England, *A new vision for prevention*, Nov 2018

Public Health England is working to a set of strategic objectives covering the period 2016 to 2020⁸. There are several sections of this strategy that would be served by the development of national protocols for GH, most notably and unsurprisingly again around the prevention of disease. Page 4 of the PHE strategy includes the following emphasis:

- improving the public's health and wellbeing
- improving population health through sustainable health and care services
- build capacity ... through application of evidence into practice
- promoting a holistic view of an individual's total health and wellbeing
- seeing public health as one system for improving health and wellbeing

Once again, at the risk of becoming repetitive, moving GH up the agenda for all healthcare professionals, through the introduction of consistent clinical guidelines and protocols, will address all of these points, for all the reasons described above

Page 6 includes the following: “prevention is core to the government’s agenda, on which we are a trusted adviser nationally and locally ... early intervention and prevention is recognised as integral to delivering the NHS efficiency challenge”

Quite rightly the NHS and PHE are fully aligned placing emphasis on prevention. Thus all of the references earlier in this document to preventing cancer, heart disease, joint disease and so on, through the introduction of guidelines that will ensure earlier diagnosis and treatment of iron overload, are as relevant here.

The Scottish Intercollegiate Guidelines Network (SIGN)

SIGN collaborate with a network of clinicians, other health and social care professionals, patient organisations and individuals to develop evidence-based guidelines which are intended to

- aid the translation of new knowledge into action
- help professionals and patients understand and use medical evidence
- reduce unwarranted variations in practice
- make sure patients get the best care available

Currently, as with NICE, there are no guidelines in respect of genetic haemochromatosis published by SIGN, despite the fact that GH is more prevalent amongst Celtic people, including the Scots, than across the rest of the UK.

SIGN will often take a lead from NICE when guidelines are developed and implemented and it is highly likely that this would be the case in respect of genetic haemochromatosis, thus impacting across Scotland in the same way as described above.

Matt Hancock

Technology >> <https://www.gov.uk/government/speeches/health-technology-can-help-spot-serious-illness-and-prevent-it>

The Secretary of State has often extolled the use of technology. In respect of diagnosing GH this could include radiography (imaging), machine learning, and taking advantage of cheaper, faster genetic testing. However, with few clinical guidelines for GH as it stands, and poor consistency and adoption where they do exist, it is difficult to see how new technologies will be applied effectively unless protocols are put in place to specify when, why and how they are to be used.

Prevention >> <https://publichealthmatters.blog.gov.uk/2018/11/05/matt-hancock-my-vision-for-prevention/>

... if we get prevention right, it holds the key to longer, healthier, happier lives and a sustainable, high quality health and care system ... it's why I made it one of my big three priorities.

Matt Hancock, Secretary of State for Health and Social Care, November 2018

Those with an understanding of the true impact of iron overload on patients and on our healthcare services believe that improved pathways for GH patients can contribute significantly to this priority.

A note about general practitioners

Multiple appointment over years (even decades) by patients with non-specific chronic conditions weigh heavily on our GP services. GPs will refer, for example, to TATT: tired all the time, used for

heartsink patients - those who make their doctors' hearts sink - who make repeated visits to the surgery but have undefined symptoms.

As well as fatigue, other chronic complaints such as joint pain, skin conditions, sexual dysfunction, undefined abdominal pain, and menstrual problems all lead to multiple GP visits and can all be caused by toxic iron. Earlier diagnosis and treatment of GH will reduce this burden on primary care.

A note about NHSBT (The Blood Service)

The primary treatment for GH is venesection (bloodletting). In most circumstances this blood is currently destroyed despite being perfectly useable. Binding guidelines and protocols around treatment could therefore result in a reliable source of donated blood, whilst also taking pressure off the hospital units that currently carry out thousands of venesections and blood disposals.

The All Party Parliamentary Group for Genetic Haemochromatosis

The recently formed APPG for Genetic Haemochromatosis will be taking the issues raised in this document to the agencies, ministers and senior NHS decision makers who may be able to influence changes in practice and/or the development of formal national guidelines.

A word from Theresa May

Whether it is cancer, heart disease, diabetes or a range of mental illnesses, we increasingly know what can be done to prevent these conditions before they develop – or how to ameliorate them when they first occur. This is not just better for our own health, a renewed focus on prevention will reduce pressures on the NHS too.

Theresa May, Prime Minister, June 2018

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