ALL PARTY PARLIAMENTARY GROUP ON RARE, GENETIC AND UNDIAGNOSED CONDITIONS

Newborn Screening

9 June 2021 via Zoom — the recording of the event can be found here.

Parliamentarians in attendance:

Liz Twist MP (Chair)
Lisa Nandy MP
Peter Dowd MP
Peter Gibson MP
Suzanne Webb MP
Office of Caroline Ansell MP
Office of Marion Fellows MP
Office of Nickie Aiken MP

MINUTES

Liz Twist MP, Chair, APPG on Rare, Genetic and Undiagnosed Conditions

Liz Twist MP welcomed attendees to the meeting and noted that this meeting has come about following on from the Westminster Hall Debate on rare diseases during which newborn screening was raised a number of times.

Liz Twist MP noted that Nickie Aiken MP had asked a question on this issue just yesterday – the Secretary of State for Health and Social Care, Matt Hancock, agreed to meet with Nickie Aiken MP and Baroness Nicola Blackwood.

Currently, in the UK, the heel prick blood test for newborns screens for between five and nine conditions, depending on whether you are in England, Scotland, Wales or Northern Ireland.

Other comparable high-income countries routinely screen for up to 50 conditions. Many people within the rare disease community see the potential of newborn screening to lead to earlier diagnosis of rare and genetic conditions before symptoms arise and, in some cases, earlier intervention can improve the child's outcome.

No new conditions have been added onto the heel prick blood test since 2017 in Scotland, 2015 in England and Wales and 2009 in Northern Ireland.

We invited the UK National Screening Committee (UK NSC), the body that advises ministers and the NHS which conditions to screen, and the Department of Health and Social Care to attend today, but unfortunately they were both unable to join us. The UK NSC have said that they would be willing to meet after the meeting to discuss any outcomes from the day. We will follow up on this after the meeting.

Speakers today include those from the clinical community and those with lived experiences of rare conditions. Liz Twist MP also noted that it was Batten Disease Awareness Day today and that Amanda Mortensen from the Batten Disease Family Association would be speaking later.

Professor Simon Heales, Great Ormond Street Hospital

Professor Simon Heales has been working in the area of inborn errors of metabolism for over 30 years; during this time there have been major changes, particularly in our ability to diagnose and an explosion in the treatments available for children with inherited metabolic conditions. The UK were leaders in the area, however, with newborn screening we are slipping behind – far behind.

Professor Simon Heales' laboratory hosts the largest newborn screening laboratory in the country where they screen for the nine conditions. They are very good at undertaking these tests but there is so much more potential. Colleagues in Europe are routinely screening for around 20 conditions, we are falling behind. We are losing our position on the world stage. The earlier you diagnose a patient the better the clinical outcomes.

We have the willingness, we have the technology but we need the investment. The return on the investment is huge: making the outcomes for people living with a rare condition better. Hospital demands and care will also be less as people are treated earlier.

Professor Laurent Servais, UK Newborn Screening Alliance & Muscular Dystrophy UK Oxford Neuromuscular Centre

Professor Servais showed a short video to attendees [see 13:00 into recording: vimeo.com/561340806]. The video shows two siblings, both with spinal muscular atrophy, type 1. The elder sibling was treated after the onset of his symptoms – the treatment has saved his life but he has profound disabilities. The younger sibling was treated before the onset of symptoms and has developed completely normally. The administration of treatment is only a few weeks apart but the impact is significant; both on the patient and the cost on the health services. Delaying treatment until the onset of symptoms costs the health service many millions of pounds (in addition to the cost of the initial treatment).

This case is not isolated. Three studies, with three different medications, have all shown that a patient treated after the symptoms will never walk and will have serious disabilities. Patients treated before the onset of symptoms will be able to walk and run and live normally.

Newborn screening for SMA is happening in many other countries. In the UK, every five days a baby is born with this condition. Two years ago newborn screening was rejected for SMA in the UK, not because of the lack of evidence or information but because of the decision making process. Since then 140 babies with SMA have been born, they, and their families will live a life managing profound disabilities and multiple hospital appointments. If we have to wait another two years before we get screening that will be another 140 babies, and some of these will die because they have been diagnosed too late. We cannot make this mistake again.

Dr Will Evans, Niemann-Pick UK

Dr Evans is the chairman of Niemann-Pick UK and father of Sam, who has Niemann-Pick type C. It's important to remember a rare disease diagnosis affects the whole family.

Niemann Pick diseases are ultra-rare inherited metabolic diseases, with approximately 130 people affected in the UK. A child with classical Niemann-Pick type C will develop normally but will start to have problems as they start school. The disease progresses until they are fully dependent on care for all day-to-day activities. Patients with classic Niemann Pick type C typically die in their late teens and early twenties.

However, there is hope. There is a significant amount of research and interest in drug development in the area. A licensed therapy already exists and is available on the NHS and more treatments are imminent. Timing of treatment is key. With neurodegenerative diseases when the neurons/ brain cells have been lost they can't be replaced. A treatment that slows or stops neuronal loss and disease progression needs to be started before the disease has progressed. Unfortunately, patients still experience a substantial diagnostic delay: typically three to five years from the onset of neurological symptoms. Newborn Screening is a potential solution for Niemann Pick type C.

A proportion of patients with Niemann-Pick type C are diagnosed when they are newborns due to liver disease. This has given the Niemann-Pick community an ability to compare those who receive an almost pre-symptomatic diagnosis, at least from a neurological disease perspective. This was the case with Sam who was diagnosed at four months old. As devastating as the diagnosis was, it enabled Will and his wife to understand and access care and support early on. It provided the opportunity to plan and make reproductive choices.

Dr Evans emphasised the value of early diagnosis and that diseases such as Niemann-Pick type C have an impact far beyond the individual affected. It is important to consider that the true value of early diagnosis can only be realised when it is considered in the context of the wider family.

Amanda Mortensen, Batten Disease Family Association

Amanda is the chief executive of Batten Disease Family Association. Batten disease is a rare, terminal neurodegenerative condition that causes children to lose their ability to talk, walk and see. Children also develop complex epilepsy and dementia. It is a devastating diagnosis that affects not just the individual but also the whole family.

The charity supports 115 children across the UK who have 13 types of Batten disease. Just one, CLN2, has a treatment – an enzyme replacement therapy. It is entirely life changing and the earlier a child starts on treatment, the better the outcome. 24 children are currently accessing this treatment across the UK. It slows down the progression of the disease so children are able to maintain skills such as walking and talking. It reduces the severity of epilepsy and improves quality of life. One child has just transitioned to adult services – historically children would have died before the age of 12. But children are not being diagnosed early enough.

Currently, families face a diagnostic odyssey and diagnosis still takes many years. Family stories of diagnosis have common themes, that parents 'sensed' something was wrong but were told to watch and wait, that early signs of speech loss of being 'wobbly' weren't taken into account alongside a first seizure, that they were told by the paediatrician 'not to go for genetic testing just yet as it's very stressful', they have had a myriad of tests but years have passed until they were tested for Batten disease. It seems there is no consistency in the system, with children seen by different professionals at different points and some opting for enzyme testing, others for genetic screening.

The test for Batten disease can be easily adapted for neonatal screening. We must identify children as early as possible as there is now a treatment that is transformational to their quality of life and health outcomes.

It is often through a diagnosis of a sibling that a child is identified early. In the UK, one family from Newcastle has two children on treatment. Their youngest child started an enzyme replacement therapy on a sibling trial before the age of two, the youngest in the UK to start treatment. The difference it has made is incredible – this child is a very able little girl at the age of five, at mainstream school and learning new skills, at an age when children not on treatment have lost most of their skills and need round the clock care. We have a duty to give other children this chance too.

Karen Harrison, Alex - The Leukodystrophy Charity

Karen is the support services manager for Alex - The Leukodystrophy Charity. She has two sons affected by adrenoleukodystrophy (ALD), a rare inherited disorder affecting 1 in 17,000. ALD causes damage to the adrenal glands and white matter of the brain, causing a progressive loss of physical and mental skills. Without timely treatment affected boys eventually lose all function, death often occurs within 18 months to two years after diagnosis, some boys will live for many years, but will be very severely disabled and dependent on others for all their care needs.

Karen's identical twin sons, Cameron and Alexander were born in 1996 and all was well until they were six years old. Alexander started to become disorientated, and his behaviour changed. After a number of tests the family eventually ended up with a Consultant Neurologist who gave the diagnosis of Adrenoleukodystrophy. They were told that this was a degenerative genetic disease and due to the fact that Alexander was symptomatic there was no treatment available, and they should take him home and make the most of the time they had left with him.

Cameron then had to be tested and he too was found to have ALD, he had no obvious symptoms at that time. There was a very small window of opportunity for Cameron to have a bone marrow transplant. Bone marrow transplant has been used effectively for decades and if given when there is very little disease affecting the brain it will halt the progression of the disease and boys will go on to live a normal healthy life. Sadly, it was just too late for Cameron who continued to deteriorate, he is now severely disabled and requires round the clock care, he is 25. Alexander died aged eight, just 18 months after diagnosis; he went through the most horrendous symptoms – he was bind, deaf, unable to speak and had no voluntary movement.

Karen sees many families where they have to lose one son to save the other: often the older brother will be diagnosed too late for treatment, but this means that the younger brother is diagnosed early and can be monitored closely using MRI scans and if needed will have bone marrow transplant in good time. In the past three months four boys have been diagnosed with ALD, three out of the four are too late for treatment and will inevitably deteriorate into a semi vegetative state. The other boy, aged two, was diagnosed due to his cousin in California being diagnosed through Newborn Screening.

In 2016 Alex TLC submitted their application to the UK National Screening Committee to have ALD added to the list of conditions screened for at birth. They were supported by specialists both in the UK and abroad and were able to show cost benefit to the NHS. Unfortunately, the application was rejected in 2017, with the NSC asking for further evidence. In October 2020 the NSC opened a Public Consultation to review NBS for ALD which closed in January 2021. Alex TLC submitted a response and coordinated a campaign to ensure as many individual responses from those affected by ALD were also submitted. The website states the review decision is estimated to be completed in March 2021, however they are still waiting.

Mandy Sanderson, Max Appeal

Mandy Sanderson works with the charity Max Appeal. In particular, Mandy helped with their newborn screening application process. Mandy also has a child with 22q deletion. Max Appeal is a charity that supports families with 22q11.2 deletion and duplication syndromes ('22q'). Max Appeal is one of the largest charities in the world supporting this condition. 22q is a genetic condition that is as common as cystic fibrosis and causes a range of health problems and learning disabilities from birth. Detection of 22q is highly variable and often dependent on presentation of symptoms.

Identification of 22q at birth would enable diagnosis, care and treatment for the large range of medical conditions and complications associated with 22q including cardiac, skeletal and immune system abnormalities, speech difficulties/delay, developmental delay and cognitive impairment. The impact of late diagnosis for patients and their families is considerable, contributing to the diagnostic odyssey and additional strain on carers. Late diagnosis reduces the opportunity for appropriate interventions and support, increasing the likelihood of adverse medical, physical and neuro-developmental outcomes. For example, 22q is the leading cause of psychosis and schizophrenia: appropriate early intervention at the first sign of delusional thinking may prevent this from being a life-long, debilitating condition.

In December 2018, an application to the UK National Screening Committee was submitted and the application was approved to proceed to the next stage in the process, a research-evidence map. The evidence map sought to establish three things: the presence of national or international guidelines on population screening, research indicating population prevalence of 22q in the UK, and the availability of a suitable screening test. It was difficult to establish the prevalence of 22q in the UK – Mandy questioned the emphasis on prevalence being UK bound. In February 2020, the UK National Screening Committee concluded that the volume and type of evidence available at that time was insufficient to progress the application further.

In order to reduce the burden of disease, disability and death and life long challenges for the babies with 22q being born every day in the UK, newborn screening is essential to ensure early diagnosis and early intervention and care; this will make the biggest difference to those living with 22q.

Georgina Morton, ArchAngel MLD Trust

Georgina Morton set up ArchAngel MLD Trust after her daughter Ava was diagnosed with Metachromatic Leukodystrophy in 2013. ArchAngel awards grants to UK MLD affected families and is spearheading a campaign pushing for review and expansion of the UK Newborn Screening Programme in conjunction with Nickie Aiken MP.

Georgina questioned why the UK is only screening for nine conditions in the UK, when we have brilliant scientists, excellent facilities, outstanding clinicians, and transformative treatments?

Patient advocacy groups have done much work in the newborn screening arena to identify the problems and flaws in the system. These boil down to a few key areas:

- Newborn screening sits within the process for *all* screening programmes for *all* conditions affecting the UK population. This results in a lengthy queue and unfavourable position for rare conditions as conditions that affect a wider number of the population, such as cancer and heart conditions, are prioritised.
- There are very few rare disease experts involved in the assessment process for newborn screening, and those that are, are not adequately involved in the decision making process.

- There are unrealistic evidence parameters specific to rare diseases. These parameters do not work as they are designed for the wider screening programmes. This means that validated sources from other countries are dismissed because it does not fit the current guidelines. The UK National Screening Committee wastes years collating evidence that has been gathered elsewhere.
- There is no time frame for which a condition needs to be assessed. Severe combined immunodeficiency (SCID) has been in the system for over 10 years.
- There is a quagmire of decision-making: inconsistent, unacceptably protracted and no accountability. There is no opportunity for patient organisations and representatives to comment during the process.

Georgina took these issues to Nickie Aiken MP. They are working with a number of rare disease patient groups with an interest in newborn screening; these groups represent hundreds of rare conditions and many thousand people affected by rare conditions. They worked with leading scientists and clinicians to develop a campaign. They called for urgent change to the system.

Nickie Aiken MP has secured a number of key meetings. The first with Baroness Blackwood who advised that the group call for key policy changes that would address the fundamental issues, not a whole system reform which would take too long. She also noted that the community must be united as policy-makers need to hear from one voice.

The campaign is now calling for three policy changes that would lead to transformation and improvement to the current newborn screening programme, and future proof it for the advances in science and technology that are on the horizon. These three changes were well received by Lord Bethell who thought they were well thought out and deliverable:

1. The formation of a dedicated team of newborn screening experts to solely evaluate conditions to be added to the newborn screening programme and to undertake the formal engagement of consultees, including clinical and scientific experts relevant to the condition/group of conditions being appraised. (Thereby taking this work out of the wider screening programme).
2. The establishment of a streamlined evidence review process for evaluation of conditions to be added to the UK newborn screening programme, which is relevant to rare diseases and automatically accepts a wide range of evidence currently available from validated and reputable sources.
3. A timeline to ensure appropriate efficiency and accountability for this process.

Discussion

Peter Gibson MP: Keep up the pressure on parliamentarians to keep pushing this forward. Peter will raise this with his meetings with the Department of Health and Social Care. Raise this campaign with your local constituency MPs.

Professor Heales: We need capacity building in the labs if we are to expand; we don't have that at the moment. But this can be done quickly with the right investment.

Professor Servais: The process needs to be easy to adapt because changes can happen very quickly: diseases that were impossible to treat five years ago are treatable today. This is good news and this progress will continue. Any programmes that we start must be able to adapt quickly. The problem with the system today is that it does not adapt. It is extremely slow even when there are treatments that exist for conditions. We should not have a system in place that requires 10 years worth of evidence from the UK. We need a system that is dynamic and can rapidly include new conditions for testing.

Gail Baxter: Early diagnosis is vital. Gail sees the difference, first-hand, that an early diagnosis can make. One daughter saved the other. Early treatment is transformative.

Sara Hunt: One voice for the campaign is key to avoid dilution of the message.

Helen Llewellyn: As the UK National Screening Committee (UK NSC) has promised to meet with the APPG, could the APPG ask the UK NSC to ensure that newborn screening is higher in its priorities and that a methods review is conducted to ensure that the evaluation of conditions to be added to the screening panel better reflects the needs of children and families affected by rare inherited conditions.

There was a consensus among those present supporting the three key policy asks presented by Georgina Morton. Attendees also called for regular, meaningful and transparent engagement with stakeholders.