Newborns with Down's syndrome to receive leukaemia test under new guidelines

June 20 2018

New genetic testing has been developed at the University of Oxford to detect early signs of a potentially fatal condition that can also develop into full blown leukaemia in children with Down's syndrome.

Despite children with Down's syndrome having around a one in 50 chance of developing acute myeloid leukaemia (AML), compared to a one in 7,000 chance for children without Down's syndrome, monitoring procedures have been unclear until now.

Early intervention greatly increases chances of survival for children who develop symptoms and new guidelines for doctors recommend that all children with Down's syndrome receive a blood test within three days of birth to identify if they are at risk.

The new British Society for Haematology (BSH) guidelines, published in the *British Journal of Haematology*, are a result of years of research and clinical studies funded by Bloodwise and Children with Cancer UK at the University's MRC Weatherall Institute of Molecular Medicine.

Around one in 10 children with Down's syndrome are born with a condition called 'transient leukaemia of Down's syndrome' (TL-DS), which goes on to develop into AML in one in five cases. The new guidelines recommend that a full blood count, which measures levels of different types of blood cell in the blood, is taken within three days of birth in children with Down's syndrome.

If blood tests reveal that there are high levels of abnormal cells in the bloodstream and there are physical symptoms, babies should be given a test, developed by the Oxford group, to screen for mutations to a gene known as "GATA1." GATA1 gene mutations are present in both TL-DS and AML in children with Down's syndrome.

TL-DS itself carries significant risks, with up to one in five children with the severe form dying within six months of diagnosis as a result of the condition—most commonly from liver dysfunction. The new guidelines recommend that all babies confirmed to have TL-DS are monitored regularly and that children who develop life-threatening symptoms should be given low-dose chemotherapy immediately.

Children with TL-DS who do not experience life-threatening symptoms should be monitored for a number of years to check for any signs of progression into leukaemia, so that treatment can start immediately if it does.

Professor Irene Roberts, at the University of Oxford, who led the research said: "Until now guidelines for the treatment of children with Down's syndrome at risk of developing leukaemia have been vague, implementation has been haphazard and children have been diagnosed late as a result. Early intervention greatly increases children's chances of survival if symptoms do develop, helping to save lives."

Professor Paresh Vyas, from the University of Oxford, said: "A simple test can ensure that those children at risk of cancer are put under the care of a specialist paediatrician. They are properly monitored and are treated straight away when symptoms develop. Importantly, it also provides reassurance to the parents of those children not at risk, removing the fear and worry of leukaemia for many families."

Dr. Alasdair Rankin, Director of Research at Bloodwise, said: "Step-

changes in care for people with blood cancer don't always come from new drugs – new tests and guidance for how doctors deliver care can make a huge difference very quickly. This new diagnostic test, the new clinical guidelines and the excellent research that has delivered them will change the lives of children with Down's syndrome and their families. Bloodwise will be keen to make sure that testing is available nationally for all newborns with Down's syndrome and that the new guidance is followed in practice."

Cliff O"Gorman, Chief Executive of Children with Cancer UK, said: "Children with Down's syndrome are far more likely to develop acute myeloid leukaemia than those without – yet until now testing and monitoring for signs of the condition has been inconsistent.

"Early intervention is crucial and these new clinical guidelines will help ensure that children with Down's syndrome who develop signs of myeloid leukaemia have the best possible chance of survival. It is vital that we continue to fund pioneering research to improve the quality of care for young cancer patients, and keep more families together."

The BSH guidelines are published online in the *British Journal of Haematology* under the title "Guidelines for the investigation and management of Transient Leukaemia of Down Syndrome."

Written by expert consultants and clinical scientists currently practising in the UK, BSH guidelines provide up-to-date evidence-based guidance on the diagnosis and treatment of haematological diseases.

More information: Oliver Tunstall et al. Guidelines for the investigation and management of Transient Leukaemia of Down Syndrome, *British Journal of Haematology* (2018). DOI: 10.1111/bjh.15390

Provided by Bloodwise