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Pioneering treatment reduces disability in premature babies with serious brain hemorrhage

The research, led by Andrew Whitelaw, Professor of Neonatal Medicine at the University of Bristol, and Ian Pople, paediatric neurosurgeon at North Bristol NHS Trust, has shown that, after a haemorrhage, the fluid inside the ventricles contains substances potentially toxic to the immature brain.

In 1998, Professor Whitelaw and Ian Pople pioneered a technique by which the inside of the brain was "washed out" to remove the toxic substances.

The Bristol team report on this pioneering work in an article published online in *Pediatrics*, the journal of the American Academy of Pediatrics.

One of the most feared complications of being born very early is bleeding into the ventricles in the centre of the brain. A large haemorrhage usually injures the developing brain with consequent cerebral palsy and serious learning difficulties in several hundred children each year in the UK. In about half of the children, fluid builds up inside the brain causing the brain and head to expand excessively. This condition is called 'hydrocephalus'.

Until now, no treatment in these premature babies has been shown to reduce disability, or improve any aspect of health. The standard approach has been to repeatedly insert needles into the spine or head to remove fluid until, after several months, a permanent surgical "shunt" drains fluid from the brain to the abdomen.

Professor Whitelaw said: "Premature babies are particularly at risk of bleeding because in the middle of pregnancy, the fetus has many fragile blood vessels in the centre of the brain. These blood vessels shrink by full term and bleeding is rare in babies born at 40 weeks."

Professor Whitelaw and Ian Pople have researched the mechanisms and treatment of the condition called 'hydrocephalus' over the last 20 years.

If a premature baby was shown by repeated ultrasound scans to have had a large haemorrhage and then expanded ventricles, the baby was anaesthetised and two tubes were inserted into the ventricles in the brain. One tube was used to continuously drain out the cola-coloured fluid while the other tube was used to let clear fluid flow in. The pressure in the brain was measured continuously and more fluid was drained out than flowed in so the brain slowly decompressed. When the fluid draining out cleared, the two tubes were removed. This took on average three days. After four years work on the feasibility and practicality of the technique, a randomised trial, funded by grants from Cerebra and the James and Grace Anderson Trust, was started.

From 2003 to 2006, 77 premature babies with large brain haemorrhages in Bristol, Glasgow, Katowice (Poland) and Bergen (Norway) were recruited. Thirty-nine babies had the ventricles washed out using the Drainage, Irrigation and Fibrinolytic Therapy (DRIFT) and 38 had standard treatment.

When they were two years old, independent assessors examined all the survivors. Of 39 infants assigned to being washed out, 21 (54 per cent) died or were severely disabled versus 27 of 38 (71 per cent) in the standard group. Amongst the survivors, 11 of 35 (31 per cent) in the DRIFT group had severe cognitive disability versus 19 of 32 (59 percent) in the standard group. Median Mental Development Index was 68 (out of 100) in the washout group, and below 50 with standard care. These results are statistically and clinically significant.

Ian Pople said: "This is the first time that any treatment anywhere in the world has been shown to benefit these very vulnerable babies. Initially known as "Drainage, Irrigation and Fibrinolytic Therapy (DRIFT)" this treatment is now called "ventricular lavage" and it is hoped that in the very near future it will be set up as a service at Southmead Hospital in Bristol."

The patient, Isaac Walker-Cox

Isaac Walker-Cox was one of the first babies to have the pioneering 'brain-washing' treatment following a brain haemorrhage after being born 13 weeks early at Southmead Hospital in Bristol.

He is now a happy nine-year-old who loves school and playing on his computer but in 2000 his parents Rebekah and Steven Walker-Cox, from Yate, South Gloucestershire, made the brave decision to allow doctors to carry out the revolutionary treatment on their fragile son to wash out toxic fluids that were inflating his brain. At that time Isaac was one of only a handful of babies who had had the Drainage, Irrigation and Fibrinolytic Therapy (DRIFT) pioneered by Andrew Whitelaw, Professor of Neonatal Medicine at the University of Bristol, and Ian Pople, paediatric neurosurgeon at North Bristol NHS Trust.

Isaac was born 13 weeks early weighing just 2lbs and 10oz at Southmead Hospital and at just 48 hours old he had a haemorrhage on the right side of his brain.

The ventricles in Isaac's brain were filling with cerebrospinal fluid (CSF) and blood causing 'hydrocephalus', where a build-up of fluid puts pressure on the brain.

The standard treatment for the majority of patients with 'hydrocephalus' after a haemorrhage is to have needles inserted repeatedly into the spine or head to drain fluid and, after two to three months to have a shunt inserted permanently connecting the brain to the abdomen. But this treatment has risks including infection and sudden blockage.

Professor Whitelaw and Mr Pople's long-term study published online in Pediatrics, the journal of the American Academy of Pediatrics, has shown that babies who have had DRIFT instead of standard treatment go on to have less developmental problems into childhood.

The study showed that at two years old children who had had DRIFT after a brain haemorrhage when they were babies were less likely to have severe cognitive disability and their mental development was higher than in children who had standard treatment.

Isaac had the DRIFT procedure when he was just two weeks old and was attached to a machine for four days to pump out the fluid.

Mrs Walker-Cox, 36, said: "We were told after the haemorrhage that Isaac may not make it through the night, that he had one per cent survival rate.

"When Professor Whitelaw told us about the research trial, we thought we didn't have anything to lose.

"Professor Whitelaw had so far carried it out on 17 babies so it was very new but we decided that if it worked it would mean Isaac did not have to have a shunt.

"We just kept watching the liquid go through the pump day after day, just waiting to see if it worked."



Isaac now has mild paralysis on the left side of his body caused by the haemorrhage but he doesn't let it hold him back.

Mrs Walker-Cox said: "We were told Isaac may not be able to walk, and we didn't think he would be able to go to a mainstream school because we expected he would have a learning disability.

"But mentally he has no problems at all, he has an above average reading age and he is very good with computers.

"He just gets on with life and is an outgoing, happy little boy.

"We are really excited to have been part of the DRIFT treatment in the early days, it's nice for Isaac too because he knows what he has been through and he feels proud."

Professor Andrew Whitelaw, a Neonatologist and Ian Pople, Paediatric Neurosurgeon at North Bristol NHS Trust, have pioneered DRIFT at the University of Bristol and it is hoped it will soon be offered, renamed 'ventricular lavage', as a service at Southmead Hospital in Bristol.

Isaac Walk-Cox lives in Yate, South Gloucestershire, with mum Rebekah, 36, dad Steven, 35, and brothers Owen, six, and Ethan, three.

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