Parent Information Sheets

ENLIVEN TRIAL
Endoscopic Lavage after Intraventricular Haemorrhage in Neonates

Thank you for agreeing to consider enrolling your child in this research study. It is important that you feel empowered to make an informed decision about whether to participate or not. The aim of this leaflet is to give you information about what intraventricular haemorrhage is, what posthaemorrhagic hydrocephalus is and about what treatments we use at Great Ormond Street Hospital.

If you have any questions the team are very happy to talk about any and all aspects of your child's treatment and please be reassured that if you decide that you do not want your child to be involved in the study, then this will not in any way impact on the quality of treatment that your child will receive.

Why do premature babies suffer brain bleeds?

Bleeding tends to occur in a region of the brain called the germinal matrix, the cause of bleeding is not completely understood but during pregnancy the newly formed blood vessels are quite fragile and the brain tissue is only loosely wrapped around them which may explain the increased risk of bleeding. The muscle layer that normally surrounds the blood vessels is also not completely formed which means that premature babies lack the ability to control the blood pressure within their brain and so fluctuations in blood pressure may also increase the risk of bleeding.

How will this bleed affect my child?

Many premature babies who suffer brain haemorrhage develop entirely normally and make the transition into adulthood without any difficulty. Unfortunately this is not the case for all babies and bleeding in the brain can cause a risk to life and can also cause problems with vision, hearing, cognition (understanding) and motor function (movement).

It has been shown that the severity of the bleed effects outcome, with more severe bleeds associated with an increased risk of developing problems. Also the development of hydrocephalus is associated with a higher risk of developing problems.

What is hydrocephalus and why does bleeding cause this to happen?

Within the brain there are chambers, called ventricles, which contain fluid (see Diagram 1 below). This fluid is known as Cerebrospinal Fluid (CSF) and it is constantly being made within the ventricles, circulated around the brain and spinal cord and ultimately reabsorbed.

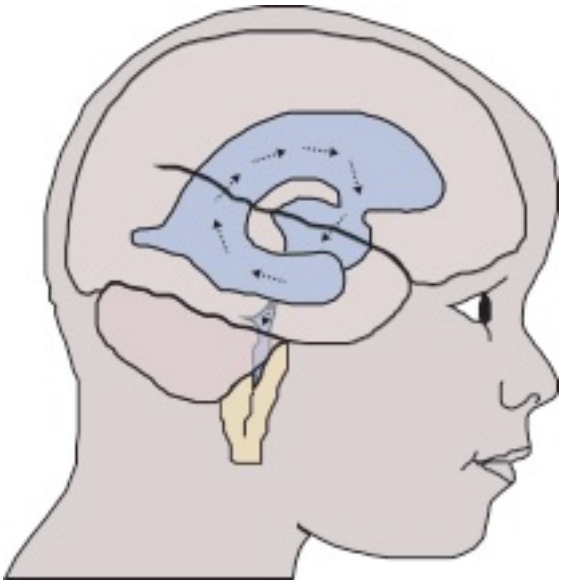


Diagram 1: *The fluid chambers (known as ventricles) within the brain are represented in blue and the flow of fluid (cerebrospinal fluid CSF) is shown by the arrows.*

Blood within the ventricle is thought to clog up this flow of CSF around the brain and, when the CSF cannot flow properly around the system is begins to back up causing increased pressure within the ventricles (see Diagram 2 below) much like a rock damming up a stream.

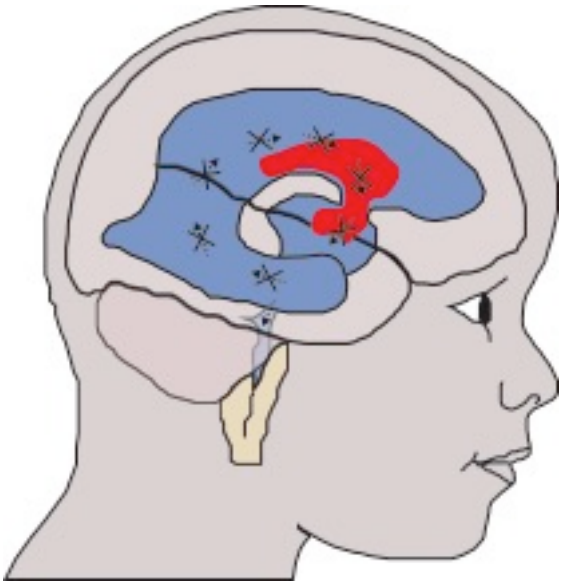


Diagram 2: *When bleeding occurs within the ventricle (shown in red) it can block the normal flow of CSF (shown as arrows with crosses through them) and this can cause the fluid to accumulate causing the ventricle to increase in size. When this happens it can put pressure on the developing brain and leads to a condition known as hydrocephalus.*

As fluid accumulates inside the ventricles, the pressure on the surrounding brain tissue also increases. This can impact on the blood supply to the brain and on the function of the brain tissue. Pressure on the brain tissue can lead to irritability and vomiting and is associated with problems controlling eye movements, blood pressure and heart rate. It also causes the size of the head to increase.

This pattern of symptoms is known as hydrocephalus and if left untreated this can significantly impact on the brain, as such surgery is used to treat hydrocephalus to prevent the build up of fluid and pressure impacting on the brain.

What treatments are used

As discussed above progressive hydrocephalus is dangerous for the developing brain and needs treatment. To do this requires an operation; under general anaesthetic a small incision is made through the skin and skull and a narrow tube is passed into the ventricle. A 'pocket' is then made underneath the scalp so that fluid is allowed to drain out of the ventricle and gets absorbed into the space underneath the scalp (see Diagram 3 below). This procedure is known as a Ventricular Subgaleal Shunt (VSG) and is the current standard of care at Great Ormond Street.

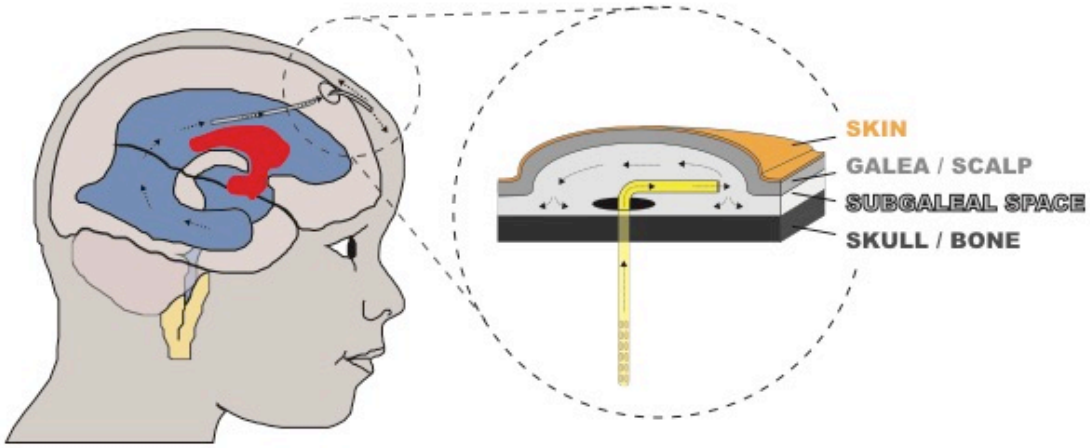


Diagram 3: *To relieve the pressure within the ventricle an operation is necessary to make a small hole in the skull. A narrow tube is then passed through the brain tissue and into the ventricle. By making a pocket underneath the scalp the fluid is allowed to drain out of the ventricle and is absorbed into this space.*

The VSG is a temporary solution, which buys time before making a decision about whether your child will need a permanent ventricular peritoneal shunt (VPS). It allows your child to gain weight, develop their immune system and thickness of skin and allows the blood in the ventricles to clear. The VSG can be used for a number of weeks and if necessary we may take off some fluid from the pocket using a needle and syringe to relieve any build up of pressure.

When your child weighs more than 2kg a decision is made whether they will need a permanent ventricular peritoneal shunt, this is essentially the same system as the VSG however instead of diverting CSF under the scalp it diverts it to the abdomen. If a ventricular peritoneal shunt becomes necessary for your child you will be fully informed about what this procedure entails.

What is Neuroendoscopy and why do you think it might help?

In addition to placing the Ventricular Subgaleal shunt as discussed above, what we propose to do is pass a small camera into the ventricle and washout the blood from the inside of the ventricle (see Diagram 4)

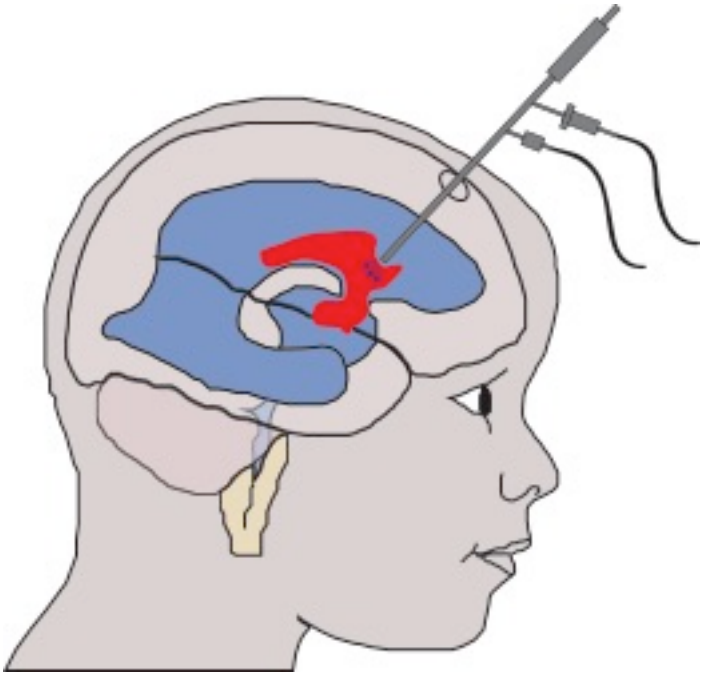


Diagram 4: *The Neuroendoscope consists of a small camera and a water outlet. The endoscope is passed into the ventricle and water is used to wash away the blood clot.*

Neuroendoscopy is a well-established technique that has been used extensively to treat other diseases and we have found the risks associated with it to be low. As such what we are proposing is a novel use of an existing technique rather than an entirely new technique.

We think that it is worth trying Neuroendoscopy for two reasons: a small trial in Germany suggested that it might reduce the risk of developing hydrocephalus and a separate trial in Bristol has shown that washing out the ventricles (using a different technique to Neuroendoscopy) may reduce the risk of developing severe disability but clear evidence is still lacking.

Is Neuroendoscopy safe?

Neuroendoscopy is a well-established technique in Paediatric Neurosurgery, however using the endoscope in this way is a more invasive procedure that will increase the surgical time and length of anaesthesia. Whilst the team at GOSH have a lot of experience in using Neuroendoscopy, and the procedure is undertaken with the greatest possible care, the risk of causing harm cannot be entirely excluded and at present the benefits of using Neuroendoscopy are unproven. This is why we feel that this study is important so that we can understand if Neuroendoscopic washout is safe and effective and if so whether it should be done in all cases of haemorrhage?

The Neuroendoscope is passed down the same tract as the ventricular subgaleal shunt, however it has a slightly larger diameter than the VSG catheter and so theoretically may cause increased damage to brain at the point where the camera is passed into the ventricle (see Diagram 5 below).

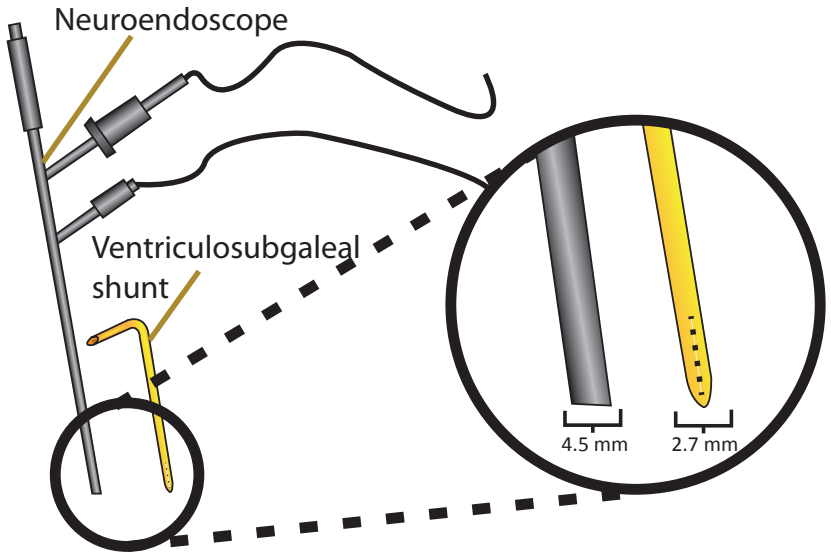


Diagram 5: *The Neuroendoscope is slightly wider than the subgaleal shunt as shown as such this requires a slightly larger hole to be made through the substance of the brain in order to pass the camera into the ventricle*

In addition, the ventricular washout with the Neuroendoscope may cause fluctuations in salt levels. We will monitor this very closely following the operation. It is very unlikely that any participants in this research will come to any harm but we are obliged to mention this possibility. In the event that something does go wrong and your child is harmed during the research study and this is due to someone's negligence then you may have grounds for a legal action for compensation against University College London or Great Ormond Street Hospital NHS trust but you may have to pay your legal costs. The normal NHS complaints mechanisms will be available to you.

If we decide to enrol our child in the study what happens then?

If you agree to participate in the study, then your child will be randomly assigned to one of the two study arms. Infants in the control group will receive the current best therapy via a Ventricular Subgaleal Shunt (as shown in Diagram 3) and infants in the intervention group will undergo intraventricular washout of the blood clot (as shown in Diagram 4), followed by insertion of a Ventricular Subgaleal Shunt. All other aspects of treatment will be identical in both arms of the study.

At the time of the operation we routinely take a sample of Cerebrospinal Fluid (CSF), which is sent to the lab for analysis. With your permission we would like to take a second sample of CSF to use for research. Taking an extra sample in this way will have no impact on your child as this CSF would normally be discarded. If you have any objections to taking a sample of CSF for research purposes then please let a member of the team know and this will not be taken.

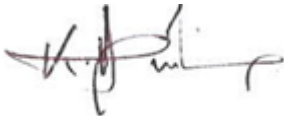
As part of the routine standard of care that we provide at GOSH, your child will undergo an MRI scan when they reach full term, this is performed to help with decision making regarding the need for ventricular peritoneal shunt, a further MRI scan will then be performed at around 6 months, to monitor brain development.

With your permission, when these MRI scans are performed (at around term and 6 months), we would like to perform some additional scans to obtain greater detail about how the brain is developing. These extra scans will prolong the time taken to scan by around 20 minutes, MRI scanning is not thought to causes any harm and the extra scan time should pose no extra threat to your child. If you do not wish your child to undergo the advanced MRI imaging then please let a member of the team know and they will be removed from this aspect of the study.

If your child should become unwell and there is a clinical suspicion that the shunt may be blocked then a CT scan may be performed at your local hospital. This is part of standard clinical care and no extra CT scans will be performed as a result of being enrolled in the ENLIVEN trial. CT scans use ionising radiation to form images of the body and provide the doctor with clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The chances of this happening to your baby are the same whether you take part in this study or not.

You can choose to remove your child from the study at any time and your decision to participate in the study, or not, will have no impact on the standard of care that you will receive. If you agree to include your child in this study, then information about them and their treatment will be stored on secure computers at Great Ormond Street Hospital for a period of around ten years, after which it will be removed.

Thank you for taking the time to read this information and for considering enrolling your child in this study.



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