Research Protocol

# Is endoscopic third ventriculostomy an effective treatment in patients with hydrocephalus and cerebrospinal fluid shunt malfunction?

Version 1.0
Date: September 11, 2006

Contents:

**Signatures of study participants:**

Darach Crimmins
Consultant Neurosurgeon

Paul Chumas
Consultant Neurosurgeon

Atul Tyagi
Consultant Neurosurgeon

Roddy O'Kane
Neurosurgical Specialist Registrar

Roberto Ramirez
Neurosurgical Specialist Registrar

Tony Goddard
Consultant Neuroradiologist

## Research Team contact details:

Darach Crimmins
Consultant Neurosurgeon
Department of Neurosurgery
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Phone: 0113 3928413
Fax: 0113 3926336
Email: Darach.crimmins@leedsth.nhs.uk

Paul Chumas
Consultant Neurosurgeon
Department of Neurosurgery
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Phone: 0113 3923297

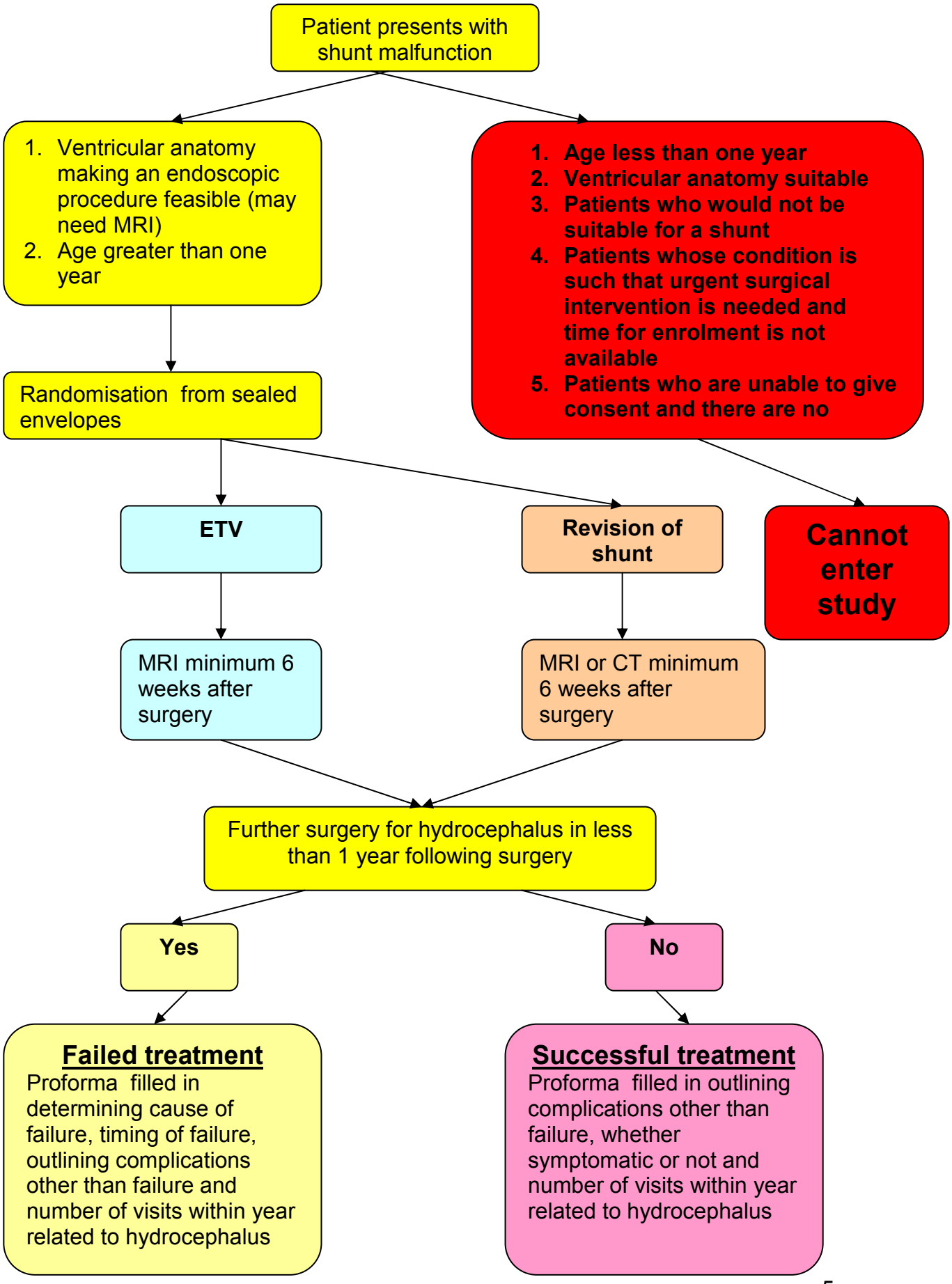
Atul Tyagi
Consultant Neurosurgeon
Department of Neurosurgery
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Phone: 0113 3928103

Roberto Ramirez,
Neurosurgical Specialist Registrar
Department of Neurosurgery
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Pager: 80-1203

Roddy O'Kane,
Neurosurgical Specialist Registrar
Department of Neurosurgery
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Pager: 80-1202

Tony Goddard
Consultant Neuroradiologist
Department of Neuroradiology,
G Floor, Jubilee Wing,
Leeds General Infirmary,
Leeds LS1 3EX
Phone: 0113 3926820

**Summary of treatment protocol**



**Introduction:**

Hydrocephalus is a pathological condition that results from overproduction or under-absorbtion of cerebrospinal fluid (CSF) or obstruction of CSF flow pathways in the ventricle or subarachnoid spaces. It can be congenital (occurring in 4/1000 live births) or acquired due to intracranial haemorrhage, infection or tumours.

Hydrocephalus is often classified into:

- Obstructive (non-communicating)
    - Tumours (obstructing CSF pathways most commonly in the posterior fossa)
    - Congenital aqueductal stenosis
    - Fibroses of leptomeninges
        - Haemorrhage
        - infection
    - Dandy-Walker syndrome
    - Vascular malformations
    - Intracranial cysts (e.g. arachnoid cysts)
    - X-linked hydrocephalus
- Communicating (due to failure of CSF absorption into the venous sinuses)
    - Venous outflow obstruction
        - Venous thrombosis
        - Platybasia
        - Craniosynostotic syndromes
        - Down's syndrome
    - Leptomeningeal inflammation
        - Haemorrhage
        - infection
    - Trauma
    - Choroids plexus carcinoma (over-production)

In general the treatment of hydrocephalus involves that of the underlying cause (for example removing an obstructive tumour or cyst) but some form of CSF diversion is often required. The mainstay of such treatment since the early 1950's has been the use of the cerebrospinal fluid shunt where the excess CSF is drained by means of a valved tube from the ventricles to a body cavity where it could be reabsorbed. The commonest shunt since the 1970s has been the ventriculoperitoneal shunt (VP shunt). Shunts however, do have problems. Up to 50% of shunts will fail within a year of implantation due to blockage, fracture, migration, malposition and infection[10,22]. Five to 10% of all newly implanted shunts can get infected[4] and this has been shown to affect cognitive development[11]. Shunts also have late complications and over 80% of shunts will have failed by 12 years (5). Other problems include overdrainage of the shunt and the slit ventricle syndrome. Alternatives to shunts have therefore been sought.[19]

Since the 1980's endoscopic procedures have been in use for the treatment of hydrocephalus[17]. The creation of a hole from the third ventricle through to

the subarachnoid space can allow CSF to bypass an obstruction, thus obviating the need for a VP shunt. The use of endoscopic third ventriculostomy (ETV) is now becoming more prevalent in the primary treatment of hydrocephalus particularly in cases of obstruction and a consensus of opinion exists regarding their high likelihood of success in these cases[13]. The use of ETV is also gaining popularity in the treatment of shunt malfunction even in cases where there was a communicating hydrocephalus to begin with. There are several papers advocating this (secondary ETV) as a worthwhile alternative to shunt revision. In some cases particularly in older patients ETV has been suggested as a treatment for shunt blockage in patients whose hydrocephalus was originally communicating[3,5,7,9,20,25].

In this unit we perform approximately 100 shunt revisions per year. In 2004, we performed 108 shunt revisions. In 47 of those cases (43.5%), a further procedure was needed because of complications with the new shunt. The 1-year survival revised shunts in 2004 was therefore 56.5%. There are series which show higher success rates (70%) with ETV following shunt failure [20]. These are retrospective.

To date there has been no prospective analysis comparing ETV to shunt revision in patients who present with shunt problems requiring surgery.

**Study objective:**

The aim of this study is to compare the success rates of ETV and shunt revision in the treatment of shunt malfunction in patients with hydrocephalus, In other words to:

- determine which group of patients are most likely to require further surgery within a one year follow-up period
- To compare immediate complication rates between the two patient groups

**Sample population:**
All patients presenting to Leeds General Infirmary with shunt obstruction will be considered for the study regardless of the original cause of their hydrocephalus.

Inclusion criteria:

1. Symptoms/signs or radiological evidence of shunt obstruction
2. Ventricular anatomy making an endoscopic procedure feasible as judged by the attending consultant neurosurgeon:
    a. Lateral and third ventricles adequate size
    b. Thin third ventricle floor
    c. Adequate pre-pontine cistern to fenestrate into with an endoscope
3. Age greater than one year

Exclusion criteria

1. Age less than one year (these children are less likely to benefit from ETV[2,6,14-16,18,23,24])
2. Small ventricles preventing passage of the endoscope
3. Patients who would not be suitable for a shunt
4. Patients whose condition is such that urgent surgical intervention is needed and time for enrolment is not available
5. Patients who are unable to give consent and there are no available next-of-kin

**Sample size:**
In order to detect a statistical significant difference ($p<0.05$) between the two groups we would require 196 patients at. The power calculations were performed by our IT department at Leeds General Infirmary (Karen Howden). This unit performs surgery for approximately 100 patients per year with shunt malfunction and we would therefore calculate that the study will take four years to complete assuming about half of patients will not be suitable for the study or will not wish to take part.

**Randomisation process:**
We intend to randomise half of our patients to each arm of the study (i.e. 100 will have a shunt revision for their treatment and 100 will have an ETV). This will be done by choosing from a collection of 200 identically sealed envelopes kept in the theatre suite. For obvious reasons the surgeon and patient cannot be blinded to the treatment to which they are randomised.

**Consent procedures:**
For each patient presenting with shunt malfunction, the surgeon will assess whether they are suitable for the study. Once suitability has been confirmed, consent will be sought in three possible ways:

1. In the case of a patient under 16: The parents of the child will be given an information sheet detailing the reasons for, aims and methods of the study. In the case of a child who has a normal conscious level and is of an age where he/she can understand the study rationale, there is a specific information sheet for the child. A consent form will be signed by the registrar or consultant taking consent and the parents of the child (and the child where appropriate). A separate information for children who can read will be provided.
2. In the case of a consenting adult, with a normal conscious level: Information on the study will be provided as above and written consent obtained by the attending registrar or consultant.
3. In the case of an adult with reduced conscious level or who is mentally unable to comprehend the study: Consent will be sought from the patient's next-of-kin. Where there is no next-of-kin available, the patient will be excluded from the study.

**Study procedure:**

Before recruitment to the trial:

The patient who presents with symptoms or signs of shunt malfunction will have a thorough clinical examination, particularly neurological examination. Fundoscopy will be performed in all patients to ascertain the presence or absence of papilloedema. Where possible, a bedside visual field assessment and visual acuity test will performed with a Snellen chart (competent older children and adults). Imaging will be performed as in all patients with suspected shunt malfunction:

- Shunt series of x-rays
- Cranial CT scan

These are not investigations exclusive to study patients but are performed routinely in such cases.
Where there is doubt as to the cause of the hydrocephalus or the suitability of the patient for ETV and the clinical condition of the patient allows the time a magnetic resonance imaging (MRI) study *may* be performed *prior* to consideration for study entry. This is done in most patients who have not had MR before as most patients presenting to us are assessed for suitability for ETV anyway. If the patient's condition is such that urgent surgery or other intervention is required, this intervention will take precedence over further investigation or entry into the study.

Once a patient is deemed suitable for trial, the patient/carer/parent/next-of-kin will be given information on the study and consent sought. Once written consent has been obtained, the patient is entered into the study. They will be given a study number and a proforma will be filled out. A sealed envelope will be opened to reveal the treatment arm and further consent for surgery will be obtained in the usual manner.

In the cases of those patients who present with shunt infection, they will not be considered eligible for the study until the infection has cleared. Treatment for shunt infection is by removal of the shunt, insertion of an external ventricular drain and administration of intravenous and intrathecal antibiotics for 10 days after the last positive CSF culture. Only at the point where a brand new shunt is considered would the patient be eligible for the study. Shunt infection is not a contraindication to ETV if infection is treated properly beforehand[23].

Those that are randomised to shunt revision will have part or all of the shunt replaced. Patients randomised to the ETV arm of the study may have the malfunctioning shunt left in situ. Once the patient has had their surgery, they will be kept in hospital until they are deemed well enough for discharge home. There will be a visual assessment prior to discharge.

Follow-up will be arranged for 6 weeks, 6 months and one year for all study patients. At the 6 week and 6 month clinic the patient will have a cranial imaging to assess ventricular size. Those that have had an ETV will have an MRI scan to determine patency of the stoma as well (this is normal practice

following such a procedure). If a shunt revision is performed, a CT or MRI will be performed. Fundoscopy and visual acuity are also assessed in clinic. This is no different from the normal follow-up of a patient who has had treatment of a blocked shunt.

Should a patient make an unscheduled presentation because of symptoms related to their hydrocephalus or surgery and recurrence of the hydrocephalus is suspected they will be investigated in the usual manner in such cases (i.e. clinical and/or radiological confirmation of failure of shunt or ETV if that is the case).

A final proforma will be filled in at the patient's exit from the study. Exit from the study can happen in 3 ways:

- The patient represents with shunt/ETV failure
- The patient is well at one year following surgery with no need for further surgical intervention
- The patient voluntarily withdraws from the study for any reason at all

**Duration of the study**

Subject to R&D and ethics committee approval, enrolment into the study will commence on January 1$^{st}$, 2007 and we would expect to enrol the 200$^{th}$ patient by December 31$^{st}$, 2010. To ensure a minimum of one years-follow-up, data accrual will continue for one year after recruitment of the 200$^{th}$ patient. Overall we would expect this study to last at most 5 years.

**Treatment efficacy assessment/endpoints:**

In each patient the following endpoints will be assessed:

<u>Primary endpoint:</u>
One-year success rate of the procedure (one-year survival of shunt or ETV)

- The procedure will be deemed a failure if the patient requires further surgical intervention within a year for treatment of their hydrocephalus. We felt that one-year follow-up was appropriate as most shunt and ETV failures occur in the first year following the procedure [9,12]. The need for further surgery will be determined clinically or radiologically. In the case of patients who are in the ETV arm of the study, a sagittal MRI demonstrating the third ventricle floor will be sought where possible.

<u>Secondary endpoints:</u>

1. Occurrence of complications from surgery
2. Ventricular size changes
3. Length of inpatient stay
4. Number of re-attendances (excluding scheduled ones at 6 weeks, 3 months and 1 year) with symptoms related to their hydrocephalus/wound or implant.

**Safety**

Where either treatment would be deemed unsafe, the patient would be excluded from the study.

The risks of surgery are:

1. Death (less than 1% for shunt and ETV)
2. Epilepsy (approximately 5% short term risk in both treatments)
3. Minor vascular injury – Both treatments involve the passage of instruments through the brain to the ventricle. The risk of bleeding from this is about 5%. Most bleeds are sub clinical and don't result in neurological deficit. The risk of a bleed causing a deficit is about 1-2% for both treatments
4. Major vascular injury: This is a risk with ETV where basilar artery injury has occurred - death from it has been reported[1]. However, most large series of patients treated with ETV, report no such injuries.
5. Infection: The shunt infection rate in this unit at present is 5%. The rate of CSF infection or ventriculitis is 0-10% in large series[8,11,21] The rate of infection
6. CSF wound leak: This occurs in up to 5% of newly implanted shunt and is a high risk factor for infection. In the case of ETV it usually means that the ETV will not work and a shunt is needed[21]
7. Overdrainage and slit ventricle syndrome. This is a rare but serious problem in children treated with shunts. It can cause severe headaches and often requires further shunt surgery. It is not a recognised complication of ETV[22]
8. Subdural haematomas. This is a complication seen with overdrainage of shunts in adults. It can mean that a patient will require surgery to remove the haematomas and shunt revision. It is also rarely seen with ETVs.

**Subject withdrawal**

Obviously, a patient or family can withdraw from the study at any point. If they withdraw at any point before the one-year follow-up, they will be excluded from analysis at the end of the study.

## Data recording and proformas

All data will be recorded prospectively on proformas by one of the investigators:
There will be a proforma for

- The initial inpatient admission, surgery and discharge
- Follow-up proforma to be filled in at one year or earlier if treatment fails

Data storage:
All proformas will be kept in paper form by the principle investigator in his office and will be transferred onto a computer database on one desktop PC in the department of neurosurgery. This will be password controlled and only the named investigators will have access to it

# ETV vs. Shunt Revision Study: admission

Hospital number 1

Surname First name Date of birth Date of entry into study

## Admission details

Date of admission

Mode of presentation
- ☐ Self referral
- ☐ Through OPD
- ☐ GP
- ☐ Other hospital
- ☐ A&E
- ☐ Other…

Cause of hydrocephalus
- ☐ IVH
- ☐ Aquaduct stenosis
- ☐ Myelomeningocele
- ☐ Chiari malformation
- ☐ Tumour
- ☐ CSF infection
- ☐ Head injury
- ☐ Dandy Walker
- ☐ Craniosynostosis
- ☐ Venous thrombosis
- ☐ Unknown
- ☐ Other

Date of first shunt insertion

Date of last shunt revision

Number of previous revisions

Previous ETV? ☐

Type of shunt: Valve

Proximal catheter

Distal catheter

Antisiphon device ☐ None ☐ Integral ☐ Separate

Rickham reservoir ☐ None ☐ Integral ☐ Separate

Site of ventricular catheter
- ☐ Frontal
- ☐ Parietal
- ☐ Occipital
- ☐ Other…

Site of peritoneal catheter
- ☐ peritoneum
- ☐ heart
- ☐ pleura
- ☐ Other…

Symptoms
- ☐ Headache
- ☐ Nausea/Vomiting
- ☐ Irritability
- ☐ Lethargy
- ☐ New or changed seizures
- ☐ Diplopia
- ☐ Fever
- ☐ Developmental delay
- ☐ Deteriorating performance
- ☐ Abdominal symptoms
- ☐ Other…

Signs
- ☐ Fever
- ☐ Papilloedema
- ☐ Bulging fontanelle
- ☐ Increasing head circumference
- ☐ Decreased L.O.C.
- ☐ Nuchal rigidity
- ☐ Cranial nerve palsy
- ☐ Parinauds/Sunsetting
- ☐ Focal deficit
- ☐ CSF leak
- ☐ Shunt reservoir not refilling
- ☐ Erythema over shunt
- ☐ Skin erosion/discharg
- ☐ Abdominal mass
- ☐ Peritonitis
- ☐ Delayed developmer
- ☐ Other…

Highest CRP

Highest WCC

ICP monitoring results
- ☐ not done
- ☐ inconclusive
- ☐ demonstrate shunt malfunction

Shunt tap
- ☐ not done
- ☐ unable to aspirate
- ☐ high pressure
- ☐ relieved symptoms
- ☐ demonstrated infection

# ETV vs. Shunt Revision Study: discharge

Hospital number 1

**Shunt xray**
- ☐ not done
- ☐ normal
- ☐ disconnection/fracture
- ☐ migration
- ☐ Other…

**CT scan**
- ☐ not done
- ☐ enlarged temporal horns
- ☐ enlarged third ventricle
- ☐ enlarged frontal horns
- ☐ effacement of cortical sulci
- ☐ periventricular lucency
- ☐ increased ventricular size compared with baseline
- ☐ Enlarged 4th ventricle
- ☐ Aquaduct patent

**MRI**
- ☐ not done
- ☐ enlarged temporal horns
- ☐ enlarged third ventricle
- ☐ enlarged frontal horns
- ☐ effacement of cortical sulci
- ☐ periventricular lucency
- ☐ increased ventricular size compared with baseline
- ☐ Enlarged 4th ventricle
- ☐ Aquaduct patent

## Surgery

Date of surgery

**Findings**
- ☐ Shunt infected (EVD intervening)
- ☐ Proximal block
- ☐ Distal block
- ☐ Valve blocked
- ☐ Overdrainage
- ☐ Other…

**Procedure**

- ☐ Shunt revision
  - ☐ Replacement of whole shunt
  - ☐ Replacement of proximal catheter
  - ☐ Replacement of distal catheter
  - ☐ Replacement of valve
  - ☐ Addition of ASD
  - ☐ Addition of reservoir
- ☐ ETV
  - ☐ ETV alone
  - ☐ ETV and EVD
  - ☐ ETV with VAD
  - ☐ ETV with lumbar drain
  - ☐ ETV and removal of original shunt
  - ☐ Other…

Complications

**MRI prior to discharge (in case of ETV)**
- ☐ not done
- ☐ flow through stoma
- ☐ inconclusive
- ☐ no flow through stoma

Date of discharge

# ETV vs. Shunt Revision Study: follow-up

Hospital number 1

Date of visit

**CT during follow-up**

- ☐ not done
- ☐ ventricle size decreased (normal)
- ☐ ventricle size decreased (still large)
- ☐ ventricle size unchanged (normal)
- ☐ ventricle size unchanged (still large)
- ☐ ventricle size increased
- ☐ Other…

**MRI**

- ☐ not done
- ☐ ventricle size decreased (normal)
- ☐ ventricle size decreased (still large)
- ☐ ventricle size unchanged (normal)
- ☐ ventricle size unchanged (still large)
- ☐ ventricle size increased
- ☐ flow through stoma (if ETV)
- ☐ Other…

Number of visits post discharge

Complications post-op — Free text

**Status**

☐ Functioning at one year ☐ Failed before one year ☐ Dead ☐ Lost to follow-up

**Symptoms in successful patients**

- ☐ none
- ☐ mild
- ☐ severe (requiring admissions

**Where failed:** Date of failure

Operation for failure
- ☐ shunt
- ☐ ETV again
- ☐ Other…

Cause of failure — Free text

**Statistical considerations:**
The primary endpoints will be compared by a chi-squared test comparing success rates at one year in each group.
The timing of failure in those treatments that do fail will be compared using the Kaplan-Meier survival curves.
Complication rates are expected to be small and we expect no statistical difference in a study this size.
Mean numbers of reattendances and mean reduction in ventricular size will be compared using student's t-test

**Data storage**
All data will be stored on a PC and in paper form in the neurosurgical department.
Patients will be identified by their hospital numbers and only neurosurgical medical staff will have access to the data

**Ethical considerations**
There are no specific ethical issues in this study. Both treatments are well-recognised alternatives for managing patients with hydrocephalus

**Publication of study findings**
We plan to publish the results of this study in Journal of Neurosurgery
Presentations of the data will be made to at academic meetings (e.g. European Society for Pediatric neurosurgery and/or the International Society for Pediatric Neurosurgery)

Study Number:

Patient Identification Number for this trial:

# CONSENT FORM

## Title of Project:

**Is endoscopic third ventriculostomy an effective treatment in patients with hydrocephalus and ventriculoperitoneal shunt malfunction?**

## Name of Researchers:

☐D. Crimmins
☐P.Chumas
☐A.Tyagi
☐R. Ramirez
☐R. O'Kane
☐T. Goddard
*Please initial box*

1. I confirm that I have read and understand the information sheet provided for the above study and have had the opportunity to ask questions.

2. I understand that my/my child's/relative's participation is voluntary and that I am/they are free to withdraw at any time, without giving any reason, without my/their medical care or legal rights being affected.

3. I understand that sections of any of my/their medical notes may be looked at by responsible individuals from Leeds General Infirmary where it is relevant to my/their taking part in research. I give permission for these individuals to have access to my/my child's/my relative's records.

4. I agree to the use of MR or CT or video images from this study being used in the medical literature

5. I agree to take part in the above study/I agree for my child/relative to take part in the study.

_____ _____ _____
Name of Patient/Parent/next-of-kin Date Signature

_____ _____ ____
Name of Person taking consent Date Signature
*(if different from researcher)*

_____ _____ _____
Researcher Date Signature

1 for patient; 1 for researcher; 1 to be kept with hospital notes

**INFORMATION SHEET (patient)**

# Endoscopic third ventriculostomy versus shunt revision in the treatment of cerebrospinal fluid shunt malfunction

*'You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish.*
*Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*
*Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy may be obtained from CERES, PO Box 1365, London N16 0BW.*

**What is the purpose of the study?**
People with hydrocephalus (fluid in the brain) are often treated with cerebrospinal fluid (CSF) shunts. These are tubes (with a valve) draining the CSF from the fluid cavities in the brain (the ventricles) to the peritoneum (in the abdomen) or the heart or the pleura (around the lungs). These shunts are prone to blockage, over-drainage or infection. In the case of such shunt malfunction, surgery needs to be carried out to rectify it. Traditionally we have replaced part or all of the shunt to treat the problem. You may have had this done before. Unfortunately, the revised shunt is also prone to malfunction and nearly half will need further surgery within a year.

More recently, we have been able to employ a different procedure to avoid the need for a shunt altogether. This treatment is called an endoscopic third ventriculostomy (ETV). An ETV involves insertion of a thin telescope (an endoscope) into the ventricles of the brain where the CSF is produced. A hole (ventriculostomy) is made in the floor of one of the ventricles (the third ventricle) to allow the CSF to drain out. A shunt is therefore not needed afterwards. There is evidence to suggest that an ETV can be as good as or maybe better than shunt revision in people that have a blocked shunt. There is definitely a lower risk of infection than with shunts but there is a slightly higher risk of bleeding from the treatment although this risk is small.

The purpose of this study is to determine whether an ETV or shunt revision is a more effective treatment in people with blocked shunts. In order to eliminate any bias, we need to randomly apply each treatment to patients who have a shunt blockage that needs surgery. Overall we need about 400 subjects to reach a valid conclusion and we estimate that the study will take about 4 years.

**How does the study work?**
If you wish to partake in the study, we may perform an MRI scan if one has not been done already. This is to determine if ETV is possible in your case. A pre-sealed envelope will then be opened indicating which treatment will be offered to you. Your will then be treated with either shunt revision or by ETV. Following surgery, we will keep you in for a few days to make sure the treatment has worked. You will be seen about 6 weeks later in the outpatients where further brain imaging will be performed to evaluate the effect of the treatment on the ventricle size.

**What other information will be collected in the study?**
If you wish to partake in the study, all their clinical details will be recorded by a neurosurgeon. They will go on to have a CT scan in the normal way and this will be interpreted in the context of their symptoms by the neurosurgeon. We may compare

this scan with old ones done when you were well (if available) to look for increasing hydrocephalus. At one year after the treatment, we will record whether the treatment worked and whether there were any complications from the treatment.

**Will there be effects on my treatment?**
Treatment of your condition will continue on in the routine fashion. Participation will not affect you in any way. Regardless of whether you enter the study or not and regardless of what type of surgery (ETV or shunt revision) you get, we will treat you the same afterwards and during follow-up as an outpatient.

**Can my child withdraw from the study at any time?**
**Yes.** You are free to refuse to join the study and may withdraw at any time or choose not to answer certain questions. You will receive the same quality of care at the hospital whether you join the study or not.

**Will the information obtained in the study be confidential?**
All data will be kept in the form of hospital registration numbers. Names and addresses of patients will not be used. Even then, these hospital numbers can only accessed by the named investigators. Anything you say will be treated in confidence, no names will be mentioned in any reports of the study and care will be taken so that individuals cannot be identified from details in reports of the results of the study.

**Will anyone else be told about my participation in the study?**
No

**What if I wish to complain about the way in which this study has been conducted?**
If you have *any* cause to complain about *any* aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study.

If you have any complaints or concerns please contact the project coordinator:
**Mr. Darach Crimmins,**
Leeds General Infirmary
LS1 3EX
(0113) 3928413
darach.crimmins@leedsth.nhs.uk

Otherwise you can use the normal hospital complaints procedure and contact the following person:
Karen Dunwoody
Patient Relations Department,
Ground Floor, Trust Headquarters,
St. James's University Hospital,
Beckett Street,
Leeds LS9 7TF
(0113) 2066261

**INFORMATION SHEET (parents)**

# Endoscopic third ventriculostomy versus shunt revision in the treatment of cerebrospinal fluid shunt malfunction

*'You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish.*
*Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*
*Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy may be obtained from CERES, PO Box 1365, London N16 0BW.*

**What is the purpose of the study?**
People with hydrocephalus (fluid in the brain) are often treated with cerebrospinal fluid (CSF) shunts. These are tubes (with a valve) draining the CSF from the fluid cavities in the brain (the ventricles) to the peritoneum (in the abdomen) or the heart or the pleura (around the lungs). These shunts are prone to blockage, over-drainage or infection. In the case of such shunt malfunction, surgery needs to be carried out to rectify it. Traditionally we have replaced part or all of the shunt to treat the problem. This may have been done in your child before. Unfortunately, the revised shunt is also prone to malfunction and nearly half will need further surgery within a year.

More recently, we have been able to employ a different procedure to avoid the need for a shunt altogether. This treatment is called an endoscopic third ventriculostomy (ETV). An ETV involves insertion of a thin telescope (an endoscope) into the ventricles of the brain where the CSF is produced. A hole (ventriculostomy) is made in the floor of one of the ventricles (the third ventricle) to allow the CSF to drain out. A shunt is therefore not needed afterwards. There is evidence to suggest that an ETV can be as good as or maybe better than shunt revision in people that have a blocked shunt. There is definitely a lower risk of infection than with shunts but there is a slightly higher risk of bleeding from the treatment although this risk is small.

The purpose of this study is to determine whether an ETV or shunt revision is a more effective treatment in people with blocked shunts. In order to eliminate any bias, we need to randomly apply each treatment to patients who have a shunt blockage that needs surgery. Overall we need about 400 subjects to reach a valid conclusion and we estimate that the study will take about 4 years.

**How does the study work?**
If you wish your child to partake in the study, we may perform an MRI scan if one has not been done already. This is to determine if ETV is possible for your child. A pre-sealed envelope will then be opened indicating which treatment will be offered. Your child will be treated with either shunt revision or by ETV. Following surgery, we will keep your child in for a few days to make sure the treatment has worked. He/she will be seen about 6 weeks later in the outpatients where further brain imaging will be performed to evaluate the effect of the treatment on the ventricle size.

**What other information will be collected in the study?**
If you wish your child to partake in the study, all their clinical details will be recorded by a neurosurgeon. They will go on to have a CT scan in the normal way and this will be interpreted in the context of their symptoms by the neurosurgeon. We may

compare this scan with old ones done when your child was well (if available) to look for increasing hydrocephalus. At one year after the treatment, we will record whether the treatment worked and whether there were any complications from the treatment.

**Will there be effects on my child's treatment?**
Treatment of your child's condition will continue on in the routine fashion. Participation will not affect him/her in any way. Regardless of whether your child enters the study or not and regardless of what type of surgery (ETV or shunt revision) they get, we will treat them the same afterwards and during follow-up as an outpatient.

**Can my child withdraw from the study at any time?**
**Yes.** You are free to refuse to join the study and may withdraw at any time or choose not to answer certain questions. Your child will receive the same quality of care at the hospital whether you join the study or not.

**Will the information obtained in the study be confidential?**
All data will be kept in the form of hospital registration numbers. Names and addresses of children will not be used. Even then these hospital numbers can only accessed by the above named investigators. Anything you say will be treated in confidence, no names will be mentioned in any reports of the study and care will be taken so that individuals cannot be identified from details in reports of the results of the study.

**Will anyone else be told about my participation in the study?**
No

**What if I wish to complain about the way in which this study has been conducted?**
If you have *any* cause to complain about *any* aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study.
If you have any complaints or concerns please contact the project coordinator:

**Mr. Darach Crimmins,**
Leeds General Infirmary
LS1 3EX
(0114) 3928413
darach.crimmins@leedsth.nhs.uk

Otherwise you can use the normal hospital complaints procedure and contact the following person:
Karen Dunwoody
Patient Relations Department,
Ground Floor, Trust Headquarters,
St. James's University Hospital,
Beckett Street,
Leeds LS9 7TF
(0113) 2066261

**INFORMATION SHEET (next-of-kin)**

# Endoscopic third ventriculostomy versus shunt revision in the treatment of cerebrospinal fluid shunt malfunction

*'You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish.*
*Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*
*Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy may be obtained from CERES, PO Box 1365, London N16 0BW.*

**What is the purpose of the study?**
People with hydrocephalus (fluid in the brain) are often treated with cerebrospinal fluid (CSF) shunts. These are tubes (with a valve) draining the CSF from the fluid cavities in the brain (the ventricles) to the peritoneum (in the abdomen) or the heart or the pleura (around the lungs). These shunts are prone to blockage, over-drainage or infection. In the case of such shunt malfunction, surgery needs to be carried out to rectify it. Traditionally we have replaced part or all of the shunt to treat the problem. This may have been done in your relative before. Unfortunately, the revised shunt is also prone to malfunction and nearly half will need further surgery within a year.

More recently, we have been able to employ a different procedure to avoid the need for a shunt altogether. This treatment is called an endoscopic third ventriculostomy (ETV). An ETV involves insertion of a thin telescope (an endoscope) into the ventricles of the brain where the CSF is produced. A hole (ventriculostomy) is made in the floor of one of the ventricles (the third ventricle) to allow the CSF to drain out. A shunt is therefore not needed afterwards. There is evidence to suggest that an ETV can be as good as or maybe better than shunt revision in people that have a blocked shunt. There is definitely a lower risk of infection than with shunts but there is a slightly higher risk of bleeding from the treatment although this risk is small.

The purpose of this study is to determine whether an ETV or shunt revision is a more effective treatment in people with blocked shunts. In order to eliminate any bias, we need to randomly apply each treatment to patients who have a shunt blockage that needs surgery. Overall we need about 400 subjects to reach a valid conclusion and we estimate that the study will take about 4 years.

**How does the study work?**
If you wish your relative to partake in the study, we may perform an MRI scan if one has not been done already. This is to determine if ETV is possible for your relative. A pre-sealed envelope will then be opened indicating which treatment will be offered. Your relative will be treated with either shunt revision or by ETV. Following surgery, we will keep your relative in for a few days to make sure the treatment has worked. He/she will be seen about 6 weeks later in the outpatients where further brain imaging will be performed to evaluate the effect of the treatment on the ventricle size.

**What other information will be collected in the study?**
If you wish your relative to partake in the study, all their clinical details will be recorded by a neurosurgeon. They will go on to have a CT scan in the normal way and this will be interpreted in the context of their symptoms by the neurosurgeon. We may compare this scan with old ones done when your relative was well (if available) to look for increasing hydrocephalus. At one year after the treatment, we will record

whether the treatment worked and whether there were any complications from the treatment.

**Will there be effects on my relative's treatment?**
Treatment of your relative's condition will continue on in the routine fashion. Participation will not affect him/her in any way. Regardless of whether your relative enters the study or not and regardless of what type of surgery (ETV or shunt revision) they get, we will treat them the same afterwards and during follow-up as an outpatient.

**Can my relative withdraw from the study at any time?**
**Yes.** You are free to refuse to join the study and may withdraw at any time or choose not to answer certain questions. Your relative will receive the same quality of care at the hospital whether you join the study or not.

**Will the information obtained in the study be confidential?**
All data will be kept in the form of hospital registration numbers. Names and addresses of patients will not be used. Even then these hospital numbers can only accessed by the above named investigators. Anything you say will be treated in confidence, no names will be mentioned in any reports of the study and care will be taken so that individuals cannot be identified from details in reports of the results of the study.

**Will anyone else be told about my participation in the study?**
No

**What if I wish to complain about the way in which this study has been conducted?**
If you have *any* cause to complain about *any* aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study.
If you have any complaints or concerns please contact the project coordinator:

**Mr. Darach Crimmins,**
Leeds General Infirmary
LS1 3EX
(0114) 3928413
darach.crimmins@leedsth.nhs.uk

Otherwise you can use the normal hospital complaints procedure and contact the following person:
Karen Dunwoody
Patient Relations Department,
Ground Floor, Trust Headquarters,
St. James's University Hospital,
Beckett Street,
Leeds LS9 7TF
(0113) 2066261

# In case of any patients who are admitted to Leeds General Infirmary with suspected CSF-shunt malfunction.

***Please contact one of the following***

**Mr. D. Crimmins** **Through LGI switch (mobile phone)**
Secretary: 28413

**Mr. Paul Chumas** **Through LGI switch (mobile phone)**
Secretary: 23297

**Mr. Atul Tyagi** **Through LGI switch (mobile phone)**
Secretary: 28103

***or Neurosurgical Registrar-on-call***

1. Abtin K, Thompson BG, Walker ML: Basilar artery perforation as a complication of endoscopic third ventriculostomy. **Pediatr Neurosurg 28:**35-41, 1998
2. Barlow P: Indications for endoscopic third ventriculostomy: a review of successful and failed cases. **British Journal of Neurosurgery 11:**456, 1998
3. Baskin JJ, Manwaring KH, Rekate HL: Ventricular shunt removal: the ultimate treatment of the slit ventricle syndrome. **J Neurosurg 88:**478-484, 1998
4. Bierbrauer KS, Storrs BB, McLone DG, et al: A prospective, randomized study of shunt function and infections as a function of shunt placement. **Pediatr Neurosurg 16:**287-291, 1990
5. Boschert J, Hellwig D, Krauss JK: Endoscopic third ventriculostomy for shunt dysfunction in occlusive hydrocephalus: long-term follow up and review. **J Neurosurg 98:**1032-1039, 2003
6. Buxton N, Macarthur D, Mallucci C, et al: Neuroendoscopic third ventriculostomy in patients less than 1 year old. **Pediatr Neurosurg 29:**73-76, 1998
7. Buxton N, Macarthur D, Robertson I, et al: Neuroendoscopic third ventriculostomy for failed shunts. **Surg Neurol 60:**201-203; discussion 203-204, 2003
8. Choux M, Genitori L, Lang D, et al: Shunt implantation: reducing the incidence of shunt infection. **J Neurosurg 77:**875-880, 1992
9. Cinalli G, Salazar C, Mallucci C, et al: The role of endoscopic third ventriculostomy in the management of shunt malfunction. **Neurosurgery 43:**1323-1327; discussion 1327-1329, 1998
10. Di Rocco C, Marchese E, Velardi F: A survey of the first complication of newly implanted CSF shunt devices for the treatment of nontumoral hydrocephalus. Cooperative survey of the 1991-1992 Education Committee of the ISPN. **Childs Nerv Syst 10:**321-327, 1994
11. Drake JM, Kestle JR, Milner R, et al: Randomized trial of cerebrospinal fluid shunt valve design in pediatric hydrocephalus. **Neurosurgery 43:**294-303; discussion 303-295, 1998
12. Fukuhara T, Vorster SJ, Luciano MG: Risk factors for failure of endoscopic third ventriculostomy for obstructive hydrocephalus. **Neurosurgery 46:**1100-1109; discussion 1109-1111, 2000
13. Grant JA, McLone DG: Third ventriculostomy: a review. **Surg Neurol 47:**210-212, 1997
14. Hopf NJ, Grunert P, Fries G, et al: Endoscopic third ventriculostomy: outcome analysis of 100 consecutive procedures. **Neurosurgery 44:**795-804; discussion 804-796, 1999
15. Jones RF, Kwok BC, Stening WA, et al: Third ventriculostomy for hydrocephalus associated with spinal dysraphism: indications and contraindications. **Eur J Pediatr Surg 6 Suppl 1:**5-6, 1996
16. Jones RF, Stening WA, Brydon M: Endoscopic third ventriculostomy. **Neurosurgery 26:**86-91; discussion 91-82, 1990

17. Kestle J, Cochrane D, Alisharan R: The initial treatment of hydrocephalus: an assessment of surgeons' preference between third ventriculostomy and shunt insertion. **Neurol Res 22:**65-68, 2000
18. Koch D, Wagner W: Endoscopic third ventriculostomy in infants of less than 1 year of age: which factors influence the outcome? **Childs Nerv Syst 20:**405-411, 2004
19. Lo P, Drake JM: Shunt malfunctions. **Neurosurg Clin N Am 12:**695-701, viii, 2001
20. O'Brien DF, Javadpour M, Collins DR, et al: Endoscopic third ventriculostomy: an outcome analysis of primary cases and procedures performed after ventriculoperitoneal shunt malfunction. **J Neurosurg 103:**393-400, 2005
21. Pople IK, Bayston R, Hayward RD: Infection of cerebrospinal fluid shunts in infants: a study of etiological factors. **J Neurosurg 77:**29-36, 1992
22. Sainte-Rose C, Piatt JH, Renier D, et al: Mechanical complications in shunts. **Pediatr Neurosurg 17:**2-9, 1991
23. Siomin V, Cinalli G, Grotenhuis A, et al: Endoscopic third ventriculostomy in patients with cerebrospinal fluid infection and/or hemorrhage. **J Neurosurg 97:**519-524, 2002
24. Teo C, Jones R: Management of hydrocephalus by endoscopic third ventriculostomy in patients with myelomeningocele. **Pediatr Neurosurg 25:**57-63; discussion 63, 1996
25. Yamamoto M, Oka K, Ikeda K, et al: Percutaneous flexible neuroendoscopic ventriculostomy in patients with shunt malfunction as an alternative procedure to shunt revision. **Surg Neurol 42:**218-223, 1994