# Table of Contents

- **Header** ................................................. 1
- **Abstract** ............................................... 1
- **Plain Language Summary** .......................... 1
- **Background** ........................................... 2
- **Objectives** ........................................... 2
- **Methods** ............................................... 2
- **Results** ............................................... 5
- **Discussion** ........................................... 5
- **Authors’ Conclusions** ............................. 6
- **Acknowledgements** .................................. 6
- **References** ........................................... 6
- **Characteristics of Studies** ........................ 7
- **Data and Analyses** ................................. 10
- **Feedback** ............................................. 10
- **What's New** .......................................... 10
- **History** .............................................. 10
- **Contributions of Authors** ...................... 11
- **declarations of Interest** ......................... 11
- **Sources of Support** ................................. 11
- **Index Terms** ......................................... 11

*Shunting for normal pressure hydrocephalus (NPH) (Review)*

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Abstract

Background
Since the condition was first described in 1965, the syndrome of normal pressure hydrocephalus (NPH) has conventionally been managed by placement of a cerebrospinal fluid (CSF) shunt.

Objectives
To determine the effectiveness of shunting procedures in promoting stability or improvement in the neurological symptoms and signs of NPH.

Search strategy
The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched on 27 March 2008 using the terms: "Shunt*" AND "normal pressure hydrocephalus". The CDCIG Specialized Register contains records from all major health care databases (The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS) as well as from many trials databases and grey literature sources.

Selection criteria
Studies included for analysis were those involving the placement of a CSF shunt for the treatment of NPH as part of a randomized controlled trial.

Data collection and analysis
No data matching the selection criteria were found.

Main results
No randomized controlled trials of shunt placement versus no shunt were found.

Authors’ conclusions
There is no evidence to indicate whether placement of a shunt is effective in the management of NPH.
There is no evidence to indicate whether placement of a shunt to remove fluid is effective in the management of normal pressure hydrocephalus.

Normal pressure hydrocephalus is a rare but potentially treatable cause of dementia. Since the condition was first described in 1965, it has conventionally been treated by placement of a shunt to remove cerebrospinal fluid (CSF) from the ventricles of the brain. No trial has yet compared the placement of a shunt versus no shunt in a randomized controlled manner. Nor have the long-term outcomes of treated and untreated normal pressure hydrocephalus been compared. There is, therefore, no evidence for the use of shunts in the management of normal pressure hydrocephalus.

**Background**

Normal pressure hydrocephalus (NPH) (Hakim 1965) is a rare but potentially treatable cause of dementia. The clinical triad is the presence of dementia, difficulty with gait (in particular, a tendency to walk with short steps), and urinary incontinence. These features occur in many other dementias but in NPH, radiological imaging of the brain shows the presence of enlarged ventricles with relative preservation of the cerebral cortex. The cerebrospinal fluid which surrounds the brain is contained within a membrane called the arachnoid. The fluid is continually produced from a collection of blood vessels lying in the cerebral ventricles (cavities within the brain) and then flows over the surface of the brain and is reabsorbed back into the veins within the skull through tiny projections of the arachnoid into the veins, known as arachnoid granulations. It is currently believed that in NPH there is a failure of reabsorption of cerebrospinal fluid through the arachnoid granulations. This may occur as a consequence of previous infection or haemorrhage in the subarachnoid space, but in many cases it is due to thickening of the arachnoid membrane, idiopathic fibrosing meningitis, which is a condition of unknown cause. Whatever the underlying cause, a pressure gradient builds up between the intraventricular system and the fluid surrounding the brain surface. Eventually, CSF formation diminishes so that a stable state is reached but the CSF pressure is reset at a high normal level, or with intermittent waves of high pressure. The increased pressure is thought to be the cause of damage to nerve cells and tracts in the brain.

Treatment is based upon the presumption that provision of a CSF diversion device from the ventricles will lead to normalization of the pressure difference and thereby to stability or improvement in symptoms and signs. The CSF is drained through a tube (shunt) from the brain ventricles either directly into the blood stream in the heart or into the peritoneal space surrounding the abdominal organs, where it is reabsorbed into the blood. This form of treatment is currently accepted practice in cases of obstructive hydrocephalus where there is blockage of CSF flow from the ventricles to the subarachnoid space surrounding the cerebrum. Insertion of a permanent CSF diversion device requires an operative procedure under general anaesthesia. The procedure can only be performed by a trained surgeon. Possible adverse outcomes can include operative complications such as bleeding or infection of the shunt or wound site, failure of the shunt due to blockage or breakage of the shunt tubing, and over-shunting resulting in a low pressure state with headache, ventricular shrinkage and the development of subdural fluid accumulations.

A recognised difficulty is the confirmation of the diagnosis and selection of those patients who will benefit from the procedure (Adams 1997). A diagnosis is often suspected when the typical clinical triad is combined with the radiological finding of ventricles enlarged disproportionately to the degree of cerebral atrophy. Additional methods used have included: monitoring of CSF pressure over prolonged periods to detect intermittent rises in pressure above normal (the A waves of Lundberg); responses of CSF pressure to subarachnoid infusions of normal saline (saline is injected by means of a lumbar puncture into the CSF lying beneath the arachnoid membrane); radionucleotide cisternography (a radionuclide liquid is injected via lumbar puncture into the subarachnoid space) showing reflux into the ventricles with delayed pericerebral diffusion; and drainage of large amounts of CSF with observation for detecting signs of temporary clinical improvement.

**Objectives**

To determine the effectiveness of shunting procedures in promoting stability or improvement in the neurological symptoms and signs of NPH.

**Methods**

**Criteria for considering studies for this review**

**Types of studies**

Randomized controlled trials involving permanent shunt procedures in NPH.
Types of participants
As there are no formalized diagnostic criteria, participants considered to have the clinical features of NPH (dementia, gait dyspraxia, and incontinence) and radiological signs (ventricular enlargement disproportionate to the degree of cerebral atrophy), and to have had other possible causes of dementia ruled out, will be included. Exclusion criteria would include the finding of an alternative cause for the clinical features or the presence of obstructive hydrocephalus.

Types of interventions
Implantation of permanent ventriculo-peritoneal or ventriculo-atrial CSF shunts.

Types of outcome measures
Stability or improvement in the clinical symptoms and signs of NPH as determined by the trialists and continuing for at least one year. Outcome measures are to include:
(i) the presence or absence of incontinence;
(ii) improvement in scores obtained on validated neuropsychological tests (such as the Mini-Mental State Examination, Rivermead Behavioural Memory Test, subtests of the Wechsler Adult Intelligence Scale (WAIS));
(iii) increase in speed of walking (measured in metres per second);
(iv) Clinician’s Global Impression of Change.

Search methods for identification of studies
The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) was searched on 27 March 2008 for all years up to December 2005. This register contains records from the following major healthcare databases: The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS, and many ongoing trial databases and other grey literature sources. The following search terms were used: “Shunt*” AND “normal pressure hydrocephalus”.

The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched separately on 27 March 2008 for records added to these databases after December 2005 to March 2008. The search terms used to identify relevant controlled trials on dementia, Alzheimer’s disease and mild cognitive impairment for the Group’s Specialized Register can be found in the Group’s module on The Cochrane Library. These search terms were combined with the following search terms and adapted for each database, where appropriate: “Shunt*” AND “normal pressure hydrocephalus”.

On 27 March 2008, the Specialized Register consisted of records from the following databases:

Healthcare databases

Conference proceedings
- ISTP (http://portal.isiknowledge.com/portal.cgi) (Index to Scientific and Technical Proceedings) (to August 2006);
- INSIDE (BL database of Conference Proceedings and Journals) (to June 2000);

Theses
- Index to Theses (formerly ASLIB) (http://www.theses.com/) (UK and Ireland theses) (1716 to 11 August 2006);
- Australian Digital Theses Program (http://adt.caul.edu.au/): (last update 24 March 2006);
- Canadian Theses and Dissertations (http://www.collectionscanada.ca/thesescanada/index-e.html): 1989 to 28 August 2006);
- DATAD - Database of African Theses and Dissertations (http://www.aau.org/datad/backgrd.htm);

Ongoing trials

UK
- National Research Register (http://www.update-software.com/projects/nrr/) (last searched issue 3/2006);
- ReFeR (http://www.refer.nhs.uk/ViewWebPage.asp?Page=Home) (last searched 30 August 2006);
- Current Controlled trials: Meta Register of Controlled trials (mRCT) (http://www.controlled-trials.com/) (last searched 30 August 2006);
- ISRCTN Register - trials registered with a unique identifier
- Action medical research
- Kings College London
- Laxdale Ltd
• Medical Research Council (UK)
• NHS Trusts Clinical Trials Register
• National Health Service Research and Development Health Technology Assessment Programme (HTA)
• National Health Service Research and Development Programme 'Time-Limited' National Programmes
• National Health Service Research and Development Regional Programmes
• The Wellcome Trust
• Stroke Trials Registry (http://www.strokecenter.org/trials/index.aspx) (last searched 31 August 2006);

Netherlands

• Nederland Trial Register (http://www.trialregister.nl/trialreg/index.asp) (last searched 31 August 2006);

USA/International

• The IFPMA Trial Results databases searches a wide variety of sources among which are:
  • http://www.astrazenecaclinicaltrials.com (seroquel, statins)
  • http://www.centerwatch.com
  • http://www.clinicalstudyresults.org
  • http://clinicaltrials.gov
  • http://www.controlled-trials.com
  • http://ctr.gsk.co.uk
  • http://www.lillytrials.com (zyprexa)
  • http://www.roche-trials.com (anti-abeta antibody)
  • http://www.organon.com
  • http://www.novartiscinclinicaltrials.com (rivastigmine)
  • http://www.bayerhealthcare.com
  • http://trials.boehringer-ingelheim.com
  • http://www.clinicaltrials.com
  • http://www.esteve.es

This part of the IPFMA database is searched and was last updated on 4 September 2006;
• Lundbeck Clinical Trial Registry (http://www.lundbecktrials.com) (last searched 15 August 2006);
• Forest Clinical trial Registry (http://www.forestclinicaltrials.com/) (last searched 15 August 2006)

The search strategies used to identify relevant records in MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS can be found in the Group’s module on The Cochrane Library.

• Letter, telephone, or personal contact was made with doctors known to have published case reports in the English language literature concerning normal pressure hydrocephalus since 1966, as identified via MEDLINE using the keywords “normal pressure hydrocephalus”, to locate details on any unpublished trials.
• Handsearching was undertaken of the following journals for abstracts of meetings at which papers are likely to have been presented: Neurology; Journal of Neurology, Neurosurgery and Psychiatry; Journal of Neurosurgery; Neurosurgery; Journal of Neurology; and Acta Neurochirurgica.
• The British Medical Journal Register of unpublished clinical trials was searched.

Data collection and analysis

Data collection and selection of studies
Both reviewers scrutinised titles and abstracts identified using the above search strategy to determine which studies satisfy the criteria for inclusion. Agreement was reached by consensus. Dr Esmonde abstracted the relevant data for inclusion in the review.

Quality assessment
Methodological quality was assessed by:
• randomization method;
• matching, where the randomized groups are tested for comparability using the characteristics of age, sex, duration, severity of symptoms as measured by Clinician’s Global Impression of Change, Mini-mental State Examination scores, performance on other neuropsychological tests, and walking speeds;
• effectiveness of patient and physician blinding, if performed (for example, head gear to conceal surgery, sham operations);
• documentation of other therapeutic exposures (for example, physiotherapy);
• adequate accounting for study dropouts and withdrawals or participants lost to follow up.

Data analysis

• Extraction of data from the relevant trials to determine odds ratios with 95% confidence intervals (CI) for stability or improvement following shunting. For continuous variables (for example, Mini-mental State Examination scores for each treatment group) the mean treatment effect, the standard error, and number of patients are to be extracted in order to calculate the mean treatment difference together with 95% CI.
• Calculation of overall odds ratios combining results from all the clinical trials. For continuous variables, results from individual studies will be combined and the weighted mean difference or standardized mean difference calculated.

RESULTS

Description of studies

See: Characteristics of excluded studies.
The studies identified for review did not include any trials of shunt versus no shunt. There is no published evidence of such a trial having been performed. Randomized controlled studies in relation to shunting are restricted to comparisons of different types of shunting devices used in the treatment of NPH.

Results of the search

The update search performed on 27 March 2008 retrieved 7 possible studies for inclusion or exclusion; after assessment, all of these studies have been excluded.

Included studies

There are no included studies in this review.

Excluded studies

See Characteristics of excluded studies.
The following studies have been excluded from the review (Black 1980; Boon 1994; Boon 1998; Chaudhry 2007; Chen 1994; Czosnyka 2000; De Jong 2000; Duplessis 1991; Keifer 2006; Meier 2006 a; Meier 2006 b; Meier 2006 c; Miyamoto 2007; Pickard 1982; Pollack 1999; Silverberg 2000; Tans 1999; Williams 2008).

Risk of bias in included studies

As the studies do not compare the value of shunting versus no shunt, it is not relevant to comment on their methodological quality.

Effects of interventions

As yet, there is no published trial of shunting versus no shunt. The study by Boon 1998 is reported and quotes data from the same participants in two other papers (Boon 1994; Tans 1999); it was a randomized controlled trial comparing the pressure sensitivity of two types of shunting device. Tans 1999 mentioned that those individuals with evidence of co-existent cerebrovascular disease who were shunted had poorer functional outcomes than those who had no evidence of cerebrovascular disease. Further comparison of shunt type is contained in the article by Pollack 1999 and in a letter reply from Czosnyka 2000, and in the studies of Keifer 2006, and Meier 2006 b. The trial of Meier 2006 a looked at the effects of different opening pressure settings in the valves used in implanted shunts in patients with NPH, but there was no control group.

Black 1980 presented a retrospective review of the outcome of placement of a CSF shunt in 62 patients who underwent the operation. Improvement in functional grading was seen in 33%, but there was no control group.
The only randomized trial of shunt placement versus a control group without shunt has been presented as phase I of an ongoing clinical trial exploring the effects of this treatment for patients with Alzheimer’s disease (Silverberg 2000). A larger confirmatory study is planned.

An attempt to predict likely responders to shunt placement in NPH was published by Chen 1994. There was no randomization and no control group. The aetiology of the NPH syndrome in the 15 participants was given as stroke in three, trauma in five, and unknown in the others. Eight patients out of 15 who had shunts ‘responded’ although the level of response was not indicated.

Williams 2008 presented results of shunting in NPH in patients where the decision for shunting had been made on the basis of initial response of gait to temporary CSF drainage. Chaudhry 2007 carried out neuropsychological testing in patients with NPH before and after temporary CSF drainage, and showed that those who had no improvement in tasks of verbal memory were less likely to show a response to shunting.

DISCUSSION

The efficacy of shunting in the treatment of normal pressure hydrocephalus has not yet been evaluated in a randomized controlled clinical trial. The exact definition of the syndrome varies between researchers. From the above trials, it can be seen that inclusion...
of individuals with enlarged cerebral ventricles involves many
diverse causes. This makes evaluation of trials difficult. Co-existent
diseases, such as cerebrovascular disease, which could cause a clin-
ical syndrome of dementia indistinguishable from that of the clas-
sical NPH syndrome was permitted in some trials (Chen 1994;
Duplessis 1991). The trials published so far have simply com-
pared the functional outcome of different shunts or the prediction
of outcome by pre-operative test lumbar drainage. No trial has
yet compared the placement of a shunt versus no shunt in a ran-
domized controlled manner. Nor have the long-term outcomes of
treated and untreated NPH been compared. The study of Meier
2006 c looked at the clinical outcome in 51 patients with NPH
treated by shunt insertion after an average of 34 months follow-up:
an excellent, good or satisfactory outcome was recorded in 67%
of patients, however, this was not a randomized trial of treatment.

AUTHORS’ CONCLUSIONS

Implications for practice

There is no evidence from randomized controlled trials that shunt-
ing is effective or ineffective in the management of normal pres-
sure hydrocephalus.

Implications for research

There is need for a randomized clinical trial of the efficacy of
shunting in the treatment of NPH.

ACKNOWLEDGEMENTS

The review authors gratefully acknowledge the help of Miss Claire
Brittain of the Alzheimer’s Society for her comments on the review.

REFERENCES

References to studies excluded from this review

Black 1980 {published data only}

Black PM. Idiopathic normal pressure hydrocephalus Results of

Boon 1994 {published data only}

Boon AJW, Tans TH, Wurzer AL, Poortvliet DCJ. Dutch Nor-
mal Pressure Hydrocephalus Study Part II. Comparison of low
and medium pressure shunts. Intracranial Pressure 1994:unknown:
unknown.

Boon 1998 {published data only}

Boon AJ, Tans JT, Delwel EJ, Egeler Peerdeman SM, Hanlo PW,
Wurzer HA, et al.Dutch Normal-Pressure Hydrocephalus Study:
randomized comparison of low- and medium-pressure shunts. Jour-

Chaudhry 2007 {published data only}

Chaudhry P, Kharkar S, Heidler-Gary J, Hillis AE, Newhart M,
Kleinman JT, et al.Characteristics and reversibility of dementia in
149–58.

Chen 1994 {published data only}

Chen IH, Huang CI, Liu HC, Chen KK. Effectiveness of shunting
in patients with normal pressure hydrocephalus predicted by tem-
porary, controlled-resistance, continuous lumbar drainage: a pilot
1430–2.

Czosnyka 2000 {published data only}

Czosnyka Z, Czosnyka M, Copeman J, Pickard JD, Pollack IF. A
randomized, controlled study of a programmable shunt valve versus

De Jong 2000 [published data only]

Duplessis 1991 [published data only]

Keifer 2006 [published data only]

Meier 2006 a [published data only]

Meier 2006 b [published data only]

Meier 2006 c [published data only]

Miyamoto 2007 [published data only]

Pickard 1982 [published data only]
## Characteristics of excluded studies

[ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black 1980</td>
<td>Retrospective review of the results of shunting of 62 patients with NPH. Not a randomized study. No control group.</td>
</tr>
<tr>
<td>Boon 1994</td>
<td>Untraced.</td>
</tr>
<tr>
<td>Boon 1998</td>
<td>Randomized study of 101 patients comparing different types of shunt. No control group.</td>
</tr>
<tr>
<td>Chaudhry 2007</td>
<td>This study looked at cognitive performance before and after shunting in patients with NPH. Not a randomized controlled treatment trial.</td>
</tr>
<tr>
<td>Chen 1994</td>
<td>Results of shunting in 15 patients with NPH (although diagnostic basis not specified). No control group.</td>
</tr>
<tr>
<td>Czosnyka 2000</td>
<td>This study only concerned the effects of magnets on various programmable shunt devices. Not a trial of shunting in NPH.</td>
</tr>
<tr>
<td>De Jong 2000</td>
<td>Same study with same participants as Boon 1998.</td>
</tr>
<tr>
<td>Duplessis 1991</td>
<td>Results of shunting in 46 patients with classical diagnostic triad. No control group.</td>
</tr>
<tr>
<td>Keifer 2006</td>
<td>A comparison of two types of pressure relief valves used in shunts for normal pressure hydrocephalus. Not a controlled randomized treatment trial.</td>
</tr>
<tr>
<td>Meier 2006 a</td>
<td>A trial to determine the optimal opening pressure for pressure relief valves used in shunts for normal pressure hydrocephalus. Not a controlled randomized treatment trial.</td>
</tr>
<tr>
<td>Meier 2006 b</td>
<td>An observational study of the effects of adjustment of the pressure setting in shunt valves used for the treatment of normal pressure hydrocephalus. Not a randomized controlled treatment study.</td>
</tr>
<tr>
<td>Meier 2006 c</td>
<td>A three year follow-up of patients with normal pressure hydrocephalus treated by shunting. Not a randomized controlled treatment trial.</td>
</tr>
<tr>
<td>Miyamoto 2007</td>
<td>A comparison of cerebral blood flow in patients with normal pressure hydrocephalus treated with shunting, with asymptomatic controls with ventricular dilatation. Not a randomized controlled treatment trial.</td>
</tr>
<tr>
<td>Pickard 1982</td>
<td>A review of the syndrome of hydrocephalus. No trial data.</td>
</tr>
<tr>
<td>Pollack 1999</td>
<td>Randomized controlled study of programmable versus conventional shunt devices. Used 377 patients with varied causes of hydrocephalus. Separate results for those with NPH not given. No sham group.</td>
</tr>
<tr>
<td>Silverberg 2000</td>
<td>Results of shunt placement in 30 patients with Alzheimer's disease. No NPH patients.</td>
</tr>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<tbody>
<tr>
<td>Tans 1999</td>
<td>Same study as Boon 1998.</td>
</tr>
<tr>
<td>Williams 2008</td>
<td>Study looking at selection of patients with NPH for shunting based on their response to temporary CSF drainage. Not a randomized controlled treatment trial.</td>
</tr>
</tbody>
</table>
This review has no analyses.

**F E E D B A C K**

**High pressures in the CSF**

**Summary**

According to the CSF hydrodynamic mechanism that I suggest on www.med-lavrencic.si/raziskava.htm, there could be severe complications in using a shunt from CSF space to extracraniovertebral location for a patient with normal pressure hydrocephalus. Namely, there is most probably a last barrier starting at around 30 mmHg of ICP that prevents further progressive volume expansion of brain or its blood volume in the pathophysiological phase of intracraniovertebral volume homeostasis. At this ICP, the CSF formation and CSF removal stops while CSF stasis physically prevents any further decrease of CSF volume and further intracranial volume imbalance. By applying a shunt that enables CSF drainage beyond 30 mm Hg of ICP, there is no ultimate barrier and extreme intracranial volume imbalance (at very high ICP) could cause severe consequences (for example, when a patient with shunt experiences traumatic brain injury or stroke that causes higher ICP than 30 mm Hg). This complication differs from shunt overdrainage syndrome with decreased ICP (a slit ventricles syndrome or a very low ICP syndrome). Comment from Darko Lavrencic (28 September 2002).

**Reply**

The authors reply that the high pressures in the CSF that you are concerned with do not occur in NPH and are, therefore, not dealt with in the review. Reply added 24 April 2003.

**Contributors**

Darko Lavrencic (contributor)
Tom Esmonde and Stephen Cooke (review authors)

**W H A T ' S N E W**

Last assessed as up-to-date: 5 September 2008.

| 9 September 2008 | New search has been performed | On 27 March 2008 an update search was performed: seven studies were retrieved for possible inclusion in the review. All seven studies have been excluded from the review |
HISTORY

Review first published: Issue 3, 2002

<table>
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<tr>
<th>Date</th>
<th>Description</th>
<th>Notes</th>
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<tr>
<td>4 May 2006</td>
<td>New search has been performed</td>
<td>May 2006: the update search revealed no new trial reports</td>
</tr>
<tr>
<td>14 March 2002</td>
<td>New citation required and conclusions have changed</td>
<td>Substantive amendment</td>
</tr>
</tbody>
</table>

CONTRIBUTIONS OF AUTHORS

Dr Esmonde is responsible for the concept of the review, drafting the protocol, collating and analysing the data, and preparing the review.

Mr Cooke is responsible for drafting the protocol, collating and analysing the data, and preparing the review.

Searches: Dymphna Hermans and Vittoria Lutje

Consumer editor for this review is Miss Claire Brittain.

This review has been reviewed anonymously by two peer reviewers.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Royal Group of Hospitals Trust, UK.

External sources

- No sources of support supplied.
INDEX TERMS

Medical Subject Headings (MeSH)
*Cerebrospinal Fluid Shunts; Hydrocephalus, Normal Pressure [*therapy]

MeSH check words
Humans