Calculation of the resistance to CSF outflow

We read the paper by Kahlon *et al.* with great interest. Comparative studies about the use of different diagnostic techniques to predict the response to shunting in hydrocephalus are of great value as they are likely to form a landmark for future clinical practice. Therefore, it is of paramount importance that the procedures taken for comparison are methodologically sound.

Unfortunately, the interpretation of the lumbar infusion study given by the authors raises our concern. For unknown reasons, the authors have taken into account only the end equilibrium pressure obtained during the constant rate lumbar infusion and neglected the baseline CSF pressure. The authors presumed that this baseline pressure was the same in everybody and equal to the value resulting from the mean taken from the whole cohort (11 mm Hg).

Interpretation of the infusion study can be biased only partially on the resistance to CSF outflow (Rcsf), with other parameters describing CSF dynamics like the baseline pressure, elasticity, etc., taken into account. The resistance to CSF outflow is, undoubtedly the most important parameter, about which a number of independent studies have been conducted in the past, including a quite multicentre Dutch trial.

The proper way to calculate Rcsf results from the well known Davson's formula:

\[ \text{ICP}_{\text{baseline}} = \text{Rcsf} \times \text{formation of CSF} + \text{Pss} \]

(where Pss is sagittal sinus pressure).

ICP reached during infusion is equal to:

\[ \text{ICP}_{\text{end infusion}} = \text{Rcsf} \times \text{formation of CSF} + \text{Infusion rate} + \text{Pss} \]

Subtracting the first equation from the second it can be derived:

\[ \text{ICP}_{\text{end infusion}} - \text{ICP}_{\text{baseline}} = \text{Rcsf} \times \text{Infusion rate} \]

From the last equation it seems obvious that the Rcsf must be calculated as the difference between end equilibrium CSF pressure and baseline CSF pressure, divided by the infusion rate (in this case 0.8 ml/min).

In cases when the pressure increases above 40 mm Hg during infusion, the Rcsf can be presumed to be greater than 40 minus baseline CSF pressure divided by the infusion rate.

There is still not complete agreement about which value Rcsf is normal or pathological (thresholds are ranging from 12 mm Hg/ml/min1 to 19 mm Hg/ml/min2, and are probably age dependent). Between 13 and 19 mm Hg/ml/min there is a “grey zone” in which patients may but they not necessarily should improve after shunting.

Is neglecting the baseline pressure likely to be a meaningful error?

Although the standard deviation of baseline CSF pressure mentioned by the authors is quite low (3 mm Hg with mean value of 11 mm Hg), this may theoretically mean that some of the patients (although less than 5%) classified as having normal pressure hydrocephalus may have baseline pressure above 17 mm Hg (that is, mean plus twice standard deviation). The “critical threshold” for CSF pressure reached during infusion study should be set for as 28, not 22 mm Hg.

We can recall our own material from Cambridge: in 133 adult patients presenting with clinical and radiological symptoms/signs of normal pressure hydrocephalus, constant rate lumbar infusion studies were performed. We calculated properly Rcsf, (that is, taking into account the baseline pressure) and recorded the end equilibrium pressure obtained during the test. The end equilibrium pressure, compared with the threshold calculated as in Kahlon *et al.* (that is, resulting from the averaged baseline pressure plus 14 mm Hg/ml/min multiplied by the infusion rate), was in disagreement with 14 mm Hg/ml/min or above in 23 patients. Therefore, by neglecting the baseline CSF pressure as done by Kahlon *et al.*, we would misjudge 18% of our tests. It is not huge, but still a meaningful fraction.

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References

1 Kahlon B, Sundbärg S, Rehnrona S. Comparison between the lumbar infusion and CSF tap tests to predict outcome after shunt surgery based on pure clinical symptoms combined with ventricular widening. J Neurol Neurosurg Psychiatry 1997; 60:549–58.

Authors’ reply

The comment by Czosnyka and collaborators to Kahlon *et al.* brings up a highly relevant question concerning the lumbar infusion test in patients with suspected normal pressure hydrocephalus. Namely, if calculations of the resistance to outflow of CSF (Rcsf) is a more adequate measure for predicting the outcome of a CSF shunting procedure than merely recording the steady state CSF pressure level reached during constant rate infusion as originally described by Katzman and Hussey. Czosnyka *et al.* claim that the latter does not take the initial pressure level (that is, before infusion is started) into account. This is not totally correct. In fact in the equation for calculating Rcsf, the initial pressure level is deducted and only the effect of the fluid volume infused per unit of time is considered. This assumes that the patient’s own CSF production is similar before as well as during the infusion of artificial CSF, which may be true but is in fact not known. CSF production may well be influenced (downregulated) by long-standing hydrocephalus.

If the measured initial resting pressure is in the high range, the difference to the infusion steady state plateau pressure level will tend to decrease and if low, the difference will tend to increase. Thus, a high initial resting pressure will tend to disqualify the patient from shunt surgery and vice versa if low. These considerations stimulated us to use the uncorrected infusion steady state pressure level as was originally described to predict the outcome of shunt surgery.

Several studies have found Rcsf to be a good predictor of outcome of shunt surgery, but almost a similar number of studies have shown a less favourable predictive value (for references, see Boone *et al.*). In two recent studies Rcsf and CSF outflow conductance were calculated in patients with suspected normal pressure hydrocephalus, undergoing shunt surgery based on pure clinical symptoms combined with ventricular widening. The results were partly divergent and while Malm *et al.* concluded that outflow conductance (reciprocal to Rcsf) had no predictive value, Boone *et al.* found that Rcsf could predict outcome of surgery with the best likelihood ratio at a cut off level of about 18 mm Hg/ml/min. In our study the consequence of using Rcsf calculations with cut off levels of 14 or 18 mm Hg/ml/min had been that 3% (1 of 32 patients) or 22% (7 of 32), respectively, of patients with verified improvement after shunt surgery should have been excluded from treatment.

At present we cannot see any obvious reason for not using the steady state infusion plateau level as a simple measure of CSF absorption capacity in clinical practice. From a theoretical basis we can agree to the reasoning by Czosnyka *et al.*, but if calculation of Rcsf in clinical practice is a better predictor than merely recording the steady state plateau pressure level remains to be proved and further data are warranted. We are currently scrutinising lumbar infusion test curves to further elucidate the role of other details than only the plateau pressure for selection of patients likely to be helped by shunt operations.

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References

probably many) who have lost contact with their biomedical roots. It was, however, disappointing to see little reference to some of the exciting new imaging studies that are exploring the links between neurobiology and attachment status. Attachment (or affiliation as it is sometimes called) is covered, but largely in relation to autism and related disorders.

Section two collects together in one place as much information as anyone could want about individual psychotropic agents, but also finds room for chapters on complementary medicine and ECT—strange bedfellows in a subsection on other somatic interventions! The emphasis on placing pharmacological treatments in a developmental context is flagged up in the preface and is a theme that runs through the book. A holistic and integrated approach to assessment and the management of children’s problems is advocated clearly throughout.

In the third section, the evidence for treatment of a range of different conditions is reviewed and explained—drug treatments are integrated with a number of other treatments not to be considered as the only treatments available. The authors’ enthusiasm for the potential value of psychopharmacology is tempered with a clear, evidence-based focus, and many chapters in this section are cautious in their interpretation of the literature and open about the absence of good randomised controlled trial evidence in a number of important conditions. Helpful algorithms suggest what would be a sensible approach to treatment, and psychological treatments are recommended, alone or in combination with drug treatments when there is evidence to support this. The MTA study showed the superiority of methylphenidate over placebo in children with ADHD, but when treatment as usual was usually methylphenidate. One possible explanation was the manner in which the prescribing was carried out in that large multicentre trial, a concept that is supported here with a chapter on the psychology of prescribing.

The book concludes with a section on research and methodological considerations, including interesting chapters on changes in research and methodological considerations, practical psychiatry, 4th edition, written. Not perhaps a book for all clinicians except at the end of the book, and no colour exposure it did have some difficulties in colour and open about the absence of good randomised controlled trial evidence in a number of important conditions. Helpful algorithms suggest what would be a sensible approach to treatment, and psychological treatments are recommended, alone or in combination with drug treatments when there is evidence to support this. The MTA study showed the superiority of methylphenidate over placebo in children with ADHD, but when treatment as usual was usually methylphenidate. One possible explanation was the manner in which the prescribing was carried out in that large multicentre trial, a concept that is supported here with a chapter on the psychology of prescribing.

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Neurosurgery of arteriovenous malformations and fistulas: A multimodal approach


This is an interesting text aimed solely at arteriovenous malformations but including the often forgotten arteriovenous fistulas. The authors consist of the Neurovascular Surgical Team at the Ludwig-Maximilians-Universität, Munich, in conjunction with the Chairman of Neuroradiology at the same institution and the Director of the Gamma Knife Centre in Munich. The spectrum of authors covers the multimodal approach described in the title of the book. The aim of the book is therefore to appeal to specialists of surgical, radiosurgical, and endovascular disciplines. Its aim is to highlight the evolution of treatment of arteriovenous malformations and arteriovenous fistulas since the first neurosurgical efforts to deal with excluding and excising these lesions to prevent the growth in what were initially adjuvant treatments, but are now part of a multimodal combination of treatments. I think the book does this very well. It begins by reiterating the basics with a literature review covering pathogenesis, epidemiology, and clinical characteristics, as well as treatment options of AVMs and fistulas of the CNS, including brain and spine.

It also considers the classification systems based on theory and the pathoanatomical relationship between morbidity intervention and thus choice of treatment. It then goes on to discuss the result of the various modalities of surgery, embolisation, and radiosurgery in a detailed literature review. This is followed by an in-depth analysis of the principles of surgery, endovascular, and gamma knife options. The relative risks and merits of each are compared. Finally, in true keeping with its clinical perspective, the book concludes with a number of case studies illustrating the combination of both surgical and endovascular approaches as well as exclusively endovascular, exclusively surgical, and finally major surgical cases.

I found the book was well structured and illustrated, making for an easy and informative read. It would be a very welcome addition to the library of any neurovascular unit and it would be of interest to all the disciplines involved in treating these abnormalities.

K O’Neill

HIV neurology


Do we need books anymore? I found myself asking this rather shocking question when an exceptionally keen medical student brought a series of current reviews relating to a patient we had seen in clinic together, downloaded from the internet within minutes of the clinical ending. HIV neurology provides at least one rationale for book publishing. Given the epidemiology of HIV in the UK, most neurologists will encounter HIV associated neurological problems rarely. Most of the physicians who look after patients with HIV disease are familiar with non-neurological problems. Neurologists will therefore tend to find themselves either considering HIV associated disease as part of the differential diagnosis in patients whose HIV status is not known, or being asked for opinions once more straightforward HIV complications have been considered. This book seems to have been designed with this in mind and is organised to allow ease of reference.

The first section provides an overview of HIV disease with a succinct and accessible summary of the virology, with an outline of general treatment. The approach to neurological diagnosis is explored including useful concepts to help neurologists abandon Occam’s razor, as they must in HIV disease. These include “time locking”, the linking of the potential complication to the stage of HIV infection; “parallel tracking”, the recognition that multiple levels of the nervous system can be involved in the same disease process to confuse the clinical presentation; and “layering”, the idea that multiple pathologies can affect the same level of the nervous system. The subsequent sections are based on the levels of the nervous system affected: predominately non-focal complications relating to the brain; focal complications, spinal cord; peripheral nerve; and finally muscle. Each section discusses the many complications on conventional lines, epidemiology, clinical features, investigations, neuropathology, pathogenesis, and treatment. These are well referenced and throughout there is strong feeling that they have been written by someone with an extensive practical experience of the clinical problems described.

Reading the book in the usual way I did find some repetition, but this is an unfair criticism as the book is intended for reference section by section. There is also an assumption that somehow all neurological symptoms suffered by patients with HIV are in some way related to HIV and that they are immune to more conventional problems. The section on “HIV headache”, a commonly occurring throbbing headache for which no cause is found and which anecdotally responds to amitriptyline, which in other clinics seems familiar enough, perhaps best illustrates this. These minor gripes aside I think this is a useful book, although expensive at £75. It is much more than the sum of the references within as it brings a thoughtful integration of the clinical approach to patients with HIV neurology. For most neurologists this book will beat the internet.

G Fuller

Ageing and dementia. Current and future concepts


This contribution represents a summary of an international symposium on “ageing and dementia”, which took place in Vienna at the end of September 2001. The programme states that as a result of the aftermath of 11 September 2001, the hitherto internationally renowned invited speakers had to be reorganised within a short time. Three key issues were addressed in the meeting—factors that contribute to brain ageing, detection of mild cognitive impairment, and preventive and therapeutic methods that alter these effects. The result is 376 pages comprising 33 contributions over a range of subjects and covering a wide array of approaches from basic science to clinical matters. The authors represent a wide span of interests and countries (although I must confess I did not read the first author of the publication was not necessarily always the presenting author at the symposium).

The concept of vascular dementia is summarised very well by the senior editor, and a discussion of the relevance of vascular changes and their rating on brain scans follows. Some discussion on basic process in the genesis of Alzheimer’s disease is intermingled with a contribution discussing a specific marker, followed by discussions of treatment approaches in Alzheimer’s disease and mild cognitive impairment.

The volume is something of a mixed bag, with a very useful overview written by leaders in the field, coupled with detailed experimental results. They represent, presumably, a faithful summary of the presentations at this particular symposium, but lack something of a thread with which to draw the contributions together. A degree of organisation with perhaps a brief introduction to particular subjects would have been helpful and easily achieved, with reference to the organisers’ aspirational themes. Some of the contributions are lengthy, while others are rather curtail.

That being said, because of its wide approach, it will have wide appeal, and one can safely say that there is something for everybody within its covers. The editors and contributors have succeeded in producing a volume that is of relevance and a pleasure to read. One cannot underestimate the difficulties the organisers had in sustaining the impetus to continue with the meeting after the terrifying events of the 11th September, and this compendium, perhaps, is a piece of evidence to show that things can and should continue as usual.

A Burns
The nucleus of Theodor Meynert (1833–1892)

In 1664 Thomas Willis described distinct subcortical structures, then called the corpus striatum. It was believed to be the “sensorium commune” as defined by Aristotle; a central structure that received sensory modalities and initiated motor acts. By 1914, Wilson wrote that the corpus striatum “seemed to fall from its high estate and depreciate in physiological significance”. It gained importance with the discoveries that lesions of these areas would result in abnormal motor functions. The corpus striatum came to be viewed as the major “extrapyramidal motor system”.

Meynert developed new techniques and used thin serial sections stained with carmine or gold with quantitative neurohistological measurements. His major aim was to relate cortical function to varied cell types and to establish the neural association fibres (radiations of Meynert) within the brain. This predicated the work of Fritsch and Hitzig in 1870.

Handbook of human and animal histology

Because of this new element in the subchlinge. Its large spindle like hyperchromatic nerve cells were measured. The nucleus of the thalamus; and anterior peduncularis; nucleus (ganglion) of the thalamus; and anterior part of the stratum zonale thalami. duncle of the thalamus; and anterior

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Meynert thereby produced the first description of the lamination and cellular diversity of the cerebral cortex in Stricker’s Handbook of human and animal histology (1872). In section three he describes a clearly extended ganglion underneath the fibres of the ansa peduncularis as the second layer of substantia innominata, named “Ganglion der Hirnschenkelschlinge”. Its large spindle like hyperchromatic nerve cells were measured. Because of this new element in the substantia innominata, Meynert distinguished four parts of the area: ansa peduncularis; nucleus (ganglion) of the ansa peduncularis; inferior (ventral) peduncle of the thalamus; and anterior part of the stratum zonale thalami.

Meynert’s powers of description were not the most lucid, and in 1896 Albert Köelliker renamed the ansa ganglion “Meynert’s basal ganglion”:

“The central, nearly superficial part of the disc-like formation of Meynert’s basal nucleus is found in the basal forebrain parallel to the ventral basis of the Nucleus lenticularis and underneath the Commissura anterior from its lateral entrance onwards; laterally, it reaches the Amygdaloid complex; caudally it extends towards the Tractus opticus; its oral part makes contact with Substantia perforata anterior, the medial one reaches the Tuber cinereum.”

Meynert was born in Dresden on 14 June 1833. His father was a historian, his mother an opera singer. When he was eight, the family moved to Vienna and the influence of artistic and bohemian living never quite left him.

As a student, he worked with Wedd and Rokitansky, who fostered his talents. He received his medical doctorate after an untitled student life, in 1861. On the basis of his thesis Structure and function of the brain and spinal cord and their significance in disease, he was appointed Privatdozent in 1865 and Director of the Prosectorium of the state psychiatric hospital in Vienna. Regarded as prophet of scientific progress, he rapidly published several pioneering discoveries. In 1873 he became professor of nervous diseases. Meynert’s novel ideas drew many visitors to Vienna, but he was considered a poor teacher. His department, Forel related, was disorderly and filthy.

He was a small melancholic man with a massive head, a sprawling bushy beard, and mane-like hair. With colleagues he was brusque and, at times, dismissive, but his son had died aged 17, his wife also died young. His admirable drawings of the brain remain in the Neurological Institute of Vienna. His concepts of the brain he obscurely summarised:

“The main function of the central organ is to transmit the fact of existence to an ego gradually shaping itself in the stream of the brain. . .If we look upon the cortex as an organ functioning as a whole then the information that subserves the processes of the mind is all that can be said. . .To think further about the cortex in these terms is impossible and unnecessary. . .But our hope to understand eventually the function of the hemispheres is raised again by the opposite assumption which leads us straight to an organology of the central surface. . .Between these two theoretical possibilities the facts have to decide.”

He studied minutely the visual, hippocampal cortex, the olfactory lobe, and septum pellucidum. He separated the cortex with white surface (allocortex) from the cortex with a grey surface (neocortex) and created the phrase “organology of the cortex”, reflecting the function of brain as an organ. Central integration was dependent on the association process. He considered the motor cortex and basal nuclei as functionally antagonistic; thus, disease would lead to extrapyramidal disorder. He went on to point out the sensory feedback from muscles to the cortex. These and other highly original ideas were published in his Klinische Vorlesungen über psychiatrie auf wissen schaftlichen grundlagen, in 1890.

Meynert was editor of the Wiener Jahr- bucher für Psychiatrie and co-publisher of the Archiv für Psychiatrie und Nervenkrankheiten (Berlin) and of Vierteljahrschrift für Psychiatrie. He was President of the Wiener Verein für Psychiatrie und Forensische Psychologie.


In 1870 he was appointed Director of the Psychiatric Clinic and he started a neurological outpatient clinic in 1887. In later years he enjoyed high civic honours. However, he suffered grave personal losses in his family and untimely died at Klosterburg on 31 May 1892.

James Papez lists many of his main publications and biographies.

References