Best evidence and the clinical decision making process

The articles by Helfenstein and Newcombe highlight the difficulties faced by clinicians in making a treatment decision for their patient when confronted by contradictory evidence. We are now faced with an ever increasing array of data of variable quality, which all need to be considered, for us to reach the best treatment decision for our patients. Systematic reviews, the cornerstone of evidence based medicine, are an important and increasingly utilised tool that use predefined objective criteria to aggregate data from trials, to provide evidence on which to base clinical decisions. However, systematic reviews have their own problems. Some, such as the finding of increased mortality with the use of intravenous albumin, have been controversial and heavily criticised. Dr Helfenstein highlights another problem with meta-analysis—that is, depending on the methodology chosen and interpretation of an individual trial within a meta-analysis can vary. Most clinicians, like myself, will not be familiar with the statistical techniques utilised in meta-analysis. Thus, the issues highlighted in these two articles will add further to the confusion felt by many.

Given these problems, what evidence should we rely on to make a clinical decision for our patient? Should the findings of a randomised controlled trial that are contrary to the findings of a meta-analysis take priority in our decision making process? Clearly, there are no simple answers to these questions. We should certainly not go back to the days when treatment was based solely on personal anecdotal experience and disregarded good trial evidence. A rigid hierarchy on which to base a clinical decision has been proposed: in this model, case reports are at the bottom end of the scale, whereas randomised controlled trials and systematic reviews are at the top end of the scale. However, there may be situations where the rigid application of this hierarchy is inappropriate. For example, observational studies may provide evidence that is as good, if not better, than that provided by randomised controlled trials. Certainly, this is the current situation when one is focusing on the harms caused by medicines, where randomised controlled trial evidence is singularly absent or unreliable. Similarly, poorly conducted randomised controlled trials, which are then included in a systematic review, can produce erroneous and contradictory results. By contrast, a good single randomised controlled trial can overturn many years of conventional “wisdom” that may have been based on observational data. For example, a meta-analysis of observational studies suggested that hormone replacement therapy (HRT) was associated with a 50% reduction in the relative risk of coronary events. Conversely, the single HERS randomised controlled trial found no benefit of HRT in secondary prevention of coronary events. The findings of HERS have been supported by angiographic studies, and the evidence taken together, has led the American Heart Association to no longer recommend the use of HRT in secondary prevention of coronary artery disease. Finally, it is also important to consider whether results from trials, where patient recruitment is often dependent on a list of specific inclusion and exclusion criteria, are applicable to an individual patient in a real-world situation. All these factors therefore have to be considered in making a clinical decision; thus, in my opinion, the answer to the problem highlighted by Helfenstein is not simple, but crucially depends on a critical appraisal of the characteristics of the evidence that is available.

M Pirmohamed
Department of Pharmacology,
University of Liverpool,
Ashton Street,
Liverpool L69 3GE, UK;
mpirmoh@liv.ac.uk

References
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artery (above), the superior cerebellar artery (below), and the posterior communicating artery (parallel) deserve further comments, especially when clinicians are faced by an acutely isolated third nerve palsy in adults. As the pupillary fibres in the third cranial nerve are located dorsally and peripherally, a dilated pupil is frequently an early sign of a compressive lesion. An aneurysm at the junction of the posterior communication artery and internal carotid artery is a common cause. Actually, around 30% of all third nerve palsies are caused by aneurysms, especially posterior communicating aneurysms.

Other causes include compression or infiltration by neoplasm, infections, large dolicho-ectatic vessels, or shifted supratentorial structures. Occasionally it may be seen in generalised polyneuropathy (Miller-Fisher variant).

References

Recurrent orogenital ulcers with papillomeloma and headaches

I enjoyed reading the self assessment question by Abbas et al published recently. It would be of great interest to know the ethnic background of this 33 year old man. In a study by Daif et al, from Saudi Arabia, Behçet’s disease accounted for almost one fourth of their cases of cerebral venous thrombosis (CVT), likely to be explained by the higher prevalence of Behçet’s disease in the Middle East.

It is imperative that all patients with CVT, even in the presence of a known aetiological factor, have a thorough diagnostic work-up, as multiple factors can be encountered in an individual patient. Also, the factor V gene mutation has been shown to be associated with a sixfold increase in venous thrombosis risk in Behçet’s disease.

Recurrent orogenital tissue plasmogen activator, rather than urokinase, can be used as a local thrombolytic agent, but must be restricted to patients without haemorrhage. It should be used after anticoagulation therapy alone has not provided sufficient clinical improvement, and after ruling out other causes of a patient’s worsening condition.

A disease once sacred.


Written by two Australian epileptologists this book follows the historical concepts of epilepsy, ranging from mythological early views of the supernatural to the modern concepts of pathophysiology and treatment. Part I is a short outline of the present understanding of epilepsy including definition and classification. Parts II, III, and IV cover the clinical manifestations of epilepsy, the nature of the epileptic process and remedies, each examined from an historical viewpoint.

Some ancients believed in the influence of bodily humours in triggering seizures, while others felt that sufferers from this malady had supernatural powers or were influenced by spirits or demons. Gradually, however, the concept of epilepsy as an illness with an underlying organic process began to be accepted along with a better comprehension of the origins and mechanisms of epileptic activity within the brain. The influence of Hughlings Jackson and the gradual acceptance of his views by his contemporaries makes particularly interesting reading.

With regard to treatments for epilepsy the early remedies are discussed; this is followed by reference to the diversity of the effectiveness of bromide, more recent drug treatments and, ultimately, the evolution of the “designer” drugs.

A major feature of the text is the liberal use of historical quotations supplemented by an extensive historical bibliography. Overall this
book provides a fascinating trip through history, following our understanding of this intriguing condition through to the present state of knowledge. It is recommended to anyone with an interest in the history of medicine and of epilepsy in particular.

R Abbott
Department of Neurology,
Leicester Royal Infirmary, UK

DIARY

**Professional Updating in Epidemiology. Design of Vaccination Programmes: From Sero-Epidemiology to Cost-Effectiveness**

8–12 July 2002, University of Warwick, Coventry, UK. The course intends to develop understanding of the epidemiological principles of vaccine programme design, including serological surveys, parameter estimation, transmission dynamic models, and cost-effective analysis of different programmes. For further information contact Dr Stephen Hicks, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (tel: +44 (0)2476 523540, fax: +44 (0)2476 523701, email: s.j.hicks@warwick.ac.uk).

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