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 model how one interprets 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 by Sackett. In his model, case reports are at the bottom end of the scale while 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 long 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 3GJ, UK; m_pirmoh@liv.ac.uk

References
Recurrent oculomotor ulcers with papillodema and headaches

I enjoyed reading the self assessment question by Abbas et al published recently.1 It would be of great interest to know the ethnic background of this 33 year old man. In a study by Daf et al, from Saudi Arabia, Behcet’s disease accounted for almost one fourth of their cases of cerebral venous thrombosis (CVT),2 likely to be explained by the higher prevalence of Behcet’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.3 Also, the factor V gene mutation has been shown to be associated with a sixfold increase in venous thrombosis risk in Behcet’s disease.4 Recombinant tissue plasminogen 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.5

Z Morcos
Department of Neurology,
University Hospitals of Cleveland,
11100 Euclid Avenue, Hanna House # 5,
Cleveland, OH 44106-5040, USA;
zyed_m@hotmail.com

References

A elderly lady with collapse

I enjoyed reading the anatomical discussion about the third cranial nerve presented by Huwez et al in a recent issue of the journal,1 and wish to make a few relevant anatomical and clinical points.

All the extracocular muscles are innervated by an ipsilaterally located subnucleus, with the exception of the superior rectus muscle, which is innervated by a contralateral subnucleus.

The particular relationship between the third cranial nerve and posterior cerebral artery (above), the superior cerebellar artery (below), and the posterior communicating artery (parallel) deserve further comments, especially when clinicians are faced by an acquired isolated third nerve palsy in adults. As the pupillary fibres in the third cerebral 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.6 Other causes include compression or infiltration by neoplasm, infections, large dilated ophthalmic vessels, or shifted supratentorial structures. Occasionally it may be seen in generalised polyneuropathy (Miller-Fisher variant).7

Z Morcos
Department of Neurology,
University Hospitals of Cleveland,
11100 Euclid Avenue, Hanna House # 5,
Cleveland, OH 44106-5040, USA;
zyed_m@hotmail.com

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Failure to develop diabetic ketoacidosis in a newly presenting type 1 diabetic patient

In a recent issue of the journal McNulty and Hardy published a very interesting case history on the failure to develop diabetic ketoacidosis in a newly presenting type 1 diabetic patient.8 Their third self assessment question was “What may be the explanation for this profoundly unwell patient with type 1 diabetes and hyperglycaemia not to have developed diabetic ketoacidosis?” The authors’ explanation is “because her insulinopenia was offset by her hypercholesterolaemia”.

However, in patients with diabetic hyperglycaemic hyperosmolar syndrome (without ketoacidosis), as in the authors’ patient3 increased concentrations of adrenal hormones (without ketoacidosis)3 are usually found.4 This makes the authors’ explanation very improbable. On the other hand, Schade and Eaton pointed out in 1977 (their p 596) that “insulin deficiency per se may not alone cause ketoacidosis”.5 An illustration of this problem is in the paper by Burge et al:9 they compared two groups of diabetic patients, with lower and higher hyperglycaemia. Ketone bodies were higher in the group with lower blood glucose. In uncomplicated diabetes mellitus, increased amounts of 34 organic acids have been identified6; it is not known whether they are insulin dependent or not. Nevertheless, they cause severe acidosis, for example, a blood pH of 6.85 was found in the patient of Vernon and Postellon in absence of acetooic and β-hydroxybutyric acids. Therefore, the authors should also ask: What are the exact mechanisms and details of development of both ketoacidosis and acido- sis without ketone bodies in diabetic patients?

V Rosival
Department of Clinical Biochemistry,
Oezer’s Hospital, Limia 5,
SK-833 OS Bratislava, Slovakia

References
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

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