letters

TO THE EDITOR

Please submit letters for the Editor's consideration within three weeks of receipt of the Journal. Letters should ideally be limited to 350 words, and sent by e-mail to: Clinicalmedicine@rcplondon.ac.uk

Rationing of medical care by age

Editor – I welcome your recent editorial for encouraging debate on this important issue (Robert Allan, *Clin Med* July/August pp 329–30). However, the concept of using age as the criteria for rationing medical care is primarily flawed. There is the temptation for using age as a surrogate for ageing but in this debate, age is not the issue; the issue is ageing and frailty. It is also important to recognise that ageing is not disease and disease is not ageing, but that in old age the disease may present as ageing.

There is no denying the fact that after the age of 60, the spectrum of pathology changes and disability rises steeply. Combinations of chronic pathology make predicting the course of illness far more complex. New patterns of disease emerge with altered response to treatment. Therefore, basic pathology, frailty and disability should be the main focus when managing patients. It will be a sad day for medicine if age alone is used for rationing healthcare and the prerogative of treating patients on clinical grounds is taken away from the attending physician.

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Current clinical uses of intravenous immunoglobulin

Editor – In their review article describing the clinical use of intravenous immunoglobulin (IVIG), El-Shanawany *et al* (*Clin Med* July/August 2006 pp 356–9) warn of anaphylaxis as a rare but severe adverse effect. Previous reports suggest that anaphylaxis is associated with IgA deficiency and the presence of anti-IgA antibodies.[1] Population studies suggest the prevalence of IgA deficiency may be as high as 1:400 in healthy blood donors.[2] Although some guidelines do not recommend essential determination of IgA prior to IVIG, others advise testing.[3,4] Fear of this potentially fatal complication may direct local hospital protocol.

In our experience the decision to test is often based on local availability and laboratory turnaround time. It is often junior doctors who are asked to arrange testing and prescribe therapy and it could therefore be argued that clear guidelines are needed to minimise patient risk. Although the clinical significance of IgA deficiency and anti-IgA antibodies is debated,[5] we would welcome the thoughts of the authors on this issue.

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In response to Hull and Hull

Hull and Hull raise a number of important points in response to our article regarding IgA deficiency (IgAD), its diagnosis, testing for anti-IgA antibodies, and guidelines for the assessment of patient prior to the use of IVIg.

The reported incidence of selective IgA deficiency in the healthy population varies from 1:223 to 1:3000.[1] IgA deficiency can occur in isolation, where it may have little effect on health (though is associated with an increase in autoimmune conditions), or in association with deficiency of other immunoglobulin subclasses and classes as in common variable immunodeficiency.

Anti-IgA antibodies should only be tested for in individuals with confirmed absent IgA using a sensitive assay which measures levels down to 0.05 g/l. If IgA levels are found to be <0.05 g/l, then, as far as we are able to determine, the patient has a complete deficiency.[2] Patients with low but detectable IgA (partial IgA deficiency) are not at increased risk of reactions to IVIg.

Current assays measure IgG anti-IgA, but the correlation between the presence of these antibodies and reactions to IVIG is no longer as certain as was once thought. High titre anti-IgA have the best association with adverse reactions. Patients with IgM anti-IgA have been successfully treated with IVIG.[3] It has also been argued that anaphylactic reactions to the small quantities of IgA in IVIG are likely to be due to IgE anti-IgA antibodies. However, this remains controversial and there is not a reliable and validated assay currently in use in diagnostic laboratories.

The urgency of the clinical setting will also affect the workup performed. In the acute setting it may be difficult to delay the administration of high dose IVIG (hdIVIG) while awaiting these results. The

checklist below (adapted from Jolles and Hughes[4]) summarises the general considerations prior to the commencement of hdIVIG.

Physician's checklist for high dose IVIg:

1. Liver function, renal function, full blood count, and hepatitis screen (avoid hdIVIG in rapidly progressive renal disease).
2. Immunoglobulin levels to exclude IgA deficiency. If no IgA present (<0.05g/l), measure anti-IgA antibodies.
3. Exclude high titre rheumatoid factor and cryoglobulinaemia.
4. Preferably ensure that a sufficient supply of a single product and batch of IVIG is available to expose the patient to a minimum number of donors and to avoid unnecessary product changes.
5. Take any baseline specimens, examination findings, or photographs required in order to later document any objective response.
6. Follow manufacturer's guidelines regarding reconstitution and rate of infusion (and maintain good hydration and fluid intake).
7. Provide patient information regarding high-dose IVIG therapy and consent.
8. Store a sample of serum so that any future research questions or matters relating to transmission of infective agents may be addressed.

If anti-IgA antibodies are detected and are at high titre it may well still be possible to use an IVIg product low in IgA (see Table 1: Properties of IVIg preparations currently available in the UK, in our original article) starting the infusion at a slow rate and, if tolerated, gradually being increased under the supervision of experienced staff and in a setting where full resuscitation facilities are available. The current generation of IVIg products are generally lower in IgA than has previously been the case. Premedication such as antihistamine, paracetamol and hydrocortisone may also be used at initiation of IVIg or during change of product. This is not generally needed for subsequent infusions. Consideration may also be given to a medic alert bracelet documenting the high titre anti-IgA antibodies should the patient require blood products in the future.

Reassuringly, the incidence of serious reactions to IVIG is low and usually due to concurrent infection or over-rapid administration. A prospective study of 459 antibody deficient patients established on IVIG showed that no serious reactions occurred in over 13,000 infusions across twelve centres and using six different IVIG products. The rate of milder reactions was 0.8%.[5] In the UK, primary immunodeficiency patients who infuse at home no longer require the automatic prescription of adrenaline auto-injectors even though incidence of complete IgA deficiency with anti-IgA antibodies is higher in antibody deficient patients (especially IgAD with IgG subclass deficiency) than the general population. Furthermore a large study demonstrated that far fewer individuals with IgAD and anti-IgA antibodies than would be expected developed transfusion reactions[6].

The diagnosis of IgAD and measurement of anti-IgA antibodies is therefore useful in defining patients at increased risk of reactions to IVIg but the presence of even high titre anti-IgA antibodies may not preclude the use of an IVIg product low in IgA where the risk–benefit ratio merits it.

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Systematic review of systematic reviews of acupuncture

Editor – Derry *et al* (*Clin Med* July/August 2006 pp 381–6) have advanced acupuncture research significantly by their review of 35 systematic reviews. Since I am an author of 14 of these articles, I feel I should comment. The analyses by Derry *et al* imply that the authors of many reviews were too 'optimistic' regarding the value of acupuncture mainly because they often based their conclusions on biased data. I think that this may well be true. We need to be more, not less, critical when assessing complementary/alternative medicine (CAM). Ironically, many CAM enthusiasts believe that the work of my team is already too critical.

Believers in acupuncture will probably point towards a range of weaknesses in the analyses by Derry *et al.* The article has, of course, several limitations but these should not distract us from its provocative conclusion: there is 'no robust evidence that acupuncture works for any indication.' Using an entirely different approach, which included a review of those trials which control for placebo effects through the use of the new non-penetrating sham devices, I recently arrived at a strikingly similar overall verdict: 'Acupuncture remains steeped in controversy. Some findings are encouraging but others suggest that its clinical effects mainly depend on a placebo response.'[1] Critical assessment like this of Derry *et al* is a very rare thing in CAM. But CAM researchers should remember that it is mainly this approach which advances healthcare.

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