Case 1—A 76 year old woman received the treatment for multifocal motor neuropathy. One week after treatment she developed a widespread erythematous, exfoliating rash, which was diagnosed after skin biopsy as being severe erythroderma. This required three months of intensive and predominantly inpatient dermatological care. The neuropathy initially responded to the intravenous immunoglobulin but then relapsed. After extensive patch testing with various brands of intravenous immunoglobulin, none of which resulted in a positive reaction, she was given a further course covered by oral steroids, but within six hours of the first dose the rash returned.

Case 2—A 66 year old man with inclusion body myositis developed itchy skin eruptions six days after receiving the Scottish preparation of intravenous immunoglobulin. Skin biopsy suggested an allergic aetiology. He had a further six courses of the same preparation at monthly intervals with oral steroid cover. No further complications developed.

Case 3—A 48 year old man with multifocal motor neuropathy developed a widespread eczematous rash 10 days after treatment with intravenous immunoglobulin. He was admitted to hospital after failure of outpatient treatment. Skin biopsy showed perivascular inflammation, hyperkeratosis, and parakeratosis without evidence of vasculitis.

Case 4—A 55 year old man received intravenous immunoglobulin for multifocal motor neuropathy. One week after treatment he developed widespread itchy, scaly eruptions, mainly on the arms and legs, which persisted for four weeks. Recovery was spontaneous and uneventful.

Serious side effects of intravenous immunoglobulin are rare. There are only a few reports of skin reactions in the literature²; although rarely life threatening, they may cause considerable distress (as they did in cases 1 and 3). A patient has been successfully treated with intravenous immunoglobulin and steroid cover after developing eczema,³ and the combination of intravenous immunoglobulin and steroid has been evaluated recently.⁴ This may well be optimal treatment, if only because the side effects of the immunoglobulin are lessened, but our experience is that the skin condition may recur despite such treatment.

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Products with low IgA content may be used in patients with total IgA deficiency

EDITOR—R A C Hughes emphasises that, on the basis of the results of recent randomised studies, intravenous immunoglobulin is as efficacious as plasmapheresis in the treatment of the Guillain-

Barré syndrome.¹ In view of the practical difficulties associated with plasmapheresis, intravenous immunoglobulin is increasingly likely to be preferred as first line treatment.

In this context Hughes states that intravenous immunoglobulin should be avoided in patients with IgA deficiency. This may mislead clinicians who are unfamiliar with immunoglobulin treatment and may result in them needlessly withholding treatment from all IgA deficient patients. Although it is true that anaphylaxis remains an important risk in some patients with selective IgA deficiency, this is virtually confined to those with the combination of severe or absolute IgA deficiency (<0.05 g/l) and high levels of antibodies to IgA.² Even in these patients the risk of anaphylaxis can be greatly reduced by the cautious use of an IgA depleted immunoglobulin product. Immunodeficient patients with high levels of antibodies to IgA (1 in 200 to 1 in 7000) have been maintained on regular replacement with an IgA depleted product with no serious adverse effects over a six year period.³

Table 1 shows the IgA content of immunoglobulin preparations currently available in Britain. Because measurement of the level of antibodies to IgA is available in only a few immunology laboratories in Britain it would be unwise to delay emergency treatment of the Guillain-Barré syndrome until the results of such measurement are available. It would be sensible to treat patients known to be totally IgA deficient, and those in whom any doubt exists, with an immunoglobulin product with a low IgA content.

Table 1—Approximate IgA content of immunoglobulin preparations

Product	IgA (mg/l)
Alphaglobin	24*
Endobulin	10-50†
Gammagard-SD	0.4-1.9*
Gamimune-N	270*
Sandoglobulin	720*
SNBTS intravenous immunoglobulin	920†
Vigam S	5†

SNBTS = Scottish National Blood Transfusion Service.

*Data from reference 4.

†Data provided by manufacturer.

Hughes's statement that intravenous immunoglobulin should be avoided in patients with renal failure also requires clarification. Temporary reversible deterioration in renal function (ranging from an asymptomatic increase in the serum creatinine concentration to anuric renal failure) associated with the use of high dose intravenous immunoglobulin (2 g/kg) is likely to be related to the toxic effect of a high sugar load on renal tubules.⁵ While the use of a single dose of 2 g/kg should be avoided in patients with pre-existing renal impairment, it may be possible to infuse lower doses at a slower rate safely in such patients.⁵ Hence, rather than renal failure being viewed as an absolute contraindication to intravenous immunoglobulin therapy, each case should be assessed on its individual merits.

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- 3 Cunningham Rundles C, Zhuo Z, Mankarious S, Courter S. Long-term use of IgA depleted intravenous immunoglobulin

lin in immunodeficient subjects with anti-IgA antibodies. *J Clin Immunol* 1993;13:272-8.

4 Buckley RH, Schiff RI. The use of intravenous immune globulin in immunodeficiency diseases. *N Engl J Med* 1991;325:110-7.

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Impact factors need to be improved

EDITOR—Because the number of citations per article is widely used to rank journals, institutions, papers, and scientists we should welcome Eugene Garfield's suggestions for improving the validity of this simple ratio.¹ The final sentence of the summary of Garfield's article, however, hardly fits the title and finds little support in the rest of the article. While good attracts good (Nobel prizewinners work with Nobel prizewinners), we would expect citations to attract citations. Yet this circular argument is reminiscent of the explanation of why the higher echelons of the civil service in Britain continue to find their most suitable recruits to be graduates of Oxford and Cambridge universities. This circular argument is barely scientific and potentially invidious.

Many factors contribute to the number of citations per paper, including the science; the nature of the research; the style of the communication (papers vary in the number of references they include, from none to over 100); editorial policy (several journals ration the number of references per article); circulation and readership (more readers equals more citations); citation bias (comparable to submission bias and publication bias); conformism (scientists often cite those papers that are currently cited); authors' tendency to cite their own work; and referees' self promotion (referees' tendency to recommend inclusion of references to their work).

A "scientific" evaluation of the citation ratio as a measure of the quality of an article might include assessments of prior agreed criteria of quality; the value added to scientific knowledge at the time that the paper was submitted for publication (not necessarily the time it was published); whether the article is deemed correct with the wisdom of hindsight—say, 30 years after publication (because many scientific observations follow a current popular paradigm or consensus); and blind scoring by a panel of judges.

One wonders whether, if independent external criteria were used, some popular articles in widely read weekly journals would still turn out to be 30 or 40 times more valuable to science than those in monthly or quarterly specialist journals, and whether the *Lancet* really is twice as good as the *BMJ*.

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- 1 Garfield E. How can impact factors be improved? *BMJ* 1996;313:411-3. (17 August.)

Non-fatal overdosing is related to polydrug use in Glasgow

EDITOR—Michael Gossop and colleagues found that 9% of 438 heroin users in London reported at least one non-fatal overdose in the previous year, and they state that the use of heroin in combination with other drugs may be a critical risk factor.¹ In our study of 1018 drug injectors recruited in Glasgow during 1993-4, 276 (27%) reported at least one non-fatal overdose requiring medical attention during the previous year.