Antiganglioside antibodies in peripheral neuropathies

Over the last decade or so serum antibodies have been shown to be associated with three groups of neurological disorders: antibodies to ion channels and other functional molecules in myasthenia gravis and related disorders; antibodies to cytoplasmic CNS antigens in paraneoplastic disorders; and antibodies to peripheral nerve antigens. Whereas the first two groups have well established diagnostic or prognostic uses, the relevance of antibodies to peripheral nerve antigens, particularly gangliosides, is less clear.

Gangliosides are sialic acid containing glycosphingolipids that are highly concentrated in certain parts of the nervous system, and which can be obtained commercially. Many laboratories are now performing in-house enzyme linked immunosorbent assays (ELISA) for antibodies to GM1, and to a lesser extent GQ1b (for nomenclature see Willison), and one needs to consider whether these antibodies are specific for disease, represent part of a pathogenic immune response against neuronal antigens, and whether their detection is helpful in the management of the patient.

Antiganglioside antibodies are typically found in inflammatory peripheral neuropathies. Miller Fisher syndrome is an acute, monophasic illness associated with inflammatory peripheral neuropathies. Miller Fisher syndrome often present after a viral or bacterial infection. Over the last few years, there have been many reports of cases associated with particular strains of Campylobacter jejuni, and lipopolysaccharide preparations from certain strains of C jejuni express ganglioside-like epitopes.23 Guillian–Barré syndrome occurs as an epidemic in certain parts of rural China; the incidence of C jejuni infection is particularly high in cases with an acute motor axonal form. Although many Chinese patients had antibodies to GM1, however, overall these did not correlate with antibodies to C jejuni or with the pattern of disease. Similarly, of 96 consecutive cases of Guillian–Barré syndrome or Miller Fisher syndrome studied by Rees et al in the United Kingdom, 26% had evidence of C jejuni infection preceded by a diarrhoeal illness. These cases had more severe motor symptoms, often with acute axonal damage, and a less good prognosis. Although in this study anti-GM1 antibodies were significantly more common in C jejuni positive than in C jejuni negative patients, infection was a more important prognostic indicator than anti-GM1 antibody positivity.

Thus there is an emerging story that antiganglioside antibodies can result from cross reactivity with bacterial antigens, and that some of them at least can have direct—probably complement mediated—effects on peripheral nerve function. Nevertheless, there is much that we need to know about the relation of these antibodies with C jejuni and other preceding infections, and about the relative roles of antibodies (and possibly
How much work do you do in a day?

Does this question induces feelings of pride, guilt, satisfaction, or indignation? Whatever the response, most histopathologists will find it difficult to answer it in a meaningful, quantified, reproducible way. It is a question which often needs to be answered, particularly when manpower changes or changes in working practices are contemplated.

Historically, the diagnostic workload of histopathologists has been assessed by the number of specimens reported. It is in this way that the Royal College of Pathologists frames its staffing recommendations. The approach is crude. Not all specimens are alike; some take much more work than others. In the past this may not have mattered, as each pathologist shared a similar pattern of work; but specialisation is advancing and will increasingly make “specimen counting” a misleading exercise. Furthermore, the workload per specimen is changing. The average number of “items of information” in a single histopathology report probably bears some relation to the work involved in its generation; this measure was found to have increased by over 200% between 1940 and 1990.1 The trend has almost certainly continued, and with the development of minimum datasets it seems likely to accelerate.

There have been several attempts to develop more sensitive methods of measuring whole laboratory workloads, of which WELCAN units are perhaps best known in the United Kingdom. Even in assessing laboratory costs the system has some problems,2–4 but it simply was not designed to measure the workload of histopathologists.

The extreme solution to this problem would perhaps be a large time and motion study to assess just how long an average pathologist takes to produce a report on each type of specimen. Workloads could then be calculated by multiplying each specimen reported by its measured weighting and adding the results together. But who would volunteer to run such a study? How would it be kept up to date? Would it be worth the effort?

In this context, the paper by Suvarna and Kay in the July issue represents a compromise. By discussion and consensus, they have sought to develop a system in which different specimens are assigned different weights in calculating a pathologist’s workload. Advantages over other systems are demonstrated. Although superficially more complex than simple specimen counting, most modern laboratory computer systems should be able to automate this sort of process with no more than minor modifications to the software. The hard work is not in using such a system, but in developing and validating it. Suvarna and Kay have made a start, but they acknowledge that their weightings are unlikely to be acceptable in all laboratories and they invite assistance. The relation between a “unit” and a measure of pathologist’s time remains a little vague, and there is no obvious mechanism to update the system as new developments require additional or alternative approaches. If this is to work, what is needed next is for other laboratories to carry out similar weighting assessments, with a view to developing a national consensus. Further validation by direct observation of pathologists’ working practices will be needed, in a variety of laboratories.

A sophisticated, validated method could have benefits beyond those proposed by Suvarna and Kay. For example, I may suspect that I spend too long examining endometrial biopsies, but tire too quickly when examining those innumerable prostatic chips. I find that I am working long hours; is this because I am obssessional with the high power objective, or am I being asked to do more work than is reasonable? How can I know? Truth is elusive, but with a national consensus on current practice we would at least have a benchmark for comparison. Most pathologists would welcome this as a form of self assessment, but there may be concern that self assessment could be replaced by peer or managerial assessment. Even so, is it not preferable to be assessed on the basis of meaningful measurements rather than specimen counts? Perhaps not—if the inaccuracy of the data is a useful excuse for its dismissal.

Do we need all this? Is it worth it? Do doctors in other specialties go to this sort of trouble? One might think that private medicine might provide a test of motivation, as histopathologists are paid not a salary, but by item of work. Here surely is an incentive to measure work accurately; but instead we usually see old, crude systems of workload measurement. Does this mean that there is no appetite for more accuracy?

Specimen counting may have been sufficient in the past, and there may be fear of the controversies that will be provoked by any change; but with increasing demands on pathologists’ time, with sub-specialisation making specimen counting meaningless, and with laboratory computerisation making it easier to be more accurate, surely our methods of workload measurement will have to improve.

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References