manufacture of intravenous immunoglobulin entails a series of alcohol precipitation steps. Recently, specific techniques have been designed to inactivate a range of viruses⁹—for example, intravenous immunoglobulins that have been heated or treated with solvent and detergent are currently on trial with some confidence that these procedures will inactivate all hepatitis viruses.

Most licensed intravenous immunoglobulin preparations are well tolerated, causing few short term side effects, although patients with hypogammaglobulinaemia commonly experience mild or moderate reactions during their first few infusions. Many of these patients carry a considerable microbial load before treatment, so it is not surprising that any sudden interaction of infused antibodies with these microbes might release inflammatory mediators, causing fever, rigors, abdominal pain, and sometimes bronchoconstriction and hypotension. As a general rule, infusing intravenous immunoglobulin during acute infection is not advised—it is better to wait until the patient improves with antibiotic treatment. A few patients with hypogammaglobulinaemia have repeated reactions, presumably due to minor contaminants in intravenous immunoglobulin, and changing to a different preparation may be helpful. The overall message, however, is that currently available intravenous immunoglobulins are well tolerated, to such an extent that an increasing number of patients with hypogammaglobulinaemia currently give themselves infusions at home. Guidelines agreed with the Department of Health state that such patients should be trained for home treatment in designated centres, of which there are now seven in the United Kingdom.

Life threatening anaphylactic reactions may occur in one important but rare combination of events. Patients with selective deficiency of IgA may develop anti-IgA antibodies in their serum after their first exposure to blood or blood products containing IgA. Routine screening is necessary to identify these patients, who should then be given preparations of intravenous immunoglobulin containing minimal amounts of IgA. A safe policy is to ensure that all patients receiving intravenous immunoglobulin are supervised by experienced staff for at least the first four infusions.

Aggressive marketing is putting pressure on pharmacies to stock only one commercial preparation of immunoglobulin, and some patients with hypogammaglobulinaemia have already been switched from one type to another, sometimes without consultation with their doctors. Any tendency to

regard intravenous immunoglobulin as a generic preparation should be discouraged as manufacturing procedures vary and the final product is only crudely standardised. Further outbreaks of hepatitis, which could not be linked to any particular preparation, could leave patients at a considerable disadvantage if they wished to claim for compensation. Doctors should acquaint themselves with the broad principles of the manufacturing process so that they know whether they are using material that has been subjected to viral inactivation procedures (so called third generation intravenous immunoglobulins) or second generation products, which from experience are considered to be safe. For those who might participate in clinical trials of new preparations, it is wise to dig a little deeper into the background and infrastructure of the manufacturer—and to feel uneasy if the company concerned has not had previous experience in making a safe intravenous immunoglobulin.

Exciting developments in treatment with intravenous immunoglobulin should take place in the 1990s. Multicentre trials are needed to test efficacy in some of the rarer autoimmune diseases, and for the commoner disorders like myalgic encephalomyelitis or asthma a double blind trial will probably be necessary. One possible benefit of the new cost cutting NHS is that doctors will be discouraged from using expensive intravenous immunoglobulins empirically until the results of formal trials are available.

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Nursing: an intellectual activity

Nurses need heads as well as hands

There are two ways of looking at nursing: which one you choose determines your whole perspective on the nursing world.

The first sees nursing as a collection of tasks or procedures which require some skill but are initiated and directed by others—particularly doctors—whose function they exist to assist. Because they require skill some training is necessary, but competent performance does not require an understanding of why the task is necessary, how it works, or what its effects will be. Within this view nursing has no knowledge base of its own, nor does it need one: its skills are essentially manual and technical and reflect the knowledge of other disciplines.

The second, quite different, view sees nursing as a particular

kind of interpersonal interaction, which has specific goals and involves particular kinds of activities. Its focus is the physical and emotional responses of people to illness, treatment, and disability. Its goal is to enable people (individuals, families, and communities) to maximise their potential for health; to enhance their ability to cope with illness and disability; and to promote physical and mental comfort, healing, and recovery. What distinguishes this perspective from the first is its intellectual component: the use of clinical judgment based on knowledge.

Assessment, planning, implementation, and evaluation all depend on clinical judgment. Assessment necessitates seeking relevant information (by observing, examining, and history

taking), synthesising and interpreting this information, and using it to identify needs and problems and the patient's current and potential ability to deal with them. Planning entails setting appropriate goals, considering alternative strategies, and selecting those most likely to achieve the goals. Implementation—putting this plan into action—includes using particular treatments (physical and interactional) and also coordinating a programme of care to ensure the best use of resources and the maximum comfort for the patient. Evaluation means seeing whether the plan has worked and revising the strategies or the goals as necessary.

The thought processes are identical with those used in medicine. Both sorts of practice require sophisticated cognitive and social skills. As the focus of nursing is human response, and as each person is unique, the complexity is infinite and the intellectual demand huge.

Enabling an old lady whose fractured femur has been mechanically repaired to regain mobility, continence, and the self confidence to return to independent living is a considerable intellectual and emotional challenge. So is teaching a couple to manage their baby's tracheostomy at home, or feeding a person whose ability to chew and swallow is compromised by a stroke, especially when the mechanical difficulty is compounded by anger and despair at the degradation of such dependency.

Unfortunately, it is the first perspective—nurses as skilled manual workers—which is the more prevalent and this explains many current ideas about the staffing mix and the deployment of the nursing workforce. Yet it cannot meet patients' expressed needs for coherent and holistic care or extant definitions of quality care.

The problem is that nurses are generally poor at articulating their knowledge and the complexity of their decision making. A recent teaching video shows a district nurse visiting an old woman with an ulcerated leg and applying a dressing. The

close up of the nurse's hands is accompanied by a soundtrack of their social conversation. There is no "thought bubble" to show the decision making process—the nurse's clinical observations and assessments go undocumented. Her knowledge is "embedded in practice"; only the manual task is visible.

Nursing is an ancient art but a young discipline, still developing and refining its conceptual framework. Only now is it beginning to define and classify the phenomena that are its concerns and its interventions and outcomes. Its knowledge base, albeit embedded in clinical practice, has still to be articulated, refined, and tested through scientific research.

Progress during the past 10 years has been dramatic. Research in nursing, especially at doctoral and postdoctoral level, is growing rapidly. For some things, such as managing pain and wounds, supporting the terminally ill, and educating patients, nursing practice can now be based on scientific research and can show clinical effectiveness. Nursing development units, based on the models established in Oxfordshire and Tameside, are growing in number and influence. A professorial clinical nursing unit associated with the new School of Health Care Studies at Middlesex Polytechnic has been established in a small hospital providing care for elderly people in Colindale.

Nursing is already valued—at least by doctors and patients if not always by managers—for its instrumental component (its technical skills) and its expressive component (its emotional, comforting, and nurturing skills). Recognition of nursing's intellectual component is now long overdue.

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The other genome

Small but significant

Mitochondria possess their own genetic material, each containing from two to 10 double stranded circular DNA molecules about 16·6 kilobases in length. Large deletions and point mutations of mitochondrial DNA have recently been associated with disease—chiefly mitochondrial myopathies and encephalomyopathies and Leber's hereditary optic neuropathy. More tantalisingly, mutations of mitochondrial DNA may play a part in neurodegenerative disease and normal aging.

Two observations, related to coding function and mode of transmission, pointed to mitochondrial DNA as a potential culprit in the pathogenesis of mitochondrial myopathies and encephalomyopathies. This clinically heterogeneous group of diseases may present with infantile lactic acidosis, progressive external ophthalmoplegia, myopathy with weakness made worse by exercise, and various syndromes predominantly affecting the central nervous system. These include myoclonic epilepsy with ragged red fibres (MERRF) and mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS). These disorders share the morphological hallmark of structural abnormalities of mitochondria in skeletal muscle, giving rise to the ragged red fibres seen in muscle biopsies stained with the modified Gomori trichrome method or succinate dehydrogenase.

Defects of the mitochondrial respiratory chain and oxidative

phosphorylation are found in most patients with these diseases.^{1,2} The respiratory chain's enzyme complexes contain 13 subunits encoded by mitochondrial DNA. In addition, if patients with mitochondrial myopathies have affected relatives in more than one generation transmission occurs much more often through the maternal line than through the paternal line. Mitochondrial DNA is exclusively maternally transmitted. Another disorder, Leber's hereditary optic neuropathy, which causes subacute blindness mainly in young men, also exhibits maternal inheritance.

The first defect of mitochondrial DNA described in association with human disease was the presence of large deletions in one population of mitochondrial DNA in the muscle of patients with mitochondrial myopathies.³ These deletions, which do not seem inheritable, occur in about 40% of affected adults, all of whom have progressive external ophthalmoplegia and some the Kearns-Sayre syndrome of progressive external ophthalmoplegia, retinopathy, conductive cardiac defects, and ataxia.^{4,5}

Deletions of mitochondrial DNA are also found in lymphocytes of patients with Pearson's syndrome, a disorder comprising neonatal pancreatic and hepatic insufficiency, pancytopenia, and lactic acidosis.⁶ Patients with Pearson's syndrome who survive may develop the features of Kearns-