NEURO-THERAPEUTICS 1950-2002

FROM THE WORLD FEDERATION OF NEUROLOGY RESEARCH GROUP ON THE HISTORY OF THE NEUROSCIENCES

Advances in many fields within the neurosciences during the last half-century have taken the form of imaging techniques, neurosurgery and diagnosis by electrical testing in various ways. However, neuro-therapeutics is the goal of all techniques of investigation and the Research Group on the History of the Neurosciences reflects interest in all these areas.

A study of the immunological mechanisms involved in **neuromuscular disease** has developed from the original techniques of Mary Walker (1888-1974) who was brought up in Wigtown in Scotland, the daughter of a judge. In her interpretation of the clinical features of **myasthenia** and their similarity to curare poisoning, she used physostigmine in 1934 and from this developed other anti-cholinesterase inhibitor treatments. Understanding of the immunological basis of myasthenia followed the work of John Simpson in Glasgow and thereafter immunosuppression with cortico-steroids and azothioprine, cyclophosphamide, plasmapheresis and intravenous gamma globulin. Nowadays the disorder can be held in remission for most patients and anti-cholinesterase drugs, though helpful in the alleviation of symptoms, are used less often when the disease process is suppressed.

In parallel with these immunological aspects of myasthenia, peripheral nerve disorders have become understood better. The immunological basis of the **Guillain-Barré Syndrome** where argument used to reign as to the value or harm done by steroids and the development of plasmapheresis and gamma globulin has enabled effective treatment for many **inflammatory neuropathies**. The mechanism or action of gamma globulin is unclear though some feel that the pooling of human serum has provided specific antibodies to suppress disease in the inflammatory neuropathies and to block receptor sites. The immunological basis of **disorders of muscle** is less clear but the classification of the **muscular dystrophies** is based now more precisely upon molecular genetic testing. Neuroscience owns much of the human genome and the **mitochondrial disorders** may be better understood as knowledge advances in these fields with resultant successful gene therapy.

Plasmapheresis is labour-intensive and expensive in equipment and time-consuming. Though useful in patients in whom gamma globulin does not work effectively, gamma-globulin therapy takes first place over Plasmapheresis in most clinical situations.

Anti-inflammatory treatment in **multiple sclerosis** is expensive too. Beta-interferon at first was thought only to reduce the number of relapses by about one-third but it seems to have a more specific action in promoting well-being. Physicians who have treated patients with beta-interferon are well used to hearing reports of improvement in disease state and a reduction in disability. Further studies may show partial recovery following beta-interferon treatment and more widespread use may become the norm. The risk-showing scheme for beta-interferon shortly to be introduced in the United Kingdom may or may not produce valid data to support this.

Other treatments in neurology are thought to slow and sometimes halt progress. The work of Gardner in **syringomyelia** is an illustration. Surgery to prevent extension of a spinal cord cavity is directed at preventing progression of the disease rather than reversal of symptoms and signs already present. Thus this disease, thought originally to be the result of failed development of the nervous system, can be associated with congenital anomalies, tumours and other cavity-producing mechanisms. The concept of the disease has changed over the years such that the disease process (in this case dissection of the cord like a cavity) produces prime understanding and the mechanisms leading to it are more plentiful than the original theory suggested.

Commensurate with this wider approach to disease processes has come the understanding that **disability** is paramount rather than disease category in the textbook index. Patients are investigated less frequently nowadays simply to produce a textbook diagnosis and more to produce successful intervention. Very often the two are linked inextricably but it is the reduction of disability which is the end point sought by the patient and therefore by his doctor. Even a slight reduction in disability is a major step forward for the disabled however minor it might appear to the outsider.

The successful vaccination scheme against **poliomyelitis** has led to a marked reduction in the incidence of poliomyelitis. The **smallpox** eradication scheme was said successful to have eliminated this disorder to the extent that existing supplies of the virus were to be destroyed. Wisely they have been preserved for biological study and, if necessary, genetic modification and the preparation of new vaccines. The advent of biological warfare makes it very important to preserve samples rather than to discard them and the potential for further knowledge simply on the basis of guesswork that they will not be required in the future.

With every success story there seems to follow a new challenge and the neuroscience of **AIDS** produces the modern challenge. The increase in AIDS parallels the decline of **syphilis** and yet the latter is increasing, as is **tuberculosis**. Increased travel opportunities for patients should create vigilance for the neuro-therapist in all countries. Fortunately neuro-therapeutics has an armamentarium for the treatment of tuberculosis and **malaria**, two of travellers' major challenges for the neurologist – but the disorders must be diagnosed first and this means great vigilance.

Progress is slow in the evaluation of neuro-therapeutics and the understanding of thrombolysis for **stroke** is in its infancy. Neurologists thought they knew the indications for **carotid endarterectomy** for stroke though this topic is open for discussion again. Other areas of neuro-vascular therapy have taken advantage of the great developments in technology. Where a lesion (in this case an **aneurysm** or **arterio-venous malformation**) can be accessed through a tube (in the arterial system) that leads directly to it, it seems only sensible to approach it in endovascular fashion. Coiling with metal implants and the injection of glue represent major neuro-therapeutic advances as indeed does the understanding that unruptured aneurysms, discovered co-incidentally, in some circumstances may not be treated in order to avoid the greater risks that treatment brings. With every treatment there comes risk and the risks must be assessed against the patient's symptoms, a basic tenet of medicine which has become better understood and better practiced over the last half century.

Members of the World Federation Research Group on the History of the Neurosciences are keen to use the understanding of the lessons of history to enhance their thinking in relation to modern and forthcoming investigation and treatment for the benefit of all patients. History is of interest. It is of importance in order that the lessons of the past can be applied to the future. Most (if not all) decisions are made on the basis of past experience in order to reduce risk and to take shortcuts to modern neuro-therapeutics. Those who would wish to join in these shorts of thoughts and who would like to join the Research Group should respond by e-mail to cgardnerthorpe@doctors.org.uk.