NEUROLOGY 2004

13 May 2004

SESSION 1
INFECTION AND THE NERVOUS SYSTEM

Chair: Dr J O'Riordan, Consultant Neurologist, Ninewells Hospital, Dundee, Scotland

CNS INFECTION IN THE IMMUNOCOMPROMISED PATIENT

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Abstract

Apart from the inherited immune deficiencies, patients may become immunodeficient from a range of disorders ranging from diabetes to immuno-suppressant drugs used in neurological, rheumatological and oncological diseases. Worldwide, HIV/AIDS is now the most common cause. This lecture will concentrate on the problems encountered in this latter group of patients. However, the basic clinical problems will be relevant to all immunodeficient patients. Although such patients will usually be managed by specialists nevertheless it is important for general physicians to be aware, as, from time to time, these patients will present via A&E on acute takes.

Outline of lecture

1. The clinical problems result from deficits in humoral and cellular immunity which makes diagnosis of infections difficult – the usual antibody responses helpful in diagnosis do not occur. As a result of an obtunded cellular response, the typical features of conditions such as meningitis are not usually apparent; multiple infections may occur; and cerebrospinal fluid (CSF) cytochemical parameters may be difficult to interpret.

2. The most common mass lesions in HIV are due to toxoplasmosis, primary CNS lymphoma and tuberculosis (TB) – the clinical, serological and radiological clues to diagnosis will be presented. A diagnostic algorithm will outline a management plan.

3. The differential diagnosis of meningitis will be discussed with some details on the diagnosis and prognostic features of cryptococcal meningitis – the commonest cause in HIV patients. The management of raised intracranial pressure in such patients will be outlined. The difficulties in the diagnosis of TB meningitis will be raised.

4. The methods of diagnosis and treatment options used for progressive multifocal leucoencephalopathy (PML) will be outlined.

Neurological infectious complications occur frequently in the immunosuppressed, especially in HIV-infected patients. The usual clinical and investigation tools are blunted in this group. With increasing experience specific management guidelines have been developed. The use of Polymerase Chain Reaction (PCR) in particular has been a great step forward.

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Key words: Cryptococcal meningitis, HIV, mass lesions, PML.

Sponsors: None.

Declaration: I have received a travel fellowship from GlaxoSmithKline to study HIV neuropathy for three months in L'Hôpital KREMLIN – Bicentre, Paris.

WHAT THE UK NEUROLOGIST NEEDS TO KNOW ABOUT TROPICAL NEUROLOGICAL INFECTIONS

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Abstract

Tropical neurological infections are uncommon in UK practice but worldwide cause substantial morbidity. Migrants to the UK, and travellers from the UK, are potentially exposed and may import these conditions. Viral and bacterial infections are seen, but protozoa and helminth parasites pose an increasing risk.

Cerebral malaria presents as a pyrexial encephalopathy, possibly to the acute neurology take, but treatment requires Infectious Disease expertise. There are ten UK deaths each year. Neurological sequelae may follow treatment, or be associated with antimalarial prophylaxis.

Sleeping sickness (African trypanosomiasis) was almost eradicated but is now again common in a central band across Africa. Travellers to the endemic zones are at risk.

Eosinophilic meningoencephalitis in south east Asia is caused by a variety of nematodes, transmitted by snails and shellfish or contaminated vegetables. Imported cases occur.

Schistosomal infection is common in backpackers who swim or bath in lakes or rivers in endemic zones. Spinal granuloma may cause a painful paraparesis which responds in early cases to antihelminth therapy.

Neurocysticercosis is the most common cause of epilepsy in parts of Latin America and other endemic areas. Migrants or UK visitors are at risk of infection with the larval form of *Taenia solium,* and many imported cases have been identified. Characteristic CT or MR appearances should lead to appropriate treatment with antiepileptic drugs and sometimes with cysticidal agent.

Neurologists should consider tropical infections in patients who have lived in or visited endemic regions.

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Key words: Tropical neurological infections.

Sponsors: None.

Declaration: No conflict of interest declared.

UPDATE ON MANAGEMENT GUIDELINES FOR MENINGITIS

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Abstract

Bacterial meningitis (BM) occurs relatively infrequently in the general population, with typically between 1,000 and 2,000 cases per annum in England and Wales. Cases occur sporadically and progression is usually rapid. Mortality untreated is very high, approaching 100% in some historical series. Prompt antibiotic treatment and appropriate supportive care have a dramatic effect on mortality and morbidity. For example, in one recent published series of 97 cases of culture positive meningococcal meningitis overall mortality was 3%. Patients with BM due to meningococcus also often have features of meningococcaemia, which are associated with a more rapid progression and a higher mortality, even with prompt appropriate treatment.

As a result of these features the evidence base for the treatment of BM is relatively poor. Management guidelines for BM in adults, based on a systematic review of the published literature and the consensus views of a panel of experts, were published in 1999 by a Working Party of the British Infection Society. These guidelines formed the basis of a treatment algorithm which was published in 2003 and which has been widely circulated in the form of a poster and educational material for health professionals and the public by the Meningitis Research Foundation (MRF).

Guidelines for the management of meningitis and meningococcaemia in children, developed on the basis of expert opinion, have also been published by the MRF and circulated in similar formats.

The guidelines draw attention to the difficulty in distinguishing between many cases of viral infection with fever and headache, and rare cases of BM. Early recognition is essential in order to facilitate prompt administration of appropriate antibiotics and supportive therapy. Adults who exhibit one or more of the following features should be referred to hospital for assessment: signs of meningeal irritation, impaired conscious level, petechial rash, patients who are febrile or unwell after a fit, and any illness in a contact of a known case of meningococcal infection. Neck stiffness is absent in up to 18% of adults with BM, and the triad of fever, neck stiffness and impaired conscious level is seen in only approximately 50% of cases.

Immediate administration of antibiotics is universally recommended, and GPs are encouraged by the Department of Health to carry benzylpenicillin on house calls, for administration prior to transferring patients to hospital. Current recommendations for antibiotic therapy of BM in hospital take account of the likelihood of infection by particular organisms, the prevalence of penicillin-resistant pneumococci and the possibility of penicillin hypersensitivity. The possibility that immediate administration of antibiotics may make subsequent microbiological diagnosis more difficult should not delay therapy, particularly since the availability of sensitive and specific serology and PCR testing for meningococcal infection. Gram staining of material from skin lesions may also allow diagnosis in

patients who have received antibiotics.

Lumbar puncture (LP) remains an important part of routine care, and computerised tomography (CT) scanning is only necessary before LP if patients have signs suggestive of raised intra-cranial pressure, such as a low (<12) or falling (>2 points fall since admission) Glasgow Coma Scale. Lumbar puncture and CT should not be allowed to delay administration of antibiotics in patients in whom BM is suspected.

The role of steroids in the management of BM has been controversial. Studies in children have shown a reduction in neurological sequelae in children with BM due to *Streptococcus pnuemoniae* and *Haemophilus influenzae*, but not in meningococcal disease. A recently published study of dexamethasone given before or with antibiotics in adults with BM showed a reduction in morbidity and mortality which was greatest in those with pneumococcal infection and who were most unwell at presentation. There was no significant benefit in patients with meningococcal infection and no effect on neurological sequelae. Animal studies have not shown benefit when steroids are given after antibiotics. Therefore the place of steroids in the management of BM in adults remains unclear, and will be discussed.

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Key words: Antibiotics, bacterial meningitis, corticosteroids, dexamethasone, meningococcaemia, therapy, *Neisseria meningitides,* steroids.

Sponsors: None.

Declaration: No conflict of interest declared.

SESSION 2
IMAGING IN STROKE

Chair: Dr M Zeidler, Consultant Neurologist, Victoria Hospital, Kirkcaldy, Fife, Scotland

MANAGEMENT OF INTRACRANIAL ANEURYSMS

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Abstract

To review and present the evidence for the optimum management of ruptured and unruptured intracranial aneurysms and to address the issue of screening for aneurysms.

Review of the latest literature and recent published and unpublished data from the International Subarachnoid Aneurysm Trial (ISAT) and from the International Study of Unruptured Intracranial Aneurysms (ISUIA) and discuss the implications for screening for cerebral aneurysms

Two recently published studies have changed the pattern of management of intracranial aneurysms. The ISUIA has provided the largest prospective observational study of unruptured intracranial aneurysms. This has shown that small incidentally found aneurysms are at very low risk of rupture but that aneurysms over 7 mm and in certain locations are at significantly higher risk of rupture, as are those small aneurysms in patients with prior subarachnoid haemorrhage (SAH) from another aneurysm.

The ISAT, a randomised trial in 2,143 patients comparing surgical clipping with endovascular coiling has demonstrated a highly significant reduction in the risk of a poor outcome (defined by death or dependency on the modified Rankin scale) at one year. The absolute risk reduction is 7·4% (30·9% after neurosurgery to 23·4% after coiling),with a relative risk reduction of 24%. The risk of re-bleeding after coiling is slightly higher in the coiling group but the late risk is very low in follow-up to five years.

Screening for unruptured intracranial aneurysms is only justified in patients with at least two first-degree relatives with SAH or in patients with adult polycystic kidney disease and a family history of SAH.

Patients with SAH from ruptured intracranial aneurysms, when the aneurysm is anatomically suitable for coil treatment, are more likely to be alive and independent at one year with endovascular coiling than neurosurgical clipping. Patients with SAH should be managed in centres with access to endovascular coiling as well as neurosurgical clipping. Medical staff should

not alarm patients with small unruptured intracranial aneurysms by telling them they have a 'time-bomb' in their head. They need to be counselled by an experienced neuroscience clinician preferably with experience of both clipping and coiling and fully informed of the risks and benefits of treatment.

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Key words: Cerebral aneurysm, endovascular treatment, subarachnoid haemorrhage, unruptured cerebral aneurysm.

Sponsors: ISAT was funded by the Medical Research Council. Dr Molyneux is part funded by the MRC. ISUIA was funded by the NINDS.

Declaration: Dr Molyneux has consultancy agreements with Micrus Corporation and Micro Therapeutics Inc.

THE LILLY LECTURE

Chair: Professor N Douglas, President, Royal College of Physicians of Edinburgh, Edinburgh, Scotland

LESSONS FROM THE NATURAL HISTORY OF MULTIPLE SCLEROSIS

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Abstract

There is good evidence that relapses in multiple sclerosis (MS) are the clinical counterpart of acute focal inflammation of the CNS whereas progression is that of chronic diffuse neurodegeneration. The classical view is to consider that MS is an organ-specific auto-immune disease, i.e. that inflammation is the cause of the neurodegeneration. The succession of relapses eventually leads to accumulation of disability and clinical progression could result from infraclinical relapses. A series of recent observations tend to challenge this classical concept.

Beta-interferons have well-known effects in MS. They lead to a 30% reduction in the relapse rate and to a more than 50% reduction in conventional magnetic resonance imaging (MRI) activity. Despite this strong effect on inflammation, the effect of interferons on disability is only marginal and possibly relapse-reduction driven. Administration of campath-1H to MS patients with a very active disease in terms of frequency of relapses, accumulation of disability and MRI activity, results in a profound and prolonged lymphopenia, and the suppression of clinical and MRI activity. In spite of this, progression of clinical disability and cerebral atrophy still occurs. The relapse rate decreases dramatically during pregnancy, notably during the third trimester, where it is reduced by 60% in comparison to the rate observed during the pre-pregnancy year. By contrast, the three-month post-partum period is characterised by a 60% increase of the relapse rate by comparison to the same period of reference. Despite these dramatic changes in the frequency of relapses, progression of disability goes on, seemingly unaffected throughout this period. Striking results have also come from the study of the natural history of MS in the Lyon MS Cohort. Progression of irreversible disability from the assignment of a score of 4 on the DSS Kurtzke scale to the assignment of a score of 6 or 7 is unaffected by the presence or the absence of a relapsing-remitting phase before the progressive phase of MS. The same observation is true regarding the presence or the absence of superimposed relapses during the progressive phase, either primary or secondary.

All these observations give some credit to the fact that relapses do not essentially influence irreversible disability in the long term in MS. They are consistent with what has been shown at the individual level in the 70s by performing serial quantitative neurological examinations over several years, and with what is currently emerging from early and serial structural brain MRI studies.

Key words: Beta-interferons, campath-1H, DSS Kurtzke scale, Lyon MS Cohort, multiple sclerosis, natural history of MS, pregnancy.

Sponsors: None.

Declaration: No conflict of interest declared.

SESSION 3
MANAGING NEURODEGENERATIVE DISEASES

Chair: Dr L Gerrie, Consultant Neurologist, Aberdeen Royal Infirmary, Aberdeen, Scotland

THE MOTOR NEURONE DISEASES

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Abstract

Sporadic motor neurone disease is a progressive and ultimately fatal neurodegenerative disease of unknown aetiology. Patients survive for a median 40 months after symptom onset. At present the cause is unknown and promising results in therapeutic trials in animal models have not been translated into effective therapies for the human disease.

Identification of specific genetic disorders with Mendelian inheritance has furthered our understanding of the biochemical basis of motor neuron vulnerability. Evidence from transgenic mice over-expressing mutant human SOD1 protein has implicated abnormalities in oxidative metabolism, glutamate uptake, mitochondrial dysfunction and axonal transport as all being potentially relevant, though the primary trigger to motor neurone degeneration remains unclear. Other motor neurone disorders such as recessive and dominantly inherited forms of spinal muscular atrophy and hereditary spastic paraparesis have demonstrated the importance of RNA handling, protein chaperone function and axonal transport for motor neurone development and maintenance. In clinical practice improvements in patient wellbeing have occurred as a result of the development of multidisciplinary teams working in specialist centres. Percutaneous endoscopic gastrostomy feeding and non-invasive ventilation are important palliative measures.

This lecture will provide an overview of the molecular basis of motor neurone diseases and review current management and prospects for future therapies

Key words: Amyotrophic lateral sclerosis, motor neurone.

Sponsors: Medical Research Council, Motor Neurone Disease Association.

Declaration: No conflict of interest to declare.

THE DEMENTIAS

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Abstract

Traditionally neurologists have seen younger or atypical patients with dementia in order to exclude treatable causes with minimal subsequent involvement in the management of the broad group of degenerative dementias. However, with the emergence of potential treatments a specific diagnosis is becoming increasingly important.

Alzheimer's disease is the prototypical dementia with impairment of episodic memory but may present with other cognitive deficits such as visual disorientation leading to diagnostic confusion. Dementia with Lewy bodies are often referred to neurologists because of the extrapyramidal features but these may only emerge years after the cognitive symptoms. The broad group of frontotemporal degenerations, presenting with a variety of language, speech and behavioural deficits, are associated with a variety of histopathologies which cannot be readily predicted from the clinical features.

Current drugs are symptomatic and include the anticholinesterases donepezil, rivastigmine and galantamine and the NMDA partial agonist memantine. Many drugs which may affect the proteinopathy of Alzheimer's disease are being developed. The immunisation trial with Ab1-42 was terminated due to the development of meningoencephalitis in some patients but limited autopsy studies suggest amyloid clearance.

References

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Key words: Alzheimer's disease, anticholinesterases, cognitive deficits, degenerative dementias, donepezil, galantamine, immunization with amyloid-beta peptide, memantine, NMDA partial agonist, rivastigmine.

Sponsors: None.

Declaration: No conflict of interest declared.

SESSION 4

DEBATE: COPYING OUTPATIENT LETTERS TO PATIENTS: SCOTLAND SHOULD FOLLOW ENGLAND AND WALES

Chair: Professor I Bone, Professor of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland

FOR

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Abstract

The Department of Health has, since 1 April 2004, required patients in England and Wales to be offered copies of all correspondence relating to their medical care. Scotland has yet to follow. However, changing patient expectations and a more equal relationship with medical professionals make the change inevitable here also.

The advantages of copying letters to patients go far beyond a display of greater openness. A letter summarising a consultation is a common courtesy as well as a valuable resource for the patient. Letters can aid understanding, provide information, empower patients and improve adherence to treatment regimens. Away from the distraction and anxiety of the hospital, patients can read and re-read about their diagnoses and management plans, the names of medications or of personnel, and lifestyle advice. A letter provides an opportunity (rarely taken) to correct errors of fact. It can be therapeutic to know that the doctor has listened and understood. Also, doctors who know that their patients will receive a written record of the consultation are likely to have more open and honest conversations with them, and to write clearer, better structured, and more accurate letters. Technical language does not need to be compromised, but both patient and general practitioners welcome clear explanations of treatment advice.

In arguing against copying letters to patients (patient anxiety, inhibition about what to include, fear of speculating about diagnoses or later being shown to be wrong) doctors highlight their traditional conservatism, caution, paternalism and insecurity. In fact, patients are less anxious knowing the doctor has been open and honest. The number of patient queries falls, not rises, after copying letters to them.

Copying correspondence to patients has many advantages to patients and clinicians. General practitioners already frequently share our letters with patients and it should now be the exception to write letters that we would not wish patients to read. Our patients' increasing demand for access to notes and letters provides the opportunity to improve our communication with them. Scotland must embrace this standard and courteous practice.

References

1 Smith PEM. Letters to patients: Sending the right message. Personal View. *BMJ* 2002; **324:**685.

Key words: Copy, letters.

Sponsors: None.

Declaration: No conflict of interest declared.

AGAINST

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Abstract

The advantages of copying letters, addressed to general practitioners, to patients are obvious; the current problem of recruitment into primary care will be obviated as that service becomes obsolete; we shall revert to the North American concept of everyone choosing their own specialist; communication and therapy will be direct between the patient and the consultant; patients will be able to make their own appointments with the specialist of their choice who will see them in the conveniently timed out-patient department of a general hospital running between the hours of 1200 and 1500 hours and 2000–2300 hours to avoid those difficult problems of taking the children to school, morning coffee, collecting the children from school and watching the early evening soaps on television.

As a future Secretary of State may say: 'Consultants in hospitals will work shifts, 8 hours at a time, of which two hours will be spent seeing patients in the clinic, two composing the careful letters which will be understandable, yet comprehensive, brief, yet all embracing and kindly, yet firm. The final four hours of each shift will be spent answering correspondence, telephone calls, e-mails and solicitors letters arising from the original correspondence!'

Key words: Copy, hoax, letters, patients.

Sponsors: None.

Declaration: No conflict of interest declared.