131P THE OPEN CAMPUS: A DISTRIBUTED LEARNING GENERAL PHARMACOLOGY COURSE

M.E. Brodie, D.W. Peterson & V. Raman.
Division of Physiology and Pharmacology, University of Hertfordshire, Hatfield, Herts. AL10 9 AB

Most pharmacology programmes will have a unit of general pharmacology that covers the major principles of pharmacodynamics and pharmacokinetics. We have also taught these areas at the start of conversion postgraduate courses and short courses to industry for students without a pharmacology background. All of these groups could use in differing ways open/distributive material to support and/or provide the primary information source for a general pharmacology unit.

We are developing a computer based general pharmacology package for use by short course participants, and as open learning material for pharmacology students on traditional university courses. The majority of the package is web-based to run on a standard browser with the appropriate plug-ins and includes its own navigational aids for ease of use. Each part of the course is a self-contained unit that is intended to be viewed in a linear manner, but it is possible to jump to any point for purposes of revision and clarification.

Some might argue that, when using a different delivery system such as computers, the style of presentation must change drastically from that used in a traditionally taught university course. We have been influenced by feedback from our students and short course participants which has indicated a strong preference for standard lectures, seminars and workshops as the primary means of delivery of the taught material. Therefore, this computer-based course has attempted to reproduce as closely as possible the teaching programme used on campus, and for short courses delivered to industrial clients. PowerPoint presentations are presented on individual web pages, but significantly enhanced with animations and interactivity to hold the interest of the student. Each slide is accompanied by a voice-over that is very similar in style to the lecturer's presentation. Practical elements for the courses are provided by the use of simulations. This has been extensively used in the kinetics components where interactive models of drug kinetic processes provide instant feedback information and data to be analysed by the student. This presentation style combined with interactivity and ease of navigation offers the benefits of a conventional live presentation with the flexibility afforded by the new technologies. Throughout the sessions there are tests that maybe used for self-assessment, or the results can be sent to a tutor via e-mail. While the package is intended to be self-contained, e-mail contact, and possible on campus tutorial sessions, and 'wet' practicals would be available for further support.

We will be demonstrating the pharmacokinetics unit of this computer-based course that illustrates the interactions of the classroom lectures, the simulated practical sessions and the self-assessment tests. We will also be showing the component of the pharmacodynamics unit that covers G-protein-coupled receptors. An external examiner has critically evaluated some individual components of the computer-based course. Also pharmacology students have used parts of the programme, but the integrated package has yet to be evaluated. This evaluation will take place when the entire course can be offered via distance learning to participants off campus.

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132P NEW ANTIEPILEPTIC DRUGS

Ley Sander, Institute of Neurology, University College London, Queen Square, London WC1N3BG and National Society for Epilepsy, Chalfont St. Peter, Bucks., SL9 0RJ

New antiepileptic drugs (AEDs) are necessary for patients with chronic epilepsy and for improving upon established AEDs as first line therapy. Ten novel anti-epileptic drugs (AEDs) have been launched worldwide in the last decade. Six of these (in chronological order of appearance: vigabatrin, lamotrigine, gabapentin, topiramate, tigabine and oxcarbazepine) are currently available in the United Kingdom.

Complete freedom from seizures with the absence of side effects should be the ultimate aim for AED treatment and the new AEDs have not entirely lived up to expectations. Only a small number of patients with chronic epilepsy have been rendered seizure-free by the addition of new AEDs. Despite claims to the contrary, the safety profile of the new drugs is only slightly more favourable when compared with the profile of the established drugs. The chronic side-effect profile for the new drugs is yet to be fully established. Recently, one of the new AEDs, vigabatrin, has been associated with a chronic side-effect which has limited its use.

Most patients with chronic epilepsy still rely on the development of novel treatment for their only hope for seizure control. This is, however, a heterogeneous group and it is unlikely that a drug that is efficacious for all patients will ever be found. Another important reason for the continued quest for new treatments is the need for safer alternatives as none of the AEDs currently available, including the new ones, are free from adverse effects.

133P SURGERY AND NON-PHARMACOLOGICAL TREATMENTS

John Duncan, Institute of Neurology, University College London WC1 and the National Society for Epilepsy, Chalfont St Peter, Bucks.

Whilst three quarters of the 30,000 people per year who develop epilepsy in the UK will be satisfactorily treated with antiepileptic drugs, the remainder will continue to have seizures and also have an annual mortality of 1 in 200.

Surgical treatment should be considered in those with medically refractory partial seizures. The optimal time for this is if three antiepileptic drugs have failed to control seizures, which will generally be 2-3 years after the onset of the epilepsy. It is estimated that there are 1,000 potential candidates for epilepsy surgery every year in the UK.

The evaluation for surgery is complex and time-consuming and is directed to finding a single epileptic focus that may be surgically removed without causing a deficit. The essential components are the clinical assessment, high quality brain imaging with MRI, recording of habitual seizures with video-EEG telemetry, neuropsychological, neuropsychiatric and social evaluations. If all data are concordant, there can be a 70% chance of the patient being rendered seizure free in the long term.

The most common operation is an anterior temporal lobe resection. The risk of a major complication of this operation is approximately 1%, with a 5% chance of a visual field defect that prevents driving and a 10% chance of a post-operative psychiatric disturbance. Other resective operations include removal of structural lesions, with and without surrounding neocortex, lobectomy and hemispherectomy.

Functional procedures that are palliative rather than curative include corpus callosotomy and multiple subpial transection. Neurosurgical resections provide a key correlation to in vivo imaging studies and also provide tissue for pharmacological investigations.

If resective neurosurgery is not feasible, vagal nerve stimulation may provide a useful palliation with efficacy that is similar to a new antiepileptic drug. In children, there has been a recent resurgence of interest in the ketogenic diet. Psychological treatments may help some individuals, particularly if emotional distress is a factor in their epilepsy. Other complementary therapies have their advocates but, at the present, there is a lack of evidence to support their widespread adoption.

134P GENETICS OF EPILEPSY

M R Johnson, Institute of Neurology, University College London, London WC1

The genetic contribution to epilepsy has been known since the time of Hippocrates. It can be categorised into three major groups according to the mechanism of inheritance: (i) Mendelian disorders in which epilepsy forms part of the phenotype; (ii) epilepsy diseases with Mendelian inheritance; (iii) epilepsy syndromes with complex inheritance.

Over 200 Mendelian disorders are recognised in which epilepsy forms part of the phenotype. These include neurocutaneous disorders, neurodegenerative disorders, inherited malformations of cortical development and an array of inherited metabolic disorders. Epilepsies resulting from this mechanism are not considered further in this talk.

This talk is concerned with the genetic basis of the idiopathic epilepsies. The idiopathic epilepsies, for which there is no detectable underlying cause other than an inherited predisposition, account for 50% of all epilepsies. The vast majority of these epilepsies are determined by complex inheritance. However, the study of rare epilepsies with simple Mendelian inheritance has established genetic principles that will likely underpin all idiopathic epilepsies.

I will attempt to review the fundamental genetic principles that constitute the genetic basis to the common epilepsies. Evidence in support of these genetic principles is presented. Such evidence derives from the combination of twin studies, family studies and genetic epidemiology. Taken together, an intellectual framework is emerging that will ultimately allow the common epilepsies to be classified on the basis of their oligogenic architecture, rather than on the basis of clinical features.

135P ANTI-EPILEPTIC DRUG MONITORING AND INTERACTIONS IN EPILEPTIC THERAPY

P N Patsalos, Pharmacology & Therapeutics Unit, National Society for Epilepsy, Chalfont St Peter, and University Department of Clinical Neurology, Institute of Neurology, London, United Kingdom.

Many pharmacological properties of traditional anti-epileptic drugs (AEDs) support suitability for therapeutic monitoring and, undeniably, during the past 10-20 years therapeutic monitoring of AEDs has had a major impact on the management of epilepsy. It is little appreciated, however, that the target ranges employed today are often based on data collected retrospectively from very few patients. Also, it should be remembered that the ranges were not established when the drugs were first introduced into clinical practice but were established many years later when analytical techniques became more widely available.

Since 1989, six new AEDs (vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine and oxcarbazepine) have been licensed in the UK and more can be anticipated within the next 2-3 years. New AEDs are initially assessed in trials (Phase II and Phase III) as adjunctive medication in patients with refractory epilepsy. The primary aim of these trials is to evaluate efficacy and to identify side effects and optimum dosage. Their secondary aim is to determine the pharmacokinetics of the drug and to investigate the possibility of any pharmacokinetic interactions with concurrent AEDs and indeed interactions with a selection of drugs used in the treatment of conditions other than epilepsy.

Even though the relationship between AED plasma drug concentrations, efficacy and side effects is not usually systematically investigated, some data are collected and these data, in these highly selected patients, provide the basis for therapeutic monitoring in clinical practice.

The current status of the usefulness of therapeutic monitoring for individualising therapy and the drug interaction profiles of the new AEDs will be reviewed.

136P EMERGING CONCEPTS IN THE TREATMENT OF STATUS EPILEPTICUS

Matthew Walker, Matthew Walker, Department of Clinical Neurology, Institute of Neurology, University of London, London WC1N 3BG

Status epilepticus (SE) is a clinical term referring to a condition characterised by an epileptic seizure or series of seizures without consciousness being regained that lasts for at least 30 minutes. Importantly, its definition is based solely upon the persistence of the seizure rather than its form, and the term thus covers all seizure types.

The necessity of differentiating SE from other seizure types is not solely clinical, but relates most importantly to the high morbidity and mortality characterised by this condition. There have been few randomised trials comparing treatments in status epilepticus, and present treatment regimes are based mainly on personal preference. Experimental data have led, however, to a number of concepts that are now shaping our approach to treatment.

Status epilepticus appears both in humans and in animal models to be a staged process that can be staged by clinical and electrographic criteria, physiological compromise, occurrence of excitotoxicity, and response to treatment. These stages lend themselves to a sequential treatment regime.

There has also been a growing realisation of the difference between the acute and chronic pharmacokinetics of drugs used in status epilepticus, which has led to the growing popularity of certain drugs over others (e.g. lorazepam over diazepam as initial treatment). Formulations of intravenous antiepileptic drugs have also been problematic, because of the poor water solubility of many of the compounds. This has led to new formulations such as fosphenytoin, a water-soluble prodrug of phenytoin.

The later stages of status epilepticus are treated with anaesthetic agents, yet we are only beginning to define the antiepileptic properties of many of these agents. Furthermore, we are still uncertain of the optimal dose and anaesthetic endpoints that we should use.

Lastly, we are only beginning to understand why seizures continue unabated, and the mechanisms underlying seizure termination. Experimental data from these studies will hopefully provide new, more effective approaches to what remains a serious condition.