SPECIAL REPORT

ILAE President’s midterm report

The “Gray Matters” section of Epilepsia provides a forum for the Journal’s owner—for almost 100 years—the International League Against Epilepsy (ILAE). As the ILAE’s centenary is approaching, and as we become involved with the project of documenting the organization’s and the Journal’s history, we have come to regret that the modern Epilepsia provides little information about the ILAE’s agenda and development. The Editors-in-Chief believe that reports from the ILAE President in the Gray Matters section would be instrumental in improving this situation in the future.

This first report, in what will hopefully be a regular series of messages, is a midterm report about the first 2 years of the present Executive Committee (EC), which was elected in 2004 and 2005 for the period 2005–2009.

THE EXECUTIVE COMMITTEE

According to our constitution, the EC includes three types of officers: six elected (President, two Vice Presidents, Secretary General, Treasurer, and the Immediate Past President), three ex officio (the President, Secretary General, and Treasurer of the International Bureau for Epilepsy, IBE), and two appointed (Editor-in-Chief of Epilepsia and Information Officer). As a result of the last elections, all elected officers came from either Europe or North America, a situation which seemed paradoxical at a moment when the ILAE had become a much more global organization than in the past, with 98 chapters in all regions of the world. It was also somewhat of an anomaly, since previous ECs had often included officers from Asia, Latin America or both.

At the 2005 General Assembly of the ILAE in Paris, an amendment to the Constitution was accepted which says that if after the global elections “any fully operational region of the ILAE is not present on the EC, the Chapters of this region shall elect an additional Vice President (VP). This VP will be a voting member of the EC and not be considered as a regional VP, but unrestrictedly share the global responsibilities of the EC.” The EC at its meeting in Paris, using the description of the “regions” in our bylaws, agreed that a region would be considered fully operational when it: has a Regional Commission that meets from one to three times per year and submits a budget; is proactive to develop, stimulate and coordinate the epileptological agenda in its part of the world; coordinates local education via formation of a regional academy; and organizes congresses under the direction of our International Director of Meetings. The Regional Commissions of the regions that were not present on the elected EC were invited to apply for such a VP, and Asia/Oceania was the only region that did so. Since this very active and dynamic region more than fulfills the established criteria, an election was held in the region for an additional VP.

One of the appointed officers, the Editor of Epilepsia, decided that he did not want to continue with this office beyond 2005. The position was put out for tender, and many interested and highly qualified candidates applied. At the end of a selection process that involved the EC (including the outgoing Editor), we selected a joint editorship—a basic researcher and a clinician—that also represents the two scientifically most active regions of ILAE, Europe and North America. One of the new Editors was at the time already serving as Information Officer. Therefore, there has been a midterm change in this office; again, a tender was put out, and the EC appointed a new Information Officer from the received applications.

At the end of these procedures, the EC now consists of:

Peter Wolf (Denmark), President
Emilio Perucca (Italy), First Vice President
Frederick Andermann (Canada), Vice President
Chong-Tin Tan (Malaysia), Vice President
Solomon Moshe (U.S.A.), Secretary General
Martin Brodie (U.K.), Treasurer
Giuliano Avanzini (Italy), Past President
Susanne Lund (Sweden), IBE President
Eric Hargis (U.S.A.), IBE Secretary General
Mike Glynn (Ireland), IBE Treasurer
Philip Schwartzkroin (U.S.A.), Co-Editor-in-Chief, Epilepsia
Simon Shorvon (U.K.), Co-Editor-in-Chief, Epilepsia
Edward Bertram (U.S.A.), Information Officer

THE PRIORITIES

The EC has set three priorities for our term of office: education, the development of epilepsy care worldwide, and translational research.

Education
It is this EC’s conviction that education of all professionals who are expected to provide care for patients with
epilepsy is the key to any progress, also that the provision of high-quality education attracts and binds young talent to our field. It is in education that we can make the best investment of our resources. It is our ambition to be pioneers in developing the best educational system of all medical specialties. A wide range of approaches has been taken to reach this goal. During the first half of our term of office, the focus of the EC has been on this priority.

1. Organization
   - Educational Commission: The ambitious horizon we have set requires concentrated and innovative work, and a new commission has been appointed to deal with it. The Commission includes representatives of all regional commissions/academies, and has subcommissions for education in French and Portuguese languages, for basic research, and for education of professionals allied with medicine. Following a comprehensive review of the present educational landscape, the Commission is now starting to work on a global master plan.
   - Academies: In both the European and the Asian/Oceanian regions, the establishment of epilepsy academies (EUREPA 1996 and ASEPA 2003) as educational arms of the regional commissions has been a very successful approach. The two academies have developed programs that are tailored to the needs of the respective regions and have contributed much to their progress. This success has encouraged the Latin American Commission to start their own educational academy in 2007 (Academia Latino Americana de Epilepsia, ALADE).

2. Activities
   - Residential Courses, Summer Schools: Residential courses are held in retreat settings and extend up to 2 weeks, during which time a limited number of postgraduate students work with a group of tutors and lecturers. The courses apply a variety of methods of active learning in groups and group design of research projects. The annual Summer Schools of San Servolo in Venice, under the aegis of the ILAE, have been taking place since 2002. The Commission on European Affairs (CEA) has, since 2005, offered a biennial Summer School on antiepileptic drug clinical pharmacology and pharmacotherapy in Eilat (Israel). In 2007, CEA started an annual “Migrating Course” on epilepsy for secondary care physicians in Central and Eastern Europe. Subregional residential courses supported by the CEA include the Baltic Sea Summer School on Epilepsy for young postgraduates (started in 2007) and the Caucasus Summer School that will take place for the first time in 2008. The Latin American Summer School (LASSE), started in 2007, will become an annual course. The first LASSE, near São Paolo, Brazil, brought together young postgraduates from all over Latin America and some Portuguese speaking Africans. All who became involved in this first LASSE consider it a key event that has opened a new era for the development of epilepsy in the region.
   - Educational seminars in underserved locations: Offerings of special seminars in underserved locations is an approach that has successfully been taken by the Asian/Oceanian Commission and Academy. Groups of senior epileptologists address primary and secondary care physicians, especially in countries without ILAE chapters. These seminars provide state-of-the-art lectures on topics relevant to issues of epilepsy care. ASEPA also offers a course and board certification in EEG.
   - Distance education: To make epileptological education accessible more widely, EUREPA has started to establish distance education modules in various fields of epileptology (Genetics, EEG, Neuroimaging, Pharmacotherapy). These modules are tutored courses that use advanced methods of interactive distance education. Their superior efficacy, compared with mere self-study using the same educational materials, has been demonstrated by a prospective evaluation with a waiting-list control group (Hézser-v.Wehrs V et al. Epilepsia 2007;48:872–879). Via VIREPA (Virtual Epilepsy Academy), a section of EUREPA, this activity is constantly renewed and expanded, and is available globally.
   - Fellowships: Fellowships for on-site training in recognized centers and institutes are an integral part of our educational approach in Asia/Oceania. The selected fellows often come from countries without established specialist care for epilepsy, and are expected to take a role in their nation’s development of epilepsy care following their training. Fellowship opportunities are also being developed in North American and Latin America (to reach out to underserved subregions), and also in sub-Saharan Africa.

3. Resources
   - Funding: The budgetary responsibility for educational activities is primarily with the organizers of these courses, who are expected to find multiple sources of sponsorship. For selected programs, support is given by the ILAE, typically as bursaries. For this purpose, the ILAE and some regional commissions use surpluses from the international and regional congresses.
   - Faculty: The expanding educational agenda requires many volunteers who are willing to serve as
ILAE, for the Global Campaign against Epilepsy which we conduct together with the IBE and the World Health Organization (WHO). To give the Global Campaign increased momentum, more responsibility has been given to the regions. Each region is expected to establish a regional Global Campaign steering committee, to include the regional Commission Chairs and the regional Mental Health Advisors of the WHO (see below). The EC plans to focus on this priority in the second half of our term of office.

Translational research
Basic research on epilepsy has increasingly become concerned with issues that are related to prevalent clinical topics. This focus has resulted in significant progress, for example in conceptual approaches of molecular genetics and functional neuroimaging. Some of our educational programs are aimed at strengthening this development.

The above-mentioned summer schools in Venice/San Servolo and Brazil (LASSE) aim at bridging basic research with clinical epileptology.

Some educational seminars at ILAE congresses also address translational research. This was the case at the Latin American congress in Guatemala 2006. An ambitious educational seminar is being planned for next year’s Asian/Oceanian congress in Xiamen (China).

Preliminary talks about possible cooperation have taken place with the Academy of Science of the Developing World (TWAS). It is hoped that this contact will become more substantial at the occasion of the meeting in China.

The Commissions
The work of our Commissions is an important and integral part of our activities. Commissions are appointed by the President as recommended by the EC. The ILAE has both regional and problem-oriented commissions.

Regional commissions
With almost 100 national chapters, the ILAE has reached a size that requires an organizational structure between the Chapters and the global EC. The regional commissions fulfill this need. Each regional commission has a membership that is partly elected by the Chapters of the region and partly appointed by the ILAE President. The regional commissions now include the following:

- Asia and Oceania
- Eastern Mediterranean
- Europe
- Latin America
- North America

The African region is the last major region with no commission of its own. The number of chapters is increasing there, and there is reason to hope that an African Commission can be established towards the end of our term of office.

The role of the regional Commissions for the further development of the Global Campaign, in cooperation with the regional structures of the IBE and the WHO, has already been mentioned above. In addition, there are joint activities of some regional Commissions that relate to our general priorities. Thus, the North American and Latin American Commissions have in 2007 initiated: an ambitious plan of exchange programs and networks for the development of underserved areas; an initiative for epilepsy care development in the Caribbean; and a specific project for the island of Hispaniola where our Chapter in the Dominican Republic will assist with developing epilepsy care in Haiti, the neighboring country.

A series of trainer courses in the Portuguese language is a joint activity of the Portuguese and Brazilian ILAE Chapters, and includes the lusophone countries of Africa. It is supported by the Commission on European Affairs and the Educational Commission, and has resulted in a bilateral fellowship program of Brazil and Mozambique.

Problem-oriented commissions
These Commissions focus on many aspects of the professional work within the ILAE’s agenda. Amongst other tasks, they elaborate reports, guidelines and recommendations that become official documents of the ILAE when they have been accepted by the EC. These Commissions comprise at present:

- Classification and terminology
- Diagnostic methods
- Education
- Epilepsy care
- Genetics
- Neurobiology
- Neuropsychiatry
- Pediatrics
- Therapeutic strategies

Each of these commissions has a defined mission, and most of them have established subcommittees and task forces to address specific problems.

On October 19, 2007, all commission chairs met in Brussels for a long-range strategic planning meeting. The progress reports of the Commissions’ activities so far provided an exciting comprehensive overview of all our activities and initiatives. What has been reported above is only...
a selection of highlights. The Commission reports provide exciting examples of the rich, varied, and enthusiastic activities ongoing at all levels, involving many different types of networks, which today are perhaps the most distinctive feature of our organization. We can be proud of this range of activity.

**The Congresses**

The ILAE was founded at the occasion of an international congress, and for many decades, the International Epilepsy Congresses were almost the only occasions of public visibility of the League. Although this situation has changed dramatically—see above for examples of ILAE’s active commission work (starting with the international classifications of seizures and syndromes), regional activities, our educational agenda, and the Global Campaign against Epilepsy—our congresses remain one of the most important parts of our activity. They provide the most important forum in epileptology for the presentation of new findings, scientific exchange and update. Global international congresses occur in odd years, and alternate with a series of regional international congresses in even years. As a consequence of the introduction of quality control measures in some of these congresses, these regional events have become increasingly attractive and economically successful. The financial surpluses which some congresses generate are at present used for two purposes: (1) to support good quality science and education at meetings of the low-budget regions; and (2) for the support of our educational programs (e.g., to provide support for young investigators to attend the future congresses, for residential courses in the region and beyond, and participation in distance education).

During the present term of office, regional congresses were held in Kuala Lumpur (Asia/Oceania) 2006, Luxor (Eastern Mediterranean) 2007, Helsinki (Europe) 2006, and Guatemala (Latin America) 2006. The traditional annual meeting of the American Epilepsy Society (AES) in San Diego was for the first time declared a joint meeting with the North American Congress of Epileptology, and will have this label every other year (and thus be in phase with the other regional congresses). The International Epilepsy Congress in 2007 took place in Singapore. The next International Congress, in 2009, will be the ILAE centenary meeting and will be held in Budapest where the ILAE was founded in 1909. Apart from the European Congress of Epileptology, all the above-mentioned congresses are joint meetings with the IBE.

**Organizational Philosophy**

The ILAE was founded, in 1909, primarily as an international society that soon established national committees. Today, the national organizations that constitute its membership are all legally independent entities, incorporated in their respective countries. Their individual memberships vary from a handful to over 2,000, and their resources and activities vary widely. Some are more aware than others that they are part of a global organization.

Since the establishment of an intermediate organizational level between the ILAE EC and Chapters—the regional Commissions—regional identities have developed in addition, as intended and expected. The challenge we face with this structure is to ensure an optimal balance between EC, Regions, and Chapters, a balance which works best to encourage participation by all those who would like to be involved in our manifold activities. One of the ongoing issues to be addressed is the adequate participation of all regions in our global agenda and in the EC. This balance is not easy to find. It is presently under intense discussion of the EC, and was also part of our dialogue with the Regional Commission Chairs last October.

**The Coming Elections**

In 2008, the procedures to elect the next EC will start under the direction of an Election Committee chaired by the Immediate Past President. The first step in this process is the election of the new President from a slate of candidates who must fulfill the precondition of having served at least one term of office on the EC. This requirement is to make sure that the candidates for President have experience with our organization. It is not yet known how many of the possible candidates will actually stand for election, but they all will be given an equal chance to present themselves publically and convince our membership that their performance and accomplishments in the service of epilepsy merit their election to the highest office of our organization. In the second step of the election process, all Chapters will be invited to nominate candidates for the other offices, and the persons who receive most nominations will then be put to a general vote. We are fortunate that around the world there are now many worthy and dedicated people—men and women—who are willing to serve on the EC. The ILAE, in spite of its dynamism and ability for renewal and progress, is a slightly atavistic organization in one respect: all its officers are, and have been for decades, only men. I feel strongly that time has come for a change, and very much hope that the Chapters will nominate some of the excellent women who are active in our Chapters and Commissions to be strong candidates with a good chance to be elected. Therefore, the next President, whoever it will be, will again be a man.

Peter Wolf
peterw@vastamt.dk
ILAE President, Denmark
Copenhagen, January 11, 2008
Primary care treatment of epilepsy with phenobarbital in rural China: Cost-outcome analysis from the WHO/ILAE/IBE global campaign against epilepsy demonstration project

In order to address the public health burden imposed by epilepsy and to stimulate expenditure into its appropriate management, there is a need to demonstrate that the interventions are not only effective and sustainable, but also affordable. Evidence for the cost-effectiveness of epilepsy treatment is currently lacking but has been identified as an important priority (Patchatok & Beran, 1995).

Phenobarbital (PB) is recommended by the World Health Organization (WHO) as a broad-spectrum first-line drug for partial and generalized tonic-clonic seizures (Kwan & Brodie, 2004; Chisholm, 2005). A demonstration project of epilepsy management at primary health level was carried out in rural China under the auspices of the WHO/International League against Epilepsy (ILAE)/International Bureau for Epilepsy (IBE) Global Campaign Against Epilepsy (Wang et al., 2006). It offered an opportunity to obtain data related to resource utilization and costs for PB treatment in primary care settings, which together with clinical outcomes can be used to inform decisions about cost-effectiveness and resource allocation in the context of low-income populations.

PATIENT POPULATION

The target population comprised patients older than 2 years with at least two convulsive seizures in the previous 12 months. Exclusion criteria were described elsewhere (Wang et al., 2006). All participants were asked to provide written informed consent (for children, consent was signed by their parents or guardians).

Fifty patients and one hundred patients were randomly selected in rural Shanghai and Ningxia, respectively, with the representative of areas with different levels of economic development.

TREATMENT AND FOLLOW-UP

The initial PB dose, 60 mg for adults and 15 mg for children, was given for a period of 2–4 weeks. Doses were then titrated according to clinical needs up to 180 mg for adults and 4–5 mg per kg for children (WHO, 2000).

Patients were followed up by rural physicians in village clinics (Shanghai) or town hospitals (Ningxia) every 2 weeks for the first month and monthly thereafter for dose adjustments, adverse events (AEs) assessment, and checks of adherence to treatment, and to receive further supplies of PB.

EVALUATION OF THE EFFICACY OF PB TREATMENT

Seizure-free cases were defined as the patients who became seizure free during the last 6 months of follow-up. Improved cases were defined as the patients with ≥50% reduction in the seizure frequency compared to the baseline (WHO, 2000). The efficacy of PB treatment was determined in terms of the percentage of seizure free and improved cases at 1-year follow-up.

COSTS

We calculated 1-year costs of running the primary care level epilepsy demonstration project in rural Shanghai and Ningxia. The unit price of PB was 2.00 yuan (US$ 0.24, at 2004 prices) per hundred 30 mg tablets, (Phenobarbital Tablets, Shanghai Jinshan Pharma Ltd., Jinshan, Shanghai, China). Costs, including drug costs, personnel, training, and operating were calculated and compared between the two study sites.

At the first visit, healthcare contacts, related medical expenses, and time during the 12 months before treatment were documented as the baseline data. The same information was then obtained for each subsequent 3-month period. We developed an economic burden questionnaire to establish the costs to patients associated with contact with (and fees paid for) other health-care services (hospital outpatient and inpatient care) at different levels of the health system (village health worker, town hospital doctor, neurologist, and hospital admission) as well as time costs associated with travel and waiting (Chisholm et al., 2000; Srinivasan et al., 2005).

STATISTICAL ANALYSIS

Continuous variables were expressed as mean and standard deviation (SD), whereas categorical variables were presented as frequencies (%). Comparisons of changes over time in the health care contacts, access time, and seizure frequency for epilepsy patients with baseline and 1-year follow-up were evaluated with the paired sample t-test or the Wilcoxon signed-ranks test, according to whether or not the data were normally distributed. All p-values and confidence intervals (CIs) were estimated in a two-tailed fashion. Differences were considered to be statistically significant at $p < 0.05$. 
GRAY MATTERS

DEMOGRAPHICS OF THE SAMPLED POPULATION
The sex and age of people with epilepsy were similar in the two areas, but the education level and yearly income of the patients in rural Ningxia were lower than those in rural Shanghai (Table 1).

COSTS OF THE DEMONSTRATION PROJECT
The total annual cost was 6,267 yuan and 12,370 yuan in rural Shanghai and Ningxia, respectively. PB cost 17% (1,050 yuan) and 23% (2,800 yuan) of the total expenses of the project in rural Shanghai and Ningxia.

COSTS OF HEALTH CARE CONTACT FROM THE PATIENT PERSPECTIVE
In the year before the demonstration project, 16 (32%) and 50 (50%) patients in rural Shanghai and Ningxia, respectively, visited town hospital doctors. Only 14 (28%) and 5 (5%) patients, respectively, made outpatient visits to a neurologist. The hospital admission rate was 22% among sampled patients in rural Shanghai, considerably higher than that in rural Ningxia (2%).

All the sampled patients in rural Shanghai were followed up by village health workers with an average of 13.56 visits. For town hospital doctor and neurologist visits, the average visits per year decreased by 2.24 and 1.72, respectively, because fewer patients were seen by town hospital doctors (11 cases) and neurologists (4 cases). As the patients in rural Ningxia were all followed up by town hospital doctors, the average visits to town hospital doctors increased from 5.76 to 13.58. The average visits to neurologist decreased by 0.07 because fewer patients (2 cases) visited neurologist during the 1-year follow-up time (Table 2).

The mean costs of health care contact with town hospital doctors in rural Shanghai decreased by 103.22 yuan. Even after allowing for the additional costs of village health worker contacts, overall expenditure was still lower than that of the baseline. In rural Ningxia, epilepsy patients were followed up by physicians in town hospitals, thus the time costs to town hospital doctors significantly increased by 9.61 as compared to that of the baseline (p < 0.001). The health care costs to town hospital doctors, however, decreased by 12.36 as compared to that of the baseline. Costs related to neurologist contacts dropped in both study sites.

In rural Shanghai and Ningxia, the total 1-year expenses per treated patient before the demonstration project were 1,494.30 yuan and 213.09 yuan, respectively, and these expenses decreased to 91.52 yuan and 45.90 yuan, respectively, during the demonstration project (p < 0.05).

OUTCOME EVALUATION
We found that 42 (84%) patients had been effectively treated and 23 (46%) patients became seizure free after one year of the PB treatment in rural Shanghai, whereas 73% patients have been effectively treated and 44% became seizure-free cases within the 100 Ningxia patients. Seizure frequency of the epilepsy patients decreased by about 60% with statistical significant in both study sites after 1 year of the demonstration project (Table 3).

A small number of cost-effectiveness studies have been carried out in high-income countries (Heaney et al., 2002), while fewer studies in developing countries provide economic data related to epilepsy treatment. In India, the annual direct cost of epilepsy per patient was US$62–93, mainly using PB, phenytoin, carbamazepine, and sodium valproate (Thomas et al., 2001; Krishnan et al., 2004). The cost-effectiveness of first-line antiepileptic drugs (AED) treatments in the developing world was studied at population level as part of the WHO’s choosing interventions that are cost-effective (CHOICE) project. In the Western Pacific region, to which China belongs, the annual patient cost of PB treatment per year was estimated at 93 international dollars (an international dollar has the same purchasing power as the U.S. dollar has in the United States) (Chisholm, 2005). Apart from this study, our study is the only economic evaluation study (cost-outcome study) of PB treatment conducted in Asian countries, reflecting the situation in rural China by using two study areas with different economic levels. Furthermore, and unlike other cost-effectiveness studies that have relied to a varying extent on assumptions, expert opinion, and modeling of underlying cost and effectiveness (Heaney & Begley, 2002), this prospective study has presented the cost-outcome of standard PB therapy by using the exact survey data obtained from the demonstration project.

Table 1. Baseline demographics of the sampled epilepsy patients treated with standard PB treatment in the demonstration project in rural areas of Shanghai and Ningxia, PRC

<table>
<thead>
<tr>
<th></th>
<th>Shanghai (N = 50)</th>
<th>Ningxia (N = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>26 (52)</td>
<td>58 (58)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>24 (48)</td>
<td>42 (42)</td>
</tr>
<tr>
<td><strong>Age (year) (mean [SD]), (range)</strong></td>
<td>31 (14), (7–65)</td>
<td>33 (12), (10–64)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate (%)</td>
<td>3 (6)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Primary school (%)</td>
<td>5 (10)</td>
<td>50 (50)</td>
</tr>
<tr>
<td>Secondary school (%)</td>
<td>42 (84)</td>
<td>42 (42)</td>
</tr>
<tr>
<td>College and above (%)</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Monthly income, yuan (mean [SD])</td>
<td>1,176 (2,064)</td>
<td>689 (806)</td>
</tr>
</tbody>
</table>
### Table 2. Health care contacts and access time for epilepsy patients treated in primary care settings (rural Shanghai and Ningxia, PRC)

<table>
<thead>
<tr>
<th>Health care contacts</th>
<th>Shanghai (N = 50)</th>
<th>Ningxia (N = 100)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (previous 1 year)</td>
<td>I-year follow-up</td>
<td>Change</td>
</tr>
<tr>
<td></td>
<td>Mean± S.D.</td>
<td>Mean± S.D.</td>
<td>Mean 95% CI</td>
</tr>
<tr>
<td>Village health worker (visits)</td>
<td>13.56±0.86</td>
<td>0.46±0.93</td>
<td>2.24±0.90, 3.58b</td>
</tr>
<tr>
<td>Town hospital doctor (visits)</td>
<td>2.70±4.54</td>
<td>0.16±0.55</td>
<td>1.72±0.65, 2.79b</td>
</tr>
<tr>
<td>Neurologist (outpatient visits)</td>
<td>5.36±13.72</td>
<td>0.00±0.00</td>
<td>0.46±3.31</td>
</tr>
<tr>
<td>Hospital admission (days)</td>
<td>5.36±13.72</td>
<td>0.00±0.00</td>
<td>0.46±3.31</td>
</tr>
<tr>
<td>Health care costs (Yuan, 2004)</td>
<td>0±0</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Village health worker</td>
<td>25.06±50.89</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Town hospital doctor</td>
<td>73.59±205.26</td>
<td>1.85±439.19</td>
<td>72.00±135.87</td>
</tr>
<tr>
<td>Neurologist (min)</td>
<td>2.65±2.10</td>
<td>1.00±0.00</td>
<td>10.83±1.85, 25.90</td>
</tr>
<tr>
<td>Hospital admission (min)</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Total</td>
<td>282.66±212.84</td>
<td>1.289.14±485.73, 2.092.55</td>
<td>202.66±837.45, 29.30±157.35</td>
</tr>
<tr>
<td>Access time (travel/waiting per visit)</td>
<td>11.62±4.24</td>
<td>0.00±0.00</td>
<td>2.70±19.11</td>
</tr>
<tr>
<td>Village health worker (min)</td>
<td>0.79±3.04</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Town hospital doctor (min)</td>
<td>7.60±12.43</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Neurologist (min)</td>
<td>80.88±198.87</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Hospital admission (min)</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Total</td>
<td>282.66±212.84</td>
<td>1.289.14±485.73, 2.092.55</td>
<td>202.66±837.45, 29.30±157.35</td>
</tr>
<tr>
<td>Access time (travel/waiting per visit)</td>
<td>11.62±4.24</td>
<td>0.00±0.00</td>
<td>2.70±19.11</td>
</tr>
<tr>
<td>Village health worker (min)</td>
<td>0.79±3.04</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Town hospital doctor (min)</td>
<td>7.60±12.43</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Neurologist (min)</td>
<td>80.88±198.87</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Hospital admission (min)</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>Total</td>
<td>282.66±212.84</td>
<td>1.289.14±485.73, 2.092.55</td>
<td>202.66±837.45, 29.30±157.35</td>
</tr>
</tbody>
</table>

a Average to 50 sampled cases in rural Shanghai and 100 sampled cases in rural Ningxia.
b p < 0.05.
c p < 0.001, Wilcoxon signed-ranks test.
d Patients were followed by village health workers, and the costs were covered by the demonstration project.
Table 3. Seizure characteristics of the study participants and efficacy evaluation of the standard PB treatment in the demonstration project in rural areas of Shanghai and Ningxia, PRC

<table>
<thead>
<tr>
<th></th>
<th>Shanghai (N = 50)</th>
<th>Ningxia (N = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (previous 1 year)</td>
<td>1-year follow-up</td>
</tr>
<tr>
<td>Disease duration (year) (mean [SD])</td>
<td>15.6 (10.1)</td>
<td>—</td>
</tr>
<tr>
<td>Antiepilepsy therapy (%)</td>
<td>29 (58)</td>
<td>50 (100)</td>
</tr>
<tr>
<td>PB dosage (mg/day) (mean [SD])</td>
<td>—</td>
<td>90 (23)</td>
</tr>
<tr>
<td>Seizure frequency (/year) (mean [SD])</td>
<td>37.3 (73.7)</td>
<td>16.0 (37.7)*</td>
</tr>
<tr>
<td>Total efficacy (%)</td>
<td>—</td>
<td>42 (84)</td>
</tr>
<tr>
<td>Seizure free (%)</td>
<td>—</td>
<td>23 (46)</td>
</tr>
<tr>
<td>Improved (%)</td>
<td>—</td>
<td>19 (38)</td>
</tr>
</tbody>
</table>

*p < 0.001, Wilcoxon signed-ranks test, comparison between baseline and 1-year follow-up.

The efficacy of PB treatment in the study needs to be interpreted cautiously because the current study was not a controlled study design, meaning that the observed improvements could be at least partly accounted for by factors uncontrolled for (including the spontaneous rate of remission for epilepsy patients plus any placebo effect present). However, the placebo effect for first-line AED treatment is likely to be low, while the expected rate for spontaneous remission among untreated chronic epilepsy patients has been recently estimated to be as low as 5% (Chisholm, 2005). Therefore, it is unlikely that the observed substantial improvements in seizure frequency in both study sites occurred by chance.

Our results demonstrate that the use of PB for the treatment of epilepsy has considerable appeal, especially in low-income regions, as there are not only clinical improvements, but also lower costs in the target population. More analysis considering cost-minimization, cost-effectiveness, and cost-benefit may be done in the future to strengthen the evidence for the generalization of PB therapy to resource-poor regions, which contain 60% of the world’s population.

ACKNOWLEDGMENTS

We thank the village health workers and the town hospital doctors in rural Shanghai and Ningxia for their efforts in the patient follow-up in this study.

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References


The challenge of epilepsy control in deprived settings: Low compliance and high fatality rates during a community-based phenobarbital program in rural Laos

According to the World Health Organization (WHO), 80% of people with epilepsy (PWE) live in poor-resource countries, and never receive treatment. Cost-effectiveness and safety profile of phenobarbital make it the recommended drug for these countries. Lao Peoples’ Democratic Republic (Lao PDR) is a small landlocked country in South-East Asia, with a sparse 5.6 million multiethnic rural population, ranking 133rd at the Human Development Index; average annual per capita income is US$491.

Epilepsy has an estimated prevalence of 7.7‰, with cysticercosis playing little etiologic role (Tran et al., 2006, 2007a). There are no national guidelines and no control program, and misconceptions and stigma toward PWE are common (Tran et al., 2007b). Despite figuring on the national essential drugs list, phenobarbital may be of limited availability. Only 53% of urban pharmacies can provide it, and diazepam short courses are the most used regimen to treat seizures (Odermatt et al., 2007). The intervention presented in this report took place over 120 km north of the capital, Vientiane, in Hinheub, in a typical Lao district hospital, with 17 health personnel including one MD for 23,000 inhabitants.

Medical practitioners pursuing continuous training at the Francophone Institute of Tropical Medicine developed a 2-year community-based phenobarbital program. The target population consisted of PWE identified in a previous prevalence survey, with cases referred by the district health personnel. Epilepsy diagnosis was clinically based on international guidelines (Freux et al., 2000). Phenobarbital (100 mg daily) was offered to all adults with active disease (≥2 generalized seizures in the previous 2-year period). Preliminary information was given to PWE and caregivers on epilepsy, treatment principles, and the importance of compliance and follow-up. We obtained each patient’s informed consent, and clearance from the Lao National Ethic Committee. Phenobarbital was provided free by the hospital every 2 months, but transportation costs were at charge of the patient. One assistant pharmacist and two nurses received a short training on the program and data management, including clinical follow-up (seizures occurrence, side effects, compliance monitoring by left over tablets count). Patients missing two appointments, or taking <80% of expected number of phenobarbital tablets, were considered low compliant; those missing three consecutive appointments were considered “dropped out.” The medical team visited the district twice a year to check data and management, and conducted a final home interview with compliant patients—on the program’s relevance and the patients/community expectations—using a semistructured questionnaire.

The potential population consisted of 53 people. Only the 46 active cases were retained. The mean age was 31.7 years, the M/F sex ratio was 1.2; 19.5% were mentally retarded. Only four people had ever received antiepileptic drugs before. Eighty percent were farmers. The average daily family income was <US$1, the mean distance to hospital was 18.6 km. Seizures frequency ranged from 2/year to 3/week. Eleven patients did not attend the program at all (24%), 16 rapidly dropped out (35%), and only 10 (22%) showed full compliance.

Premature death was a striking finding. Six of the 53 patients (11%) died within the 2-year study period (2 drowning, 1 burns, 1 fall, 2 sudden unspecified cause). Five of these were mentally retarded young males (median age 18 years), and none had been fully compliant (Fig. 1).

The 18 people who completed the program deemed it efficient and reported an improved working capacity and quality of life. Moreover, mean seizure frequency decreased from 3.5 to 0.3/month, 11 patients (69%) were seizure-free, 4 reported somnolence, and none had to withdraw because of side effects.

The main expressed difficulties were distance to the health center, transportation availability and costs (range US$1–3), and poor hospital accessibility (drug delivery failures occurred due to inadequate running hours or absent personnel). Finally, 66% of those interviewed advocated a more convenient village-based drug delivery procedure.

Phenobarbital has proved highly efficient, well tolerated, and manageable at a community level (Mani et al., 2001; Nimaga et al., 2002; Asawawichienjinda et al., 2003). Our population of PWE had low education, low income, and poor access to health care, which may all hinder compliance. The over-prevalence of death in noncompliant mentally retarded young men with epilepsy is striking;
however, the possibility that causes other than seizures may intervene, including traditional beliefs and stigma related to mental deficiency should be thoroughly investigated (Malina, 2005). The results of this pilot study suggest that a medical intervention aimed at epilepsy treatment in deprived countries might benefit from an anthropological component.

ACKNOWLEDGMENTS

We are indebted to the personnel of Hinheub district hospital, the Agence Universitaire de la Francophonie (AUF), and the French Ministry of Foreign Affairs (project CORUS number 02-811-052) which both granted the program. We thank Dr. Daniel Reinharz for his help.

Duc-Si Tran1
Jie Zen1,2
Michel Strobel1
Peter Odermatt1,3
Pierre-Marie Preux4
preux@unilim.fr
Pierre Huc4
Luc Delneuville5
Hubert Barennes1

1Institut de la Francophonie pour la Médecine Tropicale
Vientiane, Lao Peoples’ Democratic Republic
2Kunming Medical College, Kunming, Yunnan, China
3Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland
4Institut d’Épidémiologie Neurologique et de Neurologie Tropicale (EA 3174), Limoges, France
5Handicap International, Vientiane, Lao Peoples’ Democratic Republic

REFERENCES


To the Editors:

The study of mental health problems of people with epilepsy (PWE) from the Canadian Community Health Survey, reported by Tellez-Zenteno and colleagues (2007), is presented as one of few such population studies in the literature. It found higher rates of anxiety, suicidal ideation, and depression among PWE compared with the general population. These findings have broad significance not only for high-income countries like Canada, but relevance also for research and health services in low- and middle-income countries, where 80% of the PWE reside (Scott et al., 2001). The following points therefore merit consideration within the context of mental health problems in lower-income countries: (1) the historical link and present practice of psychiatrists treating epilepsy; (2) a different profile of mental health problems emerging from population studies, as compared with clinical specialty studies, of PWE; and (3) higher rates of suicidal ideation, indicating
a possible cause of mortality from epilepsy mediated by psychosocial factors.

This work highlights an important historical linkage between neurology and psychiatry through epilepsy, reflected not only in the origins of the International League Against Epilepsy itself as an interdisciplinary undertaking of neurology and psychiatry, but also in the inclusion of epilepsy as a current responsibility of WHO’s Department of Mental Health and Substance Abuse. It is important to understand that in most countries of the developing world, where neurologists are rare or absent, the majority of PWE are treated by psychiatrists (WHO, 2005).

Psychiatric morbidity identified in the Tellez-Zenteno and colleagues study focuses mainly on anxiety and depression, rather than psychoses. Schizophrenia could not be included in the analysis because of technical reasons arising from low-rates. The literature of psychiatry typically regards neuropsychiatric effects of epilepsy as “a range of biologically based psychopathology” (Sadock & Sadock, 2000), which result from central nervous system pathology or from the neuropsychopathology of seizure activity (including postictal or interictal phenomena). Findings of common mental disorders and suicidal ideation, rather than psychoses, suggest an important role of psychosocial, not just biological, factors explaining the impact of epilepsy on mental health. Furthermore, these findings highlight the importance of the impact of stigmatization affecting PWE within their families or communities (Jacoby et al., 2005). A consideration of the psychosocial underpinnings of epilepsy-related psychopathology is essential in responding to the authors’ suggestion that findings be applied to “planning health services and provision of adequate medical therapy.” Among traditional segments of society in many developing countries, cultural perceptions of cause strongly influence stigma. Therefore, attention to the social context and its particular impact is crucial in attempts to provide support and encourage help seeking and self-management (Diop et al., 2003).

Tellez-Zenteno and colleagues show that the prevalence of suicidal ideation is significantly higher among PWE. This may explain a source of mortality by suicide that reflects the severity of psychosocially-mediated aspects of the illness experience of epilepsy. A mental health component should be introduced into health system operations and sentinel surveillance activities of health demographic surveillance systems. Such a component should ensure that careful consideration of epilepsy, suicide, and indications of mental health problems are included in protocols for eliciting verbal autopsies and population-based health studies. These factors should be considered in establishing local priorities, as well as in North–South collaboration (Doku & Mallett, 2003) between industrialized and developing countries.

Response to Birbeck et al.

To the Editors:

We would like to further add to the emerging picture provided recently by Birbeck et al. regarding the use of antiepileptic drugs (AEDs) in HIV-positive patients living in resource limited settings (RLS) (Birbeck et al., 2007).

The chief concern raised by Birbeck et al. was that older AEDs—notably phenobarbitone—are prescribed widely in sub-Saharan Africa (SSA) and that this prescribing practice extends to HIV-positive people with epilepsy. The older AEDs—phenobarbitone, phenytoin, and carbamazepine—unlike the newer classes of AEDs—can significantly reduce the half-life of the also widely prescribed HIV antiretroviral agent nevirapine through cytochrome P450 enzyme induction (L’Homme et al., 2006) thereby greatly increasing the likelihood of drug resistance. As a corollary, in the same issue, Avanzini noted via endorsement of Birbeck et al., that HIV protease inhibitors may reduce serum levels of these older AEDs (Avanzini, 2007; Liedtke et al., 2004).

REFERENCES


Following these raised concerns (Birbeck et al., 2007; Avanzini, 2007) the Asia Pacific NeuroAIDS Consortium (APNAC) undertook a review of the availability and use of newer and older AEDs at APNAC sites. APNAC comprises neurologists/infectious disease clinicians, neuroscientists, neuropathologists, and neuropsychologists with a shared interest in neuroAIDS from several countries across the Asia Pacific region: India, Cambodia, Thailand, Malaysia, Hong Kong, Papua New Guinea, Fiji, and Indonesia. APNAC sites are tertiary referral hospitals with high-HIV patient caseloads.

Twelve sites across eight APNAC countries were polled to determine which AEDs are prescribed for the treatment of epilepsy in HIV-positive patients: “Often”: phenytoin 9/12, carbamazepine 5/12, phenobarbitone 0/12; “Sometimes/rarely”: phenytoin 2/12, carbamazepine 5/12, phenobarbitone 9/12. Sites were also polled to determine whether gabapentin, pregabaline, lamotrigine, or levetiracetam are available for treatment of epilepsy: one or more of these AEDs are available at seven of the 12 sites. The frequency of prescription of these newer AEDs at the seven sites was: “Often”: 0/7; “Sometimes/rarely”: 6/7; “Never”: 1/7.

Further, in a recent study of HIV-positive inpatients and outpatients undertaken by APNAC at 10 sites across eight countries (Wright et al., 2006) (Wright et al., 2007) we found that the use of nevirapine-containing regimens is common and that of 72 inpatients admitted with neurological diagnoses across these sites that 11/72 (16%) had seizures: five presented with seizures alone and six presented with seizures complicating concurrent central nervous system opportunistic infections.

In summary, the older CYP450 enzyme-inducing AEDs are prescribed commonly across the Asia Pacific region and, though the newer AEDs are available in the region, they are not commonly prescribed. Further, seizures are common in HIV-positive patients across the Asia Pacific region. Hence, we endorse Birbeck et al., Avanzini, and the recent editorial in Lancet Neurology (Birbeck et al., 2007; Avanzini, 2007; Editorial, 2007) for their collective concern about the use of older AEDs in HIV-positive populations. Our data provide the first preliminary evidence that this is a significant practical issue and not just a theoretical concern. The data provide the basis for more precise epidemiological studies, further research into drug interactions between AEDs and HIV antiretrovirals, including pharmacogenetic studies, and the immediate need for increased access to the newer, nonenzyme inducing AEDs.

Edwina Wright1,2,3
Bruce J. Brew4,5
Luxshimi Lal1,2,3

REFERENCES
Wright EJ, Brew BJ, Lal L, et al. (2006) Neurocognitive impairment, symptomatic peripheral neuropathy and depression are highly prevalent within the Asia Pacific Region: findings of the Asia Pacific
The Illinois College of Medicine

Bailey & Gibbs (1951) quickly translated these findings with epilepsy had this type of seizure (Gibbs et al., 1948). EEG focus and that around one-third of adult patients with seizures were associated with an anterior temporal lobe origin, Frederick Gibbs, in 1948, provided a physiological studies all together, simply performing “standard temporal lobectomy” in all patients with good results. As Almeida et al. discussed, there are ambiguities in Morris’s papers such that it is not clear whether his earliest resections (i.e., pre-1950) included the medial structures. Of 68 temporal lobe operations performed by Penfield between 1939 and 1949, the excisions were focused on the anterior and lateral temporal lobe, the uncus being excised in 10 cases (15%) and the hippocampus in only two (3%) (Penfield & Flanigin, 1950). In the 3 years subsequent to 1949, Penfield performed 81 temporal lobe operations in contrast to 68 in the preceding 10 years (Penfield & Paine, 1955). Furthermore, the uncus, amygdala, and hippocampus were routinely removed as well as the anterior temporal lobe anterior to the level of the central sulcus and, in some cases, (depending upon the ECoG findings), up to one centimeter posterior to it; the medial structures, explicitly the hippocampus & insula, were spared for fear of producing Klüver-Bucy syndrome.53 Bailey and Gibbs believed that the results of the radical procedure were superior (“...very good to date”) and urged its adoption in all cases.

Finally, Almeida et al., in common with previous researchers, gave insufficient recognition to the work of Arthur Morris who, at Georgetown University School of Medicine, was also developing temporal lobe surgery in patients with psychomotor seizures and anterior temporal lobe foci on surface EEG (Morris, 1950, 1956). Morris’s resections were remarkable in encompassing the medial temporal structures (uncus, amygdala, and 2–4 cm of the anterior end of the hippocampus) as well as the lateral cortex. Initially, Morris had based his resections upon ECoG, but found, as Bailey and Gibbs had, that epileptiform discharges invariably occurred diffusely within the temporal lobe, including the medial structures. Consequently, he took the bold step of abandoning intraoperative electrophysiological studies all together, simply performing “standard temporal lobectomy” in all patients with good results. As Almeida et al. pointed out, Penfield began cortical stimulation in 1928 after visiting Otfrid Foerster. However, the first definite instance of human cortical stimulation was that by Roberts Bartholow in 1874 in an awake subject, one unfortunate Mrs. Rafferty. This recognition of Bartholow’s primacy must, however, be accompanied by the observation that the experiment was ethically reprehensible (see Morgan, 1982 for a full discussion). As early as 1886, Victor Horsley, reported amongst his series of 10 operations, a case (“O.S.H.”) with “epileptiform seizures beginning at the left angle of the mouth,” in which, no structural pathology being evident, he employed “faradism” to map out and excise the “facial centre” (Horsley, 1886). This appears to be the first instance of a stimulation-guided corticectomy (although Feindel in 1997). Following Horsley, Fedor Krause in Berlin began similar work in the 1890s including excisions determined by cortical stimulation, later publishing a map of the human primary motor area (Penfield & Jasper, 1954; Wolf, 1992). Thus, it can be seen that this field had a rich history prior to the work of Penfield and, indeed, of Foerster.

Following on from Jasper’s work on seizures of temporal lobe origin, Frederick Gibbs, in 1948, provided a coherent description of psychomotor seizures as temporal lobe seizures and demonstrated that most psychomotor seizures were associated with an anterior temporal lobe EEG focus and that around one-third of adult patients with epilepsy had this type of seizure (Gibbs et al., 1948). Bailey & Gibbs (1951) quickly translated these findings into surgical practice, initiating temporal lobe operations at The Illinois College of Medicine in 1947. Their first operations excisions were limited (“unigyrectomy,” “bigryrectomy,” or “trigyrectomy”) and determined solely by the electrocorticography (ECoG) findings, but the success rate was low and therefore, after considering a number of other experimental findings, they proceeded to more radical excisions, the “radical lobectomy”: all tissue between the Sylvian fissure & the occipitotemporal sulcus, extending posteriorly at least to the level of the central sulcus and, in some cases, (depending upon the ECoG findings), up to one centimeter posterior to it; the medial structures, explicitly the hippocampus & insula, were spared for fear of producing Klüver-Bucy syndrome.53 Bailey and Gibbs believed that the results of the radical procedure were superior (“...very good to date”) and urged its adoption in all cases.

As Almeida et al. pointed out, Penfield began cortical stimulation in 1928 after visiting Otfrid Foerster. However, the first definite instance of human cortical stimulation was that by Roberts Bartholow in 1874 in an awake subject, one unfortunate Mrs. Rafferty. This recognition of Bartholow’s primacy must, however, be accompanied by the observation that the experiment was ethically reprehensible (see Morgan, 1982 for a full discussion). As early as 1886, Victor Horsley, reported amongst his series of 10 operations, a case (“O.S.H.”) with “epileptiform seizures beginning at the left angle of the mouth,” in which, no structural pathology being evident, he employed “faradism” to map out and excise the “facial centre” (Horsley, 1886). This appears to be the first instance of a stimulation-guided corticectomy (although Feindel in 1997). Following Horsley, Fedor Krause in Berlin began similar work in the 1890s including excisions determined by cortical stimulation, later publishing a map of the human primary motor area (Penfield & Jasper, 1954; Wolf, 1992). Thus, it can be seen that this field had a rich history prior to the work of Penfield and, indeed, of Foerster.

To the Editors:

I wish to make some observations on the paper “From lateral to mesial: The quest for a surgical cure for temporal lobe epilepsy” (Almeida et al., 2007). The paper arguably overemphasized the place of the work of Penfield and Jaspers at the MNI at the expense of under-recognition of other workers. This is particularly so in the case of how the importance of the medial temporal lobe in intractable epilepsy emerged and the consequent development of temporal lobectomy with inclusion of the medial structures, but also in the field of human cortical stimulation, the paper provided limited historical context.

As Almeida et al. pointed out, Penfield began cortical stimulation in 1928 after visiting Otfrid Foerster. However, the first definite instance of human cortical stimulation was that by Roberts Bartholow in 1874 in an awake subject, one unfortunate Mrs. Rafferty. This recognition of Bartholow’s primacy must, however, be accompanied by the observation that the experiment was ethically reprehensible (see Morgan, 1982 for a full discussion). As early as 1886, Victor Horsley, reported amongst his series of 10 operations, a case (“O.S.H.”) with “epileptiform seizures beginning at the left angle of the mouth,” in which, no structural pathology being evident, he employed “faradism” to map out and excise the “facial centre” (Horsley, 1886). This appears to be the first instance of a stimulation-guided corticectomy (although Feindel in 1997). Following Horsley, Fedor Krause in Berlin began similar work in the 1890s including excisions determined by cortical stimulation, later publishing a map of the human primary motor area (Penfield & Jasper, 1954; Wolf, 1992). Thus, it can be seen that this field had a rich history prior to the work of Penfield and, indeed, of Foerster.

Following on from Jasper’s work on seizures of temporal lobe origin, Frederick Gibbs, in 1948, provided a coherent description of psychomotor seizures as temporal lobe seizures and demonstrated that most psychomotor seizures were associated with an anterior temporal lobe EEG focus and that around one-third of adult patients with epilepsy had this type of seizure (Gibbs et al., 1948). Bailey & Gibbs (1951) quickly translated these findings into surgical practice, initiating temporal lobe operations at The Illinois College of Medicine in 1947. Their first operations excisions were limited (“unigyrectomy,” “bigryrectomy,” or “trigyrectomy”) and determined solely by the electrocorticography (ECoG) findings, but the success rate was low and therefore, after considering a number of other experimental findings, they proceeded to more radical excisions, the “radical lobectomy”: all tissue between the Sylvian fissure & the occipitotemporal sulcus, extending posteriorly at least to the level of the central sulcus and, in some cases, (depending upon the ECoG findings), up to one centimeter posterior to it; the medial structures, explicitly the hippocampus & insula, were spared for fear of producing Klüver-Bucy syndrome.53 Bailey and Gibbs believed that the results of the radical procedure were superior (“...very good to date”) and urged its adoption in all cases.

Finally, Almeida et al., in common with previous researchers, gave insufficient recognition to the work of Arthur Morris who, at Georgetown University School of Medicine, was also developing temporal lobe surgery in patients with psychomotor seizures and anterior temporal lobe foci on surface EEG (Morris, 1950, 1956). Morris’s resections were remarkable in encompassing the medial temporal structures (uncus, amygdala, and 2–4 cm of the anterior end of the hippocampus) as well as the lateral cortex. Initially, Morris had based his resections upon ECoG, but found, as Bailey and Gibbs had, that epileptiform discharges invariably occurred diffusely within the temporal lobe, including the medial structures. Consequently, he took the bold step of abandoning intraoperative electrophysiological studies all together, simply performing “standard temporal lobectomy” in all patients with good results. As Almeida et al. discussed, there are ambiguities in Morris’s papers such that it is not clear whether his earliest resections (i.e., pre-1950) included the medial structures. Of 68 temporal lobe operations performed by Penfield between 1939 and 1949, the excisions were focused on the anterior and lateral temporal lobe, the uncus being excised in 10 cases (15%) and the hippocampus in only two (3%) (Penfield & Flanigin, 1950). In the 3 years subsequent to 1949, Penfield performed 81 temporal lobe operations in contrast to 68 in the preceding 10 years (Penfield & Paine, 1955). Furthermore, the uncus, amygdala, and hippocampus were routinely removed as well as the anterolateral temporal lobe anterior to the vein of Labbé, that is approximately 5 cm posterior to the temporal tip. Additionally, Penfield reoperated on “a number” of his earlier temporal lobe patients in order to excise the hippocampus, sometimes with conversion of failure to success (Penfield & Jasper, 1954). Although, Penfield ascribed this development to his recognition of incisural sclerosis as the commonest cause of temporal lobe epilepsy (Earle et al., 1953) it is not clear that hippocampal/mesial temporal sclerosis was histologically identified in Penfield’s surgical specimens. In fact, it is generally accepted that this was not
possible before Murray Falconer at the Maudsley Hospital developed en bloc resections that maintained the structural integrity of the mesial structures (Falconer et al., 1953).

It may not be possible to be categorical as to who performed the first temporal lobectomy with inclusion of the medial structures. It does, however, seems clear that the notion of determining temporal lobe resections for psychomotor epilepsy by neurophysiologic rather than structural abnormality is more clearly attributable to Bailey and Gibbs and that Morris deserves at least equal recognition as Penfield, Bailey, and Gibbs in developing a standard operation that routinely included the medial temporal structures.

Nicholas F. Moran
nfm10@aol.com
Kent & Canterbury Hospital
Canterbury, United Kingdom
Department of Neurology, King’s College Hospital
London, United Kingdom

REFERENCES


ONLINE EARLY

Awad & Sarkhoo, “Public knowledge and attitudes toward epilepsy in Kuwait”
Hirsch et al., “Focal motor seizures induced by alerting stimuli in critically ill patients”
Losch de Oliveira et al., “Effects of early-life LiCl-pilocarpine-induced status epilepticus on memory and anxiety in adult rats are associated with mossy fiber sprouting and elevated CSF S100β protein”
Ozkara et al., “Surgical outcome of patients with mesial temporal lobe epilepsy related to hippocampal sclerosis”

ANNOUNCEMENTS

International Symposium on Dietary Therapies for Epilepsy and Other Neurological Disorders

This international symposium will take place April 2–5, 2008, at the Ritz-Carlton Hotel in Phoenix, Arizona (U.S.A.). The fundamental goals of this symposium are to share up-to-date information on the rapidly expanding topic of dietary therapies for epilepsy, and to define the important clinical and research questions that should be pursued in the future. The Symposium will be hosted by the Barrow Neurological Institute at St. Joseph’s Hospital & Medical Center and is sponsored by the Charlie Foundation, Citizens United for Research in Epilepsy, and Nutricia N.A. For additional information, e-mail Lindsey Kerby at Lindsey.Kerby@chw.edu or see http://www.thebarrow.org/conferences. To register online, go to http://www.peopleware.net/2836.

NEXT MONTH IN EPILEPSIA

The April issue of Epilepsia opens with two reviews dealing with Unverricht-Lundborg syndrome—one on the basic/molecular background of the syndrome (Dr. Lehesjoki and colleagues) and the other focusing on clinical characteristics (Dr. Kalviainen and colleagues). Research reports in this month’s issue are rather diverse, and include several papers with a regional/global theme, a number of reports related to pediatric issues (cognitive function in children with epilepsy, status epilepticus in children, Dravet’s syndrome, psychosocial outcomes in children after epilepsy surgery, juvenile myoclonic epilepsy), and a set of clinical studies describing various seizures/syndromes/disorders (absence status epilepticus, interictal dysphoric disorder, nocturnal frontal lobe epilepsy). The Gray Matters section will feature the results of an international survey (Dr. Baxendale and colleagues) on the use of the Wada test, along with several commentaries (including a contribution from Dr. Wada).

GRAY MATTERS

Nicholas F. Moran
nfm10@aol.com
Kent & Canterbury Hospital
Canterbury, United Kingdom
Department of Neurology, King’s College Hospital
London, United Kingdom

REFERENCES

International Symposium on Febrile Seizures and Related Conditions

The Infantile Seizure Society will host the International Symposium on Febrile Seizures and Related Conditions in Otsu, Japan on April 10–11, 2008. The ISFS aims to present a comprehensive update of the topic, and will include discussions on such issues as genetics, epidemiology, pathophysiology, imaging, treatment, education, and subsequent related conditions (including epilepsy and mesial temporal sclerosis). For additional information see the symposium website at: http://www.iss-jpn.info/ or send an e-mail to Tomoyuki Takano, secretary of the ISFS, at: iss2008@belle.shiga-med.ac.jp

7th Asian & Oceanian Epilepsy Congress

The 7th Asian & Oceanian Epilepsy Congress (AOEC) will take place in beautiful Xiamen on the southeast coast of China, May 15–18, 2008. The Scientific Program will include main sessions, and post main sessions mixed with interesting parallel sessions and platform sessions. For more information go to: http://www.epilepsyxiamen2008.org/

1st North American Regional Caribbean Congress

The 1st North American Regional Caribbean Congress on Epilepsy will take place at the Rose Hall Resort and Country Club, Rose Hall, Monego Bay, Jamaica on May 30–31, 2008. The goal of this Congress (A. Ali and R. Fisher, co-chairs) is to provide epilepsy education for medical practitioners in the Caribbean region. Limited space will be available for health professionals from other locations, particularly junior investigators and clinicians. Presentations will cover a broad range of topics, including: differential diagnosis, EEG, stigma, AEDs, pediatric issues, pregnancy, neuroimaging, epilepsy surgery, new treatment options, and specific Caribbean updates. Prospective attendees are encouraged to submit abstracts. This inaugural conference has been made possible by generous support from Novartis, the American Epilepsy Society, and the International League Against Epilepsy. For more information please contact the Jamaica Epilepsy Association (JEA) at Andrews Memorial Hospital, 27 Hope Rd, Kingston 10, Jamaica, (tel: 876-968-8274), or view the website at http://www.carinar.org.

2nd Migrating Course on Epilepsy

The new educational initiative—“Migrating Course on Epilepsy”—is a clinically oriented course, targeted to specialists at the second and third level of epilepsy care and focused on comprehensive aspects of diagnosis and treatment of epilepsy. The first course was successfully organized in Serbia. The second “Migrating Course on Epilepsy” is planned in close collaboration with the Lithuanian Society for Epileptology, for June 1–8 in Trakai, Lithuania. For more information go to http://www.ilae-epilepsy.org/Visitors/chapters/documents/MigratingCourse2announcement.pdf or http://www.epilepsy-academy.org.

4th Epilepsy Colloquium Erlangen

This international meeting will take place in Erlangen, Germany on June 6–7, 2008. The colloquium will focus on: 1) treatment strategies (including drug monitoring, emergency treatment, new treatment developments), 2) surrogate markers of epileptogenicity, 3) new approaches for quantitative measures of seizure control and neuropsychological function, and 4) study design (e.g., how to test new drugs). For more information, contact Prof. Dr. Hermann Stefan, Epilepsy Center, University Hospital Erlangen, 6-Schwabachanlage, 91054 Erlangen, Germany; e-mail: Hermann.stefan@uk-erlangen.de or visit www.epilepsiezentrum-erlangen.de

9th Eilat Conference on New Antiepileptic Drugs

The 9th Eilat Conference on New Antiepileptic Drugs will take place June 15–19, 2008, in Sitges, Spain. The program is designed to provide an in-depth progress report on new antiepileptic drugs (AEDs) in different stages of development, as well as to present new findings on second-generation treatments. In addition, sessions will be devoted to: Old and New AEDs in Generalized Epilepsies; Novel Formulations and Routes of Administration of AEDs; Common Targets and Mechanisms of Action of Drugs for the Treatment of Epilepsy and other CNS disorders; and Perspectives on New AED Discovery. Conference details can be found at: http://www.eilat-aeds.com under Forthcoming Conferences. For more information please contact the Secretariat: Target Conferences Ltd, PO Box 29041, Tel Aviv 61290, Israel, Tel: +972 3 5175150, Fax: +972 3 5175155, e-mail: eilatix@targetconf.com

8th European Congress on Epileptology

The 8th European Congress on Epileptology will take place in Berlin, Germany, September 21–25, 2008. It is presented under the auspices of the German and Israeli ILAE chapters. The online abstract submission system is now available; abstract submission deadline is 14th March 2008. For more information go to: http://www.epilepsyberlin2008.org/.
GRAY MATTERS

5th Latin American Epilepsy Congress

The 5th Congreso Latinoamericano de Epilepsia will take place in Montevideo, Uruguay on November 5–8, 2008. Jointly sponsored by the ILAE and IBE, the organizing committee is headed by A. Scaramelli (Uruguay), L. Núñez Orozco (Mexico), and S. Moshé (U.S.A.). Abstracts are due by May 31, 2008; premeeting registration deadline is September 5, 2008. For more information, contact: montevideo@epilepsycongress.org or go to http://www.epilepsymontevideo2008.org/committees.html.

Michael Prize

The Michael Prize is an international award in epilepsy which reflects a body of work. Awarded by a jury of peers, the Prize emphasizes the importance of carrying out laboratory research that can be translated into the care for patients. It is awarded biennially and is designed to recognize younger scientists (up to 45 years of age). The Michael Prize, supported by Belgian pharmaceutical company UCB, carries with it a monetary award of EUR 15,000. Nominations and applications for the 2009 Michael prize are based on manuscripts or publications that have appeared in 2007/2008 (in either English or German). Each nomination should include the CV of the nominated investigator along with the relevant manuscripts or publications. Submissions should be sent, before December 31, 2008, to: Stiftung Michael, Muenzkamp 5, D–22339 Hamburg, Germany. Further information is available at: stiftungmichael@t-online.de or http://www.stiftungmichael.de.
GRAY MATTER

CALENDAR OF MEETINGS

March 2008
- Danish Epilepsy Society Spring Meeting on Pharmacoresistance
  7–8 March
  Kolding, Denmark
  http://www.epilepsi.suite.dk
- European Project on Development of Epilepsy in Surgery Program
  18–23 March
  Brno, Czech Republic
  e-mail: cigdemoz@istanbul.edu.tr

April 2008
- International Symposium on Dietary Therapies for Epilepsy and Other Neurological Disorders
  2–5 April
  Phoenix, Arizona, U.S.A.
  http://www.peopleware.net/2836
- International Symposium on Febrile Seizures and Related Conditions
  10–11 April
  Otsu, Japan
  http://www.iss-jpn.info
- Course: Introduction to Epileptology
  April
  Dianalund, Denmark
  http://www.epilepsy.suite.dk

May 2008
- 7th Asian & Oceanian Epilepsy Congress
  15–18 May
  Xiamen, China
  http://www.epilepsyxiamen2008.org

June 2008
- 2nd Migrating Course on Epilepsy
  1–8 June
  Trakai, Lithuania
  http://www.epilepsy-academy.org/homepage/de/eurepa_activities/current_courses/19.html

August 2008
- Venice Epilepsy Summer School, 7th International Course: Bridging Basic with Clinical Epileptology–3
  August
  Venice, Italy
  e-mail: epilepsysummercourse@univiu.org

September 2008
- 8th European Congress on Epileptology
  21–25 September
  Berlin, Germany
  http://www.epilepsyberlin2008.org

November 2008
- 5th Congreso Latinoamericano de Epilepsia (ILAE & IBE)
  5–8 November
  Montevideo, Uruguay
  http://www.epilepsymontevideo2008.org