THE NEWSLETTER OF THE INTERNATIONAL LEAGUE AGAINST EPILEPSY

Epigraph

ISSUE 2 1999

Editorial

Welcome to the final issue of Epigraph this Millennium. To mark this occasion we have commissioned an article from Dr Tim Pedley, Editor-in-Chief of Epilepsia. The article looks forward to what the new millennium may bring for epilepsy. The ILAE in association with the IBE is shortly to launch the mother of all epilepsy websites and Mike Chase, our webmaster is already well advanced with this exciting initiative; in this issue he gives us a flavour of what is to come. The Global Campaign, the flagship of the ILAE/IBE/WHO partnership has changed gears. Hanneke de Boer has taken over the chairmanship of the Global Campaign and we wish her every success. She is particularly keen to enhance epilepsy services in Africa and we include a short piece on the subject in this issue. Jerome Engel's Presidential Message as ever is comprehensive and thought provoking.

My thanks go to all those who have contributed to the Bulletin Board for this issue. Our aim is to involve ILAE Chapters in the Newsletter and therefore we feel it is important for you to keep us updated of Epilepsy News in your country. We are aware of the extra demands on the part of roving correspondents to supply us with news and are grateful to you.

We take this opportunity to say farewell to Gillian Dawes, Epigraph 's Editorial Assistant. Gillian has gone onto pastures green and we would like to wish her every success for the future. Juliet Solomon, who has been Editorial Assistant for the past few issues has taken over the mantle of running the Epigraph Office. Please note our new contact details which are on the back page of this issue.

May I finish off by wishing all our readers a happy and peaceful New Millennium. This century has borne witness to significant advances in the field of epilepsy; I hope that we and our successors will see continued developments and success in the coming Millennium.

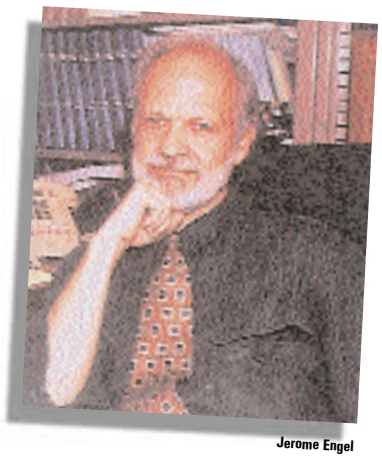
Ley Sander
Co-Editor, Epigraph

President's Message

International Congress success

With the conclusion of another extraordinarily successful International Epilepsy Congress, it is apparent that interest in epilepsy continues to rise. The registration of approximately 4,400 participants in Prague compares with 2,000 in Oslo in 1993, 3,000 in Sydney in 1995, and almost 4,000 in Dublin in 1997. Success was measured not merely by attendance, however, but more importantly by the scientific merit of the presentations, and the high quality of information transfer that took place. In this regard, it is of particular interest to note the increasing numbers of basic scientists who are contributing to our biannual international congresses, and also to regional congresses.

As we approach the new century and consider the tremendous advances in epileptology over the past hundred years, it is clear that the understanding we have gained regarding fundamental mechanisms of epilepsy has had a profound impact on clinical practice. For example, our newfound insights into neuronal disturbances responsible for enhanced excitation, decreased inhibition, and hypersynchronization characteristic of different seizure types now drive development of "designer" antiepileptic compounds. Further studies with chronic animal models of epileptic conditions, as well as with patients, are elucidating those enduring aberrations in molecular, cellular, and systems structure and function that underlie the appearance of various forms of human epilepsy. This work has already contributed greatly to new approaches for differential diagnosis and presurgical evaluation, and should ultimately suggest more specific novel strategies for treatment and prevention.



Jerome Engel

New

Neuroscience emerged as a new, vibrant field of study towards the middle of this century, in large part due to the advent of the basic research discipline of electrophysiology. For this reason, it found its initial home in EEG societies. As it gained adherents, the International Brain Research Organization was formed, and later the Society for Neuroscience in the United States, and similar regional and national neuroscience organizations appeared around the world. Over the past two decades, basic neuroscience has become arguably the fastest-growing and most exciting subspeciality of biomedical science and, indeed, we are coming to the end of what has now been recognized as the *Decade of the Brain.*

It is difficult to estimate what percentage of basic neuroscientists are working in areas relevant to epilepsy, and even more difficult to

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EPILEPSY 2000

Tim Pedley, Editor-in-Chief of Epilepsia, points to future developments in epilepsy as we move into the next millennium.

Sharing the resources and reducing the burden

Over the past century on the many accomplishments that have been made in understanding and treating epilepsy. As we end one millennium and begin another, we look ahead realizing that despite how much has been done, there is still a great deal more to do. Nonetheless, we have within our grasp the capability for treating seizures more effectively, reducing or eliminating adverse effects of therapy to a greater degree, and allowing people with epilepsy to lead more normal lives than ever before. A great deal can be achieved simply by more effective use worldwide of the already considerable body of knowledge about epilepsy and the various effective treatment options that are now available. Worldwide, more than 40% of people with epilepsy receive no treatment, and a nearly equal percentage receive inadequate or inappropriate therapy; this is indefensible. If we could use just a portion of the resources now used to treat epilepsy in the established market economies of Europe, North America, Australia, and Japan (which bear <10% of the epilepsy burden in the world but use over 80% of the resources) in the developing countries of Asia and Latin America, we could improve the lives of millions of people rapidly and relatively easily. This is part of the impetus behind the Global Campaign Against Epilepsy and, I believe, an obligation that the ILAE and the IBE carry into the new millennium.

Humans as Experimental Subjects

An important advance that can hardly be overestimated in terms of impact, has been the growing ability, as the last century has progressed, of investigators to carry out basic studies in humans. For example, intracranial monitoring techniques and the epileptogenic brain tissue removed during surgery have offered investigators opportunities to study fundamental cognitive, physiological, biochemical, and molecular issues in patients that were possible to study previously only in experimental animal models of epilepsy. Similarly, new or enhanced brain imaging methods, such as functional magnetic resonance imaging (fMRI), magnetic resonance spectroscopy (MRS), and positron emission tomography (PET) are now central to the non-invasive study of basic biological questions in the living, intact human brain. fMRI and PET, offer exciting possibilities as new ligands, activating protocols and agents, and advanced imaging methodologies become

determine how many investigators engaged in epilepsy-related basic research actually know, or care, about issues important to clinical epileptologists. Many basic neuroscientists study epileptic seizures as tools for perturbating the brain in an effort to reveal normal neuronal mechanisms. Others who investigate neuronal substrates of experimental epileptic seizures have little knowledge of the relevance of their animal models to human epilepsy. There has always been, however, a hard core of basic neuroscientists with a firm commitment to contribute to an understanding of the human condition.

Balance

Less than two decades ago, the American Epilepsy Society made a concerted effort to attract basic scientists to its annual meeting, and to enhance the productive dialogue between basic and clinical investigators. This effort began with a handful of basic researchers profoundly interested in making their investigations relevant to clinical epilepsy, and has grown to the extent that there is now perhaps an equal balance between basic and clinical presentations at the annual meeting, which now attracts over 2,000 participants. For this reason, in the US, the American Epilepsy Society has been held up as the near-perfect example of a tightly integrated, comprehensive, disease-oriented organization.

The ILAE began a similar effort to include more basic scientists in its activities with the creation of the Commission on Neurobiology of Epilepsy over ten years ago, and the adoption of the four-day Workshop on Neurobiology of Epilepsy as a fixed satellite of the biannual international congress. Basic scientists have been attending our international congresses, as well as our regional meetings (such as the European congresses), in increasing numbers. The joint IBE and ILAE executive committees recently decreed that at least one main topic of every international congress must be basic science-related. In Prague, the basic science topic was plasticity; however, many basic science presentations were also included in sessions related to the other main topics, and a significant number of the symposia contributed by commissions were concerned with fundamental mechanisms of epilepsy.

Collaborations

The current Commission on Neurobiology is chaired by Dr. Phil Schwartzkroin, who was the first PhD full-time basic neuroscientist to become president of the American Epilepsy Society. In addition to furthering its own agenda to support basic research on epilepsy, this commission has entered into collaborations with other commissions, such as the Commission on Search for Epilepsy Genes, and has established a worldwide network of basic neuroscientists interested in epilepsy. Among other activities, these investigators will be creating basic science courses at all the regional epilepsy congresses, as well as at future International Epilepsy Congresses.

Relationships

One of the major objectives of the current ILAE Executive has been to integrate basic science, as completely as possible, into the international epilepsy agenda. Clinicians needed to be convinced that basic scientists have important contributions to make to our organization; basic scientists needed to be convinced not only that they were welcome, but that their research would benefit from continuing close relationships with clinicians. Clinicians need to understand, and ultimately apply, the mechanical insights gained from basic investigations; basic neuroscientists need to know the problems faced by clinicians that might be resolved through research into fundamental mechanisms. It appears that acceptance of basic scientists by our clinical colleagues is now, for all intents and purposes, complete. However, much work remains to reach out to large numbers of investigators engaged in basic epilepsy-related laboratory research, particularly those who have limited resources to attend international meetings or become involved in other international activities. To accomplish this objective, we must provide a certain amount of financial support, and also demonstrate that the International Epilepsy Congresses have something significant to offer basic scientists interested in epilepsy that cannot be found at "pure" neuroscience meetings, such as those of IBRO and the Society for Neuroscience.

Exchange

With the completion of the Prague congress, we begin a concerted two-year effort by the Commission on Neurobiology, the chairs of the next Workshop on Neurobiology of Epilepsy (Drs. Esper Cavalheiro and Claude Wasterlain), the basic neuroscientist on the Scientist Advisory Committee of the 24th International Epilepsy Congress (Dr. Istvan Mody), and the ILAE Executive Committee, to make the Buenos Aires congress in May 2001 an exemplary integrated exchange of basic and clinical scientific information relevant to epilepsy. We must start now to plan this congress in a way that not only welcomes our basic science colleagues, but also anticipates their needs and offers a program that will be attractive to them. I can think of no better way to ensure that the League will continue to be relevant and productive into the next century.

Jerome Engel Jnr, MD, PhD

President, ILAE

available. New insights derived from these studies are, for the first time, making it possible to determine which abnormalities found in animal models of seizures have counterparts in humans; which experimental observations are valid for the human condition and which are not; and which experimental data fit within reasonable conceptual frameworks for developing further ideas.

The Molecular Genetics Revolution

Exciting developments in basic neuroscience in the middle and latter parts of this century have been related to epilepsy, either directly (e.g. in cellular studies of disease mechanisms) or indirectly (e.g. in investigations of cortical excitability and its control). However, the concept of epilepsy, or indeed of any disease, is very much a product of the scientific beliefs of the time, and the tools that are available for investigators. Thus, the focus of epilepsy research and, as a result, views of what epilepsy "is" have developed historically from anatomic, neurophysiologic, and neurochemical perspectives, to a more encompassing neurobiological construct that itself has evolved, from system to cell, from *in vivo* to *in vitro* models, and to studies of transmitters, receptors, and channels. Now, of course, we are firmly in the era of molecules and genes.

Among the more than 40 individual epileptic syndromes described in humans are about 10 that are considered familial and in which genetic determinants appear to be prominently involved. Twin studies implicate strong genetic determinants in many types of seizures and seizure disorders, especially such ones as childhood absence epilepsy, juvenile myoclonic epilepsy and idiopathic grand mal seizures. Furthermore, some inherited disorders, such as tuberous sclerosis and neurofibromatosis, are associated with brain lesions which, in turn, give rise to symptomatic epilepsies. In most cases of epilepsy, however, the role of genetic factors is not straightforward; to the contrary, it is quite complex. For example, children of parents with either localization-related or generalized epilepsy develop seizures at increased rates, although the difference is greatest for children of parents with idiopathic generalized forms of epilepsy. Thus, there may be some degree of sharing of genetic susceptibilities in both the idiopathic and degree of sharing of genetic susceptibilities in both the idiopathic and symptomatic epilepsies. This means that there are undoubtedly specific genetic determinants of the brain's susceptibility to seizures and epilepsy following a particular injury, as well as other genetic factors that determine the occurrence of individual familial idiopathic epilepsy syndromes. Probably the greatest challenge facing investigators now is to identify and characterize those genes that alter an individual's susceptibility to seizures in the presence of acquired brain pathology or as a reaction to acute or subacute cerebral dysfunction. Clues are beginning to emerge with genetic studies ongoing in families with benign familial temporal lobe epilepsy; investigation of families with hippocampal sclerosis and seizures; and the apparent link between developmental malformations and febrile seizures or hippocampal sclerosis.

Animal models have allowed definition of some "epilepsy genes" and their encoded proteins. Dr. Jeffrey Noebels has defined an epilepsy gene as "a gene expressed in the brain which, in an aberrant form, predisposes neural circuits to the paroxysmal bursting and synchronous oscillations that underlie various patterns of recurrent epileptic seizures." Information obtained from animals with single gene mutations that produce some aspect of an epileptic phenotype are elucidating two critical issues: (1) the conditional (that is, intermittent) behavior of human epilepsy phenotypes; and (2) the protein products, or lack thereof, that are responsible for the molecular aberrations underlying the abnormal excitability and synchrony responsible for the epileptic state.

In humans, several idiopathic epilepsies with a monogenic mode of inheritance have been identified. Autosomal dominant frontal lobe epilepsy is caused by mutations in the CHRNA4 gene, which codes for the a4-subunit of the neuronal nicotinic acetylcholine receptor. Mutations in two voltage-gated potassium channel genes, KCNQ2 and KCNQ3, cause benign familial neonatal convulsions. A mutation in the sodium channel fl1 subunit gene, SCN1B, on chromosome 19q has been implicated in febrile seizures and generalized epilepsies (GEFS+). Three other gene loci for autosomal dominant febrile seizures (FEB1-3) have been linked to chromosomes 8q, 19p and, most recently, 2q. In just the last months, the gene for familial adult myoclonic epilepsy (FAME) has also been linked to 8q. The only specific gene defects identified thus far in a few idiopathic epileptic syndromes result in abnormalities of ion channels that regulate cortical excitability. There is, therefore, a growing acceptance that ion-channel mutations may be a common underlying mechanism of idiopathic epilepsies.

While mutations in single genes account for some rare epileptic syndromes and familial diseases that cause epileptic seizures, the evidence from epidemiologic and family studies indicates that the majority of the idiopathic epilepsies reflect complex oligogenic inheritance patterns, not single-gene abnormalities. Multiple genes must determine the various neuronal functions which alter seizure threshold and predispose to development of clinically evident epilepsy and it is likely, as Lennox postulated 50 years ago, that these interact, to one degree or another, with acquired factors. Thus, for most epileptic disorders, it remains to be determined to what degree abnormalities of single genes, or concordance of a few key overlapping genes, determine susceptibility to seizures and the phenotypic expression of any given epileptic condition. It should soon be possible to test the hypothesis that genetic mutations in specific ion channels are associated with susceptibility to a particular type of seizure or epilepsy syndrome.

As human (or animal) epilepsy genes are identified, the next step will be to understand how particular molecular defects result in epileptic excitability. The relatively recent ability to create transgenic animal models that overexpress particular genes on the one hand, or that carry "knock-outs" on the other, is an essential strategy to address this issue. As their encoded proteins are identified, animal experiments will be necessary to show how these molecular anomalies lead to seizures. Not all gene defects will have intuitively obvious consequences for development of epilepsy. For example, the defective gene in Unverricht-Lundborg disease encodes cystatin B, a ubiquitous inhibitor of cysteine protease, a lysosomal enzyme that cannot, at the present time, be related easily to any known epileptogenic mechanism, although programmed neuronal cell death may be involved. Such data should lead eventually to a molecular classification of clinical and pharmacological seizure subtypes, and of distinct epilepsy syndromes.

Rational Drug Development

The last decade has seen the introduction of several new antiepileptic drugs, and still others, not yet marketed, are under active investigation. Most, however, have been developed as the result of serendipity, large-scale screening programs, or erroneous theories. Only three drugs that are marketed or in phase III trials - vigabatrin, tiagabine, and remacemide - have resulted from efforts to develop mechanism-specific agents. The first two of these increase GABA-mediated inhibition, vigabatrin by irreversible inhibition of GABA transaminase, the main enzyme involved in degrading GABA, and tiagabine by specific inhibition of GABA uptake into neurons and glia. In contrast, remacemide seems to have a mixed mode of action in that it (or a metabolite) acts both at NMDA receptors and at voltage-dependent NA+channels. We continue to need new drugs because existing ones tend to be relatively ineffective in severe cases of epilepsy, often have undesirable adverse effects, and are not specific for epileptogenic mechanisms.

Advances in basic neuroscience offer a number of new possibilities for novel antiepileptic or "protective" drugs in the 21st century. These will include, first, the development of drugs that prevent or abort the epileptogenic process that may occur following brain injury (e.g. trauma, stroke, encephalitis). Second, although efforts to modify excitatory neurotransmission have been largely unsuccessful to date, developments in cellular and molecular biology offer new hope. For example, it may be possible to develop antisense oligonucleotides to glutamate receptor subunits, or block/modify specific channel components. Third, we can anticipate therapies that target age-specific developmental mechanisms for childhood forms of epilepsy. Finally, neuroprotective agents to attenuate or eliminate the damaging effects of prolonged or cytotoxicity related to glutamate and unbound intracellular calcium, and interrupting repeated seizures should appear. Most likely, these will be directed to blocking the second-messenger cascade.

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The IBE/ILAE website

What do you suppose will be the most exciting new portal for clinical, research and public information on epilepsy at the beginning of the 21st Century? Right! It is "epilepsy.org," which will debut in the first half of the year 2000. We cannot be more specific regarding the time of its presentation because we recognize that it will represent a substantial undertaking to "do it right the first time," and we want the site to represent our very best effort.

Between the present and the launch of the site, we will be providing updates on our progress. We hope to obtain the input of as many individuals as possible regarding solutions to problems that we will undoubtedly confront and decisions that need to be made. For example, after it was decided to develop a Web site, the very first question that arose led to an answer that presented a major problem. It was clear that the obvious and best name for our URL (uniform resource locator, i.e., Web address) would be "epilepsy.org," but we found that the Epilepsy Ontario organization had already registered this URL. Fortunately, they were most gracious and allowed us to re-register it as the future home of the IBE/ILAE Web site. So, many, many thanks to Epilepsy Ontario.

It was decided that the site would be one that will provide comprehensive information on epilepsy, in addition to items of relevance only to the IBE and ILAE. Thus, it will contain sections of importance to members of the IBE and ILAE, as well as provide information for epilepsy specialists and the general public. We recognized that this decision to develop a comprehensive site would require that the site would have to be organized in a manner that would allow individuals to easily and intuitively find different kinds of information.

"Where is it?"

"I don't know."

"It's in here."

"I know it is. I just don't know where."

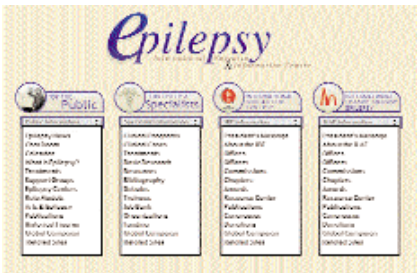
"I just can't find it. Let's go to another site."

That is a conversation that occurs countless times as frustrated individuals fail to find the information that they want among the over 3,000,000 Web pages that are available presently. On most Web sites, this problem persists as those

responsible for the site drastically under-deliver on meeting the simplest need of all: clearly communicating what is on the site and where on the site it is located. If individuals cannot find information easily and navigate between sections of a site intuitively, they certainly will not stay or return. Epilepsy.org needs to be presented and organized in a fashion that first-time visitors will have their expectations fulfilled at every click.

As a first step in developing an intuitively simple way to present information, we decided to divide the site into four basic areas: one for the general public, another for specialists, a third for the IBE, and a fourth for the ILAE. Of course, some of the same information will be accessible from more than one of these four areas, while other sets of information, that are highly focused, will be located only in the relevant areas; there will be some sections that are password-protected. Presented below are two screen captures; the first is that of the prototype Home Page, and the second shows the pull-down menus that will allow users to go directly to sections of interest to them by a single mouse click.

We are now developing a work flow pattern to develop the site, which will include deciding how and from where to obtain material for the site, how to best present this information, and numerous other fundamental matters of an organizational nature. We hope that our initial decisions are good ones, but we want to be sure and have therefore asked the members of the IBE and ILAE to critically review the prototype Web site. We intend to obtain critical evaluations at each stage of the site's development and hope that the membership of both organizations will also help in this process. Therefore, if other members of either the IBE or ILAE would like to help in this evaluation process, we would greatly appreciate their input. The prototype site is located at http://www.epilepsy.org/prototype.



Based upon the input that we receive, we will modify the site and then begin to add substantive data to fulfill our commitment to make this site the very best that we are able to present.

In order to begin to evaluate the present prototype, it is important that those who evaluate the site begin with a common foundation of knowledge regarding the current status of Web sites and the developments that suggest future directions for the communication of information on the Web.

An Overview of the Evolution of Web Sites

We don't make Web sites the way we did just four years ago. The typical welcome-to-my-home-page, menu-driven, icon-encrusted model is fast being replaced by what is called "third-generation site architecture." Though third-generation sites rely heavily on today's browser technology, the difference is not technology per se - the difference is design.

Designers know that if people don't consume their content, it doesn't matter how well structured it is. In contrast, structuralists want everyone to be able to access Web content with any browser. They don't worry much about typographic niceties or the visual lay-out of a page. To them, Web pages are documents and their interests are relegated solely to the fact that if individuals are interested in the information, they should be able to find it with a search engine. This is the situation that prevailed with first, and to some extent, second-generation sites (see below).

In contrast, for third-generation sites, design drives the user's experience of the content; it is the designer's responsibility to present content appropriately. Who cares how powerful a database is if people can't use the interface? Who cares how complete or detailed the content is if people aren't attracted to it or don't find it pleasurable to read? For example, for some third-generation sites it is important that paragraphs be indented. But structuralists think it's crazy to take the time to insert indents into paragraphs. According to hypermedia visionary Ted Nelson:

"Multimedia must be controlled by dictatorial artists with full say on the final cut."

The Web is no different from the rest of the world. From legal documents, newsletters, and the Wall Street Journal to USA Today and Wired magazine, a successful format completes the communication link between content producers and the intended audience.

First, Second and Third-Generation Sites

First-Generation Sites.

First-generation sites were linear. They were bare-bones, functional, and were intended mainly to allow scientists and others around the world to obtain basic information. When one views a typical first-generation page, the restrictions imposed by slow modems, monochrome monitors, and default browser style sheets are clear.

First-generation sites were designed by technical people. Some sites had headline banners and

were well organized; most had edge-to-edge text that ran on for pages, separated by meaningless blank lines. At best, they looked like slide presentations shown on a cement wall.

Second-Generation Sites.

Second-generation sites are basically first-generation sites with icons replacing words, tiled images replacing gray backgrounds and buttons with beveled edges. They use a top-down, bullet-list, menu-driven model to present a hierarchy of information.

Third-Generation Sites.

Third-generation sites are rapidly becoming the norm, rather than the exception. A third-generation site combines typographic and visual layout principles with creative design solutions to provide a complete experience for the visitor. Third-generation sites use metaphors and visual themes to entice and guide. They strive to make a site feel familiar and easy to navigate, with quality content and high production values. Third-generation site designers carefully specify the position and relationships of all elements on the page, retaining fine control of the layout.

Thus, a third-generation site is wrought by design, not technological competence. Third-generation sites give visitors a complete experience, from entry to exit. The cleverness of third-generation designers is not technical but visual. Design is the difference. In this way third-generation sites pull visitors through using metaphor and well-known models of consumer psychology. Just as retailers spend a lot of time tuning their environments to the customers passing by, third-generation sites are a complete experience-the more you explore, the more the entire picture of the site comes together. Third-generation design turns a site from a menu into a meal.

Building third-generation sites is hard. It takes time, dedication, and a sense of what excites the viewers. Third-generation sites usually require several people working together, pushing themselves to make every page beautiful and the entire site "work" a surfing experience.

Basic Principles of Web-based Information Communication

As people wander by a site, it is important to hold out a basket of goodies to tempt them. Gossip, news, sports scores, weather information, stock quotes, promotional sales, package-tracking services and sound files routinely lure potential viewers to a good Web site.

In contrast to the second-generation concept of a home page, third-generation sites often have either one or several core pages to organize and present the contents. Some third-generation sites have no core page at all. Core pages direct the visitor by providing links to the various neighborhood pages. Core pages hold content while continuing to entice the visitor through the site. They use content to lure and tantalize and details of images and exerpts of text to guide the viewers. Otherwise, the information remains buried behind flat, uninformative links.

Net Equity. If people talk about the site, if they come back often, if the core metaphors start with a buzz and the front door is enticing, it is possible to build net equity. Simply put, net equity is audience mindshare. One builds mindshare by making things that either are or will become familiar to the viewers.

Change Is Good. Viewers don't need to bookmark the entrance to a site - they can probably remember that. But if there is a compelling core page, they just might bookmark it. The free or really important stuff gets them there, but they come back regularly to the core of the site to see what's new.

If a site changes every month, it might as well be static. If it changes weekly, people might bookmark the pages with interesting things going on. If it changes daily, there will be big numbers on the site counter.

How many sites have "What's New!" on the front page? One shouldn't have to know how to get to What's New. If it's new, and it's important, it should be in the viewers' faces. It is therefore important to put some content on the core page - and not bury it under a "What's New!" link.

Information-Based Sites. In the information realm, sites must satisfy impatient, directed viewers; they can't afford to put too much glitter in front of the information. Nevertheless, they must be compelling without using a lot of icons and banners.

Unfortunately, most information-based sites present endless pages of text and bulleted lists, with a predictable home page up front (News/About Us/Catalog/FAQs/Help). Many have a search engine enabling visitors to find things immediately, but if viewers don't know exactly what they want, they quickly become lost and leave the site.

> Information-based sites, such as the Epilepsy portal, must offer both browse and search capabilities. Regular viewers need a page they can bookmark, preferably listing the features of the site and providing the shortest path to any given page. There should be a search window, or at least a button to a search page, on every page in the site.

Dynamic sites are becoming the norm in the information realm. Rather than bookmarking a static page, frequent users fill out a form telling the site about their needs. The site goes to work for them, sending them e-mail messages when new items of interest arise, providing a custom, made-on-demand page just for them, and generally keeping their interests in mind as they cruise the site. A good dynamic site presents opportunities to learn new things and see new offerings while trying to meet 90% of the frequent surfer's needs on the first two pages.

A good thematic site is an exercise in subtlety, good information design, and consistency. Finally, it is important never to forget that people tend to surf with their shortest attention spans turned on. As we develop the Epilepsy portal we will be keeping in mind the preceding concepts and implementing the newest methods of communication on the World Wide Web.

Michael H. Chase, PhD, Webmaster

EPILEPSY 2000

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Triggers that initiate programmed cell death will be identified, and drugs that prevent or stop apoptosis (e.g. caspase inhibitors) will become available. And it may become possible to block or modify undesirable activity-dependent gene activation, such as those that promote axonal sprouting that leads to a permanent increase in circuit excitability.

Other Future Therapies

The renewed interest in the ketogenic diet and the successful introduction of vagal nerve stimulation into the main stream of epilepsy treatment should stimulate research into other non-traditional and non-drug therapeutic approaches, such as implantable stimulators that, like programmable cardiac defibrillators, prevent either the interictal-ictal transition or spread of the seizure discharge beyond the ictal-onset zone.

Advances in technical fields, such as engineering, should allow the development of new drug-delivery systems. Ideally, for example, one would like to deliver drugs only to the neurons or critical circuits that initiate the seizure, or to a suppressor region that can abort the process. Pumps that deliver a controlled amount of individualized, very specific antiepileptic drugs in response to pre-seizure changes in brain electrical activity would be one way to do this.

Finally, molecular biology, in addition to clarifying the pathogenesis of seizures and epilepsy, may offer new therapeutic strategies. Stem cell transplants may replenish cells lost by injury (including severe seizures) and restore normal circuitry. It might also be possible to stimulate controlled neurogenesis. Gene replacement may become a viable option in the relatively rare monogenic epileptic disorders and in other epilepsies where a "susceptibility gene" can be identified.

Conclusions

As we enter the 21st century, there is an almost palpable excitement about the growing opportunities to make a difference to people with epilepsy. Laboratory and clinical investigators are collaborating to make what seems almost science fiction today the likely reality of tomorrow. The diversity with which human epilepsy expresses itself indicates that it is not a unitary problem and, therefore, that there is unlikely to be a singular solution to any of epilepsy's many facets. Nonetheless, the potential of new investigative tools, especially those of brain imaging and molecular biology, is providing unparalleled and rapidly accelerating progress in illuminating the mechanisms of epilepsy and epilepsy-related brain dysfunction, and offering greater hope than ever before for prevention, effective treatment, and even cure. I believe that the coming era will illustrate, more graphically than at any previous time, that physicians can be most effective when their practice has a sound scientific basis, and that the results of basic research will impact with increasing directness on patient management alleviating the problems of epilepsy worldwide.

Timothy A. Pedley, MD

ARGENTINA

Recently in Argentina, the National Epilepsy Law was passed by the National Senate; it has now been passed to the House of Representatives and once passed it will become effective as National Law.

Dr Silvia Kocen, head of the epilepsy center at 'R. Mejia' Hospital, University of Buenos Aires and co-founder of FUNDEPI and Mr Jorge Lovento, current Chairman of FUNDEPI, instigated the law.

The law in principle deals with the discrimination and lack of protection suffered by patients with epilepsy. Three main aspects are taken into consideration: the patient's right to access to a diagnosis and to receive free antiepileptic medication in the event that they do not have medical assistance; non-discrimination in the workplace, school or from any other social setting; and the implementation of educational campaigns aimed at informing the community, patients, their relatives and medical and non-medical professionals about what epilepsy is.

Silvia Kocen
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CHILE

In preparation for the First Latin American Epilepsy Conference next September, the Chilean Chapter has elected a new Executive Committee led by Dr. Marcel Devilat as its President. He and his colleagues would like to see as many of you as possible at the Conference.

Tomas Mesa
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GERMANY

With a view to the local global campaign, public awareness events for epilepsy are continuing on a local level. The IZE is an information center that was founded in 1985 which has as its main function the distribution of information material about epilepsy to the lay public. The information material covers many relevant areas including schooling and epilepsy, driving, women's issues etc. The homepage is www.IZEPILEPSIE. DE

Ingrid Tuxhorn
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MALTA

The Minister of Health in Malta, Dr Louis Deguara was recently invited to launch a small booklet entitled l-epilessija u t-tfal (epilepsy and children) during a well publicised press conference. The booklet was written by Dr Doriette Soler, one of the members of the Epilepsy Society of Malta (which is the local chapter of the International League Against Epilepsy), and paediatrician at St Luke's Hospital, in conjunction with Dr Simon Attard Montaldo, Head of Paediatrics. The publication of this booklet was sponsored by the Health Promotion Unit, Department of Health. As part of an on-going collaboration with the local support group, Malta Epilepsy Support Group (Caritas Malta), this booklet is the latest in a series of information guidelines written in Maltese, as part of the local campaign for Epilepsy 'Out of the Shadows'.

Janet Mifsud
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SWEDEN

Sweden has celebrated the end of the 'Decade of the Brain' which have included activities concerning epilepsy. There have been lectures for the public, exhibitions, publication of books and radio and television programmes. At the end of this year the Swedish Epilepsy Society have organised a research meeting entitled: "Epilepsy - a window to understanding the brain", and in addition a joint meeting with Swedish and Chinese epileptologists.

Eva Kumlien
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TURKEY

There are hopes to extend Epibase, the Turkish epilepsy database. An 'Epibase Bulletin' of 8 pages will be published every three months. The first bulletin due to be issued in January 2000 will contain information about epilepsy education and evaluation of the Epibase programme.

e-mail: cgurses@superonline.com

UNITED KINGDOM

A new government report (the Report of the Clinical Standards Advisory Group) is being published, in which a series of recommendations are made for changes in the way epilepsy services are organised in the United Kingdom. The aim is to produce truly 'joined up' epilepsy care with an emphasis on strengthening primary care and encouraging shared care between primary and secondary levels, and the setting of a network of around 100 Epilepsy Centres throughout the country, each covering a population of 500,000 persons. For further details on the report please contact Professor Simon Shorvon at 6th Floor, Institute of Neurology, Department of Clinical Neurology, Queen Square, London WC1N 3BG, UK or by e-mail: s.ellis@ion.ucl.ac.uk

The National Society for Epilepsy has launched a new CD-ROM, *'Epilepsy: an interactive guide for medical professionals,'* priced £79.95. It is a comprehensive, interactive mutimedia guide covering both medical and psychosocial issues.

For further information please contact Elaine Faulkner at the National Society for Epilepsy. Tel +44 1494 601 300

e-mail: elaine@epilepsyNSE.co.uk

VENEZUELA

After considerable efforts, the Venuezelan League Against Epilepsy held its first National Epilepsy Congress. This took place in the first week of November in Caracas. This meeting will be seen as a landmark in the history of the Epilepsy movement in Venezuela and was only possible with the help and support of all the scientific community in the country. We hope that it will be the first of many!

Beatriz Gonzalez Del Castillo
e-mail: becastle@telcel.net.ve

Have your say!

Contributions to the Bulletin Board are always welcome from any organisations or individuals with a 'story to tell'. Please e-mail the Epigraph Office: j.solomon@ion.ucl.ac.uk or fax on +44 (0) 20 7833 2823 or write to Juliet Solomon at Institute of Neurology, 6th Floor, Queen Square, London WC1N 3BG, UK.

African Challenge of Global Campaign

One of the most exciting challenges that the international epilepsy community, via the Global Campaign, must face during the next millennium is the fight against epilepsy in developing countries.

Through joint and concerted efforts, it is possible to make significant improvements in the field of epilepsy, such as reducing the treatment gap which affects at least 80% of people with epilepsy in the developing world. The Global Campaign Against Epilepsy supported by the ILAE, IBE and WHO, with future support from UN specialised institutions, international financial institutions and non-governmental organisations provides a unique opportunity to yield positive results.

For the African continent, the first steps will begin in 2000. An exciting initiative due to begin in 2000 are the epilepsy projects to take place in Zimbabwe and Senegal, the structure and principles of which were defined at a meeting held in Geneva in May 1999. The five-year action plan will allow the two countries to focus on epilepsy care, training information. education and epilepsy prevention. It is hoped that this initiative will mark the start of greater action within the African continent, at both regional and national levels.

A meeting is due to take place in Dakar, Senegal at the beginning of May 2000 where African countries will have the opportunity together of starting to tackle the 'Global Campaign', by clarifying policies and plans for future initiatives, with the aim of pushing epilepsy 'out of the shadows'. At this meeting, the 'African initiative against Epilepsy', supported by an 'African Declaration' will be officially adopted, in the presence of international delegates from the WHO, ILAE, IBE and various other interested parties.

For more information on the meeting in Dakar please contact:
Amadou Gallo Diop: gallo@telecomplus.sn
Hanneke de Boer: ibe@xs4all.nl

Amadou Gallo Diop, PhD
Secretary General of the
Senegalese League Against Epilepsy

Famous people with Epilepsy

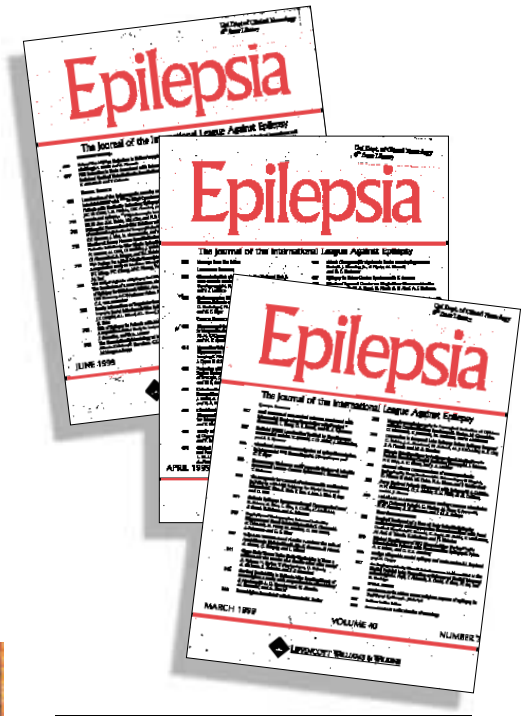
This issue's 'famous person with Epilepsy' is Joan of Arc. A national heroine, Joan of Arc is the Patron Saint of France. Also called the 'Maid of Orleans', she united the nation and decisively turned the Hundred Years' War in France's favour. Her life and death have been the subject of much controversy. The ILAE has had her listed in their pantheon of famous figures with epilepsy for some time, although it has to be admitted that the evidence she suffered from the disease is scant. She was a brave (possibly foolhardy) woman and the editors hope that her inclusion in this page does not re-ignite an Anglo-Gallic conflict (who was it that said the passage of history was always circular?) Nor do we find her necessarily a good role model for burgeoning European consensi. Nevertheless, . . .

Joan of Arc was born in the village of Domremy, in Lorraine, France in 1412, around the time that the Hundred Years' War between England and France was being renewed. She began to hear celestial voices, often accompanied by visions at the age of 13. She later idenitifed these visions as being those of St Michael who was accompanied by other angels), St Margaret and St Catherine. These voices, appearing several times a day addressed her as' Jeanne La Pucelle de Dieu'. From the onset, she was informed of her mission: she had been chosen by God to restore France and aid the Dauphin Charles, who was to be King of France and lead the army. It was not until the age of sixteen that Joan of Arc began to act on the voices, which had become more urgent.

In 1429 she led the French to a decisive victory over the English at Orléans. At the coronation of the Dauphin in the Cathedral at Rheims, she was given the place of honour. The following year, Joan led a military operation without royal suppport against the English at Compiègne, near Paris. She was

captured by Burgundian soldiers, who then sold her to their English allies. Accused of heresy for believing she was directly responsible to God rather than to the Roman Catholic Church, the ecclesiastical church condemned her to death, but the sentence was commuted to life imprisonment when she confessed her errors.

The visions might have been epileptic fits, although Joan was always reluctant to speak of the voices. She said nothing about them to her confessor and constantly refused at her trial to be drawn into descriptions of the appearance of the Saints or to explain how she recognised them. None the less, she told her judges 'I saw them with these very eyes, as well as I see you.' Later she was again condemned by a secular court, and on May 30 1431, Joan was burned at the stake in the Old Market Square at Rouen, as a relapsed heretic. At her death, those in attendance reported that the name 'Jesus' could be sighted in the flames that killed her, and a white dove was seen flying out of the pyre towards the direction of France. Even the executioner was convinced he had killed a saint. After her death, Joan of Arc's ashes were thrown into the Seine.



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Electronic databases permit easy searches to find background knowledge for present day science, however most do not retrieve information beyond mid-century. Yet the early writings, although often outdated, do contain precious gems well worth recovery. The ILAE executive has taken steps to bring the early literature on epilepsy within easy reach of everybody, by signing a contract for the reprint of the EPILEPSIA series1, 2 and 3.

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Diary Dates

If you would like to publicise an event taking place in your part of the world which would be of interest to ILAE members, we would be happy to receive the relevant information. Please provide date, venue, subject and contact details including contact person, address, telephone/fax number, email address and web site. Please forward this information to the Epigraph office (details below).

International League Against Epilepsy British Branch Annual Scientific Meeting - 'Northern Exposure' March 30th -April 1st 2000, Edinburgh, Scotland

For further details please contact: Conference 2000 81-83 Willow Street, Oswestry, Shropshire, SY11 1AJ, United Kingdom,

Fax: +44 1691 670302
e-mail: denise@conference2000.prestel.co.uk

International Meeting on the Psychobiology of Epilepsy, Berlin, 6-7 May 2000

This meeting will be organised by Professor M Trimble and Dr B Scmitz. The meeting will discuss behavioural and psychosocial problems of patients with epilepsy, covering a very wide perpspective. Speakers include internationally recognised researchers, and topics will span subjects from subtle cognitive impairment through top posticta psychoses. A heavy emphasis on mechanisms and management will be given. Information about registration (£100 sterling, or £50 for students can be obtained from: Jackie Ashmenall, St Aiden, Ealing Green,Ealing, London W5 5EN, United Kingdom.

Tel:+44 020 7829 8743/ +44 020 7840 1287
Fax: +44 0207 278 3053

e-mail: jashmenall@yahoo.com or visit our website: www.wai.co.uk/epilepsy

28th Annual Hans Berger Symposium, Clinical Neurophysiology: A New Century 21-23 May 2000

An update of technological advances and their clinical applications for physicians and technologists.

Richmond, Virginia, USA. For further information please contact: Judy Hatfield.

Tel: (804) 828 3640, (800) 413 2872.
Fax: (804) 828 7438.

10th Meeting of the European Neurological Society, 18-22 June 2000, Jerusalem, Israel

For further information please contact: Adminstrative Secretariat ENS 2000, c/o AKM Congress Service, PO Box CH-4005 Basel, Switzerland.

Tel: +41 61 686 77 11 Fax +41 61 686 77 88

e-mail info@akm.ch

http://www.ensinfo.com

5th Eilat Conference on New Anti-Epileptic Drugs (Eilat V), Israel, 25-29 June 2000

To be held at the Dan Hotel, Eilat. The programme will provide critical reviews and updated information about new AEDs in different stages of development as well as present progress reports on marketed new AEDs. For further information please contact: Target Tours Ltd, Eilat V, P.O. BOX 29041, Tel Aviv, 61290 Israel.

Tel: +972 3 517 5150 Fax: +972 3 517 5155

e-mail: trgt@netvision.net.il

11th International Cleveland Clinic-Bethel Epilepsy Symposium: Cortical Dysplasia and Epilepsy, Cleveland, Ohio, 27-30 June 2000

This meeting will be held at the Cleveland Clinic. The subject will be 'Cortical Dysplasia and Epilepsy: Pathophysiology, Diagnosis and Management'. The International Symposium will be preceded by two related meetings: The comprehensive Course (22-25 June 2000) and Neuroimaging and Epilepsy (26 June 2000). For further information, Tel: + 216 444 5178 Fax +216 444 0230

e-mail: schoepm@ccf.org

10th European Congress of Clinical Neurophysiology, 26-30 August 2000

This will be held at the Palais de Congrès, Lyon, France. For further details please contact Franck Chatelain, +33 47277 4550 Fax: +33 472 774577

e-mail: package@package.fr

Neuropathology 2000 -X1Vth International Congress of Neuropathology, 3-6 September 2000 Birmingham, UK

For further information please contact:

Congress Secretariat, 4B, 50 Speirs Wharf, Port Dundas, Glasgow G4 9TB, UK

Tel: +44 141 331 0123 Fax: +44 141 331 0234

e-mail: info@neuropathology2000.co.uk

II Latinoamerican Epilepsy Congress, Santiago, Chile, 8-10 September 2000

This is the first Latin American Epilepsy Congress committed to the ILAE/WHO/IBE slogan 'Bringing Epilepsy Out of the Shadows'. The meeting will be attended by Dr. Jerome Engel (President/ILAE) and Dr. Richard Holmes (President/IBE). For further information please contact: Dr Manuel Campos, Epilepsia 2000, Pasaje Lo Gallo 1787, Vitacura, Santiago, Chile

Tel: +56 2 232 9347 Fax +56 2 229 6731.
e-mail: mcampos@med.puc.cl

4th ILAE European Congress of Epileptology Florence, Italy 7-12 October 2000

This Congress will be held at the Fortezza Da Basso. Main topics include: 'Anatomo-Electoclinical Aspects of Frontal Lobe Seizures'; 'Sympotmatic Epilepsies'; 'What can be learned from Human Tissue Study'; Relationship between Presurgical Evaluation Strategy and Surgical Results'; 'Adverse effects of AEDs'. Contact: Maura Stella, PTS Congress, via Tevere 20, 00198 Rome, Italy.

Tel: +39 06 85 35 55 90 Fax: +39 06 85 35 60 60
e-mail: ptscongr@tin.it

5th Congress of the European Federation of Neurological Societies (EFNS 2000) Copenhagen, Denmark, 14-18 October 2000

The Danish Neurological Society celebrates its 100 year anniversary, and the EFNS 2000 Congress will be held at Copenhagen's Bella Center. Main topics are Stroke; Epilepsy; Neuropathy; Movement Disorders; Headache; Cost-Effectiveness of Treatment in Neurology; Dementia; MS and addiction-related neurological disorders. There will also be teaching courses and special lectures. For further information please contact: EFNS 2000, c/o DIS Congress Service Copenhagen A/S, Herlev Ringvej 2C, DK-2730 Herlev, Denmark.

Tel: +45 4492 4492 Fax: +45 4492 5050
e-mail: efns@discongress.com

3rd Congress of Asian Oceanic Epilepsy Organisation (AOEO), New Delhi, India, 11-13 November 2000

For further information please contact: Dr Satish Jain, Secretary General, Dept. of Neurology, Neurosciences Centre, All India Institute of Medical Sciences, New Delhi-110 029, India.

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