Epilepsy - References

Web Links

Centers for Disease Control Epilepsy
http://www.cdc.gov/Epilepsy/

Diagnosis and Management of Epilepsy in Adults Scottish Intercollegiate Guidelines Network
http://www.sign.ac.uk/guidelines/fulltext/70/
Models of Care
http://www.sign.ac.uk/guidelines/fulltext/70/section5.html

Diagnosis and Management of Epilepsy in Children – A National Clinical Guideline Scottish Intercollegiate Guidelines Network March 2005 Models of care shown from page 25
http://www.sign.ac.uk/pdf/sign81.pdf?bcsi_scan_276FAA45874D151E=0&bcsi_scan_filename=sign81.pdf

Epilepsy Information Network UK Department of Health Includes: "Evaluated examples of good practice - introduction and overview. This section demonstrates to service commissioners and providers how some organisations have already tackled aspects of service delivery described in the NSF [national service framework]. Examples of good practice are included here under each of the NSF's Quality Requirements to help service providers and commissioners take practical steps to improve services. These examples will, of course, need to be adapted to suit your local organisation.
http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/LongTermConditions/BestPractice/Personcentred/PersoncentredExample/fs/en?CONTENT_ID=4104869&chk=SubS%2B0

http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/LongTermConditions/BestPractice/GoodPracticeGuideGeneralArticle/fs/en?CONTENT_ID=4105454&chk=0ysXA8

George Washington University Medical Center Center for Health Services Research and Policy Managing Epilepsy Care: a Guide to Optional Epilepsy Purchasing Specifications to Ensure Managed Care Contracts Provide Access to Appropriate Services
http://www.gwhealthpolicy.org/newsps/epilepsy/Managing_epilepsy_care.pdf

Johns Hopkins Epilepsy Center and Epilepsy Monitoring Unit
http://www.hopkinsneuro.org/epilepsy/emu.cfm

Joint Epilepsy Council of the U.K. and Ireland (JEC)
http://www.jointepilepsycouncil.org.uk/

NHS Modernisation Agency Good Care Planning for People with Long-Term Conditions: Updated Version September 2005 "This report, commissioned by the NHS Modernisation Agency to support implementation of the National Service Framework (NSF) for People with Long-Term Conditions, is the outcome of a project which aimed to provide guidance and tools "to assist local health and social care service providers to implement evidence-based, person-centred care planning". Although the NSF focuses on neurological conditions, the guidance is intended to be more widely applicable. The report considers the benefits of, and barriers to, evidence-based, person-centred care planning". Although the NSF focuses on neurological conditions, the guidance is intended to be more widely applicable. The report considers the benefits of, and barriers to, implementation of good care planning, and identifies critical success factors. It includes case studies and a self-assessment toolkit."
http://www.networks.nhs.uk/uploads/2005_Oct/CarePlanningReportSep05.pdf

NHS Modernisation Agency Neurology Website "This site replaces the Action On Neurology website and provides information about the outcomes from the Action On Neurology programme, summarised in the report Improving Neurology Services – a practical guide.
Delivering well co-ordinated patient centred neurology services is challenging as people with neurological conditions often have complex needs requiring a range of services and support from different professionals and agencies.
The National Service Framework for Long Term Conditions (NSF) published in March 2005 describes a set of core principles in the form of Evidence Based Quality Requirements, which are designed to address the needs of people living with long term neurological conditions.
The Action On Neurology report links the outcomes and lessons learnt by the pilot sites to the relevant NSF Quality Requirements to support the implementation of the NSF and gives ideas about how to go about redesigning services. Many examples of good practice can also be found in the NSF Good Practice Guide.
See the Neurology Collaboration area to find out more about the Action On Neurology pilot sites and some of the tools they have developed to improve their services."
http://www.wise.nhs.uk/cmsWISE/Clinical+Themes/neurology/services.htm

NHS National Prescribing Centre MeReC Briefing Improving Epilepsy Services and Care 2003
http://www.npc.co.uk/MeReC_Briefings/2003/briefing_no_24.pdf

NICE Epilepsy Clinical Guideline UK [National Institute for Clinical Excellence) "The NICE epilepsy clinical guideline covers the diagnosis, treatment and management of epilepsy in children, young people, adults and older people. The guideline makes recommendations for treatment and care provided by GPs and by specialists.
It also makes recommendations about when someone should be referred to a specialist centre (a clinic or unit with particular experience and expertise in investigations or treatment of epilepsy that is difficult to diagnose or treat – sometimes called a tertiary centre)."
http://www.nice.org.uk/page.aspx?o=CG020

The Role of an Epilepsy Nurse Specialist Service Patricia Hosking The National Hospital for Neurology and Neurosurgery, London "The role of an advanced epilepsy nurse specialist service at a large tertiary referral epilepsy centre, the National Hospital for Neurology and Neurosurgery (NHNN), in supporting patients with refractory epilepsy in the hospital and community."
http://www.e-epilepsy.org.uk/pages/articles/show_article.cfm?id=101

Royal College of Nursing Competencies: a Competency Framework and Guidance for Developing Paediatric Epilepsy Nurse Specialist Services 2005
http://www.rcn.org.uk/publications/pdf/competencies_paediatric_epilepsy_nurse_specialist_services.pdf

UK Department of Health Improving Services for People with Epilepsy Action Plan in response to the National Clinical Audit of Epilepsy-Related Death February 2003
http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4010537&chk=cpRU5z

Journal References

The journal references listed were searched in the PubMed database on 19th December 2005 using the search strategy shown below. This was supplemented by a textword search for articles not yet indexed.

("hospital restructuring"[MeSH Terms] OR "efficiency, organizational"[MeSH Terms] OR "process assessment (health care)"[MeSH Terms] OR "delivery of health care, integrated"[MeSH Terms] OR "patient-centered care"[MeSH Terms] OR "efficiency"[MeSH Terms] OR "disease management"[MeSH Terms] OR "health care reform"[MeSH Terms] OR "models, organizational"[MeSH Terms] OR "ambulatory care"[MeSH Terms] OR "office nursing"[MeSH Terms] OR "ambulatory care facilities"[MeSH Terms] OR "ambulatory surgical procedures"[MeSH Terms] OR "ambulatory surgical procedures"[MeSH Terms] OR "benchmarking"[MeSH Terms] OR "surgicenters"[MeSH Terms] OR "manpower"[Subheading] OR "organization and administration"[sh] OR "utilization review"[MeSH Terms] OR "planning techniques"[MeSH Terms] OR "workload"[MeSH Terms]) AND "epilepsy"[MeSH Major Topic] AND English[Lang] AND "humans"[MeSH Terms] AND ("2003"[PDAT] : "3000"[PDAT])
The search may be repeated by clicking on the link below. This will run the search strategy shown above and limit it to all references in English from 2005 onwards.

Search now.

Check journal availability (online and print) at your Library's intranet site. Some of the articles may also be available via the CIAO interface. [Clinical Information Access Online] http://www.ciao.health.wa.gov.au Articles not available locally may be obtained through the inter-library document supply system.

Acta Neurochir (Wien). 2005 Nov 7; [Epub ahead of print]
Temporo-mesial epilepsy surgery: outcome and complications in 100 consecutive adult patients.
Sindou M, Guenot M, Isnard J, Ryvlin P, Fischer C, Mauguiere F.
Department of Functional Neurosurgery, Federative Institute of Neurosciences, Neurological Hospital P. Wertheimer, Lyon, France.
Background. We studied the surgical outcome, and the complications in a group of 100 consecutive adult patients with medically refractory epilepsy arising from the temporo-mesial structures.Methods. Hundred patients were treated surgically between 1994 and 2003 for drug-resistant epilepsy involving the temporo-mesial structures. All of them underwent a comprehensive noninvasive presurgical evaluation. Fourty-eight of them underwent depth electrodes recordings (according to the Talairach's StereoElectroEncephaloGraphic (SEEG) methodology) because the noninvasive investigations were not congruent enough to identify the epileptic zone. The patients presenting with any space-occupying lesion, or with a cavernoma, or with a strictly lateral neocortical epileptic focus, were excluded. The MRI-examination was abnormal in 87 cases, displaying a hippocampal atrophy in 69 cases. The extent of temporal resection was planned according to the results of the presurgical investigation in each particular patient. Consequently, this "tailored" resection varied from selective amygdalo-hippocampectomy (6 cases), to anterior temporal lobectomy (76 cases), or to total temporal lobectomy (18 cases).Findings. The mean post-operative follow-up period was 53 months. 85 patients were found to be in Engel's class I post-operatively (free of disabling seizures), among them 74 were in class Ia (totally seizure free). Nine patients were in Engel's class II and six were in Engel's class III or IV (failures). There was no surgical mortality. Three patients had a postoperative hematoma; two patients required a shunt insertion; in three patients meningitis occured; and two patients had postoperative ischaemia of the anterior choroidal artery territory, which resulted in a mild permanent hemiparesis. Neuropsychological complications are not addressed in detail in this article.Conclusions. These data indicate that "tailored" resective surgery for temporo-mesial epilepsy can be performed with a low rate of morbidity, and is highly efficacious. The use of invasive presurgical investigation (SEEG) may explain this high rate of success.
PMID: 16283106 [PubMed - as supplied by publisher]

Acta Neurochir (Wien). 2005 Mar;147(3):227-9.
Present and future of deep brain stimulation for refractory epilepsy.
Hamani C, Hodaie M, Lozano AM.
Publication Types: Editorial
PMID: 15666189 [PubMed - indexed for MEDLINE]

Acta Neurochir Suppl. 2003;87:115-20.
Brain stimulation: history, current clinical application, and future prospects.
Mogilner AY, Rezai AR.
Department of Neurosurgery, New York Medical College, Valhalla, New York, USA.
The dramatic effects of chronic brain stimulation in the treatment of movement disorders have spurred a renewed interest in this technique for treating a variety of other conditions. This technique has only recently begun to reach its vast clinical potential, due to a number of significant advances in basic and clinical neurosciences. Current image-guided navigation systems and intraoperative physiological mapping techniques offer more efficient, consistent, and precise targeting. Advances in neurophysiology have helped elucidate the pathophysiology of a number of disease states and thus provided for rational target selection for therapy. The latest generation of stimulation equipment allows for precise tailoring of stimulation parameters to maximize clinical benefit. These techniques are now being applied to a variety of other conditions including chronic pain, epilepsy, and psychiatric disorders.
Publication Types: Review
PMID: 14518536 [PubMed - indexed for MEDLINE]

Acta Neurol Scand. 2005 Dec;112(6):370-4.
Prognosis of epilepsy in a community-based study: 8 years of follow-up in an Argentine community.
Kochen S, Melcon MO.
Epilepsy Center, Hosp.R.Mejia School of Medicine, University of Buenos Aires, CONICET, Buenos Aires, Argentina. skochen@mail.retina.ar
OBJECTIVE: To assess the prognosis of epilepsy, the possibility of achieving remission of seizures, in patients who were identified in a population-based study carried out in Junin, a city of about 70,000 inhabitants in Buenos Aires Province, Argentina. On January 1, 1991 (prevalence day), 106 people had epilepsy, including 64 (60%) with the condition active. METHODS: Eight years later, we revisited the patients identified in the prevalence study. We analyzed risk factors in relation to remission of seizures. We also confirmed the specific cause of death. RESULTS: Ninety-six patients were revisited (10 were completely lost to follow-up). We divided them into two groups: the group in terminal remission (defined as a seizure-free period that extended from prevalence day until the visit day in 1998) which included 64 people (66.7%), and the group of those who continued to have seizures which included 32 (33.3%) patients, of whom eight (25%) died. The overall standardized mortality ratio was 2.45; the rate was two and a half times that of the general national population. CONCLUSION: The better prognosis was observed in the group with generalized idiopathic epilepsy syndrome. Patients with epilepsy secondary to underlying structural causes had the worst prognosis, with higher mortality.
PMID: 16281918 [PubMed - in process]

Acta Neurol Scand. 2003 Feb;107(2):87-95.
The ideal characteristics of antiepileptic therapy: an overview of old and new AEDs.
Steinhoff BJ, Hirsch E, Mutani R, Nakken KO.
Epilepsy Centre Kork, Landstr. 1, Kehl-Kork, Germany. b.j.steinhoff@telda.net
New and improved anti-epileptic drugs (AEDs) have made the concept of choice, according to the individual prognosis and probable response to specific regimens, increasingly feasible. Inter-individual variability in syndrome severity and complexity make individualization necessary. We propose three categories of disorder control according to the individual objectives of the patient: (1) seizure control, (2) epilepsy control and ultimately, (3) "epilepsy cure"; the latter remaining a largely idealistic target today. An AED is likely to be successful if it exhibits "optimal" characteristics, such as drug efficacy, tolerability, pharmacokinetics, interactions and cost-effectiveness. This review discusses the "optimal" characteristics of add-on AEDs, which, in addition to seizure control, will contribute to the achievement of epilepsy control and therefore address the currently unmet clinical needs of epilepsy treatment.
Publication Types: Review
PMID: 12580856 [PubMed - indexed for MEDLINE]

Acta Neurol Scand Suppl. 2005;181:68-72.
Antiepileptic drug discovery: lessons from the past and future challenges.
Klitgaard H.
CNS Research, UCB, Braine-L'Alleud, Belgium. henrik.klitgaard@ucb-group.com
Historically, most antiepileptic drugs (AEDs) have been discovered either by serendipity, or the screening of compounds using acute seizure models. However, an increasing understanding of the molecular mechanisms underlying epileptogenesis has led to more rational approaches to drug discovery, which have focused on either enhancing inhibitory gamma-amino butyric acid (GABA)-ergic, or antagonizing excitatory glutamatergic, neurotransmission. Unfortunately, AEDs generated using such strategies have poor efficacy and safety profiles, as they interfere with normal cell processes, while ignoring the complex underlying pathophysiology of epilepsy. Recently, however, the use of new epilepsy models has led to the discovery of levetiracetam, an AED with a truly unique mechanism of action, devoid of anticonvulsant activity in normal animals, but with potent seizure suppression in genetic and kindled chronic epilepsy models, and an unusually high safety margin. The recent identification of brivaracetam and seletracetam, which optimize this unique mechanism of action, may further improve the medical management of epilepsy. The experience with levetiracetam, brivaracetam and seletracetam reveals that new experimental epilepsy models can detect AEDs possessing a unique mechanism of action and thereby target the future challenge of providing clinicians novel additions to the current armamentarium of AEDs.
PMID: 16238713 [PubMed - in process]

Acta Neurol Scand Suppl. 2005;181:47-51.
The role of genetics and ethnicity in epilepsy management.
Scheffer IE.
Department of Medicine and Paediatrics, The University of Melbourne, Epilepsy Research Centre, Melbourne, Vic., Australia. scheffer@unimelb.edu.au
Recent exciting developments in epilepsy genetics have led to significant insights into the mechanisms underlying seizure disorders. Success in epilepsy genetics research to date has resulted from identification of genes responsible for rare monogenic disorders, the majority encoding either voltage- or ligand-gated ion channels. For some conditions, such as benign familial neonatal seizures, an understanding of the underlying genetics is helpful in predicting prognosis. However, for other disorders, such as autosomal dominant nocturnal frontal lobe epilepsy, phenotypic severity is determined by factors other than the major dominant nicotinic subunit mutation found in some families. Further complexity arises when single-gene mutations give rise to heterogeneous phenotypes, as typically occur with generalized epilepsy with febrile seizures plus. Another area of increasing genetic endeavour, pharmacogenetics will allow tailoring of antiepileptic medication for each patient. Pharmacogenetics explores genetic polymorphisms in genes coding for drug-metabolizing enzymes, receptors and transporters. Polymorphisms have been identified that result in marked ethnic and interindividual differences in response to treatment. With further understanding of the impact of these differences, pharmacogenetic screening is likely to guide the management of epilepsy in the future. PMID: 16238709 [PubMed - in process]

Acta Neurol Scand Suppl. 2005;181:40-6.
Issues when treating epilepsy in the elderly.
Pohlmann-Eden B.
Bethel Epilepsy Center, Bielefeld, Germany. bernd.pohlmann-eden@evkb.de
Single seizures and epilepsy are one of the most commonly encountered neurologic disorders in elderly individuals, arising as a result of complex and often multiple acquired underlying pathologies. Ischemia is by far the most frequent etiology, and is found in up to one-third of these patients, followed by tumors, which are diagnosed in approximately 10% of affected individuals. Thus, a multidisciplinary approach to its diagnosis and management is required. Antiepileptic drug (AED) therapy is the mainstay of treatment for epilepsy in the elderly, but age-specific changes in drug metabolism, increased sensitivity to side effects, and the risk of drug interactions must be considered. Some newer AEDs seem to offer advantages over the older agents in terms of their reduced drug interaction potential (due to lack of enzyme induction), and improved tolerability profiles, which is supported by few recent clinical trials. In order to achieve seizure freedom without causing intolerable side effects, treatment should be initiated with monotherapy at low doses and titrated slowly to within the recommended dose range.
PMID: 16238708 [PubMed - in process]

Acta Neurol Scand Suppl. 2005;181:36-9.
Diagnosing and predicting refractory epilepsy.
Brodie MJ.
Epilepsy Unit, Division of Cardiovascular and Medical Sciences, Western Infirmary, Glasgow, UK. martin.j.brodie@clinmed.gla.ac.uk
Over 30% of people with epilepsy will never achieve remission with antiepileptic drug (AED) therapy. These individuals are often severely disabled by their condition, have an unsatisfactory quality of life, and are at increased risk of sudden unexpected death. Early identification of refractory epilepsy would allow prompt referral to specialist services, where the diagnosis can be confirmed, seizures and syndromes classified, AED therapy optimized, and suitability for surgery assessed. Recent studies suggest that patients with symptomatic or cryptogenic epilepsy, those who experience multiple seizures before AED treatment initiation, and those with febrile convulsions, a family history of epilepsy, or psychiatric comorbidities are least likely to respond to drug therapy. Failure to achieve good seizure control with the first one or two AED monotherapies is usually sufficient to highlight the possibility of subsequent refractory epilepsy. For most of these individuals, combination therapy using AEDs with complementary modes of action is the recommended treatment approach.
PMID: 16238707 [PubMed - in process]

Acta Neurol Scand Suppl. 2005;181:17-20.
Epilepsy in children: the evidence for new antiepileptic drugs.
Verdru P.
Clinical Research, UCB, Smyrna, GA 30080, USA. peter.verdru@ucb-group.com
Childhood epilepsy remains a challenge to treat. Despite the availability of antiepileptic drugs (AEDs), >25% of children with childhood epilepsy continue to have seizures. Conventional AEDs have been the mainstay of therapy for many years but are often poorly tolerated and have a tendency to interact with other drugs. Current American Academy of Neurology guidelines support the use of four of the newer AEDs (gabapentin, lamotrigine, topiramate, and oxcarbazepine) as adjunctive treatment of refractory partial seizures in children, based on class I evidence. This paper includes a summary of the results from a recent randomized, double-blind, placebo-controlled study, which shows that levetiracetam is also effective and well tolerated in this pediatric population, and provides evidence supporting its use in refractory partial seizures in children.
PMID: 16238703 [PubMed - in process]

Acta Paediatr. 2005 May;94(5):564-7.
Sudden unexplained death in children with epilepsy: A cohort study with an eighteen-year follow-up.
Weber P, Bubl R, Blauenstein U, Tillmann BU, Lutschg J.
Department of Neuropaediatrics, Basel University Children's Hospital, Basel, Switzerland.
Aim: Sudden unexplained death is a significant cause of mortality in adults with epilepsy. Only a few data exist about this risk in childhood. Methods: Cases of sudden unexplained death in epilepsy (SUDEP) up to the age of 18?y occurring at our hospital between 1984 and 2001 were identified. The incidence rate was calculated on the basis of diagnosed epileptics registered with a statutory disability insurance scheme. Results: Four cases of SUDEP were identified during the 18-y period. The incidence of SUDEP was 4.3 per 10?000 patient-years. All children showed polytherapy-refractory epilepsy, developmental retardation and early-onset epilepsy. Two witnessed cases had shown no previous signs of seizure.Conclusion: SUDEP is rare in childhood. Children with uncomplicated epilepsy seem not to be at risk.
PMID: 16188745 [PubMed - in process]

Adv Tech Stand Neurosurg. 2005;30:51-67.
What is magnetoencephalography and why it is relevant to neurosurgery?
Lopes da Silva FH.
Section Neurobiology, Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, The Netherlands.
Magnetoencephalography (MEG) is a relatively novel technique that allows the study of the dynamic properties of cortical activity. The functional localization of brain sources of MEG signals depends on the models used and it always has a certain degree of uncertainty. Nevertheless, MEG can be very useful in

assisting the neurosurgeon in planning and carrying out brain surgery in, or around, eloquent brain areas, and in epilepsy surgery in pharmaco-resistant patients. The following three areas of application of MEG in neurosurgery are reviewed: (i) Presurgical functional localization of somatomotor eloquent cortex; (ii) Presurgical evaluation of epileptic patients. (iii) Functional localization of speech relevant brain areas. The performance of MEG in comparison with EEG and fMRI is discussed.
PMID: 16350452 [PubMed - in process]

Am J Ment Retard. 2003 Sep;108(5):293-300.
Prevalence of epilepsy and associated health service utilization and mortality among patients with intellectual disability.
Morgan CL, Baxter H, Kerr MP.
University of Wales College of Medicine, Heath Park, Cardiff., UK.
We considered the prevalence of epilepsy and associated health service utilization for a population with intellectual disability. Registers for epilepsy and intellectual disability were created using a range of datasets. Of 1,595 people with an intellectual disability, 257 (16.1%) had epilepsy. Standardized activity ratios were 3.07 (95% CI 3.00 to 3.15), 2.03 (95% CI 1.94 to 2.11), and 3.09 (95% CI 2.78 to 3.41) for inpatients, outpatients, and accident and emergency, respectively. After excluding epilepsy-related inpatient admissions, we found the standardized activity ratio was 2.55 (2.48 to 2.62). Institutionalized patients were less likely to be admitted than were those in the community (standardized activity ratio = 0.63 (95% CI 0.54 to 0.73). Patients with intellectual disability and co-existing epilepsy used secondary care services more frequently than did those with intellectual disability only.
PMID: 12901705 [PubMed - indexed for MEDLINE]

Anat Embryol (Berl). 2005 Dec;210(5-6):525-37.
Epilepsy surgery: perioperative investigations of intractable epilepsy.
Gorji A, Straub H, Speckmann EJ.
Institut fur Physiologie I, Universitat Munster, Robert-Koch-Strasse 27a, 48149, Munster, Germany, gorjial@uni-muenster.de.
Recent advances in our understanding of the basic mechanisms of epilepsy have derived, to a large extent, from increasing ability to carry out detailed studies on patients surgically treated for intractable epilepsy. Clinical and experimental perioperative studies divide into three different phases: before the surgical intervention (preoperative studies), on the intervention itself (intraoperative studies), and on the period when the part of the brain that has to be removed is available for further investigations (postoperative studies). Before surgery, both structural and functional neuroimaging techniques, in addition to their diagnostic roles, could be used to investigate the pathophysiological mechanisms of seizure attacks in epileptic patients. During epilepsy surgery, it is possible to insert microdialysis catheters and electroencephalogram electrodes into the brain tissues in order to measure constituents of extracellular fluid and record the bioelectrical activity. Subsequent surgical resection provides tissue that can be used for electrophysiological, morphological, and molecular biological investigations. To take full advantage of these opportunities, carefully designed experimental protocols are necessary to compare the data from different phases and characterize abnormalities in the human epileptic brain.
PMID: 16180018 [PubMed - in process]

Ann Emerg Med. 2004 Mar;43(3):398-400.
Comment in: Ann Emerg Med. 2004 Oct;44(4):428-9.
Comment on: Ann Emerg Med. 2004 Mar;43(3):386-97.
Fosphenytoin farewell?
Horowitz BZ.
Publication Types: Comment Editorial
PMID: 14985669 [PubMed - indexed for MEDLINE]

Ann Emerg Med. 2004 Mar;43(3):386-97.
Comment in: Ann Emerg Med. 2004 Mar;43(3):398-400.
Cost-effectiveness of oral phenytoin, intravenous phenytoin, and intravenous fosphenytoin in the emergency department.
Rudis MI, Touchette DR, Swadron SP, Chiu AP, Orlinsky M.

Department of Pharmacy, School of Pharmacy Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA. rudis@usc.edu
STUDY OBJECTIVE: Oral phenytoin, intravenous phenytoin, and intravenous fosphenytoin are all commonly used for loading phenytoin in the emergency department (ED). The cost-effectiveness of each was compared for patients presenting with seizures and subtherapeutic phenytoin concentrations. METHODS: A simple decision tree was developed to determine the treatment costs associated with each of 3 loading techniques. We determined effectiveness by comparing adverse event rates and by calculating the time to safe ED discharge. Time to safe ED discharge was defined as the time at which therapeutic concentrations of phenytoin (>or=10 mg/L) were achieved with an absence of any adverse events that precluded discharge. The comparative cost-effectiveness of alternatives to oral phenytoin was determined by combining net costs and number of adverse events, expressed as cost per adverse events avoided. Cost-effectiveness was also determined by comparing the net costs of each loading technique required to achieve the time to safe ED discharge, expressed as cost per hour of ED time saved. The outcomes and costs were primarily derived from a prospective, randomized controlled trial, augmented by time-motion studies and alternate-cost sources. Costs included the cost of drugs, supplies, and personnel. Analyses were also performed in scenarios incorporating labor costs and savings from using a lower-urgency area of the ED. RESULTS: The mean number of adverse events per patient for oral phenytoin, intravenous phenytoin, and intravenous fosphenytoin was 1.06, 1.93, and 2.13, respectively. Mean time to safe ED discharge in the 3 groups was 6.4 hours, 1.7 hours, and 1.3 hours. Cost per patient was 2.83 dollars, 21.16 dollars, and 175.19 dollars, respectively, and did not differ substantially in the Labor and Triage (lower-urgency area of ED) scenarios. When the measure of effectiveness was adverse events, oral phenytoin dominated intravenous phenytoin and intravenous fosphenytoin, with a lower cost and number of adverse events. With time to safe ED discharge as the outcome measure, the incremental cost-effectiveness ratios were 3.90 dollars and 387.27 dollars per hour of ED time saved for oral phenytoin versus intravenous phenytoin and for intravenous fosphenytoin versus intravenous phenytoin, respectively. CONCLUSION: Oral phenytoin is the most cost-effective loading method in most settings. Intravenous phenytoin is preferred if one is willing to pay an additional 20.65 dollars to 44.25 dollars per patient and willing to have more adverse events for a quicker average time to safe ED discharge. It is unlikely that intravenous fosphenytoin is justifiable in any setting.
PMID: 14985668 [PubMed - indexed for MEDLINE]

Ann Pharmacother. 2005 Dec;39(12):2029-37. Epub 2005 Nov 15.
Pregabalin: a new neuromodulator with broad therapeutic indications.
Shneker BF, McAuley JW.
1 Department of Neurology, College of Medicine, Ohio State University, Columbus, OH.
OBJECTIVE: To review pregabalin's pharmacology, pharmacokinetics, efficacy, and adverse effects in the treatment of neuropathic pain, epilepsy, and anxiety. DATA SOURCES: A MEDLINE search (1993-October 2005) for peer-reviewed English-language publications was performed. Abstracts from professional meetings were also included. Key terms were anxiety, diabetic neuropathy, epilepsy, neuropathic pain, postherpetic neuralgia, pregabalin, and seizures. STUDY SELECTION AND DATA EXTRACTION: Basic pharmacology data were extracted from animal studies; pharmacokinetic data were extracted from human studies. Multicenter, double-blind, placebo-controlled, parallel-group studies were included to describe the efficacy and adverse effects of pregabalin. DATA SYNTHESIS: Pregabalin is a new agent that exerts its pharmacodynamic effect by modulating voltage-gated calcium channels. Pregabalin has a linear pharmacokinetic profile. It is completely absorbed, not bound to plasma proteins, not metabolized, and eliminated unchanged through the kidneys. Doses must be adjusted in patients with renal insufficiency. Clinical trials showed that pregabalin is effective in neuropathic pain associated with postherpetic neuralgia, diabetic peripheral neuropathy, in partial epilepsy as adjunctive therapy, and in generalized and social anxiety disorders. The most common adverse effects were dizziness and somnolence. Few serious adverse effects were reported. Pregabalin should not be discontinued rapidly. CONCLUSIONS: Pregabalin is an effective and safe analgesic, antiepileptic, and anxiolytic medicine. It will provide a new treatment option for patients with neuropathic pain and partial epilepsy.
PMID: 16288079 [PubMed - in process]

Ann Pharmacother. 2005 Nov;39(11):1852-60. Epub 2005 Sep 27.
Optimizing antiepileptic drug therapy in the elderly.
Garnett WR.

Medical College of Virginia, Virginia Commonwealth University, PO Box 980533, Richmond, VA 23298-0533, USA. wrgarnett@hsc.vcu.edu
OBJECTIVE: To review and evaluate the medical literature concerning antiepileptic drug (AED) therapy in elderly patients. DATA SOURCES: A MEDLINE search (1982-December 2004) was conducted. Bibliographies of the articles identified were also reviewed, and an Internet search engine was used to identify additional pertinent references. STUDY SELECTION AND DATA EXTRACTION: Clinical studies and reviews were evaluated, and relevant information was included. DATA SYNTHESIS: The elderly have the highest incidence of seizures among all age groups. Complex partial seizures are the most common, followed by primary generalized tonic-clonic seizures. An accurate diagnosis may prove difficult because of a low suspicion of epilepsy in the elderly and other diseases that may mimic seizures. Most AEDs are approved for treatment of elderly patients who have partial and tonic-clonic seizures. However, a number of age-related variables should be addressed when selecting an appropriate AED. Age-dependent differences in pharmacokinetics and pharmacodynamics of AEDs must be taken into account. Drug-drug interactions must be considered since elderly people often take multiple medications. The ultimate factor that often determines AED selection is tolerability. CONCLUSIONS: Numerous factors must be considered in treating elderly patients for seizures, but maximizing the ability of patients to tolerate drug therapy is often the basis for AED selection. Special consideration should be made along several lines, including elderly patients' cognitive functioning and their tendency to respond to lower AED concentrations.
PMID: 16189285 [PubMed - in process]

Arch Dis Child. 2005 Dec;90(12):1219-22. Epub 2005 Aug 30.
The importance of acknowledging clinical uncertainty in the diagnosis of epilepsy and non-epileptic events.
Beach R, Reading R.
Norfolk and Norwich University Hospital, Norwic, UK. richard.beach@nnuh.nhs.uk
BACKGROUND: Failure to recognise diagnostic uncertainty between the epilepsies and non-epileptic events may be a factor in high rates of misdiagnosis. AIMS: To explore the results of acknowledging diagnostic uncertainty in a cohort of children presenting with paroxysmal events. METHODS: Children (29 days-16th birthday) with new presentations of paroxysmal disorders were ascertained through outpatients, admissions, and accident and emergency over a two year period in a district hospital with a catchment population of 500,000. Cases were classified by diagnosis at entry and 6-30 months later. A random selection of cases was independently assessed. RESULTS: A total of 684 cases were ascertained. Attacks were initially classified as febrile seizures (n = 212), acute symptomatic epileptic seizures (n = 5), epilepsies (n = 83), unclassified (possible epilepsy) (n = 90), isolated epileptic seizures (n = 51), and non-epileptic events (n = 243). Case review enabled reclassification of 61 of those initially unclassified--31 to an epilepsy and 27 to non-epileptic events. In 29 the final diagnosis was never clarified. These were 23 cases with confusing or absent histories and six with short lived seizure clusters. Prognosis for these 29 cases was good; 75% had been discharged. None were on long term medication. The diagnosis in the 131 cases confirmed as epilepsy was stable. Independent review of a random sample showed full concordance with one neurologist and 20% uncertainty with another. CONCLUSION: In addition to definite epilepsy or non-epileptic events it is helpful to recognise a group of cases where the diagnosis is uncertain-unclassified paroxysmal events. Reassessment of these cases enables accurate diagnosis and may prevent a hasty and incorrect diagnosis of epilepsy.
PMID: 16131503 [PubMed - in process]

Arch Dis Child. 2004 Feb;89(2):159-64.
The impact of presenting problem based guidelines for children with medical problems in an accident and emergency department.
Armon K, MacFaul R, Hemingway P, Werneke U, Stephenson T.
Norfolk and Norwich University Hospital, Norwich, UK. kate.armon@nnuh.nhs.uk
AIMS: To evaluate the impact of presenting problem based guidelines in managing children with either diarrhoea (with or without vomiting) or seizure (with or without fever). METHODS: This prospective observational study with an intervention was based on a paediatric accident and emergency (A&E) department in Nottingham. All patients (either GP or self referred) were acute attenders aged 0-15 years, with a medical presenting problem during 4 months in the spring of 1997 and 1999. Five hundred and thirty-one diarrhoea attendances (292 before guideline implementation and 239 after) and 411 seizure attendances (212 before guideline implementation and 199 after) were recorded. Evidence based and consensus ratified guidelines developed for the study were implemented using care pathway

documentation. Process (documentation, time in the department, investigations, treatment) and outcome (admission to hospital, returns to A&E) data were collected from case notes. RESULTS: The percentage of children investigated with blood tests fell significantly (haematology requests in diarrhoea presentations from 11% to 4%, biochemistry in seizure presentations from 29% to 17%). Intravenous infusions in diarrhoea presenters fell (9% to 1%), and more appropriate oral fluids were used. Management time in A&E was reduced (diarrhoea presenters: median of 55-40 minutes, seizure presenters: 80-55 minutes, but remained static for other presenting problems). Marked improvements in documentation were seen. Admission rates for diarrhoea attenders increased (27% to 34%) but remained the same for seizure (69% v 73%). CONCLUSIONS: The implementation of a presenting problem based guideline as a care pathway was associated with improvements in the quality of care by: improved documentation; reduced invasive investigations; more appropriate treatment, and reduced time spent in A&E.
PMID: 14736635 [PubMed - indexed for MEDLINE]

Aust Fam Physician. 2005 Dec;34(12):1021-5.
Febrile seizures.
Srinivasan J, Wallace KA, Scheffer IE.
Austin Health and Royal Children's Hospital, Melbourne, Victoria. jayasrisrinivasan@yahoo.com.
BACKGROUND: Febrile convulsions, or febrile seizures, are frequently encountered in paediatrics, and despite often being self limiting, these seizures strike fear in the hearts of patients' carers. OBJECTIVE: This article reviews the assessment and management of febrile seizures in children. DISCUSSION: The initial assessment of a child who convulses with fever should be directed at finding a cause for the fever, rather than the seizure itself, once the seizure has abated. A lumbar puncture should be performed if there is clinical suspicion of meningitis. Electroencephalograms and neuroimaging studies are not routinely indicated. Overall, febrile seizures carry a good prognosis, although one-third of children have recurrent attacks. Febrile seizures are genetic in origin. The risk of later epilepsy is small but increased if the child has a complex febrile seizure, neurological deficit, or a family history of epilepsy. Carers should be counselled in the management of seizures. The effectiveness of prophylactic treatment with medication remains controversial.
PMID: 16333484 [PubMed - in process]
http://www.racgp.org.au/folder.asp?id=1282

Aust Fam Physician. 2005 Dec;34(12):1017-20.
Treatment with anti-epileptic drugs.
Berkovic SF.
Epilepsy Research Centre and Department of Medicine, University of Melbourne, Austin Health, Victoria. s.berkovic@unimelb.edu.au.
BACKGROUND: The principles of epilepsy management are accurate diagnosis coupled with education, lifestyle advice, and drug therapy. There are a large number of anti-epileptic drugs now available. OBJECTIVE: This article deals with initial treatment, the role of the newer agents, and practical issues such as monitoring of therapy and the use of generic drugs. The difficult issues of when to stop therapy and management of epilepsy in pregnancy are highlighted. DISCUSSION: Accurate seizure and syndrome diagnosis determines the optimal choice of medication. In most patients with new onset epilepsy, seizures can be easily controlled with lifestyle modification and medication. In general, valproate is first line treatment for generalised epilepsy and carbamazepine for partial epilepsies. New anti-epileptic drugs offer benefits in patients who are not controlled or intolerant of the older agents. Monitoring of therapy is primarily clinical; not necessarily requiring testing for serum levels or other blood tests.
PMID: 16333483 [PubMed - in process]
http://www.racgp.org.au/folder.asp?id=1282

Aust Fam Physician. 2005 Dec;34(12):1009-15.
Epilepsy syndromes in children.
Carney P, Prowse MA, Scheffer IE.
Austin Health, Melbourne, Victoria.
BACKGROUND: Understanding the common childhood epilepsy syndromes is valuable when approaching the diagnosis and management of a child presenting with seizures. OBJECTIVE: This article discusses the common epilepsy syndromes in children and provides a guide to appropriate investigation and management of these syndromes. DISCUSSION: A careful history and examination, supported by an

electroencephalogram, are the cornerstones of epilepsy syndrome diagnosis. This, in turn, guides the need for further investigation such as magnetic resonance imaging, optimisation of therapy and prognostic counselling. Understanding the implications of a specific syndrome diagnosis helps support families who are frequently overwhelmed by a diagnosis of epilepsy in their child.
PMID: 16333482 [PubMed - in process]
http://www.racgp.org.au/folder.asp?id=1282

Aust Fam Physician. 2005 Dec;34(12):1003-8.
Fits, faints and funny turns in children.
Mackay M.
Royal Children's Hospital, Melbourne, Victoria.
BACKGROUND: Seizures and epilepsy are a common problem in childhood. There are many other paroxysmal disorders that can mimic seizures and it is important to exclude these conditions before diagnosing epilepsy and making the decision to commence anticonvulsant treatment. OBJECTIVE: This article discusses the features that differentiate seizures from nonepileptic events in children and adolescents. DISCUSSION: Diagnosis of epileptic seizures is largely dependent on the clinical history. Modes of presentation include collapse, loss of consciousness, staring, altered responsiveness, limb movements and nocturnal events. Electroencephalography is helpful in confirming the diagnosis and differentiating between focal and generalised seizures.
PMID: 16333481 [PubMed - in process]
http://www.racgp.org.au/folder.asp?id=1282

Aust Fam Physician. 2005 Dec;34(12):1000-1.
Management of epilepsy in general practice patients.
Charles J, Ng A, Britt H.
AIHW Australian GP Statistics and Classification Centre, University of Sydney, New South Wales.
The BEACH program, a continuous national study of general practice activity in Australia, gives us an overview of consultations in general practice involving the management of epilepsy. Participating general practitioners recorded the problem as 'epilepsy' in 90% of cases, while 'grand mal' was specified at about 4% of encounters and 'temporal lobe' and 'petit mal' were each specified at about 1% of encounters. This provides a backdrop against which articles in this issue of Australian Family Physician can be further considered.
PMID: 16333480 [PubMed - in process]
http://www.racgp.org.au/folder.asp?id=1282

Biomed Pharmacother. 2005 Oct;59 Suppl 1:S236-8.
Chaos analysis of electro encephalography and control of seizure attack of epilepsy patients.
Yambe T, Asano E, Mauyama S, Shiraishi Y, Shibata M, Sekine K, Watanabe M, Yamaguchi T, Kuwayama T, Konno S, Nitta S.
Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University, 4-1 Seiryo-machi, Aoba-ku, Sendai 980-77, Japan. yambe@idac.tohoku.ac.jp
In order to evaluate the EEG of patients with epilepsy, chaos analysis was performed for the subdural EEG time series data. The chaos attractor was reconstructed in the phase space and the correlation dimension. KS entropy calculated from the Lyapunov exponents was evaluated. Before the seizure attack, the KS entropy showed a lower value when compared with the time series data recorded during healthy condition. The results of our study suggest that it is possible to predict the seizure attack by the chaos analysis of the EEG signal. Further, we aim at developing an automatic control system for predicting a seizure attack by the use of local cooling of the focus with Peltier elements.
PMID: 16275501 [PubMed - in process]

BMC Fam Pract. 2005 Mar 1;6(1):9.
General practitioner attitudes to the care of people with epilepsy: an examination of clustering within practices and prediction of patient-rated quality of care.
Thapar AK, Roland MO.
School of Psychology, Cardiff University, Tower Building, Park Place, Box 901, Cardiff, UK. thaparak@cf.ac.uk

BACKGROUND: There is wide variation in the quality of care provided by primary care practices to individuals with chronic illnesses. Individual doctor attitudes and interest have been demonstrated to influence patient outcomes in some instances. Given the trend towards larger practices and part-time working, continuity of care is likely to fall and thus practice-based rather than individual general practitioner attributes and attitudes are likely to become increasingly important. The aim in this paper was to examine the extent to which individual general practitioner (G.P.) attitudes to the care of people with epilepsy cluster within practices and predict patient-rated quality of care. METHODS: The sample consisted of 1255 people with active epilepsy (a recent seizure or on anti-convulsant medication for epilepsy) and 199 GPs from 82 general practices. Measures of GP attitudes (a 17-item GP attitudes questionnaire) and patient-rated quality of epilepsy care were obtained. 1210 individuals completed initial questionnaires and 975 patients filled in final questionnaires one year later. Responses were achieved from 64 practices (83% of total) and 115 GPs (60% of total). RESULTS: 2 main factors were found to underlie GP attitudes to the care of people with epilepsy and these demonstrated clustering within practices "epilepsy viewed as a primary care responsibility" (Eigenvalue 3.98, intra-class correlation coefficient (ICC) 0.40), and "medication skills"(Eigenvalue 2.74, ICC 0.35). GP-rated scores on "epilepsy care being a primary care responsibility" were a significant predictor of patient-rated quality of GP care (p = 0.031). Other contributory factors were seizure frequency (p = 0.044), and patient-rated "shared decision making" (p = 0.022). CONCLUSION: Specific general practitioner attitudes to the care of people with epilepsy cluster within practices and are significantly associated with patient-rated quality of epilepsy care. It is important to take these findings into consideration when planning primary care interventions to ensure people with epilepsy receive the benefits of available medical and surgical expertise.
PMID: 15740630 [PubMed - indexed for MEDLINE]

BMC Fam Pract. 2003 Apr 22;4:4. Epub 2003 Apr 22.
A 'real puzzle': the views of patients with epilepsy about the organisation of care.
Elwyn G, Todd S, Hibbs R, Thapar A, Edwards P, Webb A, Wilkinson C, Kerr M.
Primary Care Research Group, Swansea Clinical School, University of Wales, UK. g.elwyn@swansea.ac.uk
BACKGROUND: Little is known about how individuals who have a diagnosis of epilepsy have experienced healthcare services or their views about how they should best be organised to meet their ongoing needs. METHODS: Focus group interviews. Individuals with epilepsy were identified in 5 practices in Wales: 90 were invited, 40 confirmed attendance and 19 individuals attended interviews in 5 groups of size 6, 5, 4, 3 and 1 (Table 2). Inclusion criteria: individuals with a confirmed diagnosis of epilepsy, aged between 18-65. The exclusion criteria were learning disability or an inability to travel to interview locations. RESULTS: The individuals in these group interviews were not 'epilepsy activists' yet they remained critical in extended discussions about the services encountered during their patient careers, wanting more information and advice about how to adapt to problems, particularly after initial diagnosis, more involvement in decision making, rapid access to expertise, preferably local, and improved communication between clinicians. A central concern was the tendency for concerns to be silenced, either overtly, or covertly by perceived haste, so that they felt marginalised, despite their own claims to own expert personal knowledge. CONCLUSIONS: Users of existing services for epilepsy are critical of current systems, especially the lack of attention given to providing information, psychosocial support and the wishes of patients to participate in decision making. Any reorganisation of services for individuals with epilepsy should take into account these perceived problems as well as try to reconcile the tension between the distant and difficult to access expertise of specialists and the local but unconfident support of generalists. The potential benefit of harnessing information technology to allow better liaison should be investigated.
PMID: 12709265 [PubMed - indexed for MEDLINE]
http://www.biomedcentral.com/content/pdf/1471-2296-4-4.pdf

BMC Health Serv Res. 2003 Dec 19;3(1):23.
Can surveying practitioners about their practices help identify priority clinical practice guideline topics?
Brouwers MC, Chambers A, Perry J; Neuro-oncology Disease Site Group.
Program in Evidence-based Care, Cancer Care Ontario, Hamilton, Ontario, Canada. mbrouwer@mcmaster.ca
BACKGROUND: Clinical practice guidelines are systematically developed statements designed to assist in patient and physician clinical decision making for specific clinical circumstances. In order to establish which guideline topics are priorities, practitioners were surveyed regarding their current practice.

METHODS: One hundred ninety-seven practitioners in Ontario, Canada were mailed a survey exploring their current practice or opinion regarding the prophylactic use of anticonvulsant drugs in patients with malignant glioma who had never had a seizure. The survey consisted of seven questions regarding the relevance of a guideline on the subject to the practitioner's practice, the proportion of clinical cases involving anticonvulsant use, knowledge of existing guidelines on this topic, interest in reviewing a completed practice guideline and three clinical scenarios. RESULTS: There were 122 respondents who returned the survey (62% rate of return). Eighty percent of the practitioners who responded indicated that less than 25% of their clinical cases involved the use of anticonvulsants; however, only 16% of respondents indicated that a practice guideline would be irrelevant to their practice. Eighty percent of respondents volunteered to review a draft version of a practice guideline on the use of anticonvulsants. The survey presented the practitioners with three scenarios where anticonvulsants in patients with brain tumours may be appropriate: peri-operatively in patients without seizures, postoperatively in patients currently using anticonvulsants, and thirdly in patients not currently using anticonvulsants or undergoing surgery. In contrast to the third situation, the first two situations yielded considerable variation in practitioner response. CONCLUSION: The survey established that there is some variation present in the current practice of anticonvulsant use in the patients with brain tumours. Whether there is an optimal treatment practice has yet to be determined. Practitioners do seem to feel that a guideline on anticonvulsant use in warranted, and most practitioners would be interested in being part of the guideline development process.
PMID: 14687426 [PubMed - indexed for MEDLINE]

BMJ. 2005 Dec 3;331(7528):1317-22.
Epilepsy in elderly people.
Brodie MJ, Kwan P.
Division of Cardiovascular and Medical Sciences, Western Infirmary, Glasgow G11 6NT. Martin.J.Brodie@clinmed.gla.ac.uk
PMID: 16322020 [PubMed - in process]
http://bmj.bmjjournals.com/contents-by-date.0.shtml

BMJ. 2004 Nov 20;329(7476):1199-200.
Comment in: BMJ. 2005 Apr 9;330(7495):846.
Revisiting phenobarbital for epilepsy.
Kale R, Perucca E.
Publication Types: Editorial
PMID: 15550407 [PubMed - indexed for MEDLINE]
http://bmj.bmjjournals.com/contents-by-date.0.shtml

Br J Gen Pract. 2004 Oct;54(507):781-3.
The outcome of initiation of antiepileptic drug monotherapy in primary care: a UK database survey.
Morgan CL, Buchan S, Kerr MP.
Department of Psychological Medicine, University of Wales College of Medicine, Cardiff, UK.
We describe the incidence of newly treated epilepsy in primary care and patterns of antiepileptic drug prescription, numbers of patients who remain on initial therapy and health service utilisation. Data was collected from 100 general practices that subscribed to the Doctors Independent Network (DIN-LINK) project. Over the study period 1531 patients were identified, equating to an annual incidence rate of 36.3 per 100 000 (95% confidence interval [CI] = 32.1 to 40.8). Of these patients, 1465 (95.7%) were started on antiepileptic drugs. Overall, 1154 (78.8%) patients remained on the original monotherapy at the 12-month stage. Primary care consultations, secondary care referrals and emergency admissions were all increased for those whose treatment was changed either to polytherapy or an alternative monotherapy.
PMID: 15469679 [PubMed - indexed for MEDLINE]

Br J Nurs. 2005 Sep 8-21;14(16):854-8.
Management and treatment options for epilepsy.
Lawal M.
Faculty of Health and Human Science, Thames Valley University, London.

Epilepsy is a major chronic condition of the nervous system affecting almost 380,000 people in England and occasionally results in death of the patient. Although epilepsy and its treatment are complex, there is evidence to support a significant gap in epilepsy care, ranging from a lack of adequate record keeping of seizure occurrence to poor referral systems. This article provides a broad introduction to the condition, discusses the incidence, disease process, diagnosis, classification and the various ways, both conventional and otherwise, in which it can be managed. By understanding the above, it will assist healthcare practitioners to improve their knowledge about management of a client with epilepsy entrusted to their care.
PMID: 16215505 [PubMed - in process]

Brain. 2005 Dec;128(Pt 12):2822-9. Epub 2005 Jul 13.
Greater functional recovery after temporal lobe epilepsy surgery in children.
Gleissner U, Sassen R, Schramm J, Elger CE, Helmstaedter C.
Department of Epileptology, University of Bonn, Bonn, Germany. ulrike.gleissner@ukb.uni-bonn.de
The purpose of our study is to evaluate whether children recover better than adults from memory deficits as a consequence of temporal lobe surgery. We compared 3 and 12 month outcomes obtained in children and adults with medically refractory epilepsy. Each candidate underwent temporal lobe resection for seizure control and children were matched with regard to pathology, onset of epilepsy, side of surgery and type of surgery with adults (N = 30 for each group, mean age at surgery 13 versus 30 years). Three months after surgery, both left-resected groups displayed a significant decline in verbal learning capacity. During the following 9 months, only the children recovered and were able to reach their preoperative level 1 year after surgery. The left-resected adults remained, for the most part, on their low level and one year after surgery, they were still significantly worse than at the time of their preoperative examination. The right-resected adults experienced a deterioration in visual memory 1 year after surgery relative to the results of the short-term follow-up; the children improved. The children also had a better outcome with regard to attentional functions and, as a trend, a better seizure outcome (Engel Outcome I--1 year after surgery: 63% adults, 80% paediatric patients). Our neuropsychological data provide evidence of greater plasticity and compensational capacity in childhood. The results can be taken as a strong argument for early surgical intervention.
PMID: 16014650 [PubMed - in process]

Brain. 2005 Nov 29; [Epub ahead of print]
Molecular and cellular mechanisms of pharmacoresistance in epilepsy.
Remy S, Beck H.
Department of Epileptology, University of Bonn Medical Center, Bonn, Germany.
Epilepsy is a common and devastating neurological disorder. In many patients with epilepsy, seizures are well-controlled with currently available anti-epileptic drugs (AEDs), but a substantial (approximately 30%) proportion of patients continue to have seizures despite carefully optimized drug treatment. Two concepts have been put forward to explain the development of pharmacoresistance. The transporter hypothesis contends that the expression or function of multidrug transporters in the brain is augmented, leading to impaired access of AEDs to CNS targets. The target hypothesis holds that epilepsy-related changes in the properties of the drug targets themselves may result in reduced drug sensitivity. Recent studies have started to dissect the molecular underpinnings of both transporter- and target-mediated mechanisms of pharmacoresistance in human and experimental epilepsy. An emerging understanding of these underlying molecular and cellular mechanisms is likely to provide important impetus for the development of new pharmacological treatment strategies.
PMID: 16317026 [PubMed - as supplied by publisher]

Brain Dev. 2005 Sep 19; [Epub ahead of print]
Reading abilities and cognitive functions of children with epilepsy: Influence of epileptic syndrome.
Chaix Y, Laguitton V, Lauwers-Cances V, Daquin G, Cances C, Demonet JF, Villeneuve N.
Unite de Neurologie Pediatrique, Hopital des Enfants, 330 av de Grande Bretagne-TSA, 31059 Toulouse Cedex, France.
Children with epilepsy are at risk of developing learning disorders. To explore the influence of the epileptic syndrome on reading abilities, we have compared the neuropsychological profile of 12 children with benign idiopathic epilepsy with rolandic spikes, 10 with temporal lobe epilepsy and 12 with idiopathic generalized epilepsy. Children underwent a selection of standardised tests designed to assess: oral

language, reading, short-term memory, attention and behavioural adjustment. Analysis of variance was adjusted according to age of onset of the epileptic syndrome, duration of the syndrome, and performance IQ for each group. Children with temporal lobe epilepsy (TLE) had significantly lower scores for reading speed and comprehension, but epileptic variables (the age of onset of epilepsy, duration and activity of epilepsy) had influenced academic performances. In the TLE group there was a clear effect of the topography of the epileptic foci (left-side TLE vs. right-side TLE) on reading profile. Furthermore, the effect of epileptic syndromes was found in phonological, semantic and verbal working memory deficits in the TLE group. To a lesser extent children with idiopathic generalized epilepsy (IGE) also exhibit cognitive deficit. The results of the present study lend support to epilepsy-specific patterns of neuropsychological dysfunction in children that should be considered to improve remediation of academic underachievement in these populations.
PMID: 16176865 [PubMed - as supplied by publisher]

Brain Res Brain Res Rev. 2004 Mar;44(2-3):141-53.
Focal treatment for refractory epilepsy: hope for the future?
Nilsen KE, Cock HR.
Clinical Neurosciences, St. Georges Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK.
Despite advances in anti-epileptic drug therapy and epilepsy surgery in recent years, intractable epilepsy remains a large clinical problem. Surgical resection, which can have an excellent outcome, is appropriate for only a minority of patients in whom an identifiable focus in non-eloquent brain can be identified. Systemic drug delivery is inevitably limited by the potential for unwanted side effects, due to actions both outside the CNS and in non-epileptic brain regions. Thus for a substantial number of patients novel treatment approaches are urgently needed. Both focal drug delivery and neuronal stem cell grafting have been evaluated in a variety of experimental epilepsy models in recent years, targeting either the seizure focus or key propagation pathways. The literature in this field is critically reviewed and considered in a clinical context. Studies in both areas are hampered by the limitations of available animal models, and by uncertainties in discerning which changes in the epileptic brain directly promote seizures, and which are compensatory. However, in many cases promising, though short-term, results have been obtained. Before such studies could be considered in humans further investigations that include long-term seizure and behavioural outcomes, in clinically relevant experimental models, are required. However, the current literature does provide proof in principle for a focal treatment approach, which may offer hope for many currently intractable patients for whom drug developments and surgical advances have proved disappointing.
Publication Types: Review
PMID: 15003390 [PubMed - indexed for MEDLINE]

Child Care Health Dev. 2005 Sep;31(5):597-602.
Comparison of a dedicated children's seizure clinic to mixed general paediatric clinics.
Mar S, Dunkley C, Al-Ansari I, Whitehouse WP.
Department of Neurology and Pediatrics, Albert Einstein College of Medicine, Bronx, New York, USA.
BACKGROUND: In the light of recent recommendations regarding the current management of children with possible epilepsy in the UK, different models of care are compared using an existing validated audit tool. METHODS: The initial clinical assessment process, investigation, management and communication regarding children referred with suspected epilepsy to general paediatric clinics or a paediatric seizure clinic was compared using the British Paediatric Neurology Association (BPNA) audit tool. Results Ninety-three children were included in the comparison. The history and description of the episodes was better documented in the Seizure Clinic (SC). Children's early development (79% vs. 50%) and school performance (86% vs. 42%) were better documented in the SC. Documentation of possible side effects relating to newly prescribed anti-epileptic drugs was poor in both groups (33% vs. 15%). CONCLUSIONS: Differences between models of epilepsy care can be detected using audit tools although there are some methodological limitations of this particular study. Future similar studies as well as informing local practice can add to the debate on the appropriate way forward in improving the care for children with epilepsy.
Publication Types: Evaluation Studies
PMID: 16101656 [PubMed - indexed for MEDLINE]

Childs Nerv Syst. 2005 Jul;21(7):546-51. Epub 2005 May 19.
Surgically amenable epilepsies in children and adolescents: clinical, imaging, electrophysiological, and post-surgical outcome data.
Terra-Bustamante VC, Fernandes RM, Inuzuka LM, Velasco TR, Alexandre V Jr, Wichert-Ana L, Funayama S, Garzon E, Santos AC, Araujo D, Walz R, Assirati JA, Machado HR, Sakamoto AC.
Department of Neurology, Ribeirao Preto School of Medicine, University of Sao Paulo, Campus Universitario, Brazil.
BACKGROUND AND PURPOSE: A large number of patients with epilepsy in the pediatric population have medically intractable epilepsy. In this age group seizures are usually daily or weekly, and response to antiepileptic therapy is poor, especially for those with neurological abnormalities and symptomatic epilepsies. However, several authors have already demonstrated similarly favorable long-term post-surgical seizure control when comparing pediatric and adult populations. In this article we aim to report the experience of the Ribeirao Preto Epilepsy Surgery Program in pediatric epilepsy surgery. PATIENTS AND METHODS: We analyzed 107 patients with medically intractable epilepsy operated on between July 1994 and December 2002, considering age at surgery, seizure type, pathological findings, and seizure outcome. All data were prospectively collected according to protocols previously approved by the institution ethics committee. RESULTS: We analyzed a total of 115 operations performed in 107 patients. There was no difference in sex distribution. Complex partial seizures occurred in 31.4% of the patients, followed by tonic seizures (25.9%), focal motor seizures (15.4%), and infantile spasms (13.3%). The most common etiologies were cortical developmental abnormalities (25.2%), tumors (16.8%), mesial temporal sclerosis (15.9%), Rasmussen syndrome (6.5%), and tuberous sclerosis (6.5%). Overall post-surgical seizure outcome showed 67.2% of the patients within Engel classes I and II, reaching 75.0% when patients with callosotomies were excluded. CONCLUSIONS: Post-surgical seizure control in the pediatric population is similar to that in adult patients, despite the fact that epilepsies in this age group are more frequently of extratemporal origin, suggesting that surgery should be considered in children as soon as intractability is determined.
Publication Types: Clinical Trial
PMID: 15906045 [PubMed - in process]

Childs Nerv Syst. 2005 May 21; [Epub ahead of print]
Effect of antiepileptic drug monotherapy on urinary pH in children and young adults.
Go T.
Department of Infants' Brain and Cognitive Development, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan, gogo@abmes.twmu.ac.jp.
OBJECTS: Since alkaline urine is a risk factor for urolithiasis, the relationship between antiepileptic drugs and urinary pH was retrospectively studied in epilepsy patients treated with antiepileptic drug monotherapy for more than 1 month. METHODS: A total of 913 urinary samples from antiepileptic drug-treated patients were compared with 780 age-matched control samples, and with 112 samples from epilepsy patients who had not been treated with antiepileptic drugs. The antiepileptic drugs administered were carbamazepine, valproate, phenobarbital, zonisamide, sulthiame, and phenytoin. CONCLUSIONS: The proportion of the acid urine in the valproate-treated patients was lower than that in controls. The proportion of the alkaline urine in the valproate-treated patients was higher than that in controls. This effect was independent of age, sex, and the serum valproate concentration. There was no significant difference in urinary pH among the epilepsy patients treated with other antiepileptic drugs, the epilepsy patients who had not been treated with antiepileptic drugs, and the controls.
PMID: 15909204 [PubMed - as supplied by publisher]

Clin Evid. 2005 Jun;(13):1588-607.
Epilepsy.
Marson A, Ramaratnam S.
University of Liverpool, Liverpool, UK.
Publication Types: Review
PMID: 16135303 [PubMed - in process]

Clin Neurol Neurosurg. 2005 Oct 10; [Epub ahead of print]
Post-traumatic epilepsy: An overview.
Agrawal A, Timothy J, Pandit L, Manju M.

Department of Neurosurgery, K.S. Hegde Medical Academy, Deralakatte, 575018 Mangalore, Karnataka, India.
Post-traumatic epilepsy (PTE) is a recurrent seizure disorder secondary to brain injury following head trauma. PTE is not a homogeneous condition and can appear several years after the head injury. The mechanism by which trauma to the brain tissue leads to recurrent seizures is unknown. Cortical lesions seem important in the genesis of the epileptic activity, and early seizures are likely to have a different pathogenesis than late seizures. Anti-epileptic drugs available for treatment are phenytoin, sodium valproate, and carbamazepine. Newer anti-epileptics are helpful, particularly in patients with associated post-traumatic stress disorders; however, no randomized controlled studies are available to prove that one of these drugs is better than the other. Current evidence is that the treatment of early post-traumatic seizures does not influence the incidence of post-traumatic epilepsy. Routine preventive anticonvulsants are not indicated for patients with head injuries, and treatment in the acute phase does not reduce death or disability rates.
PMID: 16225987 [PubMed - as supplied by publisher]

Clin Neurophysiol. 2005 Mar;116(3):716-7. Epub 2004 Dec 25.
Comment on: Clin Neurophysiol. 2005 Mar;116(3):718-28.
Electrical stimulation in epilepsy.
Alarcon G.
Publication Types: Comment Editorial
PMID: 15721086 [PubMed - indexed for MEDLINE]

Clin Neurophysiol. 2004 May;115(5):1010-20.
Comment in: Clin Neurophysiol. 2004 May;115(5):995-7.
Comment on: Clin Neurophysiol. 2004 May;115(5):1001-9.
Controversies in clinical neurophysiology. MEG is superior to EEG in the localization of interictal epileptiform activity: Con.
Baumgartner C.
Department of Clinical Epilepsy Research, Neurological University Clinic, Waehringer Guertel 18-20, A-1090 Vienna, Austria. christoph.baumgartner@univie.ac.at
OBJECTIVE: To assess whether MEG is superior to scalp-EEG in the localization of interictal epileptiform activity and to stress the 'con' part in this controversy. METHODS: Advantages and disadvantages of the two techniques were systematically reviewed. RESULTS: While MEG and EEG complement each other for the detection of interictal epileptiform discharges, EEG offers the advantage of long-term recording significantly increasing its diagnostic yield which is not feasible with MEG. Localization accuracies of EEG and MEG are comparable once inaccuracies for the solution of the forward problem are eliminated. MEG may be more sensitive for the detection of neocortical spike sources. EEG and MEG source localizations show comparable agreement with invasive electrical recordings, can clarify the spatial relationship between the irritative zone and structural lesions, guide the placement of invasive electrodes and attribute epileptic activity to lobar subcompartments in temporal lobe epilepsy and to a lesser extent in extratemporal epilepsy. CONCLUSIONS: A clear superiority of MEG over EEG for the localization of interictal epileptiform activity cannot be derived from the studies presently available. SIGNIFICANCE: The combination of EEG and MEG provides information for the localization of interictal epileptiform activity which cannot be obtained with either technique alone.
Publication Types: Comment Evaluation Studies Review
PMID: 15066524 [PubMed - indexed for MEDLINE]

Clin Neurophysiol. 2004 May;115(5):1001-9.
Comment in: Clin Neurophysiol. 2004 May;115(5):1010-20. Clin Neurophysiol. 2004 May;115(5):995-7.
Controversies in neurophysiology. MEG is superior to EEG in localization of interictal epileptiform activity: Pro.
Barkley GL.
Neuromagnetism Laboratory, Henry Ford Comprehensive Epilepsy Program, Henry Ford Hospital, Detroit, MI 48202, USA. barkley@neuro.hfh.edu
Both EEG and magnetoencephalography (MEG), with a time resolution of 1 ms or less, provide unique neurophysiologic data not obtainable by other neuroimaging techniques. MEG and EEG have often been compared to each other now although the two are complementary. Now that MEG has emerged as a

mature clinical technology, it is worthwhile to compare the relative strengths of each for the localization of interictal epileptiform activity and to describe the strengths of MEG relative to EEG in the localization of interictal epileptiform activity. The sources of MEG and EEG signals will first be reviewed. Issues relevant to solving the forward problem and the inverse problem in MEG and EEG will be addressed followed by a comparison of research concerning the detection and localization of interictal epileptiform activity by MEG and EEG. The emphasis will be upon techniques and software routinely used in clinical applications but some emerging areas of MEG research which are entering clinical practice will also be reviewed. SIGNIFICANCE: MEG is a new noninvasive neurophysiologic technique which provides unique information for the clinical evaluation of patients with epilepsy, revealing aspects of neuronal function that previously could only be obtained by invasive EEG monitoring, and giving a new window for research of neuronal activity.
Publication Types: Evaluation Studies Review
PMID: 15066523 [PubMed - indexed for MEDLINE]

Clin Neurophysiol. 2004 May;115(5):995-7.
Comment in: Clin Neurophysiol. 2005 Jan;116(1):236; author reply 237.
Comment on: Clin Neurophysiol. 2004 May;115(5):1001-9. Clin Neurophysiol. 2004 May;115(5):1010-20.
MEG: good enough.
Lesser RP.
Publication Types: Comment Editorial Evaluation Studies Review
PMID: 15066521 [PubMed - indexed for MEDLINE]

Clin Neurosurg. 2004;51:271-4.
Special lecture: Brain stimulation: perspectives for the future.
Hamani C, Lozano AM.
Division of Neurosurgery, Toronto Western Hospital, Ontario, Canada.
Publication Types: Lectures
PMID: 15571153 [PubMed - indexed for MEDLINE]

Clin Radiol. 2005 Oct;60(10):1090-9.
MR imaging of patients with localisation-related seizures: initial experience at 3.0T and relevance to the NICE guidelines.
Griffiths PD, Coley SC, Connolly DJ, Hodgson T, Romanowski CA, Widjaja E, Darwent G, Wilkinson ID.
Section of Radiology, University of Sheffield, Sheffield, UK. p.griffiths@sheffield.ac.uk
The purpose of this study is to describe our initial experience of imaging adults with localisation-related epilepsy using MR imaging at 3.0T. We discuss the findings in the context of the recently released NICE guidelines that provide detailed advice on imaging people with epilepsy in the UK. 120 consecutive people over the age of 16 years with localisation-related epilepsy were referred for clinical MR examinations from a regional neuroscience centre in England. None of the people had had MR examinations prior to the present study. High resolution MR imaging was performed taking advantage of the high field strength and high performance gradients of the system. Two experienced neuroradiologists reported on the examinations independently and the presence and type of pathology was recorded. There was complete agreement between the two reporters in all 120 cases. The overall frequency of abnormalities shown by MR was 31/120 (26%) and the commonest abnormality shown was mesial temporal sclerosis found in 10/120 (8%). Tumours were shown in 4/120, all of which appeared low grade as judged by imaging criteria. Epilepsy is the commonest neurological condition and demands a significant resource in order to provide good care for sufferers. Recent guidelines published in the UK have suggested that the majority of people with epilepsy should receive brain MR as part of their routine assessment. Our work shows that using the most sophisticated MR imaging in a highly selected population there is a modest pick-up rate of brain abnormalities. If a widespread epilepsy-imaging programme is started the detection rate is likely to be much lower. Although MR is acknowledged to be a reliable way of detecting pathology in people with epilepsy there is a dearth of information studying the health economics of imaging epilepsy in relation to patient management and outcomes.
PMID: 16179169 [PubMed - in process]

CMAJ. 2003 Feb 18;168(4):441-8.
Comment in: CMAJ. 2003 Jun 10;168(12):1523; author reply 1523-4.
Diagnosis and management of epilepsy.
Blume WT.
Department of Clinical Neurological Sciences, Epilepsy and Clinical Neurophysiology, London Health Sciences Centre - University Campus, London, ON. warren.blume@lhsc.on.ca
This article concisely describes the more common epilepsy conditions and will enable physicians to efficiently evaluate and manage these disorders. Salient aspects of the history and examination, together with electroencephalography, will usually determine the epilepsy syndrome (category), forming the basis for any further investigation and possible antiepileptic therapy. Imaging may be required in some circumstances.
Publication Types: Review
PMID: 12591787 [PubMed - indexed for MEDLINE]
http://www.cmaj.ca/contents-by-date.0.shtml

CNS Drugs. 2005;19(11):897-908.
Overtreatment in epilepsy: how it occurs and how it can be avoided.
Perucca E, Kwan P.
Institute of Neurology IRCCS, C. Mondino Foundation, Pavia, ItalyDepartment of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy.
In pharmacotherapy, overtreatment may be defined as an excessive drug load (that is, excessive drug dosages or unnecessary polypharmacy) leading to a suboptimal risk-to-benefit ratio. The risk of overtreatment in the pharmacological management of epilepsy is substantial and may have serious consequences in terms of a greater incidence and severity of adverse effects. These effects can range from subtle CNS impairment to overt toxic effects, including teratogenicity. Overtreatment also causes increased treatment costs and may even lead to a paradoxical deterioration in seizure control. The prevention and correction of overtreatment requires a thorough understanding of the situations and mechanisms that lead to inappropriate prescribing of antiepileptic drugs. These include initiating treatment in conditions where it is not indicated (for example, long-term prophylaxis after head trauma or supratentorial surgery in seizure-free patients), use of excessively fast titration rates, prescription of excessively high initial target dosages, failure to consider conditions associated with reduced dosage requirements (for example, old age or comorbidities associated with impaired drug clearance), and failure to consider the dose-response characteristics of the selected drug. Many patients whose seizures do not respond to the initially prescribed medication can be optimally managed by switching to monotherapy with an alternative agent; premature use of combination therapy represents another common form of overtreatment. Overtreatment may also result from a failure to adjust the dosage to prevent or compensate for adverse pharmacokinetic or pharmacodynamic drug interactions, and from a failure to reduce drug load in patients who have not benefited from high dosages or polypharmacy. While the measurement of drug concentrations can aid in minimising adverse effects, there is also a danger of overtreatment resulting from inappropriate interpretation of drug concentration data. Continuation of drug therapy in seizure-free patients in whom the risk-benefit ratio is in favour of gradual withdrawal may also be regarded as overtreatment.Tailoring therapy to the needs of the individual patient is the key to the successful management of epilepsy. Even though the importance of complete seizure control cannot be overemphasised, no patient should be made to suffer more from the adverse effects of treatment than from the manifestations of the seizure disorder.
Publication Types: Review
PMID: 16268662 [PubMed - in process]

CNS Drugs. 2005;19(4):347-67.
Erratum in: CNS Drugs. 2005;19(7):633.
Zonisamide: a review of its use in the management of partial seizures in epilepsy.
Frampton JE, Scott LJ.
Adis International Limited, Auckland, New Zealand. demail@adis.co.nz
Zonisamide (Zonegran, Excegran) is a new-generation, broad-spectrum antiepileptic drug (AED) currently approved as adjunctive therapy for the treatment of medically refractory partial seizures in adults in the US and as adjunctive therapy or monotherapy in the control of partial and generalised seizures in adults and children in Japan and Korea.Either as adjunctive therapy or monotherapy, zonisamide effectively reduces the frequency of partial seizures, with or without secondary generalisation to tonic-clonic

seizures, in adults and children with epilepsy. The drug is generally well tolerated and, additionally, has a favourable pharmacokinetic profile permitting once- or twice-daily administration. Direct head-to-head comparisons with other AEDs would be beneficial in fully defining the place of zonisamide in therapy. In the meantime, adjunctive therapy or monotherapy with zonisamide is a convenient, useful option for the management of partial seizures, including those refractory to other AEDs.
Publication Types: Review
PMID: 15813651 [PubMed - indexed for MEDLINE]

CNS Drugs. 2004;18(10):617-28.
Prescribing antiepileptic drugs: should patients be switched on the basis of cost?
Jobst BC, Holmes GL.
Neuroscience Center at Dartmouth, Section of Neurology, Dartmouth Medical School, Hanover, New Hampshire, USA. Barbara.C.Jobst@Hitchcock.org
To assess the costs of switching from one antiepileptic drug (AED) to another, all associated direct and indirect costs, not only drug acquisition costs, must be considered. The perspective of the healthcare system evaluated in cost-effectiveness analysis is of crucial importance. Multiple clinical factors can influence clinical decisions regarding switching AEDs. The economic cost of poorly controlled epilepsy is enormous and the most cost-effective intervention is an AED that provides total seizure control. Cost-minimisation studies have evaluated costs associated with various medications. If only efficacy and adverse events were considered, then the 'older' AEDs were generally more cost effective than the 'newer' AEDs. Most studies only examine very specific clinical situations and are not suitable for establishing general clinical recommendations. The pharmacoeconomics of AED choice is highly country specific. While switching to generic formulations is, in general, cost effective, some changes may be detrimental and more costly than remaining on the trade name preparation. For example, as a result of differences in bioavailability and possible loss of seizure control, changing patients to generic phenytoin and carbamazepine can be problematic. Fosphenytoin may only be cost effective in certain clinical situations compared with intravenous phenytoin. Seizure control should not be sacrificed on the basis of costs alone, as the major endpoint in treating epilepsy with AEDs is seizure control without adverse effects. Switching AEDs in clinical practice still depends on the individual clinical situation and choosing AED therapy solely on the basis of initial acquisition costs is unlikely to be cost effective in the long-term care of patients with epilepsy.
Publication Types: Review
PMID: 15270592 [PubMed - indexed for MEDLINE]

CNS Drugs. 2003;17(2):101-15.
Stimulation of the nervous system for the management of seizures: current and future developments.
Murphy JV, Patil A.
Pediatric Epilepsy Research Center, Children's Mercy Hospital, Kansas City, Missouri 64108, USA. jmurphy@cmh.edu
Vagal nerve stimulation (VNS) for the treatment of refractory epilepsy appears to have started from the theory that since VNS can alter the EEG, it may influence epilepsy. It proved effective in several models of epilepsy and was then tried in short-term, open-label and double-blind trials, leading to approval in Canada, Europe and the US. Follow-up observations in these patients demonstrated continued improvement in seizure control for up to 2 years. Close to 50% of treated patients have achieved at least a 50% reduction in seizure frequency. This therapy was also useful as rescue therapy for ongoing seizures in some patients; many patients are more alert. The initial trials were completed in patients >/=12 years of age with refractory partial seizures. Subsequently, similar benefits were shown in patients with tuberous sclerosis complex, Lennox-Gastaut syndrome, hypothalamic hamartomas and primary generalised seizures. Implanting the generator and leads is technically easy, and complications are few. The method of action is largely unknown, although VNS appears to alter metabolic activity in specific brain nuclei. Considering that improvement in mood is frequently found in patients using VNS, it has undergone trials in patients with depression. Other illnesses deserving exploration with this unusual therapy are Alzheimer's disease and autism. Some aspects of VNS have proven disappointing. Although patients have fewer seizures, the number of antiepileptic drugs they take is not significantly reduced. In addition, there is no way to accurately predict the end of life of the generator. Optimal stimulation parameters, if they exist, are unknown. Deep brain stimulation is a new method for controlling medically refractory seizures. It is based on the observation that thalamic stimulation can influence the EEG over a wide area. Several thalamic nuclei have been the object of stimulation in different groups of patients. Intraoperative brain imaging is

essential for electrode placement. The procedure is done under local anaesthesia. Experience with this therapy is currently limited, but growing.
Publication Types: Review
PMID: 12521358 [PubMed - indexed for MEDLINE]

CNS Spectr. 2005 Mar;10(3 Suppl 3):1-13.
Treatment-refractory epilepsy: an evidence-based approach to antiepileptic monotherapy.
Harden CL, Kanner AM, Bautista JF, Brown TR.
Comprehensive Epilepsy Center, Weill College of Cornell University, New York, NY, USA.
Treatment options for epilepsy have increased in the last decade with the introduction of several new antiepileptic drugs (AEDs). As drug selection becomes more challenging, the use of evidence-based guidelines to aid in treatment decisions has become increasingly valued. The American Academy of Neurology's (AAN) guidelines for the use of new AEDs in refractory epilepsy offers many benefits, including expert panel recommendations based on clinically relevant questions with evidence-based responses. However, lack of evidence from randomized-controlled trials, particularly as they relate to monotherapy, limits the recommendations and their use in practice. The studies of new AEDs as monotherapy in treatment-refractory epilepsy are difficult to incorporate into clinical use because they are driven by Food and Drug Administration requirements to show superiority over placebo or pseudoplacebo (ie, low dose of active drug) rather than by clinical questions. However, based on Class I evidence, the AAN guidelines have granted Level A recommendations (established effectiveness) for oxcarbazepine and topiramate monotherapy, and a Level B recommendation (probable effectiveness) for lamotrigine monotherapy in the use of refractory partial epilepsy. There is insufficient evidence to recommend gabapentin, levetiracetam, tiagabine, or zonisamide monotherapy. No monotherapy AED trials have been conducted in refractory generalized epilepsy. Because no differences in efficacy have been reported for AEDs as initial therapy of partial seizures, differences in adverse events, such as weight gain, tremor, and hair loss, are key in drug selection. More comparative studies between the AEDs are necessary for both monotherapy and add-on therapy for treatment-refactory epilepsy.
PMID: 15744225 [PubMed - in process]

Cochrane Database Syst Rev. 2005 Oct 19;(4):CD003723.
Anticonvulsant therapy for status epilepticus.
Prasad K, Al-Roomi K, Krishnan P, Sequeira R, Prasad K.
BACKGROUND: Status epilepticus is a medical emergency associated with significant mortality and morbidity, which requires immediate and effective treatment. OBJECTIVES: (1) To determine whether a particular anticonvulsant is more effective or safer to use in status epilepticus compared to another and compared to placebo.(2) To delineate reasons for disagreement in the literature regarding recommended treatment regimens and to highlight areas for future research. SEARCH STRATEGY: We searched the following electronic databases using the highly sensitive search strategy for identifying published randomised controlled trials: (1) Cochrane Epilepsy Group Specialized Register (July 2005); (2) Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2,2005); (3) MEDLINE (1966 - August 2004); (4) EMBASE (1966 - January 2003). SELECTION CRITERIA: Randomised controlled trials of participants with premonitory, early, established or refractory status epilepticus using a truly random or quasi-random allocation of treatments were included. DATA COLLECTION AND ANALYSIS: Two review authors independently selected trials for inclusion, assessed trial quality and extracted data. MAIN RESULTS: Eleven studies with 2017 participants were included. Few studies used the same interventions. Diazepam was better than placebo in reducing the risk of non-cessation of seizures (RR 0.73, 95% CI 0.57 to 0.92), requirement for ventilatory support (RR 0.39, 95% CI 0.16 to 0.94) or continuation of status epilepticus requiring use of a different drug or general anaesthesia (RR 0.73, 95% CI 0.57 to 0.92). Lorazepam was better than placebo for risk of non-cessation of seizures (RR 0.52, 95% CI 0.38 to 0.71) and for risk of continuation of status epilepticus requiring a different drug or general anaesthesia (RR 0.52, 95% CI 0.38 to 0.71). Lorazepam was better than diazepam for reducing risk of non-cessation of seizures (RR 0.64, 95% CI 0.45 to 0.90) and had a lower risk for continuation of status epilepticus requiring a different drug or general anaesthesia (RR 0.63, 95% CI 0.45 to 0.88). Lorazepam was better than phenytoin for risk of non-cessation of seizures (RR 0.62, 95% CI 0.45 to 0.86). Diazepam (30 mg intrarectal gel) was better than a lower dose (20 mg intrarectal gel) in premonitory status epilepticus for the risk of seizure continuation (RR 0.39, 95% CI 0.18 to 0.86). AUTHORS' CONCLUSIONS: Lorazepam is better than diazepam or phenytoin alone for cessation of seizures and carries a lower risk of continuation of status epilepticus requiring a different drug or general anaesthesia. Both lorazepam and diazepam are better than placebo

for the same outcomes. In the treatment of premonitory seizures, diazepam 30 mg in an intrarectal gel is better than 20 mg for cessation of seizures without a statistically significant increase in adverse effects. Universally accepted definitions of premonitory, early, established and refractory status epilepticus are required.
PMID: 16235337 [PubMed - in process]
http://www.thecochranelibrary.com/

Cochrane Database Syst Rev. 2005 Oct 19;(4):CD003032.
Ethosuximide, sodium valproate or lamotrigine for absence seizures in children and adolescents.
Posner E, Mohamed K, Marson A, Posner E.
BACKGROUND: Absence seizures are brief epileptic seizures which present in childhood and adolescence. They are characterised by sudden loss of awareness and an electroencephalogram (EEG) typically shows generalised spike wave discharges at three cycles per second. Ethosuximide, valproate and lamotrigine are currently used to treat absence seizures. This review aims to determine the best choice of anticonvulsant for a child with typical absence seizures. OBJECTIVES: To review the evidence for the effects of ethosuximide, valproate and lamotrigine as treatments for children and adolescents with absence seizures, when compared with placebo or each other. SEARCH STRATEGY: We searched the Cochrane Epilepsy Group's Specialised Register (March 2005), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 1, 2005), MEDLINE (1966 to March 2005) and EMBASE (1988 to March 2005). No language restrictions were imposed. In addition, we contacted Sanofi Winthrop, Glaxo Wellcome (now GlaxoSmithKline) and Parke Davis (now Pfizer), manufacturers of sodium valproate, lamotrigine and ethosuximide respectively. SELECTION CRITERIA: Randomised parallel group monotherapy or add-on trials which include a comparison of any of the following in children or adolescents with absence seizures: ethosuximide; sodium valproate; lamotrigine or placebo. DATA COLLECTION AND ANALYSIS: Outcome measures were: (1) proportion of individuals seizure free at 1, 3, 6, 12 and 18 months post randomisation; (2) people with a 50% or greater reduction in seizure frequency; (3) normalisation of EEG and/or negative hyperventilation test and (4) adverse effects. Data were independently extracted by two review authors. Results are presented as relative risks (RR) with 95% confidence intervals (95% CI). MAIN RESULTS: Five small trials were found, four of them were of poor methodological quality. One trial (29 participants) compared lamotrigine with placebo using a response conditional design. Individuals taking lamotrigine were significantly more likely to be seizure free than participants taking placebo during this short trial. Another trial compared lamotrigine with sodium valproate, the study lacked power to detect the difference in efficacy. Three studies compared ethosuximide, but because of diverse study designs and populations studied, we decided not to pool results in a meta-analysis. None of these studies found a difference between valproate and ethosuximide with respect to seizure control, but confidence intervals were wide and the existence of important differences could not be excluded. AUTHORS' CONCLUSIONS: Although ethosuximide, lamotrigine and valproate are commonly used to treat people with absence seizures we have insufficient evidence to inform clinical practice, and the few trials included in this review were of poor methodological quality and did not have sufficient number of participants. More trials of better quality are needed.
PMID: 16235312 [PubMed - in process]
http://www.thecochranelibrary.com/

Cochrane Database Syst Rev. 2005 Oct 19;(4):CD002029.
Psychological treatments for epilepsy.
Ramaratnam S, Baker G, Goldstein L, Ramaratnam S.
BACKGROUND: Psychological interventions such as relaxation therapy, cognitive behaviour therapy, bio-feedback and educational interventions have been used alone or in combination in the treatment of epilepsy, to reduce the seizure frequency and improve the quality of life. OBJECTIVES: To assess whether the treatment of epilepsy with psychological methods is effective in reducing seizure frequency and/or leads to a better quality of life. SEARCH STRATEGY: We searched the Cochrane Epilepsy Group's Specialized Register (July 2005), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2005), and MEDLINE (1966 to March 2005). No language restrictions were imposed. We checked the reference lists of retrieved studies for additional reports of relevant studies. SELECTION CRITERIA: Randomized or quasi-randomized studies assessing one or more types of psychological or behaviour modification techniques for people with epilepsy. DATA COLLECTION AND ANALYSIS: Two review authors independently assessed the trials for inclusion and extracted data. Primary analyses were by intention to treat. Outcomes included reduction in seizure frequency and quality of life.

MAIN RESULTS: We found three small trials (50 participants) of relaxation therapy. They were of poor methodological quality and a meta-analysis was therefore not undertaken. No study found a significant effect of relaxation therapy on seizure frequency. One trial found cognitive behavioural therapy to be effective in reducing depression, among people with epilepsy with a depressed affect, whilst another did not.One trial of group cognitive therapy found no significant effect on seizure frequency. Two trials of combined relaxation and behaviour therapy and one of EEG bio-feedback and four of educational interventions did not provide sufficient information to assess their effect on seizure frequency. One small study of galvanic skin response biofeedback reported significant reduction in seizure frequency. Combined use of relaxation and behaviour modification was found beneficial for anxiety and adjustment in one study. In one study EEG bio-feedback was found to improve the cognitive and motor functions in individuals with greatest seizure reduction. Educational interventions were found to be beneficial in improving the knowledge and understanding of epilepsy, coping with epilepsy, compliance to medication and social competencies. AUTHORS' CONCLUSIONS: In view of methodological deficiencies and limited number of individuals studied, we have found no reliable evidence to support the use of these treatments and further trials are needed.
PMID: 16235293 [PubMed - in process]
http://www.thecochranelibrary.com/

Cochrane Database Syst Rev. 2005 Oct 19;(4):CD001416.
Zonisamide add-on for drug-resistant partial epilepsy.
Chadwick D, Marson A, Chadwick D.
BACKGROUND: The majority of people with epilepsy have a good prognosis and their seizures can be well controlled with the use of a single antiepileptic agent, but up to 30% develop refractory epilepsy, especially those with partial seizures. In this review we summarize the current evidence regarding zonisamide, when used as an add-on treatment for drug-resistant partial epilepsy. OBJECTIVES: To evaluate the effects of zonisamide when used as an add-on treatment for people with drug-resistant partial epilepsy. SEARCH STRATEGY: We searched the Cochrane Epilepsy Group Specialized Register (August 2005), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2005). In addition, we contacted Eisai Limited (makers and licensees of zonisamide) and experts in the field to seek any ongoing/unpublished studies. SELECTION CRITERIA: Randomized placebo controlled add-on trials of zonisamide in people with drug-resistant partial epilepsy. DATA COLLECTION AND ANALYSIS: Two review authors independently selected trials for inclusion and extracted data. Outcomes were: (1) 50% or greater reduction in total seizure frequency; (2) treatment withdrawal; (3) adverse events. Primary analyses were intention-to-treat. Summary relative risks (RRs) were estimated for each outcome. MAIN RESULTS: Four trials (850 participants) were included. The overall RR with 95% confidence intervals (CIs) for 50% reduction in seizure frequency compared to placebo for 300 to 500 mg/day of zonisamide was 2.44 (95% CI 1.81 to 3.30). The RR for any dose zonisamide (100 to 500 mg per day) was 2.35 (1.74 to 3.17). Two trials provide evidence of a dose response relationship for this outcome. The RR for treatment withdrawal for 300 to 500 mg/day zonisamide compared to placebo was 1.64 (1.20 to 2.26), and for 100 to 500 mg per day was 1.47 (1.07 to 2.02). The CIs of the following adverse effects indicate that they are significantly associated with zonisamide: ataxia 4.50 (99% CI 1.05 to 19.22); dizziness 1.77 (99% CI 1.00 to 3.12); somnolence 1.96 (99% CI 1.12 to 3.44); agitation 2.37 (99% CI 1.00 to 5.64); and anorexia 3.00 (99% CI 1.31 to 6.88). AUTHORS' CONCLUSIONS: Zonisamide has efficacy as an add-on treatment in people with drug-resistant partial epilepsy. Minimum effective and maximum tolerated doses cannot be identified. The trials reviewed were of 12 week duration and results cannot be used to confirm longer periods of effectiveness in seizure control. The results cannot be extrapolated to monotherapy or to people with other seizure types or epilepsy syndromes.
PMID: 16235282 [PubMed - in process]
http://www.thecochranelibrary.com/

Control Clin Trials. 2003 Feb;24(1):71-7.
Data and safety monitoring board issues raised in the VA Status Epilepticus Study.
Collins JF.
Cooperative Studies Program Coordinating Center, VA Medical Center, Perry Point, MD 21902, USA. joseph.collins2@med.va.gov
The Department of Veteran Affairs Status Epilepticus Cooperative Study was a randomized, multicenter clinical trial testing four intravenous drug regimens (lorazepam, phenobarbital, phenytoin and diazepam followed by phenytoin) to treat generalized convulsive status epilepticus. During the course of the study,

two problems emerged that the study's data and safety monitoring board (DSMB) was required to address: poor recruitment and an unexpected difference in 30-day mortality between treatment groups. By the first annual DSMB meeting, recruitment was only 25.6% of expected. The DSMB recommended placing the study on probation and replacing poorly performing sites. At their second annual meeting, the DSMB recommended approval of proposed changes to the study design contingent on the study leadership removing nonproductive sites. These changes were a 2-year increase in the recruitment period and a change in study design that decreased required sample size. Nonproductive centers were terminated and the approved changes allowed the study to be successfully completed. At the second annual DSMB meeting, an unexpected doubling of mortality rates between drug groups was observed. Although not statistically significant, the finding raised serious concerns for patient safety. The DSMB recommended instituting monthly reporting on mortality and suggested additional analyses for exploring why the differences could be occurring. These analyses indicated that, by chance, older and sicker patients were being randomized to the drugs with the higher mortality rates. By the end of the study, the observed differences in mortality between drug groups had evened out. The DSMB's thoughtful recommendations, support and monitoring ensured that the study was successfully completed without endangering the study patients.
PMID: 12559644 [PubMed - indexed for MEDLINE]

Curr Neurol Neurosci Rep. 2005 Jul;5(4):322-8.
The use of monotherapy in patients with epilepsy: an appraisal of the new antiepileptic drugs.
Kanner AM, Balabanov AJ.
Department of Neurological Sciences, Rush University Medical Center, 1653 West Congress Parkway, Chicago, IL 60612, USA. akanner@rush.edu
The use of antiepileptic drugs (AEDs) in monotherapy is always preferred to a polytherapy regimen because monotherapy facilitates drug compliance, is associated with a lower risk of toxicity, and is less costly. In addition, the yield of polytherapy to render a patient seizure-free when monotherapy regimens did not is relatively low. The available data derived from randomized controlled trials suggest that standard and new AEDs appear to display comparable antiepileptic efficacy but they differ with respect to tolerability and toxicity, which may be related to their pharmacodynamic and pharmacokinetic properties. New AEDs appear to be better tolerated than standard AEDs and to have fewer pharmacokinetic interactions than standard AEDs. In this article, we review the advantages of using AEDs in monotherapy in patients with newly diagnosed and refractory epilepsies, focusing on the individual properties of the drugs that may make them more appropriate in various patient groups.
Publication Types: Meta-Analysis Review
PMID: 15987617 [PubMed - indexed for MEDLINE]

Curr Neurol Neurosci Rep. 2004 Jul;4(4):335-9.
Novel surgical treatments for epilepsy.
McKhann GM 2nd.
Department of Neurological Surgery, Columbia University Medical Center, Neurological Institute Room 428, 710 West 168th Street, New York, NY 10032, USA. gm317@columbia.edu
The surgical treatment of epilepsy is expanding in an exciting and unprecedented way. This review highlights some of the recent advances in neuroimaging that have improved epilepsy surgery. In addition, novel therapies currently being evaluated in clinical trials, including gamma knife radiosurgery, deep brain stimulation, and responsive stimulation, are discussed. Further surgical developments that will be ready for human application in the near future are highlighted.
Publication Types: Review
PMID: 15217550 [PubMed - indexed for MEDLINE]

Curr Opin Investig Drugs. 2005 Jul;6(7):680-5.
Cannabinoids as potential anti-epileptic drugs.
Smith PF.
Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago, Dunedin, New Zealand. paul.smith@stonebow.otago.ac.nz
Cannabinoids have long been recognized as having the potential for both anticonvulsant and proconvulsant effects. The increased understanding of the cannabinoid receptors and their endogenous ligands over the last decade has provided a potential mechanism of action for these apparently paradoxical effects.

Although the anticonvulsant effects of cannabinoids appear to be mediated by their action at presynaptic cannabinoid receptors, which inhibit the release of excitatory neurotransmitters such as glutamate, it is clear that they are also capable of producing proconvulsant effects through the activation of cannabinoid receptors on terminals releasing inhibitory neurotransmitters, such as gamma-amino-butyric acid. In the brain, the activation of cannabinoid receptors is carefully controlled by the rapid synthesis and degradation of endocannabinoids in a way that targets the endogenous ligands to specific sets of cannabinoid receptors. The potential problem in delivering a cannabinoid drug to treat epilepsy is the inability to control its actions at different cannabinoid receptors regulating the release of different neurotransmitters. Since the action of cannabinoids is complex, and there is a dearth of clinical trial data, it is currently unclear whether cannabinoids might be both efficacious and safe in the treatment of epilepsy.
Publication Types: Review
PMID: 16044663 [PubMed - in process]

Curr Opin Neurol. 2004 Aug;17(4):467-74.
Epilepsy.
Koepp MJ, Duncan JS.
Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, London, UK. mkoepp@ion.ucl.ac.uk
PURPOSE OF REVIEW: The purpose of this review is to consider the current and potential role of neuroimaging from an epilepsy perspective, and to illustrate that by combining appropriate imaging techniques, neuroimaging can contribute greatly to elucidating the basic mechanisms of the various forms of epileptic disorders. RECENT FINDINGS: New magnetic resonance imaging sequences (magnetization transfer imaging) and positron emission tomography ligands (serotonergic system) were biologically validated in large groups of patients with localization-related epilepsies. Investigations in genetically determined homogenous patient populations (PAX6, juvenile myoclonic epilepsy) have strengthened the link between genetic defects and neuropathological targets (anterior commissure, thalamus). Magnetic resonance spectroscopy and electroencephalogram-triggered functional magnetic resonance imaging provided converging evidence for a key role of the thalamus in the generation of generalized seizures. The role of functional magnetic resonance imaging in identifying eloquent areas of cortex and its relationship to structural lesions, in particular malformations of cortical development, has been further elucidated. Longitudinal magnetic resonance imaging studies reported progressive volume loss after febrile convulsions and in active epilepsy. SUMMARY: Neuroimaging is essential for improving the efficacy and safety of therapeutic, in particular, surgical procedures. Investigations of larger, more homogenous genetic disorders and longitudinal rather than cross-sectional neuroimaging studies have advanced our knowledge about the cause and effect of epileptic disorders, and will ultimately link defects in molecular genetics with specific neuropathological targets.
Publication Types: Review
PMID: 15247544 [PubMed - indexed for MEDLINE]

Curr Opin Neurol. 2003 Apr;16(2):213-9.
Emerging surgical and radiotherapeutic techniques for treating epilepsy.
Cohen-Gadol AA, Stoffman MR, Spencer DD.
Department of Neurological Surgery, Yale University School of Medicine, New Haven, CT 06520-8082, USA.
PURPOSE OF REVIEW: Recent advances in epilepsy surgery have developed a resurgence of interest in the use of surgical techniques for the treatment of intractable epilepsy. RECENT FINDINGS: More invasive procedures such as hemispherectomy and multiple subpial transection have become more popular. Disconnective techniques such as multiple subpial transection have provided a surgical option for patients whose epileptogenic zone resides in the eloquent cortex. Alternatively, new minimally invasive neurostimulation therapies have been introduced to preserve maximal cerebral tissue. Radiosurgery has been recently utilized in the treatment of epilepsy with preliminary promising results. SUMMARY: In this analysis, the authors will attempt to review the more recent surgical approaches and their indications for the treatment of medically intractable epilepsy. For patients with the epileptogenic zone in the noneloquent cortex, seizure focus resection remains the most reasonable approach to therapy.
Publication Types: Review
PMID: 12644751 [PubMed - indexed for MEDLINE]

Curr Opin Neurol. 2003 Apr;16(2):163-4.
The current status of neuroimaging for epilepsy: editorial review.
Duncan J.
Publication Types: Editorial Review
PMID: 12644743 [PubMed - indexed for MEDLINE]

Curr Opin Oncol. 2004 Jul;16(4):314-7.
Management of epileptic seizures.
Hildebrand J.
Institut Jules Bordet, Brussels, Belgium. hildebrand@skynet.be
PURPOSE OF REVIEW: Acquired epileptic seizures are common in cancer patients. They heavily impact on the quality of life and may affect survival. Most patients are medically treated, but the use of antiepileptic drugs (AEDs) in neuro-oncology is complicated by serious specific side effects and interference of AEDs with other commonly prescribed drugs such as chemotherapeutic agents and corticosteroids. The main purpose of this review is to help the clinician to select the most appropriate drug or drug combination, and to minimize drug side effects and drug interactions in epilepsy treatment of cancer patients. RECENT FINDINGS: Considerable progress has been achieved recently in epileptology. They include the development of new AEDs and better understanding of their subcellular mechanism of action and of drug interactions. Most studies concerning the efficacy of AEDs have not been performed specifically in neuro-oncological patients, and the extrapolation of their results to tumor-related epilepsy requires some caution. The most significant findings specific to tumor-related epilepsy are (a) the indication that their pathogenesis may be due to a decrease of focal GABA-ergic inhibition, and (b) the guidelines for prophylaxis based on a report by a subcommittee of the American Academy of Neurology. SUMMARY: The quality of life of epileptic patients has been improved by both a better control of seizures and the use of drugs with fewer side effects. Cancer patients probably benefit from this progress. However, treatment of tumor-related epilepsy faces several specific problems, and there is a real need for conducting clinical trials restricted to cancer patients.
Publication Types: Review
PMID: 15187884 [PubMed - indexed for MEDLINE]

Curr Opin Pharmacol. 2003 Feb;3(1):19-26.
Recent developments from genetic mouse models of seizures.
Upton N, Stratton S.
Neurology and GI Centre of Excellence for Drug Discovery, GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK. Neil_Upton@gsk.com
The use of genetically altered mice has revolutionised biomedical research into the genetics and neurobiological mechanisms contributing to complex human disorders such as epilepsy. Recent studies using mutant mice have expanded our knowledge of the key roles that abnormalities in synaptic function and formation play in epileptogenesis, and further illustrate just how closely some mouse models resemble human epilepsy. Broader utilisation of epileptic mouse mutants should provide new molecular targets for developing novel anti-epileptic drugs, and also improved means for predicting their efficacy in currently refractory forms of epilepsy.
Publication Types: Review
PMID: 12550737 [PubMed - indexed for MEDLINE]

Curr Probl Pediatr Adolesc Health Care. 2005 Nov-Dec;35(10):398-419.
New drugs in the treatment of epilepsy in children.
Donner EJ, Carter Snead O 3rd.
Division of Neurology and Program in Brain and Behavior, Hospital for Sick Children, Department of Pediatrics, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada.
PMID: 16321772 [PubMed - in process]

Curr Treat Options Neurol. 2005 Jul;7(4):281-290.
Pharmacotherapy of Mood Disorders in Epilepsy: The Role of Newer Psychotropic Drugs.
Kanner AM, Balabanov AJ.

Department of Neurological Sciences, Rush University Medical Center, 1653 West Congress Parkway, Chicago, IL 60612, USA. akanner@rush.edu.
Depression in patients with epilepsy (PWE) is a relatively common comorbidity that has a significant negative impact on their quality of life. Therefore, recognition and management of a comorbid depressive disorder is paramount to achieve successful comprehensive treatment in PWE. Depression in epilepsy may mimic primary depressive disorders, but in a significant percentage of depressed PWE, the clinical semiology has an atypical presentation and fails to meed any of the diagnostic criteria established in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Despite the relatively high prevalence of depression in epilepsy and its frequent atypical presentation, there has been only one controlled study (in 1979) to establish the safety and efficacy of antidepressant drugs in PWE. Accordingly, clinicians must rely on data from studies of pharmacotherapy of primary depression. These data are adequate to guide the clinician in the basic principles of pharmacotherapy of depression in PWE. Many questions are yet to be answered, including: 1) are the expectations of symptom remission to pharmacotherapy in PWE different in typical and atypical forms of depression, and do they differ from those of patients with primary depression? and 2) are the doses of antidepressant drugs necessary to yield symptom remission different between PWE and those patients with primary mood disorders?
PMID: 15967091 [PubMed - as supplied by publisher]

Curr Treat Options Neurol. 2005 Jul;7(4):273-280.
Effects of Treatment on Endocrine Function in Patients with Epilepsy.
Pack A.
Columbia University, Neurological Institute, 710 West 168th Street, 2nd Floor, Rt. 201, New York, NY 10032, USA. ap390@columbia.edu.
Antiepileptic drug (AED) treatment is associated with multiple short- and long-term side effects. Effects on endocrine function, including weight change, reproductive function, thyroid function, and bone health are examples of these side effects. Some AEDs affect weight, resulting in weight gain or loss. Levetiracetam and lamotrigine are weight-neutral agents, whereas valproate is associated with weight gain. Reproductive dysfunction is reported in women and men with epilepsy treated with AEDs. In women, the most common symptoms are hyperandrogenism, menstrual disorders with ovulatory failure, polycystic ovary-appearing ovaries or polycystic ovary syndrome, and hyperinsulinemia. These symptoms may be secondary to epilepsy or to AED treatment, particularly with valproate. In men, effects on sperm quality and motility, delayed sexual development, and small testicular size have been described in association with AED treatment. Carbamazepine reduces testosterone levels, whereas valproate increases androgen levels. Oxcarbazepine is not associated with changes in testosterone levels. Treatment with all of these agents can result in changes in sperm, including concentration, morphology, and motility. Enzyme-inducing AEDs are known to result in decreased thyroid hormones. Recent studies found reduced serum thyroid hormone concentrations in men and young girls treated with carbamazepine and oxcarbazepine. However, all patients were clinically euthyroid, and these changes were reversible after AED withdrawal. Persons with epilepsy treated with AEDs are at increased risk for fracture. Not only is this increased because of seizure activity, but also because of treatment with AEDs. AED treatment results in decreased bone mineral density, the most sensitive predictor of fracture and changes in biochemical indices of bone metabolism, including calcium, vitamin D, and markers of bone formation and resorption. Identifying each of these endocrine abnormalities is important because it may be necessary and beneficial to change AED treatment. In addition, multiple therapies exist for the treatment of polycystic ovary syndrome, infertility, and decreased bone mineral density.
PMID: 15967090 [PubMed - as supplied by publisher]

Curr Treat Options Neurol. 2005 Jul;7(4):261-271.
Experimental Electrical Stimulation Therapy for Epilepsy.
Oommen J, Morrell M, Fisher RS.
Stanford Department of Neurology, Room A343, Stanford Medical Center, 300 Pasteur Drive, Stanford, CA 94305, USA. rfisher@stanford.edu.
Electrical stimulation of the nervous system is an attractive possible therapy for intractable epilepsy, but only stimulation of the vagus nerve has been subjected to large, controlled, and completed clinical trials. Controlled trials are in progress for intermittent cycling stimulation of the anterior nuclei of the thalamus, and for cortical stimulation at a seizure focus, responsive to detection of seizure onset. Anecdotal experience has been gathered with stimulation of cerebellum, centromedian thalamus, subthalamus,

caudate, hippocampus, and brainstem. All stimulation of the central nervous system for epilepsy must be considered experimental.
PMID: 15967089 [PubMed - as supplied by publisher]

Dis Manag. 2004 Winter;7(4):333-47.
Impact of a seizure disorder disease management program on patient-reported quality of life.
Gunter MJ, Brixner D, von Worley A, Carter S, Gregory C.
Lovelace Clinic Foundation, Albuquerque, New Mexico 87106, USA. Maggie@LCFresearch.org
The objective of this study was to evaluate the impact of a comprehensive, multifaceted disease management program on self-reported quality of life (QOL) for adult patients with epilepsy. The study (1996-2000) employed a quasi-experimental research design in which primary care clinics in a southwestern integrated delivery system were assigned to either the intervention or comparison group. The impact evaluation involved a comparison of responses to a validated QOL survey before and after a disease management intervention for adult health plan members with epilepsy. The intervention consisted of both formal provider training and associated tools and reinforcements as well as direct-to-patient interventions, including a comprehensive education booklet, a seizure diary, a patient education class, and a resource list. Pre-post analysis utilizing paired t-tests was conducted to identify any pre-post differences in QOL for both the intervention and comparison group patients, as measured by the seven specific domains of the epilepsy QOL instrument (QOLIE-31). The intervention group patients showed statistically significant positive changes in two QOL domains: Seizure Worry ($p < 0.001$) and Emotional Well-being ($p < 0.05$). One other domain, Overall Quality of Life, showed improvement in the intervention group that approached statistical significance ($p < 0.06$). There were no statistically significant changes for the comparison group. A well-designed, comprehensive disease management program can improve patient empowerment and coordination of care between the patient and provider, which resulted in an improvement in quality of life, one of the most central patient outcomes in this difficult disease.
Publication Types: Evaluation Studies
PMID: 15671790 [PubMed - indexed for MEDLINE]

Drugs Today (Barc). 2005 Sep;41(9):589-97.
Zonisamide: Review of its use in epilepsy therapy.
Zareba G.
Department of Environmental Medicine, University of Rochester, School of Medicine and Dentistry, Rochester, New York, USA. grazyna_zareba@urmc.rochester.edu.
Zonisamide is an antiepileptic drug used as adjunctive therapy for refractory partial seizures in adults. Because of the multiple mechanisms of action, it shows a broad spectrum of anticonvulsant activity and has been effective in several types of seizures, including partial and generalized seizures, tonic-clonic seizures and absence seizures in patients unresponsive to other anticonvulsants. Myoclonic epilepsy, Lennox-Gastaut syndrome and infantile spasms have also been treated effectively with zonisamide. Recent clinical studies have demonstrated additional potential for therapeutic use in neuropathic pain, bipolar disorder, migraine, obesity, eating disorders and Parkinson's disease. Despite adverse events, zonisamide is relatively safe and well tolerated in patients, and shows low discontinuation rate. It has a good pharmacokinetic profile and a low drug interaction potential. Zonisamide is considered as a drug that effectively reduces the frequency of partial seizures.
PMID: 16341290 [PubMed - in process]

Drugs Today (Barc). 2004 Jun;40(6):501-15.
Vagus nerve stimulation therapy.
Wheless JW, Baumgartner J.
Texas Comprehensive Epilepsy Program, University of Texas-Houston, Epilepsy Monitoring Unit, Memorial Hermann Hospital, Houston, Texas 77030, USA. james.w.wheless@uth.tmc.edu
Until recently, antiepileptic drugs and traditional epilepsy surgery were the two primary treatment options available to patients with epilepsy. Drug therapy, however, does not always control seizures and can be associated with negative side effects. Additionally, only a minority of patients are candidates for epilepsy surgery. Vagus nerve stimulation (VNS) therapy, approved by the US FDA in 1997, is now a treatment option that is effective in reducing seizure frequency and severity as well as improving patient quality of life without the pharmacological side effects associated with traditional antiepileptic drugs. Provided here is an overview of VNS therapy and the VNS therapy system, including the history of vagal

nerve stimulation, patient selection guidelines and new indications currently under investigation for this novel therapy. Copyright 2004 Prous Science
Publication Types: Review
PMID: 15349130 [PubMed - indexed for MEDLINE]

Emerg Med J. 2003 Jan;20(1):13-20.
An evidence and consensus based guideline for the management of a child after a seizure.
Armon K, Stephenson T, MacFaul R, Hemingway P, Werneke U, Smith S.
Academic Division of Child Health, Nottingham, UK. armon@ukonline.co.uk
OBJECTIVE: An evidence and consensus based guideline for the management of the child who presents to hospital having had a seizure. It does not deal with the child who is still seizing. The guideline is intended for use by junior doctors, and was developed for this common problem (5% of all paediatric medical attenders) where variation in practice occurs. OPTIONS: Assessment, investigations (biochemistry, lumbar puncture, serum anticonvulsant levels, EEG in particular), and/or admission are examined. OUTCOMES: The guideline aims to direct junior doctors in recognising those children who are at higher risk of serious intracranial pathology including infection, and conversely to recognise those children at low risk who are safe to go home. EVIDENCE: A systematic review of the literature was performed. Articles were identified using the electronic data bases Medline (from 1966 to June 1998), Embase (from 1980 to June 1998) and Cochrane (to June 1998), and selected if they investigated the specified clinical question. Personal reviews were excluded. Selected articles were appraised, graded, and synthesised qualitatively. Statements of recommendation were made. CONSENSUS: An anonymous, postal Delphi consensus development was used. A national panel of 30 medical and nursing staff regularly caring for these children were asked to grade their agreement with the statements generated. They were sent the relevant original publications, the appraisals, and literature review. On the second and third rounds they were asked whether they wished to re-grade their agreement in the light of other panellists' responses. Consensus was defined as 83% of panellists agreeing with the statement. Recommendations in brief: For afebrile seizures all children should have their blood pressure recorded, but no other investigations are routine although a seizing or somnolent child should have blood glucose measured; all children under 1 year should be admitted. For seizures with fever, clinical signs indicating the need to treat as meningitis are given. Children should be admitted if they are under 18 months old, have had a complex seizure, or after pretreatment with antibiotics. VALIDATION: The guideline has undergone implementation and evaluation in a paediatric accident and emergency department, the results of which will be published separately. Only one alteration was made to the guideline as a result of this validation process, which is included here.
Publication Types: Validation Studies
PMID: 12533360 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Nov;46(11):1810-9.
Fasting versus gradual initiation of the ketogenic diet: a prospective, randomized clinical trial of efficacy.
Bergqvist AG, Schall JI, Gallagher PR, Cnaan A, Stallings VA.
Division of Neurology, The Children's Hospital of Philadelphia, Pennsylvania 19104, USA. bergqvist@email.chop.edu
PURPOSE: The ketogenic diet (KD) is a 90% fat diet that is an effective treatment for intractable epilepsy. Rapid initiation of the KD requires hospital admission because of the complexity of the protocol and frequent mild and moderate adverse events. The purpose of the study was to compare the efficacy of a gradual KD initiation with the standard KD initiation preceded by a 24- to 48-h fast. METHODS: Children ages 1 to 14 years with intractable epilepsy were randomized to a fasting initiation (FAST-KD) or gradual initiation (GRAD-KD). Baseline seizure activity was recorded daily for 28 days before admission and continued for the 3-month duration of the study. Effectiveness was measured in two ways: (a) the proportion of subjects with >50% reduction in target seizure type from baseline to 3-month evaluation, and (b) percentage reduction in the frequency of the target seizure type from baseline to 3-month evaluation. Blood glucose was assessed q4 to 6h, and weights, electrolytes, hydration status, vomiting, acid balance, need for interventions (citric acid and sodium citrates (Bicitra) and IV fluids) were assessed daily. Fisher's exact tests were used to examine the association between protocol and occurrence of adverse events, and longitudinal mixed-effects models were used to look for trends in tolerability data over time. RESULTS: Forty-eight subjects, 24 in each arm, were randomized. In the FAST-KD protocol, 58% of the children had >50% reduction in the target seizure type at 3 months, and 21% were seizure free. In

the GRAD-KD protocol, 67% had a >50% reduction at 3 months, and 21% were seizure free. The two protocols were equivalent in efficacy (p = 0.033). At 3 months, the FAST-KD median percentage seizure reduction rate was 78% (ranging from 100% reduction to 73% increase in seizures per week) and was 94% (ranging from 100% reduction to 161% increase in seizures per week) for the GRAD-KD protocol. By using a logarithmic transformed percentage reduction rate and an equivalence limit difference of 20%, the efficacy of the two protocols was equivalent (p = 0.0002). Children in the GRAD protocol lost significantly less weight (p = 0.006), and had fewer and less-severe episodes of hypoglycemia (p < 0.001), fewer treatments for acidosis (citric acid and sodium citrates) (p < 0.04) and dehydration (IV fluids) (p < 0.04), but no difference in vomiting was noted. CONCLUSIONS: These data suggest that in children with intractable epilepsy, a gradual initiation results in fewer adverse events and is tolerated better overall while maintaining the efficacy of the KD.
Publication Types: Randomized Controlled Trial
PMID: 16302862 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Oct;46(10):1699-700; author reply 1701-2.
Comment on: Epilepsia. 2005 Apr;46(4):470-2.
On the definition of epileptic seizures and epilepsy.
Gomez-Alonso J, Andrade C, Koukoulis A.
Publication Types: Comment Letter
PMID: 16190949 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Oct;46(10):1698-9; author reply 1701-2.
Comment on: Epilepsia. 2005 Apr;46(4):470-2.
Comment on epileptic seizures and epilepsy: definitions proposed by the International **League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE).**
Beghi E, Berg A, Carpio A, Forsgren L, Hesdorffer DC, Hauser WA, Malmgren K, Shinnar S, Temkin N, Thurman D, Tomson T.
Publication Types: Comment Letter
PMID: 16190948 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Sep;46(9):1423-5.
Photic- and pattern-induced seizures: expert consensus of the Epilepsy Foundation of America Working Group.
Harding G, Wilkins AJ, Erba G, Barkley GL, Fisher RS; Epilepsy Foundation of America Working Group.
Clinical Neurophysiology Unit, Aston University, Birmingham, UK.
PURPOSE: In August, 2004, the Epilepsy Foundation of America convened a workshop to begin to develop an expert consensus on photosensitive seizures. METHODS: Literature and data were reviewed, and consensus was derived from discussion. RESULTS: A flash is a potential hazard if it has luminance >or=20 cd/m2, occurs at a frequency of >or=3 Hz, and occupies a solid visual angle of >or=0.006 steradians (approximately 10% of the central visual field or 25% of screen area at typical viewing distances). A transition to or from saturated red also is considered a risk. A pattern with the potential for provoking seizures contains clearly discernible stripes, numbering more than five light-dark pairs of stripes in any orientation. When the light-dark stripes of any pattern collectively subtend at the eye from the minimal-expected viewing distance a solid angle of >0.006 steradians, the luminance of the lightest stripe is >50 cd/m2, and the pattern is presented for >or=0.5 s, then the pattern should display no more than five light-dark pairs of stripes, if the stripes change direction, oscillate, flash, or reverse in contrast; if the pattern is unchanging or smoothly drifting in one direction, no more than eight stripes. These principles are easier to apply in the case of fixed media, for example, a prerecorded TV show, which can be analyzed frame-by-frame, as compared with interactive media. CONCLUSIONS: A consensus view of stimuli likely to provoke visually evoked seizures can be developed.
Publication Types: Consensus Development Conference Guideline Review
PMID: 16146438 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Aug;46(8):1286-92.
Management of women with epilepsy: Are guidelines being followed? Results from case-note reviews and a patient questionnaire.

Kampman MT, Johansen SV, Stenvold H, Acharya G.
Department of Neurology, University Hospital of North Norway. Margitta.Kampman@unn.no
PURPOSE: Several international guidelines for the management of women with epilepsy (WWE) have been developed since 1989. We aimed to determine whether guidelines for the management of WWE are followed and whether active implementation of such guidelines makes a difference to clinical practice. METHODS: The study covered a 2-year period of "passive dissemination" of guidelines followed by a 2-year period of "active implementation." Documentation reflecting adherence to the guidelines was abstracted retrospectively from electronic medical records on 215 WWE aged 16-42 years. Data abstracted from case notes included counselling on contraception and pregnancy-related issues; follow-up during pregnancy; advice on supplementation of folic acid, calcium, and vitamin D; and serum folate measurements. A questionnaire assessing the knowledge of WWE issues was completed by 112 (71%) of 157 patients. RESULTS: Documentation that WWE issues had been addressed was found in approximately one third of medical case records with no measurable effect of active implementation. Only the follow-up during pregnancy seemed to have improved. Serum folate measurements in 51 women treated with enzyme-inducing antiepileptic drugs (AEDs) revealed folate deficiency in 11 (22%). Respondents to the questionnaire recalled having received information from their neurologists on the interaction between AEDs and oral contraceptives (46%), need to plan pregnancy (63%), and folic acid requirement (56%). CONCLUSIONS: Judged by a review of documentation in case notes, active implementation of guidelines had no measurable effect on clinical practice. However, the follow-up during pregnancy seemed to have improved. Patients' knowledge of WWE issues compared favorably with published studies. Better strategies are needed to secure successful implementation of guidelines.
PMID: 16060941 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Aug;46(8):1212-8.
Characterizing the patterned images that precipitate seizures and optimizing guidelines to prevent them.
Wilkins A, Emmett J, Harding G.
University of Essex, Colchester, United Kingdom. arnold@essex.ac.uk
The use of guidelines to prevent the broadcast of epileptogenic television program content has reduced the incidence of seizures in Britain and Japan. Epileptogenic content includes both flicker and patterns. The guidelines for flicker were developed on the basis of a model that related stimulus parameters to the proportion of patients affected. We here extend the model to pattern stimuli. A set of rules is advocated that keeps the level of risk to a consistent minimum and simplifies compliance. We propose that striped patterns that last > 0.5 s, occupy more than one fourth the area of the screen, and have bright stripes > 50 cd/m2 in luminance be restricted as regards the number of cycles admissible. The guidelines are estimated to protect at least two thirds of susceptible patients.
PMID: 16060930 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Jun;46(6):949-51.
Successful initiation of combined therapy with valproate sodium injection and divalproex sodium extended-release tablets in the epilepsy monitoring unit.
Boggs JG, Preis K.
Orlando Regional Healthcare, Orlando, Florida 32801, USA. jboggs@medscape.com
PURPOSE: Patients in epilepsy monitoring units (EMUs) often require aggressive initiation or reinitiation of therapy before discharge. We developed a simple dosing scheme using valproate sodium injection (VPA-IV) and divalproex sodium extended-release (VPA-ER) tablets to minimize the time required for initiation of therapy, without increasing the likelihood of seizures and adverse effects. METHODS: We identified 42 patients in the EMU, naive to VPA-IV and VPA-ER, for whom one of the discharge AEDs included divalproex sodium. On the day of discharge, patients were loaded with 20 mg/kg VPA-IV at 6 mg/kg/min, followed by approximately 20 mg/kg VPA-ER within 1 h. The discharge daily dose of VPA-ER was identical to the dose given after the IV load. We assessed tolerability and seizure occurrence during infusion, at 1 h, 4 h, and 1 week after discharge. RESULTS: All patients tolerated the VPA-IV dose followed by VPA-ER. Four patients reported mild nausea, and two patients reported mild dizziness within 4 h. No seizures or significant changes in heart rate or blood pressure occurred within 4 h, and all patients were discharged the same day. All patients denied systemic complaints at 1 week, and five had seizures during the week after discharge. All patients had improved seizure frequencies at the end of the first week. CONCLUSIONS: VPA-IV is well tolerated and convenient for rapid loading in the EMU. When promptly followed by VPA-ER, seizure control remains excellent.

Publication Types: Clinical Trial
PMID: 15946337 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Jun;46(6):901-17.
Computerized motion analysis of videotaped neonatal seizures of epileptic origin.
Karayiannis NB, Tao G, Xiong Y, Sami A, Varughese B, Frost JD Jr, Wise MS, Mizrahi EM.
Department of Electrical and Computer Engineering, University of Houston, Houston, Texas 77204-4005, USA. Karayiannis@UH.EDU
PURPOSE: The main objective of this research is the development of automated video processing and analysis procedures aimed at the recognition and characterization of the types of neonatal seizures. The long-term goal of this research is the integration of these computational procedures into the development of a stand-alone automated system that could be used as a supplement in the neonatal intensive care unit (NICU) to provide 24-h per day noninvasive monitoring of infants at risk for seizures. METHODS: We developed and evaluated a variety of computational tools and procedures that may be used to carry out the three essential tasks involved in the development of a seizure recognition and characterization system: the extraction of quantitative motion information from video recordings of neonatal seizures in the form of motion-strength and motor-activity signals, the selection of quantitative features that convey some unique behavioral characteristics of neonatal seizures, and the training of artificial neural networks to distinguish neonatal seizures from random infant behaviors and to differentiate between myoclonic and focal clonic seizures. RESULTS: The methods were tested on a set of 240 video recordings of 43 patients exhibiting myoclonic seizures (80 cases), focal clonic seizures (80 cases), and random infant movements (80 cases). The outcome of the experiments verified that optical- flow methods are promising computational tools for quantifying neonatal seizures from video recordings in the form of motion-strength signals. The experimental results also verified that the robust motion trackers developed in this study outperformed considerably the motion trackers based on predictive block matching in terms of both reliability and accuracy. The quantitative features selected from motion-strength and motor-activity signals constitute a satisfactory representation of neonatal seizures and random infant movements and seem to be complementary. Such features lead to trained neural networks that exhibit performance levels exceeding the initial goals of this study, the sensitivity goal being >or=80% and the specificity goal being >or=90%. CONCLUSIONS: The outcome of this experimental study provides strong evidence that it is feasible to develop an automated system for the recognition and characterization of the types of neonatal seizures based on video recordings. This will be accomplished by enhancing the accuracy and improving the reliability of the computational tools and methods developed during the course of the study outlined here.
PMID: 15946330 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):767-70.
Comment in: Epilepsia. 2005 May;46(5):614-5.
A comparison of epilepsy patients in a traditional ambulatory clinic and a telemedicine clinic.
Rasmusson KA, Hartshorn JC.
Department of Neurology, University of Texas Medical Branch, Galveston, 77555, USA.
PURPOSE: This article compares a traditional ambulatory clinic in an academic medical center with a telemedicine clinic. The telemedicine clinic is a joint project of the UTMB Telehealth Center and the Epilepsy Foundation of Southeast Texas, with partial funding for clinical operations provided by the Texas Department of Health. METHODS: Data were collected on all the patients (n = 155) in both clinics for 3 months in 2004. In addition to demographic information, outcome data (number of seizures, hospitalizations, and emergency room visits) were gathered. Medication compliance also was collected by using self-report and medication levels. RESULTS: Outcome variables were subjected to t test and chi(2) analysis. No significant differences were found in any of the demographic data or outcome measures between the two groups. CONCLUSIONS: Telemedicine is an acceptable alternative to in-person clinics for the provision of care to adults with epilepsy. Because telemedicine programs are designed to bring medical care closer to where patients live, these clinics provide an excellent alternative to provide consistent care in rural and geographically isolated areas. Additional studies are needed to investigate the potential costs associated with telemedicine as well as the potential for cost savings over time as patients are more able to access care and therefore may be more likely to seek the needed routine care and follow-up.
PMID: 15857445 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):751-9.

Cost-effectiveness of first-line antiepileptic drug treatments in the developing world: a population-level analysis.

Chisholm D; WHO-CHOICE.

Department of Health System Financing, and Department of Mental Health and Substance Abuse, World Health Organization, Geneva, Switzerland. ChisholmD@who.int

PURPOSE: To establish the population-level costs and cost-effectiveness of first-line antiepileptic drug (AED) treatments for reducing the treatment gap in developing countries. METHODS: A population model was applied to nine World Health Organization (WHO) developing subregions to estimate the impact of four first-line AEDs in the primary care management of (ICD-10 defined) idiopathic epilepsy and epileptic syndromes: phenobarbitone (PB), phenytoin (PHT), carbamazepine (CBZ), and valproic acid (VPA). The efficacy of treatment was gauged in terms of improvements to both disability and recovery, subsequently adjusted for treatment coverage, response, and adherence. Total population-level treatment effects (measured in disability-adjusted life years or DALYs averted) and treatment costs (measured in international dollars; IUS dollars) were combined to form ratios of cost-effectiveness. RESULTS: Across nine developing WHO subregions, extending AED treatment coverage to 50% of primary epilepsy cases would avert between 150 and 650 DALYs per one million population (equivalent to 13-40% of the current burden), at an annual cost per capita of IUS dollars 0.20-1.33. Older first-line AEDs (PB, PHT) were most cost-effective on account of their similar efficacy but lower acquisition cost (IUS dollars 800-2,000 for each DALY averted). CONCLUSIONS: A significant proportion of the current burden of epilepsy in developing countries is avertable by scaling-up the routine availability of low-cost AEDs. Critical factors in the successful implementation of such a scaled-up level of service delivery, apart from renewed political support and investment, relate to appropriate training and continuity of drug supply.

PMID: 15857443 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):743-50.

Development of a validated clinical case definition of generalized tonic-clonic seizures for use by community-based health care providers.

Anand K, Jain S, Paul E, Srivastava A, Sahariah SA, Kapoor SK.

Comprehensive Rural Health Services Project (AIIMS), Ballabgarh, India.

PURPOSE: To develop and test a clinical case definition for identification of generalized tonic-clonic seizures (GTCSs) by community-based health care providers. METHODS: To identify symptoms that can help identify GTCSs, patients with history of a jerky movements or rigidity in any part of the body ever in life were recruited from three sites: the community, secondary care hospital, and tertiary care hospital. These patients were administered a 14-item structured interview schedule focusing on the circumstances surrounding the seizure. Subsequently, a neurologist examined each patient and, based on available investigations, classified them as GTCS or non-GTCS cases. A logistic regression analysis was performed to select symptoms that were to be used for case definition of GTCSs. Validity parameters for the case definition at different cutoff points were calculated in another set of subjects. RESULTS: In total, 339 patients were enrolled in the first phase of the study. The tertiary care hospital contributed the maximal number of GTCS cases, whereas cases of non-GTCS were mainly from the community. At the end of phase I, the questionnaire was shortened from 14 to eight questions based on statistical association and clinical judgment. After phase II, which was conducted among 170 subjects, three variables were found to be significantly related to the presence of GTCSs by logistic regression: absence of stress (13.1; 4.1-41.3), presence of frothing (13.7; 4.0-47.3), and occurrence in sleep (8.3; 2.0-34.9). As a case definition using only three variables did not provide sufficient specificity, three more variables were added based on univariate analysis of the data (incontinence during the episode and unconsciousness) and review of literature (injury during episode). A case definition consisting of giving one point to an affirmative answer for each of the six questions was tested. At a cutoff point of four, sensitivity was 56.9 (47.4-66.0) and specificity, 96.3 (86.2-99.4). Among the 197 GTCS and 26 new non-GTCS patients recruited from hospitals from select SEAR Member Countries, in phase III, the sensitivity of this clinical case definition was 72% and specificity, 100%. A stratified analysis by gender in all the three phases did not show any differences between the sexes. CONCLUSIONS: Based on these criteria, we recommend that all patients with a history of two or more episodes of jerking or rigidity of limbs, having a score of > or =4 in the case definition, be identified as having GTCSs and started on antiepileptic medications. This clinical case definition can be very useful for community-based health care providers to identify and manage cases of GTCSs in the community. This should play a major role in the reduction of treatment gap for epilepsy in developing countries.

Publication Types: Multicenter Study
PMID: 15857442 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):716-9.
Adding video recording increases the diagnostic yield of routine electroencephalograms in children with frequent paroxysmal events.
Watemberg N, Tziperman B, Dabby R, Hasan M, Zehavi L, Lerman-Sagie T.
Pediatric Neurology Unit, Wolfson Medical Center, Sackler School of Medicine, Tel-Aviv University, Holon, Israel. nwatemberg@pol.net
PURPOSE: To report on the usefulness of adding video recording to routine EEG studies of infants and children with frequent paroxysmal events. METHODS: We analyzed the efficacy of this diagnostic means during a 4-year period. The decision whether to add video recording was made by the pediatric EEG interpreter at the time of the study. Studies were planned to last between 20 and 30 min, and, if needed, were extended by the EEG interpreter. For most studies, video recording was added from the beginning of EEG recording. In a minority of cases, the addition of video was implemented during the first part of the EEG test, as clinical events became obvious. In these cases, a new study (file) was begun. The success rate was analyzed according to the indications for the EEG study: paroxysmal eye movements, tremor, suspected seizures, myoclonus, staring episodes, suspected stereotypias and tics, absence epilepsy follow-up, cyanotic episodes, and suspected psychogenic nonepileptic events. RESULTS: Video recording was added to 137 of 666 routine studies. Mean patient age was 4.8 years. The nature of the event was determined in 61 (45%) of the EEG studies. Twenty-eight percent were hospitalized patients. The average study duration was 26 min. This diagnostic means was particularly useful for paroxysmal eye movements, staring spells, myoclonic jerks, stereotypias, and psychogenic nonepileptic events. About 46% of 116 patients for whom cognitive data were available were mentally retarded. EEG with added video recording was successfully performed in all 116 cases and provided useful information in 29 (55%) of these 53 patients. CONCLUSIONS: Adding video recording to routine EEG was helpful in 45% of cases referred for frequent paroxysmal events. This technique proved useful for hospitalized children as well as for outpatients. Moreover, it was successfully applied in cognitively impaired patients. Infants and children with paroxysmal eye movements, staring spells, myoclonic jerks, stereotypias, and pseudoseizures especially benefited from this diagnostic means. Because of its low cost and the little discomfort imposed on the patient and his or her family, this technique should be considered as a first diagnostic step in children with frequent paroxysmal events.
PMID: 15857438 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):664-8.
Self-reported seizure frequency and time to first event in the seizure monitoring unit.
Eisenman LN, Attarian H, Fessler AJ, Vahle VJ, Gilliam F.
Adult Epilepsy Center, Department of Neurology, Washington University Medical School, St. Louis, Missouri, USA. LEISENMAN@WUSTL.EDU
PURPOSE: To compare seizure frequency reported in the clinic with time to first diagnostic event during video-EEG monitoring. The effect of the artificial environment of the monitoring unit on self-reported seizure frequency was explored. METHODS: The 155 consecutive patients were seen in the Washington University Epilepsy Center and subsequently underwent video-EEG monitoring during 2001. Of these, 112 had a diagnostic event during monitoring; 31 left without having a definite event; and 12 could not provide an estimate of seizure frequency in the clinic. The time to first event was compared with self-reported seizure frequency. The patients were then divided into three equal groups (tertiles) based on mean seizure frequency, and time to first seizure was compared between groups. Then the numbers of patients staying >7 days without ever having an event were compared between the low and high seizure-frequency groups. Finally, Kaplan-Meier survival curves were calculated. RESULTS: No correlation was found between self-reported seizure rate and time to diagnostic event ($r = 0.18$; $p = 0.06$). Time to first event was 2.8 days in the low seizure-frequency group (mean, 2.2/month), 2.1 days in the medium (mean, 8.8/month), and 2.1 days in the high (mean, 24.1/month) groups, which were not significantly different ($p = 0.19$). Of patients in the low-frequency group, 79% had an event within 7 days. CONCLUSIONS: In the artificial environment of the monitoring unit, self-reported outpatient seizure frequency is not an accurate predictor of duration of video-EEG monitoring required to make a definitive classification of clinical events and should not contribute to the decision as to whether to refer a patient for monitoring.
PMID: 15857431 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 May;46(5):614-5.
Comment on: Epilepsia. 2005 May;46(5):767-70.
Telemedicine for epilepsy: a useful contribution.
Patterson V, Bingham E.
Publication Types: Comment Editorial
PMID: 15857424 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Apr;46(4):470-2.
Comment in: Epilepsia. 2005 Oct;46(10):1698-9; author reply 1701-2. Epilepsia. 2005 Oct;46(10):1699-700; author reply 1701-2. Epilepsia. 2005 Oct;46(10):1700-1; author reply 1701-2.
Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE).
Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, Engel J Jr.
Stanford University Medical Center, Department of Neurology, Stanford, California 94305-5235, USA. r.fisher@stanford.edu
The International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) have come to consensus definitions for the terms epileptic seizure and epilepsy. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.
PMID: 15816939 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Mar;46(3):457; author reply 457-9.
Comment on: Epilepsia. 2004 May;45(5):504-15.
Gamma knife surgery in mesial temporal lobe epilepsy.
Grabenbauer GG, Ernst-Stecken A, Ganslandt O, Stefan H.
Publication Types: Comment Letter
PMID: 15730549 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Mar;46(3):440-3.
Extended-release divalproex in child and adolescent outpatients with epilepsy.
Kernitsky L, O'Hara KA, Jiang P, Pellock JM.
Virginia Commonwealth University, Division of Child Neurology, Children's Pavilion, Richmond, Virginia 23298-0211, USA. 9lkernit@mail2.vcu.edu
PURPOSE: To determine whether valproic acid [divalproex (DVP)] extended-release, administered at a higher proportionate once-daily dosage, can be safely substituted for delayed-release or sprinkle in pediatric patients with epilepsy. METHODS: Patients between ages 6 and 17 years with stable epilepsy taking DVP were randomized to 7 days of either DVP delayed-release/sprinkle (at the usual daily dose taken before study entry) or extended-release DVP (daily dose, 8% to 25% higher than their usual dose), and then (crossed over to) 7 days of the comparator formulation. Patient's clinical status was evaluated at a screening visit and on days 8 and 15, and with telephone follow-up 1 month after study completion. RESULTS: No statistically significant difference in mean plasma VPA levels measured at the end of treatment was observed: 99, 92, and 103 mug/ml with the delayed-release tablets (n = 4), the sprinkle formulation (n = 11), and the extended-release tablets (n = 16), respectively. Seizure-control rates were stable during patients' use of the extended-release formulation. None of the study patients experienced a treatment-related adverse event. CONCLUSIONS: The total daily dose for patients taking the delayed-formulation may need to be increased by < or = 20% when they are switched to the extended-release formulation. When switching from sprinkles to the extended-release formulation, individual variability must be considered. In patients who have VPA levels near the very high end of the therapeutic range (>100 microg/ml), it may be more prudent to make only minor modifications to the total daily dose during conversion and then to individualize the DVP extended-release dose based on plasma levels.
Publication Types: Clinical Trial Randomized Controlled Trial
PMID: 15730542 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Feb;46(2):311-9.

Estimating prevalence, incidence, and disease-related mortality for patients with epilepsy in managed care organizations.

Holden EW, Thanh Nguyen H, Grossman E, Robinson S, Nelson LS, Gunter MJ, Von Worley A, Thurman DJ.
ORC Macro, Atlanta, Georgia 30329, USA. emery.w.holden@orcmacro.com

PURPOSE: The purpose of the present study was to apply computer algorithms to an administrative data set to identify the prevalence of epilepsy, incidence of epilepsy, and epilepsy-related mortality of patients in a managed care organization (MCO). METHODS: The study population consisted of members enrolled in Lovelace Health Plan, a component of Lovelace Health Systems, a statewide MCO headquartered in Albuquerque, New Mexico. Patient records were obtained from July 1996 to June 2001. Four logistic regression models with high sensitivity and specificity were applied to 1-, 3-, and 5-year time frames in which members were continuously enrolled in the MCO. Incidence was defined for patients who did not have an epilepsy-associated code in the 18 months before the first diagnosis entry. Mortality estimates in the population also were assessed by using a matched control group and linkage to a statewide death registry. RESULTS: The data yielded estimated prevalence rates of 7-10 per 1,000, depending on age, sex, ethnicity, and time interval. Annualized incidence was 47 per 100,000 for members continuously enrolled for 3 years and 71 per 100,000 for members continuously enrolled for 5 years. Crude mortality rates were 2-2.5 times higher for epilepsy patients identified with the algorithms than for the matched controls. Conditional logistic regression indicated that the odds of death for epilepsy patients as compared with controls ranged from 1.24 to 2.06. CONCLUSIONS: Accurate estimation of prevalence, incidence, and mortality rates for epilepsy is an essential component of disease management in MCOs. The algorithms in this project can be used to monitor trends in prevalence, incidence, and mortality to inform decisions critical to improving the health care needs and quality of life for patients with epilepsy.

PMID: 15679513 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Feb;46(2):280-9.

Worldwide use of the ketogenic diet.

Kossoff EH, McGrogan JR.
The Pediatric Epilepsy Center, Department of Neurology, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21287-1000, USA. ekossoff@jhmi.edu

PURPOSE: Over the past decade, the use of the ketogenic diet internationally has increased dramatically. The purpose of this survey was to evaluate the use of the diet worldwide. METHODS: With the use of the Internet, e-mail requests for information about international ketogenic diet centers (outside the United States) were made over a 9-month period. Assistance also was obtained from the Child Neurology Society and International League Against Epilepsy. Questions included patient enrollment (total and annually), year the diet was first offered, unique cultural and religious issues in the country, community opinion, and research interests. RESULTS: Successful communication was made with 73 academic centers in 41 countries outside the United States. Sixteen (39%) countries provided information from multiple centers. The median duration offering the diet was 8 years (range, 1-45 years). The average number of patients enrolled to date was 71.6 per country, with 5.4 new patients annually. Common difficulties included avoiding rice intake, tolerating higher fat-to-protein and carbohydrate ratios (e.g., 4:1), finding specific nutritional labels on foods, and handling the growing interest from large populations with limited resources. Nevertheless, cultural and religious issues were generally not limiting; physician and patient acceptance of the diet as an option is high; and most meals were similar among countries. Centers often had great pride in their programs, and international collaborative groups are forming rapidly. A website is now available with updated center information at http://www.neuro.jhmi.edu/Epilepsy/Peds/ketoworldwide.htm CONCLUSIONS: Despite occasional difficulties, the ketogenic diet is being used worldwide.

PMID: 15679509 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 9:161-8.

Evidence-based treatment of idiopathic generalized epilepsies with new antiepileptic drugs.

Bergey GK.
Department of Neurology, Johns Hopkins Epilepsy Center, Johns Hopkins University, School of Medicine and Hospital, Baltimore, Maryland 21287, USA. gbergey@jhmi.edu

With the introduction of over ten new antiepileptic drugs (AEDs) since 1993, the hope has been that at least some of these agents would be useful for not just partial seizures, but also for the primary

generalized seizures of the idiopathic generalized epilepsies (IGE). The development of evidence-based treatment guidelines in the IGE, however, faces a number of challenges, particularly after an antiepileptic drug (AED) receives approval for one indication. The majority of patients with IGE are controlled with first-line therapy if appropriately selected. Case reports or series typically appear with use in refractory patients, but these studies lack the rigor to allow formulation of guidelines. Still we are beginning to see some good class I and II data to support use of selected second-generation AEDs. It is postulated that lamotrigine (LTG), levetiracetam (LEV), topiramate (TPM), and zonisamide (ZSM) may have efficacy for a broad spectrum of seizure types including those of IGE. At the present time good class I and II evidence exists to support the use of LTG for typical absence, LEV for idiopathic myoclonic seizures, and TPM for primary generalized tonic-clonic seizures, even though only TPM has FDA approval for primary generalized seizures. This article examines the available rigorous evidence that can support these uses and also discusses some selected other reports that suggest a spectrum of efficacy for these new agents.
Publication Types: Review
PMID: 16302891 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 9:57-66.
Syndromes of idiopathic generalized epilepsies not recognized by the International League Against Epilepsy.
Panayiotopoulos CP.
Department of Clinical Neurophysiology and Epilepsies, St. Thomas' Hospital, London, United Kingdom. tom.panayiotopoulos@gstt.sthames.nhs.uk
This chapter assesses probable epileptic syndromes within the idiopathic generalized epilepsies (IGE) that have not yet been recognized by the International League Against Epilepsy (ILAE). Jeavons syndrome, a purely reflex IGE that predominantly manifests with eyelid myoclonia and electroencephalogram (EEG) abnormalities on eye closure, is the most distinct and undisputed of the syndromes. Another is autosomal-dominant cortical tremor, myoclonus, and epilepsy, a purely monogenic disorder that has been documented in numerous reports, mainly from Japan and Italy. Perioral myclonia with absences is certainly a seizure type that may constitute an IGE syndrome when it is associated with a number of other clinical and EEG manifestations. Similarly, many patients suffer for years from phantom absences, a type of mild absence, before a first generalized tonic-clonic seizure that usually occurs in adulthood. Both perioral myoclonia with absences and phantom absences are clinically significant because they are probably lifelong and are associated with a very high incidence (around 50%) of absence status epilepticus that may escape diagnosis and appropriate treatment. The position of early childhood IGE, which manifests mainly with typical absence seizures that are distinctly different from childhood absence epilepsy and other recognized IGE syndromes, is less clear. The prevalence of these syndromes is significant. Their identification allows better clinical management and is important for genetic research and counselling. In addition, their recognition permits application of exclusion criteria for a more purified definition and a better understanding of the true boundaries of the other IGE syndromes already accepted by the ILAE.
Publication Types: Review
PMID: 16302876 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 9:48-56.
Idiopathic generalized epilepsies recognized by the International League Against Epilepsy.
Nordli DR Jr.
Children's Memorial Hospital, Northwestern University, Feinberg School of Medicine, Chicago, Illinois 60614, USA. dnordli@childrensmemorial.org
There are eight syndromes currently recognized by the International League Against Epilepsy (ILAE) that would fit the original operational definition of idiopathic generalized epilepsy (IGE) syndromes, including benign myoclonic epilepsy in infancy; generalized epilepsy with febrile seizures plus, an entity in evolution; epilepsy with myoclonic absences; epilepsy with myoclonic-astatic seizures; childhood absence epilepsy; juvenile absence epilepsy; juvenile myoclonic epilepsy; and epilepsy with generalized tonic-clonic seizures only. All of these syndromes can be easily diagnosed when distinctive features are present. In some cases, such features are not present or only appear later in the course of the disease, making it challenging to distinguish the various syndromes. Electroencephalogram (EEG) is the most helpful laboratory test and often will strongly support the diagnosis of IGE, but may not be very helpful in discriminating between several of the syndromes with overlapping features. The same applies for genetic testing, although it is expected that further research exploring the genotype-phenotype relationships will

enhance our abilities to make definitive diagnoses. At the current time, clinical features are still the cornerstone of accurate classification, and accurate classification, in turn, is the best predictor of outcome.
PMID: 16302875 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 9:10-4.
Epidemiology of idiopathic generalized epilepsies.
Jallon P, Latour P.
Epilepsy and EEG Unit, University Hospital, CH 1211, Geneva 14, Switzerland. pierre.jallon@hcuge.ch
Idiopathic generalized epilepsies (IGEs) are a relatively new category of disorders defined by strict clinical and electroencephalogram (EEG) features proposed by the International League Against Epilepsy (ILAE) classification of epileptic syndromes. IGEs are usually easy to diagnose when clinical and EEG data are collected, but epilepsy is not synonymous with epileptic syndrome. So far, IGEs are studied in the large group of epilepsies of undetermined or unknown etiology although the genetic origin is now largely accepted. ILAE-proposed criteria are helpful in the clinical and therapeutic management of IGEs, but many epidemiologic studies still confuse the cryptogenic and idiopathic groups. Some syndromes in childhood, which are completely described by strict electroclinical criteria such as the absence epilepsies, juvenile myoclonic epilepsies, are usually included and analyzed in epidemiologic studies; however, other epileptic syndromes observed in infancy, such as benign familial neonatal seizures and benign myoclonic epilepsy in infancy, are quite rare and are usually excluded from epidemiologic surveys because they are difficult to describe completely in electro-clinical terms. Another strong limitation in the study of epidemiology of IGEs is the lack of EEG data, either because EEG is not available or the routine EEG is normal. This is particularly relevant in the inclusion of patients with only tonic-clonic seizures. IGEs encompass several different syndromes, and a few patients shift from one phenotype to another. The overlapping of some syndromes during infancy and adolescence increased the difficulty to individualize strictly the correct syndrome. Many discrepancies can be observed in the distribution of the different syndromes included in the group of IGEs, because the strict criteria for classifying these syndromes proposed by the ILAE are often not respected. With this understanding, the general frequency of IGEs can be assessed at 15-20% of all epilepsies. The frequency and the distribution of incidence and prevalence of the different syndromes are tentatively reported and discussed. When the term idiopathic is used following the restrictive ILAE criteria, the mortality data concerning patients with idiopathic epilepsies do not show an increased standardized mortality ratio.
Publication Types: Review
PMID: 16302871 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 1:50-1.
Quality-controlled education in epileptology: experiences from Europe and possible developments for other regions.
Wolf P.
Epilepsie-Zentrum Bethel, Klinik Mara I, Bielefwld, Germany. pwo@mara.de
As a consequence of the political system shift in Eastern Europe in the early 1990s, the new International League Against Epilepsy (ILAE) Commission on European Affairs (CEA) had to face the task of ensuring an equally good quality of epilepsy care across the whole region. A high standard of epileptologic education being the most important precondition for that, the decision was taken to make quality-controlled education a first priority. To reach this aim, an "European Epilepsy Academy" (Eurepa) was founded in 1996. Its activities comprise organization of its own educational courses, certification of other educational courses, responsibility for education at European Congresses, training of trainers in epilepsy (now 45 trainers from 27 countries), adoption of a curriculum to become a certified European epileptologist, establishment of a multinational educational network, and a "Website Academy" as a forum for discussion. In the first two years of its activity, the Academy received financial support from the ILAE (money generated by the European Congresses) but has since been self-supporting, with income from membership fees, participation fees at courses, and moderate support from pharmaceutical companies. The interest in the Academy is high, especially in those parts of Europe where epileptology was until recently not well developed. This should encourage other regional ILAE commissions to implement similar strategies, even if different regional structures will require variable regional approaches. Thus, in regions with long distances, it may be useful to include methods of distant learning and other specific features.
PMID: 15816981 [PubMed - indexed for MEDLINE]

Epilepsia. 2005;46 Suppl 1:44-5.
Development of an epilepsy comprehensive care center: a Japanese model.
Yagi K.
National Epilepsy Center, Shizuoka Medical Institute of Neurological Disorders, Shizuoka, Japan. yagi@szec.hosp.go.jp
PURPOSE: To review the requirements of a comprehensive care center for people with epilepsy. METHODS: Twenty-seven years have passed since the foundation of the Japanese Epilepsy Center in Shizuoka. The development of this center is presented as a model of an epilepsy comprehensive care center. RESULTS: Between 1926 and 1947, the Shizuoka Higashi Hospital (the former name of SMIND) served as a tuberculosis hospital. In 1975, a proposal for a special center for the care of people with epilepsy was submitted to the Japanese government. An epilepsy center (the Center) was soon built, and the tuberculosis sanatorium ended its 50-year history. The facilities of the Center include an outpatient clinic, four inpatient wards with 200 beds, a day-care center for medical rehabilitation, and classrooms for elementary and junior high school children. The Center has modern diagnostic tools such as electroencephalography (EEG), closed-circuit TV-EEG (CCTVEEG), computed tomography (CT) scan, magnetic resonance imaging (MRI), single-photon emission CT (SPECT), and magnetoencephalography (MEG). Neurosurgery for intractable seizures has been conducted at the Center since 1983. Approximately 25,000 patients with epilepsy from all over Japan have been registered since 1975. Annually, approximately 5,000 outpatients and 600 inpatients attend the Center. As of March 2002, 500 patients had received resective surgery for epilepsy. Other activities in the Center include research and specialized training of professionals, including foreign nationals, in the treatment of epilepsy. CONCLUSIONS: The experience in Shizuoka suggests that management of epilepsy should be oriented toward psychological well-being, social rehabilitation, and seizure control.
PMID: 15816979 [PubMed - indexed for MEDLINE]

Epilepsia. 2005 Jan;46(1):159-63.
Typical absence seizures triggered by photosensitivity.
Baykan B, Matur Z, Gurses C, Aykutlu E, Gokyigit A.
Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey. baykanb@istanbul.edu.tr
PURPOSE: To describe the characteristics of patients with typical absence seizures (TASs), consistently triggered by photosensitivity. METHODS: Consecutive patients having TAS induced by intermittent photic stimulation were included in the study. All clinical parameters, EEG, and video-EEG data were assessed during the long-term follow-up. Statistical analyses were performed with SPSS 10.0 software. RESULTS: Nine female and two male patients with a mean age at onset of 14 +/- 5.9 years (range, 7-27 years) and with a mean follow-up of 9 +/- 7.56 years had photosensitive TASs. They constituted 7.64% of absence epilepsies and 0.4% of all patients seen in our tertiary center. The seizures were usually subtle and had a reported frequency of 1 to 9 times daily. Seven patients were clinically photosensitive and reported that some of their TASs were induced by photic stimuli in daily life. All patients also had spontaneous TASs, and four of them had generalized tonic-clonic seizures. EEG results did not show any distinctive features when compared with those of other cases with TASs. Remission could not be achieved in five patients with antiepileptic drug treatments, and we always observed relapses after drug discontinuation or dose reduction in the remaining six cases in remission. Spontaneous remission did not occur even in the five patients older than 30 years. CONCLUSIONS: TASs triggered by photosensitivity are a rare and heterogeneous clinical condition with a marked female preponderance. It is notable that TASs do not remit in these cases.
PMID: 15660784 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Dec;45(12):1646-9; author reply 1649-51.
Efficacy and tolerability of the new antiepileptic drugs: commentary on the recently published practice parameters.
Panayiotopoulos CP, Benbadis SR, Covanis A, Dulac O, Duncan JS, Eeg-Olofsson O, Ferrie CD, Grunewald RA, Kasteleijn-Nolst Trenite DG, Koutroumanidis M, Martinovic Z, Newton RW, Parker AP, Salas-Puig J, Sander JW, Shorvon S, Watanabe K, Whitehouse WP, Youroukos S.
Publication Types: Letter
PMID: 15571526 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Nov;45(11):1397-404.

Subjective sleep disturbance in patients with partial epilepsy: a questionnaire-based study on prevalence and impact on quality of life.

de Weerd A, de Haas S, Otte A, Trenite DK, van Erp G, Cohen A, de Kam M, van Gerven J.
Centre for Sleep & Wake Disorders, Medical Centre Haaglanden, Westeinde Hospital, The Hague, The Netherlands. adweerd@sein.nl

PURPOSE: This study was designed to assess whether sleep disturbance is more frequent among patients with partial seizures and what impact on quality of life (QoL) sleep disturbance may have on patients with partial seizures. METHODS: Questionnaire booklets were mailed to 1,183 patients from four Dutch clinics. Each patient was asked to find two age- and gender-matched controls to complete the same set of questionnaires [Sleep Diagnosis List (SDL), Medical Outcomes Study (MOS)-Sleep Scale, Groningen Sleep Questionnaire, Epworth Sleepiness Scale, and the SF-36 Health Survey]. The prevalence of sleep disturbance, based on the SDL, was compared between those with partial epilepsy and controls. Mean scores on sleep and the SF-36 Physical (PCS) and Mental (MCS) Component Summary scales were compared. RESULTS: Responses from 486 patients and 492 controls were analyzed. Respondents with partial epilepsy had a highly significant, twofold higher prevalence of sleep disturbance compared with controls (38.6 vs. 18.0%; $p < 0.0001$). Most sleep-disorder subscales showed significant abnormalities in respondents with epilepsy, compared with controls. Mean SF-36 MCS and PCS scores were significantly lower in respondents with epilepsy compared with controls in both the strata with sleep disturbance and without (all p values <0.05). The presence of a sleep disturbance in respondents with epilepsy was associated with the greatest impairment in QoL. CONCLUSIONS: Sleep disturbance is more than twice as prevalent in persons with partial epilepsy compared with controls, and most domains of sleep are significantly disturbed. Persons with partial epilepsy have significant QoL impairment, and sleep disturbance further compounds this.

PMID: 15509241 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Oct;45(10):1171-5.

Navigating toward fetal and maternal health: the challenge of treating epilepsy in pregnancy.

Tomson T, Perucca E, Battino D.
Department of Neurology, Karolinska Hospital, Stockholm, Sweden. torbjorn. tomson@ kus.se

A rational approach to the treatment of women of childbearing potential with epilepsy has been hampered by the lack of conclusive data on the comparative teratogenic potential of different antiepileptic drugs (AEDs). Although, several cohort studies on birth defects associated with AED use during pregnancy have been published, these have generally failed to demonstrate differences in malformation rates between AEDs, probably mainly due to insufficient power. In particular, pregnancies with new generation AEDs have been too few. In recent years, pregnancy registries have been introduced to overcome this problem--EURAP (an international collaboration), the North American, and the U.K. AED and pregnancy registries are observational studies that prospectively assess pregnancy outcome after AED exposure using slightly different methods. Each has enlisted 3-5,000 pregnancies in women with epilepsy, and the North American and the U.K. have released preliminary observations. Thus the U.K. registry reported a higher malformation rate with valproate, 5.9% (4.3-8.2%; 95% CI), than with carbamazepine, 2.3% (1.4-3.7%), and lamotrigine, 2.1% (1.0-4.0%). Most of the more recent cohort studies have also identified a nonsignificant trend toward a higher teratogenicity with valproate. These signals need to be interpreted with some caution since none of the studies to date have fully assessed the impact of possible confounders, such as type of epilepsy, family history of birth defects, etc. However, with increasing number of pregnancies it should be possible in the near future for the pregnancy registries to take such confounding factors into account and thus make more reliable assessments of the causal relationship between exposure to specific AEDs and teratogenic risks. While awaiting more conclusive results, it appears reasonable to be cautious in prescribing valproate to women considering to become pregnant if other suitable treatment alternatives, and with less teratogenic potential, are available. Any attempt to change treatment should, however, be accomplished well before conception. The importance of maintained seizure control must also be kept in mind, and the woman who needs valproate to control her seizures should not be discouraged from pregnancy, provided that counseling at the best of available knowledge is given.

PMID: 15461670 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Sep;45(9):1158-62.
A novel nonpharmacologic treatment for photosensitive epilepsy: a report of three patients tested with blue cross-polarized glasses.
Kepecs MR, Boro A, Haut S, Kepecs G, Moshe SL.
Department of Neurology, St. Luke's-Roosevelt Hospital, New York, NY 10019, USA. gkepecs@pol.net
PURPOSE: Pharmacotherapy for photosensitive epilepsy is not always effective and is associated with well-recognized toxicities. Nonpharmacologic approaches to the management of photosensitive epilepsy have included the use of sunglasses of various types. Blue lenses have been shown to suppress the photoparoxysmal response more effectively than lenses of other colors with similar overall transmittances. Recently, cross-polarized glasses have shown promise. The axes of polarization of the two lenses of such glasses are perpendicular to one another. We tested the effect of combining the use of blue and cross-polarized lenses in three patients with photosensitive epilepsy. METHODS: We recorded the EEG response to photic stimulation, television screens, and computer monitors in three patients with photosensitive epilepsy. If photoparoxysmal responses were provoked in any of these scenarios, testing was repeated with the patient wearing nonpolarized, parallel-polarized, and blue cross-polarized sunglasses. RESULTS: One of our patients had clinical seizures that were inadequately suppressed with moderate doses of valproate (VPA) but completely suppressed with blue cross-polarized lenses. The second patient's photoparoxysmal response was suppressed by both parallel-polarized and blue cross-polarized glasses, whereas the third patient's photoparoxysmal response was not suppressed by either. CONCLUSIONS: These preliminary data suggest that blue cross-polarized lenses may be useful in the treatment of photosensitive epilepsies and that their efficacy can be predicted in the EEG laboratory. Copyright 2004 International League Against Epilepsy
Publication Types: Case Reports
PMID: 15329083 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Sep;45(9):1141-9.
Phenobarbital for the treatment of epilepsy in the 21st century: a critical review.
Kwan P, Brodie MJ.
Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong.
Summary: Phenobarbital (PB) is the most widely used antiepileptic drug (AED) in the developing world and remains a popular choice in many industrialized countries. Meta-analyses of randomized controlled trials suggest that few differences in efficacy exist between PB and other established AEDs, but its possible deleterious cognitive and behavioral side effects remain a concern in the developed world. In contrast, high degrees of efficacy and tolerability in everyday clinical use have been demonstrated consistently in observational studies in developing countries. We propose that a pragmatic, comprehensive outcomes program be carried out, perhaps under the aegis of the Global Campaign Against Epilepsy, to optimize the conditions of the use of PB, so that more people around the world can benefit from this cost-effective medication and live more fulfilling lives. Copyright 2004 International League Against Epilepsy
Publication Types: Review
PMID: 15329080 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Aug;45(8):928-32.
Evaluating the utility of inpatient video-EEG monitoring.
Ghougassian DF, d'Souza W, Cook MJ, O'Brien TJ.
The Epilepsy Program of the Alfred Hospital, The Department of Clinical Neurosciences, St. Vincent's Hospital Melbourne, Victoria, Australia. daniel@nareg.com.au
PURPOSE: Inpatient video-EEG monitoring (VEM) is widely used for the diagnosis, seizure classification, and presurgical evaluation of patients with seizure disorders. It is resource intensive and relatively expensive, so its utility continues to be debated. Few studies have specifically evaluated the utility of inpatient VEM in altering diagnosis or management of patients with seizure disorders. We sought to assess the proportion of patients for whom the preadmission diagnosis and management were altered after inpatient VEM of patients admitted for diagnostic and presurgical evaluation of seizure disorders. METHODS: Data from a consecutive cohort of patients admitted over a 3-year period to an inpatient VEM unit in a tertiary referral hospital were retrospectively analyzed. The preadmission diagnosis and management by the referring neurologist was compared with the diagnosis and management after the VEM. RESULTS: Of 131 patients, 91 (70%) were admitted for diagnostic evaluation and 39 (30%) for a presurgical workup. Mean evaluative period was 5.6 days. Mean number of seizures recorded was 2.9. No

seizures were recorded in 31% of patients. Interictal EEG showed epileptiform changes in 56 (43%). In 76 (58%), the diagnosis was altered as a result of the VEM, with the greatest change being an increase in the nonepileptic diagnosis group (7% to 31%) and the generalized diagnosis group (5% to 11%). Management was changed after the VEM in 95 (73%). CONCLUSIONS: The results of this study demonstrate that inpatient VEM has a high yield in changing diagnosis and management. Future long-term cost-benefit studies of the management changes resulting from VEM evaluation will aid in further reinforcing its role.
PMID: 15270758 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Jul;45(7):849-54.
Estimated cost of inpatient admissions and outpatient appointments for a population with epilepsy: a record linkage study.
Morgan CL, Kerr MP.
Welsh Centre for Learning Disabilities (Clinical Studies), Department of Psychological Medicine, University of Wales College of Medicine, Heath Park, Cardiff, Wales.
Purpose: This study describes the hospital costs for a population with epilepsy in 1 year (1999). The study was conducted in a defined geographic United Kingdom population of 424,000. METHODS: A register of patients with epilepsy was constructed by using a variety of data sources that had undergone a process of record linkage. Hospital admissions were coded by using Healthcare Resource Group (HRG) and costed by using published National Health Service reference costs. A population of 3,892 people with epilepsy was recorded. RESULTS: The cost of inpatient care for these patients with epilepsy was pound 2,537,386 ($4,135,939), an excess of pound 1,598,909 ($2,606,222) compared with the population as a whole. Of this, pound 320,182 ($521,897) was associated with a primary diagnosis of epilepsy, and pound 679,757 ($1,108,004) was associated with secondary diagnoses. Outpatient expenditure was pound 732,823 ($1,194,501). CONCLUSIONS: This study demonstrates that people with epilepsy use excess resources and that this is not explained solely by either the direct or indirect effects of their epilepsy. These data may help in understanding of the complex issues surrounding the health economics of epilepsy. Copyright 2004 International League Against Epilepsy
PMID: 15230712 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Mar;45(3):289-91.
Cost of epilepsy in patients attending a secondary-level hospital in India.
Krishnan A, Sahariah SU, Kapoor SK.
Comprehensive Rural Health Services Project, Ballabgarh, All India Institute of Medical Sciences, New Delhi, India. crhspaiims@sancharnet.in
The study objective was out to provide an estimate of cost of epilepsy in a secondary level hospital in northern India where a once a week epilepsy clinic is run. Cost data were based on existing information on costs of the hospital and market rates for drugs and investigations. Other necessary information was extracted from patient records for the year 2001. Both direct (consultation fees, cost of investigation, drugs and facility costs) and indirect (traveling and loss of productivity) were estimated. A 25% loss of productivity was assumed based on interviews with the epilepsy patients attending the clinic. There were a total of 184 patients attending the epilepsy clinic during the year 2001. The annual drug cost of epilepsy treatment using phenobarbitone was 11 US dollars. The cost of drugs was in the ratio 1:2:3:4 for phenobarbitone, phenytoin, carbamazepine and sodium valproate. The average annual cost of outpatient treatment of epilepsy was found to be 47 US dollars per patient. The annual cost incurred in emergency and inpatient management was estimated at 810.50 US dollars and 168.30 US dollars for all the patients attending the secondary hospital during the year 2001. The total annual treatment cost for patients attending the hospital was 11,470 US dollars. The annual productivity loss for the same patients was estimated at 20,475 US dollars. Applying these to the estimated 5 million epilepsy patients in India, it comes to about 0.2% of the GNP of the country. As disease cost is much lower than productivity loss, epilepsy treatment is a worthwhile investment for the society. Treating epilepsy patients at primary level using phenobarbitone will increase the treatment coverage and reduce treatment costs. Simultaneous efforts must be made to bring the epilepsy patients on mainstream so as to reduce the productivity loss.
PMID: 15009233 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Feb;45(2):171-8.
Direct cost of medical management of epilepsy among adults in Italy: a prospective cost-of-illness study (EPICOS).

Beghi E, Garattini L, Ricci E, Cornago D, Parazzini F; EPICOS Group.
Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy. beghi@marionegri.it
PURPOSE: To investigate the costs of epilepsy from a nationwide survey comparing adult patients included in different prognostic categories. METHODS: A 12-month prospective observational study was conducted in 15 epilepsy centers from Northern, Central, and Southern Italy. The study population included a random sample of individuals aged 18 years and older with newly diagnosed (ND) epilepsy, seizure remission (R), occasional seizures (OS), active non-drug-resistant (NDR) seizures, drug-resistant (DR) seizures, or surgical candidates (SC). Estimates of the direct costs of care of epilepsy were based on the use of diagnostic examinations, laboratory tests, specialist consultations, hospital admissions, day-hospital days, and drugs, taking the Italian National Health Service perspective. RESULTS: The sample included 631 patients (ND 62, R 158, OS 155, NDR 114, DR 128, and SC 14). The SC group had the highest total cost per patient (3,619 euros) followed by DR (2,190 euros), ND (976 euros), NDR (894 euros), OS (830 euros), and R (561 euros). For each epilepsy group, the main components of the total cost were drugs and hospital admissions. Drug costs increased from the R group to the DR group. The new antiepileptic drugs (AEDs) were the largest part of the cost of treatment. CONCLUSIONS: The costs of epilepsy in referral patients vary significantly according to the time course of the disease and the response to treatment. Hospital admissions and drugs are the major sources of expenditure.
PMID: 14738425 [PubMed - indexed for MEDLINE]

Epilepsia. 2004;45 Suppl 8:17-9.
Initiation of treatment and selection of antiepileptic drugs in childhood epilepsy.
Oka E, Murakami N, Ogino T, Kobayashi K, Ohmori I, Akiyama T, Ito M.
Department of Child Neurology, Okayama University Graduate School of Medicine and Dentistry, Okayama, Japan. okaeiji@md.okayama-u.ac.jp
PURPOSE: A retrospective study was carried out on 53 cases with childhood epilepsy to evaluate the validity of the initial selection of antiepileptic drug (AED). METHODS: We investigated the AEDs selected at the beginning of the treatment from the medical records of 53 untreated cases. A follow-up study was undertaken to evaluate the effects of the AEDs. In the second study, we investigated the AEDs of 10 cases with atypical benign partial epilepsy (ABPE), to clarify whether the initial AEDs selected for rolandic epilepsy were related to the appearance of ABPE. RESULTS: The AEDs used at the initial stage consisted of carbamazepine (CBZ), valproic acid (VPA), phenobarbital (PB), and vitamin B6. The main AEDs were CBZ and VPA for localization-related epilepsy, and VPA for generalized epilepsy. The initial selection of AEDs in 41 (85.4%) of 48 cases treated with AEDs were considered to be correct from the results of follow-up. We could not specify any AEDs that related to the appearance of ABPE. CONCLUSIONS: The selection of AED in this series was considered to be most appropriate. We proposed a criterion to determine whether to begin the AED treatment immediately at the initial seizure.
PMID: 15610189 [PubMed - indexed for MEDLINE]

Epilepsia. 2004;45 Suppl 6:3-12.
Comprehensive care of the epilepsy patient--control, comorbidity, and cost.
Bazil CW.
Comprehensive Epilepsy Center, Columbia University, New York, New York 10032, USA. cwb11@columbia.edu
Traditionally, control of seizures in patients with epilepsy is viewed as the most important clinical outcome. Yet, current antiepileptic drugs (AEDs) do not always achieve this. Around 30-40% of patients remain uncontrolled despite pharmacological intervention. Poor tolerability of AEDs is a large part of the problem and contributes as much to the overall effectiveness of therapy as efficacy. Comorbid conditions are present in many patients, and appropriate management of these can further improve seizure control and quality of life. Patients with epilepsy often experience--among other disorders--neuropsychological effects, migraines, and psychological problems (especially anxiety and depression). Sleep disturbances are also common and have been shown to contribute to the intractability of seizures in some patients. Many anticonvulsant treatments have the potential to improve--or in some cases worsen--these concurrent conditions, and these properties should therefore be considered in the total care of the patient. Finally, the costs of uncontrolled epilepsy are measured not only in terms of direct healthcare-related costs, but also in terms of lost productivity and opportunity. The indirect costs of epilepsy are substantial and account for 70-85% of total disease-related costs. Patients with uncontrolled seizures contribute disproportionately to healthcare costs, reinforcing the need for the development of newer AEDs with

improved profiles of efficacy and tolerability, but with minimal adverse effects on behavior, cognition, and sleep.
Publication Types: Review
PMID: 15315510 [PubMed - indexed for MEDLINE]

Epilepsia. 2004;45 Suppl 5:23-6.
Following catastrophic epilepsy patients from childhood to adulthood.
Glauser TA.
Department of Neurology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229-3039, U.S.A. glauser@cchmc.org
As patients with catastrophic epilepsies move from childhood to adulthood, evolving and innovative therapeutic regimens are often required. However, the goal of providing the best quality of life while minimizing both seizures and side effects remains the same. Clinicians can develop appropriate care plans by being aware of patients' changing needs. Clinical symptoms of the catastrophic epilepsies may change over time; by understanding the natural history of a patient's condition, clinicians can help ease the transition from childhood to adulthood. Additionally, as children with catastrophic epilepsies become adults, medical issues (e.g., medication side effects, tolerance, and dependence) and nonmedical issues (e.g., guardian/caretaker issue, group home applications, and respite care options) must be considered when developing strategies for patient care. Regular assessment of patients, the development of emergency plans, and maintenance of consistency in the delivery of care are also important issues to consider. Finally, a multidisciplinary care plan that incorporates resources from health-care practitioners, social service professionals, and community agencies can be valuable in optimizing treatment for patients with catastrophic epilepsies.
Publication Types: Review
PMID: 15283708 [PubMed - indexed for MEDLINE]

Epilepsia. 2004;45 Suppl 2:15-21.
The treatment of nonepileptic seizures: historical perspectives and future directions.
LaFrance WC Jr, Devinsky O.
Brown Medical School, Rhode Island Hospital, Departments of Psychiatry and Neurology, Providence, Rhode Island 02903, USA. William_LaFrance_Jr@Brown.edu
Nonepileptic seizures (NES) are neuropsychiatric disorders presenting with a combination of neurologic signs and underlying psychological conflicts. For more than a century, the medical community has accumulated data and insights about the phenomenology, epidemiology, risks, comorbidities, and prognosis of NES. However, we have not progressed much beyond anecdotal reports of treatments for NES, and no randomized, controlled trials of treatment for the disorder have been conducted. We review the diagnosis and treatment of NES and suggest directions for future research in these areas.
Publication Types: Historical Article Review
PMID: 15186340 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Jan;45(1):28-34.
Implementation strategies for a Scottish national epilepsy guideline in primary care: results of the Tayside Implementation of Guidelines in Epilepsy Randomized (TIGER) trial.
Davis J, Roberts R, Davidson DL, Norman A, Ogston S, Grimshaw JM, Davey P, Grant J, Ruta D.
Department of Epidemiology & Public Health, University of Dundee, Dundee, Scotland. j.p.l.davis@dundee.ac.uk
PURPOSE: To determine the effectiveness of two dissemination and implementation strategies to implement a national guideline for epilepsy management in primary care settings. METHODS: Three-arm cluster-randomized controlled trial. The participants were general practitioners from 68 practices in Tayside, Scotland, and 1,133 of their patients with self-reported epilepsy treated with antiepileptic medications (AEDs). Practices were randomized blind to a control, intermediate, or intensive intervention. Control: Postal dissemination of a nationally developed clinical guideline. Intermediate intervention: Postal dissemination of the guideline supported by interactive, accredited workshops, and dedicated, structured protocol documents. Intensive intervention: Intermediate intervention plus a nurse specialist who supported and educated practices in the establishment of epilepsy review clinics. The primary outcome was the SF-36 health-related quality-of-life instrument. Secondary measures were a battery of prevalidated epilepsy-specific quality-of-life instruments. These were administered at baseline and after

the intervention phase. Process of care was assessed by case-note review on number of review meetings and counseling sessions for epilepsy before and after the interventions. RESULTS: None of the intervention groups showed any change in the primary or secondary outcome measures or process-of-care measures. CONCLUSIONS: None of the intervention strategies led to improvements in patient quality of life or quality of epilepsy care. Further research is needed to discover why the interventions failed, to identify barriers to adoption of guidelines, and to develop strategies that might improve implementation and uptake in the future.
Publication Types: Clinical Trial Randomized Controlled Trial
PMID: 14692904 [PubMed - indexed for MEDLINE]

Epilepsia. 2004 Jan;45(1):1-3.
Epilepsy guidelines in the real world: the sound of music?
Stephen LJ, Brodie MJ.
Publication Types: Editorial
PMID: 14692900 [PubMed - indexed for MEDLINE]

Epilepsia. 2003 May;44(5):727-31.
ILAE Commission of European Affairs Subcommission on European Guidelines 1998-2001: The provision of epilepsy care across Europe.
Malmgren K, Flink R, Guekht AB, Michelucci R, Neville B, Pedersen B, Pinto F, Stephani U, Ozkara C; ILAE Commission of European Affairs, Subcommission on European Guidelines.
Epilepsy Research Group, Institute of Clinical Neuroscience, Sahlgrenska University Hospital, SE-413 45 Goteborg, Sweden. kristina.malmgren@neuro.gu.se
PURPOSE: To assess the needs and resources available in the provision of basic epilepsy care across Europe. METHODS: A mailed questionnaire was used, the European Epilepsy Services inventory (EESI). The EESI was distributed to all 36 European chapters of the International League Against Epilepsy (ILAE), and answers were obtained from 32, a response rate of 89%. For the purpose of studying trends across Europe, the chapters were divided into a Western, an Eastern, a Central, and a Southern group. RESULTS: The survey results showed that there was a wide range in the number of physicians and specialists involved in epilepsy care across Europe, with a trend toward higher numbers of neurologists, pediatricians, and pediatric neurologists in Eastern Europe. Many different specialties were involved in epilepsy care, and many chapters reported differences in the provision of care across their countries, with less possibility for patients to see a specialist in the least provided areas, where most epilepsy patients were cared for by general practitioners and internists. Problems with high costs of the newer antiepileptic drugs were most pronounced in Eastern Europe. Problems with lack of comprehensive care and of epilepsy specialists, with stigma and social problems, and with insufficient professional education and knowledge about epilepsy were reported all across Europe. CONCLUSIONS: Knowledge about differences in the pattern of provision of epilepsy care and about the main problems encountered by the European ILAE chapters is of importance in the continuing efforts to improve management of epilepsy all over Europe.
Publication Types: Evaluation Studies
PMID: 12752475 [PubMed - indexed for MEDLINE]

Epilepsia. 2003 Mar;44(3):273-5.
Epilepsy control in the 21st century: leave no child behind.
Pal DK.
Publication Types: Editorial
PMID: 12614380 [PubMed - indexed for MEDLINE]

Epilepsia. 2003;44 Suppl 10:27-33.
Prevention of epilepsy after head trauma: do we need new drugs or a new approach?
Benardo LS.
Department of Neurology, State University of New York Downstate Medical Center, Brooklyn, New York 11203, USA. lbenardo@sownstate.edu
Annually in the U.S. about 500,000 head injuries are severe enough to require hospitalization. Past studies of severe head trauma estimate the risk of late seizures, which are synonymous with epilepsy, to be from 26 to 53%. Furthermore, head trauma accounts for 5% of all epilepsy cases and 20% of symptomatic

epilepsy. Although potentially preventable, no effective prophylaxis for posttraumatic epilepsy currently exists. Prior attempts to prevent posttraumatic epileptogenesis used various anticonvulsants, usually given many hours after injury. Generally these studies showed these agents suppressed seizures in the first week after trauma, but had no effect on the incidence of late posttraumatic seizures. Brain trauma engages a rapid excitotoxic process triggered by glutamate release, similar to that seen with ischemia. For ischemic cell damage early and rapid delivery of agents has been a key to rescuing or protecting neurons. Yet, no study has addressed whether the rapidity of drug delivery is critical in the prophylaxis of late seizures. Perhaps excitotoxicity proximate to the brain injury also leads to the neurological deficits seen after severe trauma, initiating and promoting epileptogenesis, and that disrupting this process may prevent epilepsy. While experimental models of epileptogenesis have shown that GABAergic drugs, including valproate (VPA), may be antiepileptogenic, the timing of treatment with putative prophylactic drugs has not been studied. Recent laboratory work explored this issue using an in vitro model of posttraumatic epileptogenesis. The data suggest that a limited time domain exists for VPA to intervene in the epileptogenic process, requiring the earliest possible intervention. We contend that protection from posttraumatic epileptogenesis can be conferred only if agents are given soon after trauma. A pilot study is proposed to begin to translate these findings to explore the feasibility of early VPA delivery to severe head trauma patients admitted to Kings County Hospital Center in Brooklyn, NY, a Level 1 trauma center.
Publication Types: Review
PMID: 14511392 [PubMed - indexed for MEDLINE]

Epilepsia. 2003;44 Suppl 2:27-32.
Chronic management of seizures in the syndromes of idiopathic generalized epilepsy.
Bourgeois BF.
Department of Neurology, Harvard Medical School, Boston, MA 02115, USA. blaise.bourgeois@tch.harvard.edu
As a group, idiopathic generalized epilepsies (IGEs) have the highest rates of complete seizure control with medication. However, there are little evidence-based data to guide drug choice for treatment. Examples of IGE include absence epilepsy, generalized tonic-clonic epilepsy, and juvenile myoclonic epilepsy. Generalized epilepsies seem to be particularly vulnerable to seizure aggravation, and medications that are primarily effective against partial seizures are more commonly involved in seizure aggravation than other medications. A review of current research has shown that only a few medications can control IGE without potentially causing seizure aggravation. Broad-spectrum antiepileptic drugs such as valproate (VPA), lamotrigine, and topiramate are extremely effective at controlling a variety of seizures without causing excessive seizure aggravation. Among these drugs, VPA has the longest clinical experience history and the largest body of published data.
Publication Types: Review
PMID: 12752459 [PubMed - indexed for MEDLINE]

Epilepsia. 2003 Jan;44(1):40-5.
Interlaboratory variability in the quantification of new generation antiepileptic drugs based on external quality assessment data.
Williams J, Bialer M, Johannessen SI, Kramer G, Levy R, Mattson RH, Perucca E, Patsalos PN, Wilson JF.
Subcommission on Therapeutic Drug Monitoring and Pharmacokinetics, ILAE Commission on Therapeutic Strategies, Department of Pharmacology, Therapeutics and Toxicology, University of Wales College of Medicine, Heath Park, Cardiff, Wales. Williamsj10@cf.ac.uk
PURPOSE: To assess interlaboratory variability in the determination of serum levels of new antiepileptic drugs (AEDs). METHODS: Lyophilised serum samples containing clinically relevant concentrations of felbamate (FBM), gabapentin (GBP), lamotrigine (LTG), the monohydroxy derivative of oxcarbazepine (OCBZ; MHD), tiagabine (TGB), topiramate (TPM), and vigabatrin (VGB) were distributed monthly among 70 laboratories participating in the international Heathcontrol External Quality Assessment Scheme (EQAS). Assay results returned over a 15-month period were evaluated for precision and accuracy. RESULTS: The most frequently measured compound was LTG (65), followed by MHD (39), GBP (19), TPM (18), VGB (15), FBM (16), and TGB (8). High-performance liquid chromatography was the most commonly used assay technique for all drugs except for TPM, for which two thirds of laboratories used a commercial immunoassay. For all assay methods combined, precision was <11% for MHD, FBM, TPM, and LTG, close to 15% for GBP and VGB, and as high as 54% for TGB ($p < 0.001$). Mean accuracy values were <10% for all drugs other than TGB, for which measured values were on average 13.9% higher than spiked values, with a high variability around the mean (45%). No differences in precision and accuracy were found between

methods, except for TPM, for which gas chromatography showed poorer accuracy compared with immunoassay and gas chromatography-mass spectrometry. CONCLUSIONS: With the notable exception of TGB, interlaboratory variability in the determination of new AEDs was comparable to that reported with older-generation agents. Poor assay performance is related more to individual operators than to the intrinsic characteristics of the method applied. Participation in an EQAS scheme is recommended to ensure adequate control of assay variability in therapeutic drug monitoring.
Publication Types: Evaluation Studies
PMID: 12581228 [PubMed - indexed for MEDLINE]

Epilepsia. 2003;44 Suppl 1:51-4.
Perspectives from a developed nation.
Redhead K.
St. James Medical Practice, King's Lynn, United Kingdom. keith@redheadk.freeserve.co.uk
Epilepsy is the most common serious neurologic disorder, affecting 350,000 people in the United Kingdom. There are five neurologists per 1,000,000 population, which is better than in India but much lower than in other developed nations. Thus, a patient's day-to-day prescribing, supervision, and support depends on primary care. In the U.K., patients are entitled to register with a general practitioner (GP), who has an average of 1,841 patients. Seventy-eight percent of patients will consult their GP annually. Patients in the U.K. find that GPs are accessible and have good communication skills. There is, however, inadequate time in short consultations to provide the quality of care suggested by the latest review of services for patients with epilepsy (CSAG). This is further complicated by the heterogeneous and stigmatising nature of the condition. An improvement in the process of care in the primary-care setting can result from three important strategies: appropriately trained practice nurses running practice nurse-led clinics; structured management of care, possible because of the unique system of registration, which facilitates audit, prescription monitoring, and recall; and, finally, improved teamwork and communication based on protocols locally agreed upon between primary and secondary care. The future will tell whether these initiatives will improve the outcomes of care.
Publication Types: Review
PMID: 12558834 [PubMed - indexed for MEDLINE]

Epilepsia. 2003;44 Suppl 1:43-7.
Current status of surgery in the management of epilepsy.
Shaefi S, Harkness W.
Department of Neurosurgery, National Hospital for Neurosurgery and Neurology, London, United Kingdom.
PURPOSE: To review systematically the available evidence with regard to the current status of epilepsy surgery in the management of patients with epilepsy. METHODS: A careful search of published literature, including Medline, published reviews, chapters, and cross-references thereof. RESULTS: With medical treatment of epilepsy being unsuccessful in many cases, the importance of surgical approaches cannot be underscored. Early surgery is the treatment of choice for patients with clear-cut mesial temporal sclerosis and results in significant clinical improvement in up to 80% of cases, provided the EEG, neuropsychological, and neuropsychiatric results are in concordance with this approach. In patients with poorly defined, widespread, or dual pathology, however, invasive recordings may be necessary, and while this is performed in major centres, the outcome is rather more variable in this group. Improved surgical techniques, and the use of stereotactic approaches and image guidance procedures, have resulted in surgical resections becoming more selective. With isolated structural lesions such as dysembryoplastic tumours, low-grade astrocytomas, or focal vascular abnormalities, total macroscopic and radiological evidence of lesional excision is associated with excellent seizure-free outcome. The first randomised controlled trial of epilepsy surgery has demonstrated clearly the efficacy of these techniques, and the risk of complications. DISCUSSION: Increasing sophistication of noninvasive presurgical evaluation enables surgical candidates to be identified at an earlier stage and presents a realistic alternative to medical treatment in many cases. The introduction of minimally invasive techniques has had a significant impact on surgical practice and its associated morbidity. The future of epilepsy surgery lies with continued basic science research and its application to clinical medicine.
Publication Types: Review
PMID: 12558832 [PubMed - indexed for MEDLINE]

Epilepsia. 2000 Aug;41(8):1014-9.

Newly diagnosed epilepsy: can nurse specialists help? A randomized controlled trial. Epilepsy Care Evaluation Group.

Ridsdale L, Kwan I, Cryer C.

Division of Clinical Neurosciences, King's College School of Medicine, London, UK. L.Ridsdale@iop.kcl.ac.uk

PURPOSE: To describe a group of people with newly diagnosed epilepsy and to test the effect of an epilepsy nurse specialist on patients' knowledge of epilepsy, satisfaction with the advice provided, and psychological well-being. METHODS: Neurologists in the United Kingdom (U.K.) recruited adults with newly diagnosed epilepsy. Patients were randomized to receive the offer of two appointments with an epilepsy nurse specialist or usual medical care. The main outcome measures were a questionnaire assessing patients' knowledge of epilepsy, the Hospital Anxiety and Depression Scale, and patients' reported satisfaction with the advice and explanations provided on key epilepsy-related topics. RESULTS: Ninety people with new epilepsy completed the trial. At baseline, fewer than half the patients reported having been given enough advice on epilepsy, and there were important differences in patients' knowledge of epilepsy. Lack of a U.K. school-leaving examination pass (General Certificate School Examination) was associated with lower knowledge of epilepsy ($p = 0.03$). At follow-up, the patients randomized to see the nurse specialist were significantly more likely to report that enough advice had been provided on most epilepsy-related topics compared with the control group. There were no significant differences in knowledge of epilepsy scores. However, there were significant differences in the group who, at baseline, had knowledge scores in the lowest quartile; those randomized to the nurse had higher knowledge scores (42.7 vs. 37.2; $p < 0.01$). Compared with doctors, the nurse was highly rated for providing clear explanations. CONCLUSIONS: Patients who have less general education have less knowledge of epilepsy. The introduction of a nurse specialist in epilepsy is associated with a significant increase in patient reports that enough advice has been provided. Nurse intervention appears to help those with the least knowledge of epilepsy improve their knowledge scores.

Publication Types: Clinical Trial Randomized Controlled Trial

PMID: 10961629 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2005 Dec 9; [Epub ahead of print]

Vagus nerve stimulation does not lead to significant changes in body weight in patients with epilepsy.

Koren MS, Holmes MD.

Division of Endocrinology, Department of Medicine, University of Washington, Seattle, WA, USA.

BACKGROUND: Vagus nerve stimulation (VNS) is an FDA-approved treatment for medically intractable epilepsy. The effect of this therapy on body weight is unclear. VNS could cause weight loss by engaging vagal afferents from the gastrointestinal tract mediating satiety. METHODS: We performed a retrospective analysis of body weight changes over a period up to 2 years following VNS implantation. We studied 21 patients (13 M/8 F) 35+/-12 years old, who received a Cyberonics VNS Therapy System for medically intractable epilepsy between April 1998 and May 2004. The mean+/-SD duration of follow-up was 613.1+/-389.1 days. The study had 80% power with a type I error of 0.05 to detect a 5% weight change. Data were analyzed with repeated-measures ANOVA. RESULTS: Weight changes relative to baseline at 30, 60, 120, 360, 480, and 720 days were -0.17+/-2.33, +0.33+/-2.64, -0.32+/-3.56, +1.09+/-5.97, +1.06+/-7.47, and +0.33+/-3.69%, respectively. At all time points these differences failed to reach statistical significance. CONCLUSIONS: Vagus nerve stimulation with parameters typically used in the treatment of patients with epilepsy was not associated with clinically significant weight changes. A well-controlled prospective study is necessary for more precise evaluation of the effect of VNS therapy on body weight.

PMID: 16343997 [PubMed - as supplied by publisher]

Epilepsy Behav. 2005 Dec 5; [Epub ahead of print]

The presence and clinical implications of depression in a community population of adults with epilepsy.

Mensah SA, Beavis JM, Thapar AK, Kerr M.

Academic Department of Neuropsychiatry, Whitchurch Hospital, Cardiff, Wales, UK.

Depression is the most common psychiatric comorbidity in epilepsy, but clinical and other factors associated with this observation and their impact on detection and management of depression in people with epilepsy are poorly understood. This study used a community-based postal questionnaire of primary care-identified people with epilepsy. We were therefore able to explore depression in a nonspecialist care-identified population. Clinical and demographic associative factors were examined. The dependent variable was depression, as defined by a score of 11 or greater on the Hospital Anxiety and Depression

Scale (HADS). The prevalence of depression in our sample (n=499) was found to be 11.2% (95% CI: 8.3-13.7%). Depression was most strongly associated with unemployment. It was also associated with having had a recent seizure and complaints of side effects of antiepileptic medications. Depression was not associated with gender, marital status, or monotherapy or polytherapy antiepileptic medication. The prevalence of depression in epilepsy is greater than in the general population, with no associated female preponderance. Our findings underline important variations in the associative features between depression in the general population and in people with epilepsy, with particular implications for management of this comorbidity.
PMID: 16337435 [PubMed - as supplied by publisher]

Epilepsy Behav. 2005 Dec;7(4):708-14. Epub 2005 Nov 2.
EpiTrack: Tracking cognitive side effects of medication on attention and executive functions in patients with epilepsy.
Lutz MT, Helmstaedter C.
Department of Epileptology, University of Bonn, Bonn, Germany.
RATIONALE: Achievement of maximum seizure control with preservation or even improvement of patient's cognitive capabilities is the major aim of epilepsy therapy. EpiTrack is a brief screening tool for the tracking of cognitive side effects of antiepileptic drugs. Test selection was based on recent studies on the effects of topiramate on cognition and retrospective inspection of results from patients with antiepileptic drug (AED) side effects. METHODS: The 15-minute screening tool comprises six subtests: the Trail-Making Test (parts A and B), a test of response inhibition, digit span backward, written word fluency, and a maze test. These tests were standardized in 220 healthy subjects, 100 of whom were reevaluated after 5.3 months to obtain information on reliability and practice effects. Criterion validity was determined by correlation to other neuropsychological measures. For a first clinical evaluation, the impact of epilepsy (seizures) and medication on EpiTrack scores was evaluated cross-sectionally in 184 consecutive inpatients with chronic epilepsy. RESULTS: According to the normative data, we developed an easy scoring scheme assigning test scores on a 7-point scale. The EpiTrack is suitable for patients between 18 and 60 years of age. Age corrections were included for patients between 40 and 60 years. EpiTrack scores on subtests for both controls and patients were submitted to principal component analysis. VARIMAX rotation yielded a two-factor solution (verbal/visuo-spatial) that accounted for 63.8% of the total variance in controls. In the patient group, only one factor emerged accounting for 54.7% of variance. EpiTrack correlates with global scores of attention (r=0.85) and language (r=0.67) (P's<0.001). At a cutoff score of 25, only 2.7% of the controls were classified as impaired, while impairment was indicated in 48.4% of the patients. The score is sensitive to monthly frequency of complex partial seizures and to number of AEDs. It shows negative cognitive effects of valproate and topiramate given in mono/polytherapy. CONCLUSION: EpiTrack is a promising 15-minute screening tool for the detection and tracking of cognitive side effects of AEDs and adverse effects of seizures in patients with epilepsy. Future application will show its value in prospective follow-up studies on AED side effects.
PMID: 16266826 [PubMed - in process]

Epilepsy Behav. 2005 Dec;7(4):679-86. Epub 2005 Sep 16.
The complexity of treatments for persons with epilepsy.
Yeager KA, Diiorio C, Shafer PO, McCarty F, Letz R, Henry T, Schomer DL.
Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, 1520 Clifton Road, Atlanta, GA 30322, USA.
The purpose of this study was to describe the types of antiepileptic medication regimens and the types of actions required to take medications for a group of patients with epilepsy. The Epilepsy Medication and Treatment Complexity Index (EMTCI) was used to gather information about medications and treatments. The sample of 314 reported on 585 epilepsy medications. The majority (56%) were on more than one treatment. On average, an individual took 1.86 medications per day (range, 1-6) and 7.98 pills per day (range, 1-36 pills). Most medications (54%) were taken twice a day. The most common special instruction was taking different doses on the same day. Taking more than one tablet per dose was the most common administrative action. Data presented here raise interesting areas for further research as well as important clinical implications.
PMID: 16150652 [PubMed - in process]

Epilepsy Behav. 2005 Dec;7(4):664-78. Epub 2005 Sep 2.

I just want to be normal: A qualitative study exploring how children and adolescents view the impact of intractable epilepsy on their quality of life.

Elliott IM, Lach L, Smith ML.

Department of Nursing, Hospital for Sick Children and the University of Toronto, Toronto, Ont., Canada; Division of Neurology, Hospital for Sick Children and the University of Toronto, Toronto, Ont., Canada.

This qualitative study explores how children and adolescents with medically refractory seizures experience the impact of epilepsy on their quality of life (QOL) within the domains of physical, emotional/behavioral, social, and cognitive/academic function. Semi-structured, open-ended interviews were conducted with 49 participants (7-18 years old). These narratives constituted our data source. Analyses involved inductive generation of themes/subthemes and connection of these themes to generate a theoretical representation of their relationships. These themes reflected the negative impact of epilepsy on QOL: physical-excessive fatigue as a barrier to academic and social pursuits; emotional/behavioral-intermittent emotional distress heightened by epilepsy-related factors such as unpredictability of seizures; social-profound social isolation; and cognitive/academic-discontinuous, fragmented learning. Youths perceive seizures as the major barrier to their sense of normalcy, setting them apart from others. Findings provide direction for assessment and evidence for developing or enhancing clinical interventions and community/school-based programs that might mitigate some of these negative experiences.

PMID: 16140594 [PubMed - in process]

Epilepsy Behav. 2005 Nov;7(3):524-30. Epub 2005 Sep 27.

Do video games evoke specific types of epileptic seizures?

Piccioli M, Vigevano F, Buttinelli C, Kasteleijn-Nolst Trenite DG.

Neurology Division, II Faculty of Medicine, University of Rome La Sapienza, and Neurophysiology Section, Bambino Gesu Children's Hospital, IRCCS, Rome, Italy.

We determined whether epileptic clinical manifestations evoked by playing video games (VG) differ from those evoked by intermittent photic stimulation (IPS) or striped patterns (P). We exposed nine children who had TV- and VG-evoked seizures in daily life to 12 VG after standardized photic stimulation and pattern stimulation. Their EEGs were recorded continuously, analyzed, and then correlated with a video of their behavior. Similar types of clinical signs were seen during VG, P, and IPS, but the signs we observed were more subtle during the VG. Eight patients showed a clear lateralization. A new observation was the lowering of the eyelids to a state of half-closed. Our study suggests that the type of visual stimulus provoking a photoparoxysmal response or seizure is not particularly relevant. The children belonged to different epilepsy groups, and our findings add to the discussion on the boundaries of the epilepsy types.

PMID: 16194628 [PubMed - in process]

Epilepsy Behav. 2005 Nov;7(3):472-80. Epub 2005 Sep 2.

A randomized, double-blind, placebo-controlled trial of topiramate in adults with epilepsy and intellectual disability: impact on seizures, severity, and quality of life.

Kerr MP, Baker GA, Brodie MJ.

Welsh Centre for Learning Disabilities, Meridian Court, North Road, Cardiff CF14 3BG, Wales, UK. kerrmp@cardiff.ac.uk

This randomized, double-blind, placebo-controlled UK trial evaluated the effect of topiramate as add-on therapy on seizure frequency, seizure severity, and quality of life in patients with epilepsy and intellectual disability. There were three phases: 4 weeks baseline, 18 weeks titration to 200-400 mg topiramate/day (adults) or 5-9 mg/kg/day (children), 12 weeks maintenance. Recruitment was low (88/120); analyses were underpowered. Seizure frequency varied enormously (median 17.7, maximum 1706.2). There was no significant difference in reduction in mean total seizure frequency or number of responders between the groups. Topiramate reduced seizure frequency by >30% from baseline (placebo 1%); post hoc analyses showed a trend toward significance (R ratio, P=0.052). There were no significant differences between the groups with respect to mean seizure severity or other outcome measures. Topiramate was generally well tolerated; body weight (P=0.015) and systolic blood pressure (P=0.043) were reduced. The study suggests that topiramate reduces seizure frequency in patients with epilepsy and intellectual disability without the added burden of behavior effects, and was potentially advantageous to physical well-being.

PMID: 16140593 [PubMed - in process]

Epilepsy Behav. 2005 Nov;7(3):486-90. Epub 2005 Aug 15.

Race/ethnicity: a predictor of temporal lobe epilepsy surgery outcome?

Burneo JG, Knowlton RC, Martin R, Faught RE, Kuzniecky RI.

Epilepsy Programme, University of Western Ontario, London, Canada. jburneo2@uwo.ca

PURPOSE: The success of epilepsy surgery in temporal lobe epilepsy reaches a 64% rate of seizure freedom, based on a randomized control trial. Observational studies from epilepsy centers worldwide indicate seizure freedom rates up to 93% when the etiology is unilateral hippocampal sclerosis. Several risk factors are attributed to the recurrence of seizures following the surgical procedure. Nonetheless, whether race influences the outcome of temporal lobe surgery is unknown. The purpose of this study was to evaluate if race plays a role in outcome following surgery. METHODS: Data were obtained from the discharge database of the University of Alabama at Birmingham video/EEG monitoring unit, between 1998 and 2003, as well as the clinical charts. Seizure recurrence was evaluated 1 year following surgery. The sample consisted of all patients with a primary diagnosis of mesial temporal sclerosis (MTS) who underwent anterior temporal lobectomy. Multiple logistic regression analysis was used to model the presence of seizure recurrence after anterior temporal lobectomy for MTS. Two sets of logistic regression models were estimated to generate odds ratios (ORs) for seizure recurrence after an anterior temporal lobectomy for African-Americans or other possible ethnic/racial group present relative to non-Hispanic Caucasians. The first model incorporated only ethnicity as the independent variable and generated unadjusted ORs for seizure recurrence following the surgical procedure. The second set included the independent variables: duration of epilepsy, history of febrile seizures, lateralization of epileptogenic focus, handedness, and age. RESULTS: Seventy patients underwent surgical treatment and all of them had pathologic confirmation of MTS. Follow-up information for six was not available. Analysis of the remaining 64 patients revealed that African-Americans were more likely than non-Hispanic Caucasians to have seizure recurrence after surgery (OR=2.1, 95% CI=0.6-8.0). After potential confounders (duration of epilepsy, history of febrile seizures, lateralization of epileptogenic focus, handedness, and age) were controlled, this finding did not change (OR=1.7, 95% CI=0.3-10.7). CONCLUSION: Our data suggest that race may be an important factor related to seizure outcome following temporal lobectomy.

PMID: 16103016 [PubMed - in process]

Epilepsy Behav. 2005 Nov;7(3):481-5. Epub 2005 Aug 10.

Sleep disturbances, socioeconomic status, and seizure control as main predictors of quality of life in epilepsy.

Alanis-Guevara I, Pena E, Corona T, Lopez-Ayala T, Lopez-Meza E, Lopez-Gomez M.

Department of Neurology, National Institute of Neurology and Neurosurgery of Mexico, Mexico City, Mexico.

Improving quality of life is the most important goal for patients with epilepsy. To recognize the factors associated with quality of life in patients with epilepsy in Mexico, we performed a cross-sectional survey using the Quality of Life in Epilepsy 31 (QOLIE-31) inventory to assess the quality of life of 401 adult patients with epilepsy at the National Institute of Neurology and Neurosurgery of Mexico. Clinical and demographical data were collected. Multiple regression was used to determine which factors affected quality of life in our patients. The variables that most strongly predicted a lower QOLIE-31 total score after multiple regression were sleep disorders (P<0.001), socioeconomic status (P<0.001), female gender (P=0.002), and high seizure frequency (P=0.001). In our study, neither depression nor time of evolution of epilepsy had significant influence on QOLIE-31 scores.

PMID: 16098815 [PubMed - in process]

Epilepsy Behav. 2005 Nov;7(3):451-7. Epub 2005 Aug 8.

A structured, nurse-led intervention program improves quality of life in patients with epilepsy: a randomized, controlled trial.

Helde G, Bovim G, Brathen G, Brodtkorb E.

Department of Neuroscience, Faculty of Medicine, NTNU, N-7006 Trondheim, Norway. grethe.helde@ntnu.no

We tested the hypothesis that structured epilepsy nursing improves quality of life (QOL). One hundred fourteen adult patients with uncontrolled epilepsy were randomly assigned to either an intervention group or a control group. The intervention group was offered an interactive, 1-day group education program followed by extended nurse follow-up and counseling. The nurse was present at as many outpatient

consultations as possible and performed repeated consultations by telephone. All patients completed the QOLIE-89 before randomization and after 2 years. QOL was significantly improved from inclusion to completion of study in the intervention group (P=0.019), mainly in the subitems for Health Discouragement (P=0.01), Medication Effects (P=0.035), and Physical Role Limitations (P=0.05). To our knowledge, this is the first study to demonstrate a significant effect of a structured nurse-led intervention program in QOL of patients with epilepsy.
PMID: 16087407 [PubMed - in process]

Epilepsy Behav. 2005 Oct 24; [Epub ahead of print]
Social cognition and epilepsy surgery.
Kirsch HE.
UCSF Epilepsy Center, Department of Neurology, University of California, San Francisco, 400 Parnassus Avenue, San Francisco, CA 94143-0138, USA.
Human social behavior depends on a set of perceptive, mnemonic, and interpretive abilities that together may be termed social cognition. Lesion and functional imaging studies of social cognitive functions implicate the temporal lobes (in particular, the nondominant temporal lobe) and mesial temporal structures as critical at the front end of social cognitive processes. The frontal lobes, in turn, function to interpret and to modulate these processes via top-down control. Damage to frontal regions is associated with specific derangements in social behavior. Chronic focal-onset epilepsy and its surgical treatment commonly affect these neuroanatomic regions and might therefore impact social function. Postoperative social function helps determine quality of life for both patients and families. There is some evidence that resective seizure surgery affects social cognition, but there are significant weaknesses in our current knowledge that can be overcome with comprehensive longitudinal research.
PMID: 16253567 [PubMed - as supplied by publisher]

Epilepsy Behav. 2005 Oct 24; [Epub ahead of print]
Risk factors for psychogenic nonepileptic seizures in children and adolescents with epilepsy.
Vincentiis S, Valente KD, Thome-Souza S, Kuczinsky E, Fiore LA, Negrao N.
Laboratory of Clinical Neurophysiology, Institute and Department of Psychiatry, University of Sao Paulo, Sao Paulo, Brazil.
There is evidence that psychogenic nonepileptic seizures (PNES) remain underdiagnosed, especially in children and adolescents. Diagnosis of such events is even more difficult in patients that do have epilepsy, leading to delayed diagnosis and treatment and, consequently, iatrogenic complications. This study aimed to evaluate possible risk factors in children with epilepsy who had PNES. Seizures and epileptic syndromes were classified according to International League Against Epilepsy guidelines. Patients were evaluated with a structured psychiatric anamnesis and classified according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; Classification of Mental and Behavioral Disorders: Diagnostic Criteria for Research; and Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological Version. Risk factors such as head trauma, physical, sexual and psychological abuse, and psychiatric diagnoses, among others, were investigated. Family history of epilepsy and psychiatric illness were detected by review of medical records and/or follow-up interviews. Gender was not a predictive factor, and although older children had a higher risk for PNES, younger children also presented truly psychogenic events mimicking epileptic seizures. The most common associated psychiatric diagnosis was depression. Family histories for epilepsy and psychiatric illness were a frequent finding. An inadequate family environment was more common than sexual or physical abuse. Current knowledge obtained from adults with PNES has been used to understand children with PNES. However, this study of children with epilepsy revealed some similarities and many differences. These features may help to identify predictive factors in a population in need of adequate diagnosis of and therapy for this long-lasting pathology.
PMID: 16253566 [PubMed - as supplied by publisher]

Epilepsy Behav. 2005 Oct 21; [Epub ahead of print]
Psychosocial intervention in pediatric epilepsy: A critique of the literature.
Wagner JL, Smith G.
Division of Developmental Pediatrics, Medical University of South Carolina, Charleston, SC, USA; Division of Pediatric Neurosciences, Medical University of South Carolina, Charleston, SC, USA.
It is well documented that youth with epilepsy are at increased risk for psychopathology. The current literature supports a biopsychosocial model of adjustment to pediatric epilepsy, and implies that

interventions focused on changing youths' cognitions and illness appraisals, as well as enhancing their coping skills, may be an effective treatment for psychosocial maladjustment associated with pediatric epilepsy. The purpose of this article is to review and critique the extant literature covering psychological interventions that target psychosocial adjustment in youth with seizures followed by those aimed at reducing seizure frequency. For health care professionals treating epilepsy, establishing evidence-based interventions that target psychiatric difficulties in youth with epilepsy should be paramount in the promotion of optimal epilepsy outcomes. Thus, future recommendations for clinical endeavors and research proposals are also presented.
PMID: 16246636 [PubMed - as supplied by publisher]

Epilepsy Behav. 2005 Aug;7(1):98-105.
Patient and physician reactions to generic antiepileptic substitution in the treatment of epilepsy.
Haskins LS, Tomaszewski KJ, Crawford P.
Harris Interactive Health Care Division, Rochester, NY, USA.
BACKGROUND: The clinical and economic consequences of generic antiepileptic drug (AED) substitution are not yet fully understood. This article provides a broad perspective of generic AED substitution in five countries. METHODS: Two cross-sectional telephone-based surveys (patient and physician) were undertaken in Canada, the United Kingdom, France, Germany, and Spain. A total of 1409 interviews, 974 patients and 435 physicians, were completed. RESULTS: Across all countries studied, patients and physicians alike have elevated concerns about the safety and efficacy of generic AEDs as compared with drugs for acute care. CONCLUSION: There is an opposition to generic substitution by both patients and physicians, especially with concern over increased breakthrough seizure risk. Further evidence is required to understand how costs and effects of generic AED substitution affect patient welfare.
Publication Types: Clinical Trial Multicenter Study
PMID: 15961350 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2005 Aug;7(1):123-6.
Effect of comorbidities on medical care use and cost among refractory patients with partial seizure disorder.
Lee WC, Arcona S, Thomas SK, Wang Q, Hoffmann MS, Pashos CL.
HERQuLES, Abt Associates Inc., 4800 Montgomery Lane, Suite 600, Bethesda, MD, USA. WonChan_Lee@abtassoc.com
PURPOSE: The goal of this work was to assess the effect of comorbidities on medical care use and costs among patients with partial seizure disorder who are also refractory to initial antiepileptic drug (AED) monotherapy. METHODS: Retrospective data from the PharMetrics managed care claims database were collected for adult patients treated with AED monotherapy between January 1, 2000 and March 31, 2002. The associations of comorbidity, specifically the Charlson Comorbidity Index (CCI) and incidence of specific comorbid conditions, with total costs and with hospitalization were analyzed via econometric analysis and logistic regression. RESULTS: Five hundred forty-nine patients were identified and analyzed. The odds of hospitalization were 3.7 times greater among patients with a CCI1, than for patients without comorbidities (OR=3.7, 95% CI=1.7-7.9), while treatment costs for all medical care were 136% higher (P<0.05). Depression had the largest marginal effect on costs and on the likelihood of hospitalization. CONCLUSIONS: For patients refractory to initial AED monotherapy, the presence of comorbidities, especially depression, is associated with a substantial increase in medical care use and costs.
PMID: 15939673 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2005 Jun;6(4):520-8.
What is effective treatment of depression in people with epilepsy?
Barry JJ, Jones JE.
Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305-1008, USA. jbarry@stanford.edu
Publication Types: Review
PMID: 15876556 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2005 Feb;6(1):59-62.
The use of complementary medicines and alternative practitioners in a cohort of patients with epilepsy.
Easterford K, Clough P, Comish S, Lawton L, Duncan S.
Department of Neurology, Greater Manchester Neurosciences Centre, Hope Hospital, Stott Lane, Salford M6 8 HD, UK.
Complementary and alternative medicines (CAMs) are increasingly used by patients in the Western world. Some of the most popular herbal remedies are known to act on the cytochrome P450 system, with potential effects on antiepileptic drug (AED) levels. Few studies have explored their use in people with epilepsy. We surveyed 400 patients attending epilepsy clinics in Greater Manchester. Thirty-four percent of our patients had used or were using CAMs; the majority had not told their doctor. Use of CAMs was not predicted by age, sex, seizure frequency, number of AEDs, or dissatisfaction with conventional medicine. Patients who had gone onto higher education were significantly ($P < 0.05$) more likely to have used or be using CAMs. The majority of patients did not use CAMs for their epilepsy but for general health purposes. Most patients stated that CAMs had little or no effect on seizure frequency or severity.
Publication Types: Clinical Trial
PMID: 15652735 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2004 Dec;5(6):802-3.
Phenobarbital: a drug for the 21st century?
Brodie MJ, Kwan P.
Publication Types: Editorial
PMID: 15582826 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2004 Jun;5(3):337-42.
The impact of comorbid depression on health resource utilization in a community sample of people with epilepsy.
Cramer JA, Blum D, Fanning K, Reed M; Epilepsy Impact Project Group.
Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA. joyce.cramer@yale.edu
This study assessed the impact of comorbid depression on health care utilization and health care coverage by people with epilepsy in US communities using a postal survey questionnaire. People with untreated depression used significantly more health resources of all types assessed with and without adjustment for seizure type, seizure recency, and days with epilepsy symptoms. The number of visits to medical doctors and psychiatrists differed significantly among people with no ($N = 443$), mild to moderate ($N = 58$), and severe ($N = 148$) symptoms of depression who were not receiving antidepressant treatment (all $P < 0.001$). People with current symptoms treated with antidepressants had more medical visits than people with no current symptoms ($P=0.016$). People with current symptoms but not treated for depression had more medical and psychiatric visits than people with no current symptoms (both $P = 0.001$). These data highlight the impact of comorbid depression on health care utilization by people with epilepsy.
PMID: 15145303 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2004 Jun;5(3):277-85.
Magnetoencephalography: an investigational tool or a routine clinical technique?
Parra J, Kalitzin SN, da Silva FH.
Dutch Epilepsy Clinics Foundation, "Meer en Bosch," Heemstede, The Netherlands. jparra@sein.nl
Magnetoencephalography (MEG) is a relatively novel noninvasive technique, with a much shorter history than EEG, that conveys neurophysiological information complementary to that provided by EEG, with high temporal and spatial resolution. Despite its a priori, highly competitive profile, the role of MEG in the clinical setting is still controversial. We briefly review the major obstacles MEG faces in becoming a routine clinical test and the different strategies needed to bypass them. The high cost and complexity associated with MEG equipment are powerful hindrances to wide acceptance of this relatively new technique in clinical practice. The most straightforward advantage is based on the relative facility of MEG recordings in the process of source localization, which also carries some degree of uncertainty, thus partly explaining why the development of clinical applications of MEG has been so slow. Obviously, a decrease in the cost and the elaboration of semiautomatic protocols that could reduce the complexity of the studies

and favor the development of consensual strategies, as well as a major effort on the part of clinicians to identify clinical issues where MEG could be decisive, would be most welcome.
Publication Types: Review
PMID: 15145295 [PubMed - indexed for MEDLINE]

Epilepsy Behav. 2004 Feb;5(1):81-7.
Epilepsy surgery: patient-perceived long-term costs and benefits.
Reid K, Herbert A, Baker GA.
University Department of Neurosciences, The Centre for Research and Education, Lower Lane, Fazakerley, Liverpool L9 7LJ, UK.
PURPOSE: The goal of this study was to assess the patient-perceived costs and benefits associated with the longer-term outcomes of epilepsy surgery in patients who underwent anterior temporal lobectomy or selective amygdalohippocampectomy. METHODS: Surgery patients who were assessed in 1997 were reassessed in 2003. Demographic, clinical, and psychosocial details were collected using a validated self-completion questionnaire. Data were collected from 67 patients who had undergone surgery. RESULTS: Forty-five percent were seizure-free. There were significant differences (P<0.001) between the seizure-free (SF) and continuous seizure (CS) groups with respect to anxiety, depression, impact of epilepsy, self-esteem, mastery, stigma, affect balance, self-reported health, and quality of life. More SF patients were also employed and driving (P<0.001). Despite these differences there were no differences for regret over surgery but there were differences for satisfaction and success ratings. CONCLUSIONS: Patients who were not SF, in the longer term, had little regret undergoing surgery but were less likely to be satisfied and had a poorer psychosocial profile.
PMID: 14751211 [PubMed - indexed for MEDLINE]

Epilepsy Res. 2005 Dec 2; [Epub ahead of print]
Levetiracetam: An improvement of attention and of oral fluency in patients with partial epilepsy.
Piazzini A, Chifari R, Canevini MP, Turner K, Fontana SP, Canger R.
Regional Epilepsy Center, S. Paolo Hospital, University of Milan, Via A. Di Rudini 8, 20142 Milan, Italy.
PURPOSE: The aim of the present study is to verify whether patients with partial epilepsy receiving levetiracetam (LEV) as an add-on treatment show an improvement in cognitive function. METHODS: A neuropsychological battery of tests was administered to 35 patients with partial epilepsy before the assumption of LEV and after the achievement of the therapeutical dose of this drug, 7 weeks later. A control group of 35 patients with partial epilepsy was administered the same battery of tests twice, at the same time interval as the LEV group. The controls were administered the same pharmacological treatment, which did not include LEV in either of the two sessions. RESULTS: We found a statistically significant improvement in cognitive functioning, i.e. in attention and oral fluency, in patients receiving LEV compared to the controls. The responders to LEV were 28.6%. CONCLUSIONS: LEV as an add-on therapy improved attention level and verbal fluency in our sample of patients with partial epilepsy. It is reasonable to assume that LEV may influence the metabolism of attention and of language area, as already suggested for piracetam (PIR) from which LEV derives. Further studies are needed to confirm these findings.
PMID: 16332430 [PubMed - as supplied by publisher]

Epilepsy Res. 2005 Dec;67(3):143-51. Epub 2005 Nov 8.
Cost-effectiveness of add-on lamotrigine therapy in clinical practice.
Knoester PD, Boendermaker AJ, Egberts AC, Hekster YA, Keyser A, Severens JL, Renier WO, Deckers CL.
Department of Clinical Pharmacy, University Medical Centre Nijmegen, P.O. Box 9101, 6500 HB, Nijmegen, the Netherlands.
OBJECTIVE: This retrospective study addresses the cost-effectiveness of add-on therapy with lamotrigine in clinical practice. METHODS: Two years' observational data of 165 patients were used. Seizure frequency, adverse effects and direct medical costs were recorded for the year before and the year after the start of lamotrigine add-on therapy. Therapy effectiveness was measured by: (1) reduction in seizure frequency and (2) retention time. The incremental cost-effectiveness ratio expressed the direct medical cost per patient treated effectively with lamotrigine. RESULTS: The cost of medication was 492 (95% CI: 399-583) higher after the start of lamotrigine therapy. The extra cost of lamotrigine therapy (622) was partly offset by a reduction of the cost of co-medication (-130; 95% CI: -210 to -50). Overall, the total medical cost was 453 higher in the first year of lamotrigine therapy than in the year before the start of

lamotrigine. Lamotrigine was effective in 47% of all the patients, making the resultant incremental cost-effectiveness ratio 954 per year. DISCUSSION: Add-on therapy of lamotrigine for patients with uncontrolled epilepsy offers improved health outcomes. Lamotrigine therapy is associated with increased cost (453) and an annual incremental cost-effectiveness ratio of 954. These data, together with utility data published in the literature, support the notion that lamotrigine should be considered as an add-on therapy in for patients with refractory epilepsy.
PMID: 16288850 [PubMed - in process]

Epilepsy Res. 2005 Dec;67(3):89-99. Epub 2005 Oct 26.
Predicting seizure frequency after epilepsy surgery.
Khoury JS, Winokur RS, Tracy JI, Sperling MR.
Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107, USA.
OBJECTIVE: To identify clinical features related to seizure frequency after epilepsy surgery in patients with recurrent seizures. BACKGROUND: No studies have examined the differences between patients who have rare seizures and patients who experience frequent seizures after epilepsy surgery. Since seizure frequency correlates with morbidity and quality of life, it is desirable to know which preoperative clinical features predict postoperative seizure frequency. METHODS: Patients with recurrent seizures were placed in two categories: rare postoperative seizures (</=2 per year) and frequent postoperative seizures (>/=12 per year) using seizure frequency in the second postoperative year. Variables included preoperative seizure frequency, age of first risk, age at first seizure, epilepsy duration, age at surgery, history of febrile convulsions, tonic-clonic seizures, status epilepticus, or family history, IQ, magnetic resonance imaging (MRI), and positron emission tomography (PET). Variables were analyzed using non-parametric tests to assess relationship to postoperative seizure frequency. RESULTS: Of 475 patients who had epilepsy surgery, 111 had rare or frequent seizures in the second postoperative year. After anterior temporal lobectomy (ATL), age of first risk</=5 years and presence of mesial temporal sclerosis on MRI were associated with rare seizures (66% of patients), whereas lack of these risk factors was associated with frequent seizures (75% of patients) ($p<0.03$). For non-ATL operations, preoperative seizure frequency of >/=20seizures per month was associated with frequent postoperative seizures ($p=0.03$). No other variables influenced outcome. CONCLUSIONS: Some preoperative clinical features correlate with postoperative seizure frequency in patients with recurrent seizures after epilepsy surgery. This has implications for the surgical decision making process and early postoperative management.
PMID: 16256308 [PubMed - in process]

Epilepsy Res. 2005 Nov 28; [Epub ahead of print]
Zonisamide in the management of epilepsy-Japanese experience.
Ohtahara S.
Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Shikata-cho 2-5-1, Okayama, Japan.
Zonisamide (Zonegran((R))), a novel antiepileptic drug (AED) approved in Europe for the adjunctive treatment of refractory partial seizures in adults, has undergone extensive evaluation in pre- and post-marketing double-blind and open-label studies in Japan (where zonisamide is used widely to treat partial and generalised seizures in adults and children). These data indicate that the clinical benefit of zonisamide extends across a range of seizure types and patient ages. In an analysis based on a mixture of controlled and open studies in adults and children with partial seizures, 51-57% responded to zonisamide treatment (achieving >/=50% reduction in baseline seizure frequency). Efficacy extends across a range of generalised seizures and 22-66% of adults and children experiencing tonic-clonic, tonic, clonic, myoclonic or absence seizures responded to treatment. Even greater responder rates have been reported when zonisamide was used as monotherapy for partial seizures and generalised seizures in patients refractory to other AEDs or with newly diagnosed epilepsy. Zonisamide is also efficacious in paediatric epilepsy syndromes, including Lennox-Gastaut Syndrome, West Syndrome and Ohtahara Syndrome. Across the spectrum of epilepsy syndromes studied, zonisamide is well-tolerated with a low incidence of adverse events, which are generally mild and CNS-related. These data indicate that zonisamide represents a valuable broad-spectrum option for the treatment of epilepsy.
PMID: 16321507 [PubMed - as supplied by publisher]

Epilepsy Res. 2005 Nov 26; [Epub ahead of print]
Zonisamide as adjunctive therapy for refractory partial seizures.

Brodie MJ.
Epilepsy Unit, Western Infirmary, Glasgow, Scotland G11 6NT, UK.
Zonisamide (Zonegran((R))) has been used extensively worldwide (>2 million patient-years experience) for the effective treatment of a broad range of epilepsy indications. Four randomised, placebo-controlled trials (duration </=6 months) in the United States and Europe (848 patients in total) have shown doses of zonisamide >/=300mg/day to be efficacious in treating refractory partial seizures in adults. In a pivotal European study, zonisamide 500mg/day was significantly superior to placebo in reducing the frequency of complex partial seizures (-51% versus -16%), all partial seizures and all seizures, with dose-dependent benefit provided over a 100-500mg/day dose range. Supporting trials have confirmed significant increases in reduction in median seizure frequency (up to 41%) and responder rates (35-42%) compared with placebo following zonisamide 400-600mg/day, enabling 20-27% of patients to attain >/=75% reduction in seizure frequency. Pooled data from all four placebo-controlled trials demonstrate an excellent tolerability and safety profile; adverse events are generally of mild-moderate severity with few leading to discontinuation, and incidence of serious adverse events is comparable to placebo. These data support the use of zonisamide in combination with commonly used antiepileptic drugs to provide efficacious and well-tolerated treatment for patients with refractory partial seizures.
PMID: 16316744 [PubMed - as supplied by publisher]

Epilepsy Res. 2005 Aug-Sep;66(1-3):129-35.
The diagnostic value of initial video-EEG monitoring in children--review of 1000 cases.
Asano E, Pawlak C, Shah A, Shah J, Luat AF, Ahn-Ewing J, Chugani HT.
Department of Pediatrics, Children's Hospital of Michigan, Detroit Medical Center, Wayne State University, Detroit, MI 48201, USA. eishi@pet.wayne.edu
OBJECTIVE: We retrospectively reviewed the clinical utility of initial video-EEG monitoring in a series of 1000 children suspected of epileptic disorders. METHODS: The ages of patients (523 boys and 477 girls) ranged from 1 month to 17 years (median age: 7 years). The mean length of stay was 1.5 days (range: 1-10 days). Outcomes were classified as: 'useful-epileptic' (successful classification of epilepsy), 'useful-nonepileptic' (demonstration of nonepileptic habitual events), 'uneventful' (normal EEG without habitual events captured), and 'inconclusive' (inability to clarify the nature of habitual events with abnormal interictal EEG findings). RESULTS: A total of 315 studies were considered 'useful-epileptic'; 219 'useful-nonepileptic'; 224 'uneventful'; 242 'inconclusive'. Longer monitoring was associated with higher rate of a study classified as 'useful-epileptic' in all age groups (Chi square test: p<0.001). In addition, longer monitoring was associated with lower rate of a study classified as 'inconclusive' in adolescences (p<0.001). Approximately half of the children with successful classification of epilepsy were assigned a specific diagnosis of epilepsy syndrome according to the International League Against Epilepsy (ILAE) classification. We found only 22 children with ictal EEG showing a seizure onset purely originating from a unilateral temporal region. CONCLUSION: Video-EEG monitoring may fail to capture habitual episodes. To maximize the utility of studies in the future, a video-EEG monitoring longer than 3 days should be considered in selected children such as adolescences with habitual events occurring on a less than daily basis. We recognize a reasonable clinical utility of the current ILAE classification in the present study. It may not be common to identify children with pure unilateral temporal lobe epilepsy solely based on video-EEG monitoring.
Publication Types: Review
PMID: 16157474 [PubMed - in process]

Epilepsy Res. 2005 Aug-Sep;66(1-3):23-44.
Epilepsy and quality of life in adults: a review of instruments.
Leone MA, Beghi E, Righini C, Apolone G, Mosconi P.
Clinica Neurologica, Ospedale Maggiore della Carita, Novara, Italy. maurizio.leone@maggioreosp.novara.it
The aim of this report is to describe the state of the art of quality of life (QoL) instruments used for adults with epilepsy and to help those in the field to identify, select, and use the instruments most suitable for their purposes. We searched Medline and the Cochrane Database for articles in English, German, French, Spanish, Portuguese and Italian published by the end of 2002. Electronic retrieval was completed by hand-search. The final list included 203 articles reporting 205 studies. There were 62 validation studies and 143 clinical studies, including 7 population studies, 45 "pure" observational, 37 observational with aspects of validation and 54 experimental (38 randomized clinical trials and 16 non-randomized or non-controlled trials). Twenty-four generic and 21 specific QoL instruments were used. Eight were used in more than 10 studies, while 21 were used only once; 7/24 generic and 19/21 specific questionnaires were validated for

epilepsy. The different domains considered in the 26 questionnaires specifically validated for epilepsy are listed. We classified questionnaires according to three aspects: validation, diffusion of use, and specificity of domains. Questionnaires covering all three aspects (WPSI, ESI-55, QOLIE-89, QOLIE-31, QOLIE-10, Liverpool Batteries) should be preferred when planning a QoL study in epilepsy. However, those covering only two aspects (SF-36, SEALS, EPSES, EOS, PESOS, QOLAS) could also be useful in selected situations or may become a first-choice instrument in the future, after more widespread use or complete validation. All the other instruments should at present be considered only for second choice.
Publication Types: Review
PMID: 16154322 [PubMed - in process]

Epilepsy Res. 2005 Aug-Sep;66(1-3):63-74.
Understanding the burden of epilepsy in Latin America: a systematic review of its prevalence and incidence.
Burneo JG, Tellez-Zenteno J, Wiebe S.
Epilepsy Programme, Department of Clinical Neurological Sciences, London Health Sciences Center, University of Western Ontario, 339 Windermere Road, London, Ont., Canada N6A 5A5. jburneo2@uwo.ca
RATIONALE: Epilepsy is the most common serious neurological condition in the world, and an important cause of mortality and disability in developing countries. Because epidemiological and clinical characteristics of epilepsy vary by region, it is important to know the peculiarities of epilepsy in this area of the American continent. METHODS: We searched MEDLINE, IMBIOMED, and LILACS (The Latin-American and Caribbean biomedical database) to identify community-based studies reporting on the prevalence and incidence of epilepsy in Latin America. Studies were included if a definition of epilepsy was given, if data were obtained through standardized questionnaires and if raw population numbers were available for data confirmation. RESULTS: Thirty-three studies fulfilled eligibility criteria, 32 reported on prevalence and three on incidence of epilepsy. The median lifetime prevalence in all countries was 17.8 (range 6-43.2) per 1000 people, and the range for incidence was 77.7-190 per 100,000 people per year. There were no differences between rural and urban areas, by gender, age-group (children, adult, all ages), ascertainment method, or year of study. CONCLUSIONS: Measuring the global burden of disease in Latin America requires adequate epidemiological information. This systematic review of epidemiological studies identifies higher prevalence and incidence rates of epilepsy in the general population of Latin America than in northern hemisphere countries. The remarkable heterogeneity found between and even within countries, could be explained by several factors, importantly, socioeconomic and methodological aspects.
Publication Types: Review
PMID: 16125900 [PubMed - in process]

Epilepsy Res. 2005 Aug-Sep;66(1-3):195-8.
Inter-rater reliability of the EEG reading in patients with childhood idiopathic epilepsy.
Piccinelli P, Viri M, Zucca C, Borgatti R, Romeo A, Giordano L, Balottin U, Beghi E.
Child Neuropsychiatric Unit, University of Insubria, Macchi Foundation Hospital, Varese, Italy.
The level of agreement in the interpretation of EEG records by different experienced readers working in three child neurology tertiary centers has been evaluated. EEG recordings randomly chosen from patients with idiopathic epilepsy were included. Optimal or suboptimal agreement was found for presence of ictal and interictal discharges. Contrary to ictal discharges, the distribution and location of interictal discharges was not unanimously interpreted and agreement was unsatisfactory when assessing the background activity.
Publication Types: Multicenter Study
PMID: 16118044 [PubMed - in process]

Epilepsy Res. 2005 May;64(3):161-6.
Blood homocysteine, folate and vitamin B-12 concentrations in patients with epilepsy receiving lamotrigine or sodium valproate for initial monotherapy.
Gidal BE, Tamura T, Hammer A, Vuong A.
School of Pharmacy and Department of Neurology, University of Wisconsin, 777 Highland Ave., Madison, WI 53705, USA. begidal@pharmacy.wisc.edu
To evaluate whether the administration of lamotrigine (LTG) or valproate (VPA) changes concentrations of plasma total homocysteine (tHcy), plasma and red-cell folate and plasma Vitamin B-12, we measured these indices in a total of 20 patients with epilepsy before and after a 32-week period of monotherapy of

LTG or VPA. We found that the 32-week administration of a mean daily dose of 250mg LTG had no significant effect on any of the blood indices. On the other hand, the administration of a mean daily dose of 2070mg of VPA resulted in a 57% increase in plasma Vitamin B-12 concentrations over the baseline value and a 27% decline in plasma tHcy concentrations, although the mechanisms of such changes are unknown. Our data indicate that hyperhomocysteinemia may not be a serious clinical problem among patients with epilepsy, who receive either LTG or VPA.
PMID: 15936175 [PubMed - in process]

Epilepsy Res. 2003 May;54(2-3):131-40.
The costs of epilepsy in three different populations of patients with epilepsy.
Kotsopoulos IA, Evers SM, Ament AJ, Kessels FG, de Krom MC, Twellaar M, Metsemakers JF, Knottnerus AJ.
Department of Neurology, Maastricht University Hospital, P.O. Box 5800, AZ 6202 Maastricht, The Netherlands. iko@sneu.azm.nl
The purpose of this study was to estimate the costs of care in three different populations of patients with epilepsy (general practices (GP), University Hospital (UH), and Epilepsy Center (EC)), and to analyse the distribution of costs by type of services for each patient group. A cost diary was developed to obtain prospective information on epilepsy-attributable service use over a period of 3 months. Similar information over the previous 3 months was obtained from a cost questionnaire. In addition, a quality of life inventory (QOLIE-31) was used. Standard cost lists were applied for the valuation of the direct cost items. A sensitivity analysis was performed for certain cost items for which no reliable data were available. One hundred and sixteen patients with established epilepsy were included, and the mean costs per patient per month (in Euros) ranged from 52.08 to 357.63. Patients from GP appeared to have lower direct costs, spent less time in seeking or undergoing a treatment, and reported lower seizure frequencies and less severe seizure types than the patients from the other patient groups. Patients from the EC reported the highest productivity changes and unemployment rates and also had the lowest scores on the QOLIE-31. The cost items anti-epileptic drugs, hospital services, unpaid care, and transportation accounted for the majority of the total direct costs.
PMID: 12837564 [PubMed - indexed for MEDLINE]

Epileptic Disord. 2005 Dec;7(4):363-72.
A comparative study of mismatch negativity (MMN) in epilepsy and non-epileptic seizures.
Gene-Cos N, Pottinger R, Barrett G, Trimble MR, Ring HA.
Traumatic Stress Service, Clinical Treatment Center, Maudsley Hospital, London, UK.
This study investigated mismatch negativity (MMN) differences between subjects with non-epileptic seizures (NES), subjects with epilepsy, and healthy controls. Event-related potentials (ERPs) were obtained from 14 patients with NES, 15 patients with epilepsy and 16 healthy control subjects. A conventional MMN procedure was used with a random sequence of 12% deviant tones (922 Hz) and 88% standard tones (1000 Hz). Subjects were instructed to ignore the tones delivered through headphones whilst reading a book. Significant differences in distribution of the mismatch negativity (MMN) in patients with NES compared to controls were obtained (F3, $p </= 0.019$; Cz, $p </= 0.044$) and longer MMN duration in patients with epilepsy compared with patients with NES ($p </= 0.039$) was observed. The change that has been analyzed is one of relative (or scaled) amplitude rather than absolute amplitude. These differences observed at Cz/F3 suggest an increase in emphasis of the MMN in the frontocentral region in patients with NES compared to healthy controls, suggesting that the MMN is generated in a different way in NES compared with controls. This could indicate that one of the normal MMN generator areas does not function normally in NES. Increased absolute amplitude of the MMN has previously been observed in anxiety disorders particularly in post-traumatic stress disorder (PTSD). We discuss similarities between NES and PTSD, suggesting that the increased relative amplitude obtained in this study may be related to mechanisms of generation of NES. The prolonged duration of the MMN in epilepsy could be related to difficulties in processes associated with novelty discrimination (closure of MMN generating mechanism). This information processing dysfunction could be associated with the concentration and memory difficulties that are observed in some patients with epilepsy. This study provides electrophysiological evidence of abnormal processing of auditory stimuli in both clinical conditions when compared to healthy controls, and interictal differences between a group of patients with epilepsy and a group of patients with non-epileptic seizures, as measured by the MMN.
PMID: 16338681 [PubMed - in process]

Epileptic Disord. 2005 Dec;7(4):308-20.
A proposal for a five-dimensional patient-oriented epilepsy classification.
Loddenkemper T, Kellinghaus C, Wyllie E, Najm IM, Gupta A, Rosenow F, Luders HO.
Department of Neurology, The Cleveland Clinic Foundation, Cleveland, OH, USA, Department of Pediatrics, The Cleveland Clinic Foundation, Cleveland, OH, USA, Department of Neurology, Philipps-University Marburg, Marburg, Germany.
The recent proposal by the ILAE Task Force for Epilepsy Classification consists of a multi-axial syndrome-oriented approach. Epilepsy syndromes, as defined by the ILAE, group patients according to various, poorly defined parameters. The resulting syndromes have frequently no biological significance, with overlap among different syndromes and syndromes changing with age. Additionally, only a minority of patients can be classified syndromatically, and the axes of this classification system convey redundant information. We propose a five-dimensional, patient-oriented approach to classifying epilepsies. This approach shifts from the syndrome-oriented approach to a standard, neurological, methodological, patient-oriented approach, using independent criteria in each of the five dimensions. Similar to general neurology, the first step in each patient-physician encounter in epileptology is to take a history of the presenting symptoms and generate a hypothesis regarding the localization and etiology of the symptom within the nervous system. Therefore, the main dimensions of this classification consist of: 1) localization of the epileptogenic zone, 2) seizure semiology classified according to the semiological seizure classification, 3) etiology, 4) seizure frequency, and 5) related medical conditions. These dimensions characterize all of the information necessary for patient management, are independent parameters, and include more pertinent information with regards to patient management than the ILAE axes. All patients can be classified according to this five-dimensional system even at the initial patient encounter when no detailed test results are available. Information from clinical tests, such as MRI and EEG, are translated into the best possible working hypothesis at the time of classification, allowing for increasing precision of the classification as additional information becomes available. This patient-oriented classification envisions an epileptic seizure as an independent symptom of a central nervous system dysfunction due to different causes, with various cortical localizations, occurring at various frequencies, and in conjunction with other diseases and clinical symptoms.
PMID: 16338673 [PubMed - in process]

Epileptic Disord. 2005 Sep;7(3):253-96.
Nonconvulsive status epilepticus: Epilepsy Research Foundation Workshop Reports.
Walker M, Cross H, Smith S, Young C, Aicardi J, Appleton R, Aylett S, Besag F, Cock H, Delorenzo R, Drislane F, Duncan J, Ferrie C, Fujikawa D, Gray W, Kaplan P, Koutroumanidis M, O'regan M, Plouin P, Sander J, Scott R, Shorvon S, Treiman D, Wasterlain C, Wieshmann U.
Epilepsy Research Foundation, London, United Kingdom.
In April 2004, a group of physicians with an interest in nonconvulsive status epilepticus representing a spectrum of opinion met in Oxford, sponsored by the Epilepsy Research Foundation (a charitable organization), to discuss and debate the definition, diagnosis and treatment of nonconvulsive status epilepticus. We felt that such a meeting would be useful, as nonconvulsive status epilepticus is a subject that provokes strong reactions, perhaps largely due to the relative lack of evidence and the surfeit of opinion. The meeting was arranged such that there were formal talks followed by a discussion led by one of the attendees. We present here the extended abstracts of the main talks with the points raised by the discussants. Despite disagreements on certain issues there was much in the way of consensus. First, it was agreed that nonconvulsive status epilepticus is a term that covers a range of disparate conditions with varying prognoses and treatments. The agreed definition was thus suitably vague, A<<Nonconvulsive status epilepticus is a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in nonconvulsive clinical symptomsA>>. Secondly, it was agreed that even within a specific condition (e.g. complex partial status epilepticus), the prognosis and treatment depends upon the context in which the condition occurs (e.g. in the critically ill, in coma, in the A<<walking woundedA>> and in people with prior epilepsy). Perhaps, most importantly it was agreed that we lacked good clinical data, and the challenge was to design good studies for a condition that is underrecognised and often difficult to diagnose.
PMID: 16162436 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:39-46.
The impact of epilepsy surgery on mortality.
Ryvlin P, Montavont A, Kahane P.

Department of Functional Neurology and Epileptology, Hospices Civils de Lyon and Universite Claude Bernard Lyon 1, Lyon, France.
Patients with refractory epilepsy suffer from an increased risk of death, primarily due to seizure-related fatalities including sudden unexpected death (SUDEP), which could be conceivably avoided by surgical cure of the epilepsy. Several series have addressed this issue by comparing the mortality rate between medically and surgically treated drug resistant populations, as well as between patients, seizure free and non seizure free post-operatively. Results from some studies suggest that successful temporal lobe surgery reduced the risk of death to that observed in the normal population, whereas patients who continue to suffer recurrent seizures still present an increased standardized mortality ratio (SMR). However, other series have failed to replicate this finding, or found no difference in the overall mortality and SUDEP rates between operated and medically treated patients. All the above studies suffer various types of methodological limitations, hampering any definite conclusion regarding the impact of epilepsy surgery on mortality. However, part of the apparently discordant reported findings might be reconciled through the following framework. Patients who will eventually respond favourably or unfavourably to an anterior temporal lobectomy might already differ in the risk of seizure-related death, pre-operatively. Specifically, patients whose temporal lobe epileptogenic network extends to the perisylvian region (temporal plus epilepsy) appear to be at higher risk of failed TLE surgery, secondary generalised tonic-clonic seizures, ictal apnoea or insula-driven severe cardiac arrhytmias. This population might carry most of the SUDEP burden, both pre- and post-operatively, accounting for the lack of an obvious net reduction of seizure related deaths after temporal lobe surgery. A multicentric study has recently been launched in order to test this hypothesis, and will hopefully help to conclude on the impact of epilepsy surgery on mortality outcome.
PMID: 16120493 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:34-8.
Improving quality of life beyond seizure control.
Schachter SC.
Comprehensive Epilepsy Program, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
More than 50 years ago, Lennox and Markham urged physicians who treated patients with epilepsy to "match modern drug and surgical therapy with practical sociopsychological therapy" and to be "concerned not only with turbulent brain waves but with disturbed emotions". Indeed, while seizure frequency and severity correlate with quality of life and psychosocial outcomes for patients with drug-resistant epilepsy, numerous other epilepsy-related factors may also be significant determinants. These factors include medical and psychiatric co-morbidities, side effects of therapy, stigma, parental anxiety, employment status, seizure worry, self-esteem and self-mastery. Importantly, these epilepsy-related factors may be amenable to educational or therapeutic interventions, which if successful may benefit patients even without a concomitant reduction in seizure frequency or severity. Therefore, while further research is needed, physicians and other health care providers should comprehensively attend to these factors and refer patients with treatment-resistant seizures, when appropriate, for further evaluation and treatment to improve their quality of life beyond seizure control.
PMID: 16120492 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:27-33.
Epilepsy and common comorbidities: improving the outpatient epilepsy encounter.
Gilliam FG, Mendiratta A, Pack AM, Bazil CW.
The Department of Neurology, Neurological Institute, Columbia University, New York, NY, USA.
Epilepsy is a chronic disorder that has been associated with other specific health problems. Evidence from recent clinical and basic investigations indicates that aspects of cerebral dysfunction associated with a lowered seizure threshold may also predispose toward other disorders such as depression, cognitive impairment, sleep disorders, and migraine. Similarly, certain types of brain injury may also increase the risk of adverse antiepileptic drug (AED) effects. For example, a history of febrile seizures is associated with a three fold increase in the occurrence of negative psychiatric effects of two newer AEDs. Poor fitness and obesity are also reported at higher rates in epilepsy. Some comorbid conditions in epilepsy, such a depression and anxiety, may have a greater influence on subjective health status than does seizure rate. Management strategies employed in the outpatient clinic to maximize overall health outcomes should include screening and treatment for the commonly coexistent conditions in persons with epilepsy.
PMID: 16120491 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:22-6.

VNS Therapy versus the latest antiepileptic drug.

Ben-Menachem E, A French J.
Department of Clinical Neuroscience, Sahlgren University Hospital, Sweden.

Pro AED: The central issue in medical decision-making is risk-benefit assessment. Surgery of any type is still considered to be a major undertaking. To warrant these risks, the patient has a right to expect that they have a greater chance of a good outcome with an invasive therapy than with a non-invasive one. The main question is when, if ever, this becomes the case when comparing implantation of a VNS Therapy System versus adding an antiepileptic drug (AED)? After the first drug? The second? After all AEDs have failed? To date, no randomized trial comparing the addition of an AED against vagus nerve stimulation (VNS Therapy) has been undertaken, although several are currently being contemplated. Without this information, it is more difficult to make a case for early implementation of VNS Therapy. Unfortunately, few data are available regarding the potential for patients to become seizure-free after implantation of a VNS Therapy System. Another issue is side effects. It is important to remember that VNS Therapy also produces adverse events, albeit very different in character than those associated with AEDs, to which physicians have become accustomed. These include cough, dyspnea, pharyngitis, voice alteration and sleep apnea. A less frequently discussed, potentially negative consequence of VNS Therapy relates to the ability to obtain imaging of the patient. Patients who have undergone VNS Therapy System implantation are not candidates for imaging of the chest, breast, or abdomen. A second issue is that imaging of the brain can only be performed with MRI scanners that meet certain requirements, and as MRI technology develops, scanners meeting these requirements may become harder to find. However, to summarize, VNS Therapy is an excellent and useful treatment choice. Fortunately, the choice between AEDs and VNS Therapy is not an "either/or" decision. Each has a role in the treatment of patients with epilepsy, and the advantages and disadvantages of each should be kept in perspective.Pro VNS Therapy: VNS Therapy is no longer a new treatment for patients with refractory epilepsy. The first implant was performed in l988, and since then more than 30,000 patients have received this therapy. It is no longer considered an unusual or dangerous procedure, but it is still used almost exclusively for refractory epilepsy patients and it has not been generally accepted for use as a first line or even second line therapy. However, compared to the new AEDs, VNS Therapy has similar efficacy results in clinical trials and in many epilepsy syndromes and the long-term efficacy results are even more positive, with continued improvement in seizure reduction for up to two years. Two of the major reasons for not using VNS Therapy early are that it is a surgical procedure, and its safety during MRI procedures, especially with 3 Tesla, has not yet been elucidated. The safety profile of VNS Therapy is very favorable; the side effects being totally different from those seen with AEDs. The most important aspects are that there have been no pharmacological interactions, cognitive or sedative side effects reported, and it is safe for use in all age groups. Side effects are restricted to local irritation, hoarseness, coughing and, in a few cases, swallowing difficulties when the stimulator is on, but these tend to disappear with time. No idiosyncratic side effect has emerged during the 16 years of use. Compliance is guaranteed. The cost of the implantation of the VNS Therapy System, when spread out over 8 years (battery life), is actually less than the cost of using a new AED over an eight-year period, and real savings as regards hospital costs due to seizures can be expected.

PMID: 16120490 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:14-21.

Can drug resistance in epilepsy be minimized? Challenging commonly held beliefs.

Perucca E.
Clinical Pharmacology Unit, Department of Internal Medicine and Therapeutics, University of Pavia, and Laboratories for Diagnostics and Applied Biological Research. Institute of Neurology, IRCCS C. Mondino Foundation, Pavia, Italy.

Until more efficacious antiepileptic drugs (AEDs) that can tackle the challenge of drug-refractory epilepsy are developed, the best way to minimize inadequate seizure control is to exploit at best available treatments. There are however, discrepancies between commonly held opinions on several aspects of drug therapy, and the body of scientific evidence which exists to support them. This article highlights a few examples, discussing evidence that, contrary to common belief, (i) a significant proportion of patients with newly diagnosed epilepsy respond to concentrations of AEDs below the "therapeutic range" quoted in the literature; (ii) only a small group of patients unresponsive to low to moderate AED dosages become seizure-free after increasing dosage up to the limit of tolerability; (iii) knowledge of mechanisms of AED action can aid in the rational use of AEDs in the clinic; (iv) monitoring serum levels of new generation AEDs can be usefully exploited to improve management, and (v) at least in a subgroup of patients,

successful epilepsy surgery cannot be regarded as curative, because seizure control may be dependent upon continuation of AED therapy. It is hoped that increased awareness of these issues could eventually contribute not only to improved clinical outcome, but also to high quality studies in many areas where gaps in knowledge prevent application of truly evidence-based management.
PMID: 16120489 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:10-3.
Can we predict refractory epilepsy at the time of diagnosis?
Semah F, Ryvlin P.
Service hospitalier F. Joliot, CEA, Orsay.
The early prediction of intractability is a major challenge in epileptology. Some prognostic factors have been pointed out, most of which simply underlined that partial epilepsy is more difficult to control than idiopathic generalized epilepsy (IGE). Indeed, the main predictors are the presence of a brain lesion demonstrated by neuroimaging or suggested by a neurological deficit or a developmental delay, as well as electroclinical evidence of non idiopathic partial epilepsy. Little is known about the relationship between the location of the epileptogenic area and the chance of being seizure-free in patients with partial epilepsy. Some data suggest that temporal lobe epilepsy (TLE) is more difficult to control than other partial epilepsies, but this might only reflect the prognostic impact of hippocampal sclerosis. Indeed, several studies have shown that the majority of patients with MRI evidence of hippocampal sclerosis develop refractory epilepsy. This observation also applies to patients with malformation of cortical development (MCD). The response to the first AED is another early predictor of refractory epilepsy. At the time of diagnosis, several prognostic factors are available to predict drug resistance, but further studies are still needed to better delineate the specific role of each of these factors, and to offer a more accurate prediction of long term seizure outcome.
PMID: 16120488 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:3-9.
Mechanisms of drug resistance.
Loscher W.
Department of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine Hannover, and Center for Systems Neuroscience, Hannover, Germany.
Despite the use of new antiepileptic drugs, approximately one third of patients with epilepsy have seizures that cannot be controlled satisfactorily by medical treatment. Drug resistance may exist at the time of the first seizure or may develop later as result of the disease process. The mechanisms of these different scenarios are likely to be multifactorial, and may include alterations in brain uptake or brain targets of antiepileptic drugs. Such alterations may be constitutive (intrinsic), thus underlying de novo drug resistance in epilepsy, or induced, e.g., as a consequence of recurrent seizures or disease progression. Alterations in drug efflux ("multidrug") transporters and drug targets, such as voltage-gated sodium channels, have been found in epileptogenic brain tissue from both patients with epilepsy, and rodent models of epilepsy. However, although the multidrug transporter and target hypotheses are biologically plausible, proof-of-principle is lacking for these hypotheses. An advantage of the multidrug transporter hypothesis is that it can be validated both experimentally and clinically by combining antiepileptic drugs with inhibitors of such transporters. Selective inhibitors of the major efflux transporter P-glycoprotein are currently in clinical trials for reversing chemotherapy resistance in oncology and may soon be used to determine whether such inhibitors can prevent or reverse drug resistance in epilepsy.
PMID: 16120487 [PubMed - in process]

Epileptic Disord. 2005 Sep;7 Suppl 1:1-2.
The modern challenges of drug resistant epilepsy.
Ryvlin P.
Department of Functional Neurology and Epileptology, Hospices Civils de Lyon and Universite Claude Bernard Lyon 1, Lyon, France.
PMID: 16120486 [PubMed - in process]

Epileptic Disord. 2005 Jun;7(2):91-5.
Epilepsy in middle-aged and elderly people: a three-year observation.

Paradowski B, Zagrajek MM.
Department of Neurology, Wroclaw Medical University, Wroclaw, Poland.
An analysis of the medical documentation and investigation of 130 cases of epilepsy diagnosed in a group of people over 50 years of age (average: 65.4 years) revealed that the most common type of seizure in the group studied was partial (66.2%), followed by seizures with secondary generalization (33.8%). Epilepsy was caused by cerebrovascular disease (50.8%) considerably more often in patients over 74 years of age, craniocerebral trauma in patients addicted to alcohol (13.1%), especially those under 65 years of age, primary or metastatic neoplastic disease (10.7%), and others. The authors wish to draw attention to the leukoaraiosis factor, which might be the proepileptogenic cause of epilepsy recognized in the group of patients over 74 years of age (56.5%) and is much more frequent in this group than in the group of patients under 65 years of age (1.6%). Moreover, some drugs, such as L-dopa and Baclofen, might have been related to the epileptic seizures. In 29 patients (22.3%) the definite cause of late-onset epilepsy was unknown. The authors suggest in such cases, both follow - up tomographic examination and careful clinical examinations. In the study group of patients with initially unknown seizure etiology, some diseases, such as cerebral tumor or colon and pancreatic neoplasm, were diagnosed during follow-up examination. These processes were revealed several months after the first epileptic seizure.
PMID: 15929910 [PubMed - in process]

Epileptic Disord. 2005 Jun;7(2):83-90.
Temporal lobe epilepsy: clinical semiology and age at onset.
Villanueva V, Serratosa JM.
Neurology Department, Fundacion Jimenez Diaz, Madrid, Spain.
The objective of this study was to define the clinical semiology of seizures in temporal lobe epilepsy according to the age at onset. We analyzed 180 seizures from 50 patients with medial or neocortical temporal lobe epilepsy who underwent epilepsy surgery between 1997-2002, and achieved an Engel class I or II outcome. We classified the patients into two groups according to the age at the first seizure: at or before 17 years of age and 18 years of age or older. All patients underwent intensive video-EEG monitoring. We reviewed at least three seizures from each patient and analyzed the following clinical data: presence of aura, duration of aura, ictal and post-ictal period, clinical semiology of aura, ictal and post-ictal period. We also analyzed the following data from the clinical history prior to surgery: presence of isolated auras, frequency of secondary generalized seizures, and frequency of complex partial seizures. Non-parametric, chi-square tests and odds ratios were used for the statistical analysis. There were 41 patients in the "early onset" group and 9 patients in the "later onset" group. A relationship was found between early onset and mesial temporal lobe epilepsy and between later onset and neocortical temporal lobe epilepsy ($p = 0.04$). The later onset group presented a higher incidence of blinking during seizures ($p = 0.03$), a longer duration of the post-ictal period ($p = 0.07$) and a lower number of presurgical complex partial seizures ($p = 0.03$). The other parameters analyzed showed no significant differences between the two groups. We conclude that clinical and semiological differences exist between patients with temporal lobe epilepsy according to the age at onset. [Published with video sequences].
PMID: 15929909 [PubMed - in process]

Epileptic Disord. 2004 Mar;6(1):31-40.
Childhood epilepsy: a critical review of cost-of-illness studies.
Argumosa A, Herranz JL.
Marques de Valdecilla University Hospital and University of Cantabria, Santander, Spain.
Epilepsy is an illness with multiple consequences and costs for children, families and society. There are only a few studies published on the cost of childhood epilepsy. The different methodologies used in these studies make it difficult to compare them or even to compare the cost of childhood epilepsy treatment with that of adult epilepsy. Nevertheless, studies highlight important differences in the distribution of costs associated with childhood epilepsy and epilepsy in adults. It is understandable that direct costs represent the higher percentage of the total cost associated with childhood epilepsy treatment, given the higher number of hospital admissions and investigations, as well as the complexity of therapeutic trials, while indirect costs represent the greater proportion in adult epilepsy treatment. In addition to age, the total cost associated with epilepsy also depends on other factors such as seizure frequency, the moment at which the illness cost is estimated and the local health care system. In summary, chronic illnesses not only have an influence on the physical and psychological development of children, they also impose costs on the family and society. Childhood epilepsy has greater economic costs than those generated by more prevalent, chronic illnesses.

Publication Types: Review
PMID: 15075066 [PubMed - indexed for MEDLINE]

Eur J Health Econ. 2004 Oct;5 Suppl 1:S36-42.
Economic evidence in epilepsy: a review.
Ekman M, Forsgren L.
Stockholm Health Economics, Stockholm, Sweden. mattias.e@healtheconomics.se
Publication Types: Review
PMID: 15754071 [PubMed - indexed for MEDLINE]

Eur J Neurol. 2005 Nov;12 Suppl 4:22-9.
Epilepsy--success in clinical practice: translating trials to practice.
Gilliam FG.
Columbia University Neurological Institute, New York, NY, USA. fgilliam@neuro.columbia.edu
Success in clinical practice results from the combination of a clinician's experience, an understanding of patient preferences and factors that influence patient perceptions, and careful interpretation of data from clinical trials. However, successful clinical trials fulfil rigid methodological requirements in order to provide a basis from which to evaluate the place of a drug within a therapeutic strategy. Their translation into practice is therefore complicated by an intrinsic tension between the requirements for scientific methods that minimize error, and the need for clinically relevant data. In practice, the clinician has the flexibility to individualize epilepsy management to maximize benefits and minimize adverse effects of antiepileptic drug (AED) therapy. AED adverse effects and psychiatric comorbidity, in particular depression, have a profound impact on subjective health status; systematic screening for these confounding variables can guide clinical management and optimize quality of life. In addition, patient preferences can be acknowledged in any management plan. To achieve success in clinical practice, we need to remember that the information gleaned from clinical trials provides only part of the picture and needs to be augmented by our clinical experience, patient assessment (including routine screening for adverse effects and depression) and patient preference.
PMID: 16144537 [PubMed - in process]

Eur J Neurol. 2005 Nov;12 Suppl 4:3-11.
Ultimate success in epilepsy--the patient's perspective.
Sander JW.
Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, London, UK. l.sander@ion.ucl.ac.uk
Most people with epilepsy can live outwardly normal lives, but fear about impending seizures, driving restrictions, lack of independence, employment and social problems, medication-related adverse effects and the presence of cognitive or psychiatric complications are all concerns readily identified by affected individuals. While seizure control is the overriding goal of treatment, it is essential to realize the importance that patients place on other aspects of daily functioning. While many of the concerns identified by patients can only be managed by improved social support, others (e.g. neuropsychological impairment, medication-related adverse events, cognitive impairment, sleep disturbance) may be amenable to therapy (if available) or to the selection of a more appropriate antiepileptic drug. Each antiepileptic drug has a unique pharmacodynamic and tolerability profile. Awareness by the treating clinician of the pharmacological profile of each drug may help to minimize unwanted treatment-related effects and possibly improve the outcome of treatment from an epilepsy patient's perspective. Therefore, in order to achieve true treatment success, clinicians need to understand how individuals perceive their disorder and, where possible, address those factors that adversely affect patient quality of life. For the person with epilepsy, successful treatment involves beneficial effects on social, vocational and psychological function. This extends beyond seizure control to freedom from the fear associated with seizures, confidence in pharmacological therapy and improvements in health-related quality of life.
PMID: 16144535 [PubMed - in process]

Eur J Neurol. 2005 Nov;12 Suppl 4:1.
Defining success in epilepsy - different perspectives.
Baulac M. PMID: 16144534 [PubMed - in process]

Eur J Neurol. 2005 Jun;12(6):483-5.
Analysis of antiepileptic drugs use at a university hospital in Croatia.
Prpic I, Vlahovic-Palcevski V, Skarpa-Prpic I, Palcevski G, Boban M.
Department of Paediatrics, University Hospital Centre Rijeka, Rijeka, Croatia. igorp@medri.hr
To analyse the consumption rate of new generation antiepileptic drugs (AEDs) compared with traditional AEDs at a university hospital in Croatia. Antiepileptic drugs use was analysed retrospectively for two consecutive years, 2001 and 2002 at Departments of Neurology, Paediatrics, Psychiatry and Neurosurgery at the University Hospital Centre (UHC) Rijeka. The results obtained are expressed as number of defined daily doses (DDDs) per 100 bed days, as proposed by the WHO. The use of new generation AEDs was represented by 2% in 2001 and 5% in 2002. Majority of AEDs administered was taken by the barbiturates in both years. A wide spectrum of AEDs has been used at the Department of Paediatrics. At the Department of Neurology and Psychiatry use of barbiturates and carbamazepine predominated. The use of new AEDs at UHC has increased during the investigation period but it is still rather low compared with traditional AEDs. The similarity of our results with the result of the leading Croatian university hospitals might represent general routine AED prescription in country. Nationally based guidelines may bring more appropriate and rational approach for usage of modern AED. This task should be supported and promoted by international and national neurology associations.
Publication Types: Clinical Trial
PMID: 15885055 [PubMed - indexed for MEDLINE]

Eur J Neurol. 2005 Jun;12 Suppl 1:54-8.
Cost of epilepsy in Europe.
Forsgren I, Beghi E, Ekman M.
Department of Neurology, Umea University Hospital, Umea, Sweden.
PMID: 15877780 [PubMed - indexed for MEDLINE]

Eur J Nucl Med Mol Imaging. 2005 Nov;32(11):1311-6. Epub 2005 Aug 3.
Assessment of the role of FDG PET in the diagnosis and management of children with refractory epilepsy.
Ollenberger GP, Byrne AJ, Berlangieri SU, Rowe CC, Pathmaraj K, Reutens DC, Berkovic SF, Scheffer IE, Scott AM.
Department of Nuclear Medicine and Centre for PET, University of Melbourne, Melbourne, Australia.
PURPOSE: We performed a retrospective analysis of the results of FDG PET scans in children with refractory epilepsy referred to our centre over an 8-year period, with a view to ascertaining the impact of FDG PET on subsequent patient management. METHODS: A questionnaire was used to assess the impact of FDG PET scan on diagnosis, management and clinical decision-making processes for epilepsy surgery from the managing clinician's perspective. FDG PET scan results were also compared with MRI, EEG and SPECT results and coded according to whether the FDG PET scan provided independent information and localisation of epileptogenic regions. RESULTS: A total of 118 eligible patients under the age of 14 years were identified, with questionnaires being completed on 113 evaluable patients (96%). The pre-PET management plan consisted of consideration for surgery in 92 patients (81%) and medical therapy for the remaining 21 patients (19%). Managing physicians rated FDG PET as providing information additional to that obtained with other investigations regarding epileptogenic sites in 88 patients (77%). FDG PET had either a minor or a major impact on clinical management in 58 patients (51%), principally with regard to surgical candidacy. CONCLUSION: FDG PET has a definite role in the assessment of paediatric patients with refractory epilepsy who are being considered for surgery. In the future, analysis of FDG PET data in specific subpopulations of children with refractory epilepsy may lead to novel insights regarding aetiology.
PMID: 16078061 [PubMed - in process]

Eur J Obstet Gynecol Reprod Biol. 2005 Jun 8; [Epub ahead of print]
The relation of breech presentation at term to epilepsy in childhood.
Krebs L, Langhoff-Roos J.
Department of Gynaecology and Obstetrics, 537, University of Copenhagen, Hvidovre Hospital, Kettegaard Alle 30, DK-2650 Hvidovre, Denmark.

OBJECTIVE:: To investigate the relation between breech at term and epilepsy in childhood, and identify risk factors for epilepsy in term breech infants. STUDY DESIGN:: Register-based study of all (n=7514) singleton term infants without malformations, born between 1980 and 1994 and hospitalised with epilepsy until year 1996. For each case delivered in breech presentation (n=290), the two subsequent deliveries of non-malformed, singleton infants delivered in breech presentation at term at the same hospital were selected as controls (n=580). RESULTS:: Breech presentation was a risk factor for epilepsy (OR: 1.2 [95% CI: 1.1, 1.3]). Breech infants with epilepsy were more often small for gestational age (9.7%) than breech infants without epilepsy (4.7%). Vaginal delivery was associated with low Apgar score, but mode of delivery and low Apgar score were not related to epilepsy. CONCLUSION:: The increased risk of epilepsy in term breech infants is not related to intrapartum events, but to growth restriction in pregnancy.
PMID: 15950370 [PubMed - as supplied by publisher]

Eur J Paediatr Neurol. 2005;9(6):399-407. Epub 2005 Oct 28.
Beneficial effects on sleep of vagus nerve stimulation in children with therapy resistant epilepsy.
Hallbook T, Lundgren J, Kohler S, Blennow G, Stromblad LG, Rosen I.
Department of Paediatrics, University Hospital, SE-221 85 Lund, Sweden.
The study purpose was to evaluate sleep structure following Vagus Nerve Stimulation (VNS) in 15 children with therapy resistant epilepsy and to correlate possible alterations with changes in epileptiform activity and clinical effects. Fifteen children were examined with ambulatory polysomnographic recordings initially, and after 3 and 9 months of VNS-treatment. Sleep parameters, all-night delta power activity and movement times (MTs), used to account for arousals were estimated. Epileptiform activity was evaluated by spike detection. Seizure frequency was recorded in a diary. The severity of the seizures was scored with the National Hospital Seizure Severity Scale (NHS3). Quality of life (QOL) was assessed by a visual analogue scale. Behaviour problems were quantified by using the total score of the Child Behaviour Checklist (CBCL). VNS induces a significant increase in slow wave sleep (SWS) and a decrease in sleep latency and in stage 1 sleep. The number and density of MTs during total night sleep were significantly increased. There was also a significant increase in the number of MTs immediately related to the VNS stimulation periods. Of the 14 children with increased MTs, 10 had a reduction in epileptiform activity, and in clinical seizures, all had an improvement in NHS3, and 11 in QOL. Of the 10 children with increased SWS, eight also improved in QOL and eight in behaviour. Our findings indicate that VNS counteracts known adverse effects of epilepsy on sleep and increases slow wave sleep. This possibly contributes to the reported improvement in well-being. We also see an increase in MTs. This arousal effect seems to be of minor importance for QOL and could possibly be related to the antiepileptic mechanisms in VNS.
PMID: 16257548 [PubMed - in process]

Eur J Paediatr Neurol. 2005;9(5):339-45. Epub 2005 Jun 23.
Genetic influence on the clinical characteristics and outcome of febrile seizures-a retrospective study.
Birca A, Guy N, Fortier I, Cossette P, Lortie A, Carmant L.
Faculte de Medecine, Centre de Recherche de l'Hopital Sainte-Justine, Universite de Montreal, 3175 Cote Ste-Catherine, Montreal, Que., Canada H3T 1C5.
PURPOSE: To assess the influence of the family history (FH) of epilepsy or febrile seizures (FSs) on the clinical presentation of FSs and on their outcome. METHODS: We reviewed the charts of 482 children admitted to the Ste-Justine Hospital with FSs between 3 months and 6 years of age and followed for at least 5 years. RESULTS: Children with a positive FH of epilepsy (n=67) showed significantly more focal and recurrent FSs than those without such a FH. The risk of developing partial epilepsy (n=17) or generalized epilepsy (n=19) was significantly greater in children with focal or recurrent FSs, respectively. In children with focal FSs, only two out of 30 (6.7%) children with a negative FH of epilepsy developed partial epilepsy compared with four out of nine (44.4%) children with a positive FH. In children with recurrent FSs, as much as seven out of 34 (20.6%) children with a positive FH of epilepsy developed generalized epilepsy compared to only eight out of 161 (0.05%) of those with a negative FH. Nevertheless, when not taking into account the clinical presentation of FSs, the positive FH of epilepsy constituted a risk factor for developing generalized but not partial epilepsy. Finally, children with a positive FH of FSs (n=120) exhibited significantly more recurrent FSs than those without such a FH, but this did not modify the risk of epilepsy. CONCLUSION: The FH of FSs and/or epilepsy should be taken into account when evaluating the risk of FSs recurrence and of epilepsy.
PMID: 15979359 [PubMed - in process]

Eur Neurol. 2005;54(2):68-72. Epub 2005 Aug 23.
Clinical predictors of late-onset seizures and epilepsy in patients with cerebrovascular disease.
De Reuck J, Goethals M, Vonck K, Van Maele G.
Stroke Unit, Department of Neurology, Ghent University Hospital, Ghent, Belgium. jacques.dereuck@gmail.com
BACKGROUND: Seizures and epilepsy are harmful and worsen the disability of stroke patients. There are currently no good clinical predictors of late-onset seizures and epilepsy in patients with cerebrovascular disease (CVD). PATIENTS AND METHODS: 110 patients with delayed seizures after an ischaemic or a haemorrhagic stroke, a transient ischaemic attack or a subarachnoid haemorrhage (60 with a single seizure and 50 with epilepsy) and 366 without seizures were included in this retrospective study. The clinical syndrome, the stroke aetiology and the vascular risk factors were compared. The groups with a single seizure and with epilepsy were also analysed separately. RESULTS: There were no differences in age, gender, aetiology and vascular risk factors between the groups with and without seizures. When comparing the incidence of the clinical syndromes, ischaemic partial anterior circulation syndrome (PACS) was significantly more and transient ischaemic attack less frequent in the group with seizures compared to the control group. The severity of the neurological impairment on admission and the degree of disability on discharge after a PACS was similar in those who developed late-onset seizures compared with those who did not. Also on the Cox proportional hazards analysis, PACS appeared to be the only clinical risk factor for development of seizures and epilepsy in patients with CVD. No differences were observed in clinical predictors between patients with a single seizure and those with epilepsy. CONCLUSION: PACS is the only independent predictor for the occurrence of late-onset seizures in patients with CVD. (c) 2005 S. Karger AG, Basel.
PMID: 16118500 [PubMed - in process]

Expert Opin Drug Saf. 2005 May;4(3):571-81.
Anticonvulsant hypersensitivity syndrome: a review.
Gogtay NJ, Bavdekar SB, Kshirsagar NA.
Department of Clinical Pharmacology, Seth GS Medical College & KEM Hospital, Parel, Mumbai 400 012, India. njgogtay@hotmail.com
Anticonvulsant hypersensitivity syndrome (AHS), characterised by fever, rash and internal organ involvement, is a rare, but potentially fatal adverse event that occurs most commonly with first-line aromatic anticonvulsants, but can also occur with non-aromatic anticonvulsants such as lamotrigine and valproic acid. AHS can begin anywhere from 1 to 12 weeks after commencement of therapy and has been estimated to occur at a frequency of 1/1000 to 1/10,000 exposures. Its true incidence, however, remains unknown due to under-reporting. The disease has protean manifestations mimicking several other conditions, and the diagnosis is thus difficult. Several hypotheses have been put forward to explain the pathogenesis of AHS. These include accumulation of toxic metabolites, graft versus host disease, antibody production and viral infections. The one based on toxic metabolites has found the greatest acceptance, perhaps due to the fact that it can be proven by an in vitro test; the lymphocyte toxicity assay. Discontinuation of the offending agent with supportive, symptomatic therapy forms the mainstay of management of AHS. In addition, counselling of both the patient and first degree relatives for susceptibility to AHS is an important aspect of management. In the last decade, several new anticonvulsants have been introduced for epilepsy. In addition, for resource-poor countries, inexpensive and effective first-line drugs such as phenytoin and phenobarbitone will continue to remain important treatment options. Thus, the problem of AHS will continue, and attempts should be made to further understand the molecular basis of and individual susceptibility to AHS. Adverse event monitoring programs must also actively seek AHS reports to estimate its true incidence.
PMID: 15934861 [PubMed - in process]

Expert Opin Pharmacother. 2005 Jul;6(8):1305-12.
The role of common variation in drug transporter genes in refractory epilepsy.
Soranzo N, Goldstein DB, Sisodiya SM.
Department of Biology, University College London, Queen Square, London, UK.
Resistance to antiepileptic drugs (AEDs) is one of the most serious clinical problems in epilepsy, and along with AED teratogenicity, perhaps the major concern of epilepsy pharmacogenetics. Studying the genetics of drug resistance in epilepsy is important, as it may identify or confirm key mechanisms underlying this phenomenon that have real clinical importance; it might also offer insights into its prediction and

management. Drug resistance in epilepsy is likely to be multifactorial: overactivity of multi-drug transporters provides one likely underlying mechanism through lowering of AED concentration in the epileptogenic focus. Genetic association studies may provide a tool to assess this 'transporter' hypothesis by determining whether differences between individuals contribute to resistance phenotypes. Most of these studies have investigated one variant in the ABCB1 gene, and have provided, thus far, inconclusive evidence. This review also considers current knowledge of the role of genetic polymorphisms in multi-drug transporters in pharmacoresistant epilepsy, to highlight possible confounding factors affecting the implementation and interpretation of association studies in this field.
PMID: 16013981 [PubMed - in process]

Expert Rev Med Devices. 2005 Mar;2(2):175-89.
Improving the lives of patients with medically refractory epilepsy by electrical stimulation of the nervous system.
Murphy JV, Patil AA.
Children's Mercy Hospital, 2401 Gillham Road, Kansas City, MO 64108, USA. jmurphy@cmh.edu
Vagal nerve stimulation proved effective in animal models of epilepsy, and in open and double-blinded trials, in over 450 patients. Seizure reduction improved for at least 2 years. Almost 50% of treated patients achieve at least a 50% reduction in seizure frequency. Other advantages include termination of a seizure and improved alertness. Benefits were demonstrated in children, partial and generalized epilepsies, and in specific neurologic syndromes.
PMID: 16293054 [PubMed - in process]

Expert Rev Neurother. 2005 Nov;5(6):785-801.
Treatment options and paradigms in childhood temporal lobe epilepsy.
Ray A, Wyllie E.
Department of Neurology, Fortis Hospital, B-22, Sector 62, NOIDA-201301, UP, India. Amit.ray@fortishealthcare.com
Temporal lobe epilepsy in adults is a relatively homogenous syndrome with hippocampal sclerosis being its most common pathologic substrate. In the pediatric age group, low-grade neoplasms and cortical dysplasia are much more common than hippocampal sclerosis. Pediatric temporal lobe epilepsy has distinct semiologic, electrophysiologic and imaging characteristics as compared with its adult counterpart. The various treatment options for pediatric temporal lobe epilepsy include antiepileptic drugs, resective surgery, vagal nerve stimulation and the ketogenic diet. In spite of the multiple antiepileptic drugs currently available, 5-10% of all newly diagnosed cases will remain intractable to medical therapy and should be referred for presurgical evaluation. Resective surgery offers the best chance of seizure freedom in carefully selected patients. Future areas of research include new drug development, better imaging and localization techniques, and brain stimulation.
PMID: 16274336 [PubMed - in process]

Expert Rev Neurother. 2005 Nov;5(6):769-75.
Use of the ketogenic diet as a treatment for epilepsy refractory to drug treatment.
Murphy P.
University of Toronto, Department of Pharmacology, Medical Sciences Building, 1 King's College Circle, Toronto, Ontario, M5S 1A8, Canada. pattyannemurphy@hotmail.com
The ketogenic diet is a high-fat, low-carbohydrate and low-protein diet used in the treatment of epilepsy that does not respond to antiepileptic drugs. The diet has been found to be very effective in treating intractable epilepsy in children. There is also some evidence that the diet is useful in treating drug-resistant epilepsy in infants, adolescents and adults. This paper traces the history and development of the ketogenic diet and reviews the clinical and animal research investigating its effects.
PMID: 16274334 [PubMed - in process]

Expert Rev Neurother. 2005 Nov;5(6):753-67.
Idiopathic generalized epilepsies: clinical and electroencephalogram diagnosis and treatment.
Koutroumanidis M, Bourvari G, Tan SV.
Department of Clinical Neurophysiology and Epilepsies, Lambeth Wing, 3rd Floor, St Thomas' Hospital, London SE1 7EH, UK. Michael.Koutroumanidis@gstt.nhs.uk

This review concentrates on the principles of the clinical and electroencephalogram diagnosis of idiopathic generalized epilepsies and their treatment. The electroclinical variability of the main seizure types is detailed and particular emphasis is placed on the differential diagnosis from other seizures and nonepileptic conditions that is essential for the optimal management of these patients. The authors review the various idiopathic generalized epilepsy subsyndromes and conditions that are included in both the 1989 International League Against Epilepsy classification system and the recently proposed International League Against Epilepsy scheme, but also syndromes and forms that have not been formally recognized. Finally, the authors describe the principles of antiepileptic drug treatment with the old and newer drugs, and their specific indications and contraindications in the various syndromes and seizure types.
PMID: 16274333 [PubMed - in process]

Geriatrics. 2005 Dec;60(12):30-4.
Epilepsy in older adults: common morbidities influence development, treatment strategies, and expected outcomes.
Rowan AJ.
Mount Sinai School of Medicine; Bronx Veterans Administration Medical Center, NY, USA.
Given that that the average person has one chronic illness for each decade over age 50, one would expect that patients who develop seizures in late life would have associated medical and/or neurologic conditions. Cerebrovascular disease, hypertension, heart disease, diabetes mellitus, renal disease, and dementia all relate to epilepsy. Co-morbidities not only contribute to the causation and consequences of seizures, they also interfere with effective treatment and optimal functioning. Because seizures in older individuals can lead to serious consequences, safe and effective treatment is essential. Yet, antiepileptic drugs (AEDs) may cause adverse effects that may be worse in older patients when compared to younger patients. Multiple medications lead to a high probability that medically significant drug interactions may occur and must be monitored for in geriatric patients.
PMID: 16343034 [PubMed - in process]

Geriatrics. 2005 Dec;60(12):22-9.
Does anemia matter? Anemia, morbidity, and mortality in older adults: need for greater recognition. for older patients with epilepsy.
Dharmarajan TS, Pais W, Norkus EP.
New York Medical College, Valhall, NY; Our Lady of Mercy Medical Center, Bronx, NY; University Hospital of New York Medical College, NY, USA.
Anemia is common and under recognized in older adults and associated with increased morbidity and mortality. Estimates of prevalence of anemia in older adults vary considerably based on the setting, gender, age and definition used and likely to increase further based on aging trends. Rather than simply a consequence of aging, anemia is a marker of underlying disease, requiring investigation for an etiology. A cause is discernible in at least two-thirds of cases; management involves addressing the underlying disease process, replacement of deficient nutrients or the use of erythropoietic factors.
PMID: 16343033 [PubMed - in process]

Health Qual Life Outcomes. 2005 Nov 13;3(1):70 [Epub ahead of print]
The European DISABKIDS project: development of seven condition-specific modules to measure health related quality of life in children and adolescents.
Baars RM, Atherton CI, Koopman HM, Bullinger M, Power M.
Backgroud: The European DISABKIDS project aims to enhance the Health Related Quality of Life (HRQoL) of children and adolescents with chronic medical conditions and their families. We describe the development of the seven cross-nationally tested condition-specific modules of the European DISABKIDS HRQoL instrument in a population of children and adolescents. The condition-specific modules are intended for use in conjunction with the DISABKIDS chronic generic module. METHODS: Focus groups were used to construct the pilot version of the DISABKIDS condition-specific HRQoL modules for asthma, juvenile idiopathic arthritis, atopic dermatitis, cerebral palsy, cystic fibrosis, diabetes and epilepsy. Analyses were conducted on pilot test data in order to construct field test versions of the modules. A series of factor analyses were run, first, to determine potential structures for each condition-specific module, and, secondly, to select a reduced number of items from the pilot test to be included in the field test. Post-field test analyses were conducted to retest the domain structure for the final DISABKIDS condition-

specific modules. RESULTS: The DISABKIDS condition-specific modules were tested in a pilot study of 360 respondents, and subsequently in a field test of 1152 respondents in 7 European countries. The final condition-specific modules consist of an 'Impact' domain and an additional domain (e.g. Worry, Stigma, Treatment) with between 10 to 12 items in total. The Cronbach's alpha of the final domains was found to vary from 0.71 to 0.90. CONCLUSIONS: The condition-specific modules of the DISABKIDS instrument were developed through a step-by-step process including cognitive interview, clinical expertise, factor analysis, correlations and reliabilities. A cross-national pilot and field test were necessary to collect these data. In general, the internal consistency of the domains was satisfactory to high. In future, the DISABKIDS instrument may serve as a useful tool with which to assess HRQoL in children and adolescents with a chronic condition. The condition-specific modules can be used in conjunction with the DISABKIDS chronic generic module.
PMID: 16283947 [PubMed - as supplied by publisher]

Health Serv J. 2005 Oct 6;115(5976):22-4.
Clinical management. Fit for purpose.
Coombes R.
Care for people with epilepsy has been dogged by lack of services and long waiting lusts. There have been some pockets of improvement, aided by GPs with special interests and networks of specialists. Experts believe GPs will have a key role in providing better services for epilepsy sufferers.
PMID: 16248299 [PubMed - in process]

Health Stat Q. 2004 Spring;(21):23-9.
Trends in mortality and hospital admissions associated with epilepsy in England and Wales during the 1990s.
Bruce M, Griffiths C, Brock A, Majeed A.
Office for National Statistics.
This article examines trends in mortality and hospital admissions associated with epilepsy in England and Wales during the 1990s. Mortality data were analysed for the period 1993 to 2000. Data on hospital admissions where the main diagnosis was epilepsy were obtained from the Hospital Episode Statistics information service of the Department of Health and analysed for the period 1991/92 to 2000/01. There were about 800 deaths per year where epilepsy was the underlying cause and about 37,000 admissions where epilepsy was the main diagnosis. Both mortality and hospital admission rates for epilepsy remained relatively stable during the periods examined.
PMID: 15615150 [PubMed - indexed for MEDLINE]

Hum Brain Mapp. 2004 Jul;22(3):179-92.
EEG-fMRI of focal epileptic spikes: analysis with multiple haemodynamic functions and comparison with gadolinium-enhanced MR angiograms.
Bagshaw AP, Aghakhani Y, Benar CG, Kobayashi E, Hawco C, Dubeau F, Pike GB, Gotman J.
Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada. bagshaw@mcgill.ca
Combined EEG-fMRI has recently been used to explore the BOLD responses to interictal epileptiform discharges. This study examines whether misspecification of the form of the haemodynamic response function (HRF) results in significant fMRI responses being missed in the statistical analysis. EEG-fMRI data from 31 patients with focal epilepsy were analysed with four HRFs peaking from 3 to 9 sec after each interictal event, in addition to a standard HRF that peaked after 5.4 sec. In four patients, fMRI responses were correlated with gadolinium-enhanced MR angiograms and with EEG data from intracranial electrodes. In an attempt to understand the absence of BOLD responses in a significant group of patients, the degree of signal loss occurring as a result of magnetic field inhomogeneities was compared with the detected fMRI responses in ten patients with temporal lobe spikes. Using multiple HRFs resulted in an increased percentage of data sets with significant fMRI activations, from 45% when using the standard HRF alone, to 62.5%. The standard HRF was good at detecting positive BOLD responses, but less appropriate for negative BOLD responses, the majority of which were more accurately modelled by an HRF that peaked later than the standard. Co-registration of statistical maps with gadolinium-enhanced MRIs suggested that the detected fMRI responses were not in general related to large veins. Signal loss in the temporal lobes seemed to be an important factor in 7 of 12 patients who did not show fMRI activations with any of the HRFs. Copyright 2004 Wiley-Liss, Inc.
Publication Types: Clinical Trial PMID: 15195285 [PubMed - indexed for MEDLINE]

Hum Genet. 2005 Nov 5;:1-8 [Epub ahead of print]

Genome-wide linkage of febrile seizures and epilepsy to the FEB4 locus at 5q14.3-q23.1 and no MASS1 mutation.

Deprez L, Claes LR, Claeys KG, Audenaert D, Van Dyck T, Goossens D, Van Paesschen W, Del-Favero J, Van Broeckhoven C, De Jonghe P.

Neurogenetics Group, Department of Molecular Genetics (VIB8), University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, 2610, Antwerpen, Belgium.

Febrile seizures (FS) represent the most common seizure disorder in childhood and contribution of a genetic predisposition has been clearly proven. In some families FS is associated with a wide variety of afebrile seizures. Generalized epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome with a spectrum of phenotypes including FS, atypical febrile seizures (FS+) and afebrile generalized and partial seizures. Mutations in the genes SCN1B, SCN1A and GABRG2 were identified in GEFS+ families. GEFS+ is genetically heterogeneous and mutations in these three genes were detected in only a minority of the families. We performed a 10 cM density genome-wide scan in a multigenerational family with febrile seizures and epilepsy and obtained a maximal multipoint LOD score of 3.12 with markers on chromosome 5q14.3-q23.1. Fine mapping and segregation analysis defined a genetic interval of approximately 33 cM between D5S2103 and D5S1975. This candidate region overlapped with a previously reported locus for febrile seizures (FEB4) in the Japanese population, in which MASS1 was proposed as disease gene. Mutation analysis of the exons and exon-intron boundaries of MASS1 in our family did not reveal a disease causing mutation. Our linkage data confirm for the first time that a locus on chromosome 5q14-q23 plays a role in idiopathic epilepsies. However, our mutation data is negative and do not support a role for MASS1 suggesting that another gene within or near the FEB4 locus might exist.

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Hum Mol Genet. 2005 Oct 15;14 Spec No. 2:2491-2500.

Sacred disease secrets revealed: the genetics of human epilepsy.

Turnbull J, Lohi H, Kearney JA, Rouleau GA, Delgado-Escueta AV, Meisler MH, Cossette P, Minassian BA.

Program in Genetics and Genomic Biology, The Hospital for Sick Children, Toronto, Ontario, Canada M5G 1X8.

Neurons throughout the brain suddenly discharging synchronously and recurrently cause primarily generalized seizures. Discharges localized awhile in one part of the brain cause focal-onset seizures. A genetically determined generalized hyperexcitability had been predicted in primarily generalized seizures, but surprisingly the first epilepsy gene discovered, CHRNA4, was in a focal (frontal lobe)-onset syndrome. Another surprise with CHRNA4 was its encoding of an ion channel present throughout the brain. The reason why CHRNA4 causes focal-onset seizures is unknown. Recently, the second focal (temporal lobe)-onset epilepsy gene, LGI1 (unknown function), was discovered. CHRNA4 led the way to mutation identifications in 15 ion channel genes, most causing primarily generalized epilepsies. Potassium channel mutations cause benign familial neonatal convulsions. Sodium channel mutations cause generalized epilepsy with febrile seizures plus or, if more severe, severe myoclonic epilepsy of infancy. Chloride and calcium channel mutations are found in rare families with the common syndromes childhood absence epilepsy and juvenile myoclonic epilepsy (JME). Mutations in the EFHC1 gene (unknown function) occur in other rare JME families, and yet in other families, associations are present between JME (or other generalized epilepsies) and single nucleotide polymorphisms in the BRD2 gene (unknown function) and the malic enzyme 2 (ME2) gene. Hippocrates predicted the genetic nature of the 'sacred' disease. Genes underlying the 'malevolent' forces seizing 1% of humans have now been revealed. These, however, still account for a mere fraction of the genetic contribution to epilepsy. Exciting years are ahead, in which the genetics of this extremely common, and debilitating, neurological disorder will be solved.

Publication Types: Corrected and Republished Article Review
PMID: 16278970 [PubMed - in process]

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Susceptibility genes for complex epilepsy.

Mulley JC, Scheffer IE, Harkin LA, Berkovic SF, Dibbens LM.

Department of Genetic Medicine, Women's and Children's Hospital, North Adelaide, South Australia, Australia.

Common idiopathic epilepsies are, clinically and genetically, a heterogeneous group of complex seizure disorders. Seizures arise from periodic neuronal hyperexcitability of unknown cause. The genetic component is mostly polygenic, where each susceptibility gene in any given individual is likely to represent a small component of the total heritability. Two susceptibility genes have been so far identified, where genetic variation is associated with experimentally demonstrated changes in ion channel properties, consistent with seizure susceptibility. Rare variants and a polymorphic allele of the T-type calcium channel CACNA1H and a polymorphic allele and a rare variant of the GABA(A) receptor delta subunit gene have differential functional effects. We speculate that these and other as yet undiscovered susceptibility genes for complex epilepsy could act as 'modifier' loci, affecting penetrance and expressivity of the mutations of large effect in those 'monogenic' epilepsies with simple inheritance that segregate through large families. Discovery of epilepsy-associated ion channel defects in these rare families has opened the door to the discovery of the first two susceptibility genes in epilepsies with complex genetics. The susceptibility genes so far detected are not commonly involved in complex epilepsy suggesting the likelihood of considerable underlying polygenic heterogeneity.
Publication Types: Review
PMID: 16244322 [PubMed - in process]

IEEE Eng Med Biol Mag. 2003 May-Jun;22(3):74-80.
New horizons in ambulatory electroencephalography.
Waterhouse E.
Department of Neurology, Virginia Commonwealth University, School of Medicine, Box 980599, Richmond, VA 23298-0599, USA.
Since its inception 30 years ago, AEEG has continued to evolve--from four-channel tape recorders to 32-channel digital recorders with sophisticated automatic spike and seizure detection algorithms. AEEG remains an important tool in epilepsy evaluation. In the near future, smaller, faster, and more sophisticated AEEGs will be developed. Seizure detection/anticipation systems will allow the wearer to be forewarned of a seizure so that appropriate safety measures can be taken. With further refinement in our understanding of nonlinear dynamic analysis to define the pre-ictal state, AEEG will be coupled with an accurate seizure anticipation device in a closed-loop system, providing a time window during which therapeutic intervention can occur, to prevent a seizure. The therapeutic intervention will most likely involve vagus nerve or deep brain stimulation. An alternative is that the patient may learn to recognize early symptoms of the pre-ictal state and use behavioral biofeedback interventions to avoid a clinical seizure. In order to achieve convenient ambulatory recording and seizure detection that could realistically improve the lives of patients with refractory epilepsy, the process of miniaturization of such a device to a convenient size must be accomplished. One of the aspects of epilepsy that patients find most frustrating, and that most limits activities, is the vulnerability to sudden unexpected incapacitation due to the occurrence of a seizure. With miniaturization of AEEG and seizure anticipation technology, and advancements in our ability to identify the transition from pre-ictal to ictal state, there is realistic hope that patients with refractory epilepsy may gain control over their seizures and enjoy significantly improved quality of life.
PMID: 12845822 [PubMed - indexed for MEDLINE]

Int J Epidemiol. 2005 Nov 9; [Epub ahead of print]
Congenital structural anomalies in offspring of women with epilepsy--a population-based cohort study in Finland.
Artama M, Ritvanen A, Gissler M, Isojarvi J, Auvinen A.
Tampere School of Public Health, University of Tampere, Tampere, Finland.
BACKGROUND: Offspring of women with epilepsy may have an increased risk for congenital malformations, probably attributable to maternal antiepileptic medication. We conducted this population-based study to obtain valid and accurate estimates on major congenital malformations in the offspring of women with epilepsy, based on a large and representative patient cohort. METHODS: We identified all women (n = 6535) entitled to full reimbursement for antiepileptic medication indicated for epilepsy for the first time between 1985 and 1994 from the Social Insurance Institution of Finland database. A reference cohort (n = 14 704) was identified from the Finnish Population Register Centre. Information on children born between 1993 and 2000 (patient cohort, n = 2162; reference cohort, n = 5413) was obtained from the Medical Birth Register. Information on children born with malformation (patient cohort, n = 116; reference cohort, n = 151) was obtained from the Finnish Register of Congenital Malformations. RESULTS: The prevalence of major malformation was 54/1000 births among patients with epilepsy and 28/1000 births among mothers

without epilepsy, corresponding to a 2-fold overall risk for malformation in the offspring of women with epilepsy. The risk for spina bifida [odds ratio (OR) = 11.3, 95% confidence interval (CI) 2.34-108] and congenital anomalies of genital organs (OR = 8.38, 95% CI 2.15-47.4) was substantially elevated in the offspring of mothers with epilepsy. CONCLUSIONS: The absolute excess in the prevalence of major malformations was 26/1000 births in the offspring of mothers with epilepsy in relation to the offspring of reference mothers. The highest relative risk was observed in spina bifida and congenital anomalies of genital organs. However, these malformations cover only a small proportion of all major malformations.
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J Child Neurol. 2005 Aug 1;20(8):693-696.
Nonconvulsive Status Epilepticus Precipitated by Carbamazepine Presenting as Dissociative and Affective Disorders in Adolescents.
[No authors listed]
Nonconvulsive status epilepticus can be confused with psychiatric disorders. Inappropriate drug treatment can represent a precipitating factor. We describe two patients with idiopathic generalized epilepsy in whom nonconvulsive status epilepticus, aggravated by carbamazepine, was misdiagnosed as psychiatric disorder. A 14-year-old girl experienced a tonic-clonic seizure at age 12 years preceded by monthly episodes of confusion with awkward behavior since age 9 years. She was treated with carbamazepine, and the episodes of confusion became more frequent, leading to a diagnosis of dissociative disorder. An electroencephalogram during one of these episodes revealed nonconvulsive status epilepticus. Substitution of carbamazepine with valproic acid controlled the episodes of status epilepticus. A 23-year-old woman presented at age 16 years with a tonic-clonic seizure. Since early adolescence, she had had episodes of depressive mood, worsening of school performances, and facial tics. Carbamazepine treatment caused worsening of the depressive episodes and facial tics. An electroencephalogram during a typical episode revealed nonconvulsive status epilepticus. Carbamazepine substitution with valproate led to seizure freedom and behavioral improvement. Nonconvulsive status epilepticus should be suspected and searched for in patients with epileptic seizures and ictal or fluctuating behavioral disorders. (J Child Neurol 2005;20:693-696).
PMID: 16225818 [PubMed - as supplied by publisher]

J Child Neurol. 2005 May;20(5):416-9.
Use and value of ordering emergency electroencephalograms and videoelectroencephalographic monitoring after business hours in a children's hospital: 1-year experience.
Kothare SV, Khurana DS, Valencia I, Melvin JJ, Legido A.
Division of Child Neurology, Department of Pediatrics, St. Christopher's Hospital for Children, Erie Avenue on Front Street, Philadelphia, PA 19134, USA. sanjeevkothare@drexel.edu
Policies of administration, availability, and utility of ordering emergency electroencephalograms (EEGs) during nonbusiness hours vary widely among different EEG laboratories. In an attempt to explore further the importance of performing such emergency procedures in children, we analyzed the utility of not only emergency EEGs but also emergency longterm bedside EEGs and emergency video-EEGs at our institution in 1 year. The number of EEG studies performed in 1 year at our neurophysiology laboratory was 1821: 1212 routine EEGs, 387 24-hour ambulatory EEGs, 81 video-EEGs, and 141 long-term bedside EEGs. The number of emergency studies during the same period of time was 32 (1.8% of the total studies): 18 emergency EEGs, 8 emergency long-term bedside EEGs, and 6 emergency video-EEGs. The reasons for ordering the 18 emergency EEGs included the evaluation of (1) altered mental status (n=10), (2) paroxysmal movement (including cluster of seizures) (n=6), and (3) prolonged febrile or afebrile seizures prior to being discharged on a weekend (n=2). The eight emergency long-term bedside EEGs were done to evaluate (1) altered mental status (n=6) and (2) frequently occurring paroxysmal events (n=2). Four of the eight emergency long-term bedside EEGs were done after an abnormal emergency EEG. The six emergency video-EEGs were done to evaluate frequently occurring paroxysmal events (n=5) and altered mental status (n=1). Overall, emergency EEGs and emergency video-EEGs were useful in decision making in 30 of 32 (94%) studies. This might be related to the fact that a neurologist approved all of the studies. Appropriate strategies need to be developed to make this essential service available for patient care.
PMID: 15968926 [PubMed - indexed for MEDLINE]

J Clin Neurophysiol. 2003 Sep-Oct;20(5):299-304.

The necessity for sphenoidal electrodes in the presurgical evaluation of temporal lobe epilepsy: pro position.

Sperling MR, Guina L.

Department of Neurology, Jefferson Medical College, and Jefferson Comprehensive Epilepsy Center, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania 19107, USA. michael.sperling@jefferson.edu

Whether sphenoidal electrodes should be used in the presurgical evaluation of people with refractory epilepsy has remained controversial. Many studies have been published touting their advantages, or conversely, their lack of benefit. The present paper reviews the evidence supporting the utility of sphenoidal electrodes. In principle, sphenoidal electrodes have an advantage over laterally placed scalp electrodes in detecting inferiorly directed mesial temporal discharges. Published studies demonstrate that sphenoidal electrodes are more sensitive than scalp electrodes and sometimes detect interictal spikes and seizures not seen with scalp electrodes. While the net added yield is relatively low, perhaps 5 to 10%, those patients in whom sphenoidal electrodes provide unique localizing information have much to gain. Sphenoidal electrodes may spare some patients unnecessary intracranial electrode investigation and permit surgery for others.

Publication Types: Historical Article Review

PMID: 14701990 [PubMed - indexed for MEDLINE]

J Clin Pharm Ther. 2004 Apr;29(2):131-8.

Patterns of lamotrigine use in daily clinical practice during the first 5 years after introduction in the Netherlands.

Knoester PD, Belitser SV, Deckers CL, Keyser A, Renier WO, Egberts AC, Hekster YA.

Department of Clinical Pharmacy, University Medical Centre Nijmegen, Nijmegen, The Netherlands. p.knoester@erasmusmc.nl

OBJECTIVE: Follow-up data on the long-term effectiveness (efficacy and tolerability) of lamotrigine are limited. A useful though crude measure for effectiveness in daily clinical practice is the treatment retention rate determined from drug dispensing data. This study describes the baseline characteristics, the usage patterns and the retention rate of this antiepileptic drug (AED) in a population-based cohort of lamotrigine users in the Netherlands during the first 5 years after its registration in 1995. Data from this cohort are compared with those from the initial randomized clinical trials (RCTs) in patients with refractory epilepsy. METHODS: This retrospective cohort study used dispensing data from community pharmacies. Baseline characteristics and usage patterns were evaluated for first time users of lamotrigine in this study. Usage patterns were characterized as continued, add-on or discontinued use during the patient observation time window. Cox regression analysis was used to explore possible relationships between baseline characteristics and specific usage patterns defined. The baseline characteristics and discontinuation rates in this cohort study were compared with RCT data reported in medical literature. RESULTS: A total of 3598 lamotrigine users were identified. The mean age of the population was 39 years and 54% were female. On average, patients used two other AEDs at the start of lamotrigine therapy and approximately 6% of the patients had no history of prior AED use. The discontinuation rate was 25% after 1 year, and approximately 32% at the end of the 5-year study. Addition of another drug or discontinuation was seen in more than half of the population 3 years after the start of therapy. Concurrent use of valproic acid was associated with a better retention rate. Absence of AED history, use of antidepressants, or use of migraine abortive drugs resulted in an increased likelihood of discontinuing lamotrigine. The population from RCTs differed from the study cohort with respect to age, concurrent use of AEDs and length of follow-up. CONCLUSION: Data from RCTs cannot easily be extrapolated to daily clinical practice. In this large, observational study, lamotrigine therapy failed in a considerable number of patients, although the mean retention rate was better than previously reported by others. Population-based linkage of health care records can be used to further clarify the effectiveness of lamotrigine.

PMID: 15068401 [PubMed - indexed for MEDLINE]

J Clin Pharmacol. 2003 May;43(5):491-503.

Clinical pharmacology of topiramate versus lamotrigine versus phenobarbital: comparison of efficacy and side effects using odds ratios.

Lathers CM, Schraeder PL, Claycamp HG.

Center for Veterinary Medicine, U.S. Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, USA.

Clinical pharmacologists, neurologists, internists, and all health care givers must consider the efficacy, safety, and side effect profile of a given antiepileptic drug (AED) when determining which drug is best for a given patient. The first purpose of this paper is to address whether the "new" AEDs have advantages over the "old" drugs. The second purpose is to teach those interested in clinical pharmacology about the use of Web-based information access to answer a neurology/clinical pharmacology problem: to compare the efficacy and side effects of topiramate versus lamotrigine versus phenobarbital using odds ratios. Cost of all three AEDs was also compared. A number of new AEDs, including topiramate and lamotrigine, have been developed for chronic focal and secondarily generalized epileptic seizures. Efficacy of these drugs as anticonvulsants does not seem to be superior to that of traditional anticonvulsants such as phenobarbital. However, the advantage of the new drugs is a different spectrum of possible adverse events. Newer AEDs may or may not induce sedation and may minimize noncompliance by reducing side effects of lethargy and cognitive impairment. The difficulty in achieving therapeutic dosage because of side effects makes one consider whether these agents are "better" than the oldest and most side effect-prone AED, phenobarbital. The new AEDs have less frequent interactions, leading to improved tolerability with comedication. This exercise compares two "new" AEDs, topiramate and lamotrigine, with phenobarbital by evaluating efficacies and side effects using relative odds ratios, a method commonly used in drug development research. Development of new algorithms and/or new knowledge will bring beneficial tools to all clinical pharmacologists.
PMID: 12751270 [PubMed - indexed for MEDLINE]

J Neurol Neurosurg Psychiatry. 2005 Sep 12; [Epub ahead of print]
Malformation risks of anti-epileptic drugs in pregnancy: A prospective study from the UK Epilepsy and Pregnancy Register.
Morrow JI, Russell A, Gutherie E, Parsons L, Robertson I, Waddell R, Irwin B, Morrison P, McGivern CR, Craig J.
Royal Victoria Hospital, Belfast, United Kingdom.
BACKGROUND: Anti-epileptic drugs (AEDs) taken during pregnancy are associated with an increased risk of major congenital malformations (MCMs). The risks for different AED regimes are difficult to define from earlier studies and are mostly unknown for those containing the newly licensed AEDs (vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, oxcarbazepine, levetiracetam and pregabalin). METHODS: The UK Epilepsy and Pregnancy Register is a prospective, observational, registration and follow up study. Women with epilepsy who become pregnant, whether or not they are taking an AED, in any combination, and whose details are forwarded before the outcome of the pregnancy is known are included. The presence of MCMs recorded within the first three months of life is the main outcome measure. Findings: Full outcome data was collected on 3607 cases. The overall MCM rate for all AED exposed cases was 4.2% (95% C.I. 3.6 - 5.0%) The MCM rate was significantly higher in polytherapy (6.0%)(n=770) compared with monotherapy (3.7%)(n=2598) exposures (crude OR 1.63 [p=0.010]; adjusted OR 1.83 [p=0.002]). The MCM rate for women with epilepsy who had not taken AEDs during pregnancy (n=239) was 3.5% (95% C.I. 1.8 - 6.8%). The MCM rate was significantly greater for pregnancies exposed only to valproate (6.2% ; 95% C.I. 4.6 - 8.2) compared with those exposed only to carbamazepine (2.2% ; 95% C.I. 1.4 - 3.4)(OR 2.78 [p<0.001]; adjusted OR 2.97 [p<0.001]). There were also fewer MCMs for pregnancies exposed only to lamotrigine (3.2% ; 95% C.I. 2.1 - 4.9) compared with those exposed only to valproate OR 0.52 [p=0.015]; though statistical significance was lost using multivariate analysis (adjusted OR 0.59 [p=0.064]). While there was a trend towards more MCMs with increasing doses of valproate this was not significant. A positive dose response for MCMs was noted for lamotrigine (p=0.006) with a MCM rate of 5.4% (95% C.I. 3.3 - 8.7%) for total daily doses of more than 200mg. This MCM rate was similar to those receiving doses of 1000mg or less of valproate (5.1% ; 95% C.I. 3.5 - 7.3). For pregnancies exposed to more than 1000mg of valproate a day the MCM rate was 9.1%(95% C.I. 5.8 - 14.1%). For polytherapy combinations, those containing valproate in any combination had a significantly higher risk of MCM than polytherapy combinations not containing valproate (O.R. 2.49 [95% C.I. 1.31 - 4.70]). Interpretation: Almost 96% of live-births born to women with epilepsy did not have a MCM. The MCM rate for polytherapy exposed pregnancies was significantly greater than for monotherapy exposures. Polytherapy regimes containing valproate had significantly more MCMs than those not containing valproate. For monotherapy exposures, carbamazepine was associated with the lowest risk of MCM. While there was a trend towards lamotrigine being associated with fewer MCMs than valproate, the differences were minimised in those infants exposed to more than 200mg each day of lamotrigine.
PMID: 16157661 [PubMed - as supplied by publisher]

J Neurol Neurosurg Psychiatry. 2004 Nov;75(11):1584-8.
Inappropriate emergency management of status epilepticus in children contributes to need for intensive care.
Chin RF, Verhulst L, Neville BG, Peters MJ, Scott RC.
Neurosciences Unit, Institute of Child Health, University College London, WC1N 1EH, UK. r.chin@ich.ucl.ac.uk
OBJECTIVES: To characterise the clinical features, emergency pre-paediatric intensive care (PIC) treatment, and course of status epilepticus (SE) in children admitted to PIC. This may provide insight into reasons for admission to PIC and provide a framework for the development of strategies that decrease the requirement for intensive care. DESIGN: Cross sectional, retrospective study. SETTING: A tertiary paediatric institution's intensive care unit. PARTICIPANTS: The admission database and all discharge summaries of each admission to a tertiary paediatric institution's PIC over a three year period were searched for children aged between 29 days and 15 years with a diagnosis of SE or related diagnoses. The case notes of potential cases of SE were systematically reviewed, and clinical and demographic data extracted using a standard data collection form. RESULTS: Most children with SE admitted to PIC are aged less than 5 years, male to female ratio 1:1, and most (77%) will have had no previous episodes of SE. Prolonged febrile convulsions, SE related to central nervous system infection, and SE associated with epilepsy occur in similar proportions. Contrary to the Advanced Paediatric Life Support guidelines many children admitted to PIC for SE receive over two doses, or inadequate doses, of benzodiazepine. There is a risk of respiratory depression following administration of over two doses of benzodiazepine (chi2 = 3.4, p = 0.066). Children with SE admitted to PIC who had prehospital emergency treatment are more likely to receive over two doses of benzodiazepines (chi2 = 11.5, p = 0.001), and to subsequently develop respiratory insufficiency (chi2 = 6.2, p = 0.01). Mortality is low. Further study is required to determine the morbidity associated with SE in childhood requiring intensive care. CONCLUSIONS: As the risk of respiratory depression is greater with more than two doses of benzodiazepines, clinicians should not disregard prehospital treatment of SE. As pre-PIC treatment of SE is inadequate in many cases, appropriate audit and modifications of standard guidelines are required.
PMID: 15489391 [PubMed - indexed for MEDLINE]

J Neurol Neurosurg Psychiatry. 2003 Apr;74(4):466-70.
Clinical application of neuroimaging in epilepsy.
Wieshmann UC.
The Walton Centre for Neurology and Neurosurgery, Lower Lane, Liverpool L9 7IJ, UK. wieshmann@vizzavi.net
OBJECTIVE: To evaluate the use of neuroimaging in clinical practice and to assess the prevalence of detected structural abnormalities in epilepsy patients in a clinical set up. METHODS: 919 outpatients were identified and the scan results reviewed. A total of 677 patients had chronic active epilepsy (88 had idiopathic generalised epilepsy (IGE), 588 had localisation related epilepsy, one had symptomatic generalised epilepsy), 57 had a single epileptic seizure, 46 were in remission, and 139 had non-epileptic attacks. RESULTS: 391 patients had no scan (53 patients in this group had IGE, 182 had localisation related epilepsy, one had generalised symptomatic epilepsy, 18 had single epileptic attacks, 21 were in remission, 116 had non-epileptic attacks). Altogether 528 patients had a scan, the results were not available in 33, 163 had x ray computed tomography (CT) only, 178 had standard magnetic resonance imaging (MRI) (slice thickness 5 mm), and 154 had high resolution MRI (including a T1 weighted sequence with 1.5 mm thick slices). Some 252 of 495 scans (51%) were abnormal. Abnormalities were hippocampal sclerosis (n=128), atrophy or non-specific white matter lesions (n=35), vascular abnormalities (n=27), tumours (n=25), brain damage (n=24), malformations of cortical development (n=13). Excluding atrophy and non-specific white matter lesions the prevalence of detected abnormalities was 54% in localisation related epilepsy, 18% in single seizure patients, 16% in epilepsy in remission, and 0% in IGE and non-epileptic attacks. CONCLUSIONS: Abnormalities were detected in more than half of all patients with localisation related epilepsy, and in about one in five patients with single seizures or epilepsy in remission. Many patients had no scan or only CT or standard MRI. The true prevalence of structural abnormalities may be have been higher. Scanning did not add any information in patients with IGE or non-epileptic attacks.
Publication Types: Evaluation Studies
PMID: 12640065 [PubMed - indexed for MEDLINE]

J Neurol Neurosurg Psychiatry. 2003 Mar;74 Suppl 1:i37-41.
Taking over epilepsy from the paediatric neurologist.

Smith PE, Wallace SJ.
The Epilepsy Unit, Department of Neurology, University Hospital of Wales, Cardiff, UK. SmithPE@cardiff.ac.uk
Publication Types: Review
PMID: 12611933 [PubMed - indexed for MEDLINE]

J Paediatr Child Health. 2005 Jul;41(7):313-6.
Comment in: J Paediatr Child Health. 2005 Jul;41(7):311-2.
Drug treatment of neonatal seizures by neonatologists and paediatric neurologists.
Carmo KB, Barr P.
Department of Neonatology, Royal Alexandra Hospital for Children, Sydney, New South Wales, Australia.
OBJECTIVE: To survey anti-epileptic drug (AED) treatment of early-onset neonatal seizures by neonatologists and paediatric neurologists. METHODS: A self-administered questionnaire was posted to Australian and New Zealand neonatologists and paediatric neurologists. Participants were given the hypothetical case of a full-term infant with early-onset seizures following perinatal asphyxia and asked to nominate their preferred AED for treatment of three seizure episodes during the first 24 h. RESULTS: One hundred and seven (57%) of 187 individuals answered the questionnaire: neonatologists responded more often than neurologists (chi(2) (1,187) = 7.18, P = 0.007). Phenobarbitone was used by 95% of the respondents to treat the first episode of seizures and 75% of them used an appropriate loading dose (20 mg/kg). Phenobarbitone was used by 84 and 40% of the respondents to treat the second- and third-seizure episodes, respectively. Neonatologists used phenobarbitone, phenytoin and a benzodiazepine with equal frequency to treat a third episode of seizures, whereas neurologists rarely used a benzodiazepine. Neonatologists used significantly larger total doses of phenobarbitone than neurologists. Very few respondents used pyridoxine to treat recurrent seizures that were historically linked to perinatal asphyxia and hypoxic-ischaemic encephalopathy. Neonatologists were more likely than neurologists to discontinue AED within a few days of seizure cessation (chi(2) (1,106) = 11.60, P = 0.0006). CONCLUSIONS: Australian and New Zealand neonatologists and paediatric neurologists generally use phenobarbitone to treat neonatal seizures presumed to be owing to hypoxic-ischaemic encephalopathy, though they do not always use appropriate doses. Neonatologists use phenobarbitone, phenytoin or a benzodiazepine for second and third episodes of seizures, whereas neurologists tend not to use benzodiazepines. Neonatologists use larger total doses of phenobarbitone than neurologists in pursuit of seizure control. Neonatologists discontinue AED earlier than neurologists.
PMID: 16014133 [PubMed - indexed for MEDLINE]

JAMA. 2004 Feb 4;291(5):615-20.
The new antiepileptic drugs: clinical applications.
LaRoche SM, Helmers SL.
Department of Neurology, Emory University, Atlanta, Ga, USA. Suzette_LaRoche@emoryhealthcare.org
In the past decade, 8 new antiepileptic drugs have been approved for use in the United States, offering many new treatment options to patients with epilepsy. With expanding use of these newer agents, primary care clinicians are challenged with understanding the roles that each new agent plays in the treatment of patients with epilepsy as well as possible interactions with other pharmacological therapies. Each new medication provides a unique profile of pharmacokinetics, adverse effects, and mechanisms of action, making an appreciation of how these agents are best utilized even more difficult. Despite well-performed trials evaluating the safety and efficacy of specific antiepileptic drugs, the lack of head-to-head comparisons among them makes it difficult to endorse a single therapeutic regimen. Limited studies have compared the new antiepileptic drugs with more traditional medications and found similar efficacy but improved tolerability of the newer agents. There remains no well-established guidelines for choosing a particular antiepileptic drug or for choosing a newer agent over a traditional one. However, careful consideration of seizure type, patient comorbidities, and specific medication toxicities aids in prescribing the most appropriate medication. This article aims to familiarize the general practitioner with the appropriate roles and effective uses of the new antiepileptic drugs in specific clinical scenarios.
Publication Types: Case Reports
PMID: 14762041 [PubMed - indexed for MEDLINE]

Lancet Neurol. 2005 Oct;4(10):592-3.
Buccal midazolam as rescue therapy for acute seizures.

Scott RC.
Publication Types: Letter
PMID: 16168926 [PubMed - indexed for MEDLINE]

Lancet Neurol. 2004 May;3(5):261.
Out with the old and in with the new...epilepsy drugs.
Marshall L.
Publication Types: News
PMID: 15132138 [PubMed - indexed for MEDLINE]

Med Decis Making. 2005 Sep-Oct;25(5):511-9.
Cost-effectiveness analysis of treatments for chronic disease: using R to incorporate time dependency of treatment response.
Hawkins N, Sculpher M, Epstein D.
Centre for Health Economics, University of York, Centre for Health Economics, York, UK Y010 5DD.
When constructing decision-analytic models to evaluate the cost-effectiveness of alternative treatments, we often need to extrapolate beyond the available experimental data, as these typically relate to a limited period starting from the initiation of a new treatment or the diagnosis of the current disease state. We may also be required to extrapolate beyond the available experimental evidence to compare potential treatment sequences. Markov models are often used for this extrapolation. These models have the defining assumption that future transition probabilities are independent of past transitions. This means that, in general, transition probabilities cannot be conditional of the time spent in a given state. Where data exist to show that the risks of transition are conditional on the time spent in the treatment state, the simplifying Markov assumption can result in a loss in the model's "face validity," and misleading results might be generated. Several methods are available to incorporate time dependency into transition probabilities based on standard methods and software. These include the inclusion of tunnel states in Markov models and patient-level simulation, where a series of individual patients are simulated. This article considers the features and limitations of these methods and also describes a novel approach to building time dependency into a Markov model by incorporating an additional time dimension resulting in a "semi-Markov" model. An example of the implementation of such a model, using the R statistical programming language, is illustrated using a cost-effectiveness model for new epilepsy therapies.
PMID: 16160207 [PubMed - in process]

Med Decis Making. 2005 Sep-Oct;25(5):493-510.
Assessing the cost-effectiveness of new pharmaceuticals in epilepsy in adults: the results of a probabilistic decision model.
Hawkins N, Epstein D, Drummond M, Wilby J, Kainth A, Chadwick D, Sculpher M.
Epilepsy currently affects more than 400,000 people in the United Kingdom and 2.3 million in the United States. Drug therapy is the mainstay of treatment for patients with epilepsy, but therapies vary widely in their mechanism of action and acquisition cost. This article describes a decision model developed for the National Institute for Clinical Excellence in the United Kingdom. It compares the long-term cost-effectiveness of drugs licensed in adults for use in 3 situations: monotherapy for newly diagnosed patients, monotherapy for refractory patients, and combination therapy for refractory patients. The analysis separately considers the treatment of partial and generalized seizures. The full range of pharmaceutical therapies feasibly used in the UK health system was included in the analysis. The analysis showed that, on the basis of existing evidence, for newly diagnosed patients with partial seizures, carbamazepine and valproate are likely to be the most cost-effective mono-therapies. Carbamazepine is likely to be the most cost-effective 2nd-line monotherapy for refractory patients, and oxcarbazepine would probably be the most cost-effective adjunctive therapy for refractory patients if the willingness to pay for additional health benefits is greater than 18,000 pounds per quality-adjusted life year (QALY). For patients with generalized seizures, valproate is most likely to be cost-effective for newly diagnosed patients. For refractory patients, adjunctive topiramate is more cost-effective than monotherapy alone if the willingness to pay for additional health benefits is greater than 35,000 pounds per QALY. There is, however, considerable uncertainty regarding these results. Some of the methodological features of the study will be of value in designing cost-effectiveness analyses of other therapies for chronic conditions. These include the methods used to deal with the absence of head-to-head trial data and the need to reflect time dependency in Markov transition probabilities.

PMID: 16160206 [PubMed - in process]

Mol Psychiatry. 2003 May;8(5):463-5.
What's new in epilepsy genetics?
Ptacek LJ, Fu YH.
Departments of Neurology and Human Genetics, Howard Hughes Medical Institute, University of Utah, UT 84112, USA. ptacek@genetics.utah.edu
Publication Types: Review
PMID: 12808423 [PubMed - indexed for MEDLINE]

N Z Med J. 2005 Nov 25;118(1226):U1768.
More on nurse practitioner prescribing in New Zealand: the view and experience of an epilepsy nurse specialist who worked in the United Kingdom.
Hosking P.
Publication Types: Comment Letter
PMID: 16311622 [PubMed - in process]

Neurochem Res. 2004 Jun;29(6):1169-78.
Large-scale analysis of gene expression in epilepsy research: is synthesis already possible?
Lukasiuk K, Pitkanen A.
Laboratory of Transcription Regulation, The Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland. k.lukasiuk@nencki.gov.pl
DNA microarrays are now popular tools for large-scale studies of gene expression in the brain in both physiologic and pathologic conditions. Here, we review the few available papers describing the use of microarrays in experiments relevant to temporal lobe epilepsy. Review of the data indicates that products of genes regulated during epileptic processes belong to a variety of functional classes, including signal transduction, transcription regulation, protein synthesis and degradation, basic metabolism, and structural proteins. There is surprisingly little overlap in gene lists from different studies. This might be related to the limited sensitivity of microarrays or to differences in the experimental setup, such as the use of different animal models, time points, and microarrays. Despite obvious problems with interpretation of the vast amount of information derived from microarray experiments, these data are potentially excellent tools for creating new hypotheses about events occurring during circuitry reorganization in the brain that results in lowered seizure threshold and epilepsy.
Publication Types: Review
PMID: 15176474 [PubMed - indexed for MEDLINE]

Neuroinformatics. 2004;2(1):119-21.
Comment on: Neuroinformatics. 2004;2(1):101-18.
The utility of a federated web-based information management system in an epilepsy center.
Kirsch HE.
University of California, San Francisco Epilepsy Center, San Francisco, CA, USA.
Publication Types: Comment
PMID: 15067171 [PubMed - indexed for MEDLINE]

Neuroinformatics. 2004;2(1):101-18.
Comment in: Neuroinformatics. 2004;2(1):119-21.
A web-based federated neuroinformatics model for surgical planning and clinical research applications in epilepsy.
Cao X, Wong ST, Hoo KS Jr, Tjandra D, Fu JC, Lowenstein DH.
Department of Radiology, Brigham and Women's Hospital, Boston, MA 02115, USA. xinhuac@bwh.harvard.edu
There is an increasing need to efficiently share diverse clinical and image data among different clinics, labs, and departments of a medical center enterprise to facilitate better quality care and more effective clinical research. In this paper, we describe a web-based, federated information model as a viable technical solution with applications in medical refractory epilepsy and other neurological disorders. We

describe four such online applications developed in a federated system prototype: surgical planning, image analysis, statistical data analysis, and dynamic extraction, transforming, and loading (ETL) of data from a heterogeneous collection of data sources into an epilepsy multimedia data warehouse (EMDW). The federated information system adopts a three-tiered architecture, consisting of a user-interface layer, an application logic layer, and a data service layer. We implemented two complementary federated information technologies, i.e., XML (eXtensible Markup Language) and CORBA (Common Object Request Broker Architecture), in the prototype to enable multimedia data exchange and brain images transmission. The preliminary results show that the federated prototype system provides a uniform interface, heterogeneous information integration and efficient data sharing for users in our institution who are concerned with the care of patients with epilepsy and who pursue research in this area.
PMID: 15067170 [PubMed - indexed for MEDLINE]

Neurol India. 2005 Mar;53(1):27-31.
Telemedicine in neurology: underutilized potential.
Misra UK, Kalita J, Mishra SK, Yadav RK.
Department of Neurology, Sanjay Gandhi Post-Graduate Institute of Medical Sciences, Raebareily Road, Lucknow 226-014, India. ukmisra@sgpgi.ac.in
Advances in telecommunication which started with telephone lines, FAX, integrated service digital network (ISDN) lines and now internet have provided an unprecedented opportunity for transfer of knowledge and sharing of information. The information can be used for overlapping applications in patient care, teaching and research. In medicine there is increasing utilization of telemedicine; radiology and pathology being regarded as mature specialties and emergency medicine as maturing specialties compared to other evolving specialties which include psychiatry, dermatology, cardiology and ophthalmology. Of the emergencies, status epilepticus and stroke have high potential for improving patient management. Administration of tPA was more frequent when carried out under telemedicine guidance. Telemedicine has great potential for medical education. The principles of education are in congruence with those of telemedicine and can be closely integrated in the existing medical education system. Our experience of telemedicine as a medical education tool is based on video conferencing with SCB Medical College, Cuttack. We had 30 sessions during 2001 to 2004 in which 2-3 cases were discussed in each session. The patients' details, radiological and neurophysiological findings could be successfully transmitted. These conferences improved the knowledge of participants, provided an opportunity for a second opinion as well as modified the treatment decisions in some cases. The advances in telemedicine should be utilized more extensively in neurology, especially in emergency management, epilepsy and stroke patients as well, as it may have a role in neurophysiology and movement disorders.
Publication Types: Review
PMID: 15805651 [PubMed - indexed for MEDLINE]

Neurol Res. 2004 Jan;26(1):55-60.
A neural-network-based detection of epilepsy.
Nigam VP, Graupe D.
Department of Electrical and Computer Engineering, University of Illinois, Chicago, IL 60607-7053, USA.
Diagnosis of epilepsy is primarily based on scalp-recorded electroencephalograms (EEG). Unfortunately the long-term recordings obtained from 'ambulatory recording systems' contain EEG data of up to one week duration, which has introduced new problems for clinical analysis. Traditional methods, where the entire EEG is reviewed by a trained professional, are very time-consuming when applied to recordings of this length. Therefore, several automated diagnostic aid approaches were proposed in recent years, in order to reduce expert effort in analyzing lengthy recordings. The most promising approaches to automated diagnosis are based on neural networks. This paper describes a method for automated detection of epileptic seizures from EEG signals using a multistage nonlinear pre-processing filter in combination with a diagnostic (LAMSTAR) Artificial Neural Network (ANN). Pre-processing via multistage nonlinear filtering, LAMSTAR input preparation, ANN training and system performance (1.6% miss rate, 97.2% overall accuracy when considering both false-alarms and 'misses') are discussed and are shown to compare favorably with earlier approaches presented in recent literature.
PMID: 14977058 [PubMed - indexed for MEDLINE]

Neurology. 2005 Dec 13;65(11):1810-2.
Low-glycemic-index treatment: a liberalized ketogenic diet for treatment of intractable epilepsy.

Pfeifer HH, Thiele EA.
Pediatric Epilepsy Program, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
The ketogenic diet is often effective for intractable epilepsy, but many patients have trouble complying with the strict regimen. The authors tested an alternative diet regimen, a low-glycemic-index treatment, with more liberal total carbohydrate intake but restricted to foods that produce relatively little increase in blood glucose (glycemic index < 50). Ten of 20 patients treated with this regimen experienced a greater than 90% reduction in seizure frequency.
PMID: 16344529 [PubMed - in process]

Neurology. 2005 Dec 13;65(11):1750-3.
Do generalized tonic-clonic seizures in infancy exist?
Korff C, Nordli DR Jr.
Epilepsy Center, Children's Memorial Hospital, Chicago, IL 60614-3394, USA.
OBJECTIVE: To determine the frequency of generalized tonic-clonic seizures (GTCS) in infants (1 month to 2 years). METHODS: From a total of 2,112 patients monitored in our video-EEG lab from May 2000 through January 2005, 109 distinct seizures in 77 infants were reviewed. Eight events in eight patients were excluded because of video files insufficiently reliable to determine the clinical characteristics with precision. The clinical manifestations and electrographic features of the remaining 101 seizures in 69 infants were retrospectively analyzed. RESULTS: The authors did not observe a single GTCS. Four patients had icti that resembled GTCS, but careful analysis of these episodes revealed that three of them had a focal onset and that the fourth had a slightly different sequence of events. CONCLUSIONS: Generalized tonic-clonic seizures are rarely, if ever, seen in infants younger than age 2 in a tertiary-care pediatric epilepsy unit. Instead, they more commonly occur in older children, particularly in the well-characterized epilepsy syndromes of childhood and adolescence.
PMID: 16344517 [PubMed - in process]

Neurology. 2005 Dec 13;65(11):1744-9.
Changes in depression and anxiety after resective surgery for epilepsy.
Devinsky O, Barr WB, Vickrey BG, Berg AT, Bazil CW, Pacia SV, Langfitt JT, Walczak TS, Sperling MR, Shinnar S, Spencer SS.
New York University School of Medicine, New York, NY, USA. od4@nyu.edu
OBJECTIVE: To determine changes in depression and anxiety after resective surgery. METHODS: Data from subjects enrolled in a prospective multicenter study of resective epilepsy surgery were reviewed with the Beck Psychiatric Symptoms Scales (Beck Depression Inventory [BDI] and Beck Anxiety Inventory [BAI]) and Composite International Diagnostic Interview (CIDI) up to a 24-month period. chi2 analyses were used to correlate proportions. RESULTS: A total of 358 presurgical BDI and 360 BAI results were reviewed. Moderate and severe levels of depression were reported in 22.1% of patients, and similar levels of anxiety were reported by 24.7%. Postoperative rates of depression and anxiety declined at the 3-, 12-, and 24-month follow-up periods. At the 24-month follow-up, moderate to severe levels of depression symptoms were reported in 17.6 and 14.7% of the patients who continued to have postoperative seizures. Moderate to severe depression and anxiety were found in 8.2% of those who were seizure-free. There was no relationship, prior to surgery, between the presence or absence of depression and anxiety and the laterality or location of the seizure onset. There were no significant relationships between depression or anxiety at 24-month follow-up and the laterality or location of the surgery. CONCLUSIONS: Depression and anxiety in patients with refractory epilepsy significantly improve after epilepsy surgery, especially in those who are seizure-free. Neither the lateralization nor the localization of the seizure focus or surgery was associated with the risk of affective symptoms at baseline or after surgery.
PMID: 16344516 [PubMed - in process]

Neurology. 2005 Dec 13;65(11):1737-43.
Double-blind, placebo-controlled study of lamotrigine in primary generalized tonic-clonic seizures.
Biton V, Sackellares JC, Vuong A, Hammer AE, Barrett PS, Messenheimer JA.
Arkansas Epilepsy Program, Little Rock, AR 72205, USA. vbiton@alltel.net
OBJECTIVE: To evaluate the efficacy and tolerability of adjunctive lamotrigine in primary generalized tonic-clonic (PGTC) seizures in a randomized, double-blind, placebo-controlled trial. METHODS: Patients with a diagnosis of epilepsy with PGTC seizures who were receiving one or two antiepileptic drugs at study

entry were eligible. Patients with partial seizures were excluded on the basis of seizure history and screening EEGs. The study comprised a baseline phase, an escalation phase during which study medication was titrated to a target dose, and a 12-week maintenance phase during which doses of lamotrigine/placebo and concomitant antiepileptic drugs were maintained. RESULTS: Of the 121 randomized patients ages 2 to 55 years, 117 (58 lamotrigine, 59 placebo) entered the escalation phase and received study medication. During the escalation and maintenance phases combined, median percent reduction in PGTC seizure frequency was 66.5% with lamotrigine compared with 34.2% with placebo (p = 0.006). The corresponding numbers for lamotrigine and placebo were 60.6% and 32.8% (p = 0.038) during the escalation phase and 81.9% and 43.0% (p = 0.006) during the maintenance phase. During the maintenance phase, 72% of lamotrigine-treated patients compared with 49% of placebo-treated patients experienced a > or = 50% reduction in frequency of PGTC seizures (p = 0.014). A similar pattern of results was observed for all generalized seizures. The most common drug-related adverse events were dizziness (5% lamotrigine, 2% placebo), somnolence (5% lamotrigine, 2% placebo), and nausea (5% lamotrigine, 3% placebo). CONCLUSIONS: Adjunctive lamotrigine is effective in the treatment of primary generalized tonic-clonic seizures and has a favorable tolerability profile.
PMID: 16344515 [PubMed - in process]

Neurology. 2005 Dec 13;65(11):1730-6.
Serum antibodies in epilepsy and seizure-associated disorders.
McKnight K, Jiang Y, Hart Y, Cavey A, Wroe S, Blank M, Shoenfeld Y, Vincent A, Palace J, Lang B.
Neurosciences Group, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, Oxford OX3 9DS, United Kingdom.
OBJECTIVE: To investigate whether autoantibodies to ion channels and other neural antigens are present in the sera of patients with epilepsy and seizure-related diseases. METHODS: Sera were obtained from 139 patients, including 26 with preexisting autoimmune disease, 46 in whom an autoimmune basis was suspected, and 67 with drug-resistant epilepsy. The sera were assayed for antibodies to voltage-gated potassium (VGKC) and calcium (VGCC) channels, glutamic acid decarboxylase (GAD), gangliosides, glutamate receptor type 3, cardiolipins, DNA, and nuclear antigens; the results were compared with results from a large cohort of healthy and disease controls. RESULTS: Increased titers of VGKC antibodies (>100 pM) were detected in 16 of 139 (11%) patients with seizures but only 1 control (0.5%). Eight VGKC-positive patients presented with an acute/subacute illness, and 5 of these had the highest VGKC antibodies; 3 patients improved spontaneously, another 5 patients responded well to immunomodulatory therapy. The other VGKC-positive patients had longer disease duration (>6 years) and intermediate levels of antibodies; immunotherapies have not been tested in this group. Very high levels of GAD antibodies (>1,000 U) were found in an additional 3 patients (2.1%) with long-standing drug-resistant epilepsy. CONCLUSIONS: The presence of autoantibodies to voltage-gated potassium channels and glutamic acid decarboxylase suggests that the immune system may contribute to certain forms of epilepsy or seizure-associated disorders. Further studies are needed to determine whether the antibodies are pathogenic.
PMID: 16344514 [PubMed - in process]

Neurology. 2005 Oct 11;65(7):975.
Higher resolution MRI and image modeling for predicting surgical outcome in partial epilepsy.
Cendes F.
Publication Types: Comment
PMID: 16220587 [PubMed - in process]

Neurology. 2005 Oct 11;65(7):1098-100.
Clinical features of benign infantile convulsions: familial and sporadic cases.
Franzoni E, Bracceschi R, Colonnelli MC, Errani A, Ucchino V, Malaspina E, Moscano F, Cecconi I, Tzolas V, Marchiani V.
Department of Pediatrics, University of Bologna, Italy. emilio.franzoni@unibo.it
The authors describe the so-called benign convulsions of infancy and confirm the existence of benign nonfamilial infantile convulsions during the first 2 years of life and their benign course. The authors evaluated 58 patients: 17 subjects had a family history of benign epilepsy, and 41 did not. No clinical differences were observed between the two groups.
PMID: 16217066 [PubMed - in process]

Neurology. 2005 Sep 27;65(6):912-8.
Predicting long-term seizure outcome after resective epilepsy surgery: the multicenter study.
Spencer SS, Berg AT, Vickrey BG, Sperling MR, Bazil CW, Shinnar S, Langfitt JT, Walczak TS, Pacia SV; Multicenter Study of Epilepsy Surgery.
Department of Neurology, Yale University School of Medicine, New Haven, CT 06520-8018, USA. susan.spencer@yale.edu
BACKGROUND: In a seven-center prospective observational study of resective epilepsy surgery, the authors examined probability and predictors of entering 2-year remission and the risk of subsequent relapse. METHODS: Patients aged 12 years and over were enrolled at time of referral for epilepsy surgery, and underwent standardized evaluation, treatment, and follow-up procedures. The authors defined seizure remission as 2 years completely seizure-free after hospital discharge with or without auras, and relapse as any seizures after 2-year remission. The authors examined type of surgery, seizure, clinical and demographic variables, and localization study results with respect to prediction of seizure remission or relapse, using chi2 and proportional hazards analysis. RESULTS: Of 396 operated patients, 339 were followed over 2 years, and 223 (66%) experienced 2-year remission, not significantly different between medial temporal (68%) and neocortical (50%) resections. In multivariable models, only absence of generalized tonic-clonic seizures and presence of hippocampal atrophy were significantly and independently associated with remission, and only in the medial temporal resection group. Fifty-five patients relapsed after 2-year remission, again not significantly different between medial temporal (25%) and neocortical (19%) resections. Only delay to remission predicted relapse, and only in medial temporal patients. CONCLUSION: Hippocampal atrophy and a history of absence of generalized tonic clonic seizures were the sole predictors of 2-year remission, and only for medial temporal resections.
PMID: 16186534 [PubMed - in process]

Neurology. 2005 Aug 23;65(4):593-5.
Improved tolerability and efficacy in epilepsy patients with extended-release carbamazepine.
Ficker DM, Privitera M, Krauss G, Kanner A, Moore JL, Glauser T.
Department of Neurology, University of Cincinnati Medical Center, 231 Albert B. Sabin Way, Cincinnati, OH 45267, USA. david.ficker@uc.edu
The authors conducted a 3-month, prospective, open-label study assessing the effects of switching from immediate-release carbamazepine formulations to an equal total daily dose of carbamazepine extended-release capsules (CBZ-ERC) in adolescents and adults with epilepsy. Using validated, epilepsy-specific measures the authors found that switching to CBZ-ERC significantly improved patients' adverse events and quality-of-life measures. Switching to CBZ-ERC also improved seizure control.
PMID: 16116122 [PubMed - in process]

Neurology. 2005 Aug 23;65(4):523-8.
Familial clustering of seizure types within the idiopathic generalized epilepsies.
Winawer MR, Marini C, Grinton BE, Rabinowitz D, Berkovic SF, Scheffer IE, Ottman R.
G.H. Sergievsky Center, Columbia University, New York, NY 10032, USA. mw211@columbia.edu
OBJECTIVE: To examine the genetic relationships among epilepsies with different seizure types--myoclonic, absence, and generalized tonic-clonic--within the idiopathic generalized epilepsies (IGEs). BACKGROUND: Careful phenotype definition in the epilepsies may allow division into groups that share susceptibility genes. Examination of seizure type, a phenotypic characteristic less complex than IGE syndrome, may help to define more homogeneous subgroups. METHODS: Using the approach that found evidence of distinct genetic effects on myoclonic vs absence seizures in families from the Epilepsy Family Study of Columbia University, the authors examined an independent sample of families from Australia and Israel. They also examined the familial clustering of generalized tonic-clonic seizures (GTCs) within the IGEs in two combined data sets. Families were defined as concordant if all affected members had the same type of seizure or IGE syndrome, as appropriate for the analysis performed. RESULTS: The proportion of families concordant for myoclonic vs absence seizures was greater than expected by chance in the Australian families. In addition, GTCs clustered in families with IGEs to a degree greater than expected by chance. CONCLUSIONS: These results provide additional evidence for distinct genetic effects on myoclonic vs absence seizures in an independent set of families and suggest that there is a genetic influence on the occurrence of generalized tonic-clonic seizures within the idiopathic generalized epilepsies.
PMID: 16116110 [PubMed - in process]

Neurology. 2005 Jul 26;65(2):317-9.
Vagus nerve stimulation for epilepsy: randomized comparison of three stimulation paradigms.
DeGiorgio C, Heck C, Bunch S, Britton J, Green P, Lancman M, Murphy J, Olejniczak P, Shih J, Arrambide S, Soss J.
UCLA-Geffen School of Medicine, Los Angeles, CA, USA. cmd@mednet.ucla.edu
Vagus nerve stimulation (VNS) is an effective adjunctive treatment for intractable epilepsy. However, the optimal range of device duty-cycles [on/(on + off times)] is poorly understood. The authors performed a multicenter, randomized trial of three unique modes of VNS, which varied primarily by duty-cycle. The results indicate that the three duty-cycles were equally effective. The data support the use of standard duty-cycles as initial therapy.
PMID: 16043810 [PubMed - in process]

Neurology. 2005 Jun 28;64(12 Suppl 3):S2-11.
Current treatments of epilepsy.
Nadkarni S, LaJoie J, Devinsky O.
Comprehensive Epilepsy Center, NYU School of Medicine, 403 East 34th Street, 4th Floor, New York, NY 10016, USA. siddhu@mindspring.com
Medical therapy is the mainstay for epilepsy, with most patients well controlled on a single antiepileptic drug (AED). In this non-refractory group, many patients have medication side effects and occasional seizures. Approximately 30% of patients with partial epilepsy and 25% of patients with generalized epilepsy are not well controlled on medications. These patients are often receiving multiple AEDs, with disabling seizures and side effects. Although second-generation AEDs are safer and better tolerated than the older AEDs, there are scant data to support significant advantages in efficacy. In VA studies with older AEDS, therapy with two AEDs improved seizure control in 40% of patients but seizure freedom was achieved in only 9%. A meta-analysis of the second-generation AEDs used as adjunctive therapies shows that 12% to 29% of patients had a 50% or greater reduction in seizure frequency. Surgery and the vagus nerve stimulator provide important therapeutic options in patients whose seizures are not controlled by AEDs. Special considerations about epilepsy care must be made in pediatric populations, those with developmental delays, women, and the elderly.
Publication Types: Review
PMID: 15994220 [PubMed - indexed for MEDLINE]

Neurology. 2005 Jun 28;64(12):2136-8.
Four-year outcome after early withdrawal of antiepileptic drugs in childhood epilepsy.
Geerts AT, Niermeijer JM, Peters AC, Arts WF, Brouwer OF, Stroink H, Peeters EA, van Donselaar CA.
Department of Neurology, Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands.
Four-year follow-up of children with epilepsy included in a randomized trial of early withdrawal of antiepileptic drugs showed that 51% achieved a terminal remission of at least 2 years without medication and 21% with medication; 15% had seizures during the fourth year. Early medication withdrawal is not recommended as standard practice in children with a rapid response to medication. The authors developed a model to predict outcome if withdrawal is considered.
PMID: 15985589 [PubMed - in process]

Neurology. 2005 Jun 14;64(11):1868-73.
New onset geriatric epilepsy: a randomized study of gabapentin, lamotrigine, and carbamazepine.
Rowan AJ, Ramsay RE, Collins JF, Pryor F, Boardman KD, Uthman BM, Spitz M, Frederick T, Towne A, Carter GS, Marks W, Felicetta J, Tomyanovich ML; VA Cooperative Study 428 Group.
VA Medical Center, Bronx, NY 10468, USA. aj.rowan@med.va.gov
OBJECTIVE: To determine the relative tolerability and efficacy of two newer antiepileptic drugs, lamotrigine (LTG) and gabapentin (GBP), as compared to carbamazepine (CBZ) in older patients with epilepsy. METHODS: This was an 18-center, randomized, double-blind, double dummy, parallel study of 593 elderly subjects with newly diagnosed seizures. Patients were randomly assigned to one of three treatment groups: GBP 1,500 mg/day, LTG 150 mg/day, CBZ 600 mg/day. The primary outcome measure was retention in trial for 12 months. RESULTS: Mean age was 72 years. The most common etiology was cerebral infarction. Patients had multiple medical conditions and took an average of seven comedications.

Mean plasma levels at 6 weeks were as follows: GBP 8.67 +/- 4.83 microg/mL, LTG 2.87 +/- 1.60 microg/mL, CBZ 6.79 +/- 2.92 microg/mL. They remained stable throughout the trial. Early terminations: LTG 44.2%, GBP 51%, CBZ 64.5% (p = 0.0002). Significant paired comparisons: LTG vs CBZ: p < 0.0001; GBP vs CBZ: p = 0.008. Terminations for adverse events: LTG 12.1%, GBP 21.6%, CBZ 31% (p = 0.001). Significant paired comparisons: LTG vs CBZ: p < 0.0001; LTG vs GBP: p = 0.015. There were no significant differences in seizure free rate at 12 months. CONCLUSIONS: The main limiting factor in patient retention was adverse drug reactions. Patients taking lamotrigine (LTG) or gabapentin (GBP) did better than those taking carbamazepine. Seizure control was similar among groups. LTG and GBP should be considered as initial therapy for older patients with newly diagnosed seizures.
Publication Types: Multicenter Study Randomized Controlled Trial
PMID: 15955935 [PubMed - in process]

Neurology. 2005 May 18; [Epub ahead of print]
New onset geriatric epilepsy. A randomized study of gabapentin, lamotrigine, and carbamazepine.
Rowan AJ, Ramsay RE, Collins JF, Pryor F, Boardman KD, Uthman BM, Spitz M, Frederick T, Towne A, Carter GS, Marks W, Felicetta J, Tomyanovich ML.
From VA Medical Center (Dr. Rowan), Bronx, NY; VA Medical Center (Dr. Ramsay, F. Pryor), Miami, FL; VA Medical Center (Dr. Collins), Perry Point, MD; VA Cooperative Studies Program (K.D. Boardman), Albuquerque, NM; VA Medical Center (Dr. Uthman), Gainesville, FL; VA Medical Center (Dr. Spitz), Denver, CO; VA Medical Center (Dr. Frederick), New Orleans, LA; VA Medical Center (Dr. Towne), Richmond, VA; VA Medical Center (Dr. Carter), Dallas, TX; VA Medical Center (Dr. Marks), San Francisco, CA; VA Medical Center (Dr. Felicetta), Phoenix, AZ; and VA Medical Center (Dr. Tomyanovich), Chicago, IL.
Abstract-- OBJECTIVE: To determine the relative tolerability and efficacy of two newer antiepileptic drugs, lamotrigine (LTG) and gabapentin (GBP), as compared to carbamazepine (CBZ) in older patients with epilepsy. METHODS: This was an 18-center, randomized, double-blind, double dummy, parallel study of 593 elderly subjects with newly diagnosed seizures. Patients were randomly assigned to one of three treatment groups: GBP 1,500 mg/day, LTG 150 mg/day, CBZ 600 mg/day. The primary outcome measure was retention in trial for 12 months. RESULTS: Mean age was 72 years. The most common etiology was cerebral infarction. Patients had multiple medical conditions and took an average of seven comedications. Mean plasma levels at 6 weeks were as follows: GBP 8.67 +/- 4.83 microg/mL, LTG 2.87 +/- 1.60 microg/mL, CBZ 6.79 +/- 2.92 microg/mL. They remained stable throughout the trial. Early terminations: LTG 44.2%, GBP 51%, CBZ 64.5% (p = 0.0002). Significant paired comparisons: LTG vs CBZ: p < 0.0001; GBP vs CBZ: p = 0.008. Terminations for adverse events: LTG 12.1%, GBP 21.6%, CBZ 31% (p = 0.001). Significant paired comparisons: LTG vs CBZ: p < 0.0001; LTG vs GBP: p = 0.015. There were no significant differences in seizure free rate at 12 months. CONCLUSIONS: The main limiting factor in patient retention was adverse drug reactions. Patients taking lamotrigine (LTG) or gabapentin (GBP) did better than those taking carbamazepine. Seizure control was similar among groups. LTG and GBP should be considered as initial therapy for older patients with newly diagnosed seizures.
PMID: 15888602 [PubMed - as supplied by publisher]

Neurology. 2005 Apr 12;64(7):1131-3.
Case-control study of SUDEP.
Langan Y, Nashef L, Sander JW.
Department of Clinical and Experimental Epilepsy, RakeInstitute of Neurology, London, UK.
OBJECTIVE: To examine the influence of various factors on the risk of sudden unexpected death in epilepsy (SUDEP). METHODS: The authors investigated 154 cases in which a postmortem examination was performed. Each case had four controls with epilepsy from the community, matched for age and geographic location. Backward stepwise conditional logistic regression analysis was performed and odds ratios for risk and protection were determined. RESULTS: The risk of SUDEP was increased with a history of generalized tonic-clonic seizures in the previous 3 months (odds ratio [OR]: 13.8, 95% CI: 6.6 to 29.1). The presence of supervision at night was found to be protective (OR: 0.4, 95% CI: 0.2 to 0.8) when a supervising individual shared the same bedroom or when special precautions such as a listening device were employed (OR: 0.1, 95% CI: 0.0 to 0.3). CONCLUSION: This work lends support to the view that SUDEP is a seizure-related phenomenon and that control of tonic-clonic seizures is important in its prevention. Nocturnal supervision seems to protect against SUDEP.
PMID: 15824334 [PubMed - in process]

Neurology. 2005 Mar 22;64(6):973-5.
The frequency of intractable seizures after stopping AEDs in seizure-free children with epilepsy.
Camfield P, Camfield C.
Department of Pediatrics, IWK Health Centre and Dalhousie University, Halifax, NS, Canada. camfield@dal.ca
BACKGROUND: After 1 to 4 years, seizure-free children with epilepsy are encouraged to stop daily antiepileptic drug (AED) treatment. Approximately 70% are successful. The authors examined how often intractable epilepsy follows discontinuation of AED treatment in a population-based cohort of children with epilepsy. METHODS: The Nova Scotia population-based epilepsy cohort was used to identify children who discontinued AEDs but subsequently developed intractable epilepsy. All patients studied (ages 1 month to 16 years) developed epilepsy between 1977 and 1985, had epilepsies characterized by partial or convulsive seizures, and had at least 5 years of follow-up evaluation (n = 367). Those with benign rolandic epilepsy were excluded. Intractability was defined as one or more seizures every 3 months during the last year of follow-up review or until successful seizure surgery and failure of three or more AEDs at maximum tolerated doses. RESULTS: Overall, 71% (260/367) of eligible children became free of seizure for 1 to 4 years and discontinued AED treatment. Of this group, 70% remained seizure-free without AED treatment, but 30% had recurrences. Only three children with recurrences later developed intractable epilepsy. Two then underwent a temporal lobectomy, one successful and one only partially successful (20-year follow-up periods). The third patient continued to have intractable epilepsy for 7 years after discontinuing AED treatment but eventually entered remission. CONCLUSION: Approximately 1% of children who became free of seizure and discontinued antiepileptic drug treatment had recurrent seizures that could not be controlled again with medication. The authors were unable to predict this outcome. It remains unclear whether a similar outcome would have occurred if antiepileptic drugs had not been discontinued.
PMID: 15781810 [PubMed - in process]

Neurology. 2005 Jan 11;64(1):172-4; author reply 172-4.
Comment on: Neurology. 2004 Apr 27;62(8):1252-60. Neurology. 2004 Apr 27;62(8):1261-73.
Efficacy and tolerability of the new antiepileptic drugs I: treatment of new onset epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society.
Krauss GL.
Publication Types: Comment Letter
PMID: 15645538 [PubMed - indexed for MEDLINE]

Neurology. 2004 Nov 9;63(9):1728-30.
Short-term outpatient EEG video with induction in the diagnosis of psychogenic seizures.
Benbadis SR, Siegrist K, Tatum WO, Heriaud L, Anthony K.
Comprehensive Epilepsy Program, Department of Neurology, University of South Florida, Tampa, USA. sbenbadi@hsc.usf.edu
To analyze the yield of short-term outpatient EEG video monitoring, the authors reviewed data on all patients who underwent this procedure at their center. All patients were suspected of having psychogenic nonepileptic seizures (PNES) on clinical grounds. The total number of cases of short-term outpatient EEG video monitoring was 74. In 49 (66%) cases, the suspected diagnosis of PNES could be confirmed, thereby obviating the need for prolonged inpatient EEG video monitoring.
Publication Types: Evaluation Studies
PMID: 15534269 [PubMed - indexed for MEDLINE]

Neurology. 2004 Mar 23;62(6):990-3.
Effectiveness of broadcasting guidelines for photosensitive seizure prevention.
Takahashi Y, Fujiwara T.
National Epilepsy Center, Shizuoka MIND, Japan. takahashi-ped@umin.ac.jp
Emissions from TV programs are a dangerous light source for photosensitive individuals, because 48.9% of patients have photosensitive seizures caused by TV programs. The authors used a national survey to verify the effectiveness of current Japanese guidelines, which are based on neurophysiologic principles of photosensitivity. They show that the guidelines successfully control TV images to protect many photosensitive persons from harmful TV emissions.
PMID: 15037709 [PubMed - indexed for MEDLINE]

Neurology. 2003 Feb 25;60(4):564-70.
Meta-analysis of EEG test performance shows wide variation among studies.
Gilbert DL, Sethuraman G, Kotagal U, Buncher CR.
Division of Neurology, Cincinnati Children's Hospital Medical Center, OH 45229-3039, USA. d.gilbert@chmcc.org
BACKGROUND: EEG results are used for counseling patients with seizures about prognosis and deciding on medications. Published sensitivities of interictal EEG vary widely. OBJECTIVE: To account for variation in test characteristics between studies. METHODS: Meta-analysis. Medline search, 1970 to 2000, of English language studies. Standard methods for meta-analysis of diagnostic test performance were used to determine the ability of EEG results to distinguish between patients who will and will not have seizures. Using linear regression, the authors assessed the influence of readers' thresholds for classifying the EEG as positive, sample probability of seizure, percent of subjects with prior neurologic impairment, percent treated, and years followed. RESULTS: Twenty-five studies involving 4,912 EEG met inclusion criteria. Specificity (range 0.13 to 0.99) and sensitivity (range 0.20 to 0.91) of epileptiform EEG interpretations varied widely and were heterogeneous by chi(2) analysis ($p < 0.001$ for each). Diagnostic accuracy of EEG and the thresholds for classifying EEG as positive varied widely. In the multivariate model, differences in readers' thresholds accounted for 37% of the variance in EEG diagnostic accuracy, and no other reported factors were significant. CONCLUSION: This analysis suggests that there is wide interreader variation in sensitivity and specificity of EEG interpretations, and that this variation influences the ability of EEG to discriminate between those who will and will not have seizure recurrences. In clinical practice, interpreting the degree to which a positive EEG result predicts increased seizure risk in an individual patient is difficult. Interpreting EEG with higher specificity yields more accurate predictions.
Publication Types: Meta-Analysis
PMID: 12601093 [PubMed - indexed for MEDLINE]

Neurology. 2003 Feb 25;60(4):538-47.
Erratum in: Neurology. 2003 Apr 22;60(8):1396.
Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons.
Engel J Jr, Wiebe S, French J, Sperling M, Williamson P, Spencer D, Gumnit R, Zahn C, Westbrook E, Enos B; Quality Standards Subcommittee of the American Academy of Neurology; American Epilepsy Society; American Association of Neurological Surgeons.
Neurological Research Center, Department of Neurology #1250, 710 Westwood Plaza, Los Angeles, CA 90095-1769, USA. engel@ucla.edu
OBJECTIVES/METHODS: To examine evidence for effectiveness of anteromesial temporal lobe and localized neocortical resections for disabling complex partial seizures by systematic review and analysis of the literature since 1990. RESULTS: One intention-to-treat Class I randomized, controlled trial of surgery for mesial temporal lobe epilepsy found that 58% of patients randomized to be evaluated for surgical therapy (64% of those who received surgery) were free of disabling seizures and 10 to 15% were unimproved at the end of 1 year, compared with 8% free of disabling seizures in the group randomized to continued medical therapy. There was a significant improvement in quantitative quality-of-life scores and a trend toward better social function at the end of 1 year for patients in the surgical group, no surgical mortality, and infrequent morbidity. Twenty-four Class IV series of temporal lobe resections yielded essentially identical results. There are similar Class IV results for localized neocortical resections; no Class I or II studies are available. CONCLUSIONS: A single Class I study and 24 Class IV studies indicate that the benefits of anteromesial temporal lobe resection for disabling complex partial seizures is greater than continued treatment with antiepileptic drugs, and the risks are at least comparable. For patients who are compromised by such seizures, referral to an epilepsy surgery center should be strongly considered. Further studies are needed to determine if neocortical seizures benefit from surgery, and whether early surgical intervention should be the treatment of choice for certain surgically remediable epileptic syndromes.
Publication Types: Guideline Practice Guideline Review
PMID: 12601090 [PubMed - indexed for MEDLINE]

Neurology. 2003 Jan 28;60(2):162-3.
Comment on: Neurology. 2003 Jan 28;60(2):186-90. Neurology. 2003 Jan 28;60(2):191-5.
Success or failure with antiepileptic drug therapy: Beyond empiricism?
Brodie MJ, Leach JP.
Publication Types: Comment Editorial
PMID: 12552025 [PubMed - indexed for MEDLINE]

Neuropediatrics. 2005 Oct;36(5):302-8.
Seizure control and acceptance of the ketogenic diet in GLUT1 deficiency syndrome: a 2- to 5-year follow-up of 15 children enrolled prospectively.
Klepper J, Scheffer H, Leiendecker B, Gertsen E, Binder S, Leferink M, Hertzberg C, Nake A, Voit T, Willemsen MA.
Department of Pediatrics and Pediatric Neurology, University of Essen, Essen, Germany. joerg.klepper@uni-essen.de
BACKGROUND: GLUT1 deficiency syndrome is caused by impaired glucose transport into the brain resulting in an epileptic encephalopathy, developmental delay, and a complex motor disorder. A ketogenic diet provides an alternative fuel to the brain and effectively restores brain energy metabolism. METHODS: Fifteen children with GLUT1 deficiency syndrome were enrolled prospectively for a 2.0 - 5.5-year follow-up of the effectiveness of a 3 : 1 LCT ketogenic diet. Eight patients enrolled were described previously, seven patients were novel. RESULTS: Four novel heterozygous GLUT1 mutations were identified. 10/15 patients remained seizure-free on the ketogenic diet in monotherapy. In 2/15 patients seizures recurred after 2(1/2) years despite adequate ketosis, but were controlled by add-on ethosuximide. In one patient seizures were reduced without complete seizure control. No serious adverse effects occurred and parental satisfaction with the diet was good. 2/15 patients discontinued the diet. CONCLUSION: GLUT1 deficiency syndrome represents a complex childhood encephalopathy that can be treated effectively by means of a ketogenic diet. The response to the diet did not correlate to clinical, biochemical, or genetic features of the disease. In contrast to previous reports, our results indicate that epilepsy is not always completely controlled by a ketogenic diet and can recur in a subset of patients.
Publication Types: Clinical Trial
PMID: 16217704 [PubMed - in process]

Neuropsychopharmacology. 2005 Dec;30(12):2269-74.
Lack of pharmacokinetic interaction between oxcarbazepine and lamotrigine.
Theis JG, Sidhu J, Palmer J, Job S, Bullman J, Ascher J.
Clinical Pharmacology Unit, University of Cambridge, Addenbrookes Center for Clinical Investigation, Addenbrookes Hospital, Hills Road, Cambridge CB2 2GG, UK. Jochen_Theis@hotmail.com
Epilepsy and bipolar disorder are commonly treated by combination drug therapy, such as lamotrigine and oxcarbazepine. To ensure the safety of this combination, information on pharmacokinetics and tolerability must be available. The objective of study was to evaluate the pharmacokinetics and tolerability of coadministered lamotrigine and oxcarbazepine in healthy subjects. This randomized, single-blind, parallel-group study comprised three cohorts: lamotrigine (200 mg daily) plus oxcarbazepine (600 mg twice daily), lamotrigine (200 mg daily) plus placebo, and oxcarbazepine (600 mg twice daily) plus placebo. Serial blood samples were collected at steady state to determine serum concentrations of lamotrigine and plasma concentrations of oxcarbazepine and its active metabolite 10-monohydroxy metabolite (MHD). Pharmacokinetic parameters were determined by noncompartmental methods. Tolerability was monitored through adverse event reports, clinical laboratory results, vital signs, and electrocardiograms. A total of 47 male volunteers received study drugs. At steady state, lamotrigine AUC((0-24)) and C(max) were not significantly affected by oxcarbazepine co-therapy, nor were MHD AUC((0-12)) and C(max) significantly affected by lamotrigine co-therapy. The most common adverse events, headache, dizziness, nausea, and somnolence, occurred more frequently during lamotrigine and oxcarbazepine combination therapy than during the monotherapy. No significant changes in clinical laboratory parameters, vital signs, or electrocardiograms were reported. In conclusion, the combination of lamotrigine and oxcarbazepine does not require dose adjustments based on pharmacokinetic data. However, it is important to recognize that the combination therapy was associated with more frequent adverse events.
PMID: 16052246 [PubMed - in process]

Neurosci Lett. 2005 Oct 24; [Epub ahead of print]

Mutations in GABRA1, GABRA5, GABRG2 and GABRD receptor genes are not a major factor in the pathogenesis of familial focal epilepsy preceded by febrile seizures.

Ma S, Abou-Khalil B, Blair MA, Sutcliffe JS, Haines JL, Hedera P.

Department of Neurology, Vanderbilt University, Nashville, TN 37232-8552, USA.

GABA(A) receptors mutations have been reported in few epilepsy families with febrile seizures (FS) followed by generalized epilepsy. It is not known if such mutations may underlie FS followed by partial epilepsy, which is a more common type of epilepsy. We searched for disease-causing mutations in the genes of the alpha1, alpha5, gamma2 and delta subunits of the GABA-A receptor that were previously shown to contain epilepsy-causing mutations or epilepsy susceptibility polymorphisms. All coding and untranslated exons of these four GABA(A) subunit genes were screened in 74 unrelated patients with familial partial epilepsy preceded by FS. Most patients had temporal lobe epilepsy (TLE). We did not detect any disease-causing mutations that would be consistent with missense, nonsense or splice site mutations in any of the four analyzed genes. We conclude that these genes are not a major genetic factor in familial TLE preceded by FS.

PMID: 16256272 [PubMed - as supplied by publisher]

Neuroscientist. 2005 Feb;11(1):25-36.

Adenosine and epilepsy: from therapeutic rationale to new therapeutic strategies.

Boison D.

Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland. boison@pharma.unizh.ch

Adenosine, as the brain's endogenous anticonvulsant, is considered to be responsible for seizure arrest and postictal refractoriness. On the other hand, deficiencies within the adenosine-based neuromodulatory system may contribute to epileptogenesis. Based on these natural mechanisms and on findings that adenosine and its analogs can suppress pharmacoresistant seizures, a new field of adenosine-based therapies has emerged, including the use of adenosine receptor agonists and adenosine transport inhibitors, or the inhibition of adenosine kinase, which is thought to be the key enzyme for the regulation of intra- and extracellular adenosine levels. However, most of these pharmacological approaches are limited by strong systemic side effects ranging from a decrease of heart rate, blood pressure, and body temperature to sedation. Recently, new strategies have been developed aimed at the local reconstitution of the inhibitory adenosinergic tone by intracerebral implantation of cells engineered to release adenosine. Adenosine-releasing cells or devices implanted into or near a seizure focus offer new hopes for a side effect-free therapy for pharmacoresistant epilepsy.

Publication Types: Review

PMID: 15632276 [PubMed - indexed for MEDLINE]

Neurosurgery. 2005 Feb;56(2):318-34.

Multistage epilepsy surgery: safety, efficacy, and utility of a novel approach in pediatric extratemporal epilepsy.

Bauman JA, Feoli E, Romanelli P, Doyle WK, Devinsky O, Weiner HL.

New York University Comprehensive Epilepsy Center, and Department of Neurology, New York University Medical Center, New York, New York, USA.

OBJECTIVE: To evaluate the safety, efficacy, and utility of a novel surgical strategy consisting of multiple (more than two) operative stages performed during the same hospital admission with subdural grid and strip electrodes in selected pediatric extratemporal epilepsy. METHODS: Subdural grid and strip electrodes were used for multistage chronic electroencephalographic monitoring in 15 pediatric patients (age, <19 yr) with refractory localization-related epilepsy and poor surgical prognostic factors. Initial resective surgery and/or multiple subpial transections were performed, followed by further monitoring and additional resection and/or multiple subpial transections. RESULTS: Mean patient age was 9.7 years. Mean duration of total invasive monitoring was 10.5 days (range, 8-14 d). The first monitoring period averaged 6.5 days, and the second averaged 3.9 days. Additional surgery was performed in 13 of 15 patients. Two patients who did not undergo additional surgery had a Class I outcome. Rationales for reinvestigation included incomplete localization, multifocality, and proximity to eloquent cortex. Complications were minimal, including two transfusions. There were no cases of wound infection, cerebral edema, hemorrhage, or major permanent neurological deficit. Minimum duration of follow-up was 31 months. Outcomes were 60% Engel Class I (9 of 15 patients), 27% Class III (4 of 15 patients), and 13% Class IV (2 of 15 patients). CONCLUSION: In a very select group of pediatric patients with poor surgical prognostic factors, the

multistage approach can be beneficial. After failed epilepsy surgery, subsequent reoperation with additional intracranial investigation traditionally is used when a single residual focus is suspected. Our results, however, support the contention that multistage epilepsy surgery is safe, effective, and useful in a challenging and select pediatric population with extratemporal medically refractory epilepsy.
PMID: 15670380 [PubMed - in process]

Nurs Times. 2004 Jul 13-19;100(28):38-41.
The role of primary care nurses in the review of stable epilepsy.
Minshall I.
Northgate Village Surgery, Chester.
AIM: To assess the feasibility of primary care nurses reviewing patients with 'stable' epilepsy. Sample Practice nurses, health visitors, and district nurses drawn from all GP practices in Cheshire West Primary Care Trust. METHOD: Questionnaires were distributed to nursing staff about the management of patients considered to be stable but who require an annual review. RESULTS: Regarding their suitability for the work, there was a significant positive response from practice nurses and district nurses but less so from health visitors, while district nurses and health visitors did not feel they had the spare capacity for the work. CONCLUSION: Inclusion of epilepsy as a quality indicator in the new GP contract means practices are likely to ask primary care nurses to take a role in managing patients with stable epilepsy. From this study there is evidence of some interest in taking this work on but there are issues around capacity, manpower, and funding.
PMID: 15311538 [PubMed - indexed for MEDLINE]

Pediatr Emerg Care. 2003 Aug;19(4):221-5.
The short-term outcome of seizure management by prehospital personnel: a comparison of two protocols.
Galustyan SG, Walsh-Kelly CM, Szewczuga D, Bergholte J, Hennes H.
Emergency Medicine Section, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, USA.
OBJECTIVE: To evaluate the impact of an emergency medical service protocol with reduced diazepam dose on the intubation rate of children with seizure activity treated by emergency medical service personnel and to evaluate the short-term outcome comparing 2 emergency medical service treatment protocols. METHODS: Retrospective review of the emergency medical service and hospital databases of children 0-18 years with seizure activity. Prior to January 1996, the county emergency medical service protocol recommended a diazepam dose of 0.2-0.5 mg/kg i.v. or pr for termination of seizure activity (group 1). As of January 1996, the diazepam dose was reduced to 0.05-0.1 mg/kg i.v. or pr (group 2). Demographics, emergency medical service and emergency department interventions, and disposition data were abstracted. RESULTS: 1516 subjects met the enrollment criteria: 1003 (66%) in group 1 and 513 (34%) in group 2. Emergency medical service administered diazepam to 288 subjects: 189 (19%) in group 1 and 99 (19%) in group 2. Twenty (7%) of all treated subjects required intubation: 19 in group 1 and 1 in group 2 (relative risk 9.7, 95% CI 1.30-72.5). Mean diazepam dose was 0.17 mg/kg in group 1 and 0.13 mg/kg in group 2 (mean difference 0.04, 95% CI 0.02-0.06). No significant difference in the requirement for repeated anticonvulsant dose, complications, or emergency department interventions was noted. However, hospital admission rate was lower in group 2 (rate difference 0.06, 95% CI 0.01-0.11). CONCLUSIONS: Our study demonstrated a reduction in intubation rate and a need for hospitalization in the reduced diazepam dose emergency medical service protocol. The reduction in the diazepam dose was effective in terminating the seizure activity and did not increase the risk of adverse events.
Publication Types: Review
PMID: 12972817 [PubMed - indexed for MEDLINE]

Pediatr Neurol. 2005 Sep;33(3):166-72.
Rectal diazepam gel in the home management of seizures in children.
O'Dell C, Shinnar S, Ballaban-Gil KR, Hornick M, Sigalova M, Kang H, Moshe SL.
Department of Neurology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York 10467, USA.
This study assessed the utility of rectal diazepam gel in the home management of prolonged or repetitive seizures in children. Thirty-eight children being prescribed rectal diazepam gel by their clinician were prospectively recruited. Seizures, rectal diazepam use, emergency department visits, and quality of life data before and after study entry were recorded. The 38 children included 14 (37%) with complex febrile

seizures, and 24 with epilepsy (n = 22) or a single seizure (n = 2). There were 23 (61%) children with prolonged seizures and 15 (39%) with repetitive seizures. During the 6-month follow-up period, 12 children experienced 26 seizures which met the criteria for rectal diazepam administration. Rectal diazepam gel was administered to 8 children on 19 occasions. In 16 (84%) of these episodes, seizures stopped and no emergency department visit was required. Parental stress was decreased between baseline and 6 months in both the overall group and in all the subgroups. Home use of rectal diazepam gel is effective in aborting seizure activity, often avoiding an emergency department visit. Its use reduces morbidity and costs associated with hospital visits and provides parents a treatment option for home management of prolonged or repetitive seizures.
PMID: 16139730 [PubMed - indexed for MEDLINE]

Pediatr Neurol. 2004 Sep;31(3):198-202.
Ketogenic diet: outpatient initiation, without fluid, or caloric restrictions.
Vaisleib II, Buchhalter JR, Zupanc ML.
Division of Child and Adolescent Neurology, Department of Neurology, Mayo Clinic, Rochester, Minnesota 55905, USA.
Although the ketogenic diet has been used for more than 80 years, the optimal methods of initiating the diet and its maintenance have not been clearly defined. This retrospective study was performed to review our experience with initiation of the ketogenic diet in the outpatient and inpatient settings and maintenance of the diet without fluid or caloric restriction. We analyzed 54 patients who had medically intractable epilepsy of whom 44% manifested some degree of mental retardation, 80% had multiple seizure types, and failed on average 4.8 antiepileptic drugs. Forty-four patients underwent induction of the ketogenic diet on an outpatient basis and 21 as inpatients. Three patients in each group were fasted at the initiation of the diet. No significant differences were observed with regard to seizure control in that 62% and 71% had greater than 50% improvement in the outpatient and inpatient groups, respectively. Both groups manifested improvement in alertness and social interaction. The efficacy of a ketogenic diet in the symptomatic epilepsies was confirmed, and benefit for medically refractory childhood absence epilepsy was documented. We conclude that a prospective, randomized trial is necessary to compare outpatient vs inpatient initiation of the ketogenic diet and the utility of fluid and caloric restriction.
PMID: 15351019 [PubMed - indexed for MEDLINE]

Pediatr Neurol. 2003 Oct;29(4):302-11.
Pediatric epilepsy surgery at the University of Alberta: 1988-2000.
Sinclair DB, Aronyk KE, Snyder TJ, Wheatley BM, McKean JD, Bhargava R, Hoskinson M, Hao C, Colmers WF, Berg M, Mak W.
Comprehensive Epilepsy Program, University of Alberta, Edmonton, Alberta, Canada.
Epilepsy surgery is considered a treatment option for patients with intractable seizures. Relatively few studies of efficacy, safety, and long-term outcome are available for the pediatric age group. This study describes a 12-year experience with pediatric epilepsy surgery at the University of Alberta. Records of pediatric epilepsy surgery patients admitted to the Comprehensive Epilepsy Program at the University of Alberta between 1988 and 2000 were reviewed. All patients received preoperative and postoperative clinical evaluation, seizure charts, testing of drug levels, electroencephalogram, computed tomography/magnetic resonance imaging, neuropsychologic testing, and long-term video electroencephalogram monitoring. The patients were reassessed after surgery at 6 weeks, 6 months, and 1 year and then yearly. The duration of follow-up was 1 year to 12 years. Forty-two patients underwent temporal lobectomies; 35, extratemporal resection. The age at surgery ranged from 6 months to 16 years. Thirty-two (76%) of temporal lobe patients became seizure-free (Engel Class I) vs 24 (68%) for the extratemporal group (Engel Class I). One patient (2%) in the temporal group had an Engel Class II outcome and one patient (3%) in the extratemporal group had the same Engel Class II outcome. Three patients (4%) manifested postoperative complications, and there were no deaths. Patients reported improvement in cognitive abilities, behavior, and quality of life after the surgery. Epilepsy surgery in children is effective and safe. Many children are seizure-free after the operation and remain so, although the results of temporal lobectomy are better than for extratemporal resections. There are few complications, and children often have an improved quality of life.
PMID: 14643392 [PubMed - indexed for MEDLINE]

Pediatr Neurol. 2003 May;28(5):360-4.

Lamotrigine and valproate: efficacy of co-administration in a pediatric population.

Thome-Souza S, Freitas A, Fiore LA, Valente KD.

Laboratory of Clinical Neurophysiology, Institute and Department of Psychiatry, University of Sao Paulo Medical School, R. Jesuino Arruda, 901 Apt. 51, 04532 082 Sao Paulo SP, Brazil

This study aimed to assess the risks and benefits of the co-administration of lamotrigine and valproate in a pediatric population with refractory epilepsy. Twenty-eight children who received lamotrigine and valproate during co-medication were evaluated. Outcome measurements were established according to efficacy in seizure control, adverse effects, and tolerability. Treatment was considered effective when >50% frequency reduction was obtained. Adverse effects were also analyzed and in patients who presented them the mode of administration was compared with those who did not to verify the importance of this factor. Association of lamotrigine and valproate was considered effective in 64.3% of all patients, regardless of the seizure type. Seizure-free status was obtained in six patients. Drop attacks and secondary generalized tonic-clonic seizures were reduced in five patients, who remained under treatment despite less than the satisfactory (<50%) seizure decrease. Tremor occurred in six patients; urinary incontinence and ataxia in one. Skin rash also occurred, as an early manifestation, in two patients, both with a previous history of hypersensitivity to antiepileptic drugs. Causes for discontinuation were inefficacy of treatment in six patients and presence of adverse effects in two. In our series, seizure control was obtained in most children with refractory epilepsy, some of whom had a previous history of unsatisfactory response to lamotrigine and valproate, either in monotherapy or polytherapy. Adverse effects were uncommon, but skin rash was observed in higher proportions than in other series with lamotrigine or valproate. Nevertheless, these risks may be lessened with slow introduction and by exclusion of patients with a previous history of hypersensitivity.

PMID: 12878297 [PubMed - indexed for MEDLINE]

Pediatrics. 2004 Oct;114(4):962-4.

Which characteristics of children with a febrile seizure are associated with subsequent physician visits?

Gordon KE, Dooley JM, Wood E, Brna P, Bethune P.

Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada. kegor@dal.ca

OBJECTIVE: To reanalyze an existing data set to determine which children with an initial febrile seizure have excessive subsequent physician visits. METHODS: Individual data from a regional cohort of 75 children with a first febrile seizure and 150 febrile and 150 afebrile control subjects were linked to a comprehensive physician services database. The impact of study variables on subsequent physician utilization over the following 6 years was modeled using analysis of variance. RESULTS: Children with a known family history of febrile seizures at the time of study entry had 24% fewer physician visits. Control children with a known family history of afebrile seizures had 7% fewer visits than those with negative family histories. Children with an initial febrile seizure had 45% more physician visits when they knew of a relative with afebrile seizures than those with negative family histories. CONCLUSIONS: Knowing the family history of seizures is probably a marker of reduced physician utilization. At the time of an initial febrile seizure, knowing the family history of afebrile seizures defines a group of patients with excessive subsequent physician visits.

PMID: 15466091 [PubMed - indexed for MEDLINE]

Pediatrics. 2003 Nov;112(5):e348.

Decrease in hospital admissions for febrile seizures and reports of hypotonic-hyporesponsive episodes presenting to hospital emergency departments since switching to acellular pertussis vaccine in Canada: a report from IMPACT.

Le Saux N, Barrowman NJ, Moore DL, Whiting S, Scheifele D, Halperin S; Canadian Paediatric Society/ Health Canada Immunization Monitoring Program-Active (IMPACT).

Department of Pediatrics, University of Ottawa, Ottawa, Ontario, Canada. lesaux@cheo.on.ca

OBJECTIVE: Acellular pertussis vaccines were introduced with the promise of an improved safety profile compared with whole-cell vaccines. In 1997-1998, Canada adopted 1 combination acellular pertussis vaccine, having previously used 1 particular combination whole-cell pertussis vaccine. We hypothesized that the change would result in a decrease in hospitalization rates for seizures and reports of hypotonic-hyporesponsive episodes (HHEs) temporally related to pertussis vaccination. METHODS: Active surveillance was performed between 1995 and 2001 by the Immunization Monitoring Program-Active monitors at 12 hospitals using standard case definitions. Seizures had to occur within 72 hours after immunization with a

pertussis-containing vaccine or 5 to 30 days after immunization with measles-mumps-rubella vaccine. HHE episodes had to occur within 48 hours of receipt of a pertussis-containing vaccine. Poisson regression models were used to compare the average number of monthly admissions for seizures and HHEs before and after introduction of the acellular pertussis vaccine. RESULTS: We found a 79% decrease in febrile seizures associated with receipt of pertussis vaccine but no significant decrease in febrile seizures temporally related to measles-mumps-rubella between 1995-1996 and 1998-2001. There was a 60% to 67% reduction in HHEs associated with pertussis-containing vaccines between the same time periods, depending on case definition. CONCLUSIONS: The risks of febrile seizures and HHEs after pertussis-containing vaccine declined significantly with the introduction of acellular pertussis vaccine in Canada. Active surveillance systems are important for detecting trends in uncommon adverse events after routine immunizations.
PMID: 14595075 [PubMed - indexed for MEDLINE]

Pediatrics. 2003 Jan;111(1):194-6.
Comment on: Pediatrics. 2000 Sep;106(3):527-32. Pediatrics. 2003 Jan;111(1):1-5.
Less testing is needed in the emergency room after a first afebrile seizure.
Freeman JM.
Johns Hopkins Medical Institutions, Baltimore, MD 21247-7247, USA. jfreeman@jhmi.edu
Publication Types: Comment Review
PMID: 12509575 [PubMed - indexed for MEDLINE]

Pharmacoeconomics. 2005;23(11):1167-81.
The importance of drug adverse effects compared with seizure control for people with epilepsy: a discrete choice experiment.
Lloyd A, McIntosh E, Price M.
The MEDTAP Institute at United BioSource Corporation, London, UK.
INTRODUCTION: Antiepileptic drugs (AEDs) have been shown to reduce the severity and frequency of seizures for most patients. However, many patients experience adverse effects in order to maintain seizure control. STUDY DESIGN: A stated preference discrete choice experiment (DCE) was used to explore the preferences of people with epilepsy regarding the adverse effects and seizure control of AEDs. METHODS: The main adverse effects of AEDs were identified through a literature search and expert consultation. In addition, a national epilepsy patient advocacy group helped to identify important attributes and commented on the attributes we had already identified. The DCE included five attributes related to adverse effects (alopecia, nausea, skin rash, concentration effects and weight change) plus seizure control and cost (to estimate willingness to pay [WTP]). A cost attribute was included in the DCE in order to estimate people's WTP for changes in attribute levels. Five hundred members of a national patient advocacy group with a diagnosis of epilepsy were presented with pairs of hypothetical drug profiles with varied levels of adverse effects, seizure control and cost; they were then asked to indicate which drug they preferred. Questions were also included to collect sociodemographic data (including income) and information regarding experience of adverse effects and medication. The survey was administered via the post and the Internet. Data were analysed using a random effects probit model. RESULTS: A total of 148 surveys were returned. All attributes were significant and had the expected polarity, i.e. participants showed a preference for less severe adverse effects, greater seizure control and less cost. To achieve 100% seizure control and no adverse effects, participants were willing to pay pound709 ($US1105) per month, 95% CI pound451, pound1278 (pound1 = $US1.56, 2002 exchange rate). Participants' WTP was significantly influenced by different adverse effects; for example, people with epilepsy were willing to pay only pound174 ($US271) per month for a drug that provided seizure freedom but also caused hair loss. Segmented models showed that seizure frequency has a significant negative impact on respondents' income levels. Also, women were willing to pay twice as much as men to avoid weight gain. Participants were also willing to trade changes in seizure control for improvements in adverse effects. CONCLUSION: Participants placed a high value on gaining total seizure control with no adverse effects. This study underlines the importance that people with epilepsy place on reducing adverse effects. The study also revealed how preferences for AEDs vary in different subgroups. Management of epilepsy is usually aimed at minimising seizures within a tolerable level of adverse effects. The present study suggests that people with epilepsy have strong preferences for reducing adverse effects as well as improving seizure control. These data may be considered useful when making medical management decisions in epilepsy.
PMID: 16277551 [PubMed - in process]

Pharmacoeconomics. 2005;23(5):493-503.
Erratum in: Pharmacoeconomics. 2005;23(9):944. Blais, Lucie [added].

Economic evaluation of levetiracetam as an add-on therapy in patients with refractory epilepsy.

Blais L, Sheehy O, St-Hilaire JM, Bernier G, Godfroid P, LeLorier JJ.

Research Centre, University of Montreal Hospital, Montreal, Quebec, Canada.

OBJECTIVES: This study provides the results of a cost-effectiveness analysis of levetiracetam as an adjunctive treatment for refractory epilepsy from the Canadian Ministry of Health perspective. The main objective is to estimate the expected cost-effectiveness ratio expressed as the incremental cost per seizure-free day gained when using levetiracetam. In addition, this study examines the potential savings that might result by reducing the number of surgical evaluations and surgery when using levetiracetam. METHODS: A 1-year dose escalation decision-tree model comparing levetiracetam plus standard therapy with standard therapy alone was designed in order to combine probability, resource use and unit cost data (1999 Canadian dollars [$Can]). The short-term outcomes were derived from three phase III randomised, double-blind, placebo-controlled trials performed in 904 patients, aged 16-70 years, with at least 1 year history of epilepsy, two to four partial seizures per month, and receiving a maximum of two classic antiepileptic drugs. RESULTS: The average gain in seizure-free days attributed to levetiracetam was 19 days per patient per year and the incremental cost-effectiveness ratio (ICER) for levetiracetam add-on in the base-case scenario was $Can80.7 per seizure-free day gained per patient per year. Moreover, when surgical investigation and surgery are considered in the model, the use of levetiracetam may be dominant, with substantial savings to the overall healthcare budget. All univariate sensitivity analyses show that the model was robust to the assumptions made. CONCLUSIONS: The economic analysis presented in this paper suggests, given a wide range of assumptions, that the increased cost of treating patients (with refractory epilepsy) with levetiracetam may be partially offset by a reduction in other direct medical costs (from the Canadian Ministry of Health perspective), as a consequence of an increase in the number of seizure-free days. Moreover, potential cost savings may be foreseen when it is assumed that levetiracetam may reduce the number of candidates for surgical evaluation and surgery through a reduction of seizure frequency.

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Pharmacoeconomics. 2005;23(1):27-45.

A review of the costs of managing childhood epilepsy.

Beghi E, Frigeni B, Beghi M, De Compadri P, Garattini L.

Epilepsy Center, University of Milano-Bicocca, Monza, Italy. beghi@marionegri.it

Epilepsy is a chronic treatable condition for which new diagnostic tools and several new drugs and non-pharmacological treatments are now available. The cost profile of these options is assessed here through an overview of the available literature focusing on studies of childhood epilepsy. Several methodological problems arise when interpreting the results of economic studies in epilepsy, including the variability of the study population and costs items, the reliability of the sources of cost, the limitations of the methods of data collection and the deficiencies of the study designs, with reference to the measures of treatment benefits. International comparisons are then difficult because economic results cannot be compared on account of differences in monetary issues, clinical practice patterns and healthcare system frameworks. The economic aspects of epilepsy are different in children and adults. Differences are detectable in the incidence and expression of epileptic syndromes, social and emotional impact, availability of antiepileptic drugs, hospital admissions, diagnostic tests and referral to specialists, social assistants and other healthcare professionals. In addition, children have access to medical services only with the help of a caregiver, for whom there may be lost work days or under-employment. The mean annual cost per child with epilepsy was USD 1853 for controlled epilepsy and USD 4950 for uncontrolled epilepsy in a Spanish study performed in 1998 and the annual direct costs per child with epilepsy ranged from euro 844 for patients in remission to euro 3268 for patients with drug-resistant epilepsy in an Italian study done between 1996 and 1998. The Spanish study showed that direct costs are the major source of expenditure for children with epilepsy. These studies along with a number of other cost-of-illness studies in combined populations of adults and children showed that service use and costs increase with more severe forms of illness and seizure frequency, this being more marked in adults than in children. Moderate cost differences may be expected between children (higher) and adults (lower), particularly with reference to initial investigations. Costs of epilepsy are mostly explained by hospital admissions and drugs; in particular, drug costs tend to dominate in more well controlled epilepsy, while both hospital admissions and drugs are significant costs in less well controlled epilepsy. Newly diagnosed patients can incur significant hospital and diagnostic costs. Costs for epilepsy tend to be lower for patients cared for in

general practice or outpatient settings than in hospital settings. Seizure control by drugs, ketogenic diet or surgery is associated with a significant reduction in the costs of epilepsy.
Publication Types: Review
PMID: 15693726 [PubMed - indexed for MEDLINE]

Pharmacogenomics. 2006 Jan;7(1):89-103.
Challenges and opportunities in the application of pharmacogenetics to antiepileptic drug therapy.
Ferraro TN, Dlugos DJ, Buono RJ.
1University of Pennsylvania, Center for Neurobiology and Behavior, Room 2209, Translational Research Laboratories, 125 S.31st St, Philadelphia, PA 19104-3403, USA. TNF-@mail.med.upenn.edu , 2The Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA 19104, USA, 3University of Cincinnati, Department of Neurology, Cincinnati, OH 45267, USA.
The recent surge of interest in pharmacogenetics has provoked considerable thought regarding its relevance to antiepileptic drug (AED) therapy. Initial studies have focused on genes whose products play a putatively important role in AED pharmacology, particularly drug transporter proteins, drug metabolizing enzymes and ion channel subunits. However, there is a lack of good correspondence between results from different laboratories, and more recent findings are awaiting attempts at confirmation. Thus, there are currently no AED treatment guidelines that are informed by pharmacogenetic data. In order to begin to have clinical impact, standards specific to the conduct of future AED studies must be established. Of particular importance are the need for accurate epilepsy classification, appropriate AED selection and clear and objective assessment outcome measures. In addition, general standards for analysis and interpretation of genetic association data must be better codified and applied consistently across studies. Finally, extensive clinical research networks must be formulated and large numbers of well characterized patients must be recruited. Further development of these critical factors will optimize chances for overcoming current challenges posed by AED pharmacogenetic research and ultimately allow the realization of improved, more rational therapeutic strategies.
PMID: 16354127 [PubMed - as supplied by publisher]

Pharmacogenomics. 2005 Jun;6(4):411-417.
Complex haplotypic effects of the ABCB1 gene on epilepsy treatment response.
Hung CC, Tai JJ, Lin CJ, Lee MJ, Liou HH.
1National Taiwan University Hospital and College of Medicine, NTU, Department of Pharmacology, 1 Jen-Ai Road, Section 1, Taipei, Taiwan 100 . hhliou@ ha.mc.ntu.edu.tw , 2School of Pharmacy and Graduate Institute of Clinical Pharmacy, 3Graduate Institute of Epidemiology,, 4Department of Neurology,, 5Department of Medical Genetics, National Taiwan University Hospital and College of Medicine, NTU, 1 Jen-Ai Road, Section 1, Taipei, Taiwan 100.
Objectives: The aim of this study was to investigate the association of the complex haplotype system of the adenosine triphosphate-binding cassette B1 (ABCB1) gene with the epilepsy treatment response. Methods and results: Ten polymorphisms were genotyped in 108 drug-resistant epileptic patients, 223 seizure-free patients and 287 normal controls. Highly significant linkage disequilibrium was shown among exon 12 C1236T, exon 21 G2677T and exon 26 C3435T. Haplotypic analysis demonstrated that patients with the CGC, TGC, and TTT haplotypes were more likely to be drug resistant. Further analysis of haplotype combinations demonstrated that drug-resistant patients tended to have the CGC/CGC, CGC/TGC, CGC/TTT, and TGC/TTT haplotype combinations over the seizure-free patients and controls (all p-values < 0.0001). In contrast, patients with the TTC/TTC, TTC/CGT, TTC/TGT, CGT/CGT and TGT/CGT haplotype combinations were more likely to be seizure-free (all p-values < 0.0001 except CGT/CGT [p = 0.0063]). Conclusion: Our results showed that the three loci, C1236T, G2677T and C3435T, jointly influenced the treatment response for epileptic patients. They should be regarded together as a complex polymorphic drug-response system. These findings suggest that examination of the haplotypes of the three loci could be useful in predicting drug resistance in epilepsy.
PMID: 16004559 [PubMed - as supplied by publisher]

Pharmacol Rep. 2005 Sep-Oct;57(5):646-53.
A comparative study of vigabatrin vs. carbamazepine in monotherapy of newly diagnosed partial seizures in children.
Sobaniec W, Kulak W, Strzelecka J, Smigielska-Kuzia J, Bockowski L.

Department of Pediatric Neurology and Rehabilitation, Medical University of Bialystok, Waszyngtona 17, PL 15-274 Bialystok, Poland. kneur2@wp.pl.
Carbamazepine (CBZ) is a drug of choice for the treatment of simple or complex partial seizures and secondary generalized seizures in adults and children. Vigabatrin (VGB) is a relatively new second line antiepileptic drug and was first registered for use in Poland more than ten years ago. Few reports have been published on the comparison of efficacy of VGB in children with epilepsy. The objective of this study is to evaluate the safety, efficacy and EEG effects of initial VGB monotherapy compared with initial CBZ monotherapy in children with newly diagnosed epilepsy. We present results of a prospective, outpatient and open study carried out in the University Hospital Center in Bialystok. Twenty-six children with partial epilepsy treated with VGB and 28 patients treated with CBZ were studied. The evaluation of the efficacy of the two drugs did not reveal any significant differences. Very good (reduction > 75%) seizure control was achieved in 22 out of 26 patients (84.6%) in the VGB group. One patient had a 50-75% decrease of seizures (good effect), similarly one child had a 25-50% reduction of seizures (mild effect). In two patients, we observed increased seizures (myoclonic jerks). Very good seizure control was achieved in 17 out of 28 patients (60.7%) in the CBZ group. Good seizure control was achieved in 5 out of 28 patients (17.8%) and mild control was seen in two children. No improvement was observed in 4 (14%) of the patients. The EEG background activity was improved in VGB-treated patients. No effect on the EEG background activity was observed in CBZ-treated children. VGB seems to be a safe and effective antiepileptic drug as primary monotherapy for epilepsy in children with similar proportion of side effects as CBZ.
PMID: 16227648 [PubMed - in process]

Pharmacol Rep. 2005 Mar-Apr;57(2):154-60.
Stiripentol. A novel antiepileptic drug.
Trojnar MK, Wojtal K, Trojnar MP, Czuczwar SJ.
Department of Pathophysiology, Skubiszewski Medical University, Jaczewskiego 8, PL 20-090 Lublin, Poland. czuczwarsj@yahoo.com.
Epilepsy is one of the most widespread pathologies of human brain, affecting approximately 1% of world population. Despite the development of new methods of seizure control, chronic administration of antiepileptic drugs (AEDs) remains the treatment of choice. Nevertheless, pharmacotherapy is not always effective. In the case of single drug treatment, the number of non-responding patients is as high as 30%. Moreover, chronic medication with currently available AEDs may result in severe side-effects and undesired drug interactions. That is why in recent years intensive research has been carried out aiming at the development of new therapeutic strategies in epilepsy. The goal of this review is to assemble current literature data on stiripentol (STP), a novel anticonvulsant unrelated to any other AEDs. STP potentiates central gamma-aminobutyric acid (GABA) transmission and is characterized by nonlinear pharmacokinetics and inhibition of liver microsomal enzymes. STP has proved its anticonvulsant potency in different types of animal seizures, as well as in clinical trials. The drug seems a good candidate for adjunctive therapy in intractable epilepsy.
Publication Types: Review
PMID: 15886413 [PubMed - in process]

Postgrad Med J. 2005 Jul;81(957):442-7.
Approach to the patient with epilepsy in the outpatient department.
Hadjikoutis S, Smith PE.
The Epilepsy Unit, University Hospital of Wales, Heath Park, Cardiff CF14 4XW, UK.
Epilepsy is common and serious (prevalence 750 per 100 000) and has an impact upon employment, education, and driving. The diagnosis requires a detailed history including witness account. Clinicians must distinguish seizures particularly from syncope and psychogenic attacks. Electroencephalography and magnetic resonance brain scanning help to identify causes and classification of epilepsy, but alone rarely provide the diagnosis. Antiepileptic drug treatment is required long term and is potentially hazardous; patients should start treatment only after informed discussion with an epilepsy specialist. Patients require reliable written information, particularly the driving regulations, and the impact of seizures on employment, education, and leisure. Women must understand the potential drug teratogenic effects. Certain patient groups benefit from targeted epilepsy services, for example, learning disabled, children, teenagers, and elderly. People with epilepsy require long term specialist follow up. Although this is currently provided in mainly in secondary care (including nurse led clinics), improved liaison with primary care should enable improved access to epilepsy services. Epilepsy care should be multidisciplinary and

long term, linking primary and secondary care, and empowering patients towards improved management of their condition.
Publication Types: Review
PMID: 15998820 [PubMed - indexed for MEDLINE]

Prev Chronic Dis. 2005 Jul;2(3):A12. Epub 2005 Jun 15.
The role of state public health agencies in addressing less prevalent chronic conditions.
Wheeler FC, Anderson LA, Boddie-Willis C, Price PH, Kane M.
Association of State and Territorial Chronic Disease Program Directors, 1107 Rutland Dr, West Columbia, SC 29169, USA. wheeler@chronicdisease.org
INTRODUCTION: State-based chronic disease programs typically focus on the most prevalent chronic conditions, such as cancer, diabetes, and cardiovascular disease, but interest in less prevalent chronic conditions (LPCCs), such as epilepsy, is growing. In our study, we examined the perceived roles of state health departments in addressing LPCCs and used this information to develop recommendations for state health departments that are considering developing LPCCs programs. We also compared the identified state health department roles for LPCCs with roles related to healthy aging, as well as to the essential elements of existing state-based chronic disease programs, to determine whether future LPCCs programs would have any unique requirements. METHODS: Participants used concept-mapping techniques to generate a set of 100 statements on steps that state health departments could take to address LPCCs. The participants sorted and rated each statement according to importance and feasibility. We used a sequence of multivariate statistical analyses to generate a series of maps, or clusters, and rating graphics. We reviewed the findings and produced recommendations for state health departments. We used a similar process to examine roles of state health departments in addressing healthy aging. RESULTS: The participants grouped the LPCCs statements into nine clusters, which they rated as moderately feasible and important. The healthy aging statements were grouped into eight clusters. Clusters for LPCCs and healthy aging were similar. We also compared LPCCs clusters and the essential elements of existing state-based chronic disease programs and found that they were similar. CONCLUSION: The similarities between LPCCs clusters and essential elements of existing state-based chronic disease programs highlight an important point. State health departments that are considering establishing LPCCs programs should use strategies that have already been used by other public health agencies to develop chronic disease prevention and control programs.
PMID: 15963314 [PubMed - in process]

QJM. 2003 Feb;96(2):87-9.
Epilepsy: time for review.
Smith PE, Leach JP.
Publication Types: Editorial
PMID: 12589006 [PubMed - indexed for MEDLINE]

Radiol Clin North Am. 2006 Jan;44(1):111-33.
MR Imaging of Epilepsy: Strategies for Successful Interpretation.
Vattipally VR, Bronen RA.
Yale University School of Medicine, New Haven, CT, USA.
The first half of this article is devoted to providing an introduction and overview for MR imaging of epilepsy. Several MR imaging epilepsy topics will be discussed in great detail in separate articles, such as hippocampal sclerosis, developmental disorders, and functional MR imaging. The remainder of this review will discuss strategies for successful interpretation of MR images from the seizure patient and how to avoid potential pitfalls.
PMID: 16297685 [PubMed - in process]

Scott Med J. 2005 Aug;50(3):114-7.
Review of patients in general practice with a diagnosis of epilepsy: development of a practice nurse checklist and an assessment of resource implications.
Duncan R, Barlow G, Smith AC.
West of Scotland Regional Epilepsy Service, Southern General Hospital, Glasgow. r.duncan@clinmed.gla.ac.uk

BACKGROUND: SIGN has recommended annual review of all patients with epilepsy. Annual review is rewarded in the new GMS contract. There is no information on how or by whom reviews should be carried out, nor on resource implications for secondary care. AIMS: To determine whether a practice nurse can deliver annual review of patients with epilepsy, and to estimate the resource implications of such review. METHODS: Evaluation of a practice nurse checklist against review by neurologist in 62 patients with epilepsy identified from a practice list of 6240 from Southwest Glasgow LHCC, and audit of case records in 1259 patients with epilepsy identified from the whole LHCC population of 96,565. RESULTS: There were 8 discrepancies between nurse and doctor reviews in a first iteration, but none in the second. Changes suggested a training effect. The review process generated 19 epilepsy nurse appointments, 7 requests for cerebral imaging and 3 requests for video EEG. Twelve patients required continuing follow up. The LHCC audit identified a large number of patients who had inadequate documentation of information and advice (over 90% in some domains). 28.6% had not been seen by a specialist, 40.7% had not had cerebral imaging, and only 37.4% were seizure free. CONCLUSION: Annual reviews of patients with epilepsy can be carried out by practice nurses, but some training is required. The review process is likely to increase the burden on secondary care and have a significant adverse effect on neurology waiting times.
PMID: 16163997 [PubMed - indexed for MEDLINE]

Seizure. 2005 Dec 3; [Epub ahead of print]
Comparison of short-term outcome between surgical and clinical treatment in temporal lobe epilepsy: A prospective study.
Yasuda CL, Tedeschi H, Oliveira EL, Ribas GC, Costa AL, Cardoso TA, Montenegro MA, Guerreiro CA, Guerreiro MM, Li LM, Cendes F.
Department of Neurology, State University of Campinas, Campinas, SP 13083-970, Brazil; Division of Neurosurgery, Department of Neurology, State University of Campinas, Campinas, SP 13083-970, Brazil.
OBJECTIVE: To compare the efficacy of medical and surgical treatment for refractory mesial temporal lobe epilepsy associated with hippocampal sclerosis (MTLE). METHODS: A prospective controlled non-randomized study of 26 patients with MTLE who underwent surgical treatment and 75 patients with MTLE who underwent medical treatment between August 2002 and October 2004. All patients failed to achieve seizure control with at least two first line antiepileptic drugs (AED) for partial seizures before entering the study. We used Kaplan-Meier survival analyses as a function of time of seizure recurrence to obtain estimates of 95% confident interval of seizure freedom and log-rank test to compare the status of seizure control between the two groups. RESULTS: The cumulative proportion of patients free of all seizures (Engel's class IA) was higher in the surgical group (73%) compared to the clinical group (12%) ($p<0.0001$). In the surgical group, 2 of 26 patients (7.7%) had transient adverse effects and 2 of 26 patients (7.7%) had a permanent deficit related to the surgical procedure. In the clinical group 7 patients (9.3%) major adverse events during follow-up, including burns and status epilepticus. CONCLUSIONS: Surgical treatment for patients with MTLE who failed to achieve seizure control with two previous AED regimens was more efficient than medical treatment with further trials of AED.
PMID: 16337144 [PubMed - as supplied by publisher]

Seizure. 2005 Dec;14(8):597-605. Epub 2005 Nov 8.
The LAM-SAFE Study: Lamotrigine versus carbamazepine or valproic acid in newly diagnosed focal and generalised epilepsies in adolescents and adults.
Steinhoff BJ, Ueberall MA, Siemes H, Kurlemann G, Schmitz B, Bergmann L; The LAM-SAFE Study Group.
Epilepsiezentrum Kork, Kehl-Kork, Germany.
OBJECTIVE: To investigate efficacy and safety of lamotrigine (LTG) versus carbamazepine (CBZ) or valproic acid (VPA) in newly diagnosed focal (FE) and idiopathic generalised (GE) epilepsies in adolescents and adults. METHODS: Open-label randomised comparative multicentre 24-week monotherapy trial in newly diagnosed epilepsy patients of >/=12 years of age. Patients with FE were treated with LTG or CBZ, those with GE received LTG or VPA. The primary efficacy variable was the number of seizure-free patients during study weeks 17 and 24. RESULTS: Two hundred and thirty-nine patients were included. One hundred and seventy-six patients suffered from FE and 63 from GE. In the FE group, 88 patients each were treated with CBZ or LTG. Ninety-four percent of the CBZ patients and 89% of the LTG patients became seizure-free according to an intent-to-treat analysis (not statistically different). The rate of patients discontinuing treatment due to adverse events or a lack of efficacy was 19% with CBZ compared to 9% with LTG (not statistically different). In the GE group, 30 patients received VPA and 33 LTG. During study weeks 17 and 24, 61% of the LTG patients and 84% of the VPA patients had become seizure-free (not statistically significant). The drop-out rate due to lack of efficacy or adverse events was 12% with LTG and

3% with VPA (not statistically different). CONCLUSIONS: This study indicates that the effectiveness of LTG in focal and generalised epilepsy syndromes as initial monotherapy in patients >/=12 years is in the range of standard first-line antiepileptic drugs.
PMID: 16278088 [PubMed - in process]

Seizure. 2005 Dec;14(8):606-10. Epub 2005 Nov 4.
A population audit of first clinic attendance with suspected epilepsy.
Dunkley C, Albert D, Morris N, Williams J, Whitehouse WP.
Department of Paediatric Neurology, Queen's Medical Centre, Nottingham NG7 2UH, UK.
OBJECTIVE: To assess the quality of clinical care at first clinic attendance in children with suspected epilepsy from a defined geographical population. METHOD: All hospital- and community-based consultant paediatricians in Nottingham City region, UK, were asked to collaborate with a retrospective clinical audit identifying children seen between January 2001 and March 2002. The British Paediatric Neurology Association (BPNA) audit tool (Appleton R, Besag F, Kennedy C, et al. An audit of children referred with suspected epilepsy. Seizure 1998;7(6):489-95) was used to analyse the initial outpatient assessment. RESULTS: All consultants agreed to participate. A total of 147 children were identified as meeting the inclusion criteria. The sequence of events during the episodes was well recorded (91%). Other aspects of the history were less well recorded. Twelve percent were given a diagnosis of epilepsy, 26% non-epileptic and 62% uncertain. Documentation of early development and school performance was low (41%). Twenty-four percent of the children had no written documentation confirming physical and neurological examination. Documentation describing referral to an epilepsy nurse or support group was seen in 11%. Drug treatment and doses and follow-up plans were recorded in nearly all cases where applicable. DISCUSSION: A managed clinical network for children with epilepsy in Nottingham and the surrounding Trent region is currently being discussed which will consider alternative models of care for children with epilepsy. A revision of the BPNA audit tool has been produced with the BPNA Audit group and is available for other centres via the BPNA website's 'clinical toolbox' ().
PMID: 16275142 [PubMed - in process]

Seizure. 2005 Dec;14(8):534-40. Epub 2005 Sep 19.
What is the current evidence on decision-making after referral for temporal lobe epilepsy surgery? A review of the literature.
Uijl SG, Leijten FS, Parra J, Arends JB, van Huffelen AC, Moons KG.
Rudolf Magnus Institute for Neuroscience, Department of Clinical Neurophysiology, hp F02.230, UMC Utrecht, P.O. Box 85500, 3508 GA Utrecht, The Netherlands.
OBJECTIVES: Many patients thought to have temporal lobe epilepsy, are evaluated for surgical treatment. Decision-making in epilepsy surgery is a multidisciplinary, phased process involving complex diagnostic tests. This study reviews the literature on the value of different tests to decide on whether to operate. METHODS: Articles were selected when based on the consensus decision whether to perform temporal lobe surgery, or on the consensus localization or lateralization of the epileptic focus. The articles were scrutinized for sources of bias as formulated in methodological guidelines for diagnostic studies (STARD). RESULTS: Most studies did not fulfill the criteria, largely because they addressed prognostic factors in operated patients only. Ten articles met our inclusion criteria. In most articles, a single test was studied; SPECT accounted for five papers. Unbiased comparison of the results was not possible. CONCLUSION: Surprisingly little research in epilepsy surgery has focused on the decision-making process as a whole. Future studies of the added value of consecutive tests are needed to avoid redundant testing, enable future cost-efficiency analyses, and provide guidelines for diagnostic strategies after referral for temporal lobe epilepsy surgery.
PMID: 16169751 [PubMed - in process]

Seizure. 2005 Nov 21; [Epub ahead of print]
Is primidone the drug of choice for epileptic patients with QT-prolongation? A comprehensive analysis of literature.
Christidis D, Kalogerakis D, Chan TY, Mauri D, Alexiou G, Terzoudi A.
Section of Public Health, Panhellenic Association for Continual Medical Research (PACMeR), Thoma Pashidi 31, TK 45445 Ioannina, Athens, Greece.
Sudden unexplained/unexpected death (SUDEP) in epilepsy is a major cause of death accounting for 7-17% of the mortality among epileptic patients. Prolongation of QT-interval has been issued as a major

mechanism in SUDEP since it is associated with fatal cardiac arrhythmias. This condition may be further precipitated by anti-epileptic treatment. Despite thorough literature research, we did not find any reports suggesting that primidone is responsible for QT-prolongation. On the contrary, all the retrieved reports addressed that the drug shortened QT-interval and corrected signs and symptoms of the underlying disease.
PMID: 16309926 [PubMed - as supplied by publisher]

Seizure. 2005 Jul;14(5):347-53.
Seizure-related injuries in a group of young people with epilepsy wearing protective helmets: incidence, types and circumstances.
Deekollu D, Besag FM, Aylett SE.
The National Centre for Young People with Epilepsy, Lingfield, Surrey RH7 6PW, UK. david_jsd@hotmail.com
PURPOSE: To provide information on the incidence, types and circumstances of injuries sustained in a group of young people with epilepsy using protective helmets. METHODS: Thirty-three residential students (21 M, 12 F, age range 5-21, mean 14.5 years) attending a special epilepsy centre over 1 year were provided with helmets. The types of protective measures, seizure frequency, types of injuries, circumstances and outcome were recorded. RESULTS: Fourteen thousand seven hundred and fifty-one seizures were recorded in the 33 patients, which resulted in 59 injuries. The seizure-related injury risk was 4/1000 seizures. Scalp and facial bruises were the commonest injury (51%). Additional protective measures, such as bed guards and padding of dinner tables and sinks, were used for 57% of these students. Helmets were in use in 46% of the accidents; 68% of these accidents resulted in facial or scalp injuries, which required medical attention in 48%. Helmets were not in use in 41% of accidents; 57% of these accidents resulted in facial or scalp injuries, which required medical attention in 36%. Data on wearing of helmets in the accidents were unavailable in 13%. CONCLUSIONS: Injuries continue to occur despite the use of helmets. Changes to the helmet design and modifications to suit the seizure type may improve the protection offered by helmets.
PMID: 15896983 [PubMed - indexed for MEDLINE]

Seizure. 2005 Apr;14(3):207-12.
Educational problems with underlying neuropsychological impairment are common in children with Benign Epilepsy of Childhood with Centrotemporal Spikes (BECTS).
Vinayan KP, Biji V, Thomas SV.
Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala 695011, India.
INTRODUCTION: Benign Epilepsy of Childhood with Centrotemporal Spikes (BECTS) is one of the most common childhood epilepsies with a good prognosis regarding the seizure and neuropsychological outcomes. However, recent reports indicate the presence of neuropsychological problems in a significant percentage of children with BECTS. Our study was aimed to examine the educational performance and neuropsychological functions along with clinical and electrographic characteristics in a cohort of children with BECTS. METHODS: We identified a cohort of children with BECTS by screening medical and EEG recordings of patients attending our institute. Data were collected with a standard protocol. Their educational performance was evaluated by an interview with the parents. Neuropsychological and language tests were administered to children who had educational problems. Statistical analysis was done using the chi2-test. RESULTS: Fifty children (29 boys and 21 girls; mean age of onset of epilepsy 7.84+/-2.87 years) who met the criteria for BECTS were included in this study. Atypical seizure characteristics for BECTS were observed in 26 (52%) children. EEG showed typical centrotemporal spike and wave discharges in all children, 42% of them had a tangential dipole in the frontocentral region. An additional extra-rolandic focus in the EEG was found in seven children (14%). Educational problems were identified in 27 children (54%); 19 of them had neuropsychological or language impairment ($p=0.003$). We found a statistically significant correlation between the occurrence of educational problems and the absence of a tangential dipole in the EEG ($p<0.001$). Abnormal language function had a significant correlation with atypical seizure semiology ($p=0.021$). CONCLUSION: This study shows that a significant number of children with BECTS have neuropsychological impairment and educational problems.
Publication Types: Clinical Trial
PMID: 15797356 [PubMed - indexed for MEDLINE]

Seizure. 2005 Jan;14(1):46-51.

Estimating the economic burden of status epilepticus to the health care system.

Penberthy LT, Towne A, Garnett LK, Perlin JB, DeLorenzo RJ.

Department of Internal Medicine, Medical College of Virginia, Virginia Commonwealth University, 1200 East Broad Street, West 10 West 402, P.O. Box 980306, Richmond, VA 23298, USA. lpenberth@hsc.vcu.edu

PURPOSE: Status epilepticus (SE) is a major neurological condition associated with significant morbidity and mortality. No studies to evaluate the cost burden of SE have been performed to date. This study estimates the direct cost related to an inpatient admission for SE in an urban academic medical center. METHODS: Cases of SE were defined based on a standard 30 min or greater seizure duration. The inpatient claims data were analyzed for 192 patients admitted with SE from 1 July 1993 through 30 June 1994. Patient demographic and clinical characteristics associated with increased cost were identified using multiple regression. The direct costs for SE were compared with other common DRGs. RESULTS: The median reimbursement for a patient with SE was dollar 8417. The average length of stay for all SE patients was 12.9 days. Age groups (17-45 and 46-64) and etiology (acute CNS) were the only patient factors significantly associated with increased cost. SE patients had 30-60% higher reimbursements than patients admitted for other acute health problems including acute myocardial infarction or congestive heart failure. CONCLUSIONS: The direct inpatient costs for SE are high compared with the direct costs of admissions for other major conditions such as acute myocardial infarction or congestive heart failure. Data from this study were used to estimate a dollar 4 billion annual direct cost for inpatient admissions for SE. Given the incidence and the high costs, further more detailed evaluation of these costs may be useful in assessing the adequacy of reimbursement for this subset of patients with epilepsy.

PMID: 15642500 [PubMed - indexed for MEDLINE]

Seizure. 2004 Dec;13(8):587-90.

Vagus nerve stimulation therapy: 5-year or greater outcome at a university-based epilepsy center.

Spanaki MV, Allen LS, Mueller WM, Morris GL 3rd.

Department of Neurology, Medical College of Wisconsin, 9200 W. Wisconsin Avenue, Milwaukee, WI 53226, USA. mspanaki@mcw.edu

OBJECTIVE: This retrospective study documented long-term outcome of patients receiving vagus nerve stimulation (VNS) therapy for pharmacoresistant epilepsy. METHODS: Medical charts of 28 patients implanted for 5 years or longer were reviewed for changes in seizure frequency after 1 year of VNS therapy and at follow up, which ranged from 5 to 7 years. Numbers of antiepileptic drugs (AEDs) taken by the patients were also computed at 1 year and follow up. One patient had died and one had discontinued VNS therapy; data were available for 26 patients. Results: The median percent change in seizure frequency from baseline increased from -28% ($P = 0.0053$, Wilcoxon signed-rank test) at 12 months to -72% ($P < 0.0001$) at follow up. Some patients whose seizure frequency was not reduced during the initial 12 months of VNS therapy did experience reductions in seizure frequency during the follow-up period. CONCLUSION: In this retrospective study, the effectiveness of VNS therapy increased over time. Physicians should be aware that response to VNS therapy may be delayed for some patients.

PMID: 15519919 [PubMed - indexed for MEDLINE]

Seizure. 2004 Dec;13(8):553-64.

The Department of Health Action Plan "Improving Services for People with Epilepsy": a significant advance or only a first step?

Besag FM.

Specialist Medical Department, Bedfordshire and Luton Community NHS Trust, Twinwoods Health Resource Centre, Milton Road, Bedford, Beds MK41 6AT, UK. FBesag@aol.com

The government in England has supported the production of a number of reports on services for people with epilepsy over the last three or four decades but these have not come with any promise to provide resources or to achieve change. In recent years, the voluntary agencies have worked with government in undertaking some very worthwhile initiatives. The publication of the audit on epilepsy-related deaths and the commitment of the Chief Medical Officer have led to the production of an Action Plan entitled "Improving Services for People with Epilepsy". This Plan covers many of the key issues in the management of epilepsy and is seen as an important first step towards actual improvement of services. There is certainly a consensus that improvement is necessary with too many people receiving inadequate diagnosis and management leading, in some cases, to avoidable morbidity and mortality. A critical overview of the Action Plan and a suggested 10-point model Action Plan are presented. Whether the further necessary steps following the Department of Health Action Plan will be taken, remains to be seen. All those

responsible for the management and wellbeing of people with epilepsy very much hope that the required measures will be taken to ensure significant long-term improvements in services.
PMID: 15519915 [PubMed - indexed for MEDLINE]

Seizure. 2004 Oct;13(7):523-8.
Review of the legal obligations of the doctor to discuss Sudden Unexplained Death in Epilepsy (SUDEP)--a cohort controlled comparative cross-matched study in an outpatient epilepsy clinic.
Beran RG, Weber S, Sungaran R, Venn N, Hung A.
Epilepsy Research and Services & Strategic Health Evaluators, Suite 5, Level 6, 12 Thomas Street, Chatswood, NSW 2067, Australia. roy.beran@unsw.edu.au
INTRODUCTION: Acknowledging informed consent and warning of material risk, the present study examined the current debate regarding early discussion of Sudden Unexplained Death in Epilepsy (SUDEP). It sought to confirm the profile of those prone to SUDEP and to determine the basis for disclosure to patients. METHODS: Patients with SUDEP attending an Australian outpatient epilepsy clinic between 1985 and 2000 were compared to an age, gender and epilepsy type cross-matched control group to ascertain risk factors for SUDEP and similarities to published parameters. These were evaluated as the basis for actions in negligence for either disclosure or failure to disclose. RESULTS: Twenty-one SUDEP patients were identified: aged 18-70 years; the majority had localisation-related epilepsy (13:8, 62%); male to female ratio was 3:1; and 15/21 used polypharmacy, compared with 8/21 controls (P = 0.02951). Handedness, alcohol use or deterioration of epilepsy were unrelated. DISCUSSION: This population mirrored the literature and confirmed an absence of risk factors amenable to modification. As discussion of SUDEP with males with localisation-related epilepsy on polypharmacy could not alter outcome it is unlikely that failure to disclose could be causal and hence successful in an action for negligence. Conversely, disclosure, in the absence of the patient seeking the information, may causally adversely affect quality of life hence providing successful action in negligence. Duty of care dictates open and frank discussion with those seeking the information. Thus, each case must be managed individually and doctors are advised to document the decision-making process.
PMID: 15324833 [PubMed - indexed for MEDLINE]

Seizure. 2004 Jun;13(4):223-5.
Zonisamide monotherapy in a multi-group clinic.
Newmark ME, Dubinsky S.
Department of Neurology, Kelsey-Seybold Clinic, Houston, TX 77025, USA. Menewmark@kelsey-seybold.com
OBJECTIVE: Reports on zonisamide monotherapy are limited despite favourable preliminary data, and typically restricted to tertiary referral centres. The goal of this study is to report clinical experience with zonisamide monotherapy in a large, multi-group clinic setting. METHODS: We reviewed the charts of patients treated with zonisamide monotherapy in the Neurology Department of the Kelsey-Seybold Clinic (Houston, Texas) during an 18-month period. We analysed subgroups of patients who were naive to antiepileptic drug (AED) therapy (Group 1) and those who had previous exposure to AEDs (Group 2). RESULTS: The study included 54 paediatric and adult patients with a variety of seizure types: 15 patients in Group 1 and 39 patients in Group 2. Mean maintenance zonisamide dosages in the two groups were similar (193 mg/day in Group 1 vs. 218 mg/day in Group 2). Thirty-eight patients (70.4%) continued zonisamide monotherapy, with 7 patients (13.0%) adding a second AED and 9 patients (16.7%) switching to a different drug. Of the 24 patients who became seizure free on zonisamide monotherapy, 11 were on the 100-mg initial dosage. Zonisamide monotherapy was well tolerated. CONCLUSIONS: Zonisamide monotherapy is safe and effective for a variety of seizure types and may be appropriate as first-line therapy in some cases.
Publication Types: Clinical Trial
PMID: 15121129 [PubMed - indexed for MEDLINE]

Seizure. 2004 Mar;13(2):87-94.
The role of the clinical nurse specialist in epilepsy. A national survey.
Goodwin M, Higgins S, Lanfear JH, Lewis S, Winterbottom J.
Neurology Department, Northampton General Hospital, Cliftonville, Northampton NN1 5BD, UK. Melesina.Goodwin@ngh.nhs.uk

PURPOSE: To review and describe the key roles of the UK clinical nurse specialist in epilepsy (CNSE), and to identify the specialist nurses' contribution to care through an exploration of CNSE's perceptions of their roles. METHOD: Using the Delphi technique [Applied Project Design and Analysis, 3rd ed., Churchill Livingstone, London, 2000, p. 243] a national survey of all known UK CNSEs was completed. One hundred and thirty questionnaires identifying nine key hypotheses central to the role of the CNSE were distributed and 76 valid questionnaires returned. RESULTS: The response rate was 63% and was geographically representative of the UK population of CNSEs. CNSEs were employed in a range of hospital and community settings with differing patient groups. Seventy-two percent of respondents held higher academic nursing qualifications but only 36% had previous epilepsy or neurology experience. Thirty percent of respondents had been employed in the role of CNSE for more than 5 years and 84% were employed as a G or H grade nurse. Only 39% of CNSEs held nurse-led clinics and of those 32% were responsible for all decisions made during their clinic. Furthermore, 40% of CNSEs saw new patients who had not previously been reviewed by one of the medical team. The level of responsibility for drug management was mainly at a monitoring and advisory level but a small number of CNSEs held much greater responsibility. The responses to the nine hypotheses were compared using cross tabulations. CONCLUSION: The findings of the study and the review of the CNSE in the UK revealed that the key roles of the CNSE were difficult to define. Yet, the respondents identified that there were common core features central to their contribution to care as specialist nurses.
PMID: 15129836 [PubMed - indexed for MEDLINE]

Seizure. 2004 Jan;13(1):3-14.
A systematic review of the contribution of qualitative research to the study of quality of life in children and adolescents with epilepsy.
McEwan MJ, Espie CA, Metcalfe J.
Department of Psychological Medicine, University of Glasgow, Scotland, Glasgow, UK. c.espie@clinmed.gla.ac.uk
A sizeable literature focusing on QOL in children and adolescents with epilepsy has been produced over the last few years. However, relatively little emphasis has been placed on defining these issues from direct exploration of children's and adolescents' views. Qualitative methodologies are proposed in this review as an appropriate means of eliciting such information. This review systematically investigated the extent to which studies of QOL in children and adolescents with epilepsy have used recognised qualitative methodology. Articles for inclusion were identified by searching the term 'epilepsy', combined with 'adolescent(s) and/or child(ren)' and 'psychosocial and/or quality of life'. Selected articles were reviewed and rated using CASP Guidelines for qualitative research by two independent raters. Seventeen studies were retrieved through literature search. Of these six used some form of qualitative methodology either individually or combined with quantitative methods. However, only one study met quality criteria for selection in this systematic review. A summary of both selected and excluded studies is presented and methodological limitations discussed. Recommendations for appropriate methodology for investigation of QOL issues in children and adolescents are given.
Publication Types: Review
PMID: 14741177 [PubMed - indexed for MEDLINE]

Seizure. 2003 Dec;12(8):555-60.
Annual direct medical cost and contributing factors to total cost of epilepsy in Oman.
Al-Zakwani I, Hanssens Y, Deleu D, Cohen A, McGhan W, Al-Balushi K, Al-Hashar A.
Department of Pharmacy, Sultan Qaboos University Hospital, Muscat, Oman. ial-zakwani@healthcore.com
OBJECTIVES: To describe the pharmaceutical use, health care resource utilisation patterns, and annual direct medical cost of epilepsy as well as determining the impact of various demographic and clinical characteristics on total costs of epilepsy in Oman. METHODS: Medical and pharmacy data were collected for 6 months on all patients aged > or =13 years attending the Sultan Qaboos University Hospital. Unit pharmacy and medical costs were retrieved for each patient, and multiple linear regression was utilised to analyse the impact of various demographic and clinical characteristics on total cost. RESULTS: A total of 486 patients were seen over the study period. Annual direct medical costs of epilepsy amounted to 1,426 US dollars. In-patient care, the antiepileptic drug (AED) lamotrigine and specialist visits, respectively, were the first, second and third most significant predictors of total cost. Age was associated positively, and was the most significant predictor of total costs among demographic and clinical parameters. CONCLUSIONS: This analysis, the first economic study of epilepsy in Oman, could assist in health care allocation of scarce resources and in pharmacoeconomic analysis of AEDs. Besides in-patient admission,

our findings demonstrate that the newer drugs are significant predictors of total cost, and hence any incremental benefits derived from them must be rigorously assessed for their cost-effectiveness.
PMID: 14630493 [PubMed - indexed for MEDLINE]

Seizure. 2003 Dec;12(8):539-44.
Outcomes from a nurse-led clinic for adolescents with epilepsy.
Stephen LJ, Maxwell J, Brodie MJ.
Epilepsy Unit, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow, Scotland, UK.
PURPOSE: Epilepsy is the commonest serious neurological condition to affect adolescents. We established a nurse-led clinic for young people with suspected or diagnosed epilepsy. Outcomes in all patients referred during the first 4 years after its inception are reported. METHODS: A total of 301 adolescents were seen at the clinic during 1996-1999. Epilepsy was excluded in 135 (45%), including 5 receiving antiepileptic drug (AED) therapy. A single seizure occurred in 22 (7%) others. Seventy-six patients (25%) had treated epilepsy and 68 (23%) were newly diagnosed. RESULTS: More than 1 year's seizure freedom was achieved by 53% of patients, 76% with one AED, 16% with two and 3% with three. Four (5%) patients remained seizure free off medication. Sixteen (11%) were lost to follow-up. Outcome was better ($P<0.05$) for newly diagnosed (59% seizure free) than for treated (47% seizure free) epilepsy and for idiopathic generalised (60% seizure free) than for partial (46% seizure free) seizures ($P<0.02$). Magnetic resonance imaging of brain was obtained in 63 (85%) patients with localisation-related epilepsy. Findings were abnormal in 43%, including nine with cortical dysplasia, eight with mesial temporal sclerosis and two with gliomas. CONCLUSIONS: Epilepsy can be difficult to diagnose in adolescents. Outcomes were surprisingly poor suggesting the need for improved services for this patient population.
PMID: 14630490 [PubMed - indexed for MEDLINE]

Seizure. 2003 Dec;12(8):523-8.
Treatment of epilepsy in general hospitals: do patients and neurologists agree on success or failure?
Aldenkamp AP, Van Donselaar C.
Department of Neurology, University Hospital of Maastricht, Maastricht, The Netherlands. aldenkampB@kempenhaeghe.nl
OBJECTIVE: Opinions of patients and neurologists about aspects of their epilepsy and their treatment were compared. METHOD: Thirty-two neurologists, working in general hospitals, included 198 patients aged 16 years or more. Both neurologist and patient independently completed a questionnaire consisting of simple open questions about the epilepsy and the drug treatment. The average characteristics for this group are very similar to characteristics of the general population: age and gender distribution, highest completed educational level, occupational participation and family circumstances are not statistically significant from the general population. RESULTS: Neurologists and patients appear to agree about most areas that we assessed: seizure count, severity of epilepsy, efficacy and tolerability of the treatment and impact of the epilepsy and treatment on daily life (as expressed in the 'Quality of Life ratings'). Detailed analysis showed that this agreement is partly artificially increased by the group with good outcome and less strong or even absent for the more severe epilepsies. For seizure count, we see 96.4% agreement for the group with low seizure frequency and 73.1% agreement in case of high seizure frequency. For the evaluation of severity of the epilepsy, 73.2% agreement is found for mild classification and 16.6% agreement for the severe classification. Agreement on Quality of Life (QOL) is almost complete in patients with excellent QOL (91% agreement) and almost absent for a low QOL (17% agreement). Finally, the same pattern is found for reports on side-effects of the medication. Both neurologists and patients report side-effects in about 40% of the cases. This suggests excellent agreement but individual data show that agreement is only satisfactory for the milder epilepsies (16.2% vs. 16.2%). For the more severe agreement is almost absent (4.1% of the neurologists vs. 13.4% of the patients). DISCUSSION: Possibly, it is more difficult for the neurologist to perceive and appraise all relevant factors in the case of complex epilepsies. Alternatively, subjective definitions and assumptions of patients differ from the standards set by the neurologists in the case of continuing seizures.The clinical relevance of our findings is that, especially in the cases of more severe and refractory epilepsies, patients' opinions are of utmost importance and we cannot take our own opinions and evaluations at face value.
PMID: 14630487 [PubMed - indexed for MEDLINE]

Seizure. 2003 Jul;12(5):249-56.

Cost-utility analysis of vagus nerve stimulators for adults with medically refractory epilepsy.
Forbes RB, Macdonald S, Eljamel S, Roberts RC.
Department of Neurology, Royal Victoria Hospital, Belfast, Northern Ireland, UK. raeburnforbes@aol.com
INTRODUCTION: The cost-utility of vagus nerve stimulator (VNS) devices for medically refractory epilepsy has yet to be estimated. METHODS: Using a meta-analysis of randomised controlled trials of VNS, we estimate that six people require implantation in order for one person to experience a 50% reduction in seizure frequency. Costs averted from improved epilepsy control were ascertained from published literature. Values for health states were obtained from a series of 42 seizure clinic attenders using time trade-off techniques and the EQ-5D health status instrument. The cost per quality adjusted life year gained was estimated and the values obtained were tested in a sensitivity analysis. RESULTS: Improved epilepsy control averted, on average, 745 pounds sterling health care costs per annum. People with epilepsy had great difficulty performing the time trade-off experiment, but those who managed to complete the task valued a 50% reduction in their own seizure frequency at 0.285 units. For a programme of six implants, the baseline model estimated the cost per quality adjusted life year gained at 28,849 pounds sterling. The most favourable estimate was equal to 4785 pounds sterling per quality adjusted life year gained, assuming that the number needed to treat was similar to published series in which one response was obtained for every three implants. The least favourable estimate was equal to 63,000 pounds sterling per quality adjusted life year gained, when EQ-5D utility values were used. The cost per quality adjusted life year gained was not sensitive to changes in length of stay, nor complication rates, but was significantly influenced by cost of device and device battery life expectancy. CONCLUSION: There is not a strong economic argument against a programme of VNS implantation, although care should be taken to try and identify and treat those most likely to benefit.
Publication Types: Meta-Analysis
PMID: 12810336 [PubMed - indexed for MEDLINE]

Seizure. 2003 Jun;12(4):229-36.
Seizures and therapy in adolescents with uncomplicated epilepsy.
Raty LK, Wilde-Larsson B, Soderfeldt BA.
Faculty of Health Sciences, Department of Neurology, Linkoping University, Linkoping, Sweden. lena.raty@kau.se
PURPOSE: This study aimed to describe seizures and their therapy among Swedish adolescents, aged 13-22, with active but uncomplicated epilepsy. METHOD: The adolescents answered questionnaires (158/193). Data were also obtained from medical records. RESULTS: Epileptic seizure types could be specified in 92.1% of the cases. Predominant types were Primary Generalised Tonic-Clonic Seizures and Partial Complex Seizures with Secondary Generalisation. Clinical diagnoses by physicians were unspecified in 25.8%. Ninety percent were on antiepileptic drugs (AEDs), most commonly valproate and carbamazepine. New AEDs were used in 9.3% of the cases and polytherapy in 13.9%. More than 40% of the respondents had seizures despite AED treatment. Side effects of AEDs were experienced by 61%, most commonly tiredness, concentration difficulties and headache. Patients on polytherapy experienced significantly more side effects. The choice of a new AED over a traditional one was not related to seizure type or seizure control. CONCLUSIONS: Many adolescents had persistent seizures despite treatment at a specialist regional epilepsy centre. This, plus the high reported rate of side effects of AED treatment, suggests that treatment is not optimal for the group studied. As traditional AEDs strongly dominated treatment possibly newly marketed AEDs are underused in this group.
PMID: 12763471 [PubMed - indexed for MEDLINE]

Seizure. 2003 Mar;12(2):77-84.
Implementing good practice in epilepsy care.
Frost S, Crawford P, Mera S, Chappell B.
Centre for Community Neurological Studies, Leeds Metropolitan University, Calverley Street, Leeds LS1 3HE, UK.
Examples of evidence-based guidelines for epilepsy care exist. However, guidelines are of little use if they are not recognised, implemented and supported. The object of this study was to establish the degree to which good practice guidelines for epilepsy have been implemented and to identify positive and negative factors that affect their implementation. Semi-structured questionnaires were sent to 750 randomly selected health professionals working in primary and secondary care in England. The sample comprised nurses (200), adult consultants (including learning disability consultants) (300), paediatric consultants (150) and general practitioners (100). Aspects of good practice are being implemented in some areas, but

not generally, therefore service provision is likely to remain fragmented until this is addressed. Professionals have been prevented from successful implementation of guidelines to sustain good practice due to a number of factors, most notably lack of time, workload, competing priorities and staffing levels. Factors that have promoted and encouraged the successful adoption and application of good practice include inputs from epilepsy specialist nurses (ESNs), appropriate, timely and accessible professional development opportunities and the support and enthusiasm of colleagues.
PMID: 12566230 [PubMed - indexed for MEDLINE]

Seizure. 2003 Mar;12(2):74-6.
Prescribing and the epilepsy specialist nurse.
Hosking P.
Department of Neurology, National Hospital for Neurology & Neurosurgery, University College Hospitals NHS Trust, Queen Square, London WC1N 3BG, UK. patricia.hosking@uclh.org
Increasingly, the epilepsy nurse specialist has become an integral part of the specialist epilepsy team. Nurse specialists, who practice at an advanced level, frequently advise patients on diagnosis and antiepileptic drug changes. The inclusion of antiepileptic drugs to the nurse Prescribing Formulary would allow specialist nurses to provide a more enhanced service to patients.
Publication Types: Review
PMID: 12566229 [PubMed - indexed for MEDLINE]

Stud Health Technol Inform. 2003;95:549-53.
How many neurologists/epileptologists are needed to provide reliable descriptions of seizure types?
van Ast JF, Talmon JL, Renier WO, Hasman A.
Department of Medical Informatics, University of Maastricht, The Netherlands. w.vanast@mi.unimaas.nl
We are developing seizure descriptions as a basis for decision support. Based on an existing dataset we used the Spearman-Brown prophecy formula to estimate how many neurologist/epileptologists are needed to obtain reliable seizure descriptions (rho = 0.9). By extending the number of participants to the required level we found that the number of participants needed to obtain a reliability coefficient of 0.9 were in accordance with the number of participants determined from the Spearman-Brown prophecy formula. Systematic differences between the participants were minor and not statistically significant.
PMID: 14664044 [PubMed - indexed for MEDLINE]

Suppl Clin Neurophysiol. 2004;57:477-84.
Advances in EEG telemetry.
Schomer DL.
Clinical Neurophysiology, Comprehensive Epilepsy Program and Neurology, Harvard University, Boston, MA 02215, USA. dschomer@bidmc.harvard.edu
PMID: 16106648 [PubMed - indexed for MEDLINE]