ACF Hui 許志輝
P Kwan 關國良

Epilepsy in Hong Kong: a literature review

癲癇症在香港：文獻回顧

Objective. To review data on the causes, clinical features, and management of patients with epilepsy in Hong Kong.
Data sources. MEDLINE and Chinese Current Medical Contents were used to search the literature. A manual search of the *Hong Kong Medical Journal, Hong Kong Practitioner,* and *Chinese Medical Journal* (1982-2002) was also undertaken.
Study selection. Key words for the literature search were 'epilepsy' and 'Hong Kong'.
Data extraction. All relevant articles in English or in Chinese language were reviewed.
Data synthesis. Overall, disease characteristics and the response to both medical and surgical treatments of epilepsy among local Chinese patients with epilepsy was found to be comparable to that reported for patients in western countries. Knowledge of epilepsy among the general population was more limited than expected from the international literature, and attitudes to epilepsy relatively more negative, adding to the psychosocial burden for people with epilepsy.
Conclusion. Further research in Hong Kong on aspects of epileptology is indicated with a view to developing more innovative and effective therapy.

目的：回顧香港癲癇症患者的病因、臨床病徵及治理方法。
資料來源：於 MEDLINE 及 Chinese Current Medical Contents 資料庫內作文獻檢索。另以人手搜尋由 1982 至 2002 年的《香港醫學雜誌》、《香港家庭醫學學院月刊》及《中華醫學雜誌》。
研究選取：以「癲癇症」及「香港」為關鍵詞檢索文獻。
資料選取：回顧所有有關的中文及英文文獻。
資料綜合：整體來說，本地華人癲癇症患者，其病發的特徵，以及對內外科療法的反應，與西方國家的同類型病人接近。香港一般市民對癲癇症的認識，比國際文獻所預期的更有限；而他們對待癲癇症的態度亦較為負面，從而增加癲癇症患者的心理壓力。
結論：香港有需要就癲癇症學的各個方面進行更多研究，以發展更創新及更有效的療法。

Key words:
Chinese;
Cross-cultural comparison;
Epidemiology;
Epilepsy

關鍵詞：
華人；
跨文化比較；
流行病學；
癲癇症

Hong Kong Med J 2004;10:185-9

Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong
ACF Hui, FRCP, FHKAM (Medicine)
P Kwan, PhD, FHKAM (Medicine)

Correspondence to: Dr ACF Hui (e-mail: cfhui@cuhk.edu.hk)

Introduction

Existing knowledge on the epidemiology and treatment of epilepsy has been derived mainly from studies conducted overseas. However, differences in ethnic composition, disease prevalence, and socio-economic factors mean that the findings from these studies may not be entirely applicable to the Chinese communities. For example, in China around 50% of patients with epilepsy have no regular access to medical treatment.[1] Local data are important in order to assess the magnitude of the problem and to target resources to patients and projects most in need. This article aims to summarise current knowledge of epilepsy in Hong Kong by reviewing relevant articles on the topic.

Methods

We performed a search of the electronic databases MEDLINE and Chinese Current Medical Contents using the key words 'epilepsy' and 'Hong Kong', and also conducted a manual search of both English- and Chinese-language journals (*Hong*

Kong Medical Journal, Hong Kong Practitioner, Chinese Medical Journal) from 1982 to 2002.

Results

Epidemiology

The prevalence of active epilepsy in people aged 15 years or over in Hong Kong has been estimated at 1.54 per 1000.[2] This figure may be an underestimate as it was based on a study of a hospital cohort. Using the figures derived from epidemiological studies conducted in other Chinese communities (China, Singapore) where the prevalence is 3 to 5.7 per 1000,[1,3,4] approximately 40 000 people in Hong Kong could be expected to have active epilepsy.

The risk of recurrence after a first unprovoked and untreated generalised tonic-clonic convulsion was studied in 126 people, using Kaplan-Meier survival analysis.[5] The cumulative probability of a second attack at 1, 2, and 3 years was 30%, 37%, and 42%, respectively. Multivariate analysis showed that an abnormal cranial computed tomography (CT) scan was associated with an increased risk of recurrence.

Aetiology

Epilepsy is a heterogeneous condition. Among the patients in the Hong Kong Epilepsy Registry survey in 1997 with identifiable causes, the most common aetiologies included: cerebrovascular disease (26.2%); a history of central nervous system (CNS) infection, such as meningitis or encephalitis (26.0%); head trauma (11.4%); perinatal insult (9.7%); congenital brain malformation (7.4%); hippocampal sclerosis (5.9%), and intracranial neoplasm (5.6%).[6] Cerebrovascular disease is a relatively common cause of seizures, reported to occur in 3.4% of cases within 1 year of an acute stroke in a recent study.[7] Disorders listed in the International League Against Epilepsy's revised classification of epilepsies and epileptic syndromes, such as Lennox-Gastaut syndrome, benign childhood epilepsy with centrotemporal spikes, childhood absence, and juvenile myoclonic epilepsy are increasingly being recognised in Hong Kong.[6,8,9] Rare causes of repeated seizures, such as neuronal ceroid lipofuscinoses, insulinomas, porphyrias, and drug overdoses have also been described.[10-13] Although neurocysticercosis is an important cause of epilepsy in poor countries, this is an unusual cause in local Chinese.[14] Systemic lupus erythematosis is more common in Chinese populations and seizure disorders are found in 16% to 28% of affected individuals.[15,16]

Psychosocial impact

Epilepsy imposes an enormous psychological, social, and economic burden on patients and their families. One Hong Kong cost-of-illness study involved a retrospective cohort of 745 individuals treated medically from 1992 to 1996. Reported total direct costs were USD 0.98 million, and indirect costs USD 1.32 million during this period.[17]

Although the public's perception of epilepsy is more positive in Hong Kong than in other Chinese communities, such as in China and Taiwan, it appears to be more negative than in western societies. A recent study in Hong Kong of 1128 members of the public without seizures and without relatives with epilepsy, found that 71% of respondents believed that epilepsy was an inheritable disorder, and 57.7% considered inserting an object into the person's mouth during an attack constituted appropriate first aid.[18] Attitudes towards people with epilepsy were also studied: 32.2% indicated they would not allow their children to marry individuals with epilepsy, 27.5% considered pregnancy to be inappropriate for an individual with epilepsy, and 22.5% of employers indicated they would terminate an affected workers' employment contract. A belief peculiar to Chinese communities is that mutton consumption during pregnancy can lead to epilepsy in the offspring. Two percent, mainly older respondents, believe that epilepsy is due to possession by evil spirits.

A study of 70 individuals with epilepsy in Hong Kong using the Washington Psychosocial Inventory revealed that many patients had difficulties with emotional, interpersonal, vocational, and financial adjustment.[19] Discrimination was reported by 70% of patients as a direct result of having epilepsy.[19]

Epilepsy also affects carers. Three quarters of carers interviewed in a recent Hong Kong study were found to have low scores on the Chinese versions of the Epilepsy Outcome Scale and the World Health Organization Quality of Life Measure.[20] Severe depression was also found in 14%.

Clinical features

A large retrospective review was undertaken of 2952 patients with epilepsy over the age of 10 years seen at eight public hospitals with a neurological service. Primary and secondary generalised tonic-clonic convulsion was the most common seizure type—presumably as this is the most readily recognised type.[6] Complex partial, simple partial, and myoclonic seizures occurred in 28.3%, 14.4%, and 1.4% of cases, respectively. Overall, mental retardation was found in 14.1% and cerebral palsy in 2.1% of patients; these two figures were twice as high in the subpopulation with refractory epilepsy. Approximately one fifth (20.3%) had refractory epilepsy as defined by persistent seizures despite appropriate treatment with at least two drugs.[6] This compares favourably with findings from prospective studies in western countries.[21]

In childhood epilepsy, abnormal neurodevelopmental status and the presence of more than three seizures in the second 6-month period after treatment have been identified as early predictors of intractability.[22] Wong[23] found that 7.6% of children with autistic spectrum disorder have recurrent seizures, and Kwong and Wong[24] reported only two of 124 children with Down's syndrome reviewed suffered from epilepsy (due to Lennox-Gastaut syndrome and infantile spasms), a percentage which is notably lower when

compared with the case series reported in white patients.[23,24] Among 105 children with West syndrome studied in Hong Kong, the majority had a poor outcome—multiple disabilities in 16 cases, cerebral palsy in 22, mental retardation in 94, and Lennox-Gastaut syndrome in 13.[25]

A retrospective review of 37 Chinese children admitted to a hospital in Hong Kong with the diagnosis of status epilepticus (SE) from 1989 to 1993 found a mortality rate of 11%. Death in these cases was attributed to the underlying aetiology rather than to seizures per se.[26] Neurological complications were reported in 27%. Acute CNS pathologies were the most common cause (observed in 60%), followed by idiopathic (11%), pre-existing CNS insult (13%), febrile illness (5%), and progressive encephalopathy (11%). The authors concluded that the outcome was favourable in patients with normal baseline neurological status, and without acute CNS insult or progressive encephalopathy.

Among adults presenting with SE, the most common identifiable aetiologies were cerebrovascular disease (23%), lack of compliance with anticonvulsants or drug withdrawal (15%), and metabolic derangement (12%)[27]; alcohol-related SE was noted to be uncommon when compared with series from the US and Europe. Of the 107 cases reviewed, 82 (77%) required admission to the intensive care unit, with a mean stay of 3.6 days, and 65 patients (61%) required ventilation, with a mean duration of 2.7 (standard deviation, 5.6) days. Increasing age, delay in treatment, SE due to cerebrovascular disease, and CNS infection were associated with poor outcome (mortality and/or morbidity).[27] Non-convulsive SE has also been reported, highlighting the importance of electroencephalography (EEG) in patients with altered mental status.[28-30]

Medical management

The majority of patients with epilepsy in Hong Kong are managed in the public sector.[31] First-line antiepileptic drugs are the mainstay of therapy but there are no local randomised controlled trials investigating the use of these therapeutic agents. Data obtained from the 1997 Hong Kong Epilepsy Registry survey indicate that the four most commonly prescribed antiepileptic drugs are phenytoin (38.7%), carbamazepine (32.8%), valproate (22.4%), and phenobarbitone (11.1%).[6] Monotherapy is used in the majority of cases (57.4%). The effects of phenytoin, as measured by brain-stem auditory evoked potentials, have been studied in local patients. Chan et al[32] demonstrated that phenytoin produces abnormalities both peripherally on the auditory nerve/cochlea, as well as centrally on brain stem conduction.

Kumana et al[33] conducted a comparison study of diazepam pharmacokinetics in healthy Chinese and white volunteers. Serum concentrations of diazepam and desmethyldiazepam were measured using enzyme-linked immunoassay and high-performance lipid chromatography. Mean peak diazepam concentration (Cmax) was similar in both groups but in the Chinese group, mean diazepam apparent volumes of distribution were smaller and time to Cmax (tmax) was more often prolonged.[33] The authors attributed these differences to the greater body fat and stature of those in the white volunteer group.

The effects of more recently developed antiepileptic drugs, topiramate, and vigabatrin have been studied in local patients. Thirty children with intractable seizures received vigabatrin as add-on treatment[34]; the epilepsy was cryptogenic in 16 cases and symptomatic in 12. Vigabatrin 40 to 80 mg/kg per day was titrated according to clinical response for up to 2 years. Overall, 43% of children experienced a 50% to 75% reduction in seizure frequency. There was no relationship seen between response to vigabatrin therapy and age of onset, type of seizure, aetiology, and presence/absence of mental retardation. A small, observational study has also indicated that vigabatrin is effective for treating infantile spasms.[35]

Topiramate was also used as an add-on therapy in a multicentre open-label trial of 103 patients, including the local Chinese patients.[36] Of these patients, 53% had a more than 50% reduction in seizure frequency, 31% had a 75% reduction, and 12% became seizure free. In contrast to studies from the West, there were no reports of gastro-intestinal upset, speech disturbance, or psychomotor slowing, but the overall withdrawal rates were similar at 7%.

A prospective trial looked at the effect of increasing anticonvulsant medication dose in seizure-free cases with low serum anticonvulsant levels.[37] Seventy-nine subjects were randomised to either:

(1) a study arm in which drug levels were maintained in the subtherapeutic range; or
(2) another arm in which the dose was increased until the therapeutic range was reached.

The study showed that the dose increment did not lead to significant improvement in seizure control but did lead to the occurrence of more neurotoxic side-effects. These results suggest that increasing the anticonvulsant therapy dose in a patient with relatively well-controlled epilepsy is unnecessary. The need for expensive drug monitoring could also be reduced.[37]

An increased risk of thrombocytopenia with valproate therapy has also been described in a Hong Kong population.[38] Children with a trough level of 450 μmol/L or above, or a daily dose of 40 mg/kg or above, were shown to be more likely to develop thrombocytopenia, although the thrombocytopenia was mild in most cases.

Surgical management

Investigations such as EEG, CT, and magnetic resonance imaging (MRI) are widely available in Hong Kong, while long-term video-EEG monitoring, single photon emission computed tomography and positron emission tomog-

raphy are performed in a growing number of specialist centres.[6,39,40] Vagus nerve stimulation is an adjunctive treatment for patients with refractory partial-onset seizures who are not suitable for epilepsy surgery.[41] The procedure was first introduced in South-East Asia in Hong Kong during the mid-nineties, with results comparable to those reported overseas.[41,42] In patients with an epileptic syndrome amenable to surgery, resection is the most effective mode of therapy; those with mesial temporal lobe abnormalities on MRI were more likely to proceed to surgery than those with extrahippocampal lesions.[40] Results from one surgical centre showed that eight of 11 patients became seizure free following temporal lobe resection for intractable epilepsy.[43] Nine of these reported significant improvement in social functioning as a result. No major postoperative complications or deaths were reported in this series.

Using the Chinese version of the World Health Organization Quality of Life Measure Abbreviated Version, validated in Hong Kong, Ho et al[44] found that the quality of life of participants after successful surgery was still poorer than that of 157 healthy controls, suggesting that additional factors are important in determining quality of life other than seizure control alone.

Discussion

Data from studies over the past decade have provided a clearer picture of the clinical characteristics of patients with epilepsy in Hong Kong. One of the most valuable contributions has been made by the territory-wide survey conducted in 1997 which showed that overall, clinical features of epilepsy (such as seizure types and prognosis) in patients in Hong Kong appear to be comparable to those of their western counterparts.[6] The effectiveness of antiepileptic drugs and surgery, a further major focus of research activities again has yielded similar findings to those reported overseas. This suggests that broadly speaking, disease characteristics and the response to treatment among local Chinese patients with epilepsy can be expected to be comparable to that seen in western countries. This helps to validate the extrapolation of findings generated in Europe and North America to the Chinese populations and vice versa. Important differences, including differences in pharmacokinetic profile, and attitude to and knowledge of the condition do exist, however.

Differences seen in pharmacokinetic profile were attributed to differences in body composition in one study.[33] Genetic polymorphisms contribute significantly to variations in drug response in both pharmacokinetic and pharmacodynamic terms among ethnic groups.[45] For instance, polymorphisms in the hepatic cytochrome P450 enzyme system result in differences in the metabolism of phenytoin.[46] There is also considerable ethnic variation in the frequency of polymorphism of the *MDR1* gene.[47] This gene has been shown to be associated with response to drug therapy in patients with epilepsy, and it is possible that such genetic variations might influence the response to specific antiepileptic drugs in different ethnic groups.[47,48]

Differences in public attitude towards patients with epilepsy between Hong Kong Chinese and their western counterparts reflect underlying cultural differences in the perception of this condition.[18,19,49,50] The Hong Kong Epilepsy Association and the Community Rehabilitation Network are non-governmental organisations that offer advice and support to people with epilepsy and their families in the form of quarterly newsletters, regular group and educational meetings, and a website (http://www.hkepilepsy.com). Local studies concerning public knowledge of epilepsy and attitudes towards people with epilepsy should be encouraged since they have direct relevance to health education and promotion. These studies have a valuable role in our efforts to bring epilepsy "out of the shadows".[51]

Future research directions

Despite the efforts of clinicians over the past decade, knowledge gaps are clearly evident in many important aspects of epileptology. Understanding epileptogenic mechanisms through insights from genetics, imaging, electrophysiology, and developmental biology has been identified as the key to developing more innovative and effective therapies.[52] In keeping with this overall strategy and to produce data that are directly applicable to the Chinese communities, future research in Hong Kong should focus on the following directions:

(1) Epidemiology: one of the priorities is a community-based prevalence and incidence study. Without such information, sensible allocation of resources cannot be made for clinical service and research purposes;
(2) Natural history: the natural history of epilepsy in response to treatment is still poorly understood. Hong Kong has a major methodological advantage in this regard since it is routine practice for patients presenting with a first seizure to be admitted to hospitals for investigation and observation. The majority of in-patients with epilepsy are managed in public hospitals, where medical records are linked by a territory-wide database;
(3) Genetics: a growing number of gene mutations associated with familial epilepsy syndromes have been identified. Genetic polymorphisms may play an important role in disease susceptibility, as well as response to drug treatment. Ethnic variations in these polymorphisms should be studied so that pharmacogenetically based prescription may be realised;
(4) Psychosocial aspect: there is a growing trend to include psychosocial outcome in the evaluation of treatment effectiveness; psychometric testing is also an essential part of presurgical evaluation. Many of the tools for assessment of psychological function and quality of life have not been translated and validated among Chinese patients; and
(5) Basic science: there has been a lack of basic research on epilepsy in Hong Kong. Investigation in this area is

needed for a better understanding of the mechanisms of seizures and epileptogenesis.

References

1. Wang WZ, Wu JZ, Wang DS, et al. The prevalence and treatment gap in epilepsy in China: an ILAE/IBE/WHO study. Neurology 2003;60: 1544-5.
2. Fong GC, Mak W, Cheng TS, Chan KH, Fong JK, Ho SL. A prevalence study of epilepsy in Hong Kong. Hong Kong Med J 2003;9: 252-7.
3. Li SC, Schoenberg BS, Wang CC, Cheng XM, Zhou SS, Bolis CL. Epidemiology of epilepsy in urban areas of the People's Republic of China. Epilepsia 1985;26:391-4.
4. Tan CT, Lim SH. Epilepsy in South East Asia. Neurol J Southeast Asia 1997;2:11-5.
5. Hui AC, Tang A, Wong KS, Mok V, Kay R. Recurrence after a first untreated seizure in the Hong Kong Chinese population. Epilepsia 2001; 42:94-7.
6. Ng KK, Ng PW, Tsang KL; Hong Kong Epilepsy Study Group. Clinical characteristics of adult epilepsy patients in the 1997 Hong Kong epilepsy registry. Chin Med J (Engl) 2001;114:84-7.
7. Cheung CM, Tsoi TH, Au-Yeung M, Tang AS. Epileptic seizure after stroke in Chinese patients. J Neurol 2003;250:839-43.
8. Kwong KL, Chak WK, Wong SN, So KT. Epidemiology of childhood epilepsy in a cohort of 309 Chinese children. Pediatr Neurol 2001;24: 276-82.
9. Ma CK, Chan KY. Benign childhood epilepsy with centrotemporal spikes: a study of 50 Chinese children. Brain Dev 2003;25:390-5.
10. Ko CH, Kong CK, Chow TC, Lee KC. Classic late infantile neuronal ceroid lipofuscinosis in a Chinese patient. Hong Kong Med J 2001;7:93-6.
11. Hui AC, Ma RCW, Ozaki R, Kay R, Cockram CC. Seizure recurrence in temporal lobe epilepsy. Int J Clin Pract 2001;56:63-4.
12. Chow KM, Hui CF, Lam CW, et al. Clinical and genetic features of variegate porphyria in a Chinese patient. Chin Med J (Engl) 2001; 114:424-7.
13. Hui AC, Wong TY, Chow KM, Szeto CC. Multifocal myoclonus secondary to tranexamic acid. J Neurol Neurosurg Psychiatry 2003; 74:547.
14. Heap BJ. Cerebral cysticercosis as a common cause of epilepsy in Gurkhas in Hong Kong. J R Army Med Corps 1990;136:146-9.
15. Wong KL, Woo EK, Yu YL, Wong RW. Neurological manifestations of systemic lupus erythematosus: a prospective study. Q J Med 1991; 81:857-70.
16. Mok CC, Lau CS, Wong RW. Neuropsychiatric manifestations and their clinical associations in southern Chinese patients with systemic lupus erythematosus. J Rheumatol 2001;28:766-71.
17. Mak W, Fong JK, Cheung RT, Ho SL. Cost of epilepsy in Hong Kong: experience from a regional hospital. Seizure 1999;8:456-64.
18. Fong CY, Hung A. Public awareness, attitude, and understanding of epilepsy in Hong Kong Special Administrative Region, China. Epilepsia 2002;43:311-6.
19. Lau VW, Lee TM, Ng PK, Wong VC. Psychosocial adjustment of people with epilepsy in Hong Kong. Epilepsia 2001;42:1169-75.
20. Lee MM, Lee TM, Ng PK, Hung AT, Au AM, Wong VC. Psychosocial well-being of carers of people with epilepsy in Hong Kong. Epilepsy Behav 2002;3:147-57.
21. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314-9.
22. Kwong KL, Sung WY, Wong SN, So KT. Early predictors of medical intractability in childhood epilepsy. Pediatr Neurol 2003;29:46-52.
23. Wong V. Epilepsy in children with autistic spectrum disorder. J Child Neurol 1993;8:316-22.
24. Kwong KL, Wong V. Neurodevelopmental profile of Down syndrome in Chinese children. J Paediatr Child Health 1996;32:153-7.
25. Wong V. West syndrome--The University of Hong Kong experience (1970-2000). Brain Dev 2001;23:609-15.
26. Kwong KL, Lee SL, Yung A, Wong VC. Status epilepticus in 37 Chinese children: aetiology and outcome. J Paediatr Child Health 1995; 31:395-8.
27. Hui AC, Joynt GM, Li H, Wong KS. Status epilepticus in Hong Kong Chinese: aetiology, outcome and predictors of death and morbidity. Seizure 2003;12:478-82.
28. Yan Liu X, Wong V. Spectrum of epileptic syndromes with electrical status epilepticus during sleep in children. Pediatr Neurol 2000;22: 371-9.
29. Chow KM, Hui AC, Szeto CC, Wang AY, Li PK. A confused uraemic woman. Lancet 2001;357:278.
30. Chow KM, Wang AY, Hui AC, Wong TY, Szeto CC, Li PK. Nonconvulsive status epilepticus in peritoneal dialysis patients. Am J Kidney Dis 2001;38:400-5.
31. Department of Health of Hong Kong SAR. Annual Departmental Report. 2000-2001:132.
32. Chan YW, Woo E, Yu YL. Chronic effects of phenytoin on brain-stem auditory evoked potentials in man. Electroencephalogr Clin Neurophysiol 1990;77:119-26.
33. Kumana CR, Lauder IJ, Chan M, Ko W, Lin HJ. Differences in diazepam pharmacokinetics in Chinese and white Caucasians--relation to body lipid stores. Eur J Clin Pharmacol 1987;32:211-5.
34. Wong V. Open label trial with vigabatrin in children with intractable epilepsy. Brain Dev 1995;17:249-52.
35. Kwong L. Vigabatrin as first line therapy in infantile spasms: review of seven patients. J Paediatr Child Health 1997;33:121-4.
36. Lim SH, Kwan MC, Sjahrir MI, et al. An open label trial of topiramate as adjunctive therapy in Asian patients with refractory partial epilepsy. Neurol J Southeast Asia 2001;6:121-7.
37. Woo E, Chan YM, Yu YL, Chan YW, Huang CY. If a well-stabilized epileptic patient has a subtherapeutic antiepileptic drug level, should the dose be increased? A randomized prospective study. Epilepsia 1988; 29:129-39.
38. Ko CH, Kong CK, Tse PW. Valproic acid and thrombocytopenia: cross-sectional study. Hong Kong Med J 2001;7:15-21.
39. Ng KK, Tang KW, Cheung YL, Li PC. Brain MRI of hippocampal volumetry in patients with refractory temporal lobe epilepsy. Chin Med J (Engl) 2000;113:254-6.
40. Hui AC, Lam JM, Chan YL, et al. Role of magnetic resonance imaging for preoperative evaluation of patients with refractory epilepsy. Hong Kong Med J 2003;9:20-4.
41. Hsiang JNK, Wong LKS, Kay R, Poon WS. Vagus nerve stimulation for seizure control: local experience. J Clin Neuroscience 1998;5:294-7.
42. Hui AC, Lam JM, Wong KS, Kay R, Poon WS. Vagus nerve stimulation for refractory epilepsy: long term efficacy and side-effects. Chin Med J (Engl) 2004;117:58-61.
43. Leung GK, Fan YW, Fong KY. Temporal lobe resection for intractable epilepsy: review of 11 cases. Hong Kong Med J 1999;5;329-36.
44. Ho A, Ng KK, Chan CC, Lee TM. Quality of life of people with epilepsy following temporal lobectomy: a preliminary report. Percept Mot Skills 2000;91:1035-9.
45. Roses AD. Pharmacogenetics and the practice of medicine. Nature 2000;405:857-65.
46. van der Weide J, Steijns LS, van Weelden MJ, de Hann K. The effect of genetic polymorphism of cytochrome P450 CYP2C9 on phenytoin dose requirement. Pharmacogenetics 2001;11:287-91.
47. Ameyaw MM, Regateiro F, Li T, et al. MDR1 pharmacogenetics: frequency of the C3435T mutation in exon 26 is significantly influenced by ethnicity. Pharmacogenetics 2001;11:217-21.
48. Sisodiya SM, Lin WR, Harding BN, Squier MV, Thom M. Drug resistance in epilepsy: expression of drug resistance proteins in common causes of refractory epilepsy. Brain 2002;125:22-31.
49. Lai CW, Lai YH. History of epilepsy in Chinese traditional medicine. Epilepsia 1991;32:299-302.
50. Lee TM, Yang SH, Ng PK. Epilepsy in Chinese culture. Am J Chin Med 2001;29:181-4.
51. De Boer HM. "Out of the shadows": a global campaign against epilepsy. Epilepsia 2002;43(Suppl 6):7S-8S.
52. Jacobs MP, Fischbach GD, Davis MR, et al. Future directions for epilepsy research. Neurology 2001;57:1536-42.