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EDITORIAL

At the age of seventy, Joop Loeder MEd, the former honorary executive director of EPICADEC, passed away. In this issue an "In Memoriam" focuses on his battle to help those for whom social circumstances aggravate the impact of epilepsy.

The ILAE-IBE-WHO initiative '*EPILEPSY out of the shadows*' is making progress, as evidenced by the German government, which has organized a meeting on epilepsy as a public health problem in Europe. Professor Maheshwari from New Delhi has been asked to describe the Asian situation and his contribution is reproduced in this issue.

While Nepal's size is small relative to the whole of the India continent, its poor economy has led to major problems in health care. Attempts to incorporate systematic epilepsy care into primary health care have foundered. In this issue Doctors Eisler and Lajtai present their views.

A study by Dr Kaiser from the Institute of Tropical Hygiene and Public Health in Heidelberg conducted in the Kabarole District of West Uganda has also investigated whether it is feasible to introduce epilepsy treatment into the primary health care services. Dr Van Wieringen has written a précis of this paper and while the outcome is positive Dr Kaiser emphasizes the importance of establishing a reliable supply of antiepileptic medication. People who have epilepsy, irrespective of type of epilepsy and regardless of circumstances, have an increased mortality rate, due in part to convulsive status epilepticus. The epidemiology of status epilepticus in the developing world and its contribution to mortality is not well known. An editorial paper takes up this issue and calls for information from workers in the developing world. The column "From the Literature" deals with an interesting thesis

from Nimal Senanayake of Sri Lanka who discusses Reflex Epilepsies and underlines the regional differences.

As always, the editors welcome comments or request to publish information, or developments in research in specific areas.

Harry Meinardi

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Epilepsy out of Shadows

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At a meeting “Epilepsy as a public health problem in Europe “ in Heidelberg, October 1998, organized by the German government in collaboration with the World Health Organization (WHO) and the German Chapter of the International League Against Epilepsy (ILAE), problems of epilepsy care were reviewed. Although the focus was on European conditions, the worldwide situation was taken as a reference.

For the Far East Maheshwari presented the following report. The ILAE has taken an important step to coordinate efforts for epilepsy care in the Far East by establishing a Commission on Asian and Oceanic Affairs represented by the following countries: *Australia* (Chr. Rower); *China* (Li Shichuo); *India* (M.C Maheshwari: Secretary); *Indonesia* (Mahar Mardjono); *Japan* (Masakazau Seino: Chairman); *Korea* (Byung In Lee); *Singapore* (Shin-Hui Lim); *Taiwan* (Jing Jane Tsai). The population range of the countries varies enormously, from three million to 1.2 billion and the number of people with epilepsy is sometimes an estimate based upon a small or more extensive epidemiological study (table 1).

Table 1.

	Population	Prevalence	Incidence	Estimated Number
Australia	18 million	5-8/10 ³	50-100/10 ⁵	90-14.4x10 ³
China *	1.2 billion	4-5/10 ³	25/10 ⁵	4.5-6.0 million
India *	900 million	ca 10/10 ³		ca 9 million
Indonesia	200 million	5-10/10 ³		1-2 million
Japan *	120 million	8.2/10 ³	145/10 ⁵ (< 10 yr.age)	ca 1 million
Korea	43 million			
	3 million	3-4/10 ³		3-4x10 ³

Singapore*				
Taiwan *	21 million	6.85/10 ³ (Tainan)		ca 144x10 ³

* epidemiological studies

In all member countries the classic antiepileptic drugs (AEDs) phenobarbital, phenytoin, ethosuximide, primidone, carbamazepine and valproate can be obtained (the situation with respect to recently developed AEDs is presented in table 2). However, obtainable is not the same as being available when needed.

Table 2. Are new AEDs available other than PB, PHT, ESM, PRM, CBZ, VPA?

Australia	VGB, LTG, GBP, TPM
China	LTG (VGB on trial)
India	GBP, CZP (VGB, LTG, FBM without approval)
Indonesia	GBP, LTG (VGB, TPM in the near future)
Japan	ZNS (VGB, LTG, TPM, CLB, TGB, GMP on trials)
Korea	ZNS, VGB, LTG
Singapore	VGB, LTG, GBP, TPM, OXC
Taiwan	VGB, LTG

VGB: vigabatrin; LTG: lamotrigine; GBP: gabapentine; TPM: topiramate; CZP: clonazepam; FBM: felbamate; CLB: clobazam; TGB: tiagabine; ZNS: zonisamide; OXC: oxcarbazepine.

Table 3. Financial coverage by health authorities

Australia	doctor's fee, EEG, MRI, drug levels, hospitalization are covered Only \$3 –10 per prescription required.
China	paid by government for public servants, but not for non-government employees
India	PB/PHT available to poor patients free of cost in government or charitable hospitals
Indonesia	public servants and their families are covered by health insurance, and others by their companies
Japan	almost all expenses including medication/hospitalization/surgery are covered by health insurances

Korea	national health insurance covers 50% (except MRI) for eight months per year
Singapore	standard AEDs, MRI and surgery are subsidized by government, whereas newer AEDs are not
Taiwan	all medical and surgical expenses are covered by health insurance

Table 4. Neuroimaging

Australia	CT, MRI, SPECT, PET (2)
China	CT, MRI, SPECT in most UH, and PET(1)
India	CT, MRI, MRA/MRS (tertiary hosp.)
Indonesia	CT, MRI, SPECT
Japan	CT, MRI, SPECT, MRS, PET, MEG
Korea	CT (primary), MRI (tertiary)
Singapore	CT, MRI, SPECT
Taiwan	CT, MRI, SPECT, PET (1)

The latest AEDs are always the most expensive and many countries do not have the health system infrastructure whereby this burden is carried by the community instead of the individual with epilepsy. Table 3 shows the financial coverage, not only of AEDs but also of diagnostic investigations by health authorities in the area.

All countries have access to CT and MRI facilities and most have SPECT and a few have PET. MEG is available only in Japan (table 4). Such tools play an important part in the selection of medication refractory patients for epilepsy surgery. However, the percentage of patients who are found to be suitable for such treatment greatly varies between member countries because of the differing definitions used between member countries and the availability of epidemiological data. The number of patients operated on for epilepsy relative to the number of medication refractory and for whom surgical therapy is not feasible may need special residential care, a facility that is available only in Japan. There is also great disparity in monitoring people with active epilepsy (having seizures despite having treatment) and those in seizure remission but who are still receiving treatment with regard to both the use of EEG-examinations (table 6) and the use of measurement of serum levels of AEDs (table 7).

The information presented is based on what doctors do with the patients they treat. The problem of the treatment gaps, how many patients with epilepsy never see a doctor and why, is not taken into consideration in this overview. The huge differences in care for a condition that is more or less the same everywhere does point to the need for an active development of protocols for optimal diagnosis and therapy and pressure on governments to make these available for all who need them. WHO should play an important role in this field but the regional offices have shown very little initiative and sometimes, if approached, little inclination to deal with epilepsy even though it is a scourge that affects both the patient and the family. Fortunately, headquarters in Geneva are now participating in the global campaign "Epilepsy out of the Shadows", and it is to be hoped that the picture will be quite different when redrawn in the first year of the next millennium.

Table 5.

	Medication refractory patients*		Surgeries
Australia	40%	ca 10x10 ³	ca 150/yr
China	25%	ca 1.1-1.5 million	ca 200/yr
India	25-30%	ca 2.25-2.7 million	Very few
Indonesia			None
Japan	13-25%	> 100x10 ³	ca 150/yr
Korea			ca 500('95)-300('96)
Singapore	10-15%	> 3x10 ³	20-25/yr
Taiwan	20-50%	> 3x10 ³	ca 50/yr

* the definition varies

*Table 6. How often EEG examination are performed for patients
(1) with active epilepsy, (2) in seizure remission*

	(1)	(2)
Australia	1-2/yr	none
China	on demand	none

India	> 2/yr	none (govern. hosp.)
Indonesia	2/yr	on indication
Japan	whenever necessary	> 1 x/yr
Korea	on demand	when AED withdrawn
Singapore	practice varies	ibid.
Taiwan	1-5/yr	0-1/yr

Table 7. Is blood AED monitoring carried out as a part of routine examinations?

Australia	when seizures are poorly controlled
China	not routinely, but applicable in university hospitals
India	available in private clinics and in very few government hospitals
Indonesia	only on indication
Japan	once every month or more whenever necessary
Korea	not routinely
Singapore	not routinely, but applicable when necessary
Taiwan	yes, according to medication settings

Epilepsy in Nepal
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Nepal is a landlocked country between China and India divided into three major geographical belts: the 20 km wide lowland of Terai, the broad area of the hills, and the Himalayas, featuring the world's highest peaks. The 20 million-strong population, 90% of whom live in rural areas, is made up of: Indo-Aryan, Mongolian and the indigenous Nepali people. Hindus speak Sanskrit-based Nepali and live under the caste system and Mongolians, who are mostly Buddhist, comprise many ethnic groups speaking different Tibeto-Burmese languages. Nepal is a Hindu Kingdom and Hinduism is the official religion. The Constitution describes the country as a "multiethnic, multilingual, democratic, independent, indivisible, sovereign, Hindu, and Constitutional Monarchical Kingdom." Nepal was closed to the outside world for more than a hundred years and this seclusion, together with its remoteness, preserved an exceptional cultural heritage.

According to the Human Development Index Nepal lies 145th out of a total of 160 countries; it has only a few surfaced roads; most of the people do not have electricity or safe water, and while literacy is 40%, this level is achieved after an average of only 1.8 years of schooling.

Health status

In 1952 there were 12 physicians for 8.7 million people, and the average life expectancy was 28 years. Today there are about 1,500 doctors practicing western-style medicine and the life expectancy is 54 years. However, the national health situation is still among the worst in the world. Carbohydrates, protein, vitamin A, iron and iodine deficiency bring high mortality rates among children and mothers -over half the child population is malnourished. The maternal mortality rate is at least a

hundred times higher than in a western country, and 20% of the children die before the age of five. The health infrastructure only treats about 20% of the population and is frequently inadequate; most of the hospitals do not have even basic life saving capabilities, so it can be seen that the problem of epilepsy is not high on the list of priorities for the health authorities of Nepal. The only prevalence study was performed by Dr M.K. Nepal, Dr. V.D Sharma and P.M. Shrestha. In a door-to-door survey, 823 households were studied and a prevalence rate of 0.733 was found. Only generalized tonic-clonic seizures were examined.

Epilepsy caring and the medical sector

Epilepsy is classified as a mental disease in Nepal and comes within the professional remit of psychiatrists. There are twenty psychiatrists and four neurologists in the country and the most widely used drug is phenobarbital, but phenytoin, carbamazepine, sodium valproate and clonazepam are also on the market. Epilepsy surgery is not available, nor is the seizure and syndrome classification of the International League Against Epilepsy widely used. There are only six EEG appliances in the whole country, all of them are in Kathmandu, and one electrophysiologist. There are two MRIs, both of which are in Kathmandu, and two more will be established in the near future. phenobarbital, phenytoin, carbamazepine and diazepam monitoring are available at the Tribhuvan University, and valproate is under preparation.

Non-Governmental Organizations

The Nepali Epilepsy Association and the Korean Rose Club

Special care for epilepsy patients was begun in 1981 when a Korean Christian missionary, Dr.Chong Cheul Park, proposed the foundation of the Nepali Epilepsy Association (NEA) under the aegis of his organization, the Korean Rose Club. Some years later the two organizations separated and in 1991 the Rose Club founded a busy, well organized general hospital in Dolkha. People often call it an epilepsy hospital because epilepsy patients are given special consideration.

The United Mission to Nepal

The United Mission to Nepal (UMN) is the oldest and biggest INGO in Nepal, comprising 39 Christian agencies from 17 different countries. Their approach involves a widespread mental health consideration and involves publishing booklets which contain the most basic information about epilepsy for community mental health workers.

EPICADEC and the SECON group

EPICADEC has built up contacts in Nepal over the past eight or nine years. In 1996, following five years of consultations an international workshop was held with the cooperation of the Tribhuvan University Institute of Medicine. This provided the impetus for both sides and in 1997 a new NGO was established for this project by social workers, the SECON group (Society for Epilepsy Care of Nepal). The project is under negotiation.

Ayurvedic and Tibetan Insutitutes

Ayurveda and Tibetan medicine are traditional medical systems that function quite well with chronic illnesses. The Ayurvedic institutions are a part of the official health care system and now some Ayurvedic doctors send the patients with epilepsy to allopathic doctors for western type medicine because they find it is more effective.

Jhankiries

Up to 90% of the sick go first to traditional healers such as Jhankiries, the representatives of the aboriginal, shamanistic healing beliefs. Such traditional systems believe that epilepsy is given as a punishment by evil spirits. It is the healer's function to find out the sins and to treat the person accordingly. They beat drums, sprinkle holy water on the patient's forehead, suggest different kinds of rituals such as wearing treated beads, holding bunches of keys, worshipping different gods, or sacrificing animals. A common belief is that smelling dirty shoes or clothes expels the evil spirits. The UMN offers mental health training for the Jhankiries and the process has been encouraging: Jhankiries can differentiate epileptic seizures from pseudo-seizures, stating that they can cope only with the latter.

Conclusions and future possibilities

Nepal is rich in culture and natural beauty, but extremely poor according to the health and life standards of the West. Those involved in the intellectual, political and economic advancement make huge efforts to follow the western model but it is almost impossible to do so without considering the most basic means of attaining cost-effectiveness. The external funds and aids are frequently misused and the projects are often insensitive to local conditions. Most of them have failed and have made local people suspicious of or resistant to any kind of western proposals. Trying to improve epilepsy caring here we have to take all this into account.

The possible structure of support for community based epilepsy care

Until recently organized epilepsy caring was non-existent. A future structure should have four levels:

1. Community level
2. District level
3. Regional level

4. Special centre level at Kathmandu

Ad 1.

It is possible to train Jhankaries to refer epilepsy patients to the health workers or to the psychiatrist. The community health workers, together with local private pharmacy owners, could be the first point of contact with the network, beginning, in the case of recurrent tonic-clonic seizures, with phenobarbital. The patients who do not react to phenobarbital therapy, or who have other types of seizures than tonic-clonic seizures, should be referred to the doctor at the district hospital level.

Ad 2.

At the district hospital level there should be at least one general practitioner (GP) and these should be provided with a national guideline about the basics of seizures and syndromes. The problematic patients they could refer to the regional psychiatrist, to other nearby doctors with expertise in epilepsy or the special epilepsy centre in Kathmandu.

Ad 3.

Psychiatrists would have to work in the first regional diagnostic centres, and would be provided with EEG and serum level examination facilities. There are some doctors outside Kathmandu who use significant amount of carbamazepine and it is reasonable to see them as the beginnings of a framework forming a rural epilepsy caring network, and support them with regular information and special training.

Ad 4.

The special centres in Kathmandu will be developed by their own experts who have a special interest in epilepsy. They are the ones who could ask for national or international (WHO, World Bank, etc.) funding. The best support would be the provision of short, individual training courses in centres of excellence abroad.

Suggestion for short-term epilepsy control projects

1. The first and easiest way to inform GPs about the basics of epileptology. It would be helpful to support and facilitate the preparing, printing and distribution of guidelines about epilepsy control for GPs and specialists. The next step would be general awareness campaign through radio.
2. Pilot studies for working epilepsy caring models. We suggest two models, one for a regional hospital with a psychiatrist who has special interest in epileptology, and one for a district hospital with poor facilities. The main point of both is to inform the local people (Jhankaries, private pharmacy owners, health workers, teachers and village officers) about health and epilepsy, and to support local doctors in caring for epilepsy patients.

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***An Investigation into the Process of
Introducing Antiepileptic Treatment into
Primary Health Care Services in Western
Uganda***

PRECIS OF PAPER BY DR CH. KAISER FOR MASTER OF
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The East African country of Uganda covers 241,039 square kilometers, has 14.67 million inhabitants (at the 1991 census), with a life expectancy of 48 years. The Kabarole District in western Uganda (altitude around 1300 meters) had a population calculated at 741,000 in 1991 and estimated at 882,000 in 1998. People in this area live mainly from subsistence farming and from work in several large tea estates. Two areas of the district are endemic for onchocerciasis (a microfilarial infestation causing "river blindness") with an estimated 80,000 people at risk of infection. With the introduction of an ivermectin treatment programme and the concomitant restructuring of the health facilities, it became apparent that the prevalence of epilepsy was high in these areas –2:1000 involving some 1400 people. Thus, epilepsy treatment became a new issue in the health services of the district.

In 1991 research activities had identified and treated patients with epilepsy within a distance of up to 10 km from the Kyarusozzi Health Unit (HU). After the survey was completed, the task of carrying on monthly (outreach) clinics was handed over to the HU staff. Unfortunately, by mid-1993, the treatment activities of the HU had come to a standstill. In two other HUs (Kijura HU and Nyamabuga HU) integrated epilepsy treatment was apparently never realized. It is uncertain whether there is a causal relationship between onchocerciasis and epilepsy. In 1994, Dr Ch. Kaiser of the Institute of Tropical Hygiene and Public Health of the University of Heidelberg, Germany, led a further research project in the area of the Kabende Parish in the northern periphery of the district to investigate this relationship. The area was not covered by the first line structures of the district health services as in the Kyarusozzi HU. As part of the research project a pilot study into a self-help group *distribution approach* to treatment was started, the aim being to install a more viable treatment

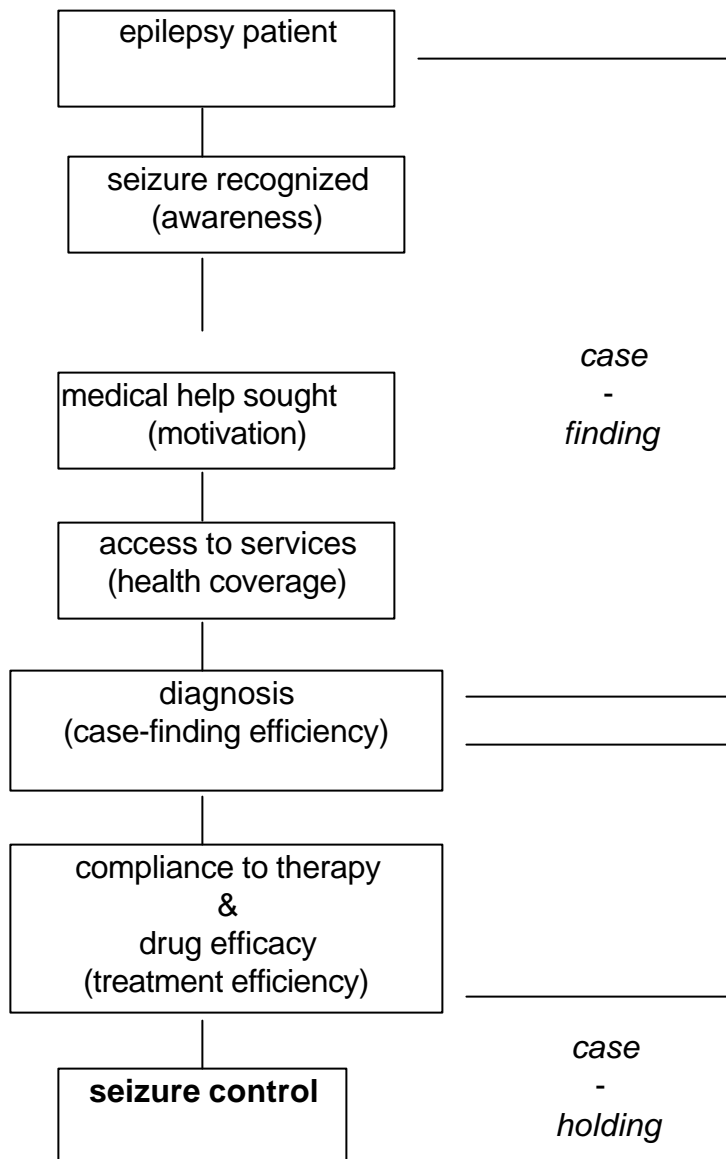
infrastructure. By 1996, this pilot study had shown that medical visits of a district health team member, and drug supplies at six-monthly intervals with involvement of the community in organizational tasks, were very successful.

In 1996, the district health Services, as represented by the district health management team (DHMT) and the district medical officer (DMO), decided to launch a programme to introduce antiepileptic treatment in the endemic areas using the existing HUs as well as establishing a distribution approach. It is important to evaluate such measures in order to find ways to address the problem in local conditions and this could prove relevant to other areas in sub-Saharan Africa with a comparable medical infrastructure. In 1997, Dr Kaiser and co-workers evaluated the programme using Piot's model of tuberculosis management. In figure 1 the management of epilepsy therapy is described using the terminology of the tuberculosis model by analogy.

Once the seizure has been recognized as a sign of disease by the patient or person in his or her environment (*awareness*) everyone must agree that the disease needs medical treatment (*motivation*). Health *coverage* can be split up into zones which may be comprehensive, but which are frequently reduced from a "curative zone" – the potential case-finding area – where patients who are aware of their disease could find their (financial and geographical) unrestricted ways to the health facility if told that treatment is available there, or to a "preventive zone" where the treatment capacities of the facility are insufficient due to scarce resources. The more skilled the health worker and the better the organization of the service the greater the *case-finding efficiency*. Of greater importance than finding is keeping the patient following start of treatment in which *treatment efficiency* is ultimately dependent on the patient adhering, and the organization guaranteeing access, to drug intake over an unforeseeable length of time. There are four government health units in or near the northern onchocerciasis focus providing primary health care (PHC) to its population; each is staffed by three or four health workers. Three of these HUs were constructed in the 1970s and were rehabilitated 10 to 15 years ago; they are Kijura HU, Kyarusizi HU, Nwamabuga HU. A fourth HU at Kigoyera was opened in 1996, and in Kabende Parish at the northern end of the area a small unit staffed by one nurse began work in 1997. In different locations the treatment structure was organized, broadly speaking, according to two systems: that of the health unit (HU) and that of the distributor approach (DA). The investigation aimed at a qualitative description and evaluation of the elements of each system and its interrelations. Semi-structured interviews and group discussion were applied at different levels of the treatment structure viz. the DHMT, the HUs, the community and, finally, the patients and their families. This part of the investigation focused on issues such as drug management, information/communication, organization and health worker tasks. Another aspect was the drug availability at district, health centre and patient/community levels. In the case of the HU, activities were limited to its actual location at which patients could present themselves at any time. Case-finding was therefore passive and depended on the motivation and the initiative of patients, both in establishing contact with the health services and subsequent maintenance. The

yield in case-finding at the beginning of the programme was relatively low, but in the long run a steady increase of new patients was observed. This led to a low but steady growth in drug demand and of staff workload. Drug therapy was always linked to counseling and appropriate information of the treatment. The HU afforded an *integrated approach* but gave the health worker sufficient flexibility to adjust attention given to a patient to his or her individual needs. Time spent at a first visit of 30 minutes and 10 minutes for a follow-up visit worked well. The case-holding rate over 18 months was 23-28%. A patient register was sufficient to keep records necessary for patient follow-up. In contrast, in the distributor approach, it was found that in order to reach as many patients as possible, community members had to be actively involved in case finding as well as periodic efforts by the health service to identify and enroll patients in the treatment programme.

Fig.1: The process of epilepsy therapy



This resulted in a high number of patients admitted to treatment over a short time and a fast increase in drug demand. The initiative to follow-up, i.e., case-holding, lies with the health services, while the patients and their caretakers have the role of mere recipients of the drug. This meant that the flow of drugs was taken out of the immediate control of HU staff, and arrangement that is appropriate to delivery of drugs to the patient but does not necessarily secure the flow of information from the health worker to patient and vice versa. Consequently, there is a dislocation in the constituents of treatment, an arrangement that is not comprehensive and of lower quality than the HU integrated approach. Furthermore, the time available per visit (10 minutes at first contact, and less than five minutes at follow-up) resulted in low average dose of drugs, no appropriate dosage adjustment, low information level and general dissatisfaction with treatment. It appeared that there were no specific guidelines available for epilepsy treatment at HU level. A copy of the Ugandan National Standard Treatment Guidelines, which contains some notes on antiepileptic drug (AED) dosage was in place at two out of the four HUs reviewed. Although the dosage regimens followed at the HUs were compatible with the national guidelines, the health workers did not refer to them when describing their actual practice. The health workers' knowledge of AED treatment was based on the medical school training and on oral information they had collected in occasional discussions with the mental health coordinator of the district. All health workers knew about an appropriate starting dose, that the treatment had to be continuous and that there is a risk of recurrent seizures if treatment is discontinued.

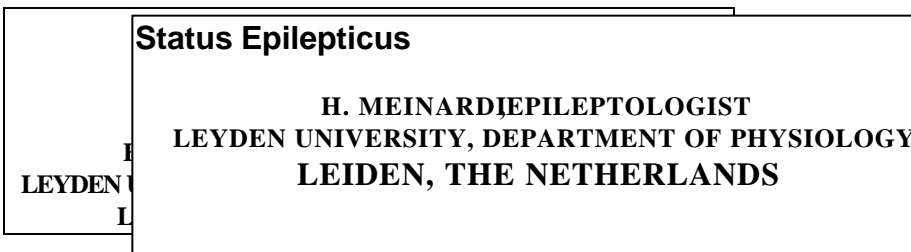
There were some shortcomings in the health workers' knowledge on dosage adjustment. Usually, they increased the dosage only if the frequency of seizures did not change at all. When they observed a reduction in seizure frequency "to a satisfying degree" they did not increase the dosage any further even if side effects were absent. This practice is not in accordance with the general recommendations which aim to achieve full seizure control by gradually increasing the dosage as long as seizures persist and there are no unacceptable side effects. In the locations providing treatment with the *distributor approach* the criteria for dosage increase were entirely unclear. Since the start of the programme, epilepsy treatment in terms of drug consumption had improved. The major limitation for further improvement was insufficient drug availability. The factors contributing to non-availability of drugs were the insufficient supplies from higher levels, restrictive regulations impeding the

use of alternative sources, a growing demand for drugs from areas outside the programme area and political influence on allocation preferences.

Finally, recommendation made were:

- The promotion of complete integration of programme activities into existing primary care facilities;
- The development of locally applicable guidelines of treatment and their use as a reference tool in the supervision of the HUs in the programme area;
- Efforts to improve drug availability by the district health services should be increased as well as introducing a minimum stock system.

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Whether or not the sword of Damocles delivers a deadly blow to a person with epilepsy getting a seizure is usually not death due to nerve cells dying from excessive discharging, but due to consequences such as a fatal fall. In status epilepticus there is a far more direct relation between seizures and fatal outcome. The Commission on Classification and Terminology of the International League Against Epilepsy at first defined status epilepticus as the situation in which a seizure persists for a sufficient length of time, or is repeated frequently enough, to produce a fixed and enduring epileptic condition. The definition was accepted in 1981 and has been only slightly modified since. It reads: "The term status epilepticus is used whenever a seizure persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur". The classification also specifies that status epilepticus may be further defined as partial or generalized. However, disregarding classification rules, there is a more commonly used distinction that distinguishes between Convulsive Status Epilepticus and Non-Convulsive Status Epilepticus. The vagueness of "persists for a sufficient length of time" has led to disagreement between authors and following a meeting on status epilepticus a time span of 30 minutes was proposed and subsequently often used. Recently, Lowenstein et al. argued against this definition. They address in particular generalized convulsive status epilepticus and argue that a generalized tonic clonic seizure rarely lasts longer than five minutes. The diagnosis of status epilepticus, therefore is not only referring to a prolonged seizure, but also to a situation in which the normal compensatory mechanisms instrumental

in limiting seizure time to maximal five minutes are absent or fail. They also point out that most protocols to prevent status recommend that medication should be administered if a seizure has lasted more than five or ten minutes. However, this may also be interpreted that such action is not interrupting status epilepticus but preventing status epilepticus. Meldrum argues that outcome is related to duration and that the consequences of status epilepticus are more common after the quoted period of 30 minutes. But he also points out that next to duration another important factor is the condition of the brain following these ongoing excessive discharges, that is, is it in a stable condition or suffering from acute pathology. His suggestion is to label the period between five and 30 minutes as “incipient” or “threatening” or “early status epilepticus”.

It should be borne in mind that such a discussion is the prerogative of an affluent society that has the access to, and means by which, a status epilepticus can be interrupted as soon as it threatens. The data about occurrence of status epilepticus vary. For example, Hausar suggests 65,000 cases per year for the United States, while DeLorenzo et al. suggests that the occurrence are closer to 150,000. Shorvon estimates the occurrence of Generalized Convulsive Status Epilepticus to be 180-280 per million in the UK and the USA, while Complex Partial Status Epilepticus would happen in 35 per million.

Information from developing countries is scarce. Sridharan et al. from Libya mention that of 568 patients older than 15 years 55 had status epilepticus. Jilek-Aall and Rwiza report from rural Tanzania that 14.5% of epilepsy related deaths were due to status epilepticus. In the early 1970s a hospital based study in five major cities of India revealed that of 3,424 patients, 73.4% had no a history of cluster attacks or of status epilepticus. Some time in the course of illness, 20% had cluster attacks, 3.8% had one or more episodes of status epilepticus and 2.8% had both cluster attacks and status epilepticus.

Amongst the participating factors for status epilepticus, fever ranks highest in children, and cerebrovascular causes ranks highest in adults. In both children and adults medication change follows these as a risk factor. This highlights a real problem in developing countries: often, phenobarbital is the only affordable drug. Fortunately, its adverse effects profile has also advantages in a less developed society. On the other hand, it is also notorious for the occurrence of withdrawal seizures, which arise when the dose is reduced, irrespective of whether the new steady state serum level is still in the therapeutic range. An experienced physician from Sri Lanka once claimed that the prevalence of seizures in people with epilepsy under medical care was not different from those who did not see a doctor. This finding was interpreted as due to (forced) non-compliance with subsequent withdrawal seizures. Hard data about this topic, however, have not been published.

Whether it is possible to interrupt threatening status epilepticus obviously depends on the circumstances and means available. Although emphasis is on evidence-

based medicine nevertheless there are remarkable differences in drug use between countries. In Europe, once it was proven that intramuscular diazepam is erratically absorbed and given the problem of administering an intravenous injection to convulsing patient, a diazepam solution for rectal application was introduced. Rectal diazepam proved to have satisfactory pharmacokinetics and the added advantage that the compressible plastic vial ending in a stiff tube which can be easily introduced into the rectum also could be handled by parents or partners of the patient. Each vial contains 10 mg diazepam. However, interruption of a threatening status epilepticus by lay people only plays a role once the diagnosis of epilepsy has been established, and it is not uncommon that status epilepticus is the first seizure manifestation. Diazepam does have a drawback that, although its lipophilic properties help it to penetrate the brain rapidly after administration, these same properties are also responsible for its extensive redistribution and concomitant fall in brain concentration; because of this several authors in the USA prefer lorazepam. Instead of rectal administration Liu Yu Xi has advocated a nasal spray. This suggestion has not had much follow-up but recently the intranasal use of midazolam, a water-soluble benzodiazepine, has been reported.

Before the benzodiazepines became available phenytoin and phenobarbital, and a mixture of barbiturates (phenobarbital and allobarbital) were used for intravenous administration. Barbiturates and benzodiazepines tend to suppress respiration; phenytoin is less likely to but the vehicle to make it injectable is rather alkaline and extravasal injection is quite painful. In addition the effect of phenytoin on the conduction of heart muscles demand that it is injected slowly. If seizures recur after 10 mg rectal diazepam (in an adult) a second dose can be given but transportation to a medical facility then becomes necessary. In the emergency room the patient will be prepared for continuous intravenous administration of fluids and medication and for arterial monitoring and blood sugar levels will be checked for hypoglycaemia. The automatic administration of glucose has been abandoned as hyperglycaemia appears to increase the risk of neuronal damage. When glucose is administered thiamine (100 mg) is added, particularly when a person's nutritional condition is unknown. It is also advisable to administer pyridoxine 50-100 mg. A number of different protocols are possible. In the Netherlands Scholtes advocates starting in the emergency room with clonazepam 1 mg i.v. and once indwelling catheters have been inserted to continue with 0.5-1 mg clonazepam per minute until seizures stop or respiratory depression becomes evident. If after ten minutes seizures continue, then phenytoin sodium 15-18 mg/kg is administered at a speed of 50 mg/minutes. If half an hour after admission to the emergency room the status has not been interrupted the patient is transferred to the intensive care unit for endotracheal intubation; pharmacological muscle relaxation (vecuronium) and EEG monitoring. Phenytoin is replaced by midazolam infusion 0.3-0.6 mg/kg/hour. If midazolam does not stop the seizures within an hour a thiopental drip is started, initially 10-30 mg/kg/hour, subsequently (after reaching burst suppression on the EEG-monitor) at 5-20 mg/kg/hour.

Obviously, while arrest of status epilepticus is tried, diagnostic procedures and laboratory test to determine the cause as well as measures to avoid complications due to aspiration, thrombosis, keratitis, and gastric ulcers have to be addressed.

If, after several attempts, say at 4-8 hour intervals, the tapering of thiopental leads to reappearance of seizure discharges, other drugs may be tried, such as chlomethiazole, paraldehyde (cave plastic tubings), etomidate, althesin or other general anaesthetics. From India (Mani, Bangalore), also for adults, a shorter and more attainable protocol under restricted conditions is given.

Aside from nursing and medical care as needed, serum glucose is determined. A drip with 50% dextrose is started and 100 mg thiamine given plus, in children less than one and a half year of age, 100-200 mg pyridoxine.

STAT either 10 mg diazepam or 4 mg of lorazepam is administered in the course of 2 minutes.

If seizures persist after:

10 minutes phenytoin with a speed of 50 mg/minute is administered in a total dose of 300-500 mg;

30 minutes repeat first treatment, i.e., 10 mg diazepam or 4 mg lorazepam in the course of 2 minutes;

60 minutes repeat step two, i.e., phenytoin with a speed of 50 mg/minute in a total dose of 300-500 mg;

90 minutes phenobarbital 100 mg (in a minute) repeat 4 to 6 times within the next 24 hours. Indisputably in developing countries and especially in rural areas the options presented may already exceed the available means. The editors of Epicadec News would welcome suggestions, which have been found helpful under circumstances of restricted means.

From the Literature

Reflex epilepsy: clinical and neurophysiological studies in a tropical country in Asia

Thesis for Ph.D. degree by N Senanyake Catholic University Nijmegen
The Netherlands ISBN 955-599-105-7 printed at Sarvodaya Vishava Lekha
Sri Lanka.

In the revised International Classification of Epilepsies and Epileptic syndromes (ICE) of 1989 reflex epilepsies are classified both under localization related, and generalized categories. Accordingly, an epilepsy characterized by specific modes of seizure precipitation is one in which a consistent relationship can be recognized between the occurrence of one or more definable non ictal events, and subsequent occurrence of specific stereotyped seizure.

Senanayake quotes the ICE on page 10 of this thesis: "Three types of precipitation are mentioned:

1. Seizures precipitated by specific sensations or perceptions (**reflex epilepsies**), occurring in response to discrete and specific stimuli; usually, in individual patients, there is a simple specific stimulus or a limited number of clearly related stimuli.
2. Seizures precipitated by sudden arousal (startle epilepsy), where the stimulus must be unexpected in nature.

3. Seizures precipitated by integration of higher cerebral function, such as memory or reading”.

As, under 1. the word “reflex epilepsy” is added between brackets, one can suppose that 2. and 3. are **not reflex epilepsies** in sensu stricto. But this turns out not to be the case, Senanayake recognizes that a definition problem exists on page 11 because “a drawback for a sensible classification of these reflex epilepsies is that many of them have not been studied sufficiently, and appendix II of ICE (...) can only be considered as a preliminary solution.”

In 1985 the ICE offered extra criteria for definition like the response latency to discriminated simple and complex forms of reflex epilepsy. One of the few things one can regret in Senanayake’s thesis is that, based on his extensive material, no attempt is found to improve this definition problem. After the prologue (mainly dealing with this definition problem) Senanayake gives an excellent overview of the existing knowledge or mentions fields where knowledge is lacking. In startle epilepsy one misses the EEG findings except in Tay Sachs disease.

The most valuable and most interesting part of this thesis both for clinical practice and from neurophysiological viewpoints are parts 2, 3 and 4, which offer a wealth of information concerning self-induced epilepsy, epileptic seizures evoked by high cerebral function and eating epilepsy; the relationship between some of these epilepsies and geographical and genetical factors is especially intriguing. The link with other phenomenological classification, such as juvenile myoclonic epilepsy, are brought in, as are the relevant treatment options. It is good to know that most reflex epilepsies respond to conventional antiepileptic drugs. In Senanayake’s experience 85.9% of his patients with eating epilepsy will be seizure free or “satisfactorily controlled” by medication. Many received clobazam. In other reflex epilepsies, such as photosensitive epilepsy, valproate is mostly helpful, sometimes with additional clobazam. In seizures evoked by card games and draughts, phenytoin controlled tonic-clonic seizures and jerks. However, a criticism arises in case two of the self-induced seizures (page 48-49); why was it that a patient who was six months pregnant was not treated by specific antiepileptic medication? This presumably was because she was pregnant. Surely, in this phase of pregnancy 20-30 grand mal seizures a month must be more harmful for the fetus than the drugs.

The most puzzling part of the reflex epilepsy syndrome is the pathogenic mechanism. In eating epilepsy attempts to find a seizure triggering mechanism have either been unsuccessful or have produced variable results (page 91). This includes mastication, swallowing, passage of food along the oesophagus, gastric distension, richness of the meal, chemical substances and lifting food with the fork or cutting food. In the last case, subsequent loss of the second, third and fourth digits of the right hand in an accident stopped the seizures. In seizure induction by cognitive functions like reading epilepsy card games, draughts and arrhythmic the pathophysiological mechanism is not yet established.

Three factors suggested by Forster (1977) seem, in Senanayake's experience, applicable to the situation in which his patient developed seizures and EEG dysrhythmias: complex decision-making, sequential decision-making and stress. In epilepsy arithmetics it is hypothesized that the dominant parietal lobe provides the neural substrate for triggering calculation and spatial processing, but probably one or both frontal lobes are involved as well (page 79). In some of Senanayake's patients the seizures were provoked by several kinds of stimuli in the course of lifetime, e.g., first these patients had nocturnal seizures, later on seizures were provoked by punchy, a local game with six tiny sea shells used as a die, the scores of each players are indicated by marker on a chart (page 56). Most chapters of the thesis have been published as scientific articles in the international literature. Not the least interesting is the study of familial eating epilepsy (chapter 7 and *J Neurol* 1990;237:388-391) where in nine families with 59 siblings 20 had eating seizures (34%). In another study of 120 cases (*Epilepsy Res* 1990;5:74-79) 20 (16,7%) patients had a brother with epilepsy; 9 (7.5%) has a sister with epilepsy, and 4 (3.3%) had a parent with epilepsy. I quote (page 101): " This study provides evidence for a strong genetic susceptibility in yet another form of idiopathic partial epilepsy with focal EEG abnormalities. It is postulated that the genetic susceptibility lies in a central mechanism as in all other epilepsies, whilst the triggering mechanism of the eating seizures is dependent on yet unidentified multiple stimuli which are more environmentally determined".

As was mentioned already in chapter 6 Senanayake suggests that during eating the amygdalae become the site of additional stimulation, lowering the seizure threshold and leading to rapid generalization of seizures. The evidence of genetic susceptibility is endorsed by the geographical distribution of the different types of reflex epilepsy: In the western world photosensitivity is well known but in South India hot water epilepsy and in Sri Lanka eating epilepsy are more prevalent.

Dr Nimal Senanayake became senior professor at the University of Ceylon, Peradeniya, Sri Lanka in 1992. He has been the dean of the faculty of medicine since 1993. He is a fellow of the Royal Society of Medicine, Royal Society of Tropical Medicine and Hygiene, Royal Colleges of Physicians (London and Edinburgh), Ceylon College of Physicians and the National Academy of Science of Sri Lanka. He is a corresponding fellow of the American Academy of Neurology and a founder member of the Asian and Oceanic Epilepsy Association and the Epilepsy Association of Sri Lanka. He is honorary secretary of the tropical neurology research group (Asian division) of the world Federation of Neurology. He is a referee for the *New England Journal of Medicine* and editor or member of the editorial board of several medical journals. Professor Senanayake also writes scripts for television dramas; he won several awards in this field. He is a modest and affable man, and probably to play punchy with him is as much pleasure as to read this excellent thesis.

Piet Voskuil

In Memoriam Joop Loeber
(Johannes Nicolaas Loeber)

1928-1998

On December 10, 1998 the organizations that work towards eradication suffering from epilepsy lost one of their prominent leaders. Joop Loeber held a master's degree in economy from the Erasmus University in Rotterdam and initially followed his father, who had a trading company in the former Dutch East Indies and subsequently in Indonesia, into business. Later, Joop returned to the Netherlands and took a management position with the Dutch national railways. But business gave him little scope for demonstrating his concern for people, particularly those to whom fate had been unkind, so he applied for, and was successful in getting the post of general secretary (manager) of "The Power of the Small", an organization founded in 1895 that raised money to help care for people with epilepsy. When Joop took charge it had 300,000 contributors (2.5% of the Dutch population).

The Power of the Small was part of a larger organization: the Christian Society for the Nursing of People with Epilepsy, which had established a special centre for epilepsy in Heemstede. This comprised a hospital for assessment and treatment (including neurosurgery), rehabilitation units with primary and secondary schools, residential units for chronic care, and outpatient department network covering the Netherlands above the river Rhine, and a research department in collaboration with Leyden University. In this large organization Joop's talents in public relations soon led to his appointment as head of the department of public relations, in addition to the management of the charity fund. This Dutch special centre for epilepsy has been involved with epilepsy care on an international level from its earliest beginning.

Joop Loeber's appointment by the executive committee of the International Bureau for Epilepsy as editor of International Epilepsy News in 1977 was a logical and, as time proved, a fortunate step. When the proposed merger of the International League Against Epilepsy and the International Bureau for Epilepsy into Epilepsy International was rejected by its members, IBE reduced the involvement of physicians and elected Francesco Castellano as president and Joop Loeber as treasurer. Members of the new IBE executive threw themselves into the task of establishing its new position as an equal partner of ILAE, and one that would represent people with epilepsy and their companions. In this position Joop was more than the steward of the IBE finances, he was also the energy behind the organization of self-help groups worldwide. His erudition, level-headedness and managerial skills made him the obvious successor to Francesco Castellano as

President of IBE in 1985. After his term as Past President, which ended his membership of the executive, he continued to serve as manager of the permanent office of IBE in Heemstede.

The organization through which Joop Loeber was employed, the Christian Society for the Nursing of People with Epilepsy (CSNPE), celebrated its centennial in 1982. All jubilee-gifts offered to the Society were set aside to help improve epilepsy care in countries where it still reflected the state of care in the Netherlands at the time the CSNPE was founded in 1882. Three projects were set up with those in Indonesia and Sri Lanka being particularly successful. However, some of the ample gifts bestowed on the CSNPE for its centennial celebrations still remained and these were transferred to a new foundation, Epilepsy Care Developing Countries (EPICADEC), of which Joop Loeber became the first honorary executive director.

His sustained, outstanding achievements on behalf of people with epilepsy were formally recognized by the IBE and the ILAE when, in 1995, he was selected to be the first recipient of the ILAE/IBE Lifetime Achievement Award. Among an almost endless list of contributions his singular involvement in improving epilepsy care in the developing world had a prominent place.

Joop Loeber was not only an energetic and efficient professional, he was also a very likeable and cooperative colleague who established friendships throughout the world. For his friends everywhere Joop's death came much too soon, and the campaign to improve epilepsy care lost one of its greatest champions.

Harry Meinardi