

The Assessment and Management of Epilepsy – Prof VU Fritz



Summary

Epilepsy is still one of the most common neurologic disorders, one which poses difficult challenges to the physicians. Giving clear practical guidelines, the author helps to assess and classify epilepsies and evaluates the different medical managements available today.

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KEYWORDS:

Epilepsy; Convulsions;
Diagnosis; Drug Therapy.

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Epilepsy is one of the most common neurologic disorders, as well as one of the most frequent and difficult challenges faced by today's physicians.

To best assess the type of seizure a description from the patient and also from someone who has witnessed the patient's attack is required. In Tables I & II a series of questions is listed which can be put to both the patient and an observer. These questions may help decide whether the event was a seizure and may help to localise the pathology.

The classification of Epilepsies

There are 2 major forms of seizure patterns, generalised and partial seizures. Terminology has changed and the term "absence" has come into general use in recent years. Although some still prefer the familiar synonym

"petit mal", absence may be a better description. The hallmark of the absence attack is a sudden onset, interruption of ongoing activities, a blank stare, possibly a brief upward rotation of the eye. The absence may be simple, begin in early childhood or adolescence, and be short, paroxysmal without warning and cessation is likewise sudden without postictal confusion or depression. These absences are usually not of a known organic aetiology and are easy to control medically.

However, absences may also be due to brain lesions or cerebral metabolic disturbances and be associated with other phenomena such as mild clonic components, diminished postural tone (atonic absences) automatisms or autonomic phenomena such as enuresis. In the former type of absence the rhythmic 3 per second cyclic spike and wave discharge is typical. In the organic form, the ictal EEG pattern may be "atypical" and demonstrate very fast rhythmic discharges, or asymmetrical sharp and slow wave discharges. Therapy may also be less successful and seizures more difficult to control.

Probably the most acceptable classification still in use today is that presented by the *Commission on Classification and Terminology of the International League against Epilepsy* which was published in *Epilepsia* in 1981 and approved by the International League against Epilepsy in September 1981. This classification is easily applied to patients with epilepsy and also more accurately reflects the nature and heterogeneity of the epileptic seizure. The classification, summarised in Tables III & IV is broadly divided into Partial and Generalised seizures. Electroencephalographic features will not be discussed further.

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Curriculum vitae

Professor Fritz obtained a MBChB at Wits in 1967 and after some time in Internal Medicine at the Johannesburg Hospital, obtained the FCP(SA). Her major research interest at this time was in cardiology. She re-specialised in Neurology and in 1982 became a Principal Neurologist at the Johannesburg Hospital. In 1986 she succeeded Professor H Reef when he retired, and in 1988 was appointed to the Chair of Neurology at the University of the Witwatersrand Medical School, and Chief Neurologist at the Johannesburg Hospital. Her particular research interest is in Strokes and Transient Ischaemic Attacks, and in 1986 she obtained a PhD for her project on strokes. Prof Fritz has a long list of scientific publications to her credit, involving topics such as epilepsy, multiple sclerosis, headaches and strokes. She is the recipient of many research grants and served on the council of the South African Neurological Association.

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Table I. Questions for Patient

1. What were you doing before the attack?
2. What was the first thing you noticed that seemed to be abnormal?
3. What happened after that until you lost consciousness?
4. Were you fully unconscious ie a period where you were totally unaware of your environment?
5. What is the first thing you remember after return of consciousness?
6. Were you confused?
7. Did you lose control of your bladder?
8. Did you bite your tongue?
9. Were you tired and did you go to sleep?
10. Did your muscles ache?

Partial Seizures

These are epileptic attacks of localised onset: 1) Simple partial seizures in which consciousness is preserved, 2) Complex partial seizures in which consciousness is altered, and 3) Partial seizures (of either type) that progress to generalised tonic-clonic attacks.

Carefully assess what patient as well as witness are describing

Consciousness in this context is defined as responsiveness to

exogenous stimuli. The progression of partial seizures allows for an understanding of "secondary generalisation" ie a continuum of the spread of the abnormal discharge to finally produce a tonic-clonic attack. Auras therefore may occur in isolation and are in fact simple partial seizures. When they progress to a generalised tonic-clonic seizure, this is secondary generalisation.

Complex partial seizures are frequently associated with automatic behaviour ie complicated behaviour that requires integration of higher cortical structures and for which the patient has no recollection. Typical automatisms include chewing, lip

Table II. Questions for family

1. Was patient unconscious (ie lack of responsiveness)?
2. Position when attack occurred?
3. Was the patient able to control the seizure?
4. Was this a single episode or a series?
5. Did patient recover between attacks?
6. What was patient's colour?
7. Ask all the "patient's" questions and ascertain events before and after the seizure from questions in Table I.
8. What did the patient look like during the event eg rigid, jerking, teeth clenched?
9. What medications does the patient use?

smacking, scratching, running, disrobing. These may be perseverative ie the continuation of an act initiated prior to loss of consciousness eg chewing food, drinking or walking.

Table III. Classification of Epilepsies

- Partial (beginning locally)
- A. *Simple partial (consciousness not impaired)*
 1. With motor signs (ie: march (Jacksonian), versive, postural, phonatory).
 2. With somatosensory or special sensory symptoms, (light flashes, lugging, somatosensory, visual, auditory, olfactory, gustatory, vertiginous).
 3. With autonomic symptoms or signs (epigastric sensation, pallor, sweating, flushing, pilo erection, pupillary dilatation).
 4. With psychic symptoms (very rare-usually part of complex partial seizures).
 - B. *Complex partial seizures.*
 1. Beginning as simple partial seizures and progressing to impairment of consciousness.
 - A. With no other features.
 - B. With features in A 1-4.
 - C. With automatisms.
 2. Unconscious from the onset with similar features to B above.
 - C. *Partial seizures evolving to generalised tonic-clonic convulsions (secondary generalised).*

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Table IV. Classification of Epileptic Seizures

<i>Generalised Seizures</i>	
A. 1) Absence seizures	
a) Impaired consciousness only	
b) With mild clonic component	
c) With atonic component	
d) With tonic component	
e) With automatisms	
f) With autonomic components	
2) Atypical absences	
Tone changes more pronounced than typical absences and onset and cessation is not as abrupt.	
B. Myoclonic seizures – single or multiple	
C. Clonic seizures	
D. Tonic seizures	
E. Tonic/clonic seizures	
F. Atonic (astatic seizures)	
Combinations of the above may occur.	

Generalized Seizures

In these seizures no locus of onset can be determined. There are various types:

1. Absences, or atypical absences as described above.
2. Myoclonias. This is a surprisingly

- stereotyped movement, not random flailing about.
3. Clonic seizures. Generalised convulsive seizures lacking a tonic phase.
4. Atonic seizures. Precipitous loss of tone frequently postural, allowing patient to fall to the floor suddenly.
5. Generalised tonic-clonic seizure termed "primary" if there is no antecedent partial or other seizure. Secondary generalised tonic-clonic seizures are more frequent, usually preceded by an aura and associated with some form of underlying organic disorder (eg trauma, encephalitis etc).

Table V. Pharmacokinetic and Therapeutic Date

Drug Family	Daily dose	Half Life	Side effect prominence	Type of epilepsy
Hydantoins (phenytoin)	5-7mg/kg	24 hrs	moderate	Major generalised complex partial
Carbamazepine	10-30mg/kg	12 hrs	moderate	Partial seizures major generalised
Benzodiazepines Diazepam	0,5mg/kg 8 hourly	30 hrs	high	Absences minor generalised (myoclonic, atonic)
Clonazepam	0,1-0,2mg/kg	30 hrs	high	
Succinimides Ethosuxumide	20-30mg	40 hrs	low	Absences
Barbiturates Phenobarb	3-8mg/kg	96 hrs	high	Major generalised
Sodium Valproate/ Valproic Acid	20-30mg/kg	8 hrs	low	Absences minor generalised major generalised (fair) partial seizures (poor)

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A generalised approach to treatment of these forms of epilepsy is shown in Table V.

Seizures as a manifestation of systemic disease

In the previous section the epilepsies have been classified. However, convulsions can occur without a patient having a true epileptic syndrome. In all patients it is

Convulsions can occur without a true epileptic syndrome

important to remember that many metabolic illnesses and drugs can be the cause of a convulsion.

In hepatic, renal, electrolyte disorders (hypo and hypernatraemia, hypomagnesaemia, hypophosphataemia, hypoglycaemia, hypoparathyroidism, rarely hyperthyroidism and porphyria) seizures usually occur with confusional states, delirium or coma. Hyperglycaemia may cause focal status epilepticus. Vasculitic and connective tissue diseases produce convulsions in \pm 15% of patients (especially SLE) but are usually associated with cutaneous or other neurological signs.

Drug induced seizures may be produced by a number of mechanisms eg INH lowers brain levels of GABA, theophylline elevates cyclic GMP, psychotropic agents and antipsychotic tranquilisers are frequently epileptogenic. Table VI is a list of some drugs that may cause convulsions. Withdrawal of drugs especially anticonvulsants may

precipitate seizures and even cause status epilepticus. Alcohol and barbiturate withdrawal are the commonest seizure precipitants and have been studied very fully.

Medical Managements of Seizures

Having decided to institute treatment, the physician must choose an agent from the wide array of available anticonvulsants. One must make use of the known pharmacokinetics of these drugs to determine dosing schedule and to use serum concentration studies

Table VI. Some drugs causing seizures.

(Messing & Simon)

- Contrast agents (aqueous, iodinated).
- Antihistamines.
- Psychotropics and antidepressants.
- Beta blockers (eg propranolol).
- General anaesthetics (Ketamine, Halothane).
- Hypoglycaemia agents (eg Insulin)
- INH.
- Lidocaine and Procaine.
- Bronchodilators eg Theophylline.
- Metronidazole.
- Penicillins.
- Phenobarbital.
- Phenytoin.
- Prednisone (with hypocalcaemia)
- Amphetamines.
- Cefazolin.

effectively. A plan for determining when and how anticonvulsants may be withdrawn is also needed.

The Choice of Anticonvulsants

The primary determinant of anticonvulsant choice is the seizure type.

Table V lists drugs of choice for the commoner seizure types. The first

Metabolic illnesses as well as drugs can cause convulsions

agent listed for each seizure type should be tried first. If it is ineffective, when pushed to the threshold of symptomatic toxicity, then a different agent should be substituted and the first withdrawn. In general, monotherapy (even at relatively high doses) is better tolerated and may be more effective than a polypharmaceutical approach. If the likely agents are ineffective, then a combination may be tried. Choosing agents with different mechanisms of action is theoretically enticing. Given the fragmentary state of such knowledge, however, one should not be dogmatic in this regard.

The results of the Veteran Administration Co-operative Study of anticonvulsants in adults with partial or generalised convulsive seizures, showed that carbamazepine and phenytoin were equally likely to be tolerated and effective. Primidone was less tolerable, and phenobarbital was less effective. In a given patient, however, primidone may be better tolerated than carbamazepine or phenytoin. The choice of an optimal

agent should be guided by studies such as this, but must be individualized.

The use of serum concentrations ("levels")

The role of serum anticonvulsant concentrations ("drug levels") in the management of seizure patients is commonly misunderstood. There are five situations in which anticonvulsant concentrations are useful; initiation of therapy, assessment of compliance, autoinduction, some decisions about increasing dosage, and toxicity in patients on multiple drugs.

The timing of levels is crucial to their interpretation. When seizure control is of concern, a predose (ideally, prior to the first dose of the day) level should be obtained. When toxicity is to be evaluated, the optimal time to obtain the sample is during the suspected toxic symptoms.

Although total and free (unbound) serum levels and salivary levels (reflecting the free drug concentration) can be obtained, the

After 2 years of no seizures, consider slow withdrawal of medication

total level forms the basis for most studies of "therapeutic" and "toxic" concentrations.

Because patients vary in their absorption, metabolism, and clearance of drugs, the usually recommended milligram-per-kilogram doses are only a general

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guide. Once a steady state has been achieved (five or more half-lives of the drug at a constant dose), a predose serum level can be obtained to ensure that the patient's drug concentration is within the "therapeutic" range. This range is determined from a large population; for a given patient, a higher than

Sleep deprivation and ethanol withdrawal will always pose a risk

"therapeutic" level may be tolerated well and give effective seizure control. Conversely, another patient may experience toxicity at a level below the upper limit of "therapeutic". Hence, this initial level can only be used to ensure that the dose chosen for this patient is providing approximately the expected level. Further dosage adjustments depend on seizure control and side effects, rather than the anticonvulsant concentration.

When seizures persist or recur at "therapeutic" doses, a predose level may suggest either poor absorption or poor compliance. This distinction depends on asking the patient about compliance, the dosage schedule, and intercurrent illnesses that may alter drug absorptions. The patient may also be taking another agent that alters anticonvulsant metabolism. Even immunizations may effect drug kinetics.

Autoinduction occurs after four to eight weeks of carbamazepine therapy in some (but not all) patients, causing the level to fall and, on occasion, seizures to recur. Some

physicians routinely obtain a predose level at 6 or 8 weeks to investigate this possibility. Others instruct the patient to report back at this time, measuring levels only as dictated clinically. Either approach appears acceptable.

When a patient's seizures are not controlled at the anticipated therapeutic dose, but side effects are absent, the dose should be increased slowly in small increments until toxic symptoms first appear. One then returns to the highest tolerable dose; the level is irrelevant in this decision. In some circumstances, the level may be used to help decide the magnitude of a dosage change but not whether it is indicated.

Toxic effects in a patient on a single drug are an indication to lower the dosage, regardless of the level. If the patient is taking two (or more) drugs with similar toxic symptoms, a level obtained during these symptoms is very useful in deciding which agent to reduce.

Specific Anticonvulsant Agents

The large number of anticonvulsants and the vast amounts of data about them preclude an inclusive discussion here. "Drugs for Epilepsy" (Medical Letter January 1989), should be

Acute management is far more important than establishing the cause in status epilepticus

consulted for more information. The relevant pharmacokinetic parameters of the more common anticonvulsants are summarized in Table V. Only a

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few general comments are presented below.

Carbamazepine

The risks of carbamazepine (aplastic anaemia and hepatotoxicity) have been greatly exaggerated; this drug is very useful and should be employed as a first line agent in appropriate seizure types. Its utility is somewhat diminished by its insolubility, which precludes a parenteral preparation. It causes less cognitive dysfunction than phenytoin or barbiturates.

Symptomatic toxicity consists primarily of diplopia, nausea, and head discomfort; these symptoms require lower doses. They are common upon introduction and when the dose is increased. The drug should be started at a low dose (eg, 200mg bd) and increased every 3 days. Most patients experience an asymptomatic decrease in the peripheral white blood cell concentration; if the total granulocyte count falls below 1 000/ml, the drug should be discontinued. The Syndrome of Inappropriate ADH Secretion may be a late complication.

The term "absence" is now commonly used

Generic carbamazepine has recently become available, but experience with it is too limited to recommend for or against its use.

Allergy to carbamazepine is usually confined to dermatologic symptoms. When no other anticonvulsants can be used, the drug can sometimes be reintroduced with steroid coverage,

and the latter subsequently withdrawn without recurrence of allergic symptoms. Carbamazepine may occasionally exacerbate seizures in children: this happens very rarely in adults.

Phenytoin

Long a standard choice, phenytoin remains a useful drug. Its tendency to cause gingival hypertrophy, coarsening of facial features, and cognitive dysfunction must be considered. Phenytoin may be given orally or intravenously (in loading doses) to achieve a therapeutic level rapidly.

Side effects that require dosage reduction include ataxia and, at very high levels, confusion or somnolence. Because phenytoin saturates its clearance enzymes in the high therapeutic range, dosage increments should be small (10 to 50mg) when the level exceeds 17mg/ml. For the same reason, one or two doses of phenytoin should be withheld (to allow the level to fall) when toxicity is present.

Mild elevation of transaminases (especially gamma-glutamyl transpeptidase) and alkaline phosphatase are common and seldom require discontinuation of phenytoin. Greater than 1.5-fold increases of alkaline phosphatase should prompt a search for other etiologies of this abnormality. Folate deficiency may occur.

Chronic administration occasionally produces symptomatic cerebellar dysfunction or peripheral neuropathy. These symptoms indicate a change in

therapy. Phenytoin allergy ranges from minor rash to a syndrome of fever and lymphadenopathy resembling lymphoma. Rarely, the Stevens-Johnson syndrome occurs.

Phenobarbital

Sedative side effects of phenobarbital diminish over weeks, but some patients are never completely free of them. This drug is now most useful as an added agent when carbamazepine or phenytoin alone

Urgent sugar, urea and electrolyte measurements are always justified

are insufficient. Its major advantage is the lack of serious side effects. The rapid withdrawal of barbiturates (or benzodiazepines) may trigger seizures.

Primidone

Primidone has an anticonvulsant effect independent of the phenobarbital produced by its metabolism. Some of its toxic side effects are contributed by another metabolite, phenylethylmalonamide. The extreme sedation produced by this agent may be minimized by starting at a dose of 50mg qhs and slowly increasing every 3 days.

Sodium Valproate

Of the available preparations of this drug, sodium valproate is much less likely to produce gastrointestinal side effects and is usually worth the extra expense. As with carbamazepine, the

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risks of this agent have been greatly exaggerated. As a single agent, it rarely causes serious toxicity in patients above the age of 6 years.

The mild hyperammonemia occasionally noted during valproate therapy is of renal, rather than hepatic, origin. If asymptomatic, it does not indicate a need for drug withdrawal.

Ethosuximide

This drug is often used as primary therapy for absence seizures; it has minimal gastrointestinal toxicity. It does not protect against the generalized convulsions that may occur as children with absence seizures reach early adulthood. This situation indicates either a change to sodium valproate or the addition of carbamazepine or phenytoin. The use of phenytoin alone in these patients may markedly increase the frequency of absence episodes.

Benzodiazepines

Of the benzodiazepines, clonazepam is the most commonly used as an anticonvulsant. Sometimes effective in myoclonic seizures, these drugs may produce a temporary (2 to 6 months) decrease in the frequency of seizures of other types. Sedation is prominent, especially when the dosage is increased. Withdrawal seizures are prominent with all benzodiazepines.

Experimental Anticonvulsants

Research is currently underway on several new anticonvulsants that exploit our recent advances in understanding epileptic mechanisms. Some of the more promising include GABA agonists or enhancers

(vigabatrin) NMDA antagonists (MK-801), lamotrigine, calcium antagonists (flunarizine), and zonisamide.

Discontinuing Anticonvulsant Treatment

No definite rules can be established regarding the discontinuation of anticonvulsant therapy. While some patients clearly enter prolonged or permanent remissions of their seizures, it is difficult to predict who will relapse.

Patients who have been seizure free for 2 or more years may wish to consider slow withdrawal from their medication. The same factors that predict recurrence after a single seizure suggest that the patients will

Table VII. Factors leading to status in treated epileptics.

- Poor therapeutic compliance.
- Rapid changes in dosage.
- Altered drug pharmacokinetics eg
 - altered absorption
 - altered metabolism or elimination (hepatic or renal cause)
 - drug interaction.
- Intercurrent infection (non CNS)
- Alteration in underlying pathology (eg change in behaviour of tumor)
- Alcohol
- Cerebrovascular episode
- Metabolic abnormalities
- CNS infection.

suffer a relapse off medication. However, even in the face of an EEG with epileptiform activity, the patient may wish to try stopping treatment. The life-style issues must be considered; the risk of recurrent seizures necessitates that patients again stop driving or placing themselves in other potentially hazardous situations. Sleep deprivation and ethanol withdrawal will always pose a risk for these patients.

Status Epilepticus

Repeated seizures occur under a variety of circumstances eg fatigue, alcohol, emotion. 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. Status epilepticus may also be divided into partial (eg Jacksonian) or generalised.

No history of previous seizures is obtained in 70% of children and 45% of adults presenting with status epilepticus.

Some factors leading to status in treated epileptics are shown in Table VII. Table VIII demonstrates causes of generalised convulsive status in previously undiagnosed epileptics. These factors, eg metabolic, infection, trauma, tumors, drug overdosage and uncontrolled hypertension with encephalopathy, infarct or haemorrhage should always be corrected if possible.

However, efforts to establish a cause must generally take second place to the acute management of convulsive status. Urgent sugar, urea and electrolyte measurements are always justified.

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Treatment of Status

Principles of management

Time is of the essence. Nevertheless, a few minutes spent in clinically assessing the patient for head injury, reading medic alert bracelets and obtaining a history from accompanying persons is always worthwhile.

Basic rules:

- Start treatment at home or in casualty but if possible admit to hospital.
- Don't push a spoon or spatula into the mouth, especially during the tonic phase - The patient won't choke on his tongue but may choke on a tooth.
- Protect the head with a cushion or lap and turn to one side. Active restraint will aggravate violence.
- Give O₂, monitor cardiorespiratory status and check glucose, give sugar if *any* suspicion of hypoglycaemia.
- Normal saline drip, insert between seizures.
- Use bolus therapy whenever possible.
- Don't give up.
- If control not obtained in sixty minutes, get to a centre with a respirator (don't move without an endotracheal tube) especially if drugs which suppress respiration are used.
- Don't hesitate to use Pentothal and a respirator if no control is obtained in 60 minutes.

A protocol for suggested drug management is shown in Table IX

Diazepam, bolus therapy is the drug of choice to control the acute seizure, Clonazepam may also be used.

A maintenance drug for long term seizure control must always be started immediately. Phenytoin is the drug of choice. If the patient has previously received Phenytoin then use Phenobarbitone. After 3 doses of 10mg each IV Diazepam (max dosage 30mg) given at 15-20 minute intervals reassess. If status persists then use Thiopentone. Patient must be intubated and ventilated.

Less common drugs that are occasionally used are: Lorazepam (Ativan) Heminevrin (Chlormethiazole), Carbamazepine

Table VIII. Some causes or contributing factors to status in previously undiagnosed epileptics.

Tumor
Vascular
Infections
Trauma
H/T encephalopathy
Idiopathic
Alcohol or other drug withdrawal
Drug overdose or intoxication, Vit B deficiency, eclampsia, cardiac arrhythmias, hypotension,
<i>Metabolic:</i> hypoxia, hypercapnia, cerebral oedema, metabolic acidosis, uraemia, liver failure, hyper/hypoglycaemia, hyper/hypocalcaemia, hyper/hyponatraemia, hypomagnesaemia, hyper/hypothermia.

(Tegretol), Paraldehyde, Sodium Valproate and Lignocaine.

Diagnostic work-up is begun after the initial therapeutic steps. Therapeutic failures are generally due to a failure to diagnose or control the cause of status epilepticus or to achieve adequate anticonvulsant blood levels.

If Phenytoin plasma level is known or can be assumed, the following formula can be used to calculate a loading dose. Loading dose (mg)=0,65 x wt (kg) x (C desired - C current) where C desired and C current are plasma concentrations in micrograms/ml.

An integral part of intensive monitoring is the frequent use of anti-epileptic drug levels in plasma. However, these levels are only guides and certain points should be considered.

1. Drug monitoring is a guide to changes in therapy not a substitute for clinical judgement.
2. Expected therapeutic plasma drug levels are average values, each patient has an individual optimal value.
3. In refractory seizures gradually increase dose to establish maximally tolerated dose for that individual.
4. Always do levels in patients on multiple drugs and those with toxic side effects.
5. Non-compliance is *much* commoner than malabsorption and altered metabolism.
6. Peak and trough levels should be established and the reliability of the laboratory assay confirmed prior to interpreting results.

'ROHYPNOL' ROCHE

Components:

Flunitrazepam

Indications:

Tablets: sleep disturbances, whether occurring as an isolated functional disturbance or as a symptom of an underlying chronic disease.

Ampoules: pre-anaesthetic medication; induction of anaesthesia; maintenance of anaesthesia.

Dosage/Administration:

Treatment of insomnia. Adults: 1 - 2 mg; elderly patients: 0,5 - 1 mg, immediately before going to bed.

Anaesthesia:

Adults:
Premedication: 1 - 2 mg i.m.
Induction of anaesthesia: 1 - 2 mg by slow i.v. injection.
Maintenance of anaesthesia: if the amount used for inducing anaesthesia is inadequate, further small doses may be injected slowly.
Children:
For premedication and induction of anaesthesia: 0,015 - 0,030 mg per kg by i.m. or slow i.v. injection.

Contra-indications:

Severe chronic hypercapnia.
Hypersensitivity to benzodiazepines.

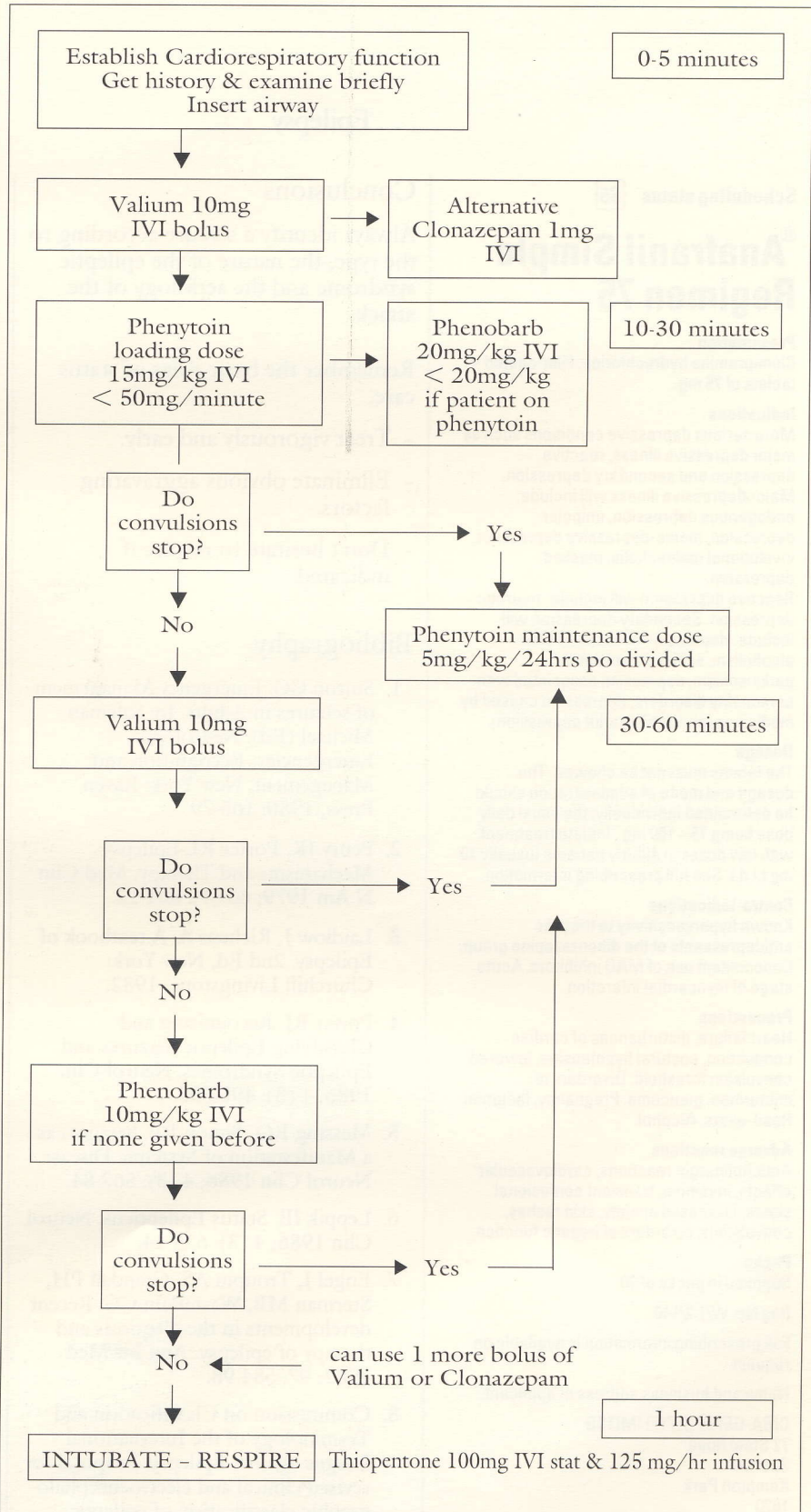
Precautions:

General: elderly patients with organic cerebral changes. Avoid alcohol during treatment.
Pregnancy.
Discontinue breast feeding.

Packs:

Tablets 2 mg: 30's, 100's.
Ampoule pack containing:
5 ampoules with 2 mg of active ingredient in 1 ml solution;
5 ampoules with 1 ml of sterile water for injections as diluent, to be added prior to i.v. or i.m. injection.

Table IX Status Treatment Protocol



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Conclusions

Always identify a seizure according to the type, the nature of the epileptic syndrome and the aetiology of the attack.

Remember the basic rules of status care.

- Treat vigorously and early.
- Eliminate obvious aggravating factors.
- Don't hesitate to respire if indicated.

Bibliography

1. Sutton GG. Emergency Management of seizures in Adults. In: Salzman Michael (Ed). Neurologic Emergencies, Recognition and Management. New York: Raven Press, 1980: 165-79.
2. Penry JK, Porter RJ. Epilepsy: Mechanisms and Therapy. Med Clin N Am 1979; 63 (4): 801-12.
3. Laidlow J, Richens A. A textbook of Epilepsy. 2nd Ed, New York: Churchill Livingstone, 1982.
4. Porter RJ. Recognising and Classifying Epileptic Seizures and Epileptic Syndromes. Neurol Clin 1986; 4 (3): 495-508.
5. Messing RO, Simon RP. Seizures as a Manifestation of Systemic Disease. Neurol Clin 1986; 4 (3): 563-84.
6. Leppik IE. Status Epilepticus. Neurol Clin 1986; 4 (3): 633-44.
7. Engel J, Troupin AS, Crandall PH, Sterman MB, Wasterlain CG. Recent developments in the diagnosis and therapy of epilepsy. Ann Int Med 1982; 97: 584-98.
8. Commission on Classification and Terminology of the International League against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic

seizures. Epilepsia 1981; 22: 489-501.

9. Ward CD. Status Epilepticus. Hospital Update 1987; 190-200.
10. Fritz VU. Neurological Emergencies may not be recognised. Trauma, Journal of Accident and Emergency Medicine 1985; (Oct) 13-7.
11. A guide to the Management of Common Medical Emergencies in Adults. 2nd Ed, University of the Witwatersrand Medical School, 1987: 54-5.
12. Fritz VU "Convulsions". J Cont Med Ed SA 1988; 6: 40-6.
13. The Medical Letter. "Drugs for Epilepsy" 1989; 31 (issue 783): 1-4.
14. Bleck TP. "Epilepsy". Disease a Month. Bone RC (Ed) Year Book Medical Publishers. 1987: 651-60.

Scheduling status **S5**

Anafranil Simple Regimen 75

Presentation

Clomipramine hydrochloride. Film-coated tablets of 75 mg.

Indications

More serious depressive conditions such as major depressive illness, reactive depression and secondary depression. Major depressive illness will include: endogenous depression, unipolar depression, manic-depressive depression, involuntal melancholia, masked depression.

Reactive depression will include: neurotic depression. Secondary depression will include: depression associated with alcoholism, schizophrenia and parkinsonism, depression associated with personality disorders, depression caused by medicines (and senility with depression).

Dosage

The tablets must not be chewed. The dosage and mode of administration should be determined individually, the usual daily dose being 75 - 150 mg. Initiate treatment with low doses in elderly patients (usually 10 mg t.i.d.). See full prescribing information.

Contra-indications

Known hypersensitivity to tricyclic antidepressants of the dibenzazepine group. Concomitant use of MAO inhibitors. Acute stage of myocardial infarction.

Precautions

Heart failure, disturbances of cardiac conduction, postural hypotension, lowered convulsion threshold. Disorders of micturition, glaucoma. Pregnancy, lactation. Road-users. Alcohol.

Adverse reactions

Anticholinergic reactions, cardiovascular effects, insomnia, transient confusional states, increased anxiety, skin rashes, convulsions, disorders of hepatic function.

Packs

Supplied in packs of 30.

Reg No. W/1.2/140

Full prescribing information is available on request.

Name and business address of applicant.

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72 Steel Road
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Kempton Park
1620
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