PREVALENCE OF EPILEPSY IN RURAL EGYPT

Submitted Thesis In Partial Fulfilment For
Master Degree In Neuropsychiatry

BY

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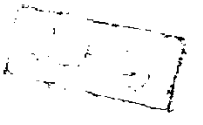

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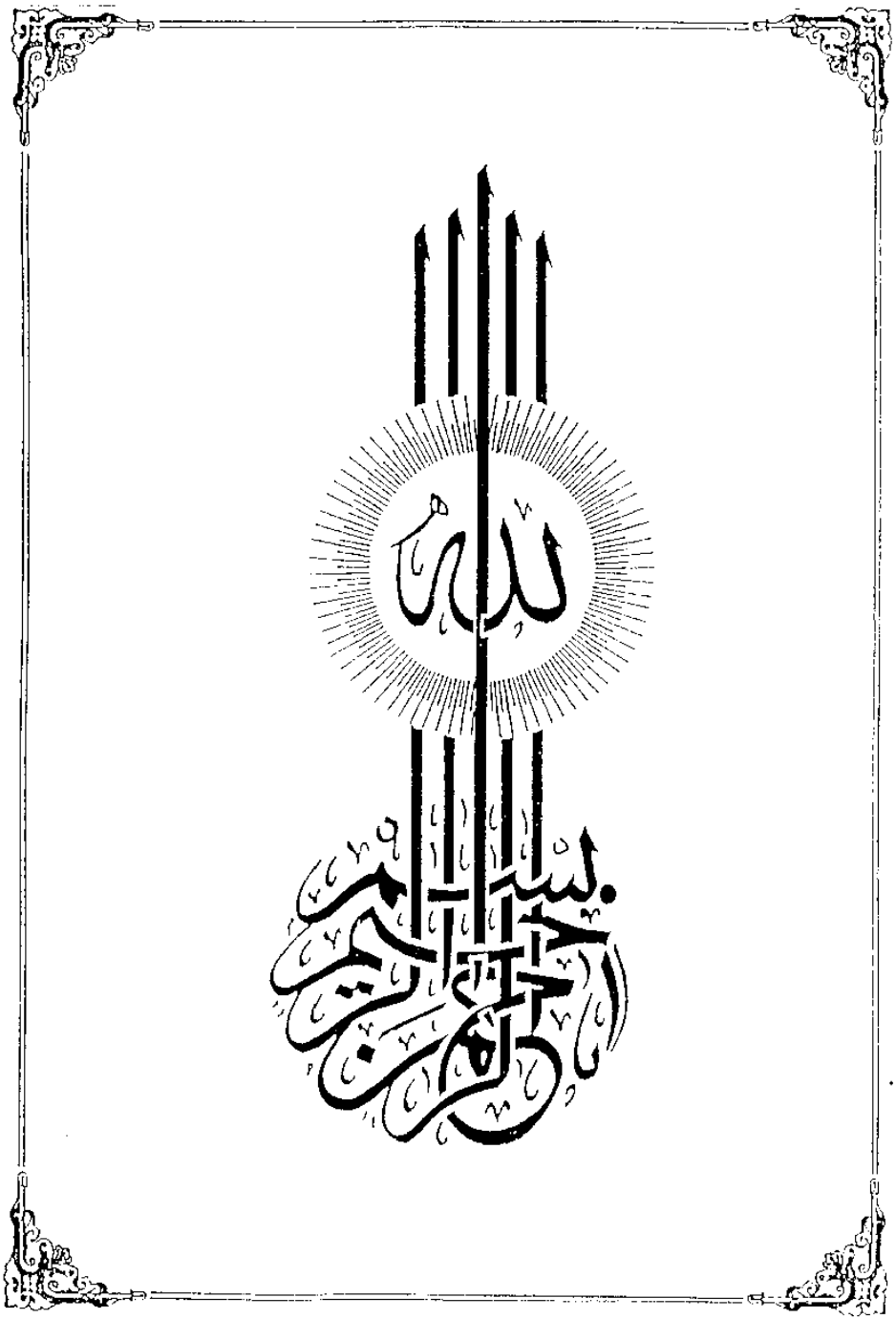
TO MY WIFE AND DAUGHTER REHAB



ACKNOWLEDGMENT

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C O N T E N T S

INTRODUCTION

Epilepsy is a paroxysmal and transitory disturbances of the function of the brain, which develop suddenly, cease spontaneously and exhibits a conspicious tendency to recurence.

Though in its most typical forms it is characterized by the sudden onset of loss of conciousness, which may or may not be associated with tonic spasm and clonic contraction of the muscles. Many varieties of epileptic attack occur, their distinctive feature depends upon difference in the site of the origin, extend of spread and nature of disturbance of function.

Epilepsy is thus a symptom and in some cases local lesion in the brain plays the chief part in causation, in other the cause is quite unknown.

A generalized attack has long been known as "Grand Mal". An attack characterized by loss of consciousness only without falling and without as a rule motor accompaniment as "Petit Mal"(Brain 1977)

The essential feature of epilepsy varies so widely in character that a definition of it, except in very

general terms, is not easy to give. It may be said that it is the expression of a sudden and transient disturbance of cerebral functions. If the disturbance be widespread, there will be loss of alteration of conciousness. If the disturbance be localized, conciousness may be imparied. In either case sudden and transient symptoms, motor sensory or purely mental may be present. They commonly take the form of positive symptoms that is motor spasm, abnormal sensation or special sense phenomena (Walsh 1970).

These clinical paroxismal neurological disorders are due to sudden synchroneus high voltage discharge arising from a number of hyperexcitable neurones and neurochemical and electrical changes occur with disturbances of the inhibitory mechanisms and spread of electrical discharges beyond the locus (Philip Maries 1976).

GENERAL CONSIDERATION OF EPILEPSY:

As the term "the epilepsies" suggest there is no disease (epilepsy) but a group of disorders, the epilepsies, which probably involve similar patho-physiological mechanism but which occur in different anatomic regions of the brain have different aetiologies and are associated with different electro-encephalographic appearance. For convenience, however, throughout this consideration the word epilepsy is

used as a synonym for "the epilepsies".

Epilepsy is best regarded as a symptom of disturbed cerebral function, (Epilepsy is disordered regulation of energy released within the brain).

The poroxismal cerebral dysrhythmias in epilepsy that manifest themselves clinically as epileptic fit and electro-encephalographically as seizure discharges are not caused by mysterious agents but by some physical causes that can produce serious disturbances in any other organ for example the heart. The same thing that can cause severe cardiac disorder can produce the cerebral dysrythmias of epilepsy for example, trauma, infection, O_2 lack, tumours, abscesses, toxins and general metabolic diseases. But the injury that produces epilepsy can not be too severe. It must produce an intermediate non-lethal degree of injury to cerebral neurones. Such injury usually is not visible with the naked eye or even with microscope. When neurons are killed they do not produce epileptic seizure. Therefore destructive lesions, the kind that shows so clearly in gross pathological studies and in microscopic section (for example areas of softeing, atrophy and scarring) are not so likely to be associated with epileptic seizures as lesions that occur when neurons are harmed but not destroyed,

when their intimate chemistery is upset not enough to make their function abnormal and the pathology of epilepsy is not structural but physiological (Gibbs 1958 and Southerland 1974).

So epilepsy shows in electroencephalogram but not in stained sections and this does not mean that epilepsy is not due to real injuries. The injuries that produce epilepsy are not extreme but just as real as those that produce structural damage.

Around area of destruction in which function has been abolished there is often a zone of less severe injury in which seizure activity develop which correspond to mild injury and in this state seizure activity is likely to occur.

To put this in a nutshell: Epilepsy is what the brain does when it is slightly injuried, for this reason epilepsy is a common and also a treatable disorder (Gibbs 1958).

Thus when one is confronted with a patient where history suggest an episode or episodes of disturbed cerebral function, the clinician has to consider the following possibilities (Southerland 1974):

1. Epilepsy.

2. Disturbed cerebral blood flow:
   (a) Physiological e.g. vasovagal fainting attacks.
   (b) Organic e.g. the drop attacks of vertebro-basilar arterial disease.
3. Brain Pathology e.g. lesion involving brain stem, tumour of ventricular system.
4. Disorders of blood compisition e.g. hypoglycaemia, deminished blood cortisol, drugs.
5. Psychoneurotic conditions and catatonic states.
6. Narcolepsy-Catalepsy syndrom.
7. Malingering.

THE NATURE OF EPILEPSY:

The precise mechanism involved in the excessive neuronal discharge of epilepsy remain obscure.

Nerve tissue is excitable tissue and its excitability is influenced by various factors and mechanism.

(1) Individual neurones are kept in state of excitability by virtue of a concentration gradient of Na^+ ions across the neuronal cell membrane. This gradient is maintained by the so-called "Sodium pump" (The enzyme Na^+; K^+, K Linkined adinosine triphosphatase). The sodium pump is an energy requiring mechanism. If the Na concentration

gradient increases, the neurone become hyperpolarized and more difficult to activate, if the gradient lessens the neurones excitability increased. The sodium dependent high affinity choline transport system has a number of properties which strongly suggest that it has an important role in a functioning cholinergic neuron. These properties includes it is possibily unique localization to cholinergic neurone (Kuhar et al., 1976, Pert and Snyder 1974), its molecular specificity for choline (Simon et al., 1976), it is coupling to choline acetyle transferase which suggests that, it may be a rate-limiting step in synthesis of acetyl choline (Barken and Mittage 1975, Lofrense et al., 1975), it is subserving of a releasable pool of acetyle choline (Mulder et al., 1974), and it is coupling to neuronal activity in such a way that it is capacity changes in parallel with the need for choline and acetyle choline synthesis (Simon et al., 1975 and Brodferd 1976).

(2) Neuronal excitability at synapses is altered by the release onto the synaptic cell membrane of excitatory and inhibitory transmiter substances. Thus the release of acetyle choline has an excitatory effect while gama-aminobutyric acid (GABA) exerts a powerful inhibitory action at certain synapses. It is possible that defective

inhibition is at least as important as excessisive excitation and excessisive neuronal discharge. It is also possible that such discharges may result from constitutional metabolic derangment in synthises or availability of (GABA) and possibily other inhibitory substances. For example, there is evidence that pyridoxal phosphate is essential for the synthesis of GABA, and that pyridoxine diffeciency may result in convulsion in children due to lower seizure threshold. Also in cerebral scare at the prephery of which graphic elements with convulsive pattern were found the activity of glutamic oxaloacetic transaminase was found to be decreased (Pierre M. Dreyfus 1976 and Stephen 1971). Also drugs that inhibit glutamate decerbonylase (GAD), do so by interfering with the synthesis or co-enzyme function of pyridoxal phosphate can be shown to induce seizures in animal (Meldrum 1976). Meldrum and Sicaic (1976) found that bicuculline which is a plant alkaloid that blocks the inhibitory action of GABA at a post-synaptic sites when injected intervenously in light anesthetized rats it induces electrocorticographic seizures that continue with unreduced intensity for more than two hours in paralysed artificially ventilated rats (Meldrum 1976 and Philip 1976).

Also from the biochemical point of view, under some condition admenstration of p-chlorphenylalanine (P-CP) to rats produces an increase in their susceptibility to seizur and also increases cerebral excitability.
Koe and Weissman (1968) found that rats givin one injection of P-CP are more likely than controls to exhibit tonic extension seizures. Also the effect of P-CP is not clear but there are two possibilities:

(A) P-CP has a direct effect on neurenal membrane, and a single dose of drug lower seizure threshold in susceptible rats.

(B) It causes depletion of serotonine which might cause increased cerebral excitability (Wrichard J. 1971).

(3) Certain collections of neurons, inhibitory pools, exist and exert a controlling action on other parts of the nervous system preventing discharges occurring repeatedly. Damage to such a neuronal pool from, for example, traumatic, infective, vascular or neoplastic causes would result in loss inhibition and a tendency to epilepsy in the area of brain normally regulated by the pool (Aurther 1972).

(4) Nervous tissue may be rendered hyperexcitable by a variety of factors which act diffusely. These include pyrexia, hypoxia, hypocalcaemia, hypoglycaemia, over