Thus, the venous ulcer, far from being an *ischaemic* lesion, is a *hyperaemic* lesion. It is sitting on a honeycomb of dilated venules which in fact is rather like a haemangioma. The longer the ulcer has been present the more profuse and sponge-like is the venous sump on which the ulcer sits. Moreover, as time goes on, this hyperaemic area acquires an increased arterial supply; and this venous "sump" under the ulcer can be filled equally well from the arterial or venous side of the circulation, and therefore can be shown equally well by an arteriogram or a venogram (see Fig. 9).

Finally, the cause of destruction of the strategic valve in the ankle-perforating veins, and therefore the cause of their incompetence, is deep thrombosis in the majority of cases. Post-thrombotic ankle-perforator incompetence is therefore the main immediate cause of the ulceration, induration, and swelling of the ankle, which is such a prominent feature of the post-thrombotic syndrome of the leg.

Treatment of Perforator Leaks

The treatment of high-pressure leaks at the ankle, perforator leaks, and their effects, is to relieve the unnatural venous hypertension in the subcutaneous tissues of the ankle region. This can be done by conservative methods or by operation.

Conservatively.—(1) By putting the patient flat, with the feet a little above heart level (raising the foot of the bed). (2) By applying an elastic compressing force from the outside (this is the basis of the elastic-stocking and elastic-bandage method of healing ulcers).

Operatively.—By finding and ligating the incompetent perforating veins. They must be ligated *at source*—that is, either below or as they emerge from their holes in the deep fascia. This simple measure will control and heal early cases of ankle ulceration. In the more widespread and long-standing cases, as much as possible of the haemangioma-like venous sump round the ankle must be removed as well, to get a good and lasting result. The exact technical methods of achieving this have been dealt with elsewhere (Cockett, 1955; Dodd and Cockett, 1956).

Conclusion

In this short paper I have attempted to deal only with the main mechanical principles underlying the pathology of varicose veins and venous ulcers. *En passant*, as it were, a very beautiful and intricate piece of physiology has been explored—the mechanism of venous drainage of the subcutaneous tissues of the leg and ankle in the erect position. Only if this physiology and the exact anatomy of the main perforating veins are mastered does the story of varicose veins and venous ulcers become intelligible. Once it is mastered the art of diagnosing the exact site of the venous leak or leaks in a patient who presents with varicose veins or an ulcer becomes an interesting clinical exercise.

Successful surgery then depends to a great extent on just how much time and care the surgeon is prepared to spend on his patient. The proper performance of the various flush ligations of the perforating veins at all levels in the limb needs time and care. The ancillary procedures, like stripping and skin grafting, need scrupulously careful operative technique and aftercare. Successful surgery of varicose veins cannot be done in ten minutes at the end of a long list.

REFERENCES

Cockett, F. B. (1955). *Brit. J. Surg.*, 43, 260.
Dodd, H., and Cockett, F. B. (1956). *The Pathology and Surgery of the Veins of the Lower Limb.* Livingstone, Edinburgh.
Höjensgard, I. C., and Stürup, H. (1952a). *Acta physiol. scand.*, 27, 49.
—— —— (1952b). *Acta derm.-venereol. (Stockh.)*, 32, Suppl. 29, p. 169.

AETIOLOGICAL ASPECTS OF AMMON'S HORN SCLEROSIS ASSOCIATED WITH TEMPORAL LOBE EPILEPSY*

BY

J. B. CAVANAGH, M.B., M.R.C.P.
Honorary Senior Lecturer in Neuropathology

AND

A. MEYER, M.D.
Professor of Neuropathology

Department of Neuropathology, Institute of Psychiatry, Maudsley Hospital

The cornu Ammonis has in recent years received much attention in the discussion of the pathological processes associated with temporal lobe epilepsy. The problem and its historical development have been outlined in several publications coming from the Maudsley group—for example, Meyer (1954), Falconer *et al.* (1955), Meyer and Beck (1955)—and in order to avoid repetition the reader is referred to these publications. In the present paper it is intended to deal with certain aspects of the pathology and aetiology of this condition, which in previous papers were either omitted or reported upon in inadequate detail.

The present report is based upon 40 cases in which radical temporal lobectomy has been carried out by Mr. Murray Falconer.

Subdivision of the Pathological Findings

In order to maintain a proper perspective it would be best to outline briefly the various pathological changes that have been met with in this material.

Focal Lesions

Our material conforms with that of Earle, Baldwin, and Penfield (1953) in that about one-third of the cases (13 out of 40) showed a sharply circumscribed abnormality, sometimes visible to the naked eye. Table I lists these changes and defines their location. In two of the cases with tumours the lesion was of such an extent as to be of little interest with regard to the functional disturbances recorded. On the other hand, small well-defined tumours in the early stage of their development and vascular lesions were found restricted to very narrow limits. Interesting though these focal lesions may be, they are not, however, the subject of the present paper. It should be noted that in no case was definitive Ammon's horn sclerosis encountered in this group, although this region was encroached upon by an angiomatous malformation in one instance.

Diffuse and Disseminated Lesions

The pathological changes in the remaining two-thirds of the cases may be divided into two subgroups—namely, (1) those cases in which Ammon's horn sclerosis was present in addition to other diffuse lesions in the lobe, and (2) those cases in which little or no abnormality of importance was encountered. The changes and their distribution are shown in Tables II and III, where they are arranged in order of severity. In the Ammon's horn sclerosis group the changes encountered were diffuse laminar nerve-cell loss in the cortex involving chiefly layers II and III; partial or complete loss of nerve cells in the pyramidal layer of Ammon's horn; and gliosis of the white matter and of the subpial layer of the

*Being expanded from a communication read before the Second International Congress in Neuropathology in London, September, 1955.

TABLE I.—*Distribution of Focal Lesions Encountered*

Case and Sex	Age at Onset and Operation	Grand Mal	Lesion	Side of Lobectomy	Meningeal Fibrosis	Marginal Gliosis	Gyri: Middle C	Gyri: Middle W	Gyri: Inferior C	Gyri: Inferior W	Gyri: Fusiform C	Gyri: Fusiform W	Gyri: Hippoc. C	Gyri: Hippoc. W	Ammon's Horn	Uncus	Amygdaloid
Sin. F	14/12 26/12	–	Glial hamartoma	L.	▲	▲	N.A.	N.A.	■	■	■	■	N.A.	N.A.	N.A.	N.A.	N.A.
Ros. M	30 46	–	Trauma	R.	■	○	N.A.	N.A.	■	■	■	■	N.A.	N.A.	N.A.	N.A.	N.A.
Woo. F	47 48	+	Vascular lesion	L.	▲	▲	○	○	■	■	■	○	○	○	○	○	○
Val. F	21 23	–	Meningioma	L.	▲	▲	○	○	○	○	■	■	○	○	N.A.	N.A.	N.A.
Mar. M	18 32	+	Oligodendroglioma	L.	○	▲	○	○	○	○	■	■	○	▲	○	○	N.A.
Par. F	22 28	+	White matter gliosis	R.	○	▲	○	○	○	▲	○	■	○	■	○	○	N.A.
Mun. M	25 35	–	Astrocytoma	R. dominant	○	■	○	▲	○	▲	○	▲	■	■	○	■	▲
Kie. F	9 14	–	Glial hamartoma	R.	○	▲	○	○	○	○	○	○	■	■	○	■	■
Lew. F	30 43	+	Angioma	L.	○	■	○	▲	○	▲	○	▲	○	▲	○	■	N.A.
Har. F	49 51	–	Oligodendroglioma	R.	○	○	○	▲	○	■	○	■	○	▲	□	□	■
Wak. M	51 56	–	,,	R.	○	○	○	■	○	■	○	■	○	■	□	□	■
Ste. F	18 40	–	Angioma	L.	○	○	Scattered remnants of angioma and softening								▲	N.A.	N.A.
Lar. M	38 42	+	Vascular lesion	L.	▲	▲	▲	○	○	○	○	▲	○	▲	○	○	○

■ = + + Severity. ▲ = + Severity. □ = Doubtful lesion. ○ = No abnormality. N.A. = Not available. C = Cortex. W = White matter.

TABLE II.—*Ammon's Horn Sclerosis Group with Diffuse and Disseminated Lesions Arranged in Order of Severity. The Various Possible Aetiological Agencies are Given*

Case and Sex	Age at Onset and Operation	Status at Onset	Grand Mal	Difficult Birth	Other Causes	Side of Lobectomy	Meningeal Fibrosis	Marginal Gliosis	Gyri: Middle C	Gyri: Middle W	Gyri: Inferior C	Gyri: Inferior W	Gyri: Fusiform C	Gyri: Fusiform W	Gyri: Hippoc. C	Gyri: Hippoc. W	Ammon's Horn	Uncus	Amygdaloid
Esh. F	4 13	–	+	–	Hemiplegia following measles	L.	○	■	▲	■	■	■	■	■	■	■	■	■	■
Man. F	11 25	+	+	+	—	L.	○	■	■	■	■	■	■	■	■	■	■	■	■
Ren. F	2 13	+	+	+	Meningitis at 11/12	L.	○	■	■	■	■	■	■	■	■	■	■	▲	■
Nob. F	4½ 18	+	+	–	—	L.	○	■	○	■	■	■	▲	■	▲	■	■	■	■
Pat. M	3 13	–	–	+	—	L.	○	■	■	■	■	■	■	■	■	■	■	N.A.	N.A.
Lov. M	3 11	+	+	–	Teething convulsions 2 years	L.	▲	■	▲	▲	▲	▲	▲	▲	▲	▲	■	■	□
Gam. F	8 18	–	–	–	Head trauma 8 years	L.	▲	■	■	▲	○	▲	○	▲	○	■	■	■	□
Nev. M	9 16	–	–	–	—	R.	▲	■	▲	■	▲	■	▲	■	▲	■	■	N.A.	N.A.
Joh. F	2 21	+	–	–	Status at 23/12	R.	○	■	□	■	□	■	▲	■	▲	■	■	■	□
Wal. M	2 22	–	–	+	—	R.	■	■	▲	■	▲	▲	▲	▲	■	■	■	■	N.A.
Har. M	2 36	+	+	–	—	R.	▲	■	○	▲	□	▲	□	▲	□	■	■	■	■
And. F	1 23	+	+	+	—	L.	▲	■	□	▲	□	▲	□	▲	▲	▲	■	■	□
Tur. E. F	2 22	+	+	–	Whooping cough 1/12 before status	L.	▲	▲	□	▲	□	▲	□	▲	□	▲	▲	N.A.	N.A.
Pri. M	2 23	+	+	–	Teething convulsions	R.	▲	▲	○	○	○	○	○	○	○	○	■	N.A.	N.A.
Tur. J. F	14 20	+	+	+	—	L.	▲	▲	□	▲	□	▲	□	▲	□	▲	▲	■	■
Chu. M	40 49	+	+	–	—	L.	▲	■	○	■	○	■	▲	■	▲	■	N.A.	N.A.	N.A.
Ric. M	2 32	–	–	–	—	L.	■	■	N.A.	■	▲	■	▲	▲	▲	▲	N.A.	N.A.	N.A.
Mac. M	2 45	+	+	+	Status compl. Ch. pox	R.	○	■	□	■	□	■	□	■	▲	▲	▲	N.A.	N.A.
Kev. F	4/12 43	+	+	–	—	L.	○	▲	○	▲	○	▲	○	▲	○	▲	▲	N.A.	N.A.

■ = + + Severity. ▲ = + Severity. □ = Doubtful lesion. ○ = No abnormality. N.A. = Not available. C = Cortex. W = White matter.

TABLE III.—*Group with Minimal Lesions and no Ammon's Horn Sclerosis Arranged in Order of Severity and Showing Possible Aetiological Factors*

Case and Sex	Age at Onset and Operation	Status at Onset	Grand Mal	Difficult Birth	Other Causes	Side of Lobectomy	Meningeal Fibrosis	Marginal Gliosis	Gyri: Middle C	Gyri: Middle W	Gyri: Inferior C	Gyri: Inferior W	Gyri: Fusiform C	Gyri: Fusiform W	Gyri: Hippoc. C	Gyri: Hippoc. W	Ammon's Horn	Uncus	Amygdaloid
Lee M	8 38	–	–	–	—	L.	○	■	□	▲	□	▲	□	▲	□	▲	□	N.A.	N.A.
Str. F	2 21	–	+	+		L.	○	▲	○	○	▲	○	▲	○	▲	○	□	□	○
Par. M	18 25	–	+	+	Boxer	R.	○	▲	○	□	○	□	○	□	○	□	□	□	N.A.
You. F	13 45	–	+	–	Head injury at 13 years	L.	○	▲	○	□	○	□	○	□	○	□	□	□	□
						L.	▲	▲	○	□	○	□	○	□	○	▲	○	○	○
Cha. F	16 27	–	+	–	Wh. cough at 2½ years	R.	▲	▲	□	○	□	○	□	○	□	○	N.A.	N.A.	○
Tay. M	14 27	–	+	+	Sinusitis at 16 years T.B. hip with meningismus at 12 years	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○
Par. M	18 25	–	+	–	Otitis media	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○
Fau. M	18 45	–	+	–	Head injury at 18 years	R.	○	□	○	○	○	○	○	○	○	○	○	○	○

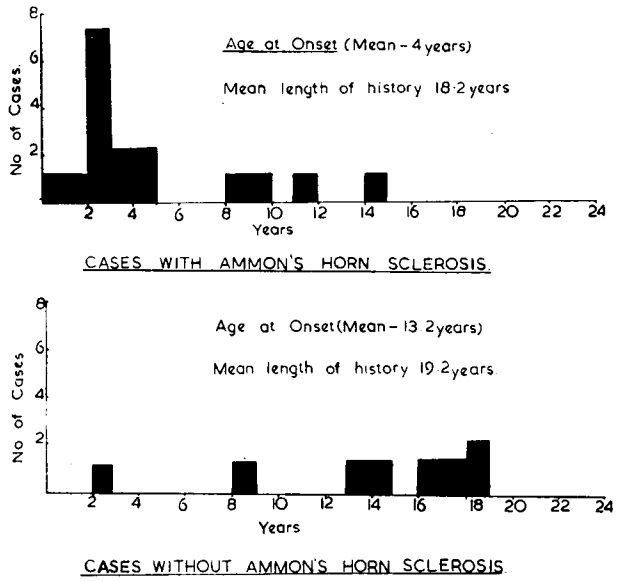
■ = + + Severity. ▲ = + Severity. □ = Doubtful lesion. ○ = No abnormality. N.A. = Not available. C = Cortex. W = White matter.

cortex. Furthermore, in about half the cases in which the amygdaloid nucleus was included in the specimen, focal loss of nerve cells in the basal groups was found; in other cases only severe gliosis could be discerned in this region, and thus the possibility of a slight loss of nerve cells in these instances could not be ruled out. In no case was damage to this region found where Ammon's horn was normal. All these changes were judged to be of considerable age, and no significant alterations in the neurons or glia of a recent nature were encountered in any part of the resected lobes.

In those cases of subgroup (2) (Table III) not showing Ammon's horn sclerosis, subpial gliosis and gliosis of the white matter of moderate severity were the only abnormalities found. The cortical layers in this group did not appear to be altered in any way.

Possible Aetiological Factors Leading to the Ammon's Horn Sclerosis

In Tables II and III are also listed those factors that may be considered to contribute to the lesions encountered in both subgroups. When cases showing Ammon's horn sclerosis are compared for these factors with those not



Histograms of the age of onset of epilepsy of the cases in Tables II and III.

showing this change some important correlations emerge. With regard to the age of onset of the epileptic history, it will be seen in the Chart that there is a heavy concentration of those cases with Ammon's horn sclerosis beginning their history at the average age of 4 years, while the other subgroup shows a mean age of onset at about 14 years. The mean length of history is, however, the same in the two subgroups. It is well known that epilepsy may follow its precipitating cause by one to several years, and the figures of Bridges (1949) indicate that about 84% of cases in which epilepsy was probably ascribable to birth trauma developed convulsions before the fifth year of life, while the onset after this time was infrequent. However, if birth injury was a consistently important feature in the development of Ammon's horn sclerosis it would be expected that a marked difference in the incidence of a history of birth difficulty would be encountered in the two subgroups. In fact, this is not the case, as is shown in Table IV, where only a slight increase appears in the number of cases in the Ammon's horn sclerosis subgroup that gives such a history.

On the other hand, if the incidence of grand-mal seizures in addition to psychomotor attacks is considered a greater incidence is found in the first than in the second subgroup. Closer examination shows, however, that this is not simply due to the greater number of major seizures occurring in

TABLE IV.—*Aetiological Correlations of the Cases With and Without Ammon's Horn Sclerosis*

Relation of Ammon's Horn Sclerosis to Possible Birth Trauma

	Total	Possible Birth Trauma	Age at Onset of Cases
Group *with* Ammon's horn sclerosis	17	7 (41%)	1, 2, 2, 2, 3, 11, and 14 years
Group *without* Ammon's horn sclerosis	9	3 (33%)	2, 13, and 18 years

Relation of Ammon's Horn Sclerosis to Major Convulsions

	Total	Major Convulsions During Illness	Status at Onset
Group *with* Ammon's horn sclerosis	17	13 (76%)	11 (64%)
Group *without* Ammon's horn sclerosis	9	4 (44%)	—

these cases with Ammon's horn sclerosis, for in fact several of them were subsequently subject to only minor attacks, but is due to the remarkably high incidence (64%) of status epilepticus at or preceding the onset of the epileptic history. Because of the incompleteness of our material and the necessarily provisional nature of the present grouping of the cases, the association between Ammon's horn sclerosis and an early history of status epilepticus may well prove to be even more striking. Thus, of those cases in the Ammon's horn sclerosis group that do not give a history of status epilepticus, one individual dates her temporal lobe seizures from an attack of measles that was complicated by hemiplegia probably having its origin in a vascular accident; while another patient, a few weeks before the onset of her minor seizures, had a mild closed head injury which was probably responsible, either directly or indirectly, for the lesions encountered. It is clear, therefore, that this interesting relationship between status epilepticus, particularly in early infancy, and Ammon's horn sclerosis may be even more impressive than was at first apparent. Its meaning is, however, still obscure in many respects.

Scholz (1936, 1951), following the lead of Spielmeyer, has regarded Ammon's horn sclerosis as the consequence of vasomotor disturbances, particularly vascular spasm, associated with the epileptic convulsions. He even explains the lobar atrophy, hemiatrophy, and total atrophy of the brain, sometimes encountered in this condition, as consequences of vasomotor disturbances and anoxia caused particularly by severe serial convulsions. It is important to stress that in most of Scholz's cases, as well as in most of ours and in those of Zimmerman (1940), the onset of the convulsions has been in infancy. Apparently status epilepticus rarely leads to severe lesions of this type in later life. One is therefore compelled to conclude either that the brain of infants is more vulnerable to the stress of epileptic convulsions than that of adults or that other factors are involved. It has been stated that the oxygen requirements of the infant's brain up to the age of 4 years are higher than those of the adult and may be up to 50% of the total oxygen consumption; but, according to McIlwain (1955), allowance must be made for the fact that the weight of the infant's brain approximates the sum of the liver, kidneys, heart, and spleen. There is at present, therefore, no definite evidence of an increased vulnerability of the infant's brain to oxygen deprivation during epileptic attacks or to anoxia of any other origin.

Scholz has suggested that perhaps the occurrence of status epilepticus during the exanthematous fevers and acute allergic reactions may have to be implicated in order to explain this increased danger to vascular damage. In fact, most of Zimmerman's (1940) cases developed convulsions during acute febrile conditions, and in our material it will be seen from the tables that there is frequently an acute febrile episode accompanying the initial status epilepticus. The exact mechanism of this relationship remains unknown,

though pyrexia itself would, by stimulating cell metabolism, tend to increase demand for oxygen. The febrile illnesses were not, however, usually of severe type in themselves.

One must therefore not entirely preclude the possibility that one link in the chain of events leading to the status epilepticus is not yet known and that at least in some of the cases the convulsions are a symptom of the damage already done and are not entirely its cause. This was the conclusion, for instance, of Alajouanine (1954) when he summed up the discussion of temporal lobe epilepsy held in Marseilles. A similar opinion has been expressed by Bini and Callieri (1955) from their own extensive experience.

Purdon Martin (1955) has restated his view that thrombosis of cerebral venous channels may follow comparatively trivial head injury, but that by the time the body reaches the post-mortem room any consequent pathological changes may, because of their relatively minor nature, be readily overlooked. From the pathological standpoint Lindenberg (1955) has drawn attention to the possibility that after sometimes trivial head injury, as well as during the course of acute febrile conditions, cerebral oedema may develop, giving rise to epileptic convulsions and focal anoxic lesions in consequence of pressure developing on certain arteries. Because of their anatomical relationship to the free tentorial edge, the medial structures of the temporal lobe and, above all, the Ammon's horn are especially liable to be the seat of changes of this type on account of pressure upon the long penetrating branches of the anterior choroidal and posterior cerebral arteries. Lindenberg's view of the pathogenesis of the type of lesion that has been so often encountered in our series is an important one and one that agrees, in principle, with the hypothesis implicating tentorial herniation during excessive moulding of the head at birth put forward by Earle *et al.* (1953). Further, it has the advantage of wider application, since birth injury cannot be considered, from the evidence presented here, as an exclusive pathogenetic factor. In fact, because raised intracranial pressure is likely to occur during the course of anoxias of various origin, including the cyanotic stage of severe epileptic convulsions, the puzzle of Ammon's horn sclerosis and related selective phenomena may have been brought nearer solution.

Relationship of Ammon's Horn Sclerosis to Temporal Lobe Epilepsy

Stauder (1935–6) and Sano and Malamud (1953) found in their cases, which they regarded as definite or probable temporal lobe epilepsy, an occurrence of Ammon's horn sclerosis approaching 100%, if one excludes those cases with a focal fronto-temporal traumatic lesion. This impressive correlation must be considered against the overall incidence of Ammon's horn sclerosis in all forms of epilepsy, which over several series has averaged at 50% (Scholz, 1951 ; Gastaut, 1954).

Our present figure is 70%—a fairly high incidence, though substantially less than Sano and Malamud's and Stauder's. It must be taken into account, however, that only one lobe was available for investigation in practically all our cases. Furthermore, the second subgroup (Table III) is almost certainly heterogeneous and may well include cases that should belong to the focal group, but with the lesion outside the material available for study. A history of head injury or infective process apt to lead to intracranial thrombophlebitis is common in this small subgroup, but is unusual in the Ammon's horn sclerosis group.

Recent experimental work, which has been reviewed in our previous publications already referred to, has shown that Ammon's horn may be of considerable importance as a general activator of brain function (Herrick, 1933 ; Green and Arduini, 1954), as part of the so-called visceral brain (MacLean, 1954) or as participating in the cerebral control of emotion and emotional expression (Papez, 1937 ; Bucy and Klüver, 1940). A lesion of Ammon's horn may thus, theoretically at least, be one of the direct factors underlying the automatic and emotional features of temporal lobe attacks.

Closer scrutiny reveals, however, some contradictions which it is difficult to resolve at present. Cadilhac (1955) and Passouant *et al.* (1955) have shown that powerful afterdischarges may be elicited on stimulation of Ammon's horn. G. Pampiglione and M. A. Falconer (1956, personal communication) have even been able to reproduce some features of the patient's psychomotor attacks by Ammon's horn stimulation before the temporal lobe was removed. On the other hand, Penfield and Jasper (1954) in man, and Gastaut (1953) in cats, have failed to obtain these responses, whereas both electrical and chemical stimulation of the amygdaloid complex and the periamygdaloid region can induce psychomotor attacks.

Some of our pathological findings seem to underline similar difficulties. It is seen in Table II that in most cases of our second group Ammon's horn sclerosis is associated with severe and often widespread lesions in other parts of the temporal lobe, thus rendering it difficult to decide which is the effective epileptogenic lesion. Even more striking is the virtual absence of Ammon's horn involvement in our focal group (Table I).

A final judgment on the causal relationship between Ammon's horn sclerosis and temporal lobe epilepsy must naturally be deferred until these uncertainties have been clarified by further clinico-pathological and experimental research. If there should be a positive correlation, it would be likely to be of a rather complex and indirect nature : a lesion of Ammon's horn, though not itself involved in the mechanisms of the attack, may " fire " the adjacent amygdaloid complex via pathways which are, at least anatomically, not yet known. Perhaps if MacLean's general concept of a balanced activity between Ammon's horn and the amygdaloid complex influencing the subcortical centres, and through them the cortex, contains an essential truth, then destruction or disorganization of one element by throwing the system out of equilibrium might be expected to disturb the stability of its hypothetical antagonist. It may be that temporal lobe seizures materialize only through this remote influence upon the hypothalamic centres, thalamic nuclei, reticular formation, and cingular cortex. One or the other of these possible indirect relationships may explain why the removal of Ammon's horn in some of our cases had a beneficial clinical effect on the epilepsy, even though this structure was histologically found to be normal.

Crome (1955) has drawn attention to yet another difficulty by pointing out that Ammon's horn sclerosis may be found in severely damaged brains of mental defectives who had shown no epileptic seizures during life. Morel and Wildi (1954), analysing the same question from another standpoint, have even arrived at the conclusion that there is a greater incidence of Ammon's horn lesions (not always the accepted form of typical Ammon's horn sclerosis) in non-epileptics (41%) than in epileptics (20.5%). Both groups of workers had to rely, however, upon the presence or absence of major epileptic attacks ; their studies were not restricted to clinically defined psychomotor epileptics. Morel and Wildi included all cases that had experienced one or more major convulsions. In the severely retarded mental defectives described by Crome it was naturally difficult to be sure that clinical features of seizures of temporal lobe type had not in fact been present. As Gastaut (1954) so convincingly points out, it is only in the psychomotor group that the association with Ammon's horn sclerosis becomes significant.

It is, of course, generally accepted that Ammon's horn sclerosis is not exclusively found in epileptic brains, but that it often occurs in anoxic conditions of all types. The question arises whether unilateral Ammon's horn sclerosis in an otherwise undamaged brain will invariably give rise to temporal lobe epilepsy. This question is difficult to answer at present.

If general experience in post-traumatic epilepsy may serve as a guide, the anatomical lesions cannot be regarded as the only factor responsible for the resultant focal epilepsy. The importance of a constitutional factor both in convulsions

generally and in temporal lobe epilepsy has recently been re-emphasized in Ounsted's (1955) preliminary report on his survey of epileptic children, but the point at which this would be operative is still obscure. It may be that Ammon's horn sclerosis or any other focal lesion in the temporal lobe would give rise to epilepsy only if additional factors were present. It is pertinent in this respect to observe that, even in animal experiments, during electrical or chemical stimulation of the medial centres of the temporal lobe it may be necessary sometimes, in order to produce temporal lobe attacks, to lower the animal's seizures threshold with small doses of leptazol.

Summary

Ammon's horn sclerosis has been encountered in resected temporal lobes of 19 out of 27 cases (70%) suffering from temporal lobe epilepsy. The mean age of onset of the epileptic history when Ammon's horn sclerosis was present lay at the fourth year of life, but in less than half of the cases only a history of birth trauma could be elicited. The association with a history of status epilepticus preceding the psychomotor seizures was encountered in at least 64% of these cases; this association was not encountered in those cases without Ammon's horn sclerosis.

The importance of the various pathogenetic mechanisms is discussed, particular stress being laid upon cerebral oedema as a major factor.

The association between Ammon's horn sclerosis and temporal lobe epilepsy is of considerable interest; although this relationship is not yet fully understood, it is probably not simple or direct. The possible mechanisms involved are briefly discussed in the light of recent conceptual developments concerning temporal lobe epilepsy.

We wish to thank Dr. Denis Hill, of the Department of Clinical Neurophysiology, and Mr. Murray Falconer, of the Guy's–Maudsley Neurosurgical Unit, and their associates for detailed clinical records of the cases studied in this series, to which we have had access.

REFERENCES

Alajouanine, T. (1954). *Colloque de Marseilles. Les lésions de l'épilepsie.* Acta Medica Belgica, Bruxelles.

Bini, L., and Callieri, B. (1955). *Recenti Progr. Med.*, **19**, 1.

Bridges, E. M. (1949). *Epilepsy and Convulsive Disorders in Childhood.* McGraw-Hill, New York.

Bucy, P. C., and Klüver, H. (1940). *Arch. Neurol. Psychiat. (Chicago)*, **44**, 1142.

Cadilhac, J. (1955). *Hippocampe et épilepsie.* Paul Dehan, Paris.

Crome, L. (1955). *Lancet*, **1**, 882.

Earle, K. M., Baldwin, M., and Penfield, W. (1953). *A.M.A. Arch. Neurol. Psychiat.*, **69**, 27.

Falconer, M. A., Hill, D., Meyer, A., Mitchell, W., and Pond, D. A. (1955). *Lancet*, **1**, 827.

Gastaut, H. (1953). *Epilepsia*, **2**, 29.

—— (1954). *Colloque de Marseilles. Les lésions de l'épilepsie.* Acta Medica Belgica, Bruxelles.

Green, J. D., and Arduini, A. A. (1954). *J. Neurophysiol.*, **17**, 533.

Herrick, C. J. (1933). *Proc. nat. Acad. Sci. (Wash.)*, **19**, 7.

Lindenberg, R. (1955). *J. Neuropath.*, **14**, 223.

McIlwain, H. (1955). *Biochemistry and the Central Nervous System.* Churchill, London.

MacLean, P. D. (1954). *J. Neurosurg.*, **11**, 29.

Martin, J. P. (1955). *British Medical Journal*, **2**, 467.

Meyer, A. (1954). *Colloque de Marseilles. Les lésions de l'épilepsie.* Acta Medica Belgica, Bruxelles.

—— and Beck, E. (1955). *Proc. roy. Soc. Med.*, **48**, 457.

Morel, F., and Wildi, E. (1954). *Colloque de Marseilles. Les lésions de l'épilepsie.* Acta Medica Belgica, Bruxelles.

Ounsted, C. (1955). *Eugen. Rev.*, **47**, 33.

Papez, J. W. (1937). *Arch. Neurol. Psychiat (Chicago)*, **38**, 725.

Passouant, P., Gros, C., van Bogaert, L., and Cadilhac, J. (1955). *Rev. neurol. (Paris)*, **92**, 96.

Penfield, W., and Jasper, H. (1954). *Epilepsy and the Functional Anatomy of the Human Brain.* Churchill, London.

Sano, K., and Malamud, N. (1953). *A.M.A. Arch. Neurol. Psychiat.*, **70**, 40.

Scholz, W. (1936). *Allg. Z. Psychiat.*, **104**, 589.

—— (1951). *Die Krampfschädigungen des Gehirns.* Springer, Berlin.

Stauder, K. H. (1935-6). *Arch. Psychiat. Nervenkr.*, **104**, 181.

Zimmerman, H. M. (1940). *J. Pediat.*, **13**, 859.

BENACTYZINE IN PSYCHONEUROSIS

A CONTROLLED CLINICAL TRIAL IN HOSPITAL PATIENTS

BY

C. P. SEAGER, M.B., B.Ch., D.P.M.
Senior Registrar

AND

A. LEITCH, M.D., D.P.M.
Consultant Psychiatrist

Barrow Hospital, near Bristol

Ross (1949) has commented at length on the difficulties inherent in the evaluation of the results of treatment where psychoneurotics are concerned. He was discussing the results obtained by the Weir Mitchell method, but the remarks he then made apply equally well to-day in the assessment of the new group of drugs named by Fabing (1955) the "ataractics," also described as "tranquillizing agents." These drugs are stated to relieve the tension and anxiety so often complained of by psychoneurotic patients, and have been used singly, in combination with each other, with psychotherapy, and with E.C.T.

Benactyzine is a new member of this group, and work has been done in Denmark to demonstrate its activity in "normalizing" the behaviour of disturbed experimental animals (Jacobsen and Sonne, 1955; Jacobsen and Skaarup, 1955) and also in relieving the symptoms of human patients (Munkvad, 1955; Jensen, 1955). The drug is pharmacologically a member of the anticholinergic group, with a mild atropine-like action, and its peripheral effects have been long established. Work on its central effects was first carried out in Denmark, and led to its trial clinically because of its activity in increasing the emotional threshold for external stressful influences and its ability to induce a blocking of thoughts, which suggested that it would be useful in cases where there is persistent rumination.

The series of cases so far published have included only one controlled trial (Raymond and Lucas, 1956) on psychiatric patients. Munkvad gave placebo tablets during his work with the drug, but points out that he was aware that the patient was on a placebo. It has been shown (Wolf and Pinsky, 1954) that it is very easy for the investigator to be led astray in spite of all his efforts at objectivity when this method is used. For this reason we have used the self-controlled, self-recorded clinical trial, which has proved its value on previous occasions (Hogben and Sim, 1953; Hare *et al.*, 1956).

Case Material

The patients studied were all in-patients of a neurosis unit which is organized for the treatment of acute non-psychotic illness. The usual duration of stay in the unit is from 4 to 12 weeks. The patients were all of average or above average intelligence and were fully co-operative in the trial. Patients were selected for the trial if anxiety and tension were prominent symptoms, and the diagnoses of the group were as follows: anxiety state 6, neurotic depression 7, obsessional state 2, hypochondriacal state 1.

Sixteen patients started the trial, but only 13 completed it. Of the three who failed to complete it, all were on benactyzine and gave up during the first period of the trial; two of these became worse clinically and it was considered advisable to stop the administration of the drug; one of