

recent memory and higher intellectual abilities, but compatible with no loss of employment status except in professional, executive, and similar occupations. Moderate impairment falls between the two above, and is usually associated with a drop in employment status.

Physical Disability.—This excludes purely ocular disabilities, and refers mainly to the consequences of weakness or other disturbances of the limbs. Those with C.N.S. signs are not included unless there is frank disability—which depends mainly on the severity of the signs and the nature of the patient's work.

Summary

Some results of a psychiatric study of 261 cases of subarachnoid haemorrhage are presented, dealing especially with comparisons between operative and conservative treatment of 209 patients with single aneurysms of the posterior communicating (P.C.), middle cerebral (M.C.), and anterior communicating (A.C.) arteries. The background and trial organization are briefly described.

Psychiatric morbidity is high. Of those with aneurysms in the trial comparisons 45% were regarded as unimpaired or nearly so; 24% were mildly, 18% moderately, 10% severely, and 3% very severely affected. Patients with no demonstrable aneurysms (30) had lower morbidity rates.

Most of the psychiatric and psychological morbidity is due to brain damage, but anxiety and depressive states also occur in the absence of such damage, and may be very severe.

Patients with M.C. aneurysms have a significantly higher morbidity with surgical than with conservative treatment, especially women with left-sided lesions. Possible reasons for this are mentioned. Patients with aneurysms at other sites do slightly but not significantly better with surgery.

A group of 13 patients with apparently improved personalities is described. This improvement is regarded as a leucotomy effect.

The incidence of epilepsy is 10% overall in patients with single aneurysms. No case of epilepsy occurred in those with A.C. aneurysms or with no demonstrable aneurysm. The rate was 24% in those with M.C. and 7% in those with P.C. aneurysms. There was no difference between operative and conservative treatment in this respect.

Several tables have had to be omitted to save space. Details will be sent on request.

I wish to express my gratitude to all those who made this study possible. The patients examined were under the care of Mr. Wylie McKissock, who originally suggested the study, Mr. A. E. Richardson, and Mr. L. S. Walsh, all of whom gave every help and much valuable advice. Professor Desmond Curran provided me with facilities and gave me encouragement. I have had essential statistical advice from Mr. P. M. Payne and Mr. H. Gwynne Jones; and there are many others, not named here, to whom I am also most grateful. Financial support for computer analysis was provided by St. George's Hospital Medical School.

REFERENCES

- Crawford, M. D., and Sarner, M. (1965). *Lancet*, 2, 1254.
 Crompton, M. R. (1962). *Ibid.*, 2, 421.
 Logue, V., Durward, M., Pratt, R. T. C., Piercy, M., and Nixon, W. B. L. (1967). *Brit. J. Psychiat.* In press.
 McKissock, W., Richardson, A., and Walsh, L. (1960). *Lancet*, 1, 1203.
 ——— (1962). *Ibid.*, 2, 417.
 ——— (1965). *Ibid.*, 1, 873.
 ——— and Walsh, L. (1956). *Brit. med. J.*, 2, 559.
 Norlen, G., and Barnum, H. S. (1953). *J. Neurosurg.*, 10, 634.
 Richardson, A. E., Jane, J. A., and Payne, P. M. (1964). *Ibid.*, 21, 266.
 ——— Yashon, D. (1966). *Arch. Neurol. (Chic.)*, 14, 172.
 Rose, F. C., and Sarner, M. (1965). *Brit. med. J.*, 1, 18.
 Walton, J. N. (1956). *Subarachnoid Haemorrhage*. Edinburgh.

Psychiatric Aspects of Pernicious Anaemia: A Prospective Controlled Investigation

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Brit. med. J., 1967, 3, 266-270

Though a wide spectrum of psychiatric symptoms has been attributed to vitamin-B₁₂ deficiency, the factors which predispose individuals to this form of illness rather than to haematological or neurological manifestations remain unknown. The frequency of mental symptoms in pernicious anaemia has not been established. Inquiries based on the retrospective analysis of general hospital case records have reported mental symptoms in only 2 to 4% of patients (Young, 1932; Cox, 1962), whereas in selected patients with chronic neurological disabilities the incidence of such symptoms has been as high as 60% (McAlpine, 1929; Holmes, 1956). No investigations to date have been carried out prospectively on unselected patients with pernicious anaemia admitted to general hospitals, and none have controlled the non-specific effects of physical illness and fatigue on the mental states of patients. Despite these uncertainties, interest in the psychiatric symptoms of pernicious

anaemia has been renewed and routine screening tests to detect latent pernicious anaemia have been advocated for all psychiatric patients (Strachan and Henderson, 1965; Hunter and Matthews, 1965).

The present investigations were carried out, firstly, to determine the incidence of psychiatric symptoms in patients with pernicious anaemia and, secondly, to evaluate the importance of vitamin-B₁₂ deficiency in their development. The method used was a comparison of the psychiatric symptoms in patients with pernicious anaemia and in a control series of patients with other types of anaemia, both groups being matched for age, sex, and haemoglobin level. It was predicted that if vitamin-B₁₂ deficiency caused mental symptoms, their incidence would be higher in the pernicious anaemia group and their remission would not occur until after treatment with vitamin B₁₂.

Selection of Patients

Pernicious Anaemia.—Patients with suspected pernicious anaemia were seen through the co-operation of physicians and

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haematologists, and treatment with vitamin B₁₂ was withheld until the first psychiatric interview had been completed. In many of the patients a definitive haematological diagnosis had not been established, and several patients were later transferred to the control series when complete investigations had shown a normoblastic type of anaemia. In this way some of the interviews were carried out blindly. Between 1963 and 1966 38 patients were referred as possible cases of pernicious anaemia and interviewed before treatment had begun. Of the 38 patients, 27 are described in this report—25 with Addisonian pernicious anaemia and two with post-gastrectomy intrinsic factor deficiency. Of the remaining patients, two were excluded because of uncertainty in the final diagnosis. Six were transferred to the control series, and three were rejected because of difficulties in examining the mental state on account of deafness, mental subnormality, and advanced physical deterioration.

Control Patients.—The criterion for admission to the control group was a presentation with symptoms of anaemia with little evidence of disabling primary disease. To avoid possible bias in the frequency of psychiatric symptoms in the control group, patients with the following types of anaemia were excluded: (1) anaemia associated with chronic infective and toxic conditions such as renal disease, ulcerative colitis, etc.; (2) anaemia of carcinomatosis and reticuloses; (3) acute haemorrhagic anaemia; (4) pregnancy anaemia; and (5) folate deficiency megaloblastic anaemia. Twenty-one control patients were examined, 18 with chronic iron-deficiency anaemia, two with primary hypoplastic anaemia, and one with a benign haemolytic anaemia.

Methods of Examination

The examination consisted of an interview, a psychological test for organic brain damage, and a personality questionnaire.

Interview.—Two or more interviews were carried out, the first before treatment, and the second early in treatment at the time of the maximum reticulocyte response. The length and structure of the interviews varied with the physical state of the patients. At every interview the mental state was formally examined for changes in affect, orientation, and intellectual function and for the presence of obsessional symptoms, hallucinations, and delusions. Most patients were well enough to allow a comprehensive history to be taken and when possible the interview was conducted in a private room.

Psychological Test.—The synonym learning test (S.L.T.), an auditory word-learning test, was administered to patients before and after treatment with vitamin B₁₂. This test contains a factor of short-term memory and has been validated and standardized on an elderly psychiatric population (Kendrick *et al.*, 1965; Kendrick, 1965). Patients of low intelligence may be misclassified as brain damaged on this test (Kendrick, 1964), and for this reason all the patients had their verbal intelligence assessed on the synonym section of the Mill Hill vocabulary scale Form I Senior (Raven, 1958).

Questionary.—After their mental state had returned to normal, patients were given the Maudsley personality inventory to complete. This questionnaire measures two dimensions, neuroticism (N) and extroversion (E) by means of a self-rating scale of 48 questions (Eysenck, 1959).

Assessment of Psychiatric Symptoms and Method of Rating

Some of the symptoms which occur in the psychoneuroses and in depression may also be found in patients with anaemia who have no psychiatric illness. In the present investigations, for example, fatigue and loss of weight were regarded as physical and not psychogenic in origin. The severity of the psychiatric symptoms was measured by the degree to which *psychiatric* symptoms had interfered with the normal habitual activities of the patient. In terms of social disability three

grades were defined: (1) mild, if disability occurred in one or more minor areas only—for example, recreation; (2) moderate, if working-time or efficiency had been appreciably diminished; and (3) severe, if unable to follow usual employment.

With this method of rating symptoms it was sometimes necessary to judge whether disability had been caused by psychiatric symptoms rather than by physical incapacity. In general it was possible to make this distinction, and when there was doubt the disability was not regarded as psychiatric.

Follow-up Study

Patients were asked to co-operate in a follow-up study after leaving hospital by a home visit, an outpatient appointment, or a postal questionnaire.

Results

Incidence and Severity of Psychiatric Symptoms

The psychiatric symptoms included depression, anxiety, loss of libido, irritability, poor concentration, and impaired memory. The only paranoid state encountered was in one of the control patients. Some psychiatric symptoms were present in 82% of the pernicious anaemia patients compared with 52% of the controls, the higher incidence in the former group reflecting symptoms rated as mild. Psychiatric symptoms rated as moderate or severe were present in approximately one-third of both groups of patients. Six of the patients with pernicious anaemia and three of the control patients had a moderate or severe depression.

Incidence and Severity of Psychiatric Symptoms

	Pernicious Anaemia Patients				Control Anaemic Patients			
	Mild	Mod.	Severe	Total	Mild	Mod.	Severe	Total
Normal ..				5				10
Depression ..	7	4	2	13	4	2	1	7
Memory impaired ..	4	1	2	7	1	1	1	3
Irritable ..	2			2				
Paranoid state							1	1
Total ..	13	5	4	27	5	3	3	21

Factors Predisposing to Psychiatric Symptoms

Physical.—In pernicious anaemia the presence or severity of the psychiatric symptoms did not correlate with age, duration of illness, physical complications of the illness, loss of weight, neurological involvement, haemoglobin level, or serum vitamin-B₁₂ levels.

Psychological.—The neuroticism score on the Maudsley personality inventory did not correlate with the presence of psychiatric symptoms. There was, however, a positive association between depressive symptoms in pernicious anaemia and a past history of depressive illness ($\chi^2=6.51$; $P<0.02$). Of the 13 depressed patients, seven had a personal or family history of depressive illness. Among the 14 patients who were not depressed, none had a history of previous depression.

Effect of Hospital Admission on Mental State of Patients

Early in this investigation it was observed that the psychiatric histories given by the pernicious anaemia patients did not correspond with their mental states shortly after admission to hospital. Eight of the patients reported that their mood had returned to normal shortly after or even before admission to hospital, and related this to the excellent prognosis received from their physicians. This tendency to spontaneous remission was well illustrated in the following case.

The patient, a 47-year-old policeman, had previously been in excellent physical and mental health. To siblings had a history

of depression, treated with electric convulsion treatment. For six months the patient had become increasingly concerned by unexplained fatigue. He lost his confidence and became unable to control traffic or meet people. He became deeply depressed with ideas of unworthiness. Suicidal thoughts were present and he was referred for a psychiatric opinion. A blood count showed the presence of a macrocytic anaemia. He was told the result of the test and was referred to a physician. For the next two weeks while he was on the waiting-list for admission to a medical ward his depression remitted completely. "I was better as soon as I knew that it was my blood and not my nerves, doctor." At the first psychiatric interview his mental state was completely normal except for impaired memory on the synonym-learning test.

In most of the control patients the cause of anaemia was unknown on admission and the prognosis was uncertain. Not surprisingly, fewer of the control anaemic patients showed spontaneous improvement after hospital admission.

Memory Impairment: The Synonym-learning Test

(Figs. 1 and 2)

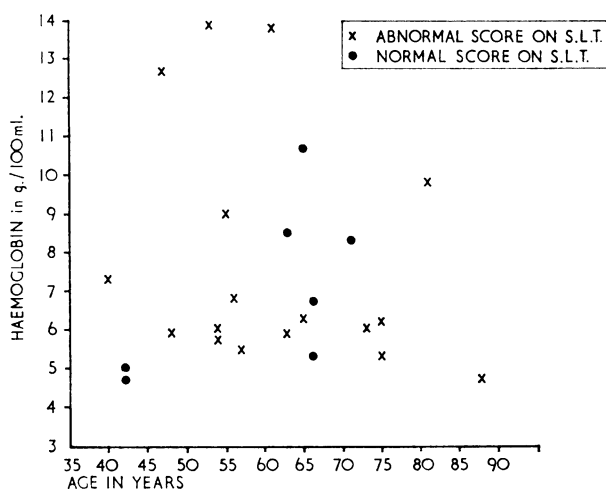
Of 24 pernicious anaemia patients, 17 showed abnormal short-term memory on the synonym-learning test, with scores

experienced until after the vitamin-B₁₂ treatment. None of the control patients, except two who had received large blood transfusions, were able to record a comparable feeling of well-being and alertness in the early phase of treatment.

On the Synonym-learning Test.—Twelve patients with brain-damage scores agreed to be retested, and nine of them were found to have a normal score early in treatment. After the first vitamin-B₁₂ injection the time for the synonym-learning test score to return to normal varied between 10 and 27 days, with a mean interval of 16 days. Serial testing in two patients revealed a considerable improvement on their synonym-learning test scores as early as 20 hours after the first injection. Three patients with persistently abnormal scores had clinical evidence of senile and arteriosclerotic dementia; and during the follow-up study two of them were found to have died after a stroke.

Follow-up Study

The results of a follow-up study one year after leaving hospital are incomplete, since only nine of the pernicious anaemia patients returned a postal questionnaire or attended for interview. Of this small number, three have relapsed with depres-



S.L.T. v. Age +0.09 (N.S.)
S.L.T. v. Haemoglobin +0.06 (N.S.)
Age v. Haemoglobin -0.10 (N.S.)
S.L.T. v. Haemoglobin: Age constant +0.05 (N.S.)
S.L.T. v. Age: Haemoglobin constant +0.10 (N.S.)

Using Kendall's τ (Siegel, 1956)

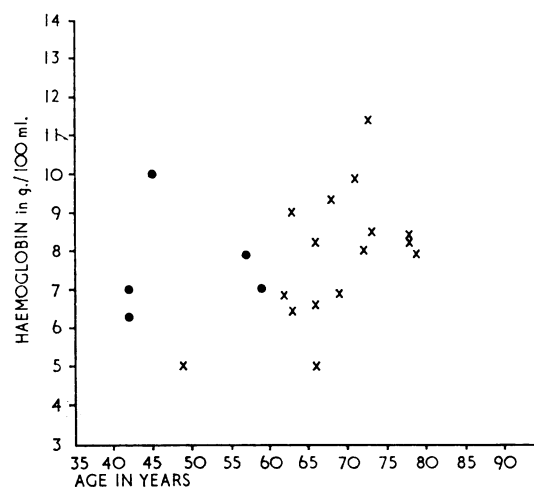


Figure 2
S.L.T. v. Age +0.44 (P < 0.01)
S.L.T. v. Haemoglobin +0.04 (N.S.)
Age v. Haemoglobin +0.28 (P < 0.05)
S.L.T. v. Haemoglobin: Age constant -0.12 (N.S.)
S.L.T. v. Age: Haemoglobin constant +0.44 (P < 0.01)

FIG. 1.—Relation between age, haemoglobin level, and performance on the synonym-learning test in pernicious anaemia.
FIG. 2.—Relation between age, haemoglobin level, and performance on the synonym-learning test in control anaemic patients.

in the range (0-53) associated with brain damage. In pernicious anaemia a brain-damage score was not related either to age or to haemoglobin level. Of the 21 control patients, 16 also had brain-damage scores on this test, but in this group there was a positive correlation between advanced age and an increasingly abnormal score (+0.44; $P < 0.01$ Kendall's τ ; Siegel, 1956).

Effects of Vitamin B₁₂

On the Mental State.—At the second psychiatric interview 10 of the patients declared that they were more cheerful and were taking a new interest in ward activities and conversations. Confirmation of this improvement was sought whenever possible by an interview with the sister and resident doctor in charge of the ward. Nevertheless, it proved difficult to assess whether these changes in mood were the continuation of a previously noted spontaneous remission, the effects of the vitamin-B₁₂ injections, or a combination of both. Fourteen patients reported an increased well-being and mental alertness which they had not

sive symptoms despite regular vitamin-B₁₂ injections and the maintenance of normal blood values. One other patient has required admission to a psychiatric unit for management of his depression with electric convulsion treatment.

Discussion

In pernicious anaemia the accompanying psychiatric symptoms do not necessarily have a uniform relation to vitamin-B₁₂ deficiency. The present investigation has suggested that the main syndromes encountered—depression and memory impairment—have a different origin and significance.

Depression in Pernicious Anaemia

Klerman (1966), in a review of antidepressant drugs, has commented on the frequency of depressive symptoms in conjunction with acute and chronic physical illness. Psychiatric studies in general medical wards have reported that 20% of

the patients developed a clinical depression after the onset of an illness likely to be fatal or severely disabling (Helsborg, 1958; Stewart *et al.*, 1965). If minor neurotic symptoms had been included the frequency of depressive reactions would have been higher. The results of the present investigations in which 6 out of 27 pernicious anaemia patients and 3 out of 21 control patients developed a moderate or severe depression are consistent with these previous studies.

Patients attributed their depression to the consequences of their physical handicap. It is of interest that after they had received a favourable prognosis many of the pernicious anaemia patients showed a spontaneous remission of depressive symptoms before treatment with vitamin B₁₂. Had this investigation been carried out retrospectively these remissions might have been attributed to the effect of specific therapy with vitamin B₁₂. Because there were patients in both groups who did not develop psychiatric symptoms or in whom such symptoms were mild despite severe physical incapacity, personality characteristics and constitutional factors may have been decisive in determining the appearance of psychiatric sequelae. Evidence that those who developed depressive symptoms were constitutionally vulnerable was indicated by their high incidence of previous depressive reactions, and by a tendency to relapse after discharge from hospital.

In summary, the evidence relating to vitamin-B₁₂ deficiency and depressive illness is tenuous. Depressive symptoms are not more common in pernicious anaemia than in other types of disabling physical illness. When depression accompanies pernicious anaemia it would appear to be related less to the direct effect of vitamin-B₁₂ deficiency than to the uncovering of a constitutional predisposition to depressive illness precipitated by the anxiety of unexplained fatigue and physical incapacity.

Loss of Memory and Pernicious Anaemia

In pernicious anaemia a short-term loss of memory has been demonstrated on the synonym-learning test. In contrast with the control series this memory impairment was independent of age or anaemia. Memory changes may occur in depression, but few of the patients were clinically depressed at the time of testing. After receiving vitamin B₁₂ many patients experienced a rapid sense of well-being and mental alertness. The cellular effects of vitamin B₁₂ can be observed after a few hours without implicating placebo-responders. Cells in the bone marrow begin to revert to normoblastic type after nine hours, and in bone-marrow cultures the R.N.A./D.N.A. ratio in the cell returns completely to normal within 24 to 48 hours (Thomas and Lochte, 1958). After one week electroencephalographic abnormalities begin to improve (Samson *et al.*, 1952; Walton *et al.*, 1954) and cerebral oxygen consumption shows a moderate increase (Scheinberg, 1951). The earliest changes in the synonym-learning test were observed after 20 hours; in nine patients a reversion to completely normal scores on this test took on average 16 days. Parallel electroencephalograms would have been interesting, but facilities for this were not available.

Did the nine patients with reversible synonym-learning test scores after vitamin B₁₂ have a mild dysmnesic syndrome, and if untreated could this have proceeded to an established dementia? Recent evidence suggests a hypothetical, biochemical, and pathological basis for memory disturbances in pernicious anaemia. Vitamin B₁₂ has been implicated in the enzymatic incorporation of amino-acids into proteins (Neill and Weaver, 1958) and in the synthesis of R.N.A. (Nieweg *et al.*, 1952). Memory may be encoded and preserved in the molecular structure of certain nucleic acids, including R.N.A. (Dingman and Sporn, 1961). Intact hippocampal and mammillary zones are essential for the process of remembering (Brierley, 1961), and damage to those areas has been described in pernicious anaemia (Ferraro *et al.*, 1945).

Misdiagnosis of Psychiatric Illness in Pernicious Anaemia

In both the anaemic and vitamin-B₁₂-deficient patients physical fatigue was the most common symptom encountered, and was frequently the initial symptom. In several patients this unexplained fatigue had resulted in psychiatric referral as cases of neurosis or neurasthenia. One patient with an earlier history of difficulty in swallowing associated with a Plummer-Vinson syndrome had been referred as a case of hysteria.

Vitamin-B₁₂ Deficiency as a Cause of Psychiatric Illness

Studies of serum vitamin-B₁₂ levels in mental hospital patients have indicated some of the difficulties which exist in attributing the psychiatric illness to vitamin-B₁₂ deficiency (Edwin *et al.*, 1965; Hansen *et al.*, 1966; Shulman, 1967a, 1967b). In a survey of 1,012 psychiatric patients 0.88% were found to have pernicious anaemia (Henderson *et al.*, 1966). This is no higher than the incidence of pernicious anaemia in a normal population. Latent pernicious anaemia is present in 5 to 6% of patients with iron-deficiency anaemia (Beveridge *et al.*, 1965; Dagg *et al.*, 1966). From epidemiological data on the incidence of iron-deficiency anaemia (Kilpatrick, 1961) the normal incidence of pernicious anaemia is 0.5%, rising to 1% over the age of 65. The results of the present investigation have suggested that except in the organic psychoses there is little evidence to support the mass screening of psychiatric patients for vitamin-B₁₂ deficiency. Even when dementia occurs in pernicious anaemia it is often impossible to exclude a coincidental arteriosclerotic or senile dementia, as in three of the patients in the present report.

It is concluded that psychiatrists should be alert to the possibility of vitamin-B₁₂ deficiency in three situations: patients thought to be at risk clinically—for example, anaemic or post-gastrectomy patients, patients with unexplained fatigue, and patients with confusional states or dementia of unknown origin.

Summary

The psychiatric status of 27 patients with pernicious anaemia and 21 control anaemic patients is described. Approximately one-third of both groups had psychiatric symptoms rated as moderate or severe.

Before treatment the most frequent symptoms were depression and memory impairment. Of the psychiatric symptoms encountered only memory impairment appeared to be related to vitamin-B₁₂ deficiency. The role of vitamin-B₁₂ deficiency in the production of mental symptoms is reviewed. Except for research purposes there is no evidence to support the routine screening of psychiatric patients for pernicious anaemia.

I am grateful to the many physicians and haematologists who co-operated in this investigation, and would especially like to thank Dr. L. Bernstock, consultant clinical pathologist, St. Helier Hospital, for continued interest and encouragement; Dr. C. K. Kendrick for instruction in the use of the synonym-learning test; and Mr. W. I. Hume for assistance with the statistical analysis.

Part of this investigation was submitted as a dissertation for the Academic Postgraduate Diploma in Psychological Medicine, University of London, 1964.

REFERENCES

- Beveridge, B. R., Bannerman, R. M., Evanson, J. M., and Witts, L. J. (1965). *Quart. J. Med.*, **34**, 145.
 Brierley, J. B. (1961). *Geront. clin. (Basel)*, **3**, 97.
 Cox, E. V. (1962). In *Vitamin B₁₂ and Intrinsic Factor*, edited by H. C. Heinrich, p. 590. Stuttgart.
 Dagg, J. H., Goldberg, A., Gibbs, W. N., and Anderson, J. R. (1966). *Brit. med. J.*, **2**, 619.

- Dingman, W., and Sporn, M. B. (1961). *J. psychiat. Res.*, **1**, 1.
 Edwin, E., Holten, K., Norvum, K. R., Schrupf, A., and Skaug, O. E. (1965). *Acta med. scand.*, **177**, 689.
 Eysenck, H. J. (1959). *Manual of the Maudsley Personality Inventory*. London.
 Ferraro, A., Arieti, S., and English, W. H. (1945). *J. Neuropath. exp. Neurol.*, **4**, 217.
 Hansen, T., Rafaelsen, Ole J., and Rødbro, P. (1966). *Lancet*, **2**, 965.
 Helsing, H. C. (1958). *Acta psychiat. scand.*, **33**, 303.
 Henderson, J. G., Strachan, R. W., Swanson Beck, J., Dawson, A. A., and Daniel, M. (1966). *Lancet*, **2**, 809.
 Holmes, J. MacD. (1956). *Brit. med. J.*, **2**, 1394.
 Hunter, R., and Matthews, D. M. (1965). *Lancet*, **2**, 738.
 Kendrick, D. C. (1964). *Psychol. Rep.*, **15**, 188.
 — (1965). *Brit. J. Soc. clin. Psychol.*, **4**, 141.
 — Parboosingh, R., and Post, F. (1965). *Ibid.*, **4**, 63.
 Kilpatrick, G. S. (1961). *Brit. med. J.*, **2**, 1736.
 Klerman, G. L. (1966). *Int. J. Psychiat.*, **2**, 73.
 McAlpine, D. (1929). *Lancet*, **2**, 643.
 Neill, D. W., and Weaver, J. A. (1958). *Brit. J. Haemat.*, **4**, 447.
 Nieweg, H. O., Van Buchem, F. S. P., and Kroese, W. F. S. (1952). *Acta med. scand.*, **142**, 45.
 Raven, J. C. (1958). *Guide to Using the Mill Hill Vocabulary Scale with the Progressive Matrices Scales*. London.
 Samson, D. C., Swisher, S. N., Christian, R. M., and Engel, G. L. (1952). *Arch. intern. Med.*, **90**, 4.
 Scheinberg, P. (1951). *Blood*, **6**, 213.
 Shulman, R. (1967a). *Brit. J. Psychiat.*, **113**, 241.
 — (1967b). *Ibid.*, **113**, 252.
 Siegel, S. (1956). *Non-Parametric Statistics: For the Behavioural Sciences*. New York.
 Stewart, M. A., Drake, F., and Winokur, G. (1965). *Dis. nerv. Syst.*, **26**, 479.
 Strachan, R. W., and Henderson, J. G. (1965). *Quart. J. Med.*, **34**, 303.
 Thomas, E. D., and Lochte, H. L. (1958). *J. clin. Invest.*, **37**, 166.
 Walton, J. N., Kiloh, L. G., Osselton, J. W., and Farrall, J. (1954). *Electroenceph. clin. Neurophysiol.*, **6**, 45.
 Young, R. H. (1932). *J. Amer. med. Ass.*, **99**, 612.

Stenosis and Occlusion of Vessels in Cerebral Infarction

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Brit. med. J., 1967, **3**, 270-274

The contribution of cerebral vascular disease to the morbidity and mortality of an ageing population has led to a notable increase in studies of the condition in many branches of medicine. Stenosis and occlusion of the extracranial part of the cerebral blood supply has been the subject of several pathological studies (Hutchinson and Yates, 1957; Duffy and Jacobs, 1958; Martin *et al.*, 1960; McGee *et al.*, 1962). Schwartz and Mitchell (1961) reported on the results of a study of the neck vessels in 93 unselected necropsies. They showed that atheroma of the neck vessels increased with age in all patients and that stenosis of severe degree may occur without evidence of cerebral infarction. On their findings they accepted a direct relation between thrombotic occlusion of neck vessels and cerebral infarction but felt that the significance of stenosis in this context was uncertain.

This communication concerns part of a study of the pathology of cerebral infarction and reports the prevalence of stenosis and occlusion of the cerebral arteries in a series of patients with cerebral infarction and compares these findings with an unselected series of patients who died of unrelated causes.

Material and Methods

The material for the study was obtained from 145 necropsies performed at the North Staffordshire Royal Infirmary. During the time of the investigation all 57 cases found to have a cerebral infarct were included in the infarct group. Cases of emboli obviously arising from the heart and cases of paradoxical embolism were excluded. The control group consisted of 88 cases where there was no evidence of cerebral infarction and the age at death was over 45. No deliberate selection was made, but as it was not always possible to remove the cervical spine in a particular case coming to necropsy the cases were not consecutive.

The brain was removed and fixed in 10% formalin in the routine manner. The arch of the aorta was divided above the

aortic valve at the level of the third dorsal vertebra; the subclavian arteries were divided beyond the origin of the vertebral arteries and the major vessels were then mobilized. After sectioning the cervical spine at the level of the seventh cervical vertebra a saw cut was made through the base of the skull on a line which ran through the anterior, middle, and posterior fossae on both sides. This provided a specimen containing the aorta and the neck vessels throughout their entire course. The carotid arteries were then exposed in the carotid canal with bone forceps. After examination of the arch of the aorta, the innominate artery, the common and internal carotid arteries, the subclavian artery, and the extravertebral part of the vertebral artery were examined by transverse section at 1-cm. intervals throughout their course. The cervical spine was decalcified with 10% hydrochloric acid and after three weeks the vertebral portion of the vertebral artery was exposed and examined.

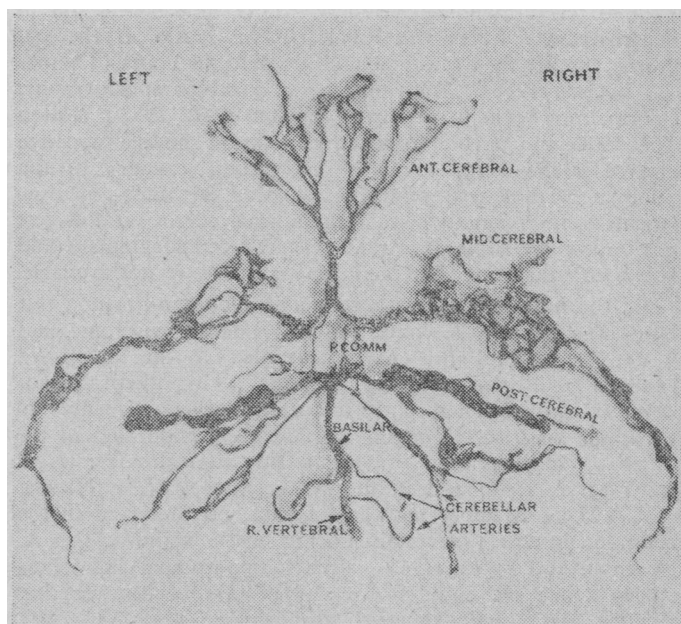


FIG. 1.—Specimen showing the intracranial vessels dissected from the brain preparatory to examination for stenosis and occlusion.

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Dr. Battacharji was awarded the Ph.D. at the University of Birmingham for a thesis entitled "The Role of Extracranial and Intracranial Arteries in Cerebral Infarction."