Clinicopathological Conference

Two neurological cases

DEMONSTRATION AT THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

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The quarterly clinicopathological conference was held at the Royal College of Physicians on 27 July 1978 with Professor W B Matthews (1) in the chair. The first case was presented by Dr Nigel Hyman (2).

First case—clinical summary

DR HYMAN: This patient was a 66-year-old retired army officer who complained of episodic loss of vision in the right eye in the two weeks before his outpatient appointment in December 1976. There was complete loss of vision which occurred up to three times a day. He said it was like a curtain going across the visual field of his right eye from right to left over a few seconds: vision was lost for up to an hour. For four weeks he had also had a constant occipital headache, which, although severe enough to keep him awake, was not exacerbated by straining or coughing.

His medical history showed mild diabetes diagnosed six years before and he was on a restricted carbohydrate diet. In 1970 he had had palpitations, and an electrocardiogram (ECG) had shown ventricular extrasystoles. He also had gout and took phenylbutazone when necessary. On examination he was obese.

His corrected visual acuities were 6/9 in the right eye and 6/5 in the left. His visual fields were normal and fundoscopy showed nothing abnormal. There were no carotid bruits but he had a soft basal systolic murmur. His blood pressure was 120/70 mm Hg on the right and 110/60 mm Hg on the left. Neurological examination showed no abnormalities. The erythrocyte sedimentation rate (ESR) was 31 mm in the first hour (Westergren); ECG showed ventricular extrasystoles; the echocardiogram was normal apart from some thickening of aortic valve cusps; a right carotid angiogram (direct puncture technique) showed irregularity of the artery near the bifurcation and tortuosity within the carotid siphon (fig 1). While he was in hospital his attacks of blindness stopped spontaneously and he went home taking no treatment. His headaches had also stopped. He was advised to take aspirin if necessary.

He was readmitted as an emergency four months later with unsteadiness on his feet and a week's history of double vision. For 24 hours he had had severe headache and loud noises in his head. On the morning of admission his speech was slurred. He had a headache and was dysphagic. He was alert but dysarthric with horizontal nystagmus to the right on right lateral gaze. His pupils were small but reacted to light. He had partial left ptosis and absent gag reflex. His uvula deviated to the left and his tongue deviated to the right. He had sensory loss to pinprick over his right face and minimal finger-nose incoordination with the left arm. His blood pressure was 130/60 mm Hg and his ESR 33 mm in the first hour. The next morning his breathing

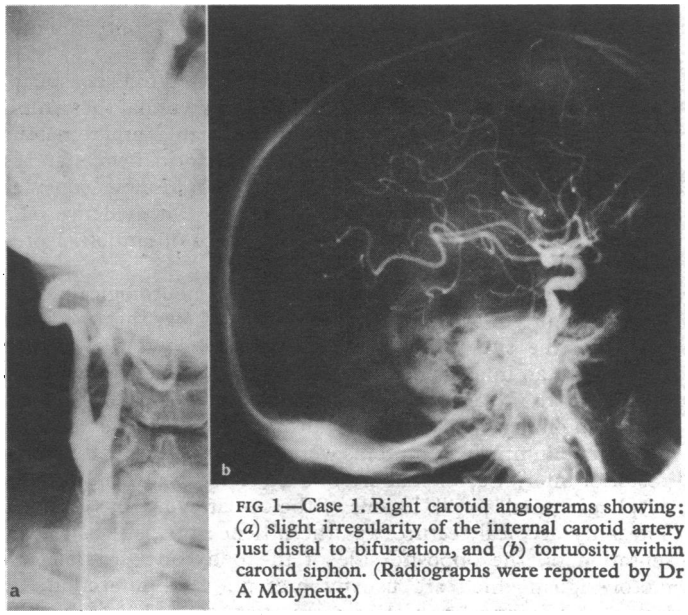

FIG 1—Case 1. Right carotid angiograms showing: (*a*) slight irregularity of the internal carotid artery just distal to bifurcation, and (*b*) tortuosity within carotid siphon. (Radiographs were reported by Dr A Molyneux.)

stopped and he died. The whole neurological disease thus lasted about five months.

PROFESSOR MATTHEWS: Does anyone wish to ask any questions?

MEMBER OF AUDIENCE: What about this patient's smoking?

DR HYMAN: He did not smoke cigarettes.

Diagnosis

PROFESSOR MATTHEWS: I now call on Sir Roger Bannister to discuss this case.

SIR ROGER BANNISTER (3): Firstly, I looked on this as a problem of transient visual obscuration. The fact that the attacks were confined to the right eye, were stereotyped, and occurred two or three times a day for two weeks implies a disturbance of flow in the right retinal circulation. The problem is whether this was due to embolism, spasm, or insufficiency of flow. The fact that there were no abnormalities on fundoscopy and that the attacks were stereotyped makes emboli less likely, although platelet emboli might do this. Spasm used to be a subject of dispute but it sometimes occurs with migraine. We have no reason to think that this man had migraine. I think the pattern suggests insufficiency with some reversible disturbance of flow.

Headache in a man of 66 could be due to cranial arteritis. This is associated with arterial insufficiency and not always with temporal arterial lesions. But the insufficiency (and the blindness) miraculously disappeared without treatment. The ESRs were

31 and 33 mm in the first hour, and that is hardly in the range for cranial arteritis. But we cannot forget about it as a possible condition.

The patient was a diabetic so he may have had atheroma. He had ventricular ectopic beats, which seem to have been from different foci, and one must consider intermittent arrhythmias. Some of the first cases of unilateral visual obscuration were the result of paroxysmal fibrillation, which lowers the blood pressure and might, with added distal atheromatous lesions, cause this type of attack. The blood pressure was a little lower in the left arm. So I am obviously thinking of proximal extracranial stenotic disease. There was no carotid bruit. In any case which ends like this with a brain stem infarct we must consider subclavian stenosis and a "steal" syndome. But we have no further support for this. So we cannot get any further as to the site of vascular lesions. As a neurologist I cannot attach much significance to the thickened aortic cusps. I am looking for some cardiac lesion which would give a low blood pressure or low output which, in association with lesions of the carotid artery such as kinking and tortuosity in the syphon, might have contributed to the early part of the story.

The remission was surprising. He was advised to take aspirin, an innocuous treatment, when it had been shown that the carotid angiogram excluded any surgically remediable atheromatous lesion. To be haemodynamically important on its own, stenosis has to be more than 50-60%. But we would now consider exploration even if there were less stenosis but evidence of a plaque or irregularity that might be a source of emboli. I presume that no firm diagnosis was made then.

He was admitted finally with an acute neurological event after intermittent symptoms, which make it clear that the brain stem was the site of the threatened blood flow; the episode ended with an infarction, clearly due to occlusion of the vessels supplying the lateral part of the medulla—the well-known lateral medullary infarction syndrome affecting the medulla and cerebellum. The symptoms were almost classically those of a posterior inferior cerebellar artery occlusion: dysarthria, vertigo, dysphagia, small pupil, lesions of the ocular sympathetic fibres. The only atypical feature was the absence of disturbances of sensation on the opposite side of the body and contralateral motor signs, which are usually present. This infarction, by virtue of affecting brain stem respiratory control, was fatal.

I conclude that this was an unusual case of cerebrovascular disease. Some usual features were absent. He was not hypertensive; atheroma was not widely shown; there was no obvious cardiac lesion or silent infarction. I therefore return to the raised ESR, fluctuating lesions in more than one vessel, and the tortuosity. Tortuosity of this degree, which is like an ox-bow lake type of tortuosity, has been said to be haemodynamically important if it occurs in association with abnormalities in the siphon. The position and rotation of the head may affect it. That may have been haemodynamically important and there may have been an arteritic process, although there was only partial evidence for it and it appears to have fluctuated.

PROFESSOR MATTHEWS: Thank you for a very thorough analysis. Dr Trevor Hughes, will you tell us what you found?

PATHOLOGICAL FINDINGS

DR HUGHES (4): At necropsy the lungs showed congestion and early bronchopneumonia. There was moderate atheroma of the aorta and large arteries. The aortic valve was moderately rigid due to calcification. The heart was somewhat dilated and there was some greyness of the myocardium. The slight coronary atheroma seemed out of proportion to the well-marked myocardial fibrosis.

In histological sections there was some thrombosis within the coronary arteries but this was not obviously associated with atheroma. There was also a perivascular inflammatory exudate, mainly of plasma cells and lymphocytes. The cerebellum, brain stem, and cerebrum looked normal in the fresh state and after formalin fixation, but a section of the medulla showed acute infarction, with shrunken ischaemic neurones. The left vertebral artery at the foramen magnum was occluded by thrombus, which was partly organised (fig 2). The inflammatory reaction was related to the tunica media, which in a nearby artery (fig 3) showed degeneration of the tunica elastica and a line of multinucleate giant cells. The right vertebral artery was also thrombosed above the foramen magnum, with similar histological features. This giant cell arteritis was generalised but most severe in the vertebral arteries.

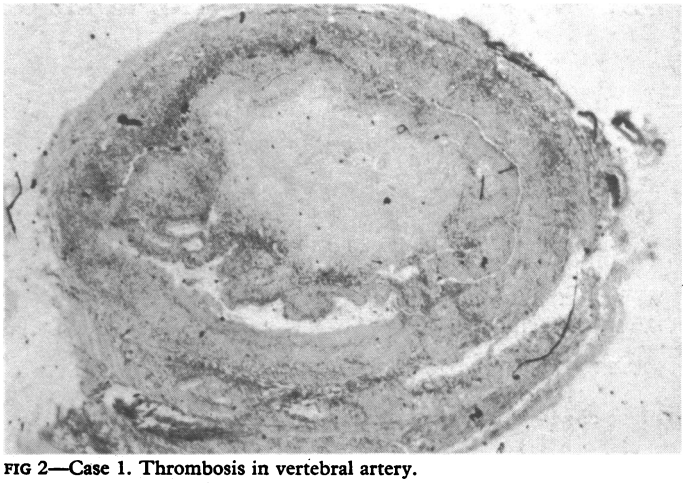

FIG 2—Case 1. Thrombosis in vertebral artery.

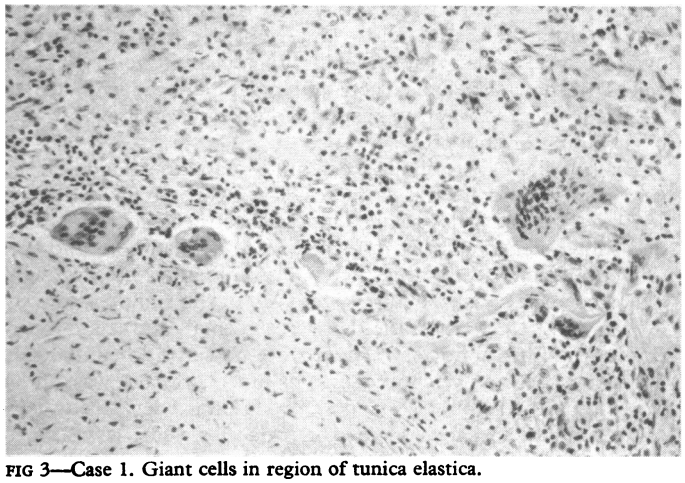

FIG 3—Case 1. Giant cells in region of tunica elastica.

PROFESSOR MATTHEWS: If we consider the original symptoms, was the carotid artery affected?

DR HUGHES: Sections showed a similar inflammation but not as florid a picture as in the vertebral arteries.

SIR ROGER BANNISTER: One is always going back to recall unusual cases. I have diagnosed temporal arteritis with an ESR under 50 and negative biopsy findings—which is not unusual. The lesson is that in any patient with unexplained fluctuations in cerebral blood flow cranial arteritis must be the presumed diagnosis. If this man had been treated with a trial of steroids he might well not have died.

Possible treatment and causes

MEMBER OF AUDIENCE: Would steroids really have helped? The condition was pretty advanced.

SIR ROGER BANNISTER: They do not reverse the process

quickly, but if patients who have impaired vision are given 100 mg of prednisone a day the condition may not spread further. Steroids may have to be given for a year, the dose being reduced slowly according to the ESR.

DR PYKE (5): Were there any changes in the ophthalmic arteries?

DR HUGHES: I'm afraid they were not examined.

MEMBER OF AUDIENCE: Could we be brought up to date on the cause of giant cell arteritis? Is there anything in the idea that it is due to hypersensitivity to birds, the patients being pigeon fanciers or having some other contact?

SIR ROGER BANNISTER: Usually there is some preceding illness, which has been called polymyalgia rheumatica. I have always assumed that it was of unknown cause but had some relationship to autoimmune disease.

PROFESSOR MATTHEWS: I'm not really keen on the bird sensitivity theory.

MEMBER OF AUDIENCE: We had a patient with an abdominal aneurysm with many obscure neurological problems. She had an ESR of 80 mm in the first hour so we were confident she had giant cell arteritis. The pathological findings at necropsy were entirely degenerative.

PROFESSOR MATTHEWS: Our case is unusual in that the retinal vessels were clear and only the larger arteries in the neck were affected; this explains the transient symptoms without occlusion.

MEMBER OF AUDIENCE: When Dr Hawley and myself wrote a paper on temporal arteritis we found no patients aged under 60; even now we've not seen it under 55. In itself this is rather odd and suggests that the bird fancier theory is not right. The relationship with polymyalgia rheumatica which we suggested at that time is now generally accepted. There may be quite acute shifts in the symptoms. Has anyone seen a true case under the age of 55?

MEMBER OF AUDIENCE: Can I take up the question of steroids in slowing down or preventing progression? The visual attacks and headaches got better. Would anyone really have put him on to steroids? If so for how long and what would one be treating?

PROFESSOR MATTHEWS: I would have put him on steroids if I had known the diagnosis, to prevent him from going blind.

SIR ROGER BANNISTER: When the symptoms remitted the ESR was over 30 mm in the first hour. If there was no other adequate explanation for the symptoms I would have given steroids and the ESR would have dropped to 15 mm and I would have thought he had temporal arteritis and continued for a couple of months using the ESR to guide me.

Second case—clinical summary

DR HYMAN: This patient was a 66-year-old right-handed white woman, who was admitted in July 1975. Nine weeks earlier she had developed red, watering eyes. She was thought to have haemorrhagic conjunctivitis and her eye symptoms responded to chloromycetin. After that she had aches and pains in her arms and legs and her vision gradually deteriorated. In the three weeks before admission her vision deteriorated more rapidly: she thought she was almost blind. In addition she could not dress or feed herself.

She had been born in India and lived there until 1947. She had spent several years in Greece and Malta and then in Oxfordshire. She smoked heavily, admitted to drinking four whiskies a day, and came into the ward heavily armed with whisky.

She had been taking thyroxin tablets for years (for no clear reason) and had had tricyclic drugs for depression. For about two years she had had symptoms suggestive of renal colic and complained of excessive thirst and constipation.

She was obese and did not look ill. General examination showed no abnormalities, but neurological examination showed pink optic discs without definite papilloedema. Her visual acuity was reduced to finger counting and, although this made visual field assessment difficult, she had a left homonymous hemianopia. The pupils reacted to light but there was failure of conjugate upward gaze. There was no motor weakness or reflex abnormality, but sensory inattention was detected on the left side. Attempts to copy shapes confirmed the left-sided inattention. Her speech was normal. She was orientated but had impaired delayed recall of verbal material.

Her ESR was 8 mm in the first hour (Westergren); blood count normal; Wassermann reaction negative; and chest and skull radiographs normal. Blood values were normal except that the serum calcium concentration was persistently about 12·5 mg/100 ml (3·1 mmol/l) and went as high as 18·3 mg/100 ml (4·6 mmol/l). The phosphate concentration varied from 2·5 to 3·0 mg/100 ml. She was investigated as a case of primary hyperparathyroidism but the results, which were inconclusive, were not, we think, relevant to her underlying neurological condition. The blood urea value on admission was 24 mg/100 ml (4·0 mmol/l). Her intravenous pyelogram, isotope brain scan, thyroid and liver function tests were normal. Her electroencephalogram (EEG) showed bursts of diffuse delta activity, bilateral and maximal in the frontal and temporal areas (fig 4). On the air encephalogram there was moderately severe diffuse cerebral and cerebellar atrophy. The cerebrospinal fluid obtained then was normal.

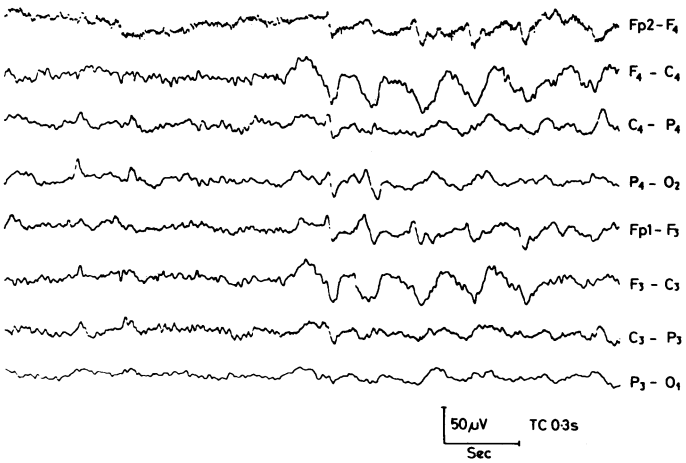

FIG 4—Case 2. EEG on admission.

She became increasingly drowsy and two weeks after admission developed myoclonus in her left arm, which became weak and hypertonic.

PROFESSOR MATTHEWS: The calcium abnormalities were an additional red herring and were never properly explained.

MEMBER OF AUDIENCE: I find it difficult that the alarming calcium concentration can remain unexplained. What was the parathyroid hormone concentration?

DR HYMAN: 0·74 ng/ml; up to 0·9 ng/ml is normal.

MEMBER OF AUDIENCE: The skeletal survey was normal?

DR HYMAN: Yes.

MEMBER OF AUDIENCE: What sort of assay was done? In the presence of high serum calcium concentrations that level of parathyroid hormone is abnormal.

PROFESSOR MATTHEWS: We were guided by our metabolic colleagues.

PROFESSOR MILNE (6): The main risk of such a large serum calcium concentration is rapidly deteriorating renal failure. Could we be told whether the blood urea concentration remained normal?

DR HYMAN: The blood urea did not rise above the upper limit of normal.

MEMBER OF AUDIENCE: Could cerebral sarcoidosis cause something like this?

PROFESSOR MATTHEWS: Certainly it could. There is also a paper in the *Revue Neurologique* describing hemaniopia as a presenting symptom of hypercalcaemia resulting from taking calciferol.[1]

MEMBER OF AUDIENCE: The chest radiograph was said to be normal; but in a long-term illness an investigation is sometimes not repeated. Was the *x*-ray examination repeated? From the case history you might be tempted to believe that the abnormal calcium and cerebral dysfunction were both due to carcinoma of the bronchus.

DR HYMAN: The chest *x*-ray film was not repeated. Her deterioration was in fact very rapid.

Diagnosis

PROFESSOR MATTHEWS: Would you like to comment, Sir Roger?

SIR ROGER BANNISTER: Naturally I got excited about the calcium values and thought about parathyroid disturbance. But I took their lack of explanation at its face value and went back to consider the neurological implications of the history.

I could not make much of the illness nine weeks before admission. One naturally suspects the birth in India might indicate exotic rare disease, such as tropical or parasitic diseases with neurological effects, but I rejected all these and thought that we should start with a woman who had unexplained bilateral visual deterioration. She was fond of whisky and smoked a lot. Bilateral deterioration at this rate must have been central scotomata, and toxic causes, such as alcoholic amblyopia, must be considered. But quite quickly we get on to the physical findings. The disc appearances were a little surprising—with such impaired visual acuity they did not show pallor. They were not swollen so there is no evidence of an arteritic process or raised intracranial pressure—which would not in any case give visual deterioration of this kind. It is very difficult to test visual fields with this degree of acuity but I accept the homonymous hemianopia. Defects of upward gaze are interesting, indicating lesions in the upper midbrain. There were no pupillary defects to go with that, to suggest a lesion in the region of the pineal gland. The left sensory inattention puts us in the right parietal lobe, and this agrees with the homonymous hemianopia. The inability to draw supports the non-dominant hemisphere lesion.

Was there anything to suggest a dominant hemisphere lesion? There was dyscalculia, a feature of Gerstmann syndrome, a left angular gyrus lesion, the other features being right-left disorientation (which she had), finger agnosia, and agraphia. All this means is that we have secure evidence of bilateral damage. The memory impairment adds to that. So how many lesions were there? There were bilateral optic nerve lesions, a right hemisphere parieto-occipital lesion, a left angular gyrus lesion, and perhaps bilateral temporal or frontal lesions; to these there may have been added some further neurological deficit. The result which interests me most, if the calcium problems are not relevant, is the EEG showing bursts of delta activity, which confirms the bilateral and widespread nature of the process. The technetium scan was normal, so that there was no neoplastic process. Then we have the final illness with myoclonus. Was this noise-sensitive myoclonus, jerking with loud noises?

DR HYMAN: Noise certainly exacerbated it.

SIR ROGER BANNISTER: My conclusion is that this patient had progressive subacutely advancing and ultimately fatal generalised brain damage. In view of the onset with visual impairment, it probably affected white matter more than grey matter. This puts us into a group of diseases, much written about and in a state of flux regarding classification, which includes both non-viral and viral diseases. Some of the non-viral ones are being pushed into the viral category as techniques of brain biopsy get more advanced. The non-viral ones that crossed my mind were those connected with malnutrition and alcoholism. The case did not quite fit that. There is a disturbance called central pontine myelinolysis and this could be present in someone who started with an alcoholic amblyopia, but I get the feeling that she was a social drinker rather than an alcoholic and it does not quite fit the pure picture of a central pontine lesion. We should therefore have to add another alcoholic syndrome, the Marchiafava-Bignami syndrome, in which the white matter of the corpus callosum is affected particularly. These diseases would not be so rapidly and progressively fatal.

I come now to the group thought to be viral. These include progressive multifocal leucoencephalopathy, in which there is usually some systemic or generalised disease such as Hodgkin's disease or neoplasia, and we have no evidence of that, although these conditions sometimes may not come to light until necropsy. There are some rapidly progressive diseases in this group in which the virus does not merely disturb immunity but is itself active. These include the herpes simplex encephalitides, but the patient had no inflammatory changes in the cerebrospinal fluid (CSF), and the brain was not swollen on air encephalography. Subacute sclerosing panencephalitis is excluded because it affects a different age group but has quite similar EEG changes.

So we are left with two groups—a subacute herpes encephalitis, but I would expect a more abnormal CSF; and, lastly, the Jakob-Creutzfeld group. These conditions are very rare but have now been proved to be due to a slow virus, transmitted to chimpanzees. There are several forms, and although it is an obscure diagnosis I think it fits most closely to the neurological syndrome.

There is the classical form with pyramidal and extra-pyramidal features, which is not quite right for this case. There is a form with predominant involvement of the visual system, the Heidenheim type, and I think it could be put in that category. There is also the type first described by Jones and Nevin as the spongiform encephalopathy.[2] In conclusion, I believe this woman had a diffuse degeneration affecting white matter more than grey which may well have been a slow virus encephalopathy.

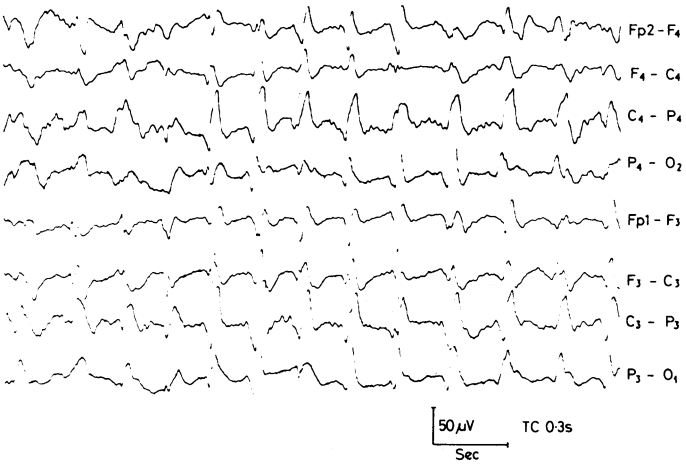

FIG 5—Case 2. Repeat EEG, showing deterioration. (EEGs were reported by Dr E W Poole.)

DR HYMAN: To complete the story, there was progressive deterioration after admission. A further EEG showed continuous stereotyped discharges (fig 5). She developed myoclonus in all four limbs, assumed a decerebrate posture, and died 35 days after admission.

PROFESSOR MATTHEWS: Dr Hughes, will you show us the pathological findings.

PATHOLOGICAL FINDINGS

DR HUGHES: The cause of death was pulmonary collapse and congestion, with multiple small pulmonary infarcts due to emboli from thrombosed leg veins. Apart from the central nervous system the tissues and organs were otherwise unremarkable. The brain weighed 1050 g and was moderately atrophied (fig 6). The atrophy of the cerebral gyri was most obvious as a widening of the sulci. A portion of the right parietal lobe was

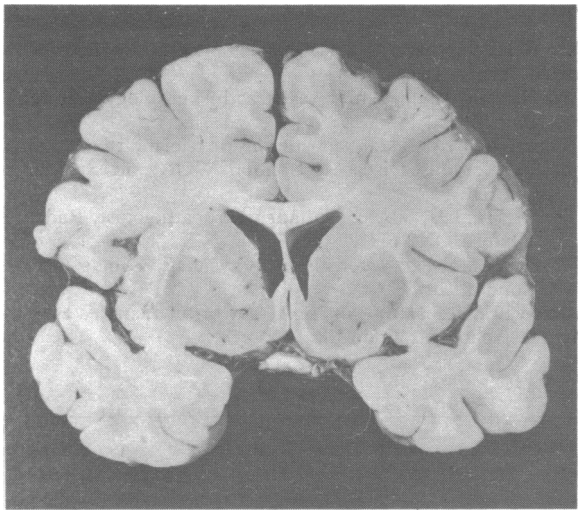

FIG 6—Case 2. Coronal slice of cerebrum showing cerebral atrophy.

homogenised and injected intracerebrally into guinea pigs. The generalised cerebral atrophy was also evident at the base. The major cerebral arteries were affected by a little fibrous thickening and some streaks of atheroma. A coronal slice at the level of the optic chiasm showed atrophy without focal lesions. At higher magnification the cortical ribbon was thin and sparse. Histologically this was a primary grey-matter disease with secondary white-matter degeneration. The neuronal degeneration (fig 7) was present throughout the cerebral cortex in every place examined and also in the internal nuclei. There were striking pathological changes: degeneration of neuronal cell bodies leading to a severe neuronal depletion; astrocytic proliferation leading to an increased cellularity of grey matter, which concealed the neuronal depletion; and a spongiform change with large vacuoles and small vesicles (fig 8), which was diagnostic. There were interstitial vesicles and large perineuronal and pericapillary spaces. The other finding was a negative feature: a complete absence of any inflammatory reaction. These features are typical of Creutzfeldt-Jakob disease.

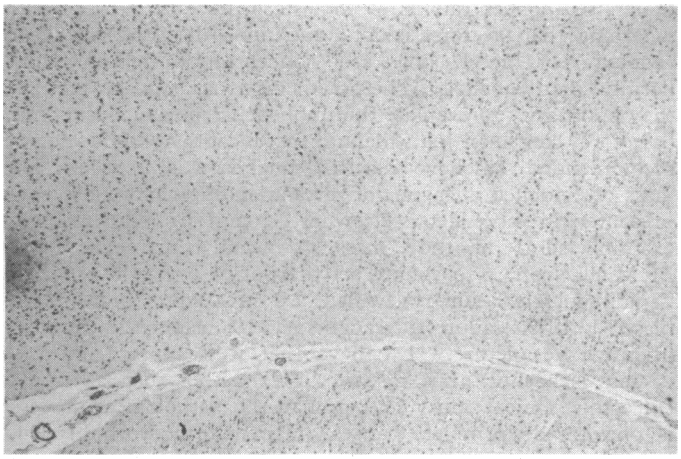

FIG 7—Case 2. Frontal cortex showing neuronal degeneration.

PROFESSOR MATTHEWS: You found no cause for hypercalcaemia?

DR HUGHES: I found no parathyroid tumours, no metastatic calcification, and no calculi in the kidney. The bones were normal.

PROFESSOR MATTHEWS: Again Sir Roger was right. Would you like to comment?

Changing neurological concepts

SIR ROGER BANNISTER: I have not seen a case: they are so rare. The progressive disease without inflammatory changes in the CSF means that there was no reaction against the virus from the immune mechanisms because of the blood-brain barrier, which affects the development of immunity within the central nervous system. This extraordinary disease has altered our whole concept of neurology. The theoretical implication is also important to a neurologist. We wonder how many other progressive neuronal degenerations have yet to be explained on the basis of this kind of response. I do not know currently just which virus is incriminated. One practical point is that these slow viruses are virtually indestructible by normal methods of sterilisation and there have been cases reported to be caused by needles which have been inadequately sterilised before a stereotactic EEG so that intracerebral inoculation has occurred.

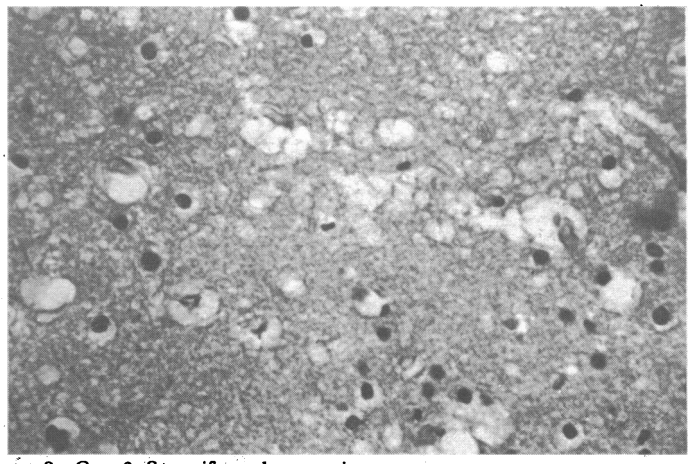

FIG 8—Case 2. Spongiform degeneration.

PROFESSOR MATTHEWS: This case was both topical and full of red herrings, some of which were not explained.

MEMBER OF AUDIENCE: What happened to the guinea-pigs?

DR HUGHES: We think that we transferred the disease. We used six guinea-pigs, with several controls. After 18 months one of the guinea-pigs became sick. We killed it, and the brain had the same changes as in the human disease. We have killed another one, which was healthy and showed nothing abnormal, and the others are still alive.

MEMBER OF AUDIENCE: Was the conjunctivitis a red herring?

PROFESSOR MATTHEWS: It was a very severe conjunctivitis. I don't know how it fits; it is not a feature of Creutzfeldt-Jakob disease.

MEMBER OF AUDIENCE: I am interested in the infectivity of the disease. Does this apply to the neurologists' pin?

SIR ROGER BANNISTER: I think it is an intracerebral inoculation, rather than general or systemic.

PROFESSOR MATTHEWS: I know one neurologist who says you should flame the pin. But there has been no indication that peripheral inoculation has transmitted the disease.

PROFESSOR MILNE: Has it not been transmitted by corneal grafting?

SIR ROGER BANNISTER: Yes. And that is rather closer to the brain. The eye is an extension of the brain.

MEMBER OF AUDIENCE: Can it be transmitted by eating animal brains?

PROFESSOR MATTHEWS: Not many of us eat sheep's brains, but many eat spinal cord attached to lamb chops. The virus has never been seen. We know it is there only by its production of disease. It is resistant to 40% formalin for many months. I

thought I detected some clustering of cases in some villages north of Oxford, but the statistics are difficult in a disease so rare. There is another suspected cluster to the east of London. Institutional clusters have not been seen.

This conference was recorded and edited by Dr W F Whimster. We regret that the names of the speakers from the audience were not picked up on the tape, so they remain unidentified.

References

[1] Nick, J, *et al*, *Revue Neurologique*, 1971, **125**, 15.
[2] Jones, D, and Nevin, S, *Journal of Neurology and Psychiatry*, 1954, **17**, 148.

APPOINTMENTS OF SPEAKERS

(1) Professor W B Matthews, DM, FRCP, professor of clinical neurology, Oxford University
(2) Dr N M Hyman, MRCP, senior registrar in neurology, Churchill Hospital, Oxford
(3) Sir R Bannister, DM, FRCP, consultant physician, the National Hospital for Nervous Diseases, London WC1, and St Mary's Hospital, London W2
(4) Dr J Trevor Hughes, MD, consultant neuropathologist, Radcliffe Infirmary, Oxford OX2 6HE
(5) Dr D A Pyke, MD, FRCP, consultant physician, King's College Hospital, London SE5
(6) Professor M D Milne, MD, FRCP, professor of medicine, Westminster Medical School, London SW1

The Other Side

Fats and atheroma: a retrial

J I MANN

British Medical Journal, 1979, **1**, 732-734

Summary and conclusions

The controversy over medical endorsement of dietary measures to reduce cholesterol intake has been reconsidered. The results of several published reports that apparently do not confirm the association between diet, cholesterol concentrations, and ischaemic heart disease (IHD) were found to be largely inapplicable to the argument. Results of primary prevention trials, however, suggested that lowering the cholesterol concentration had a beneficial effect in reducing morbidity from IHD. The "average Western diet" is particularly associated with accelerated or premature atherosclerotic disease, yet the saturated fatty acid component of the diet may be only one of several factors relevant to IHD. Such diets are usually high in refined carbohydrate and total energy intake.

Disordered nutrition generally, and other environmental and constitutional factors seem to be important in the aetiology of IHD. A prudent diet, incorporating decreased intake of fats, simple sugars, and refined carbohydrate, with polyunsaturated fats comprising less than 25% of total energy intake, may be the best method of reducing the incidence of IHD and other diseases of overnutrition.

Introduction

Sir John McMichael has held another inquest[1] and concluded that medical endorsement of cholesterol-reducing measures should be withdrawn. He considers that polyunsaturated fats may actually be harmful. I request a retrial, not because I regard a diet high in polyunsaturated fat as the single most important aspect of a diet more prudent than the current Western diet, but because Professor McMichael has suggested that raised concentrations of cholesterol have little to do with atheroma, that atheroma is not a nutritional disorder, and that a reduction of blood cholesterol concentration may be more harmful than beneficial. The practising doctor who has not had the opportunity to evaluate the published reports in detail may therefore conclude that dietary modification should not be recommended. I believe that this conclusion is not valid. The mass of evidence in favour of recommending change has been presented in more detail elsewhere,[2 3] and I shall principally examine some of the "mass of negative evidence" that McMichael offers to counteract the positive reports based on "epidemiological surveys which are misleading and grossly biased by their failure to recognise and consider the complete investigative picture." I believe that it is more helpful to discuss ischaemic heart disease (IHD) rather than atheroma, since this clinical entity, rather than the pathological process, is one of the principal causes of premature morbidity and mortality in most Westernised countries and factors other than atheroma may be concerned.

Negative evidence

Sir John McMichael cites a number of investigations which do not apparently confirm the association between diet, cholesterol levels, and IHD: "Diets with a high and low fat content that were consumed by different monastic orders did not alter the incidence of coronary disease." This statement is based on an interesting *cross-sectional* investigation by Groen *et al*[4] of 181 Trappist and 168 Benedictine monks; the former consuming a frugal vegetarian diet and the latter a mixed "Western" diet. There was indeed no difference in the prevalence of IHD between the two groups, but the most striking finding in this study (which can be criticised from several points of view) is the virtual absence of major ischaemic events in either group —only one out of the 349 monks studied had evidence of myocardial infarction (a Trappist with diabetes and appreciable hypercholesterolaemia). The authors' principal conclusion concerned the protective effect of a monastic life against ischaemic heart disease. Professor

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