states of the U.S.A. and in Japan this early peak is lacking. MacMahon suggested that Hodgkin's disease was an infectious condition in the young and a neoplasm in the old. The bimodality could equally be explained if older people acquired the disease from their children, bearing in mind the postulated long incubation period.[15] Another recent development has been the appearance of an early peak among Japanese living in the U.S.A. Mason and Fraumeni[16] have interpreted this shift in the American-Japanese curve towards that of the white Americans as consistent with an environmental influence affecting all ages rather than with an infective agent affecting only young adults. Clarke, Anderson, and Davidson[17] have recently presented an alternative working hypothesis in which a transmissable form of Hodgkin's disease may occur at any age.

Where, then, do we stand at present? On current evidence it is premature to conclude that case-to-case transmission of Hodgkin's disease occurs in the school, surgery, or family home. Furthermore, the postulated increase in incidence in these situations is only of the order of two-to-eightfold, which in practical terms represents a negligible hazard in a disease with an overall incidence of around 4 per 100 000 population per year. Doctors, teachers, spouses, and close relatives of patients with this disease may take heart from these facts.

[1] Vianna, N. J., Greenwald, P., and Davies, J. N. P., *Lancet*, 1971, **1**, 1209.
[2] Vianna, N. J., *et al.*, *Annals of Internal Medicine*, 1972, **77**, 169.
[3] Klinger, R. J., and Minton, J. P., *Lancet*, 1973, **1**, 168.
[4] Smith, P. G., Pike, M. C., and Kinlen, L. J., *Lancet*, 1973, **1**, 433.
[5] Vianna, N. J., and Polan, A. K., *New England Journal of Medicine*, 1973, **289**, 499.
[6] Milham, S., *New England Journal of Medicine*, 1974, **290**, 1329.
[7] Bahn, A. K., *New England Journal of Medicine*, 1974, **291**, 207.
[8] Hoover, R., *New England Journal of Medicine*, 1974, **291**, 473.
[9] Vianna, N. J., *et al.*, *Lancet*, 1974, **2**, 131.
[10] Smith, P. G., Kinlen, L. J., and Doll, R., *Lancet*, 1974, **2**, 525.
[11] Vianna, N. J., *et al.*, *Lancet*, 1974b, **2**, 854.
[12] MacMahon, B., *Cancer Research*, 1966, **26**, 1189.
[13] Falk, J., and Osoba, D., *Lancet*, 1971, **2**, 1118.
[14] MacMahon, B., *Cancer*, 1957, **10**, 1045.
[15] Wagener, D. J., *Lancet*, 1974, **1**, 880.
[16] Mason, T. J., and Fraumeni, J. F., *Lancet*, 1974, **1**, 745.
[17] Clarke, E. A., Anderson, T. W., and Davidson, J. W., *Lancet*, 1974, **1**, 745.

Transient Ischaemic Attacks

Transient ischaemic attacks (T.I.A.s) are a common presenting symptom of cerebrovascular disease. The characteristic clinical picture is one of a focal neurological deficit of abrupt onset, lasting up to 24 hours, and leaving no residual signs. In about 30% of cases a completed stroke occurs after one or more T.I.A.s, usually within 3 years,[1 2] but the prognosis is rather better in attacks arising in the vertebrobasilar artery territory.[3]

Most T.I.A.s are due to the passage of an embolus through the cerebral circulation. More rarely they are caused by reduction of perfusion through a grossly narrowed vessel—the "haemodynamic crisis" of Denny-Brown—secondary to sudden blood loss, hypotension, or a fall in cardiac output.

T.I.A.s are characterized by their sudden onset, often in waking hours, and by the repetitive nature of the symptoms in an individual—they may recur several times a day. As has recently been shown by Grindal and Toole,[4] headache may be prominent in up to 25% of patients during or after an attack. Its location is variable, but in vertebrobasilar attacks it is often in the neck or occiput, while pain is more typically frontal or temporal in carotid attacks. An earlier report[5] noted a higher incidence of headache in non-dominant hemisphere lesions and considered that dysphasia might mask it when the speech was affected in lesions of the left hemisphere. The mechanism of the headache is uncertain, but it may be related to distension of pain-sensitive nerve fibres in the arterial wall at the site of impaction of the embolus; dilatation of collateral vessels has also been suggested.

In the carotid territory the common symptoms are unilateral weakness of the face, arm, or leg, with or without speech disturbance. Hemianopic field defects occur in posterior cerebral artery occlusion and also (in association with hemianaesthesia) in ischaemic lesions of the internal capsule. Transient monocular blindness (amaurosis fugax)[6] may afford the diligent observer the chance of seeing bright yellow cholesterol crystals or whitish fibrin-platelet plugs traverse the retinal vessels. More often the history of a "curtain" or "shutter" crossing the visual field points unmistakably to a source of embolus in the carotid or great vessels, including the aorta and the heart itself.

A bruit localized over the carotid artery is a good clue to a stenosis or even an occlusion; a similar bruit in the supraclavicular fossa or the posterior triangle of the neck suggests a subclavian or vertebral stenosis. Usually this is accompanied by a diminished radial pulse and a drop of blood pressure of over 20 mm Hg in the arm. The common symptoms of vertebrobasilar attacks are vertigo, diplopia, fortification spectra, hemianopia, and paraesthesiae especially around the lips and face; there may also be ataxia, slurred speech, and numbness of both arms or legs, or of one side. Hemiparesis and hemisensory disturbance seem to carry a greater risk of a forthcoming infarct. A variant of this picture is the "subclavian steal syndrome," in which symptoms are precipitated by exercise of the arm, which increases the demand for blood. The narrowed subclavian artery then "steals" blood from the vertebral artery. The reversed flow can be seen at angiography and can be treated by endarterectomy—if symptoms are disabling.

Investigation of carotid T.I.A.s is designed to find treatable factors and thus prevent a disabling stroke. Age is a poor guide, and most reasonably fit patients merit assessment in a neurological unit. Tests will include a full blood count, E.S.R., radiographs of chest and skull, electrocardiogram, and fasting blood glucose, lipids, and urea. Exhaustive routines are not justifiable—an individual assessment of each case should determine the need for further investigation. Evidence of widespread coronary and peripheral vascular disease will often contraindicate angiography; so too will sustained hypertension, unless a localized neck bruit suggests a surgically remediable stenosis.

With these exceptions angiography is usually indicated in patients with carotid T.I.A.s. The morbidity is less than 0·5% and the mortality almost negligible in skilled hands. The aim is to show the extent and number of vascular stenoses or occlusions (multiple or clinically unsuspected lesions being common) and to exclude lesions such as meningiomas or angiomas which may mimic a stroke.

In patients with vertebrobasilar T.I.A.s the incidence of surgically correctable lesions is small. Only those cases with severe symptoms related to neck movement suggesting vertebral compression by removable cervical osteophytes or those with subclavian steal syndrome should be considered for surgery, and hence for angiography.

Before contemplating surgery, an arch aortogram showing all four major neck vessels is necessary: initial enthusiasm may be dampened by the multiple lesions often seen. In an isolated carotid stenosis operation carries a better outlook than anticoagulants or doing nothing.[7] Thromboendarterectomy carries a mortality rate[8] of about 1%, and postoperative

neurological signs persist in about 2% of patients. At follow-up 10% die of a stroke in the next ten years.

Patients deemed unsuitable for surgery are often treated with anticoagulants. Most trials show some statistically significant benefit over placebo, but how clinically significant this is remains debatable.[1 9] Their use in arterial disease has little scientific rationale and is not without hazard. It may be that such simple remedies as aspirin, one dose of which inhibits platelet aggregation for over three days, will prove equally effective. The basis of T.I.A.s surely is to be found in the genesis of the widespread disorders which cause atheroma; improvement in our presently empirical modes of treatment is likely to be based on effective and preventive methods.

[1] Millikan, C. H., *Stroke*, 1971, **2**, 201.
[2] Acheson, J., and Hutchinson, E. C., *Quarterly Journal of Medicine* 1971, **40**, 15.
[3] Marshall, J., *Quarterly Journal of Medicine*, 1964, **33**, 309.
[4] McAllen, P. M., and Marshall, J., *Lancet*, 1973, **1**, 1212.
[5] Grindal, A. B., and Toole, J. F., *Stroke*, 1974, **5**, 603.
[6] Wells, C. E., *Archives of Neurology*, 1961, **5**, 490.
[7] Fisher, C. M., *Archives of Ophthalmology*, 1952, **47**, 167.
[8] Marshall, J., *Medicine*, 1974, **31**, 838.
[9] Bauer, R. B., *et al.*, *Journal of the American Medical Association*, 1969, **208**, 509.
[10] Pearce, J. M. S., Gubbarry, S. S., and Walton, J. N., *Lancet*, 1965, **1**, 6.

Hypotensive Treatment for Acute Myocardial Infarction

The prompt recognition and consequent immediate treatment of arrhythmias in coronary care units has left the main causes of death as heart failure and cardiogenic shock. These complications are related[1] to the amount of cardiac muscle necrosis: large infarcts have a higher mortality than small ones. That might, perhaps, have been expected, but the effect was somewhat masked before the otherwise lethal but treatable arrhythmias had been reduced in coronary care units, chiefly by the skill of the nursing staff. If, then, some means could be found for reducing the extent of the infarction, this might further lessen mortality—a hope which until recently appeared to be difficult or impossible to achieve.

After an acute myocardial infarction there is an ischaemic zone around the area of irreversible necrosis, and this zone may or may not survive.[2] Factors which reduce myocardial oxygen consumption favour the survival of the ischaemic zone,[3] and these include a lowered velocity of contraction, decreased tension in the ventricular wall, and slowing of the heart rate. Efforts to change these factors in a favourable direction might lessen the size of eventual infarction and reduce the risks of death from heart failure and shock.

A method for assessing the size of myocardial infarction has been pioneered by American workers at San Diego and St. Louis.[4] They have studied the rate of rise of the enzyme creatinine phosphokinase (CPK) after myocardial infarction. By serial studies they have been able to predict the ultimate peak levels of CPK from measurements during the first seven hours after admission. They claim that the serum levels of this enzyme, particularly when the cardiac isoenzyme is analysed, indicate the extent of myocardial necrosis, and that treatment which leads to observed CPK levels being lower than those predicted from the initial values can reasonably be considered to have reduced the size of the final infarct. These authors have now found[5] that in 14 previously hypertensive patients who were admitted to hospital with acute myocardial infarction, lowering of blood pressure with trimetophan (a ganglion blocking agent) resulted in CPK levels 24% less than the predicted values. The assumption is that some 24% of jeopardized myocardium was thus salvaged from infarction. Their patients were not markedly hypertensive, the mean arterial pressure was 114 mm falling to 88 mm with treatment.

Coronary blood flow to the left ventricle is largely dependent on aortic diastolic pressure, so it might seem paradoxical to treat myocardial infarction with hypotensive agents. Until now there has been considerable concern in the management of acute infarction to avoid the undue hypotensive effects of analgesics, and most centres temporarily stop or reduce hypotensive therapy in patients with known hypertension after acute infarction. To suggest, therefore, that hypotensive treatment may be beneficial is revolutionary: the findings of Shell and Sobel indicate a way in which an inroad might possibly be made on the residual mortality. The mechanism seems logical enough—the treated patients showed a reduction in the mean left atrial pressure (the left ventricular filling pressure) while they continued to maintain a satisfactory cardiac output.

This series of 14 patients is too small for any firm conclusions to be drawn about hypotensive treatment and prognosis after acute infarction. Shell and Sobel suggest that the time has come for more extensive studies of hypotensive treatment after myocardial infarction both to assess the difference between predicted and observed CPK values and, more important, the effects on survival and other clinical features. Clearly such studies will need very careful monitoring of blood pressure. Many patients with acute myocardial infarction have hypertension at admission, probably due to anxiety, heart failure, or pain, while later readings may often be normal. It could be dangerous to inflict hypotension on such patients. The blood pressure should be reassessed after treatment with analgesics and for heart failure where indicated, before hypotensive therapy is started. It could well be that such trials will show a reduction in mortality in hypertensive and perhaps also in normotensive patients.

[1] Harnarayan, C., *et al.*, *British Heart Journal*, 1970, **32**, 728.
[2] Cox, J. L., *et al.*, *American Heart Journal*, 1968, **76**, 650.
[3] Maroko, P. R., *et al.*, *Circulation*, 1971, **43**, 67.
[4] Sobel, B. E., *et al.*, *Circulation*, 1972, **46**, 640.
[5] Shell, W. E., and Sobel, B. E., *New England Journal of Medicine*, 1974, **291**, 481.

Anaesthetists' Environment

Anaesthetists may have to work long hours, sometimes in theatres with no daylight and poor ventilation, and often without adequate time for rest and food; and the need for constant vigilance and the exacting demands of major surgery in poor risk patients might be expected to be associated with an increase in morbidity and mortality in both the anaesthetist and his patient. In fact, one recent report[1] has suggested that the death rate in anaesthetists was lower than that expected. Despite earlier findings there is no evidence that anaesthetists have a higher risk of death from coronary artery disease or from malignancies of the lymphoid and reticuloendothelial tissue. Unexpectedly high rates[2] of cancer and other disease of the liver and kidney may occur in anaesthetists, however, though Spence *et al.*[3] found no increase in the overall incidence of malignant disease among British anaesthetists. The suicide rate is considerably higher than expected and is the second or third highest of the specialty groups.[1]