BRITISH MEDICAL JOURNAL

LONDON SATURDAY 20 JUNE 1970

Pointers

Review Body's Report: Mr. J. H. Gunlake, until his resignation a member of the Review Body, corrects some misunderstandings about the award (p. 726). The B.M.A. Council decides on its contingency plans (*Supplement*, p. 201, and leader at p. 682). Meetings of Central Committee for Hospital Medical Services, Hospital Junior Staffs Council, and General Medical Services Committee (*Supplement*, pp. 208 and 209). Correspondence (p. 726).

Medical Schools: The Dean of Medicine at Southampton University discusses the two existing types of medical school and suggests that a third type is needed (p. 683).

Heart Valve Replacement: A leader on this page discusses the outlook after operation.

Haematuria in Childhood: A study of the value of various investigations, especially renal biopsy, in assessing the prognosis of symptomless haematuria (p. 687). Leader at p. 678.

Hepatitis: Incidence of autoantibodies and Australia antigen in acute and chronic infective hepatitis (pp. 693 and 695).

Breast Cancer: Enzyme activity of biopsy specimens may help to distinguish tumours likely to recur early and respond to hormone therapy (p. 698).

Clindamycin: Clinical use (p. 703).

Digoxin Maintenance: Results of stopping treatment suggest that maintenance therapy is often unnecessary (p. 705). Leader at p. 680.

The "Empty" Sella: Leader (p. 679) and case report (p. 709).

Other Clinical Studies: Hypercalcaemia in thyrotoxicosis (p. 701), gut glucagon in reactive hypoglycaemia (p. 706), pancreatic carcinoma (p. 708), and cerebral malaria (p. 710).

Clinicopathological Conference: From the Royal Postgraduate Medical School (p. 711).

Super-specialization in Surgery: Mr. John Charnley describes his centre for prosthetic hip replacement and its general implications (p. 719).

Mark Akenside, 1721-70: Poet and Harveian orator (p. 722).

Personal View: Dr. Dewi Rees on being called out to accidents (p. 725).

Supplementary Report of Council: See *Supplement*, p. 206.

A.R.M. Supplementary Agenda: See *Supplement*, p. 207.

Medical Officers of Health: Agreement on pay (*Supplement*, p. 209).

G.M.C.: Disciplinary cases (*Supplement*, p. 210).

Hazards of Heart Valve Replacement

Both the immediate operative risks and the likelihood of late postoperative complications must be weighed against the expected natural course of the disease when replacement of heart valves is being considered. The development of real symptoms of left ventricular dysfunction in a patient with aortic valve disease means that life may end suddenly at any time and at best is unlikely to be prolonged for more than two years. The immediate risk of aortic valve replacement is now less than 10% in major centres, and the chance of a patient continuing to survive for more than two years after operation is greater than 80%.[1 2] Surgery therefore offers a favourable option.

In the patient with mitral valve disease the downhill course once symptoms have developed is very much slower and more predictable, while the mortality of mitral valve replacement is higher than for the aortic valve in most centres.[3 4] Poor general health is more likely to be an adverse factor than in the case of lone aortic valve disease, which has usually not caused trouble for long enough to affect the patient's vitality. The patient with mitral disease may develop both pulmonary vascular obstruction and tricuspid reflux. This combination lowers the cardiac output and takes the pressure off the mitral valve so that the patient is less breathless, but she ultimately faces a rather higher operative risk. The timing of mitral valve replacement is consequently fraught with difficulty; symptoms are likely to be relieved, but the long-term prognosis may not necessarily be improved. Pulmonary hypertension will regress,[5] but the best management of tricuspid reflux is still not agreed.[6]

What kind of future can the owner of an artificial valve look forward to? Thromboembolism is still the biggest single risk. Long-term anticoagulant therapy confers some measure of protection, and the prothrombin activity should be kept continuously within the therapeutic range. Despite the claims made for each new valve, the incidence of embolism usually turns out to be much the same as for the long-established Starr valve. In a recent review of 404 patients followed over a five-year period at the Mayo Clinic, G. E. Duvoisin and his colleagues described a 33% incidence of postoperative embolism after mitral valve replacement and 31% after aortic valve replacement. No less than 15% of all patients who sustained an embolus died.[7] T. J. Yeh and his coworkers[8] reported an incidence of emboli after mitral valve replacement which was 1·7 times higher in patients with atrial fibrillation than in those with sinus rhythm, and the Mayo Clinic workers reported similar experiences. In a recent double-blind study in Boston it was found that the incidence of embolism was lower in patients who received dipyridamole as well as anticoagulants after cardiac valve replacement. Dipyridamole may inhibit the formation of platelet thrombi on implanted heart valves, and these early encouraging results await confirmation from more extensive trials of the drug.[9]

In contrast to all artificial prostheses so far designed, valves of human or animal origin are almost completely free of the risk of thromboembol-

ism.[10 11] Aortic valve homografts are, however, troublesome to procure and technically more difficult to insert than prostheses. They are not always haemodynamically perfect, and their longevity still awaits proof. During the last two years inverted aortic valve homografts have been put in the mitral ring after mounting on a metal frame, and autogenous fascia lata has been prepared in a similar fashion. The early results are encouraging; these valves also seem to confer freedom from embolic hazard, but the risk of late failure is still unknown. Thromboembolism can kill or maim, but haemodynamic failure is usually gradual and remediable. Many surgeons believe that this security from the tragedy of late coronary embolism puts the advantage firmly on the side of the homografts.

Even artificial valves are not immune from mechanical failure. A dehiscence may develop between the natural annulus and the sewing ring of the prosthesis. Regurgitation then gives rise to early postoperative haemodynamic deterioration and the frequent complication of mechanical haemolysis.[12] Degenerative changes may distort the silicone rubber poppet of the caged aortic ball valve.[13] This "variance" of the ball is a late complication that has only once been reported in the mitral valve, which is opened at lower pressure and therefore less violently. The variant ball becomes misshapen and discoloured; free mobility is lost so the ejection click gets softer, the ejection murmur louder, and the sounds may vary from beat to beat. A regurgitant murmur and mechanical haemolysis may follow, but dehiscence is distinguished from variance by its earlier onset. Both complications can be successfully corrected surgically.

A poor surgical result may also come about from failure of the myocardium despite a prosthesis working perfectly well. Much used to be said about "the myocardial factor," with the implication that surgical intervention might be delayed too long. While poor cardiac output inevitably leads to poor coronary blood flow (and the normally high oxygen extraction rate of the myocardium leaves little reserve for this) the main cause for postoperative myocardial failure may be myocardial damage consequent upon the operation itself. In Portland, U.S.A., N. R. Niles and J. R. Sandilands examined the hearts of 62 patients who had died at all stages up to six years after valve replacement.[14] They found ischaemic necrosis or scars in 57 of the 62 cases. These were attributable to thrombosis on the prosthesis with coronary occlusion or embolism in 28 of the 36 late deaths. In 13 cases the infarcts appeared temporally related to the operation: these tended to be haemorrhagic, patchy, or miliary and most heavily affected the inner layers of the left ventricular walls. These important observations have clear bearing on the once common postoperative low-output syndrome, which has now become rare even in high-risk cases. The improvement is attributable to better control of coronary perfusion and to prevention of air and particle embolism.

Infection on artificial prostheses is another major problem. Infection which is acquired at the time of surgery is likely to be due either to a resistant hospital staphylococcus or to a ubiquitous organism of low pathogenicity, which is often almost equally hard to treat. Positive blood cultures may not be obtained because of the broad-spectrum antibiotics usually prescribed to "cover" surgery, yet early diagnosis is particularly vital in these cases. Later infections are caused by similar organisms to those which infect diseased natural valves, and are therefore most commonly due to *Streptococcus viridans* in patients with teeth and Gram-negative bacteria in elderly patients with disease of the gastrointestinal or urinary tracts. Fungus endocarditis is particularly sinister. The spores probably enter the heart at the time of surgery, but their growth is so insidious, the constitutional reaction often so slight, and the incidence of fungi in the blood stream likely to be so sporadic that recognition may be delayed for many months. Infection in a prosthesis is a very grave complication and in some cases surgical excision may offer the only chance of a cure.[15 16]

Notwithstanding this formidable list of potential hazards the chances of a given patient with an artificial valve avoiding trouble are steadily improving. The operative risk still lies between 5% and 25%, but at present we can expect that up to 70% of the survivors of cardiac valve replacement will be alive, well, and able to work five years after surgery. It is reasonable to hope that if a patient has avoided embolism, infection, and mechanical breakdown over this length of time that the prosthesis will be so well endothelialized and incorporated that the chances of the next 5 or 50 years being as good are even brighter.

Haematuria in Childhood

The causes of haematuria in childhood include structural abnormalities of the renal tract such as hydronephrosis, polycystic kidney, and tumours of the kidney or bladder; stones and crystals; trauma; meatal ulcer; infections caused by bacteria (including tuberculosis), viruses, or schistosomata; acute and chronic glomerulonephritis; Henoch-Schoenlein syndrome; haematological disorders such as sickle-cell anaemia and leukaemia; haemorrhagic disorders including haemophilia and scurvy; systemic diseases such as endocarditis and disseminated lupus; and certain drugs and poisons. Lists of this kind are of very limited use to the clinician: they suggest unreal diagnostic dilemmas and bemuse those who try to remember them. In practice a child who presents with haematuria as the main problem is most likely to have acute glomerulonephritis, urinary infection, renal trauma, or the well-recognized but still puzzling disorder of recurrent haematuria, discussed by Drs. E. F. Glasgow, M. W. Moncrieff, and R. H. R. White at page 687 of this week's *B.M.J.* A rational scheme of investigation for diagnosis of the commoner causes will also disclose most of the rarer ones.

The urine must first be examined to confirm that the discoloration is due to blood. The simplest test is Hemastix or

1 Herr, R. H., Starr, A., Pierie, W. R., Wood, J. A., and Bigelow, J. C., *Annals of Thoracic Surgery*, 1968, **6**, 199.
2 Otto, T. J., Cleland, W. P., and Bentall, H. H., *Journal of Cardiovascular Surgery*, 1969, **10**, 339.
3 Morrow, A. G., Oldham, H. N., Elkins, R. C., and Braunwald, E., *Circulation*, 1967, **35**, 962.
4 Starr, A., Herr, R. H., and Wood, J. A., *Journal of Thoracic and Cardiovascular Surgery*, 1967, **54**, 333.
5 Braunwald, E., Braunwald, N. S., Ross, J., and Morrow, A. G., *New England Journal of Medicine*, 1965, **273**, 509.
6 Braunwald, N. S., Ross, J., and Morrow, A. G., *Circulation*, 1967, **35**, Suppl. No. 1, p. 63.
7 Duvoisin, G. E., Brandenburg, R. O., and McGoon, D. C., *Circulation*, 1967, **35**, Suppl. No. 1, p. 70.
8 Yeh, T. J., Anabtawi, I. N., Cornett, V. E., and Ellison, R. G., *Circulation*, 1967, **35**, Suppl. No. 1, p. 77.
9 Sullivan, J. M., Harken, D. E., and Gorlin R., *Circulation*, 1969, **39**, Suppl. No. 1, p. 149.
10 Barratt-Boyes, B. G., Lowe, J. B., Cole, D. S., and Kelly, D. T., *Thorax*, 1965, **20**, 495.
11 Ross, D., *Surgery*, 1968, **63**, 382.
12 Kastor, J. A., *et al.*, *Journal of Thoracic and Cardiovascular Surgery*, 1968, **56**, 279.
13 Bonnabeau, R. C., and Lillehei, C. W., *Journal of Thoracic and Cardiovascular Surgery*, 1968, **56**, 258.
14 Niles, N. R., and Sandilands, J. R., *Diseases of the Chest*, 1969, **56**, 373.
15 Roberts, W. C., and Morrow, A. G., *Archives of Pathology*, 1966, **82**, 164.
16 Braniff, B. A., Shumway, N. E., and Harrison, D. C., *New England Journal of Medicine*, 1967, **276**, 1464.