

Apparent recurrence of Q fever endocarditis following homograft replacement of aortic valve

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A 39-year-old man with aortic stenosis and regurgitation developed Q fever endocarditis. After 15 weeks of chemotherapy with tetracycline the damaged aortic valve was replaced with a homograft. Organisms were present in the excised valve. Some months later the valve began to leak and the endocarditis recurred fatally. Because of the nature of rickettsial infection neither a course of chemotherapy nor an operation can guarantee a cure of Q fever endocarditis. Chemotherapy should be continued indefinitely even after operation.

Coxiella burnetii, the causative organism of Q fever, is being increasingly recognized as a cause of infective endocarditis (Marmion *et al.*, 1953; Kristinsson and Bentall, 1967). It appears to affect especially the aortic valve of male patients. This report concerns such a patient in whom the infection recurred after prolonged chemotherapy and surgical replacement of the damaged aortic valve with a homograft. The behaviour of the rickettsiae and the reasons why such an infection may never be eradicated from the body are discussed.

Case report

This man spent much of his youth in contact with cattle and sheep in Australia but returned to England in 1958, aged 30, as a grocer in Kent. He had been rejected for military service because of his heart, though there was no history of rheumatic fever. In 1960 he was diagnosed as having aortic stenosis and regurgitation.

During 1966 he became unduly breathless on exertion. After a mass radiograph which showed cardiomegaly he was referred in April 1967 to his local hospital where he was found to have signs of bacterial endocarditis, namely fever, finger clubbing, splinter haemorrhages, and splenomegaly; but repeated blood cultures on admission were negative. Treatment was begun with saline penicillin and streptomycin but he continued pyrexial with rigors and a raised sedimentation rate. Cloxacillin and then cephaloridine were substituted for his original antibiotics and his clinical and laboratory evidence of infection disappeared over a period of six weeks. However, before discharge, serological testing showed a complement-fixation titre to *Coxiella burnetii*, the Q fever organism, phase 2 antigen, of more than

1 in 10240. He left hospital in June 1967 with a badly leaking aortic valve, taking antifailure treatment and tetracycline 250 mg. q.d.s.

He was admitted to the London Hospital in October 1967 aged 39. Chemotherapy with tetracycline had been continued for three and a half months and was stopped six weeks before admission. He had developed cardiac asthma. Cardiac catheterization and angiography confirmed the clinically gross aortic reflux and left ventricular failure. There was no clinical evidence of infection. Blood count and sedimentation rate were normal and the complement-fixation titre had fallen to 1 in 5120.

At operation by Mr. E. J. M. Weaver in November 1967 the damaged aortic valve was excised and replaced with a freeze-dried homograft (Fig. 1 taken at operation). Cephaloridine was administered after surgery. Recovery from the operation was uneventful and there was no evidence of aortic incompetence. He was discharged on digoxin alone.

Examination of the excised valve showed it to be calcified and tricuspid. Each cusp bore granulations, but the right coronary cusp had been perforated. Neither bacteria nor rickettsiae could be shown under the microscope. However, intraperitoneal inoculation of valve fragments into a guinea-pig caused a rise in its complement-fixation titre to *Coxiella burnetii* over seven weeks from 1 in 10 to 1 in 640. This strongly suggested that viable organisms which had survived the period of 15 weeks of chemotherapy were present in the valve.

The patient was seen two months after operation in January 1968. His blood pressure was 145/100 mm. Hg. On auscultation only a soft ejection systolic murmur was heard. There was no aortic reflux. The complement-fixation titre to *Coxiella burnetii* had fallen to 1 in 1280. However, three months after operation his blood pressure was 140/70 mm. Hg and he had an aortic diastolic

murmur which was even more obvious after another two months in April 1968.

The patient was next seen in October 1968, 11 months after operation. Again he claimed that he was well but he looked ill. He had a tachycardia and severe aortic reflux giving him a blood pressure of 160/50 mm. Hg. There was no splenomegaly or splinter haemorrhages. Objections were raised to his immediate admission. While his blood was being cultured he was admitted from his new home in the Midlands to a local hospital, with a left femoral vein thrombosis.

The complement-fixation titre was now 1 in 10,240, similar to that before treatment and eight times his post-operative figure. Neither bacteria nor rickettsiae were isolated from the blood, and a moderate pyrexia settled *pari passu* with his venous thrombosis. He was treated initially with anticoagulants and cardiac drugs and later with tetracycline. He apparently improved though he was troubled by nocturnal chest pain. While awaiting transfer for re-operation he suddenly became anuric with left ventricular failure. He was moved to the London Hospital but suffered a cardiac arrest on arrival associated with prerenal uraemia. After resuscitation severe brain damage was evident and he died three days later, in January 1969, aged 41.

At necropsy the new aortic homograft valve cusps were extensively ulcerated and perforated (Fig. 2). There were multiple tan-coloured vegetations on the ventricular surfaces. The suture lines were intact. The subject was perfused with formalin before section to prevent dissemination of the organism, and culture for rickettsiae was therefore not attempted. Again neither bacteria nor rickettsiae could be seen on microscopy, even with specific staining.

Discussion

This patient was treated for infective endocarditis in a manner that would have been curative if the infection had been bacterial; he had 15 weeks of specific chemotherapy followed by excision of the site of infection, the damaged aortic valve, and replacement with a competent homograft valve. Though the operation was necessary for mechanical reasons rather than infection, from which he appeared at the time to be free, valve replacement is now considered as reasonable in resistant cases of infective endocarditis with deteriorating cardiac status (*British Medical Journal*, 1968; Braniff, Shumway, and Harrison, 1967), and is recommended for Q fever endocarditis (Kristinsson and Bentall, 1967). Nevertheless, all replacement valves whether prosthetic or homograft may be the site of infective endocarditis *de novo* (McGoon, Ellis, and Kirklin, 1965; McDonald *et al.*, 1968) and Q fever endocarditis of a prosthetic valve has been described (Morgans and Cartwright, 1969).

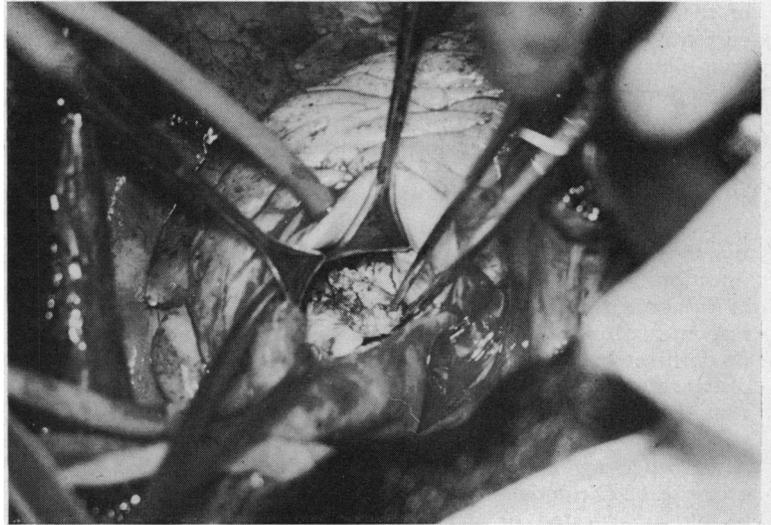
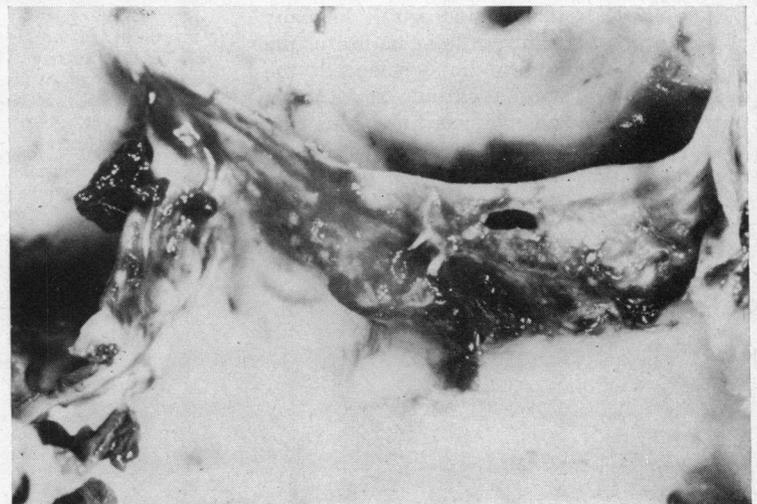


FIG. 1 Operative photograph of the heart to show the damaged aortic valve seen through the aortotomy.

Despite the prolonged use of tetracycline in this patient, the valve fragments removed at operation still provoked a rising titre to Q fever antigen in the guinea-pig. While the chemotherapy had been specific, tetracycline and other recommended anti-rickettsial drugs seem to be rickettsiostatic rather than rickettsiocidal. Though apparently effective at the time, a limited, even though protracted, course of chemotherapy could not, therefore, guarantee eradication of the organism. That excision

FIG. 2 Post-mortem close-up view of homograft aortic valve cusps showing vegetations and perforation.



of the infected site did not prevent a recurrence would suggest (though reinfection from outside cannot be excluded) that there were dormant intracellular organisms elsewhere in the body at the time of operation which infected the new valve. Such extracardiac foci of infection do not usually persist in bacterial endocarditis, but corroborative evidence for this supposition is provided by the observed behaviour of rickettsial infections.

Rickettsia prowazeki, the related organism responsible for epidemic typhus, is known to lie dormant in the body giving rise to Brill's disease after an interval of many years (Brill, 1898; Price *et al.*, 1958). Recurrent or chronic attacks of Q fever may occur on the same basis. Patients with Q fever may relapse after a course of chemotherapy and a proportion go on to repeated or persistent episodes. Indeed, *Coxiella burneti* has been isolated from the placentas of Czech women in a village where a Q fever outbreak had occurred years previously (Syrůček, Soběšlavský, and Gutvirth, 1958). The subjects were symptom free.

Contact with cattle and sheep, especially at calving and lambing, is a potent cause of Q fever infection (Connolly, 1968), and such evidence of prolonged latent infection might suggest that this patient could have been infected before 1958 during his ranching days in Australia. However, he might also have been infected more recently while resident in Kent, as a large proportion of the reported British cases of Q fever have occurred there. Some of these patients give no history of contact with animals and might be infected from contaminated milk even though it has been pasteurized (Marmion and Stoker, 1958).

While Q fever endocarditis closely resembles subacute bacterial endocarditis in many of its features, the intracellular nature of the organism, its ability to lie dormant in the tissues or to sustain a chronic septicaemia independent of an endocarditis, plus the absence so far of a rickettsiocidal drug, mean that eradication of the organism cannot be guaranteed either by a course of chemotherapy or by excision of the affected valve.

Despite the risk of resistant bacterial superinfection, these patients should take tetracycline or a related drug indefinitely. Had this patient been so treated his replacement aortic valve might not have been destroyed.

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