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Changing Face of Infective Endocarditis

The liberal use (and abuse) of antibiotics has radically altered the disease so exhaustively catalogued by Horder¹ and Osler² in 1909. Not only have the clinical features changed but so have the patients, the infecting organisms, and the underlying cardiac fault.

When seen today the textbook combination of protracted fever, anaemia, finger-clubbing, petechiae, splenomegaly, and systemic embolism is usually a sign of belated diagnosis and a deeply entrenched infection or of an inaccessible or antibiotic-resistant infecting agent. The classic victim, a young adult with rheumatic heart disease and *Streptococcus viridans* endocarditis following tooth extraction, is more rarely seen than formerly owing to the decreasing incidence of rheumatic fever and the use of penicillin to cover dental work in patients known to be at risk.

The character of infective endocarditis has always departed furthest from the classical at the extremes of age. In childhood the pneumococcus and meningococcus used to select an apparently normal aortic valve as well as congenital anomalies such as aortic stenosis, ventricular septal defect, and patent ductus. Cardiac infection by these penicillin-sensitive organisms has now virtually disappeared, but endocarditis accompanying staphylococcal septicaemia still occurs and even increases.³ In infancy the portal of entry is usually a septic lesion of the skin and the seat of attack a normal tricuspid valve. Staphylococcal tricuspid endocarditis also attacks drug addicts using intravenous injections.

P. Hughes and W. R. Gauld⁴ have recently drawn attention to an apparently real increase in the incidence of endocarditis in old age. In elderly and edentulous persons genitourinary, gastrointestinal, and biliary-tract disease provide alternative sources of bacteraemia, and penicillin-resistant infections with *Staphylococcus pyogenes* and *Str. faecalis* have become common. In old age the disease is often extremely insidious in onset and protracted in course. Heart disease may not be noted, and infection may in fact affect the normal ageing valve, particularly the aortic valve, where atherosclerosis provides a nidus for it to start.

In a previously fit patient with a cardiac murmur blood cultures should be set up if fever or malaise persist and are unexplained for more than a few days, but absence of murmurs does not preclude the diagnosis, particularly in an elderly person. A dilemma develops when blood cultures are unexpectedly sterile. Non-bacterial thrombotic endocarditis may complicate terminal illness (marantic endocarditis)⁵ or systemic lupus (Libman-Sacks endocarditis),⁶ but more often previous administration of antibiotics is responsible. An unwelcome product of the antibiotic era is an "endocarditis lentissimus" which is peculiarly resistant both to diagnosis by positive blood culture and to effective treatment. Sometimes a history of repeated courses of antibiotics may not be readily obtained because the patient has dosed himself with antibiotic tablets

left over from previous bronchitis. Alternatively, when blood cultures are stubbornly negative⁷ an exotic organism which is slow growing, or has special growth requirements, or simply cannot be cultured extracellularly, should be suspected—such as *Brucella*, *Candida*,⁸ or a rickettsia.⁹ All reported cases of Q fever endocarditis have so far been fatal, for the rickettsiae are insensitive to bactericidal drugs, and an uneasy truce rather than cure is the best that can be achieved with tetracycline and chloramphenicol.

Cardiac surgery has brought iatrogenic endocarditis, usually a staphylococcal infection introduced during operation.^{10 11} The situation is particularly serious when a valve prosthesis becomes infected. Bacteria permeate the valve's woven "skirt," whence they can rarely be eradicated by medical treatment. Surgery can help in desperate circumstances. Well-timed excisions of the valve harbouring inaccessible or antibiotic-resistant organisms or intracellular rickettsia, or exchange of an infected prosthesis, may offer the only hope of cure.

Unexplained fever in a patient with rheumatic heart disease poses a common problem. Infective endocarditis rarely attacks patients in advanced heart disease with heart failure; pulmonary infarction or infection, systemic embolism, or active rheumatism is more likely to be the cause of their symptoms.¹² However, bacterial endocarditis is easy to miss, and treatment has to be instituted if doubt remains. In a patient with apparent mitral valve disease a myxoma in the left atrium can mimic infective endocarditis almost perfectly.¹³ Here the combination of an unusually high erythrocyte sedimentation rate, abnormal protein pattern on electrophoresis, and intravascular haemolysis in a patient with unusual mitral murmurs and sterile blood cultures should suggest the need to undertake angiography.

Why infective endocarditis should show a predilection for certain cardiac sites and anomalies has been a source of speculation. S. Rodbard's theory has most appeal.¹⁴ He proposed that infection occurs first on an area of damaged intima, the "jet lesion," which develops at the low-pressure end of a high-velocity stream of blood. The disease is thus common in mild aortic regurgitation, severe aortic stenosis, and mild mitral regurgitation, but rare in mitral stenosis and advanced valve disease with heart failure, rare in congenital defects with pulmonary hypertension, and virtually unknown in the ostium secundum type of atrial septal defect.¹⁵

Reduction in the incidence of infective endocarditis depends on the patient as well as his doctor knowing that preventive measures are needed. Penicillin cover before dental extrac-

tion or tonsillectomy is certainly important. Less well known is it that a transient bacteraemia may follow normal childbirth,¹⁶ which should be covered by penicillin and streptomycin in patients with rheumatic or congenital heart disease. The high incidence of unrecognized minor aortic-valve lesions in elderly men indicates a need for routine bactericidal prophylaxis to cover urethral instrumentation.^{17 18}

Prevention of recurrent infective endocarditis depends on removal of the source of infection. As *Str. viridans* invasion through the mouth is by far the commonest cause of recurrence, this means impeccable dental care, and since *Str. viridans* endocarditis is virtually unknown in edentulous persons a second attack despite such care is an indication for dental clearance.

Prescription of long-term antibiotic treatment to prevent infective endocarditis is unwise and rests on a misunderstanding. Unlike rheumatic fever, which follows infection only by the β -haemolytic streptococcus, almost any organism can cause infective endocarditis. *Str. viridans* infection is the usual one only because the mouth is the usual portal of entry. A change in the mouth's flora simply ensures that any recurrence will be with the penicillin-resistant organism which has replaced *Str. viridans*.¹⁹ The decreased proportion of cases of endocarditis seen nowadays due to penicillin-sensitive organisms exemplifies this point, and there is much to be said for using sulphonamide rather than penicillin for prophylaxis against rheumatic fever, since the low dose required to prevent infection with β -haemolytic streptococci is insufficient to remove the less sensitive *Str. viridans* from the mouth.

T.N.M. Marches On

The International Union Against Cancer (U.I.C.C.) has always given special attention to the problem of the clinical classification of malignant tumours. The practice of dividing cancer cases into groups according to so-called stages arose from the known fact that the crude survival or apparent recovery rates were higher for cases in which the disease was localized than for those in which the disease had extended beyond the organ of origin.

These groups are often referred to as "early" or "late" cases, erroneously implying some regular progression with time. In fact the stage of disease at the time of diagnosis may be a reflection not only of the rate of growth and extension of the neoplasm but also of the type of tumour, the tumour-host relationship, and the interval of time between the first symptom or sign recognized by the patient and the time of diagnosis or treatment. These complex interrelationships are an obstacle to any perfect classification. Though this is a different concept from staging, it is equally a challenge to the recording of precise information on the extent of the disease. This will make possible a clinical description which may serve a number of related objectives. These are, briefly, to aid the clinician in the planning of treatment, in making a prognosis, in assisting in the evaluation of the results of treatment, and facilitating the exchange of information between centres and individual specialists.

The basic requirements of any system are that it should be simple, practical, and sensible. If it is not these things it will have little chance of being adopted on a world-wide scale. The seed of the T.N.M. system, as it is generally called, was planted by P. F. Denoix in Paris and germinated between

¹ Horder, T. J., *Quart. J. Med.*, 1909, 2, 289.

² Osler, W., *ibid.*, 1909, 2, 219.

³ Bain, R. C., Edwards, J. E., Scheifley, C. H., and Geraci, J. E., *Amer. J. Med.*, 1958, 24, 98.

⁴ Hughes, P., and Gauld, W. R., *Quart. J. Med.*, 1966, 35, 511.

⁵ Barry, W. E., and Scarpelli, D., *Arch. intern. Med.*, 1962, 109, 151.

⁶ Harvey, A. M., Shulman, L. E., Tumulty, P. A., Conley, C. L., and Schoenrich, E. H., *Medicine (Baltimore)*, 1954, 33, 291.

⁷ Blount, J. G., *Amer. J. Med.*, 1965, 38, 909.

⁸ Andriole, V. T., Kravetz, H. M., Roberts, W. C., and Utz, J. P., *Amer. J. Med.*, 1962, 32, 251.

⁹ Evans, A. D., *Brit. med. J.*, 1963, 1, 1613.

¹⁰ Hoffman, F. G., Zimmerman, S. L., Bradley, E. A., and Lapidus, B., *New Engl. J. Med.*, 1959, 260, 152.

¹¹ Geraci, J. E., Dale, A. J. D., and McGoon, D. C., *Wis. med. J.*, 1963, 62, 302.

¹² Elster, S. K., Pader, E., and Horn, H., *Arch. intern. Med.*, 1963, 112, 476.

¹³ Goodwin, J. F., Stanfield, C. A., Steiner, R. E., Bentall, H. H., Sayed, H. M., Bloom, V. R., and Bishop, M. B., *Thorax*, 1962, 17, 91.

¹⁴ Rodbard, S., *Circulation*, 1963, 27, 18.

¹⁵ Sellors, Sir T. H., *Brit. med. J.*, 1967, 1, 385.

¹⁶ Redleaf, P. D., and Fadell, E. J., *J. Amer. med. Ass.*, 1959, 169, 1284.

¹⁷ Barrington, J. F., and Wright, H. D., *J. Path. Bact.*, 1930, 33, 871.

¹⁸ Vogler, R., and Dorner, E., *Bull. Emory Univ. Clin.*, 1961, 1, 21.

¹⁹ Garrod, L. P., and Waterworth, P. M., *Brit. Heart J.*, 1962, 24, 39.