

INFECTIOUS DISEASES OF THE HEART

Infectious heart disease related to certain infections is present in epidemic proportions in sub-Saharan Africa.

MPIKO NTSEKHE

MD, FCP (SA)

Senior Consultant

The Cardiac Clinic
Department of Medicine
Groote Schuur Hospital and
University of Cape Town

Mpiko Ntsekhe is a Senior Consultant in the Division of Cardiology and Director of the Cath Lab at Groote Schuur Hospital. He qualified in medicine from Columbia University's College of Physicians and

Surgeons. His postgraduate training in internal medicine and cardiology was completed in Cape Town. His research interests include infectious diseases affecting the heart, and heart disease in patients with HIV.

BONGANI MAYOSI

MB ChB, DPhil

Professor and Head

Department of Medicine
Groote Schuur Hospital and
University of Cape Town

Bongani Mayosi qualified in medicine from the University of KwaZulu-Natal in Durban, and trained in internal medicine and cardiology in Cape Town. From 1998 to 2001 he worked under Hugh Watkins as a research fellow in cardiovascular medicine at Oxford University. His research interests include genetics of heart disease, treatment of tuberculous pericarditis, and prevention of rheumatic fever.

Sub-Saharan Africa is in the midst of three epidemics which predispose patients to infections of the heart. These epidemics are rheumatic heart disease, tuberculosis, and human immunodeficiency virus (HIV) infection. Whereas rheumatic heart disease predisposes to infective endocarditis, tuberculosis is the leading cause of pericarditis in Africa, and HIV affects the cardiovascular system in multiple important ways. In this overview we provide a clinical approach to common infectious diseases of the heart in patients presenting at primary and secondary care levels.

INFECTIVE ENDOCARDITIS

Cardiac risk factors

Patients with valvular heart disease (i.e. abnormal native or prosthetic valves), congenital heart disease, patches or conduits are at risk of developing infective endocarditis. Table I lists dental and non-dental procedures for which antibiotic prophylaxis is recommended by the American Heart Association to prevent infective endocarditis. Some authorities divide these into high, moderate and low-risk conditions. Although this may have some theoretical value, practically it is not useful because the advice for prevention is the same for all groups.

Prevention

The cornerstone for prevention of infective endocarditis is the maintenance of adequate oral health care by means of

annual visits to a dentist or an oral hygienist, twice daily tooth brushing, and daily use of dental floss and other plaque-removing devices. The use of antibiotic prophylaxis before invasive procedures is widely accepted. Tables II and III outline the recommended prophylactic antimicrobial regimens.

Initial clinical approach in suspected infective endocarditis

The following rules are helpful to guide the initial management of the patient with an underlying cardiac predisposition to infective endocarditis and a febrile or constitutional illness:

- Infective endocarditis is rarely an acute illness that requires immediate intervention. Antibiotic therapy needs to be delayed until appropriate investigations have been conducted and other causes of a febrile illness have been excluded.
- Clinical suspicion of infective endocarditis in the presence of haemodynamic instability and/or congestive heart failure, however, is an indication for urgent referral to a centre where valve replacement surgery is possible.

Ensure that a minimum of three blood cultures are taken from different sites, at least 1 hour apart, preferably in association with a temperature spike.

Table I. **Common dental and surgical procedures where endocarditis prophylaxis is recommended**

- Any dental procedures known to induce gingival or mucosal bleeding, including professional cleaning
- Tonsillectomy and/or adenoidectomy
- Surgical operations that involve intestinal or respiratory mucosa
- Bronchoscopy with a rigid bronchoscope
- Sclerotherapy for oesophageal varices
- Oesophageal dilation
- Biliary tract surgery
- ERCP with obstruction
- Cystoscopy
- Urethral dilatation
- Urethral catheterisation if urinary tract infection is present
- Prostatic surgery
- Incision and drainage of infected tissue
- Prolonged or difficult vaginal delivery

Table II. **Recommended regimens for dental, oral and upper respiratory tract procedures**

Standard regimen	Amoxicillin 2 g orally 1 hour before procedure
Patients unable to take orally	Ampicillin 2 g IV at induction or IM 30 minutes before procedure
Penicillin-allergic patients and those on long-term penicillin prophylaxis for rheumatic fever	Clindamycin 600 mg orally 1 hour before procedure
Penicillin-allergic patients unable to take orally	Clindamycin 600 mg IV over 10 minutes 30 minutes before procedure

Table III. **Recommended regimens for genitourinary or gastrointestinal procedures**

Standard regimen	Ampicillin 2 g IV plus gentamicin 1.5 mg/kg up to 30 minutes before procedure
Penicillin-allergic patients and those on long-term penicillin prophylaxis	Vancomycin 1 g over 1 hour plus gentamicin 1.5 mg/kg up to 30 minutes before procedure

It is essential to examine the patient with suspected infective endocarditis carefully and repeatedly over several days for peripheral stigmata of the disease. Pay close attention to the skin (petechiae), hands (clubbing,

splinter haemorrhages, Osler's nodes), conjunctivae (petechiae), and urine (microscopic haematuria).

If after 3 - 4 days there is no diagnosis or alternative explanation for the

febrile illness, it is advisable to refer the patient to a health facility with the relevant expertise for the management of cardiac disease.

TUBERCULOUS PERICARDITIS

Tuberculous (TB) pericarditis is uncommon in the First World, but very common in developing countries, and the incidence appears to be increasing in sub-Saharan Africa in parallel with the HIV/AIDS epidemic. The disease presents in three forms: pericardial effusion, constrictive pericarditis, and effusive-constrictive pericarditis.

Tuberculous pericardial effusion

Pathology

Pericardial effusion is the commonest mode of presentation with or without tamponade. The effusion is bloodstained in over 95% of cases, and may even resemble venous blood. The absence of parenchymatous lung disease and the presence of hilar lymphadenopathy in many of these patients suggest a direct spread from a TB hilar node to the pericardium.

Clinical presentation

Systemic symptoms are variable. Typical pericardial pain is uncommon and the classic ECG features of pericarditis are not common. The chest radiograph shows an enlarged globular heart, small pleural effusions on one or both sides, and evidence of pulmonary tuberculosis in 30 - 40% of cases. The echocardiogram shows features of pericardial effusion, typically associated with soft-tissue density masses, thickening of the visceral pericardium, and fibrinous strands.

Diagnosis

A definite diagnosis of TB pericarditis is based on the demonstration of tubercle bacilli in the pericardial fluid or on histological section of the pericardium. The diagnosis should be confirmed by pericardiocentesis. Fluid should be sent for microscopy (to identify acid-fast bacilli (AFB)) and culture of tubercle bacilli.



Sub-Saharan Africa is in the midst of three epidemics which predispose patients to infections of the heart. These epidemics are rheumatic heart disease, tuberculosis, and human immunodeficiency virus (HIV) infection.

It is essential to examine the patient with suspected infective endocarditis carefully and repeatedly over several days for peripheral stigmata of the disease.

The chances of a positive culture are improved by bedside inoculation of the fluid into double-strength Kirschner culture medium. Pericardial biopsy and drainage offer the advantage of a histological diagnosis and early complete drainage of the pericardium. This can be performed via the sub-xiphisternal approach under local anaesthesia.

A probable diagnosis is made when there is proof of tuberculosis elsewhere in a patient with unexplained pericarditis. Palpation in the supraclavicular fossa will frequently reveal enlarged lymph nodes, which should be biopsied. AFB-positive sputum will only be found in about 10% of cases. Tuberculin skin testing is of little value in endemic and non-endemic areas.

Several tests have been developed for the rapid diagnosis of tuberculosis in the pericardial fluid (albeit indirect). Polymerase chain reaction can identify DNA of *Mycobacterium tuberculosis* rapidly from only 1 µl of pericardial fluid (sensitivity 75%, specificity 100%). An adenosine deaminase (ADA) level > 40 U/l has a sensitivity of 83% and a specificity of 78%. A high interferon-γ level is also a highly sensitive (92%) and specific (100%) marker of TB pericarditis.

Treatment

This is by means of standard four-drug antituberculosis chemotherapy for 6 months. Overall mortality is about 26% (40% in patients with clinical evidence of HIV infection; 17% in those with no clinical signs of HIV infection). Repeat pericardiocentesis is required in about 15% of patients, and during a 2-year follow-up period about 10% of patients will require surgical pericardiectomy. While some favour the addition of steroids to conventional therapy, their role in improving survival is not clearly established, particularly in HIV infection.

Tuberculous pericardial constriction

Clinical presentation

Most cases have an active inflammatory fibrocaseous tissue surrounding the heart, involving visceral and parietal pericardium. The clinical presentation is highly variable – from asymptomatic to severe signs and symptoms of constriction. The diagnosis is often missed on cursory clinical and echocardiographic examination. It is uncommon to find concomitant pulmonary tuberculosis, and pericardial calcification is found in < 5% of cases.

Treatment

The initial management of patients with non-calcific TB constrictive pericarditis is with antituberculosis therapy, and since the process is an active fibrocaseous condition resolution of constriction occurs in 15 - 20% of patients with medical management over 3 - 4 months. Pericardiectomy is recommended if no improvement has occurred after 6 weeks of anti-tuberculosis treatment or unsatisfactory improvement after several months of treatment. By contrast, calcific TB pericarditis is treated by early pericardiectomy and antituberculosis chemotherapy.

Effusive-constrictive tuberculous pericarditis

Features

This mixed form is a common presentation of TB pericarditis. There

is increased pericardial pressure due to effusion in the presence of visceral constriction. The echocardiogram shows porridge-like exudation with loculation of the fluid.

Treatment

This is by standard four-drug therapy. The role of adjuvant steroids is not known. The mortality is about 10% and about 30% of cases will come to pericardiectomy over 2 years of follow-up.

HIV AND THE CARDIOVASCULAR SYSTEM

The clinical effects of HIV on the heart are relatively uncommon compared with the impact of HIV infection on the lungs, gastrointestinal tract, central nervous system and the skin. There are similarities in the pattern of cardiovascular involvement in people living in developed and developing countries, but with differences in the causative organisms. The main presentations are the following:

- pericardial effusion
- cardiomyopathy
- pulmonary hypertension
- large-vessel aneurysms
- metabolic complications associated with antiretroviral drug use.

Pericardial effusion

This is the major cardiovascular manifestation of HIV infection in people living in sub-Saharan Africa. Whereas in Western countries a large effusion is usually idiopathic in 80% of patients with AIDS, the disease is caused by tuberculosis in over 80% of Africans living with HIV. Purulent pericarditis is not uncommon, while involvement with Kaposi's sarcoma and B-cell lymphoma is thought to be rare. Treatment of TB pericarditis is with a standard antituberculosis regimen similar to that used in HIV-negative patients, and the short-term outcome is also similar. The role of adjuvant steroids is uncertain.

Left ventricular dysfunction

This is found in 50% of acutely ill hospitalised patients.

Cardiomyopathy

This occurs in 15% of ambulatory asymptomatic patients living with HIV. Myocarditis is said to occur in the majority of cases of cardiomyopathy in the West, whereas it is uncommon in Africans with HIV-associated cardiomyopathy. Patients with HIV-associated cardiomyopathy should be treated as for heart failure and considered for antiretroviral therapy. The prognosis is poor, with a median survival of 100 days without anti-retroviral drugs.

Pulmonary hypertension

HIV-associated pulmonary hypertension has an estimated prevalence of 1/200 among HIV-infected patients – much higher than the 1/200 000 prevalence of primary pulmonary hypertension in the general population. Primary pulmonary hypertension is found in 0.5% of hospitalised AIDS patients and is a cause of cor pulmonale and death. The pathogenesis is poorly understood. Once a diagnosis has been established therapeutic options are limited, although there is some evidence to suggest that antiretroviral therapy may reverse the process.

Arterial aneurysm

HIV-related arterial aneurysm is a distinct clinical and pathological entity associated with advanced HIV disease. HIV-related aneurysms affect young patients (median age 30 years) with no risk factors for atherosclerosis, occur mainly in peripheral arteries

(carotid, distal superficial femoral and popliteal sites), are usually multiple (1 - 10 per patient), and have been reported more frequently in Africa than elsewhere. The inflammatory process is thought to involve the vasa vasorum of the adventitia, with sparing of the media and intima. The most frequent mode of presentation is that of a painful mass of increasing size. The diagnosis is confirmed by duplex sonography or computed tomography. Arterial angiography is performed to delineate the extent of aneurysm. Serological testing for syphilis, typhoid, and autoimmune disease is indicated. Treatment is by operative intervention for symptomatic aneurysm in patients with an acceptable surgical risk and good anticipated life expectancy.

Metabolic abnormalities

The use of protease inhibitor antiretroviral agents is associated with the following metabolic abnormalities: fat redistribution (lipodystrophy), increased total cholesterol and triglycerides, decreased HDL, impaired glucose tolerance and increased intra-abdominal fat. These changes translate to a small increase in the risk of myocardial infarction with the long-term use of protease inhibitors. It is prudent to avoid them in patients with other cardiovascular risk factors if possible, to modify risk factors, and to treat the metabolic complications when they arise according to standard guidelines.

In summary, the three most important cardiac infections in people living in Africa are infective endocarditis, TB pericarditis and HIV-related cardiovascular disease. Recognising those at high risk for infective endocarditis and implementing a plan for primary prevention is the single best intervention for that condition. In patients with suspected TB pericarditis, excluding pyogenic, malignant and other inflammatory causes while establishing a diagnosis of tuberculosis is particularly important. Finally, establishing the clinical stage of HIV, knowing what the diagnostic possibilities are and having a clear strategy for evaluation and therapy are most important in the HIV-infected patient with a cardiac presentation.

Further reading

Baddour LM, Wilson WR, Bayer AS, *et al.* Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: A statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association-Executive Summary: Endorsed by the Infectious Diseases Society of America. *Circulation* 2005; **111**: 3167-3184.

Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. *Circulation* 2005; **112**: 3608-3616.

Ntsekhe M, Hakim J. Impact of human immunodeficiency virus infection on cardiovascular disease in Africa. *Circulation* 2005; **112**: 3602-3607.

IN A NUTSHELL

Sub-Saharan Africa is in the midst of three epidemics which predispose patients to infections of the heart. These epidemics are rheumatic heart disease, tuberculosis, and human immunodeficiency virus (HIV) infection.

Patients with valvular heart disease (i.e. abnormal native or prosthetic valves), congenital heart disease, patches or conduits are at risk of developing infective endocarditis.

Infective endocarditis is rarely an acute illness that requires immediate intervention.

TB pericarditis presents in three forms: pericardial effusion, constrictive pericarditis, and effusive-constrictive pericarditis.

Treatment of TB pericarditis is by means of standard four-drug antituberculosis chemotherapy for 6 months.

The clinical effects of HIV on the heart are relatively uncommon, compared with the impact of HIV infection on the lungs, gastrointestinal tract, central nervous system and the skin.

Pericardial effusion, as a result of TB pericarditis, is the major cardiovascular manifestation of HIV infection in people living in sub-Saharan Africa.