NON SPECIFIC AORTIC ARTERITIS

(TAKAYASU'S DISEASE)

The Cape Town Experience

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I would like to pay tribute to the late Professor Val Schrire. It was he who provided the initial interest in aortic arteritis at the University of Cape Town. He instituted research on the subject and his publications remain widely acclaimed. His article (Fig. 1) published in the Quarterly Journal of Medicine in 1964 is regarded as a classic, a milestone in the understanding of the condition, and is quoted throughout the world literature. Furthermore, he is accredited with providing the most succinct and currently acceptable nomenclature of the condition, viz. "Non-specific arteritis of the Aorta."

FIG 1.

ARTERITIS OF THE AORTA AND ITS MAJOR BRANCHES[1]

By V. SCHRIRE and R. A. ASHERSON

(From the Cardiac Clinic, Groote Schuur Hospital, Council for Scientific and Industrial Research Cardiovascular-Pulmonary Research Group, and Department of Medicine, University of Cape Town)

Many patients were in the care of eminent surgeons of Groote Schuur Hospital. Acknowledgement is due to Professors JH Louw, DR de Villiers, M Barnard, EJ Immelman and S Cywes for their interest in the subject, and the contributions they have made to vascular surgery during the past three decades.

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TO

JANET

ABSTRACT

Non-specific aortic arteritis remains a disease of unknown aetiology, in which the treatment is empiric, the indications for surgery controversial and the prognosis unpredictable. Most series emanate from the Far East, with few contributions from Africa. The pattern of disease as seen in Cape Town has not been documented since the study of Schrire and Asherson in 1964, containing 18 cases. (1)

In this study at Groote Schuur and Red Cross Childrens Hospital from 1952 to 1987, only patients who had been extensively investigated and subjected to angiography were included. Strict inclusion criteria excluded patients with specific forms of aortic arteritis. 220 patients were studied of which 77% were female. Mean age 25(1-66). 68% were "Coloured" or Asian, 24% Black and 8% White.

Involvement of the entire aorta was seen in 62%. The aortic arch was involved in 70% but isolated arch disease occurred in only 9%. Aortic bifurcation disease occurred in 30%, an unusually high incidence. 93% had occlusive disease. 50% had aneurysms, which usually occurred together with occlusive disease. 7 patients presented with ruptured aneurysm.

Hypertension due to renal artery stenosis or to coarctation was the commonest presentation (76%). 103 (47%) patients had cardiac disease (hypertensive cardiac failure or aortic incompetence.) Upper or lower limb claudication was present in

77 patients with gangrene in only 11. 43 patients had clinical evidence of cerebrovascular disease.

54 patients are known to have died, with cardiac failure responsible for almost 50%. Follow-up of 5-20 years was possible in 40% of patients. Two-thirds showed no further progression in this period. Vascular reconstruction was performed in 43 patients (21%). Other treatment modalities included corticosteroids (11%) and antituberculous therapy (28%). Proven tuberculosis was present in only 20% of cases.

The pattern of disease in Cape Town tends to be diffuse, usually with extensive branch vessel involvement, and thus seldom amenable to reconstructive vascular surgery. Hypertension and cardiac failure are the commonest presenting symptoms and the most frequent cause of death. The aetiology of this condition remains obscure and the pathogenetic link with Tuberculosis is controversial. A significant number of patients have "burnt out" disease, and prolonged survival has been observed.

CONTENTS

1. INTRODUCTION

Non-specific aortic arteritis, also called Takayasu's disease is a condition of unknown aetiology, with the pathogenesis and natural history little understood, and the treatment still poorly defined. The scant literature available on the subject comes mainly from Japan and the Soviet Union, with very few contributions from Africa. The largest published African series contains less than 25 patients [121]. The disease as seen in Africa would appear to differ from that seen in Asia, however, this has never been clearly documented.

The University of Cape Town Medical School and Groote Schuur Hospital have detailed records of a 36 year experience in this condition. In 1964, Professor V Schrire described 18 patients in a publication regarded worldwide as a major contribution to the understanding of this disease. The current study is a sequel to this: it includes 220 patients , and is the second largest reported series in the world.

There are four main controversies surrounding the condition of nonspecific aortic arteritis. These include the aetiology, pathogenesis, natural history and, the treatment of the disease.

Genetics, immunological factors, nutritional aspects, and chronic bowel infection have all been implicated in the aetiology of this disease. Although the genetic link is not yet clearly defined,

there is undoubted evidence that the disease occurs more commonly in patients with certain histocompatibility antigens.

The immune hypothesis is based on several facts:

- immune complex deposition in the aortic media
- the presence of anti-aortic antibodies
- defective T-lymphocyte function
- the association with Tuberculosis
- the association with other immune-related disorders such as Crohns disease and glomerulonephritis.

The condition is known to occur in the poorer socio-economic groups, but the reason for this is uncertain. Nutritional deficiency may contribute to fragmentation of the aortic media. The Asian literature has implicated parasitic intestinal infections in the aetiology and has submitted immunological evidence to support this.

The relative importance of these aetiological factors remains uncertain.

Concerning the pathogenesis of the disease, many unanswered questions remain:

- What is the initial trigger to the immune response?
- Why is there a predilection for the aorta and major elastic arteries?

- What determines the site of involvement and whether "dilating" or "occlusive" disease occurs?
- How is the age and sex predilection explained?
- Which factors determine the progression of the disease?

The natural history of aortic arteritis is variable, with prognostic factors ill-defined. Recent prospective studies have shown four distinct patterns of disease progression, with cardiac and hypertensive complications having the greatest influence on prognosis [9,12].

Several clinical classifications have been proposed for this disease. The classification of Nasu in 1976 (Fig 1) is the most universally accepted and is frequently referred to in this text.

Fig. I Nasu Classification 1976[133]

I Aortic arch only
II Thoracic aorta only
III Abdominal aorta only
IV Diffuse

Therapeutic options include reconstructive vascular surgery, corticosteroids, and anti-tuberculous therapy.

Surgery was previously considered hazardous, with risk of anastomotic disruption and false aneurysm formation. However, successful vascular surgery is currently being performed on a large percentage of patients in Japan and the Soviet Union. The indications for surgery depend firstly on the anatomical extent

of the lesions and secondly on the severity of the symptoms. The disease pattern seen in Cape Town would appear to be more diffuse, with segmental branch vessel involvement. It is thus less suitable for reconstructive surgery.

The role of corticosteroids, the indications, dosage and duration of treatment remain uncertain. However, recent evidence would suggest definite benefit, with reduction in the inflammatory "activity" of the disease, halting of disease progression, and even return of pulses in some cases.[19]

1.1 AIMS

The aims of this study are:

1. To document the Cape Town experience in non-specific aortic arteritis and to analyse the spectrum of disease seen during a thirty-six year period.

2. To categorise the clinical presentation of the condition and to correlate this with the angiographic findings.

3. To review the pathology of the disease and to correlate this with aetiological factors.

4. To assess the validity of diagnostic criteria and the numerous classifications available for the condition.

5. To evaluate the treatment modalities, including the role of surgery, in this condition.

6. To establish the natural history of the disease in Cape Town and the factors affecting the prognosis.

7. To review the literature and to correlate previous studies with the present one.

1.2 HISTORICAL PERSPECTIVE AND NOMENCLATURE

Although aortic arteritis occurs mainly in Asia and has traditionally been considered an oriental condition, the first reports of the disease were made in Britain, and cases have been described in virtually every country of the world. The first clinical description of the disease was given by Adams in 1827, reporting a sixty-eight year old man with absent pulses. (cited in 1). Savory (1856), an English physician, reported the first case in a young woman, a patient with absent pulses in both arms and the left side of her neck [65]. Broadbent (1875) reported a similar presentation in a fifty year old man.

The disease was first described in Asia in 1908[62] by Takayasu and Onishi at a congress of the Japanese Opthalmologic Society. Takayasu, a Japanese opthalmologist described a patient with unusual ocular manifestations, fundoscopy showing a curious ringlet of anastomosing arterioles and venules surrounding the optic disc. At the same congress, in the discussion that followed, Professor Onishi described a more typical case, who, in addition to the eye signs had absent pulses. Thus the link between eye disease and pulselessness was established. Ironically Onishi has been forgotten, whereas Takayasu who was merely confused by a retinal vascular ring, has his name attached to a disease he never described. The eponym "Takayasu's disease" was first used in 1952, by Caccamise and Whitman, who thought they were describing the first case outside Japan.

The terminology of non-specific aortic arteritis is diverse and confusing, indicative of how little is known and understood about the condition. The syndrome has been given the following titles.:

1. "Reversed Coarctation" (Giffin 1939)
2. "The Aortic Arch Syndrome" (Frovig 1946)
3. "Pulseless disease" (Shimizu and Sano 1951)
4. "Young female arteritis" (Ross and McKusick 1953)
5. "Branchial arteritis" (Koszewski and Hubbard 1957)
6. "Obliterative Brachiocephalic arteritis" (Gibbons and King 1957)
7. "Syndrome of Occlusion of Supra-aortic trunks" (Martorell 1961)

Involvement of the aorta and vessels arising beyond the arch was initially thought to be a distinct disease entity. Terminology included:

"Elongate coarctation" (Milloy and Fell 1959)

"Sub-isthmic coarctation" (Morris, De Bakey, Cooley, Crawford 1960)

"Stenosing aortitis" (Sen, Kinare, Parulkar 1962)

"Middle aortic syndrome" (Sen, Kinare, Engineer, Parulkar 1963)

"Central aortitis" (Asherson and Gordon 1964)

Schrire and Asherson (1964)[1] were the first to name the disease "Arteritis of the Aorta and its major branches," and Sen called it "Non-specific Aortic arteritis." The latter two names are favoured for their accuracy and for encompassing the diverse spectrum of the disease.

1.3 DIAGNOSTIC CRITERIA

Since the first description of the disease more than 150 years ago, the most controversial aspect has been the diagnosis of the condition. This controversy has centred on the establishment of definitive diagnostic criteria, the proof of diagnosis, and the differentiation of the condition from other forms of arteritis and from atherosclerosis.

Prior to the availability of angiography , the diagnosis was based on the clinical findings, and confirmed only at autopsy. Although the clinical presentation provides valuable clues to the diagnosis, and is important in the assessment of complications, clinical features alone are inaccurate in defining the nature and extent of the disease. Pan-aortography is now regarded as essential to the diagnosis, and should be performed on all patients suspected of having this condition.

The histopathology may provide additional proof of the diagnosis and should be regarded as a useful adjunct to the clinical and angiographic findings. The diagnosis cannot be made on histology alone as several arteritides have identical findings. However, in the appropriate clinical setting, with compatible angiography, histopathology usually provides proof of the diagnosis.

Amongst the most important advances in the understanding of this condition has been the establishment in 1973 of specific diagnostic criteria by the Aortitis Research Committee of Japan[5]. These were based on 4 aspects. Symptoms, clinical signs, laboratory and histological findings, and angiography.

1. Symptoms

(1) Ischaemia to the central nervous system, the upper and lower extremities and to the kidneys.

(2) Associated non-specific systemic symptoms, such as fever, arthralgia, skin rashes, all suggestive of a systemic inflammatory process.

2. Clinical signs

Pulselessness / impaired pulse volume / unequal pulses.

Vascular bruits: supraclavicular, neck, abdominal, renal.

Aneurysms

Cardiac findings

Associated hypertension

Fundoscopic findings

3. Laboratory investigations

Biochemical and haematological results suggestive of a systemic inflammatory process:

Erythrocyte Sedimentation rate

C- Reactive protein

Gammaglobulin

Histopathology on surgical or autopsy material

Serology negative for syphilis.

4. Angiography

(1) Pan-aortography including the aortic bifurcation

(2) Pulmonary angiography

(3) Cardiac catheterisation studies with pressure measurements of the main vessels and cardiac chambers.

1.4 DIFFERENTIAL DIAGNOSIS

The differential diagnosis of aortic arteritis is extensive, and includes the following conditions:

1. Atherosclerosis
2. Collagen diseases:

Rheumatic fever

Rheumatoid arthritis

Ankylosing spondylitis

Systemic lupus erythematosis

Reiters syndrome

3. Infections:

   Tertiary syphilis

   Rubella

   Tuberculous arteritis

4. Congenital:

   Coarctation

   Congenital fibroelastosis

   Congenital hypercalcaemia

   Familial arteriopathy (Macaroni arteries)

   Neurofibromatosis

   Cogan syndrome

5. Post-traumatic

6. Other inflammatory conditions:

   Behcèts disease

   Giant cell arteritis

   Kawasaki disease (Mucocutaneous lymph node syndrome)

2. PATIENTS AND METHODS

The computerised record systems of Groote Schuur and Red Cross Childrens' Hospitals were used to identify the patients. Only patients who were coded as having "non-specific aortic arteritis" after being thoroughly investigated were included in the study. The main sources of information included the records of the following departments at Groote Schuur and Red Cross Hospitals:

(1) Cardiology. 133 patients (60%) underwent cardiac catheterisation studies and were carefully followed by the cardiac unit. Excellent records were maintained on these patients.

(2) Nephrology unit

(3) Hypertension clinic

(4) Vascular suite of the Department of Diagnostic Radiology

(5) General medicine and General Surgery

(6) Department of Pathology

The study was performed retrospectively over a period of 36 years (1952-1987), and included 220 patients.

The inclusion criteria were strictly in accordance with the Aortitis Research Committee of Japan[5].

Aortic angiography (including arch studies) was performed on all patients and was regarded as essential to the diagnosis. All specific forms of aortic arteritis were excluded, as were patients with single vessel disease and patients with a doubtful diagnosis.

Patients who conformed with the Japanese diagnostic criteria but never underwent aortic angiography were excluded from the study. Definitive histological proof of the diagnosis was obtained in as many patients as possible. This was available in 57 patients (20%) either from surgical specimens or from autopsy material.

Patients with the so-called "middle aortic syndrome" sometimes posed a diagnostic dilemma. This condition usually occurs in middle-aged females who characteristically have short stocky proportions. The nature of this syndrome is probably atherosclerosis, and these patients were excluded unless concomitant aortic arch disease was present.

Information regarding the long-term outcome of patients was obtained from the records available in the various medical and surgical departments. In many instances contact was made telephonically and through correspondence with the patients or their medical practitioners. Although this was a retrospective study, I personally examined and assessed more than 50 of these patients.

3. CASE REPORTS

The selection of case reports illustrates the diverse spectrum of the disease seen in Cape Town, and the available therapeutic options.

Case No. 1

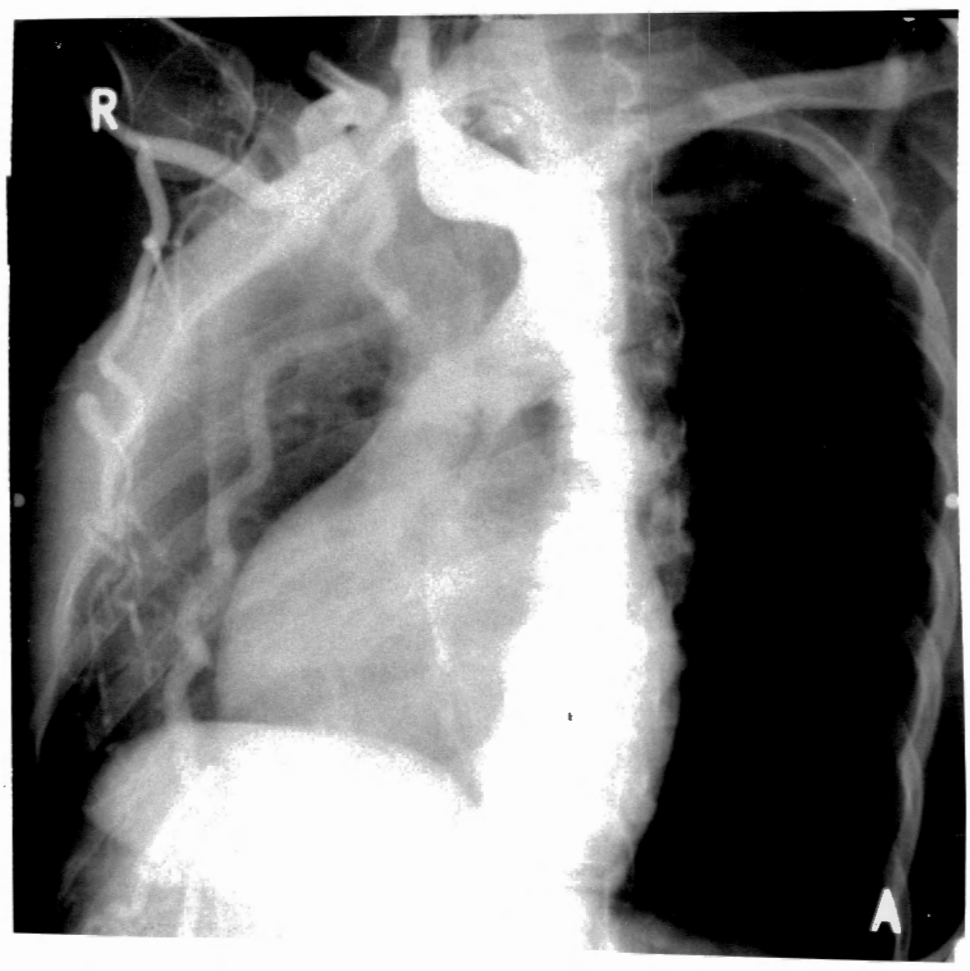
This 19 year old black female presented to a general practitioner in 1985 with a one year history of severe headaches. She also had intermittent claudication involving calves, thighs and buttocks bilaterally. Blood pressure was $^{210}/_{140}$. Femoral and distal pulses were absent bilaterally. Prominent subclavian arterial pulsation was evident in both supraclavicular fossae. Fundoscopy showed grade II hypertensive retinopathy only. The following investigations were all normal: biochemistry, haematology and ESR; collagen screen, serum immuno-globulins and complement; chest radiograph, mantoux. Angiogram: stenosis of the descending aorta from T6 to T11. Ascending aorta and arch normal. Both subclavian and innominate vessels dilated, considered to be due to distal stenosis of the aorta, and not intrinsic subclavian disease. The following arteries were entirely normal: coronary, carotid, abdominal aorta, bifurcation, renal, mesenteric, iliac and common femoral.

The patient underwent thoracotomy in April 1985 with insertion of a graft from the ascending aorta to the distal descending aorta. She became normotensive and was well at a recent assessment in 1987, with normal pulses and requiring no medication.

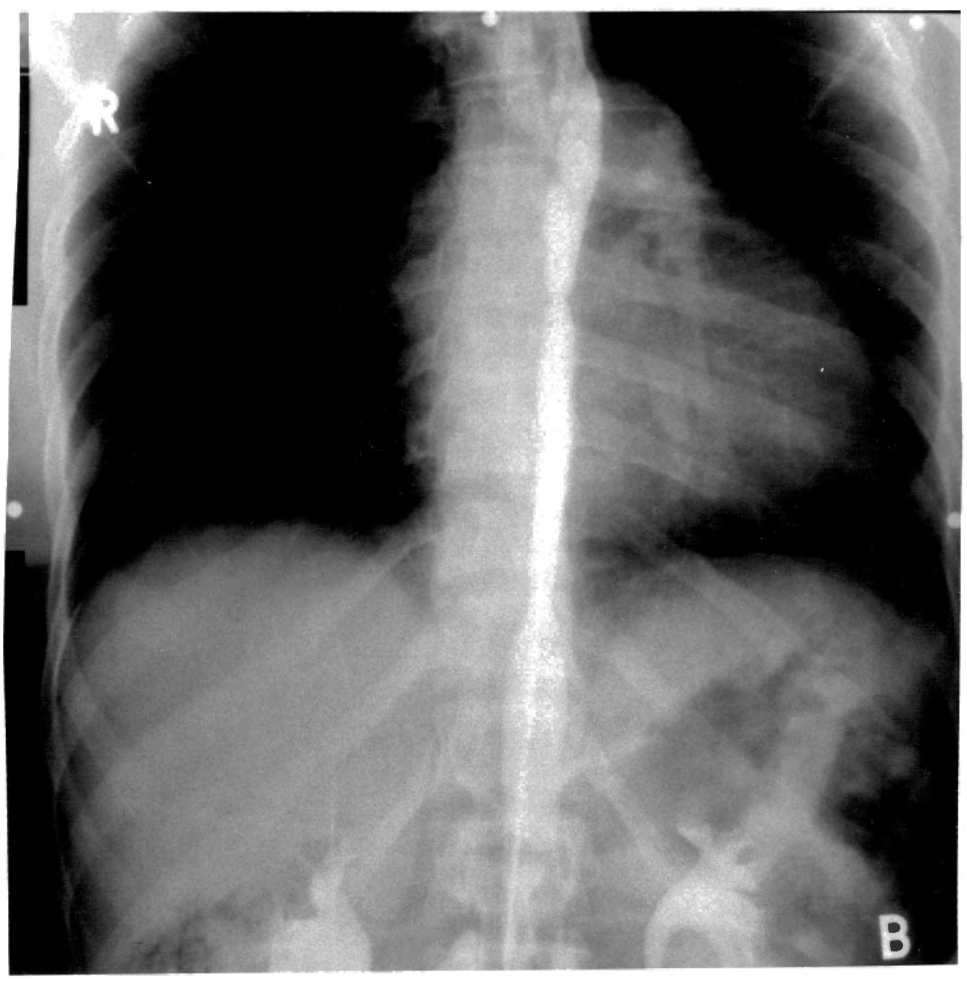
Comment

This patient represents a classic case of type II disease (Nasu 1976), presenting with severe hypertension on the basis of aortic coarctation. The localised nature of the disease, her relative youth and the absence of cardiac and renal complications made this patient highly suitable for surgery.

Case No. 1.



CASE No. 1. DESCENDING AORTAGRAM.



Case No. 3

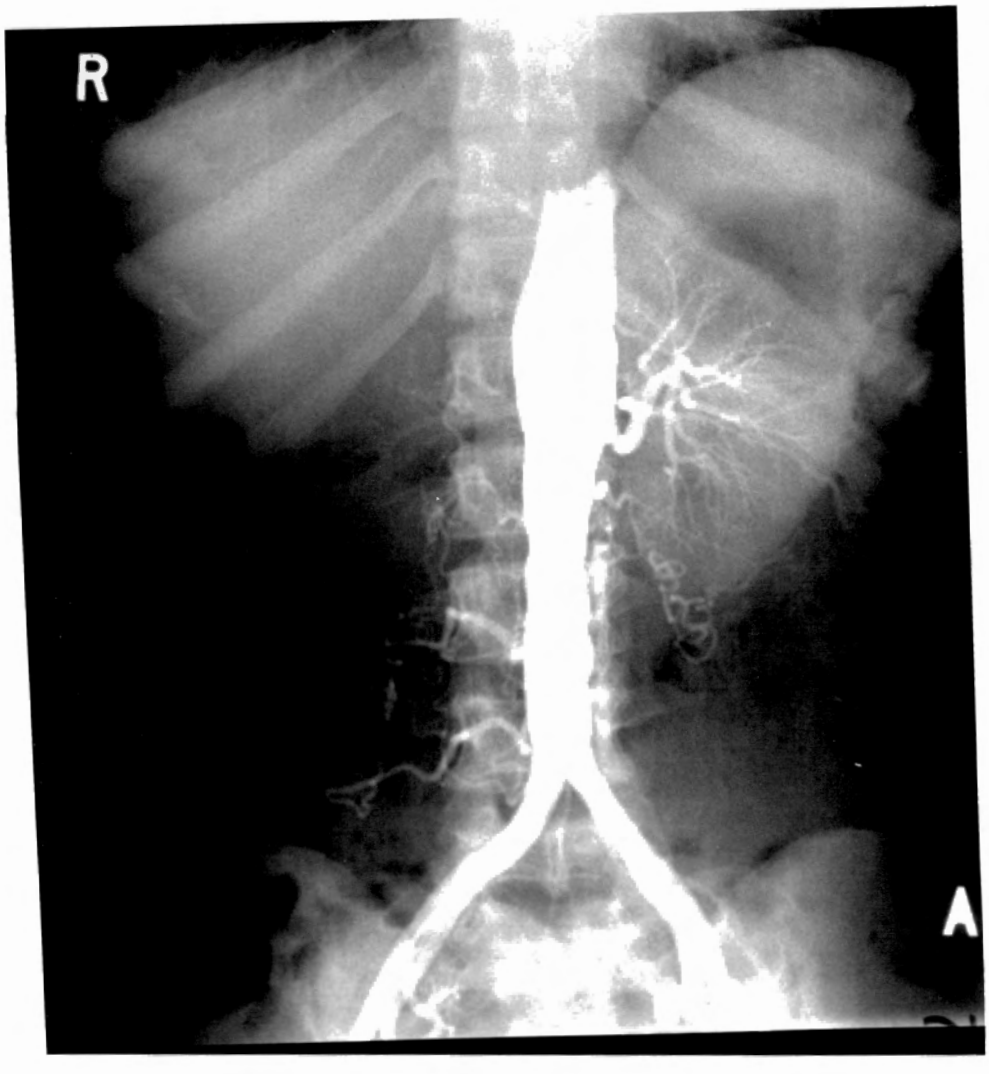
This 27 year old Coloured female presented in 1983 with hypertension ($BP^{240}/_{140}$) and congestive cardiac failure.
Apart from a diminished left brachial pulse, all pulses were equal. There was a left subclavian bruit, and hypertensive retinopathy. Renal function was impaired, with creatinine clearance 32 ml/min. Intravenous pyelography showed a small atrophic right kidney. Relative renal function on isotope scan was 82% left 18% right. The ESR was 30. Aortography showed irregularities of the aortic arch, left subclavian artery, and a small aneurysm of the abdominal aorta. Right renal artery occluded. Left side normal. Occluded coeliac, S.M.A. and I.M.A., with collateral supply to the bowel from the iliac vessels. Renal vein renin ratio was >1,6 with suppression on the left. Cardiac catheterisation studies confirmed left ventricular failure, considered to be due to hypertensive heart disease.

The cardiac failure was controlled with digoxin and a diuretic. A right nephrectomy was performed, and the diastolic blood pressure was reduced to 90 mm Hg on no further treatment. Prophylactic mesenteric revascularisation was carefully considered, but not performed. She has remained well for 5 years since the operation.

Comment

An example of diffuse disease, both "dilating" and "occlusive" in nature, the case illustrates a problem of renovascular hypertension and its cardiac sequelae. Nephrectomy remains a worthwhile procedure in selected cases.

CASE NO. 3. ABDOMINAL AORTAGRAM.



Case No. 4

A 23 year old "Coloured" male initially seen in 1984 with a duodenal ulcer. He presented a year later with headache, hypertension ($^{190}/_{140}$) and proteinuria. He had a renal artery bruit (Lt.). Renal function was impaired with a creatinine clearance of 14 ml/minute. The right kidney was small and had only 7% of function. Aortography showed a saccular abdominal aortic aneurysm, involving the origins of renal arteries. Arch and descending aorta normal. Occluded right renal artery. Stenosis left renal artery. The S.M.A. was occluded at the origin. Renal vein renin levels were high with a ratio of less than 1.6.

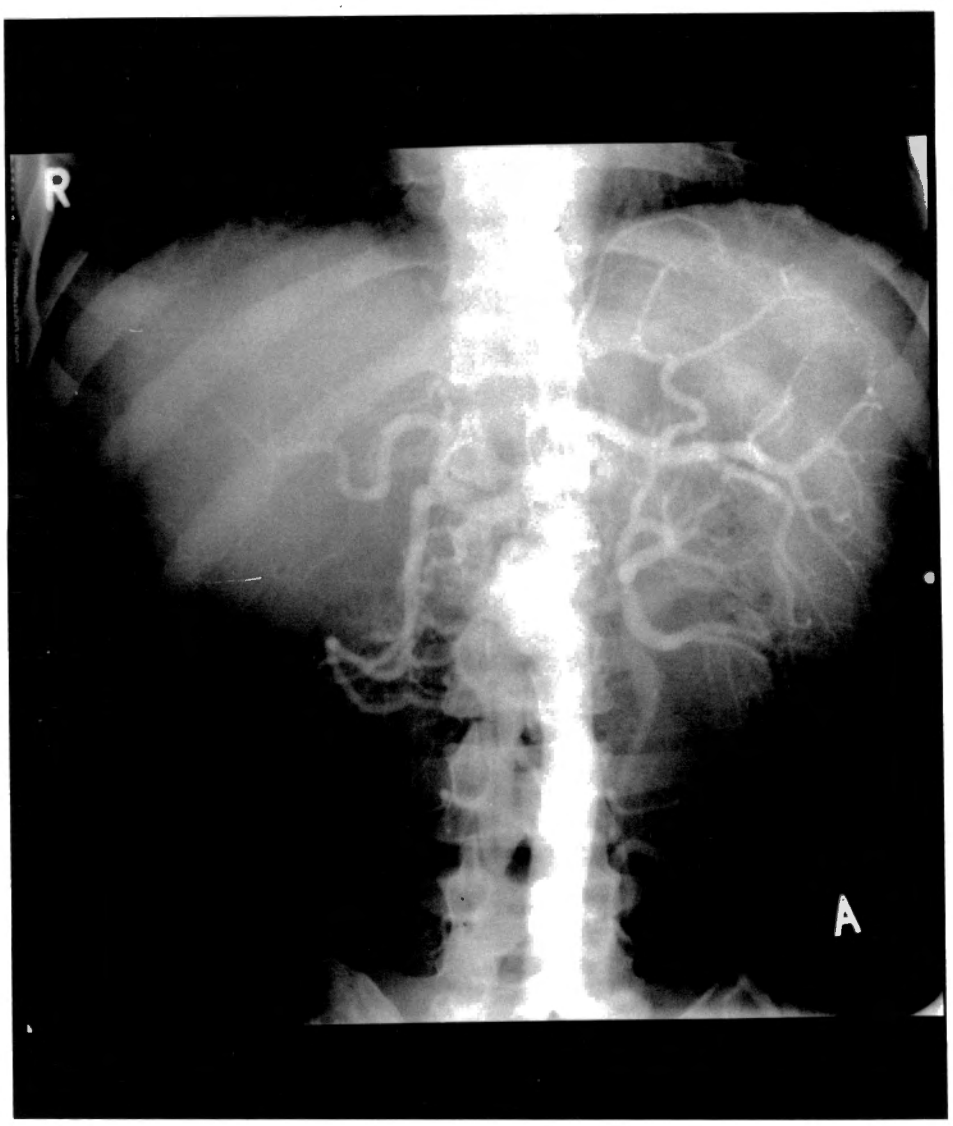
An aortic tube graft was inserted, with proximal anastomosis between the origins of the coeliac and superior mesenteric arteries. Dacron side grafts were anastomosed to both renal arteries and the S.M.A Renal biopsy on the right showed a viable kidney.

Post-operatively his blood pressure was maintained at 90 mm Hg with a diuretic only, and he has remained well. Histology of the aorta confirmed Takayasu's disease. His renal function has significantly improved since surgery.

Comment

An example of the "middle aortic syndrome", with "dilating" and "occlusive" aspects present, the case illustrates a dilemma in the management of renovascular hypertension. With the current emphasis in the literature on renal preservation, previous

criteria for nephrectomy based on kidney size (<9cm) and relative function (<20%) are no longer valid. Furthermore, it has been shown that revascularisation may improve renal function, as occurred in this patient. Nephrectomy in this patient, with non-lateralising renal vein renins, may not have controlled the blood pressure and may have led to renal failure requiring long-term dialysis.



Case No. 5

27 year old "Coloured" female from the country districts presenting initially in 1967 with a neck swelling, clinically a carotid aneurysm. Angiography confirmed the diagnosis and showed diffuse disease, "dilating" and "occlusive" of the entire aorta and main branches. BP $^{270}/_{140}$. Cardiac catheterisation showed aortic incompetence. ESR 90. She was treated with anti-hypertensive medications only, and was lost to follow-up for 10 years. Readmitted in 1978 with a ruptured internal iliac aneurysm. She underwent successful emergency surgery. Repeat angiography showed some disease progression, with a dilated ascending aorta, arch, innominate, right subclavian. The left carotid aneurysm was enlarged. Occluded left subclavian, stenosed descending aorta, aneurysm of the abdominal aorta, and right renal artery. In 1980 she had a stroke, causing a right hemiplegia. She died a year later of another stroke.

Comment

A typical example of the diffuse form of the disease occurring in Cape Town, the case illustrates the significance of aneurysms in this disease. Aneurysms due to aortitis do rupture, irrespective of size, and should be operated on electively whenever possible. Another complication of aneurysms, viz. embolisation, caused repeated strokes and led to the demise of the patient.

Case No. 6

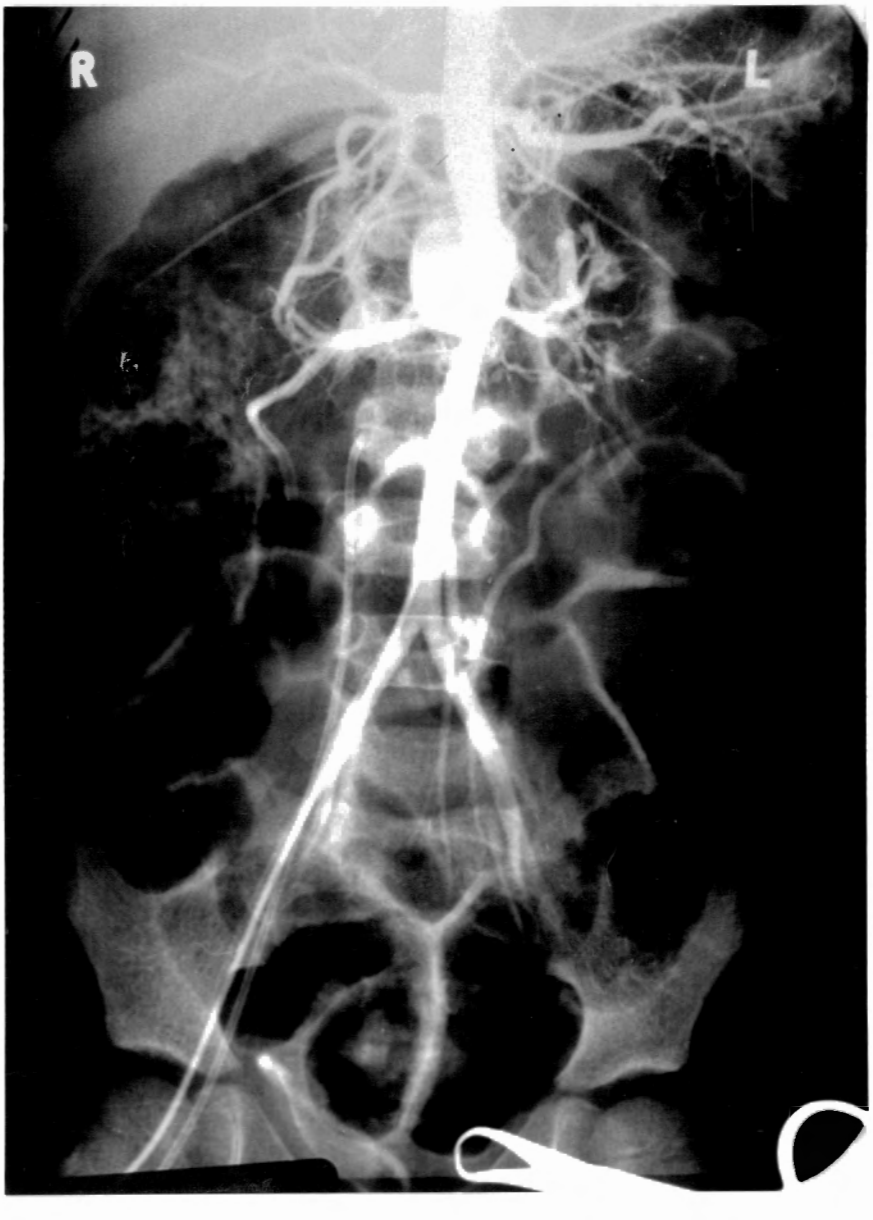
This 10 year old Coloured girl presented with a pulsatile mass in her abdomen and severe hypertension. Examination confirmed an abdominal aortic aneurysm and a renal bruit. All pulses were present and equal. Angiography showed a normal proximal aorta, an abdominal aortic aneurysm, an occluded right renal artery and severe stenosis of the left renal artery with some branch vessel disease. Renal vein renin ratios were high bilaterally, with a ratio of <1.6. The right kidney was atrophic.

She underwent aneurysm resection, insertion of a "tube" graft, right nephrectomy and left renal autotransplantation with anastomoses to the iliac vessels. The anastomosis was performed "ex vivo", under magnification with the kidney "cold perfused" with ringers solution. The divisions of the ipsilateral internal iliac artery were anastomosed to the branch vessels of the renal artery, and the renal vein was anastomosed to the external iliac vein. The hypertension was cured, the renal function remained within normal limits, and she has been well at a 5-year reassessment.

Comment

Another case of renovascular hypertension emphasising its prevalence in this series of patients. The choice surgical procedure for renal artery stenosis in Takayasu's disease is aorta-renal bypass using autogenous artery. Saphenous vein and dacron are also acceptable graft materials. There is no place

for "endarterectomy" in aortic arteritis as the pathology involves the media of the artery, with the intima relatively spared. Auto-transplantation is a more complex procedure reserved for segmental branch vessel disease.



Case No. 7

This 6 year old Transkeian girl presented in 1980 with an acute chest infection. A pulse deficit was noted in the right arm. Pulmonary tuberculosis was proven on sputum examination. There were no other findings on physical examination. Angiography showed irregularity of the innominate artery, and occlusion of the right subclavian. The aorta appeared normal. Pulmonary angiography showed arteritis with bilateral pulmonary artery aneurysms. The tuberculosis was treated and she received a course of corticosteroids.

She was reasonably well until 1985 when she developed right sided cardiac failure, and was noted to have an absent right carotid pulse. Repeat angiography in 1986 showed progression of the pulmonary arteritis and occlusion of the right common carotid artery. The aorta remained normal. Cardiac catheterisation studies confirmed right ventricular failure, pulmonary hypertension and cor pulmonale. There was no progression of the pulmonary tuberculosis to account for the pulmonary hypertension. The cardiac failure was treated adequately with diuretics.

Comment

Takayasu's disease is the only form of aortic arteritis that may have associated pulmonary arteritis, and the incidence of this may be as high as 50%. As occurred in this case, progression of the pulmonary arteritis may be independent of the systemic disease. Pulmonary angiography is now performed routinely on patients with aortic arteritis. The pulmonary angiogram on this patient is shown below.

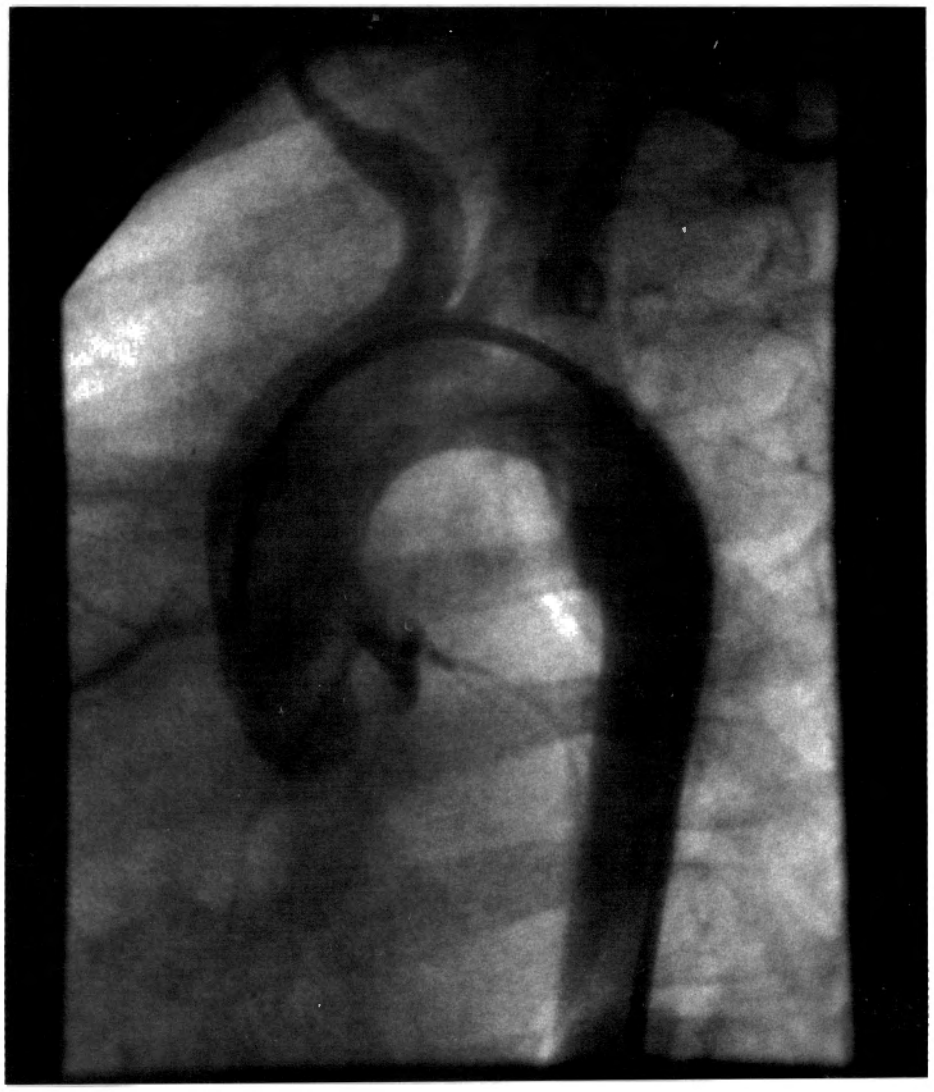
Case No. 8

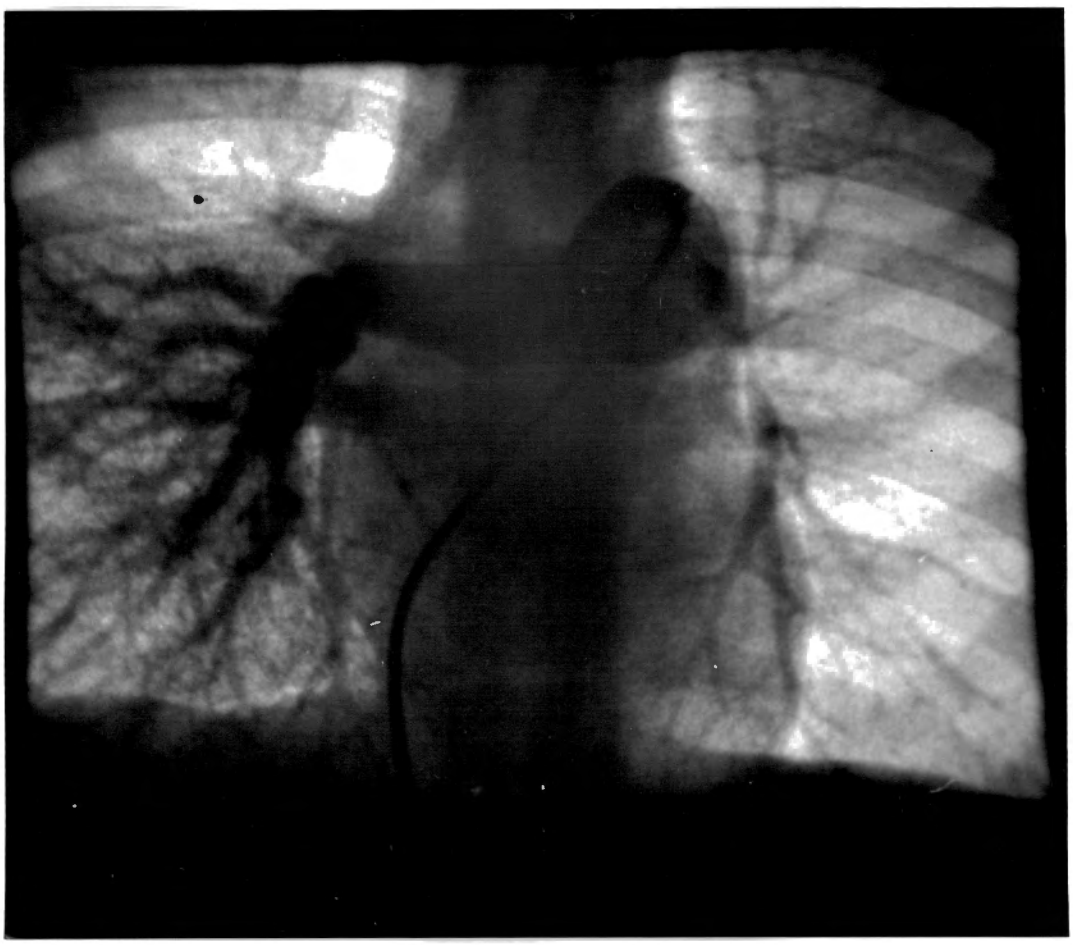
This 42 year old patient presented with mild cardiac failure, valvular heart disease, and erythema multiforme. Cardiac catheterisation confirmed the presence of aortic incompetence, mitral stenosis and left ventricular failure. Lower limb pulses had a reduced volume compared with other pulses. Aortography showed dilatation of the ascending aorta and arch. The descending and abdominal aorta had occlusive disease. The branches were spared of disease.

In view of aggravating cardiac failure, she underwent aortic valve replacement in 1987. The ascending aorta was simultaneously replaced with a dacron prosthesis. Her cardiac status improved significantly following surgery.

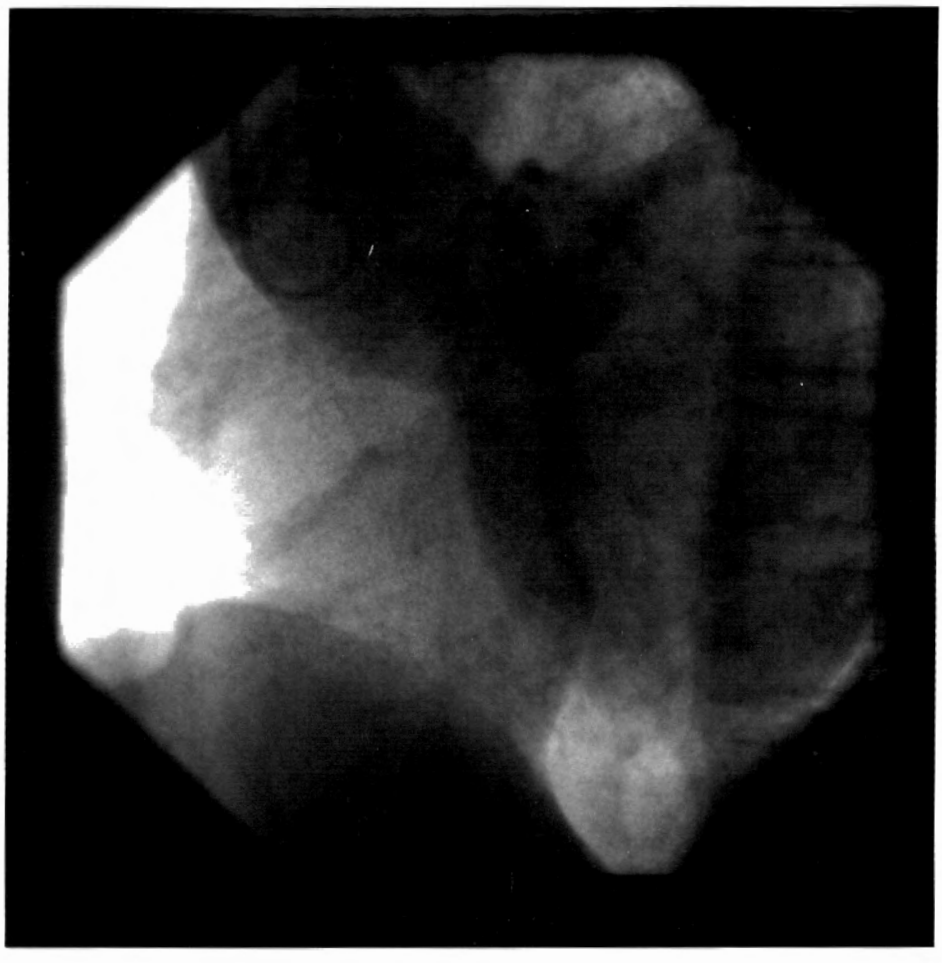
Comment

Aortic incompetence is a common finding in Takayasu's disease, usually associated with dilating disease of the ascending aorta and a dilated valve ring. The valve cusps may have histologic evidence of arteritis. Aortic incompetence is surpassed only by hypertensive heart disease as the commonest cause of cardiac failure in Takayasu's disease. Response to valve replacement is usually good, although the long-term results are unknown. The aortogram showing aortic valve insufficiency is shown below.

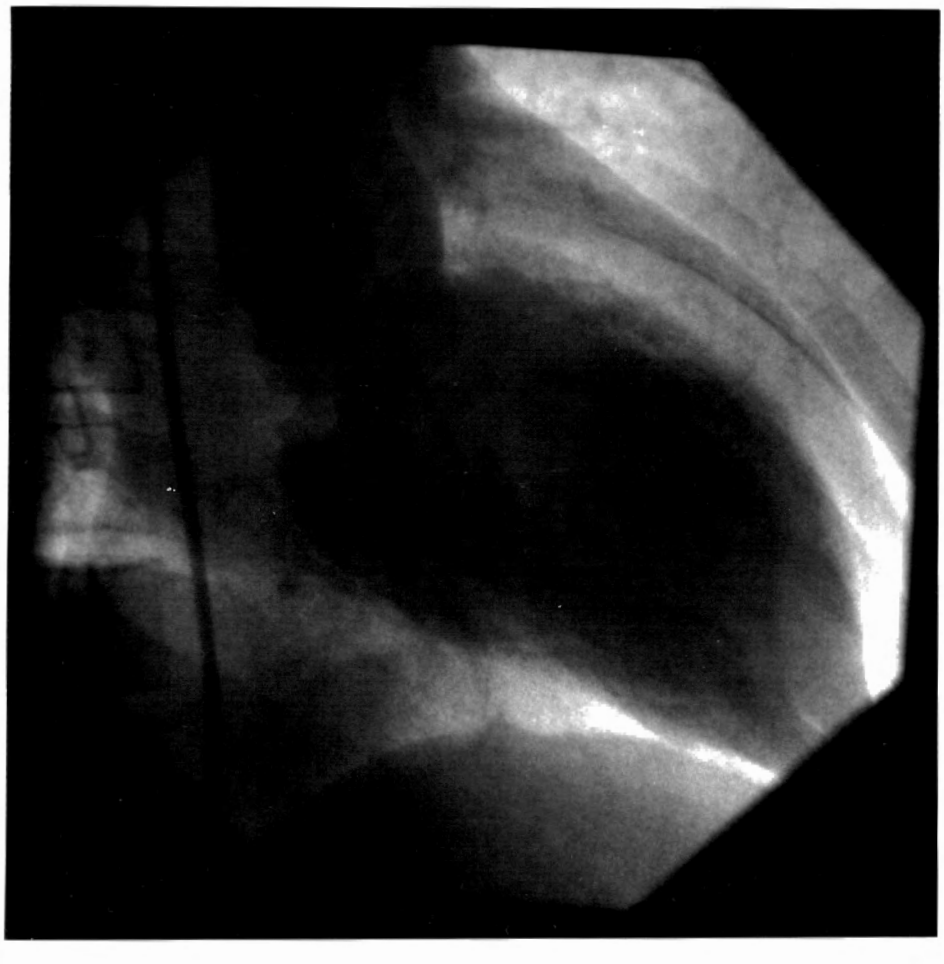




CASE NO. 8.



AORTOGRAM.



VENTRICULOGRAM.

Case No. 9

12 years old and severely ill, this child was admitted to hospital in 1986 with erythema nodosum, pulmonary tuberculosis, tuberculous pericarditis, severe hypertension and cardiac failure. She had abdominal and carotid bruits, and absent pulses in the right arm. The ESR was 118. Angiography showed diffuse disease with multiple aneurysms and stenoses of all parts of the aorta. The aortic bifurcation was stenosed. There was bilateral carotid stenosis, occlusion of the right subclavian, bilateral renal artery stenosis and mesenteric stenosis. Pulmonary angiography was normal.

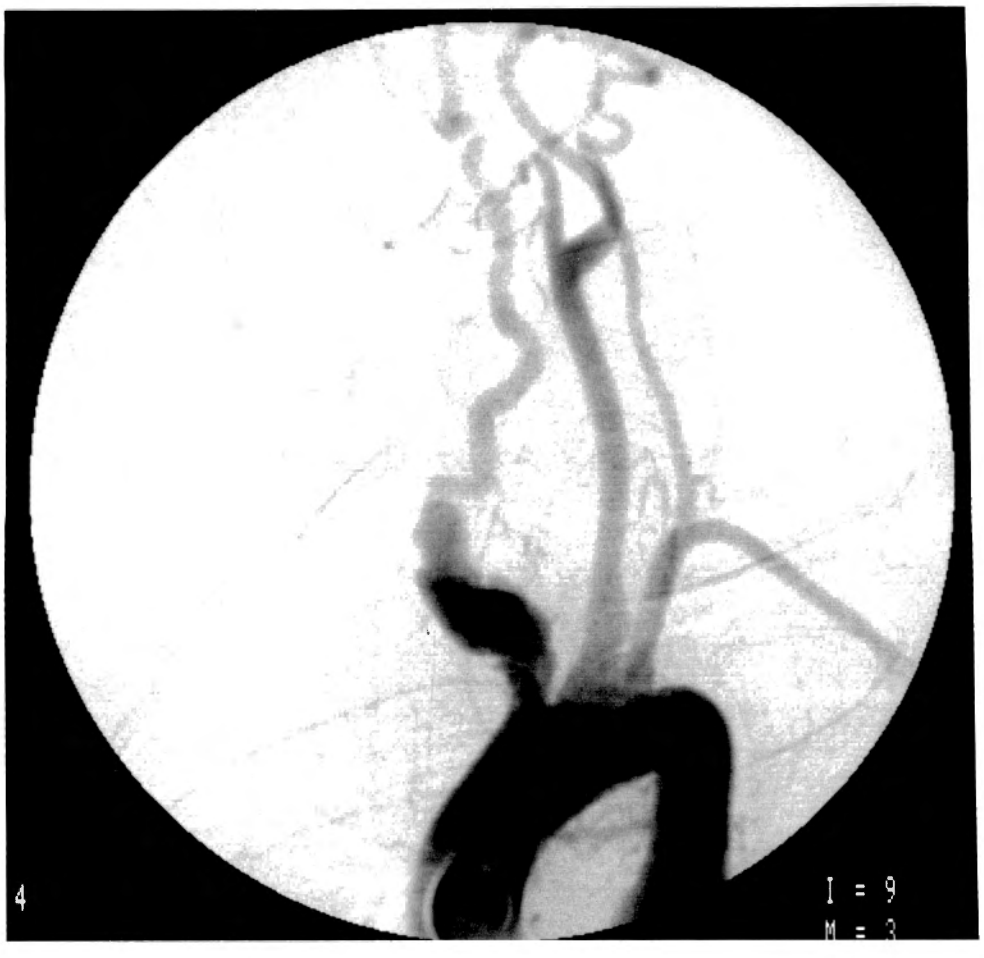
Despite intensive medical care, she died of intractable cardiac failure, considered to be primarily due to hypertensive heart disease. Autopsy confirmed the clinical diagnoses.

Comment

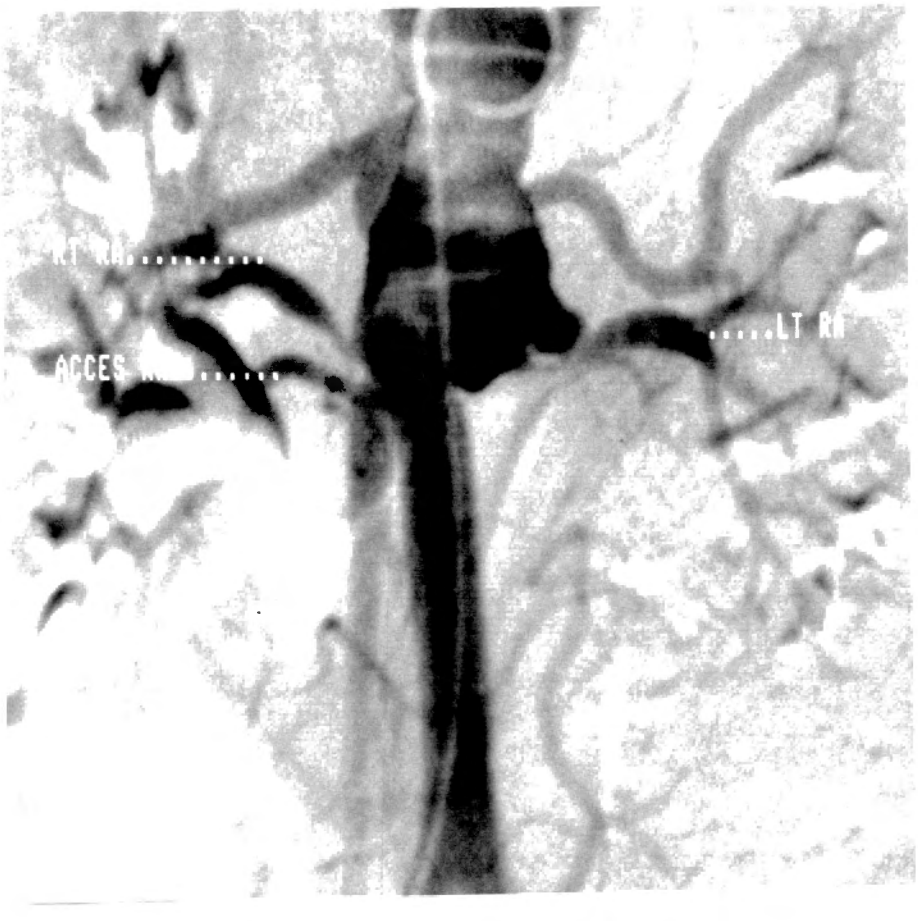
An example of the type IV disease (Nasu 1976), the case emphasizes the importance of hypertension and cardiac failure, both as presenting problems and as a cause of death in aortic arteritis.

CASE NO. 9.

AORTIC ARCH.



ABDOMINAL AORTA.



Case No. 10

This 29 year old patient presented in 1986 with a critically ischaemic right foot, with non-healing ulceration. She had a one year history of intermittent claudication involving all four limbs. Examination showed a "threatened" right lower limb, normal blood pressure and heart, and absent pulses in all four limbs. ESR 110. Chest X-ray showed cavitation of the right upper lobe, and the mantoux test was ulcerating. Angiography: dilated ascending aorta and arch, stenosis of the abdominal aorta and bifurcation occlusion of the right common iliac, and stenosis on the left. There was bilateral superficial femoral artery disease, with occlusion of the trifurcation of the popliteal artery bilaterally. Both subclavian arteries were occluded.

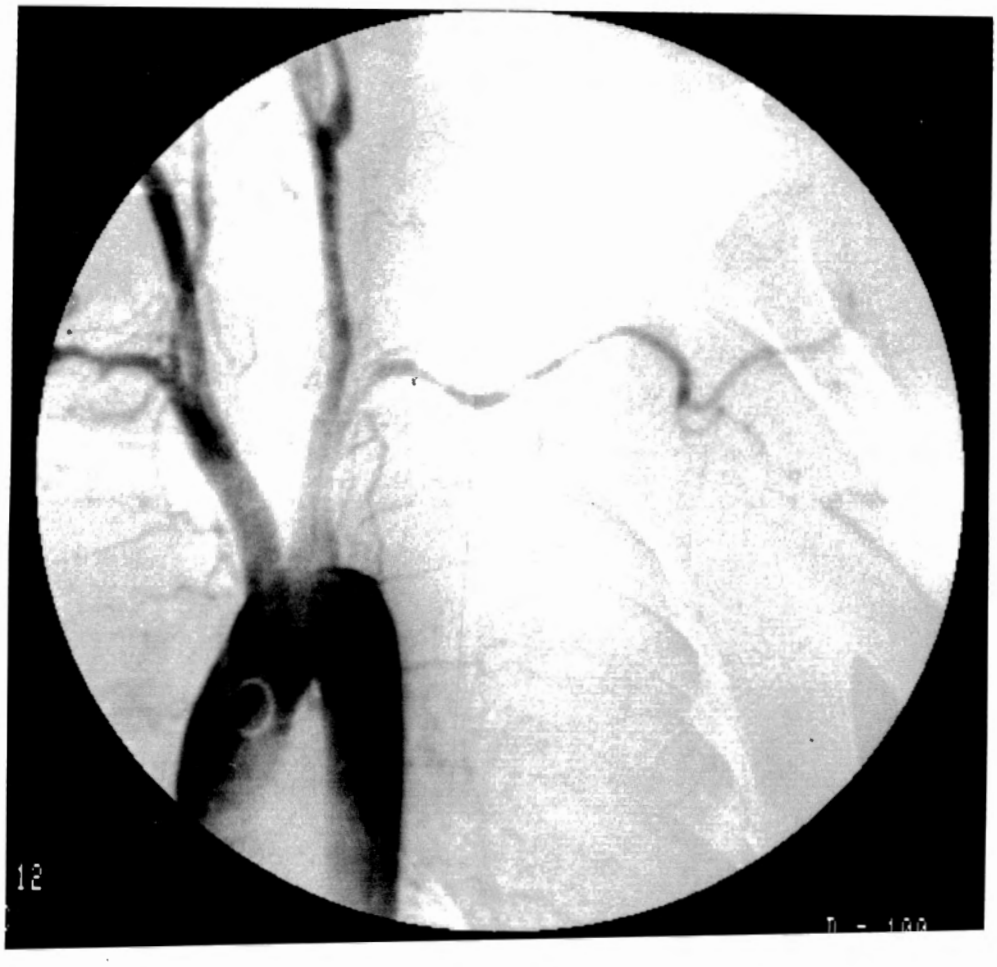
In view of the extensive aortic and distal disease, vascular surgery was considered inappropriate. She underwent a below knee amputation on the right and had a full course of anti-tuberulous therapy. Her condition has remained unchanged at 2 years. Histology confirmed arteritis of the superficial femoral artery. The ischaemic foot ulcer had non-specific histological findings.

Comment

An example of diffuse vascular disease, the case also illustrates an unusual feature of Takayasu's disease: involvement of distal limb vessels. Schrire and Asherson [1] were the first to

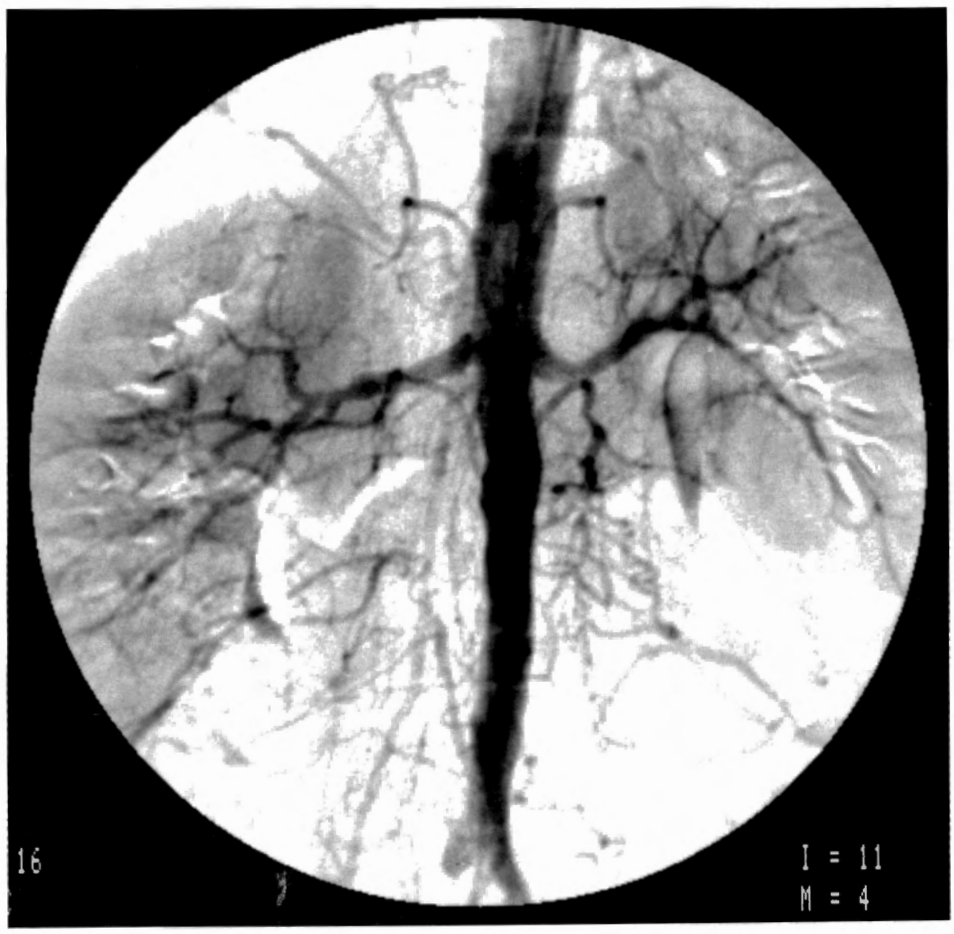
document peripheral vascular disease as a feature of this condition. However, peripheral vascular occlusion in aortic arteritis is usually embolic in nature, with no evidence of distal vessel arteritis.

CASE NO. 10. ARCH AORTOGRAM.



CASE NO. 10.

ABDOMINAL AORTOGRAM.



Case No. 11

This 32 year old Coloured male presented in 1986 with a large abdominal aortic aneurysm which was asymptomatic. Examination also revealed a carotid aneurysm. He was normotensive, and all peripheral pulses were present. Angiography showed aneurysms of the descending aorta, abdominal aorta, aortic bifurcation, left common carotid and left subclavian artery. There was no associated occlusive disease.

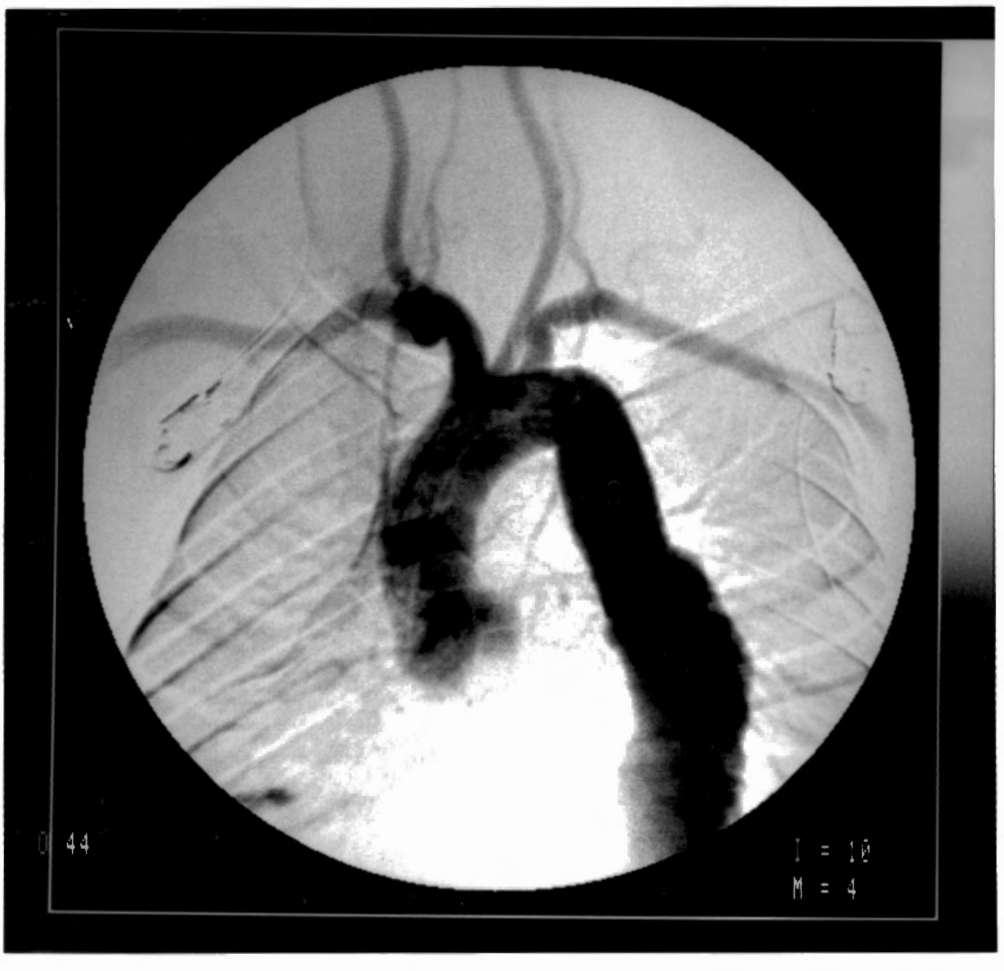
The abdominal aortic aneurysm ruptured while the patient was in hospital. He underwent emergency surgery with a dacron aorto-bi-iliac graft. The post-operative course was uneventful and he is currently awaiting surgery to the carotid aneurysm. Histology confirmed the diagnosis of aortic arteritis.

Comment

The case is an example of multiple aneurysms, without associated occlusive disease. This occurred in only 7% of the current study, and is regarded as exceptionally rare in Asia and the Soviet Union.

CASE NO. 11.

ARCH AND DESCENDING AORTOGRAM.



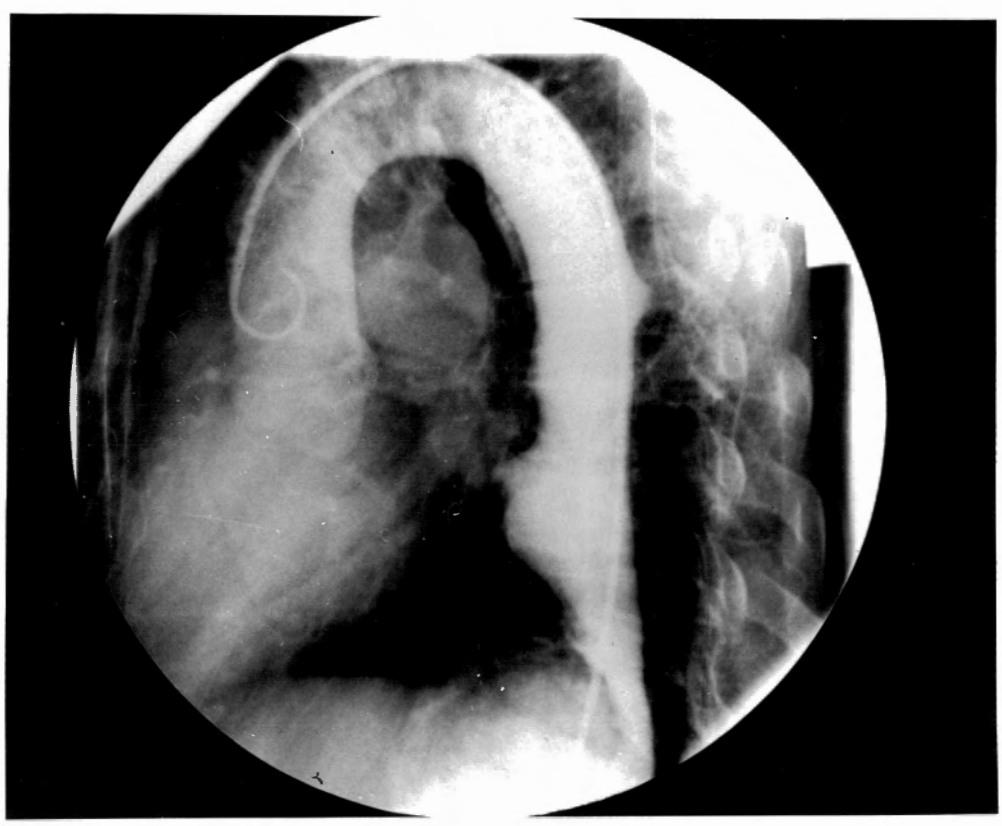
Case No. 12

This 54 year old patient presented with chest pain and dysphagia. On physical examination she was hypertensive and had an abdominal aortic aneurysm. Angiography showed a descending aortic aneurysm, separate abdominal aortic aneurysm, bilateral pulmonary artery aneurysms, with the remainder of the vasculature normal.

She underwent aneurysmectomy of the thoracic aorta with insertion of a tube graft and has made a good recovery. The histology of the aorta confirmed arteritis. She is awaiting planned surgery for the abdominal aorta.

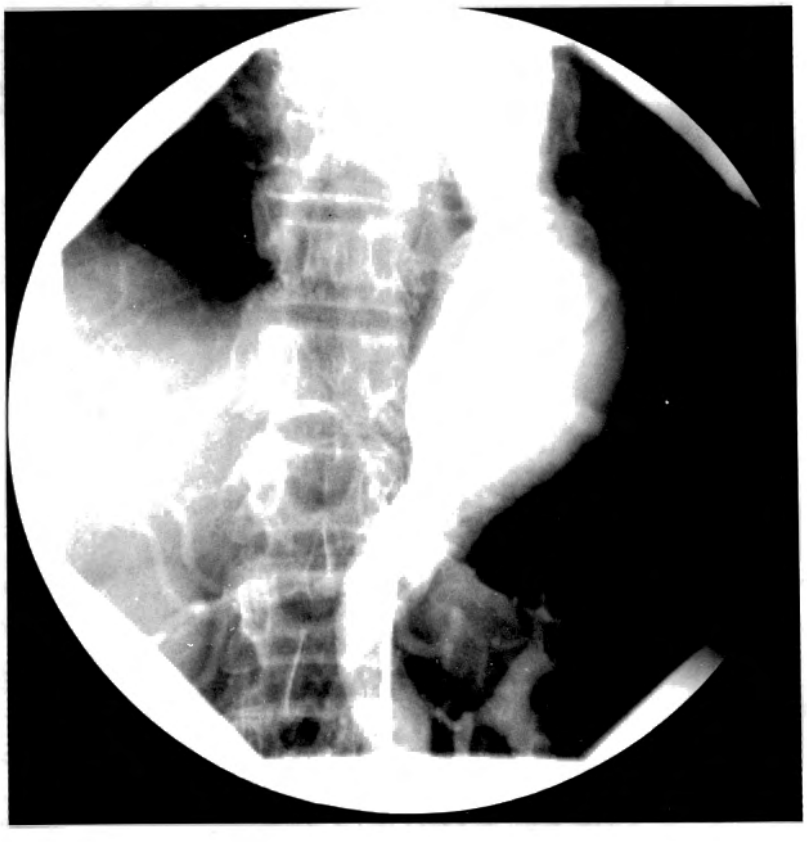
Comment

Another example of dilating disease unassociated with an occlusive pattern, the case also illustrates pulmonary artery involvement.



CASE 12.

ABDOMINAL AORTOGRAM.



Case 13

An 18 year old patient with severe hypertension. He had a previous history of pulmonary tuberculosis and proven tuberculous adenitis of the neck. He also had mild left ventricular failure. Renal function was normal. Isotope renogram and pyelography showed an atrophic right kidney with minimal function. Angiography: Aneurysms of the descending and abdominal aorta, and of the left subclavian. The right renal artery and S.M.A. were occluded and the left renal artery stenosed. Right renal vein renin was very high, with contralateral suppression and a ratio of >1.6.

Cardiac catheterisation confirmed hypertensive heart disease with mild left ventricular failure.

He underwent a right nephrectomy with dramatic response of his blood pressure, and has remained normotensive on a mild diuretic only.

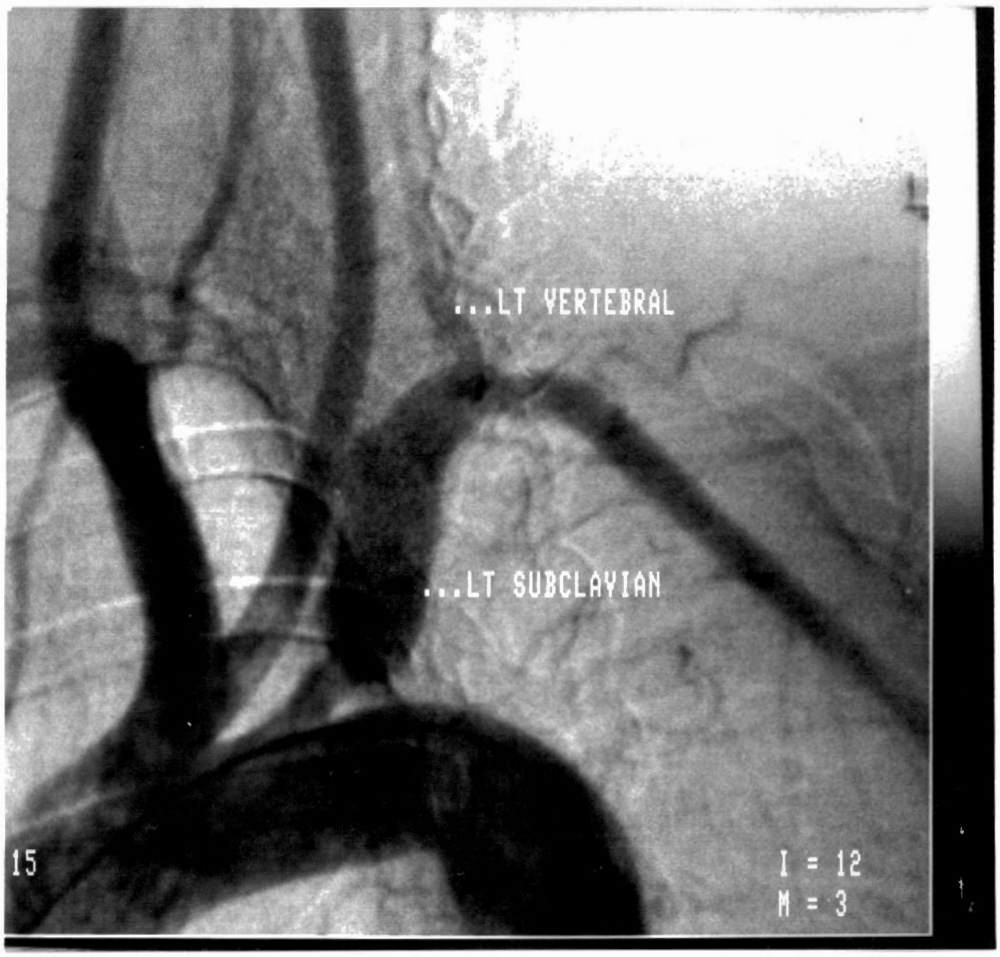
Comment

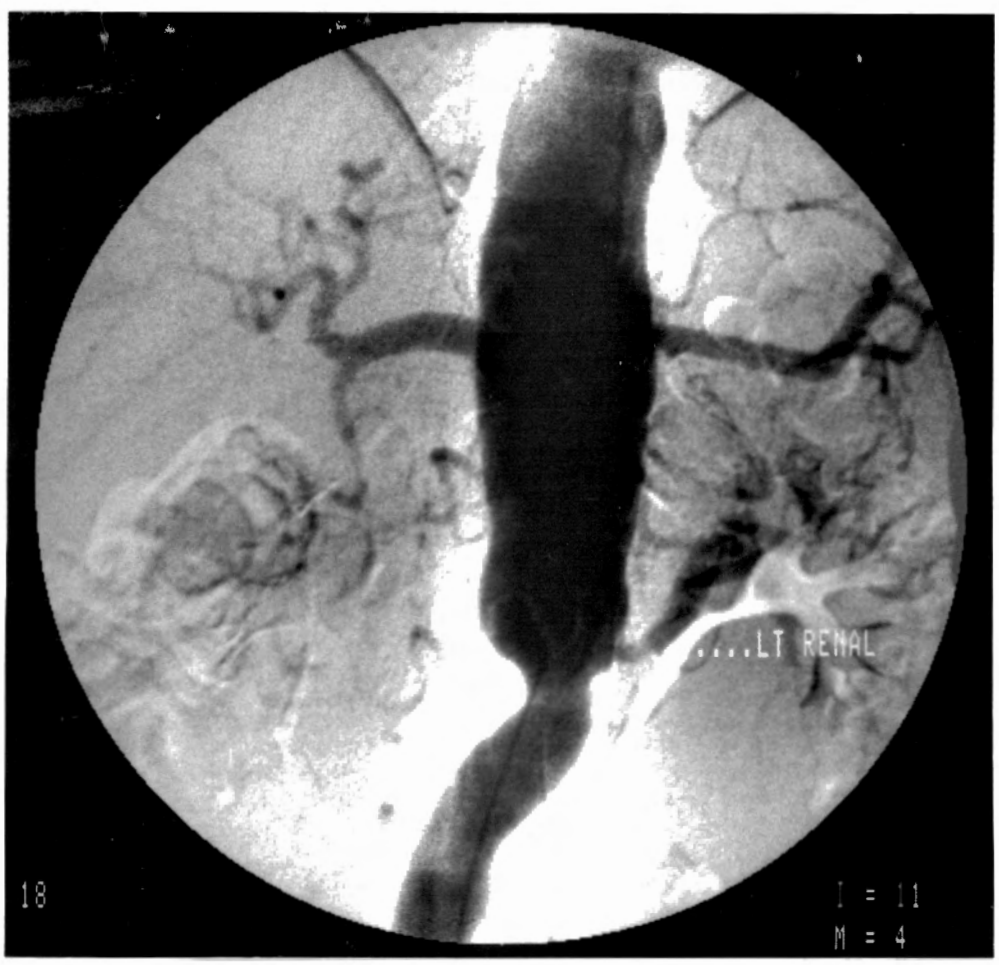
An ideal case for nephrectomy which remains an effective and safe operation in selected patients. There are two indications for nephrectomy in aortic arteritis:

(1) severe branch vessel disease, not suitable for reconstructive surgery, causing intractable hypertension

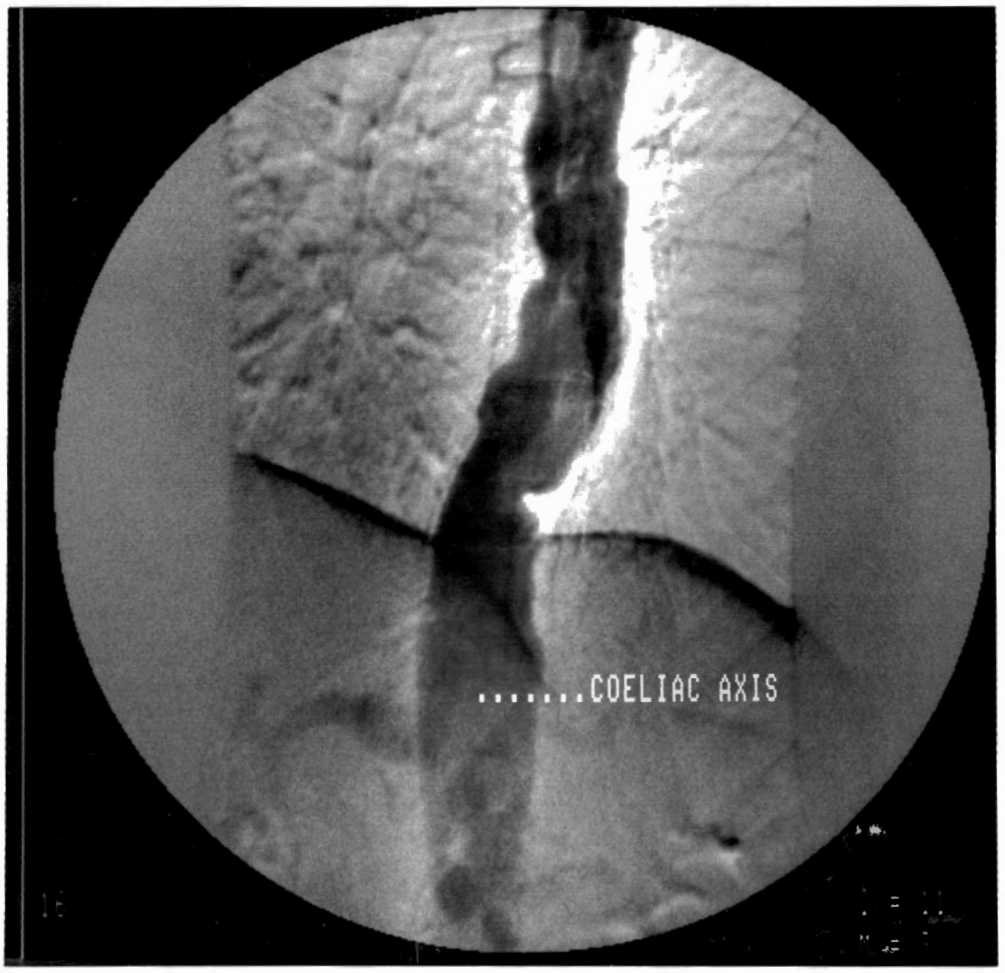
(2) an atrophic poorly functioning kidney which is renin-producing.

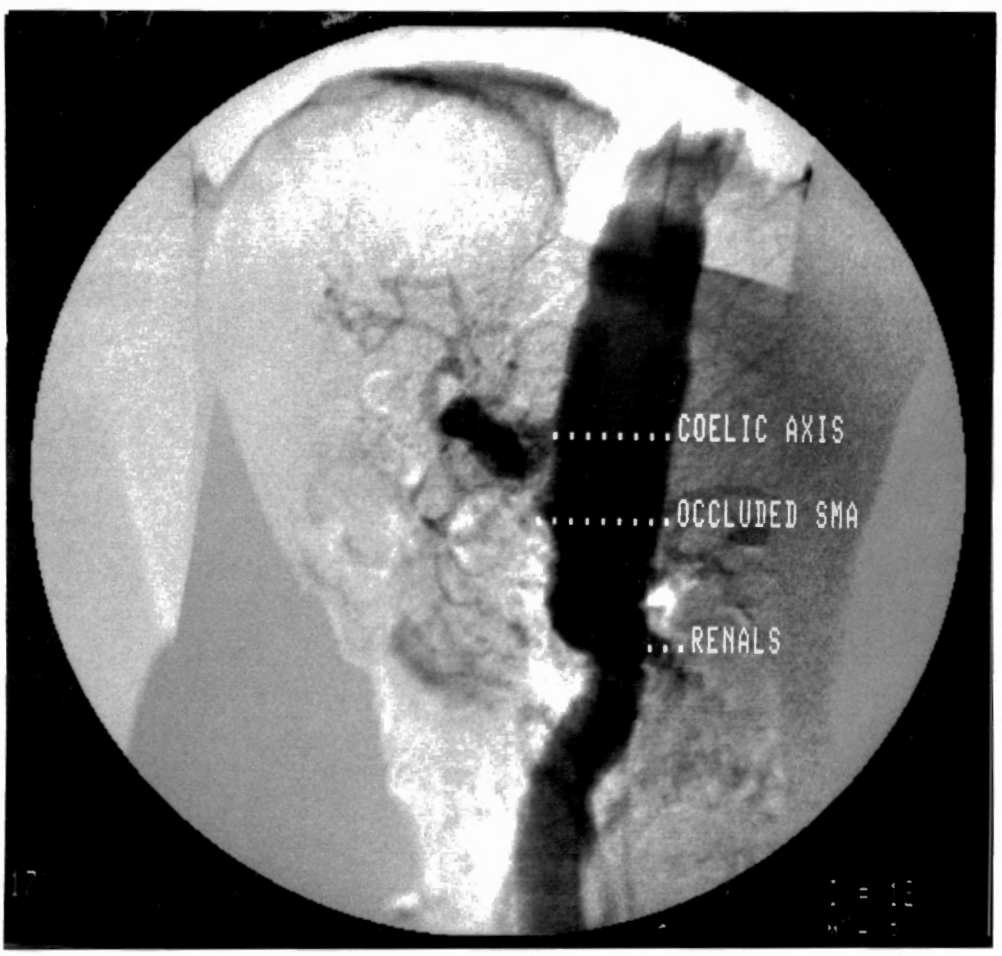
CASE NO. 13.





CASE NO. 13.





Case no. 14

This 17 year old patient was investigated for hypertension in 1973. He was asymptomatic, and the only other clinical findings were bilateral renal artery bruits. Angiography showed a normal aortic arch, both dilating and occlusive disease of the descending aorta, narrowing of the abdominal aorta, bilateral renal artery stenosis.

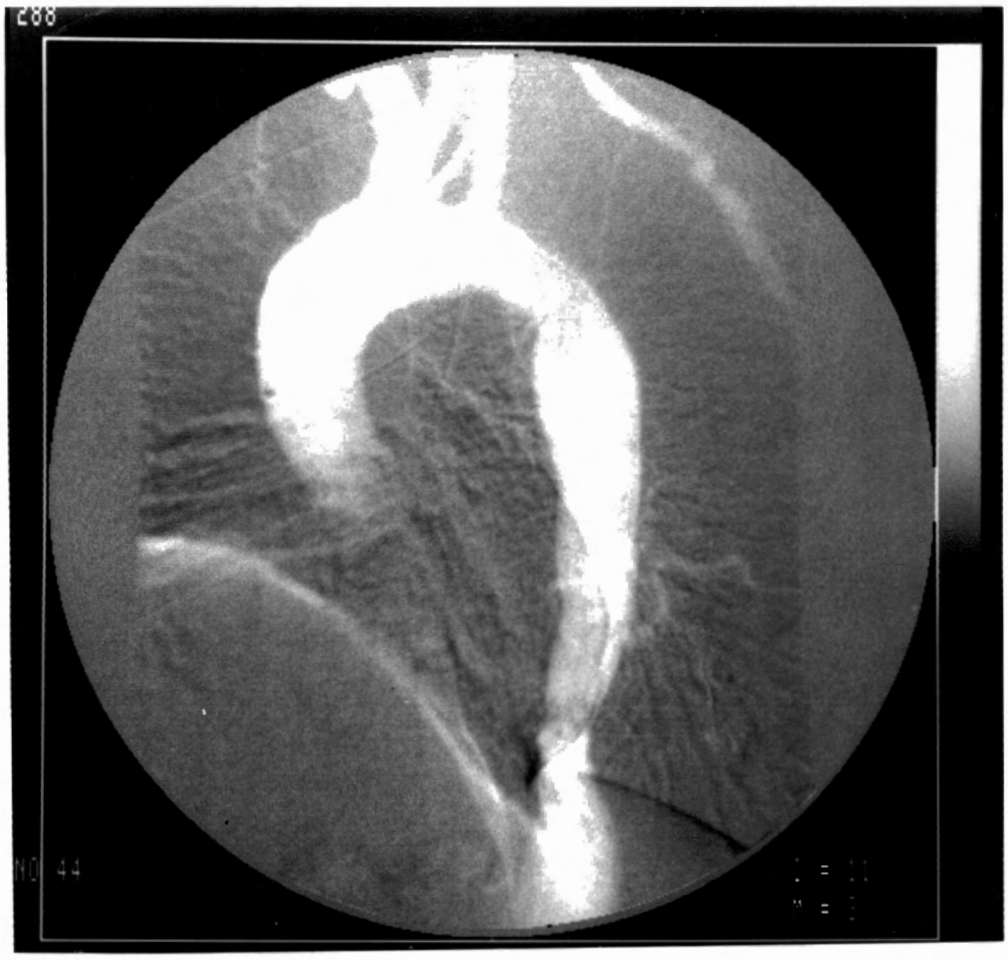
Surgery was considered unwarranted in view of the diffuse nature of the disease, and the adequate medical control of the hypertension.

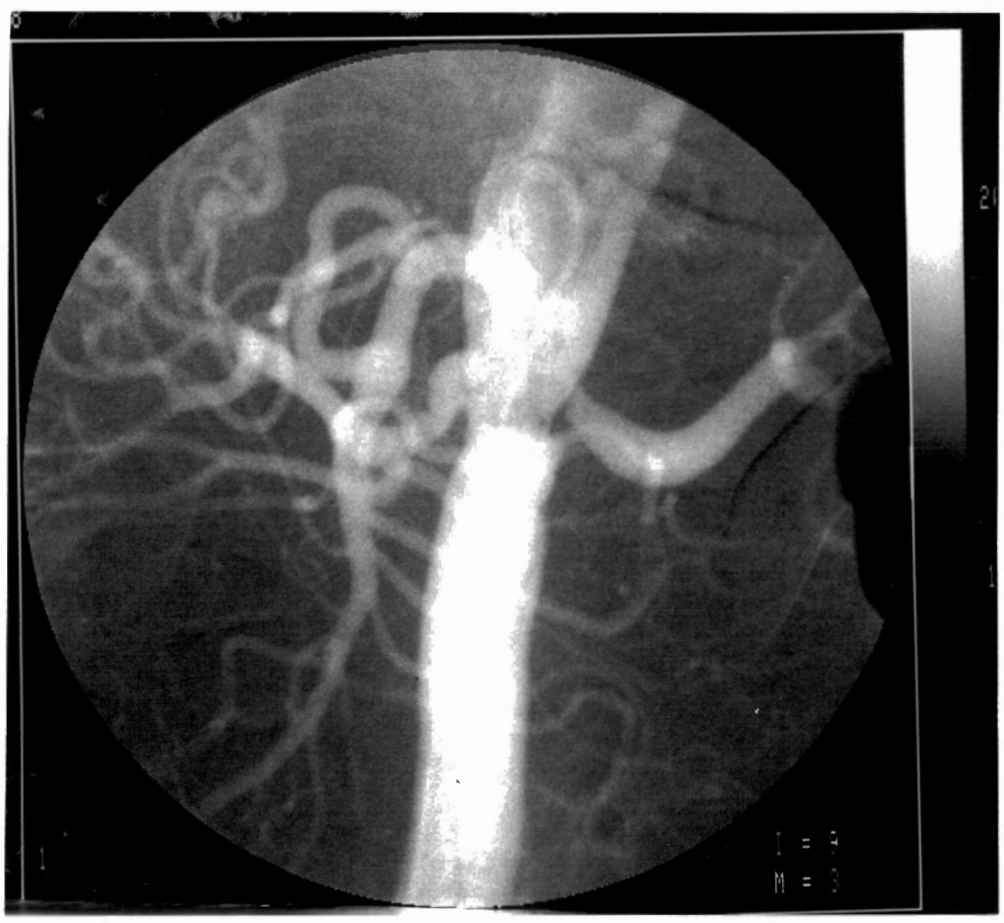
The patient defaulted on follow-up visits, despite several efforts by the Hypertension clinic to locate him. He was next seen in 1987 and found to be clinically unchanged. He was mildly hypertensive, but there was no evidence of cardiac or other sequelae of the disease. Repeat aortography showed no progression of the arteritis. Raised renal vein renin levels were no higher than vena caval levels, and were non lateralising.

Comment

67% of patients in this study developed "burnt out" disease with no progression of the arteritis. The case also demonstrated difficulties in assessing the cause of hypertension in patients with diffuse disease.

CASE NO. 14. AORTOGRAM.





Case no. 15

This 39 year old female presented in 1956 with hypertension, pulse deficits and abdominal bruits. She also had mild cardiac failure and a degree of aortic incompetence. Angiography showed irregularities and stenosis of the entire aorta, and a saccular abdominal aortic aneurysm.

Both subclavian vessels were stenosed and the left common carotid artery occluded. Two of the 3 mesenteric vessels were occluded. Cardiac catheterisation confirmed mild aortic incompetence and cardiac failure. She was regularly seen at the clinic until 1980, and her clinical and angiographic findings remained the same. She died of a stroke in 1981.

Comment

Cardiac and cerebrovascular sequelae are the commonest cause of death in aortic arteritis, despite a prolonged survival in some patients.

Case no. 16

This 27 year old patient presented in 1987 with hypertension in pregnancy. She complained of intermittent claudication of both legs for 1 year.

Examination: BP $^{200}/_{100}$, reduced pulses both legs, renal artery bruit. Heart normal. A limited angiogram showed stenosis of the abdominal aorta, the bifurcation and both iliac vessels, and right renal artery stenosis.

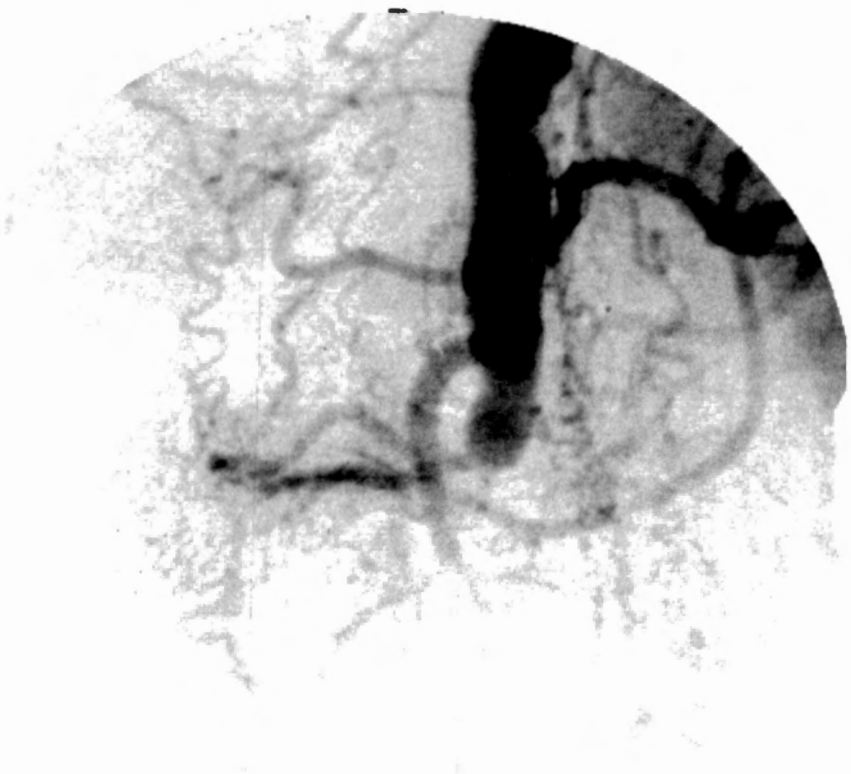
Her blood pressure was adequately controlled with medical treatment and her pregnancy was uneventful, with delivery of a healthy baby. Subsequent panaortography showed a normal descending aorta and arch. Renal vein renin levels were raised on the right, with contralateral suppression and a ratio of >1.6. She is currently being evaluated for elective aortic and renovascular surgery.

Comment

Hypertension in pregnancy is a common presentation in young females with aortic arteritis. The major risks to the mother and fetus relate to the effects of hypertension. If the blood pressure is adequately controlled, the pregnancy should be allowed to follow a normal course. In this patient, the fetus was protected from the effects of hypertension by the occlusive disease of the distal aorta. Also the internal iliac vessels were spared of disease, allowing normal placental and fetal growth.

CASE No. 16.

ABDOMINAL AORTOGRAM.



Case no. 17

This 23 year old patient from Transkei presented with hypertension in her first pregnancy. She was 30 weeks pregnant and had not previously been clinically assessed. Examination also showed a large asymptomatic abdominal aortic aneurysm. Peripheral pulses and cardiac examination were all normal. Ultrasound of the abdomen showed a 30 week pregnancy and a 9 cm aneurysm which was infrarenal. She was kept in hospital and after much deliberation it was decided to induce labour as soon as the baby was "mature". She delivered a healthy boy at 36 weeks. Elective aneurysmectomy was planned for the early post-partum period, however, the patient insisted on deferring the surgery. The aneurysm ruptured a week later and she died at home.

Comment

Large aneurysms remain life-threatening in this condition and should be treated surgically. The world literature is unable to answer the 2 major questions that arise from this case.

(1) the delivery of the baby - when and by what method?

(2) the timing of aortic surgery - before, during or after delivery?

The risk of aneurysm rupture is probably higher in pregnancy and in labour owing to pressure effects, but this is unproven. Caesarian section would probably increase the risk of rupture

owing to release of collagenase and elastase. But would aortic surgery be physically possible with a gravid uterus or even a bulky post-partum uterus obstructing the surgeon's exposure? These and other questions are discussed in more detail in the chapter on "Aortic arteritis in pregnancy".

Case no. 18

This 13 year old patient presented in 1973 with hypertension and cardiac failure. Examination revealed cardiomegaly, grade $^{2}/_{4}$ aortic incompetence, absent pulses in both legs and multiple bruits.

Angiography: Diffuse dilating and occlusive disease of the entire aorta, stenosis of the right renal artery, occlusion of the left, with a non-functioning kidney. Cardiac catheterisation studies confirmed systemic hypertension, left ventricular failure, aortic incompetence and normal pulmonary vessels. The hypertension and cardiac failure were easily controlled with medication and he was assessed 3-monthly at the cardiac clinic for 14 years. Due to the diffuse nature of his disease, reconstructive surgery was considered not feasible. Repeat cardiac catheterisation in 1984 showed some progression of the disease since the 1973 study:

- occlusion of the left coronary artery
- large aneurysm of the intra-atrial appendage
- aneurysm of the innominate artery.

In 1985 his general condition deteriorated and he developed progressive renal failure and intractable cardiac failure which was the cause of his death in 1986.

Comment

An example of the diffuse disease (Nasu type IV) with the complications of cardiac and renal failure which frequently lead

to the patient's demise. Current evidence in the literature would favour an aggressive surgical approach towards reno-vascular hypertension, not only for blood pressure control, but also to improve renal function.

Case no. 19

This 24 year old patient from the country districts was admitted to hospital in 1978 with a stroke. She also had a 1 year history of intermittent claudication of both forearms, and of symptoms suggestive of vertebro-basilar insufficiency. Examination showed pulse deficits of both arms and both carotid arteries, and a right hemiparesis. ESR was 140. Chest radiograph was suggestive of pulmonary tuberculosis, and acid-fast bacilli were seen in her sputum. Fundoscopy showed an ischaemic retinopathy. Angiography: irregularities and stenosing disease of the aortic arch, bilateral common carotid and subclavian artery occlusion. Both vertebral arteries were stenosed. The remainder of the aorta was normal.

Initial treatment consisted of tuberculous therapy, and a course of corticosteroids. She then underwent a right femoro-axillary dacron bypass graft, with a side-arm graft to the right common carotid artery. The histology of the subclavian artery was typical of Takayasu's disease.

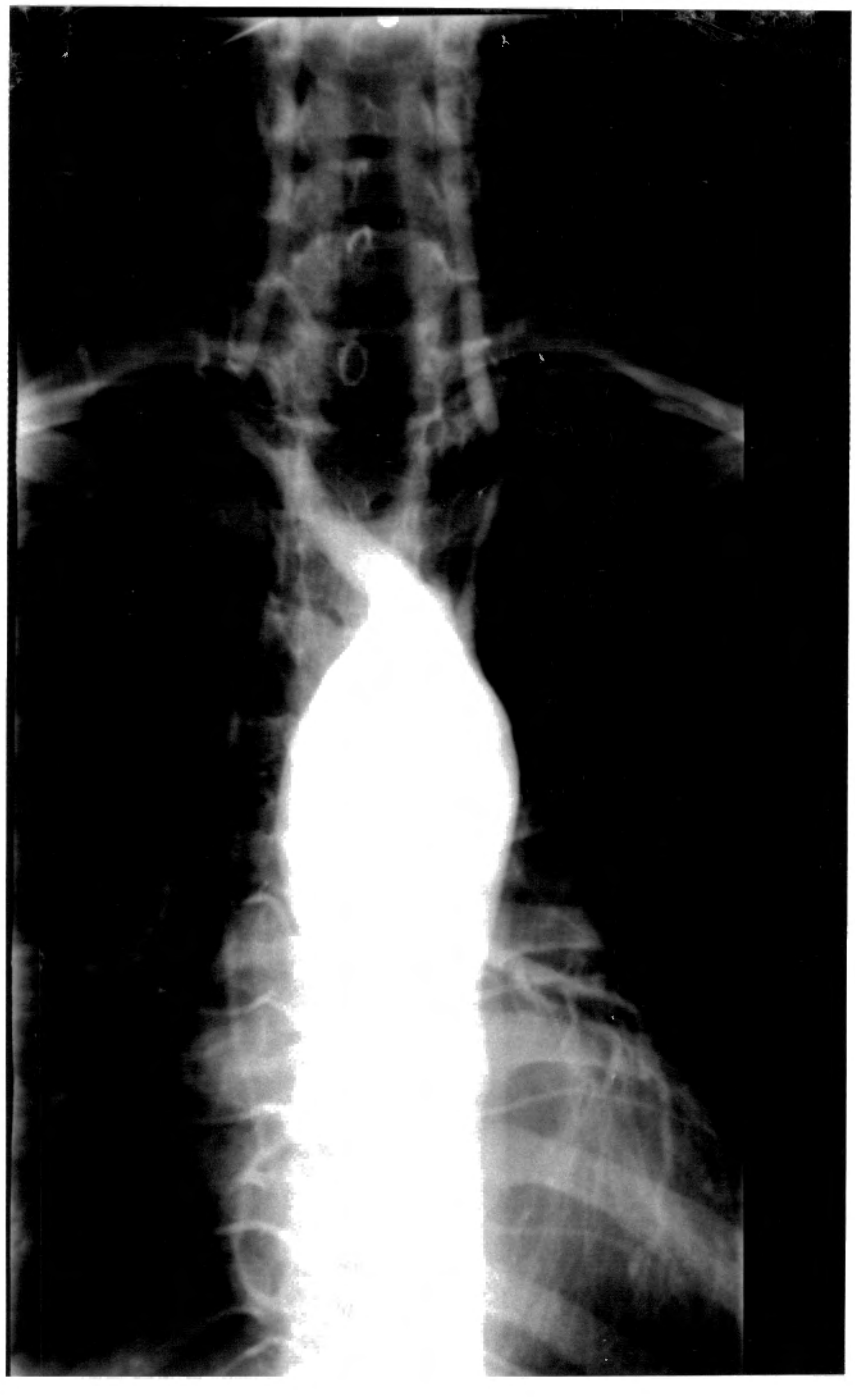
After 1 year she had minimal neurological deficit. The vertebro-basilar symptoms disappeared and the graft remained patent, with pulses present in the arm and neck. She was subsequently lost to follow-up and all attempts to trace her failed.

Comment

An example of isolated aortic arch disease (Nasu type I) which occurred in only 9% of the series. Carotid artery disease was frequently bilateral and associated vertebral disease was common.

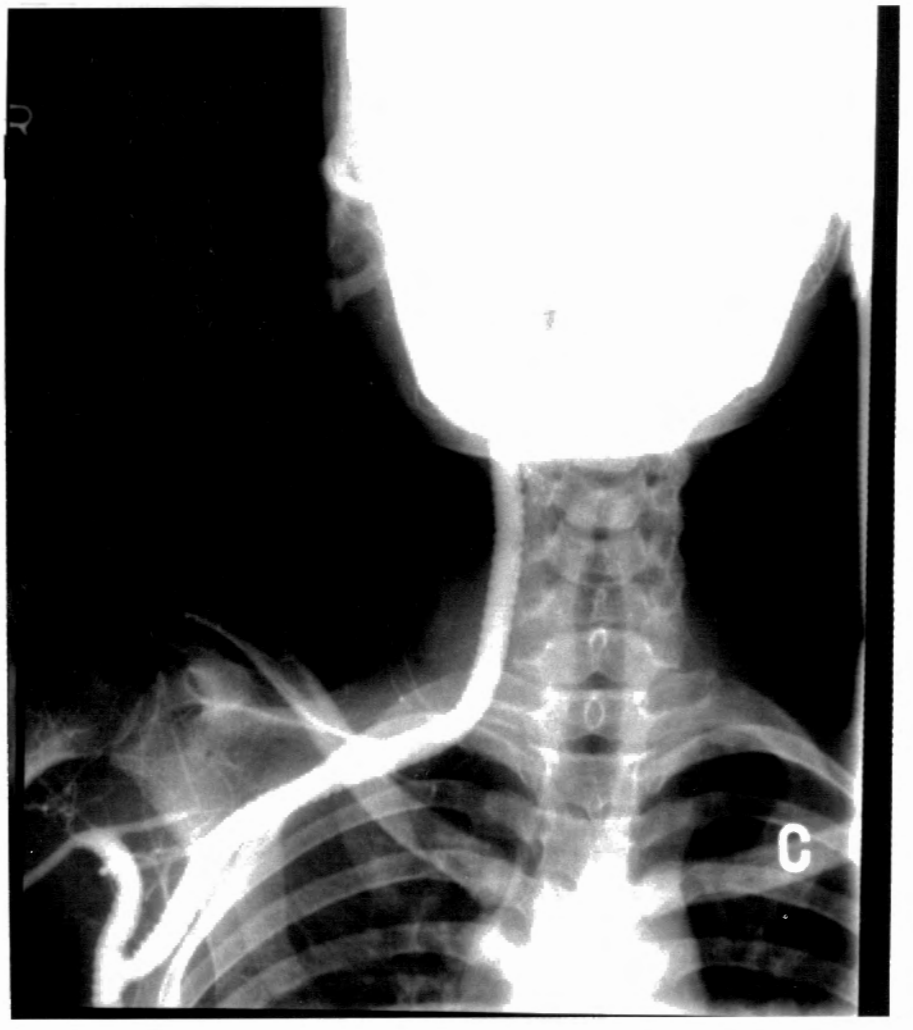
This represents a major threat to the patient with the risk of stroke, and revascularisation should be undertaken. Surgical options include bypass grafting from the aortic arch, the axillary or femoral artery. The donor artery should be free of disease. "Endarterectomy" is not a surgical option in arteritis.

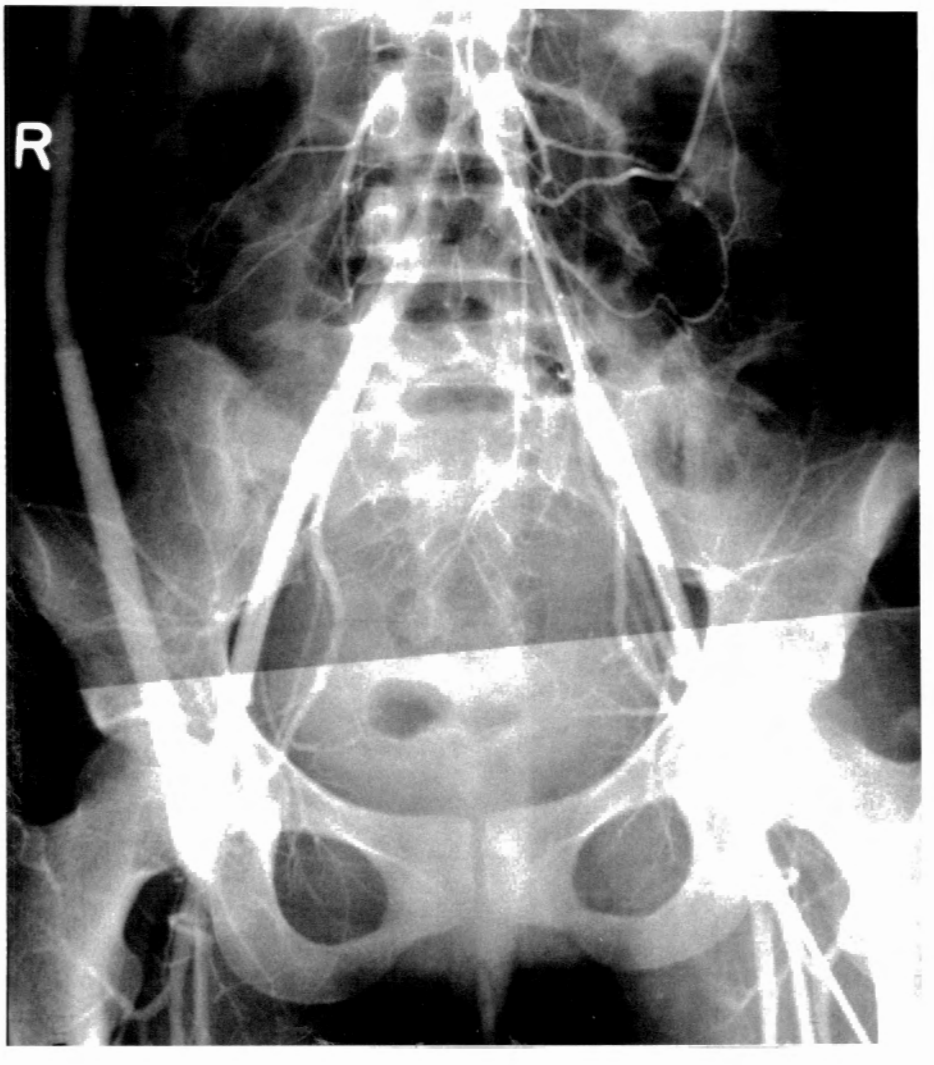
ARCH AND DESCENDING AORTIC ANGIOGRAM.



CASE NO. 19.

GRAFT ANGIOGRAM.





Case no. 20

This 36 year old patient's presentation in 1971 was that of angina pectoris. She was also found to be hypertensive ($^{205}/_{140}$) and to have impaired renal function.

Angiography: - stenosing disease of the abdominal aorta and bifurcation. Bilateral renal artery stenosis, with equivocal renal vein renin levels.

- coeliac artery stenosis, S.M.A. occlusion, and left carotid stenosis

Cardiac catheterisation showed normal ventricles, with diffuse main stem coronary artery disease, and systemic hypertension.

Treatment comprised medical control of the hypertension and angina. She was seen regularly at cardiac clinic. She was readmitted in 1973 with an acute myocardial infarct which caused her death. Autopsy confirmed the clinical diagnosis.

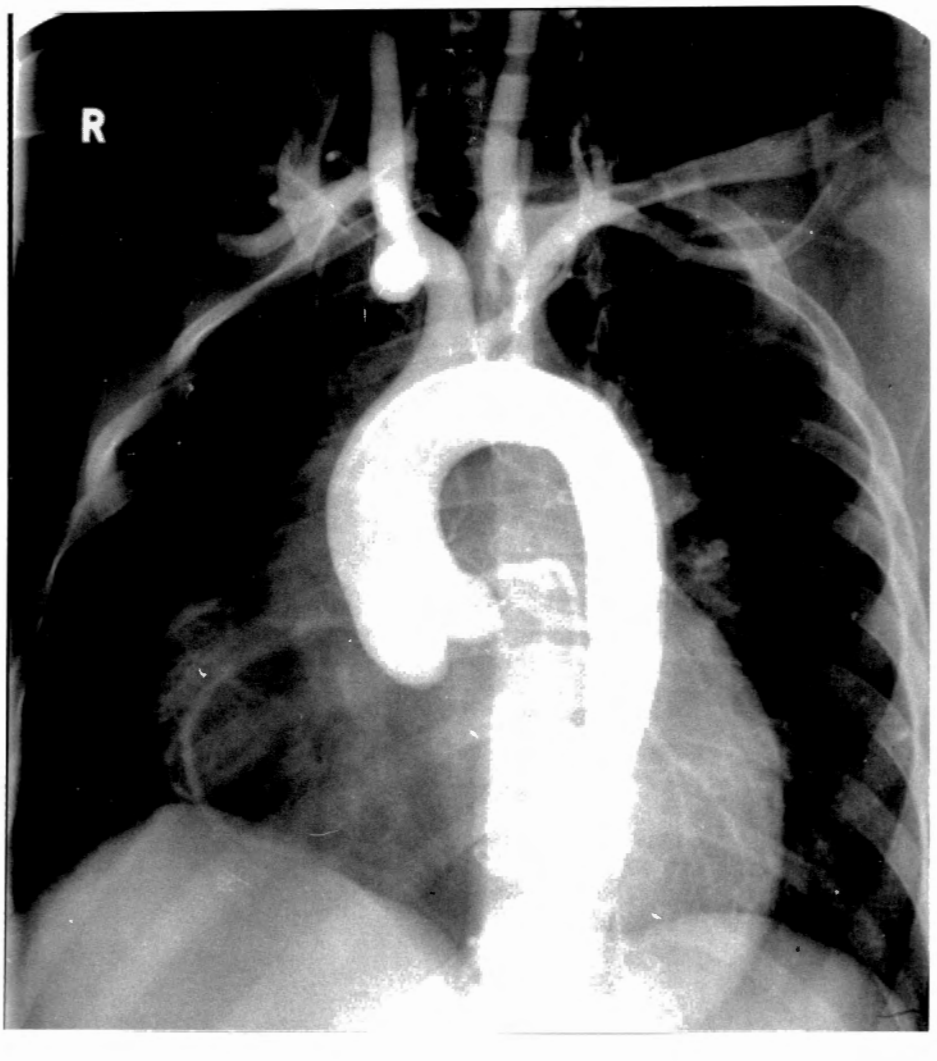
Comment

The patient represents an example of coronary arteritis occurring as part of the disease spectrum. The risk of myocardial ischaemia is often aggravated by associated hypertensive heart disease, cardiomegaly and valvular disease.

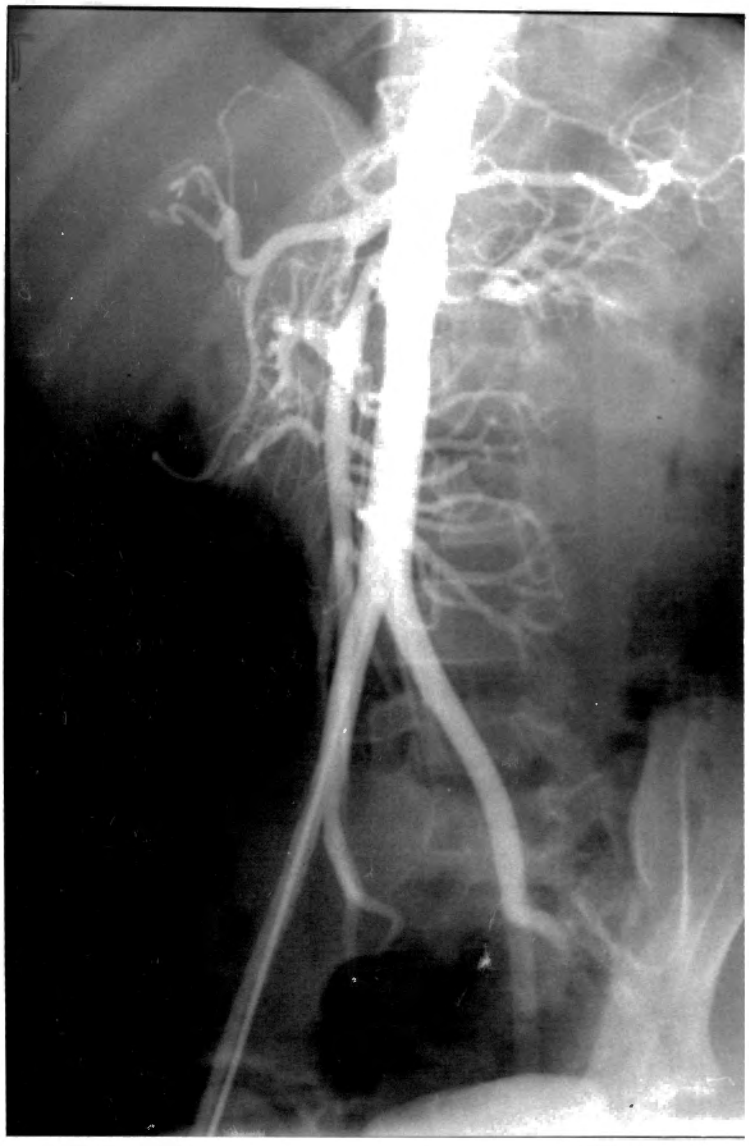
The following ten cases have been included merely to illustrate certain angiographic features.

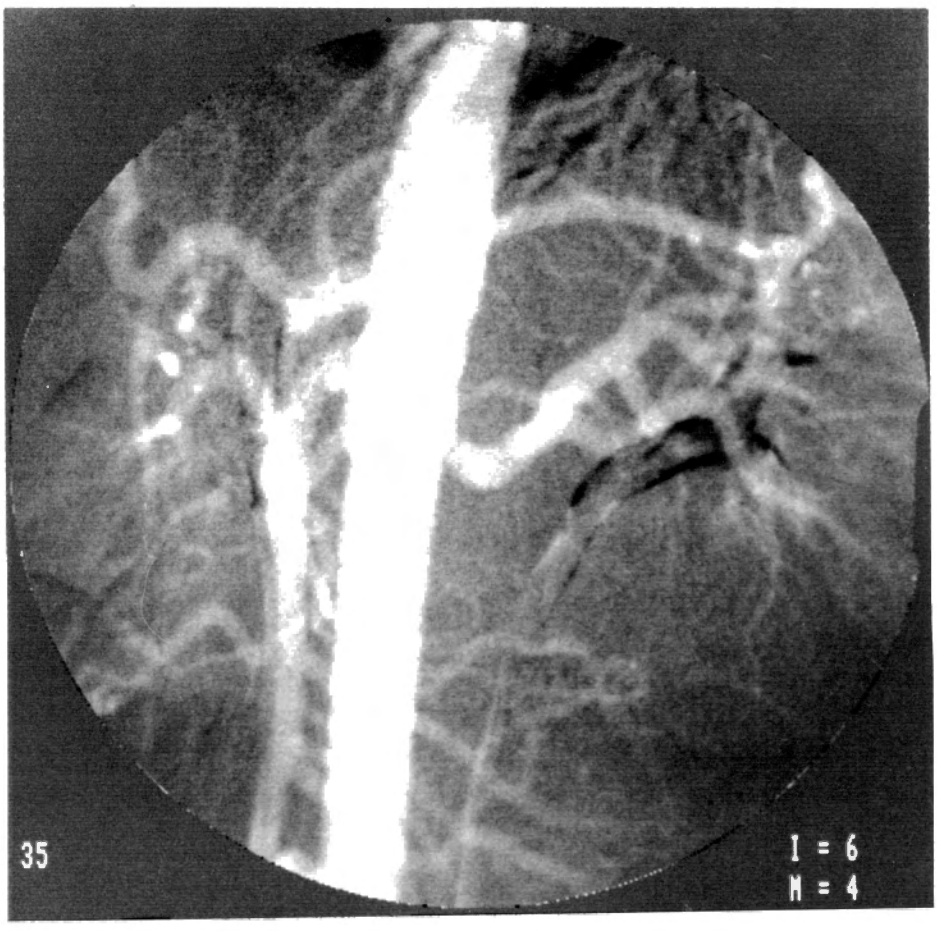
Case 21

This 10 year old child presented with hypertension due to renal artery stenosis. Angiography (see below) showed narrowing of the descending aorta, left common carotid stenosis, bilateral renal artery stenosis, and some irregularities of the abdominal aorta (see magnified view). The enclosed films are a repeat study performed after 5 years of medical treatment only. A percutaneous transluminal angioplasty of the renal arteries was unsuccessful. P.T.A. is seldom beneficial in arteritis owing to the diffuse fibrosis of the media of the artery and to intense peri-arterial inflammation.



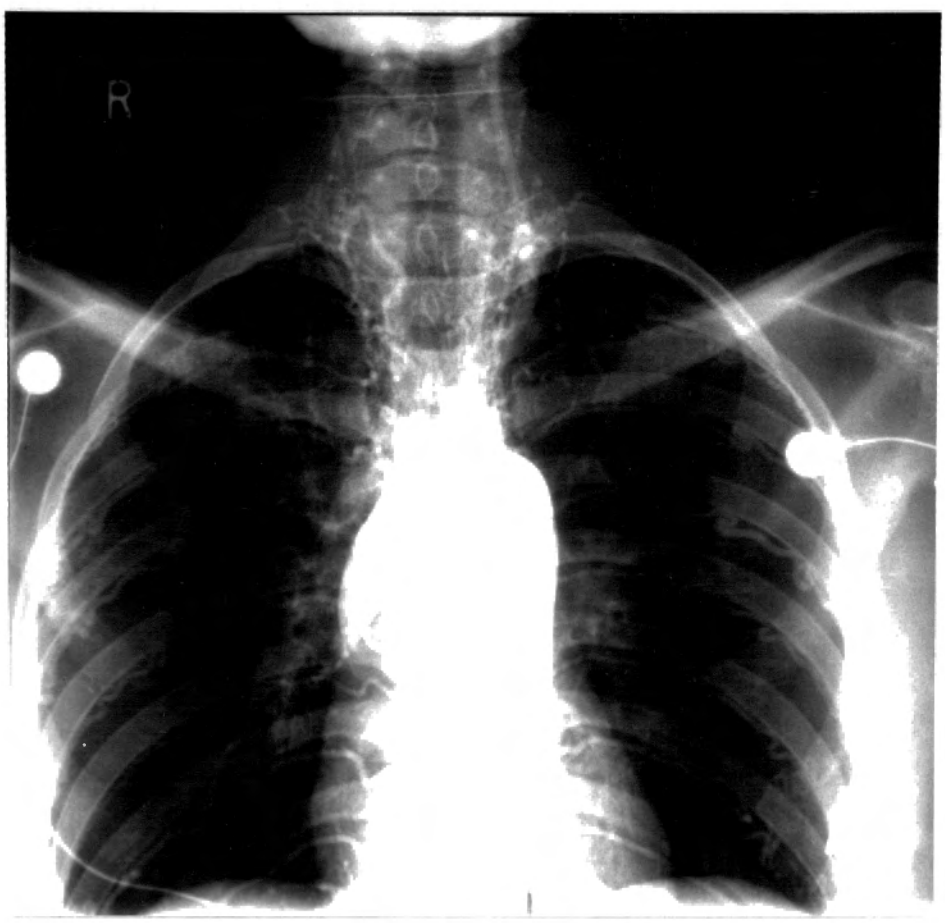
CASE NO. 21.





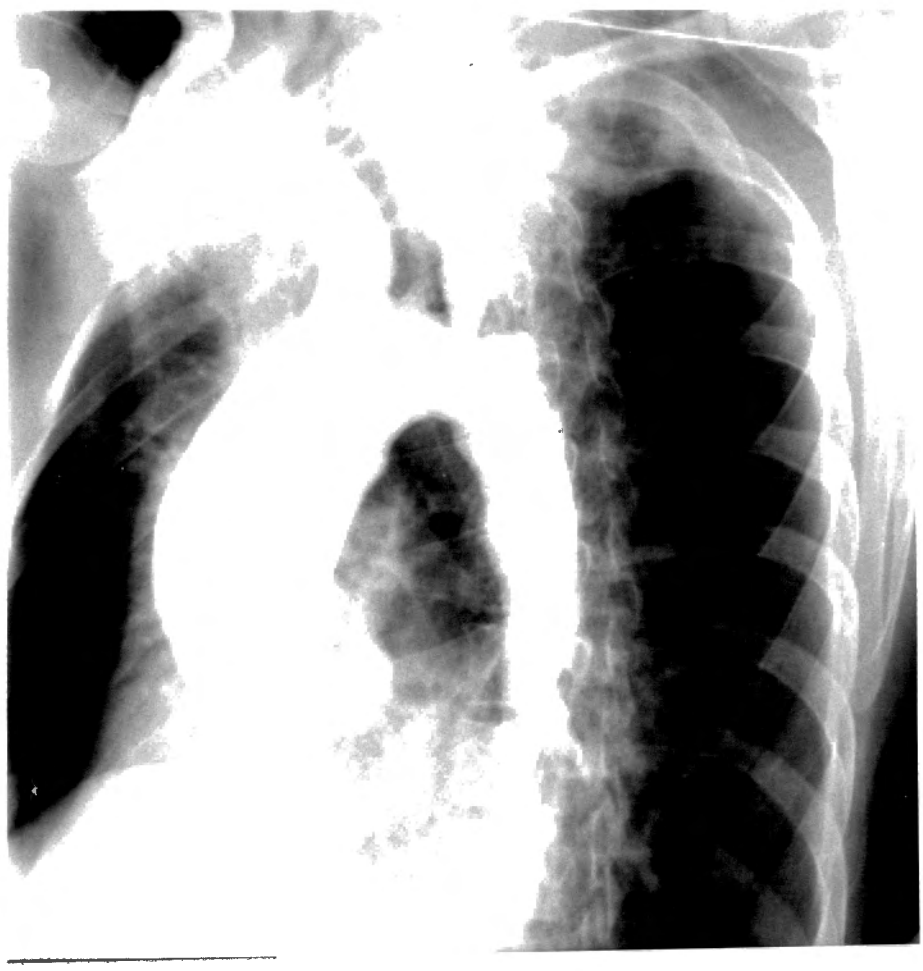
Case 22

This 34 year old patient presented with cerebral ischaemic episodes including blindness induced by arm movement. The angiogram shows occlusion of both common carotid arteries, both vertebral arteries and both subclavian arteries. A subclavian steal syndrome was demonstrated bilaterally. A femorobicarotid graft was performed in this patient.

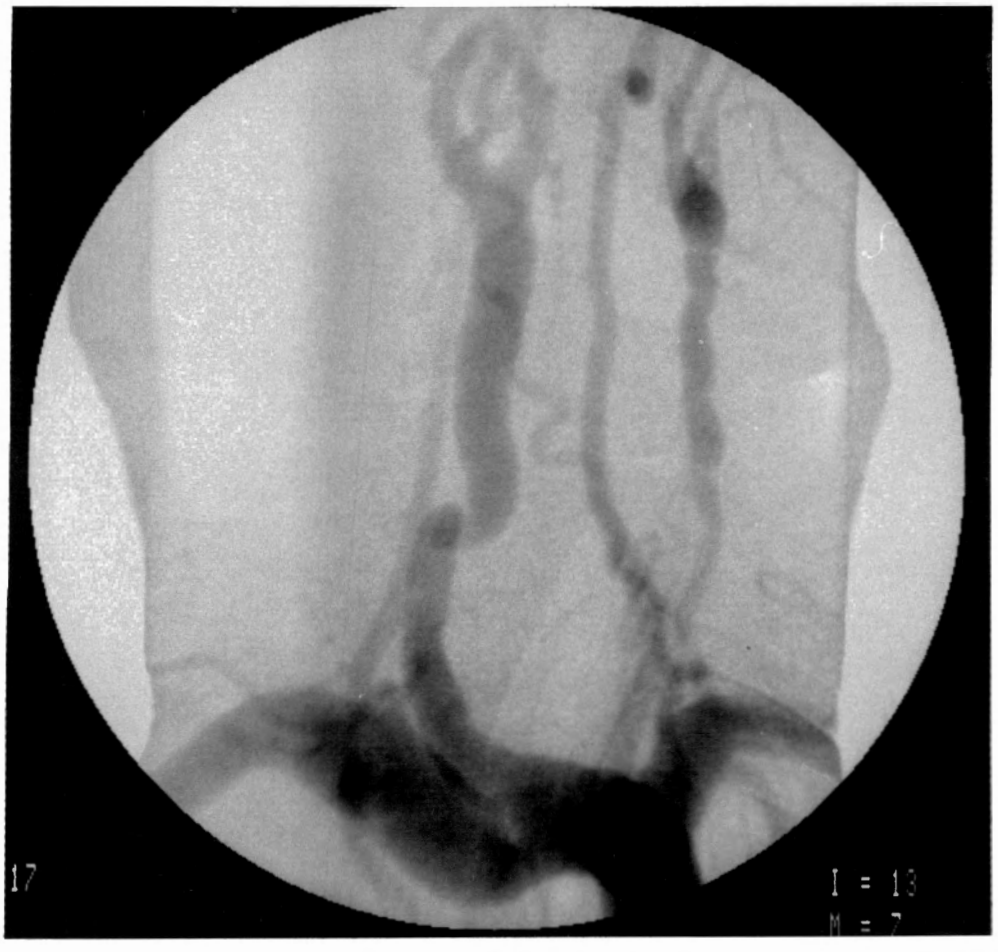


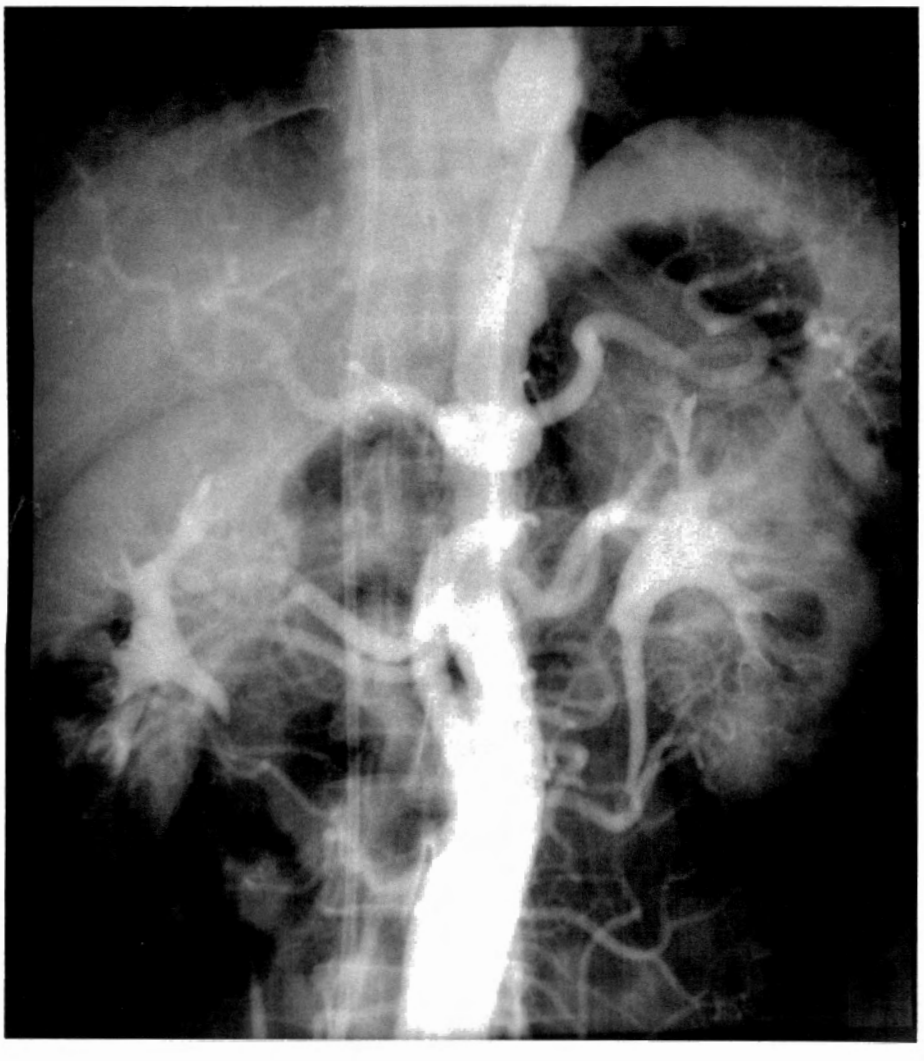
Case 23

An example of diffuse "dilating" and "occlusive" disease involving the entire aorta. Aortic valve incompetence was proven on cardiac catheterisation. The innominate aneurysm is shown on the angiogram, and the left common carotid artery is stenosed.



CASE NO. 23. AORTIC ARCH BRANCHES.

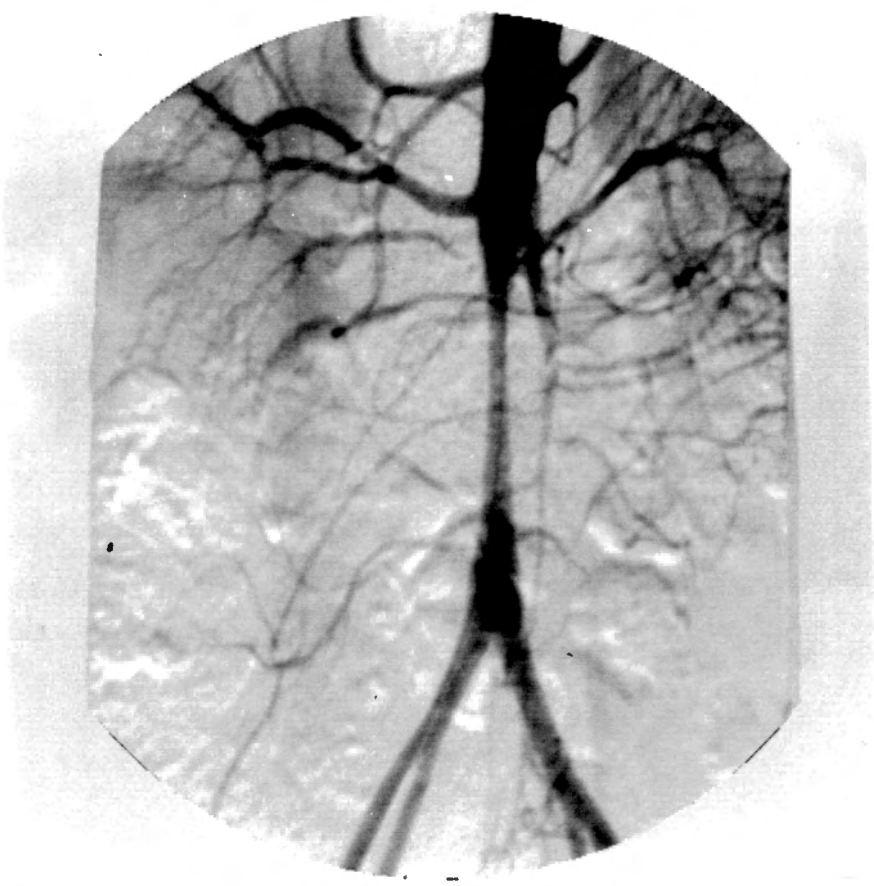




ABDOMINAL AORTA.

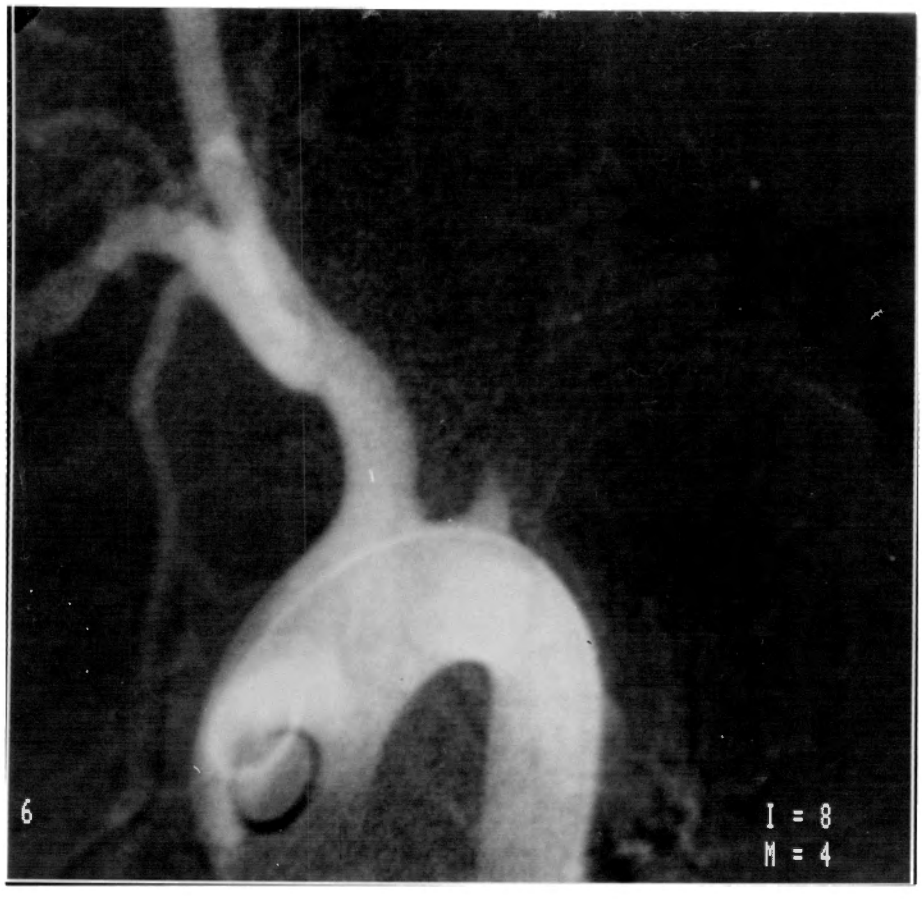
Case 24

This 13 year old patient presented with hypertension, fever of unknown origin, arthralgia and erythema nodosum. The angiogram shows diffuse occlusive disease of the abdominal aorta, with bilateral renal artery stenosis. The E.S.R. was 160. She responded well to corticosteroids.



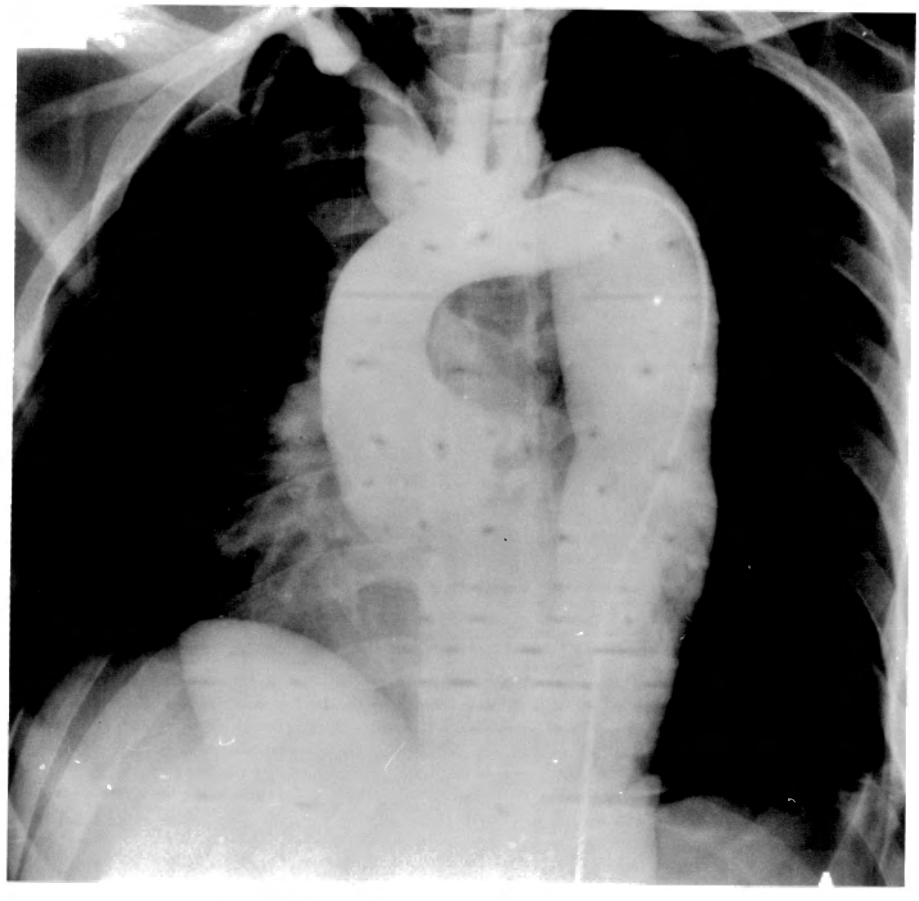
Case 25

This 20 year old patient had severe intermittent claudication of the left arm. She underwent a right subclavian - left axillary bypass graft. Histology of the left subclavian artery confirmed arteritis.



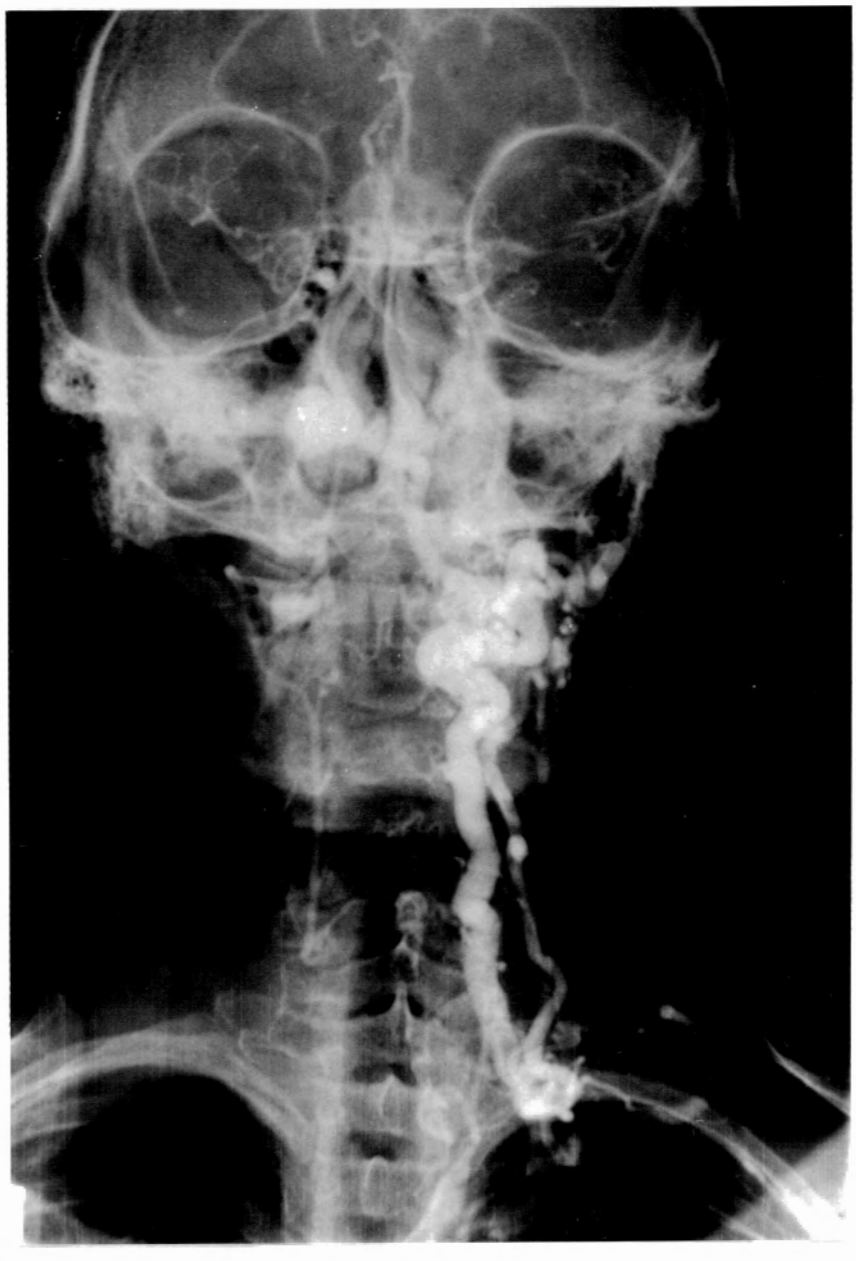
Case 26

22 year old asymptomatic patient with a diffusely dilated aorta. Cardiac catheterisation showed a left coronary artery aneurysm and a normal aortic valve.



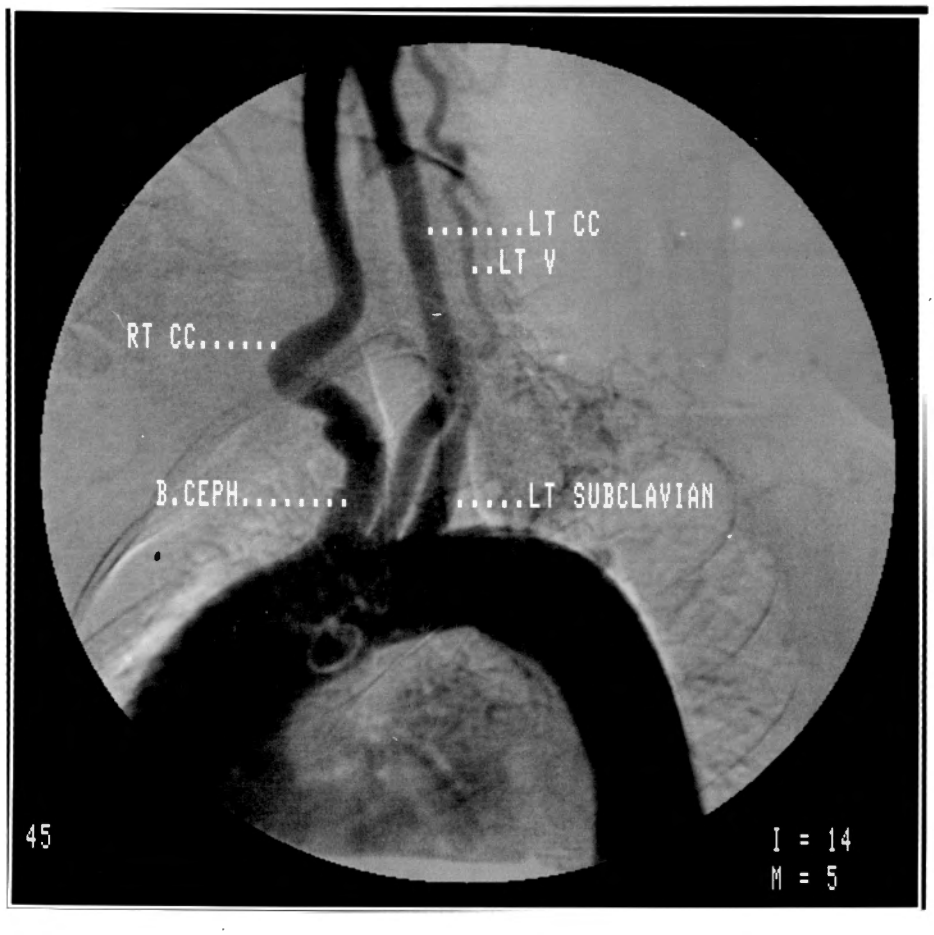
Case 27

This patient presented at age 14 with a stroke. The angiogram shows a large left vertebral artery as the only blood supply to the brain. The aortic arch and descending aorta showed evidence of arteritis.



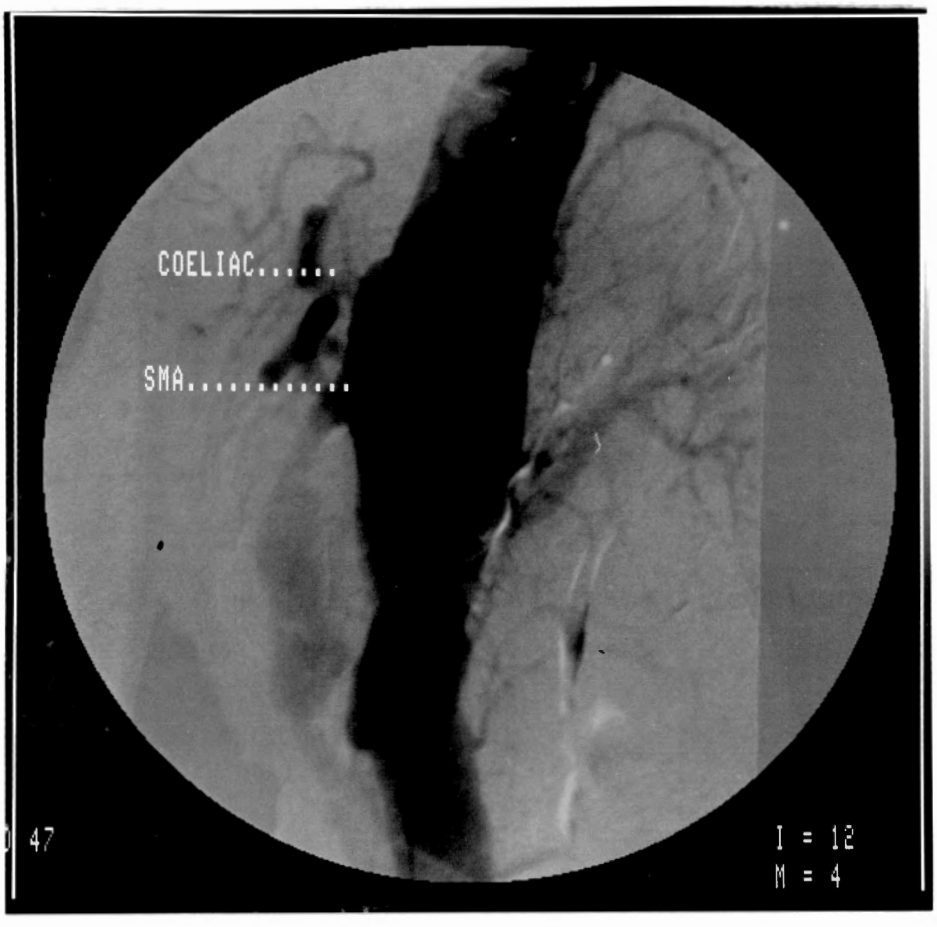
Case 28

This 29 year old patient presented with aortic valve incompetence and pulse deficits in both arms. The angiogram shows a dilated ascending aorta, occluded subclavian arteries bilaterally, and an abdominal aortic aneurysm.



CASE NO. 28.

ABDOMINAL AORTIC ANGIOGRAM.

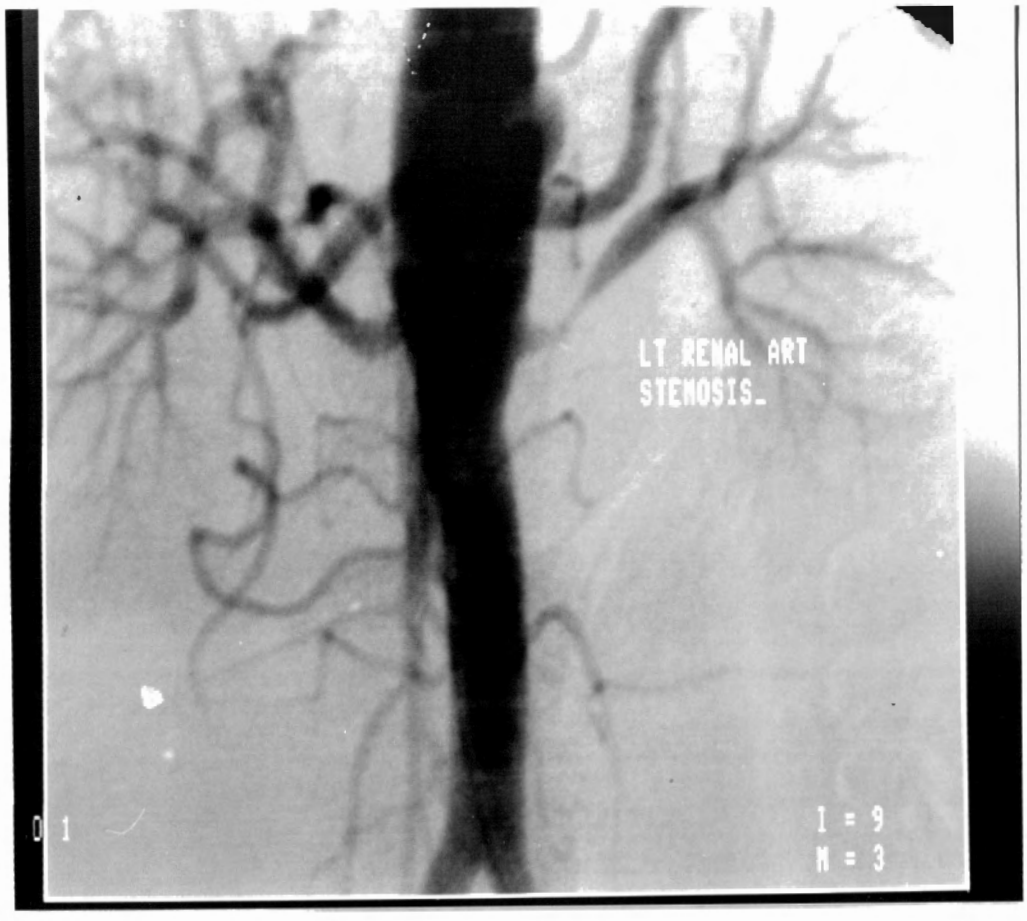


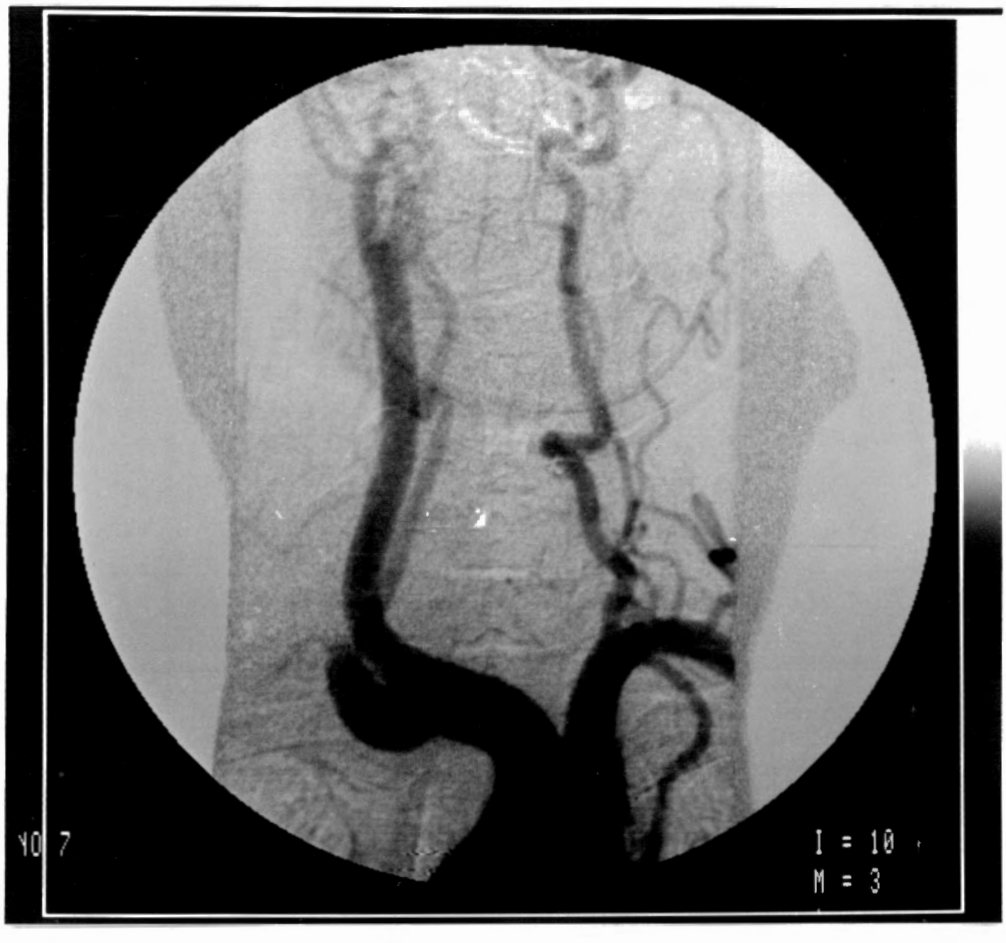
Case 29

This 33 year old patient initially presented to hospital in 1974 with severe hypertension. She underwent surgery for coarctation of the descending aorta, with good results. In 1987 she again became hypertensive and repeat angiography showed significant progression of the disease: aneurysm of the abdominal aorta, left renal artery stenosis, occlusion of right subclavian, right internal carotid and left common carotid arteries. She had no symptoms of cerebral ischaemia, although she did have intermittent claudication of the right arm. In this case, percutaneous transluminal angioplasty of the stenosed renal artery was beneficial, and the hypertension is currently controlled by a diuretic only.

This patient illustrates the problem of progression of the arteritis and emphasises the importance of long-term reassessment of these cases. This patient may still require surgery for both renovascular hypertension and cerebral ischaemia.

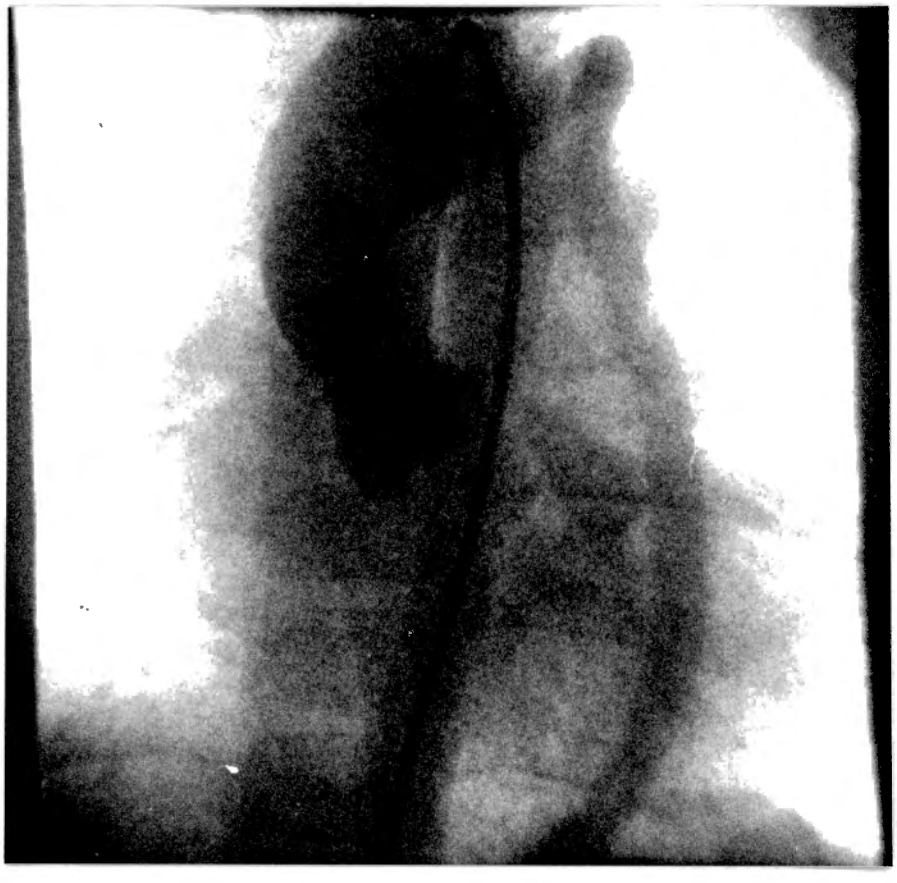
CASE NO. 29.





Case 30

This 4 year old child presented with cardiac failure and hypertension due to stenosis of the descending and abdominal aorta. The angiogram performed one year after surgery shows a patent graft from the ascending to the abdominal aorta.



4. RESULTS

1. AGE, SEX AND RACE

The study included 220 patients and represents a 36 year experience (1952-1987) in non-specific aortic arteritis at Groote Schuur Hospital.

The mean age of presentation was 25 years, with age range 1 to 66. 33 patients (15%) were aged 10 years or less.

There were 170 females (77%) and 50 males. 150 patients (68%) were Coloured or Asian, 52 Black (24%) and 18 Caucasian (8%).

2. CLASSIFICATION AND SPECTRUM OF DISEASE

The commonest form of disease was a diffuse arteritis, with extensive involvement of the aorta and its branches. The spectrum of disease is shown in Fig. 1.

Classification (Nasu 1976) (109) (133)

I	Aortic arch only	9%
II	Thoracic aorta only	5%
III	Abdominal aorta only	14%
IV	Diffuse disease	72%

Classification (Ueno 1976)

I	Isolated aortic arch	9%
II	Thoraco-abdominal aorta	23%
III	Combined I & II	61%
IV	Aneurysmal disease only	7%

"Dilating" disease occurred in 111 patients (50%), most of whom also had stenoses and occlusions of the major arteries. Isolated "dilating" disease occurred in only 16 patients (7%).

"Occlusive" disease occurred in 204 patients (93%). The only anatomic site where "dilating" disease occurred more commonly than "occlusive" disease was the right side of the aortic arch (ascending aorta and proximal half of the arch). 70% of the disease pattern at that site was "dilating", whereas 85% of left sided arch disease was "occlusive" (Fig 2).

FIG 1.

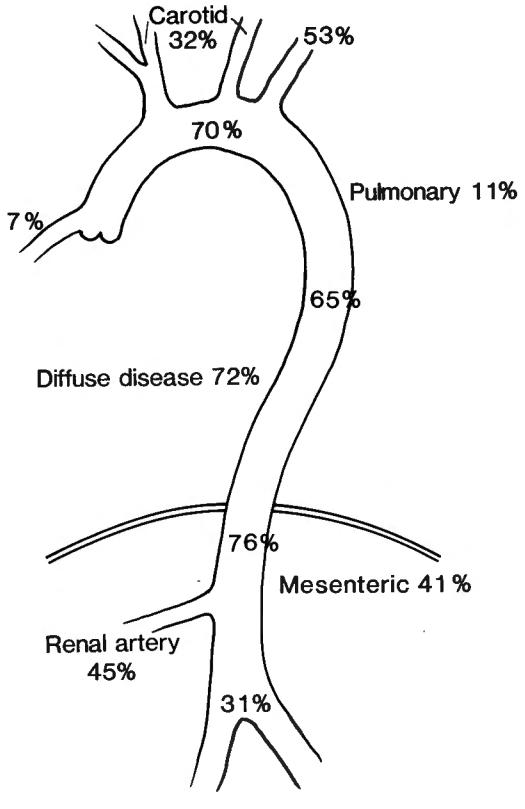
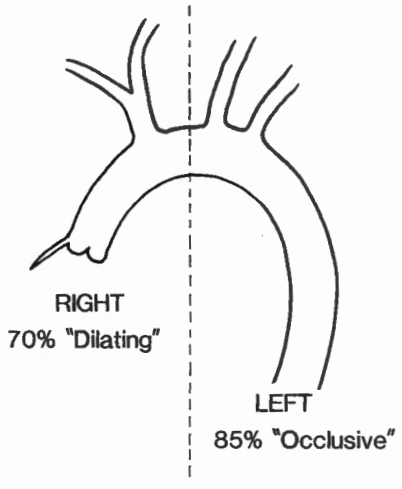


FIGURE 2.



3. CLINICAL PRESENTATION

The commonest clinical presentation was hypertension, occurring in 76% of patients. Cardiac disease was also prominent (47%). The symptoms of ischaemia indicated the precise anatomic location of the arteritis. Table I shows the incidence of the presenting clinical problems.

Table I

Hypertension : 76%	N = 168
Hypertension in pregnancy : 20 patients	
Cardiac disease : 47%	N = 103
Intermittent claudication : 30%	N = 66
Cerebrovascular symptoms : 19%	N = 43
Impaired renal function : 15%	N = 33
Symptomatic aneurysms : 12%	N = 27
Ruptured aneurysms 7 patients	
Non-specific inflammatory symptoms (eg. arthralgia, fever, skin rashes): 10%	N = 22
Gangrene : 5%	N = 11
Angina : 4%	N = 9

4. HYPERTENSION

168 patients (76%) presented with hypertension. The pathogenesis is shown in Table 2.

Table 2

(1) Renal artery stenosis only : 65 patients (39%)

(2) Coarctation of the aorta : 51 patients (30%)

(3) Both (1) and (2) : 28 patients (17%)

(4) Other / unknown : 24 patients (14%)

Renal artery stenosis could be implicated in the pathogenesis of the hypertension in 93 patients (55%). Some of these patients also had aortic coarctation. Of the patients with renovascular hypertension, nearly a half (47%) had bilateral disease.

24 patients had hypertension of uncertain origin. The majority of these probably had essential hypertension. Other mechanisms that have been implicated in aortic arteritis include:

(1) loss of elasticity in the aortic wall

(2) baroreceptor instability

(3) cerebral ischaemia

20 patients presented with hypertension in pregnancy.

Hypertension was certainly the commonest presentation and the most frequent cause of death in this series. The majority of serious cardiac, renal and cerebrovascular complications were related to hypertension. 80% of all known deaths occurred due to hypertension-related causes.

5. CARDIAC DISEASE

103 patients (47%) developed cardiac complications (Table 3). Cardiac catheterisation studies were performed on 133 patients (60%).

Table 3

	Total patients	103	(47%)
(1)	Cardiac failure	N = 74	(34%)
(2)	Hypertensive heart disease (total no.)	N = 66	(30%)
(3)	Valvular heart disease (total no.)	N = 48	(22%)
(4)	Both hypertensive & valvular disease	N = 24	(11%)
(5)	Ischaemic heart disease	N = 13	(6%)
(6)	Other		
	Proven pulmonary hypertension	13	
	Cor pulmonale	1	
	Intra-arterial aneurysm	1	
	Peri-carditis (non-infective)	1	

5.1. Cardiac failure

74 patients developed a degree of cardiac failure, viz. $^1/_3$ of the entire study. More than half of the known deaths (54% of deaths) occurred due to cardiac failure.

The commonest cause of cardiac failure was hypertensive heart disease. Another important cause was valvular heart disease, and some patients had both pathologies.

5.2. Valvular heart disease

48 patients (22%) had valvular heart disease. Aortic incompetence (A.I.) was the commonest pathology and occurred in 34 patients. Mitral valve disease occurred in 22 patients, 8 of whom also had aortic incompetence. The incidences are shown in Table 4.

Table 4

Aortic incompetence (A.I.)		34 patients
AI alone	26	
A.I. + Mitral stenosis (MS)	3	
A.I. + Mitral incompetence (MI)	5	
Mitral valve disease (Total)		**: 22 patients**
M.I. alone	12	
M.S. alone	1	
M.I. + M.S.	1	
Mitral + Aortic disease	8	

Disease of the ascending aorta, which is usually "dilating" in nature commonly occurred in association with aortic incompetence. 3 patients underwent aortic valve replacement for intractable left ventricular failure due to severe valvular incompetence. Of these 3 patients, 2 had simultaneous excision of the ascending aorta with insertion of a graft. 1 patient had both aortic and mitral valve replacement. Mitral valve replacement was performed in 1 patient, and 2 patients underwent mitral valvotomy.

5.3. Ischaemic heart disease

13 patients had clinical evidence of ischaemic heart disease. 9 of these patients had angina pectoris and 4 had proven myocardial infarction. 2 patients died as result of infarcts. These patients all underwent coronary angiography, showing stenotic or occluded vessels.

Asymptomatic coronary occlusive disease was shown in 4 patients. A further 4 patients had coronary aneurysms present, and one of these aneurysms was associated with a coronary "steal" from the thoracic aorta.

5.4. Other cardiac disease

Pulmonary hypertension was proven in 13 patients. This represented 11% of patients who underwent cardiac catheterisation studies. Pulmonary angiography was not performed as a routine until 1986. However, nearly all patients who underwent cardiac catheterisation had pulmonary pressures measured. Of the 13 patients, only 5 had pulmonary arteritis. The remainder had pulmonary hypertension secondary to valvular heart disease. The 5 cases of pulmonary arteritis all had pulmonary artery aneurysms.

6. PERIPHERAL VASCULAR DISEASE

77 patients (35%) presented with a problem of intermittent claudication and/or peripheral gangrene. (Table 5)

Table 5

Intermittent claudication:	66 patients	(30%)
Upper limb	28	
Lower limb	33	
Both upper and lower limbs	5	
Gangrene:	11 patients	(5%)

Gangrene was confined to the lower limb in all patients, except one who also had a gangrenous finger.

Upper limb claudication occurred due to occlusion of the subclavian artery (Table 6). However, there were many patients with subclavian disease who were asymptomatic due to adequate collateral supply. There were 128 patients (58%) with subclavian arteritis, and the nature of the disease was "occlusive" in 88% of cases.

Table 6

Subclavian arteritis :	128 patients	(58%)
Left	108 patients	
Right	69	

Bilateral disease was present in 49 of these cases

Intermittent claudication of the lower limb usually involved calf, thigh and buttock, in keeping with a proximal occlusion. Arteritis of the common iliac artery occurred in 46 patients, 7 of whom had aneurysms.

Common femoral involvement occurred in 17 patients. Peripheral gangrene requiring amputation was usually due to distal embolisation.

7. NEUROLOGICAL COMPLICATIONS

43 patients (20%) developed neurological sequelae. (Table 7)

Table 7

Transient ischaemic attacks (TIA)	:	13
Stroke	:	25
Other	:	5
Hypertensive encephalopathy	:	3
Spastic Paraplegia	:	1
Raised intracranial pressure	:	1

6 Patients died as a result of cerebrovascular accident.

8. RENAL FAILURE

33 Patients (15%) had significantly impaired renal function, defined as follows:

(1) Creatinine clearance <50% expected for age

(2) Serum creatinine/urea increased to more than twice the upper limit of normality.

The majority of these patients (29) had impaired renal function at the time of diagnosis. 4 Patients developed renal failure 10 years after the initial diagnosis. 2 patients underwent haemodialysis.

There were 2 causes of renal failure:

- arteritis of the renal vessels with resultant chronic ischaemia
- hypertensive nephropathy

Renovascular surgery was performed in 6 patients with renovascular hypertension and impaired kidney function. This consisted of 4 aorta-renal bypasses, and 2 renal autotransplantations.

11 patients underwent nephrectomy for severe branch vessel disease and for atrophic renin-secreting kidneys.

9. TUBERCULOSIS

Proven tuberculosis occurred in 45 patients (20%). The tuberculosis was almost exclusively pulmonary, with visceral and abdominal TB not encountered. A few children had tuberculous adenitis or meningitis.

Diagnostic criteria for pulmonary tuberculosis included

(1) acid-fast bacilli seen on sputum examination.

(2) chest radiograph highly suggestive of TB together with an ulcerating/grade IV mantoux .

Overall, 62 patients received anti-tuberculous therapy, some on speculation of an aetiological association between aortic arteritis and tuberculosis.

10. PATHOLOGY INVESTIGATIONS

(1) Haematology

Routine investigations performed were haemoglobin, leucocyte count, differential white blood cell count, platelet count, and erythrocyte sedimentation rate (E.S.R.) The only abnormalities found were a raised ESR in 114 patients and a relative eosinophilia in less than 10% of cases. The E.S.R. reflected the "activity" of the disease, and was elevated in patients with systemic symptoms and progressive arteritis.

(2) Biochemistry

The following biochemical tests were routinely performed, and no specific abnormality was shown:

Serum electrolytes, blood glucose, chloride, bicarbonate, proteins, calcium, inorganic phosphate, cholesterol and lipid screen, urate, bilirubin, alkaline phosphatase, lactate dehydrogenase, gamma glutamyl transferase, and liver transaminases. 33 patients had significantly impaired renal function.

(3) "Collagen screen"

Routinely performed, the collagen vascular screen included Rheumatoid factor, lupus cells, antinuclear factor, scat and latex tests, anti-DNA antibody titre, serum complement, VDRL, serum immunoglobulin levels. The results were non-specific with no clear pattern shown. Less than 10% had evidence of immune complex formation. False positive tests for syphilis occurred in 8 patients.

Investigations performed selectively included kidney biopsy, and biopsies of skeletal muscle and temporal artery. Only renal biopsies yielded positive results, showing a non-specific glomerulo-nephritis.

Non-specific aortic arteritis was shown histologically in 57 cases (26%) from either surgical or autopsy specimens.

(4) Tissue antigen typing

HLA tissue typing was performed in only 24 patients with arteritis.

With respect to the antigens controlled by the A,B, or C loci, there was an increased frequency of B52, B44, B4, B6 and A26. B cell antigens encoded in the D region of the immune response gene showed no specific pattern. However, MB 3, a determinant on the DQ molecule was present in more than half the cases tested. However, the small number of cases studied and the lack of a control group preclude meaningful interpretation of these results.

11. ANGIOGRAPHY

Pan-aortography was regarded as essential to the diagnosis and was performed in all patients. 133 (60%) underwent cardiac catheterisation which included measurement of cardiac pressures, assessment of myocardial function and coronary angiography. Table 8 shows regional incidence of the aortic and branch vessel disease.

Table 8

(1)	Ascending aorta		N = 52 patients (24%)
	Dilating disease	:	N = 36
	Occlusive disease	:	N = 12
	Both patterns of disease	:	N = 4
(2)	Arch aorta		N = 76 (35%)
	Dilating	:	N = 31
	Occlusive	:	39
	Both	:	6
(3)	Descending aorta		N = 142 (65%)
	Aneurysms	:	N = 36
	Stenoses	:	N = 88
	Occlusions	:	N = 1
	Both patterns of disease	:	N= 17

(4)	Abdominal aorta		167 patients (76%)
	Stenoses	:	85 patients
	Occlusions	:	25
	Aneurysms	:	35
	Both patterns of disease	:	22
(5)	Bifurcation aorta		68 (31%)
	Stenoses	:	48
	Occlusions	:	15
	Aneurysms	:	4
	Both	:	1
(6)	Common Carotid artery		70 patients (32%)
	Right only	:	11
	Left only	:	32
	Bilateral	:	27
	Stenoses	:	28
	Occlusions	:	25
	Aneurysms	:	13
	Both disease patterns	:	4

(7)	Coronary artery		16 (7%)
	Stenoses	:	7
	Occlusions	:	8
	Aneurysms	:	4

1 patient had a coronary steal from the thoracic aorta.

(8)	Innominate artery		38 (17%)
	Stenoses	:	11
	Occlusions	:	8
	Aneurysms	:	16
	Both patterns	:	3

(9)	Subclavian artery		128 (58%)
	Left only	:	59
	Right only	:	20
	Bilateral	:	49
	Stenoses	:	35
	Occlusions	:	73
	Aneurysms	:	16
	Both	:	4

(10)	Mesenteric arteries		91 patients
	Stenoses	:	31
	Occlusions	:	54
	Aneurysms	:	6

Coeliac artery	21	patients
Superior mesenteric	38	
Inferior mesenteric	32	

(11) Renal arteries	99	(45%)
Right only	25	
Left only	27	
Bilateral	47	
Stenoses	72	
Occlusions	21	
Aneurysms	2	
Both occlusive & aneurysmal disease	4	

(12) Common iliac arteries	46	
Stenoses	19	
Occlusions	20	
Aneurysms	5	
Both	2	

(13) Common femoral artery	17	cases (all occlusive)
Superficial femoral	8	

(14) Vertebral arteries 9

Stenoses : 6
(3 bilateral, with associated carotid disease, 2 of whom had vascular surgery)

Occlusions : 3

(All had associated common carotid stenoses)

Subclavian steal shown in 4 patients

(15) Pulmonary arteries 13
(viz. 11% of those who had pulmonary angiography)

Stenoses 8

Aneurysms 4

Both 1

(16) Internal iliac artery 4 patients

Stenoses 1 (bilateral)

Aneurysms 3 (1 ruptured)

(17) Popliteal artery 1 patient (Aneurysm)

This patient had multiple aneurysms.

(18) Other vascular involvement

1 Basilar artery aneurysm

1 Splenic artery occlusion

1 Sinus of valsalva aneurysm

1 Superior vena caval and iliac vein occlusion.

(19) Disease incidence (anatomic site)

- Abdominal aorta : 76%
- Ascending aorta/arch & branches : 70%
- Descending aorta : 65%
- Subclavian artery : 58%
- Renal artery : 45%
- Mesenteric arteries : 41%
- Carotid : 32%
- Aortic bifurcation : 31%

(20) Incidence of aneurysms / "dilating" disease

- Abdominal aorta	57 patients	(26%)
- Descending aorta	53	(24%)
- Ascending aorta	40	(18%)
- Aortic arch	37	(17%)
- Subclavian	20	(9%)
- Innominate	19	(9%)
- Carotid	17	(8%)
- Renal artery	6	(2.7%)

Certain aspects arising from these results warrant special mention:

1. The ascending aorta, aortic valve ring, innominate artery and "right side" of the aortic arch were involved primarily by "dilating" disease. This was the only anatomic site where "dilating" disease was more prevalent than "occlusive" disease.

2. The frequent involvement of the left subclavian artery (53%, N=17). In some cases this was the only manifestation of aortic arch disease.

3. The high incidence of renal artery disease (45%), with bilateral involvement in a half of these patients.

4. The relatively high incidence of aortic bifurcation disease (31% N=68). It has only recently been recognised that the Aortic bifurcation and common iliac arteries may be involved by Takayasu's disease. There is little mention in the literature, on this aspect of the disease.

5. The coronary arteries are not spared by the disease process. There were 16 patients with angiographic evidence of coronary artery disease, four of whom had coronary aneurysms. In some of these cases the pathology was probably atherosclerosis. Histologic proof of arteritis was available in only 3 cases.

6. The high incidence of Common Carotid artery disease. (32% N=70). This was bilateral in 39% of cases, and associated vertebral artery disease was common.

7. 50% of the entire series (N = 111) had aneurysms present. Associated "occlusive" disease was usually found in the same patients. Many of the patients with "dilating" disease had multiple aneurysms. This incidence is higher than reported in the large Japanese and Asian series. Nasu [6] found a 17% incidence of aneurysms, and Yamato [5] 30%.

   The high incidence of abdominal aortic aneurysms (26% N=57) is noteworthy. Aneurysm of the descending and abdominal aorta together accounted for nearly a half of all aneurysms in the series.

8. Pulmonary arteritis is a diagnostic feature of Takayasu's disease. Pulmonary artery disease is not seen in any of the other causes of aortic arteritis. There is no correlation between the extent of the arteritis of the pulmonary and systemic circulations. The arteritis of the two systems appear to occur independently. Pulmonary angiography, pulmonary perfusion scanning and the measurement of pulmonary artery pressures has been routinely performed in certain Japanese studies. The reported incidence of pulmonary arteritis in Takayasu's disease is 50%.

12. TREATMENT

The treatment options available included both medical and surgical modalities (Table 9).

Table 9

(1)	Anti-tuberculous therapy	62 patients	(28%)
(2)	Corticosteroids	N=18	(8%)
(3)	Surgery		
	(a) Vascular reconstruction	N=43	(20%)
	(b) Cardiac surgery	6	
	(c) Other procedures		
	eg. Nephrectomy, amputation.		

(1) ANTI-TUBERCULOUS THERAPY

62 patients were treated with anti-tuberculous medication. 45 patients (20%) had proven tuberculosis. Another 17 had suspected but unproven TB.

Although the treatment was effective in controlling tuberculosis, there was no obvious effect on the arteritis, and there was no survival benefit.

(2) CORTICOSTEROIDS

25 patients (11%) were treated with corticosteroids. All patients responded with a reduction in the "activity" of the

disease as assessed by the E.S.R. However, there was no evidence of reversal of the arteritis or of a return of pulses.

(3) SURGERY

3.1 Vascular reconstruction

46 procedures were performed in 43 patients (20%):

Aortic surgery	36
Subclavian/carotid	4
Renovascular surgery	6

The overall short-term results of reconstructive surgery were good. The long-term results were limited by the cardiac complications of the disease, and by progressive arteritis. Details of the surgery are given in the next chapter.

3.2 Cardiac Surgery

(a) Aortic valve replacement. 3 patients

2 of these had replacement of the ascending aorta performed at the same operation. 1 patient also had a mitral valve replacement. All 3 patients were significantly improved by the surgery, and have been well at a minimum of 12 months follow-up.

(b) Mitral valve replacement 2 patients

(c) Mitral valvotomy 2 patients

3.3 Other procedures

(a) Nephrectomy 11 patients

There were 2 indications for nephrectomy in the treatment of renovascular hypertension.

- severe branch vessel disease, not suitable for reconstructive surgery
- an atrophic renin-secreting kidney.

2 patients had nephrectomy after failed aorta-renal bypass grafting.

All 11 patients had significantly improved blood pressure control following the procedure.

(b) Amputations	8 patients
Above knee	2
Below knee	5
Toe amputation	1

(c) Laparotomy only 3 patients

These patients underwent laparotomy with the intention of performing aortic reconstruction. The definitive procedure was abandoned in view of the operative findings. One patient had a supra-renal aortic aneurysm, and two patients had severe peri-aortitis and retroperitoneal inflammation.

(d) Femoral embolectomy 2

(e) Lumbar sympathectomy for hypertension 1 patient

(f) Termination of pregnancy 2 patients

This was performed for severe hypertension.

(g) Percutaneous transluminal angioplasty for renovascular hypertension : 3 patients

This was unsuccessful in two, and the hypertension was improved in the third patient.

13. RECONSTRUCTIVE VASCULAR SURGERY

46 procedures were performed in 43 patients.

1. Aortic Aneurysms

(1) Abdominal aorta — 3 patients

One had concomitant aortorenal bypass graft.

One presented with a ruptured internal iliac aneurysm.

The results of surgery, both short-term and long-term, were good, in all 3 patients, with a minimum 24 month follow-up.

(2) Supra-renal aortic aneurysm — 2 patients

One patient had nephrectomy and contralateral auto-transplantation of the kidney. Both patients have been well 5 years after the operation.

(3) Thoracic aorta — 5 patients

One was a thoraco-abdominal aneurysm.

One patient had a ruptured aneurysm, and died post-operatively.

The 4 elective cases had good results.

(4) Ascending / arch aorta — 3 patients

One patient died in the early post-operative period.

2 patients had simultaneous aortic valve replacement, with control of the aortic incompetence and good long-term results.

2. Aortic Occlusive Disease — 23 patients

(1) Abdominal aorta — 8 patients

Aorta - bi-iliac grafts — 6

Aorta-bifemoral grafts — 1

Axillo-bifemoral grafts — 1

One patient had simultaneous nephrectomy for renovascular hypertension and a non-functioning kidney. Follow-up information was available for a minimum of 2 years, and there were no operative deaths. The axillo-bifemoral graft was patent at 8 years.

(2) Thoracic aorta — 15 patients

The operation performed for occlusive disease of the thoracic aorta was a dacron bypass graft from the ascending aorta to the lower thoracic/abdominal aorta. The first procedure of this nature at Groote Schuur Hospital was performed by Professor JH Louw in 1961, with the patient on the cardio-pulmonary bypass apparatus. The patient remained well for 5 years, and was then lost to follow-up.

One patient died intra-operatively. The remaining patients had good early and late operative results. One patient had simultaneous renal artery implantation into the graft.

3. Renovascular Surgery — 6 patients

4 aorto-renal bypass grafts.

2 had early graft thrombosis necessitating nephrectomy.

2 renal autotransplantation procedures.

Both patients remain normotensive at 4 years.

4. Carotid Surgery 3 patients

1 Femoro-bicarotid graft.

Early failure necessitated revision, which blocked at 1 year and the patient died subsequently.

1 Axillo-carotid graft

1 Femoro-axillary-carotid graft.

The patient was lost to follow-up at 1 year.

5. Upper limb revascularisation

1 Axillo-axillary graft, which occluded within the first 3 months, and was not revised owing to minimal symptoms.

14. MORTALITY AND OUTCOME

Long term follow-up was available in 85 patients (39%) for a minimum of 5 years. (Table 10)

Table 10

5 years	45 patients	20%
10 years	32 patients	15%
20 years	8 patients	3.6%

(a) Natural history of the disease

The following sequelae were noted in the 85 patients:

(1) No clinical progression of disease : 56 patients (66%)

(2) Cardiac complications : 17 patients (20%)

- Cardiac failure due to hypertensive heart disease : 10
- Myocardial infarction : 2
- Cor pulmonale : 1
- Pulmonary hypertension and pulmonary aneurysm formation : 1
- Aortic incompetence requiring valve replacement : 2
- Coronary occlusion on angiogram : 1

(3) Stroke : 6 patients

(4) Renal failure : 3

(5) Progression of arteritis : 13

(8 confirmed on repeat angiography)

(b) Repeat angiography

20 patients had repeat angiography to assess progression of the disease. The results are listed below, with the years after the initial angiogram in parenthesis.

6 patients (5 years): No progression seen, "burnt out" disease.

4 patients (10 years) : No progression seen, "burnt out" disease.

1 patient (12 years) : Developed innominate aneurysm and coronary artery occlusion.

1 patient (15 years) : Developed bilateral common carotid stenosis and an innominate aneurysm.

1 patient (2 years) : Developed right subclavian artery occlusion

3 patients (10 years) : Developed aortic arch disease.

2 patients (5 years) : Developed abdominal aortic and renovascular disease

2 patients (2 years) : Patent thoracic aortic graft shown two years after surgery.

(c) Mortality (Table 11)

There were 54 known deaths. (25%)

Table 11

Hypertensive heart disease with cardiac failure		N=26	(48%)
Renal failure		N=5	(9%)
Stroke		N=6	(11%)
Ruptured aneurysm		N=6	(11%)
Abdominal aorta	3		
Thoracic aorta	2		
Arch aorta	1		

Post-operative deaths	N=3	(6%)
Myocardial infarction	N=2	(4%)
Aortic thrombosis	N=1	(1%)
Suicide	N=1	(2%)
Cause not established	N=4	(7%)

Discussion

5. CLINICAL MANIFESTATIONS OF AORTIC ARTERITIS

1. GENERAL ASPECTS AND CLASSIFICATION

The Cape Town experience in non-specific aortic arteritis, also known as Takayasu's Disease, was previously documented by Professor Schrire in 1964,[1] describing 19 cases. The current study is a sequel to this, spanning a period of 36 years and involving 220 patients. The number of patients is surpassed only by the 300 cases described by Pokrovsky[83,86] from Moscow in 1986. The inclusion criteria were strictly in accordance with those established by the Aortitis Research Committee of Japan[5] in 1973. All patients were thoroughly investigated, and all patients underwent angiography.

The Cape Town experience in Takayasu's disease is that of an extensive disease pattern, with diffuse aortic arteritis and multisystem involvement. This is the most obvious and overriding feature of the clinical and radiological manifestations of the condition in Cape Town. The majority of patients had extensive aortic and branch vessel involvement with degrees of visceral ischaemia. Most patients presented late, with severe complications already established. These complications included primarily the effects of longstanding hypertension and also the effects of visceral ischaemia. Many patients had cardiac failure, with irreversible myocardial damage. The majority of patients were unsuitable for reconstructive surgery owing to both

the diffuse nature of the aortic arteritis, and the severity of the visceral complications.

The clinical manifestations of the disease are a mirror image of the anatomic involvement of the arteritis. The symptoms comprise:

(1) the effects of visceral and limb ischaemia

(2) the complications of hypertension, especially the cardiac, cerebrovascular and renal effects.

(3) symptomatic aneurysms

(4) systemic symptoms denoting "activity" of the disease.

Arteritis confined to the aortic arch and its 3 main branches typically presents with the clinical effects of a reduced blood supply to the head and upper limbs. This is described by Ueno as the classic "pulseless disease" (Ueno Type I)[4]. Thoracic and abdominal aortic involvement usually presents with hypertension and possible visceral ischaemic symptoms. Ueno regards this as the "Hypertensive disease" (Type II). Aortic bifurcation and common iliac artery involvement usually leads to intermittent claudication of the thigh and buttocks, and possible Le Riche syndrome. Combinations of these types may occur, presenting as the "Extensive disease" (Ueno type III). Ueno regards Aneurysmal disease as a distinct entity in aortic arteritis (type IV). The currently favoured classification is that of Nasu, introduced in 1976[5][133].

Nasu's classification recognises the isolated abdominal aortic involvement as a distinct entity. Fig. I.

Fig. I

Ueno (1976)[4]

I	"Pulseless Disease"
II	"Hypertensive Disease"
III	"Extensive Disease"
IV	"Aneurysmal Disease"

Nasu (1976)[133,5]

I	Aortic arch only
II	Thoracic aorta only
III	Abdominal aorta only
IV	Diffuse disease

The Nasu classification is universally applicable in Aortic Arteritis and its simplicity is a hallmark. However, it lacks detail and is merely a broad description of anatomic distribution. It does not correlate anatomic location with other aspects of the disease, such as clinical presentation, management options and prognosis. For example, subclavian artery stenosis with irregularities of the descending aorta has the same classification as bilateral carotid artery occlusion associated with severe renal artery stenosis and middle aortic syndrome. However, the clinical presentation, management options and in particular the long-term prognosis are entirely different.

Pokrovsky has introduced a comprehensive classification which he has applied to 300 patients.(83)

(1) Pathology
1. Acute inflammation
2. Subacute inflammation
3. Chronic inflammation

(2) Morphology
1. Stenosis
2. Deforming
3. Aneurysm

(3) Anatomical Site
1. Arch of Aorta
2. Thoracoabdominal
3. Both

(4) Organ Ischaemia — 4 degrees.

(5) Syndromes : 10

1. Aortic arch syndrome
   (a) Takayasu's syndrome
   (b) Pulseless disease
2. Aortic coarctation syndrome
3. Renovascular hypertension
4. Abdominal aortic ischaemia
5. Aortic bifurcation syndrome

6. Coronary syndrome
7. Combined syndrome of coarctation and renovascular hypertension (Middle aortic syndrome).
8. Syndrome of Arch and renovascular hypertension (Takayasu-Denerey syndrome).
9. Syndrome of renovascular hypertension and bifurcation disease.
10. Pulmonary artery syndrome.

In the following text, the clinical aspects of aortic arteritis are discussed. The clinical and therapeutic aspects of systemic hypertension and cardiac disease are addressed in separate chapters.

2. AGE, RACE AND SEX

Non-specific arteritis of the aorta may present at any age, but is commonly diagnosed in the 2nd-4th decades. There is an undoubted female predominance.[17,14] The condition is reported worldwide, but the incidence is highest in Japan and Asia. The large series from Japan [5,4,13,109] and the Soviet Union[86] had a female predominance of 90%, compared with the 77% at Cape Town. The average age at presentation in these series was 30 years, which is similar to the mean age in the Cape Town study.

3. PATTERN OF DISEASE

The pattern of disease in Cape Town is similar to that seen in Japan and the Soviet Union (Fig. 2)

Fig 2	Japan	Cape Town
I Aortic arch only	10%	9%
II Thoracic aorta only	18%	5%
III Abdominal aorta only	4%	14%
IV Diffuse disease	68%	72%

The commonest form of the disease encountered was a diffuse aortitis with extensive involvement of the aorta and its branches.

"Dilating" disease occurred in 50% of cases in this study, usually in association with "occlusive" disease. Isolated aneurysms occurred in only 7% of cases. This differs from the large Japanese studies where "dilating" disease occurs in only 10-15%, with isolated aneurysms very rare. The only anatomic site where dilatation occurred more commonly than stenosis was the ascending aorta and brachiocephalic artery. 70% of the disease pattern involving the "right" side of the aortic arch was "dilating". This is in keeping with the Japanese experience.[5,137] True aneurysms most commonly involved the descending or abdominal aorta. The incidence of abdominal aortic aneurysm was 26%(N=57) in the Cape Town study. This is a particularly high incidence compared with other series.

Concerning the anatomical distribution, certain other aspects are noteworthy. In comparison with other studies, the Cape Town series had a high incidence of involvement of the aortic bifurcation, common carotid arteries and the left subclavian artery.

4. PERIPHERAL VASCULAR DISEASE

66 patients presented with intermittent claudication, and 11 patients developed peripheral gangrene. This represents a higher incidence than that reported in Japan and the Soviet Union. The intermittent claudication occurred equally in the arm and leg whilst gangrene was confined to the lower limb.

Claudication of the arm was usually due to an occluded subclavian artery. Left subclavian arteritis occurred in 108 patients (49%). The majority of these patients were asymptomatic, and surgical intervention was rarely warranted. The frequent involvement of the left subclavian artery is a well-described phenomenon[4,5,6], and it was formerly postulated that this may represent the anatomic starting point of the disease. A subclavian steal syndrome was shown in 4 patients.

Intermittent claudication of the lower limb usually involved the calf, thigh and buttock, and may form part of a Le Riche syndrome. Occlusive disease of the aortic bifurcation and the common iliac arteries were responsible for these symptoms. The prevalence of aortic arteritis involving these regions has only recently been recognised.[121,5,3]

Complete occlusion of the distal aorta was first described in Takayasu's disease by Professor Isaacson from Johannesburg in 1961[55]. He was also the first to report Takayasu's disease in South Africa (1959)[51]. In the current study there was a 31% incidence (N=68) of aortic bifurcation disease. Femoral and distal artery involvement by the arteritic process is exceedingly rare. 17 patients were noted to have femoral artery disease angiographically, but histologic proof of arteritis was available in only 2 cases. The majority of these patients were considered to have superimposed atherosclerosis.

Peripheral gangrene is rare in Takayasu's disease and there is little mention of it in the literature. It is speculated that the usual cause is distal embolisation. It was Schrire and Asherson[1] who first described peripheral gangrene as a feature of aortic arteritis.

5. NEUROLOGICAL COMPLICATIONS

43 patients (20%) developed neurological sequelae as a result of cerebrovascular disease. These clinical manifestations were predominantly transient ischaemic attacks and stroke, and were directly responsible for the death of 6 patients. Certain patients present with "global", non-localising symptoms of cerebral ischaemia. These findings concur with the results of most major studies from Asia.

70 patients (32%) had angiographic evidence of arteritis of the common carotid artery, and almost a half of these cases had bilateral disease. Most of these patients were asymptomatic. The arteritis was limited to the common carotid artery, with sparing of the bifurcation and internal carotid. Of note is that 17 patients had common carotid aneurysms. Aneurysms are probably a greater risk to the patient than occlusive disease. Apart from the risk of rupture, aneurysms are a potential source of cerebral emboli, and thrombosis may also occur.

The indications for surgery in cerebrovascular disease include:

(1) aneurysms of the common carotid artery

(2) reversible symptomatic occlusive disease

Reconstructive vascular surgery is imminently feasible in most cases because the arteritis is usually limited to the origin of the common carotid artery.

6. RENAL FAILURE

33 patients (15%) developed significantly impaired renal function. Renal failure was primarily responsible for 5 deaths, and contributed to the demise of several other patients. The causes of renal failure in Aortic Arteritis include:

(1) Chronic ischaemia due to arteritis of the renal artery.

(2) Hypertensive nephropathy

(3) Glomerulonephritis.

Two types of glomerular lesions have been recognised in Takayasu's disease [46], but their clinical significance is still controversial.

(1) an axial mesangial glomerulonephritis. Electron microscopy has shown intramembranous and mesangial electron dense deposits, consisting of IgG, IgM and C3. This occurred in patients with "active" arteritis.

(2) a centrilobular mesangial thickening associated with a hyaline deposition. This occurred in patients with quiescent disease.

The genesis of the axial type may be on the basis of immune complex deposition caused by active aortitis. Glomerular ischaemia caused by vascular lesions may be responsible for the centrilobular type. [151,46] The centrilobular lesions are identical to those seen in other conditions causing chronic renal ischaemia.

The following measures should be undertaken to prevent renal failure in aortic arteritis.

(1) The blood pressure should be adequately controlled.

(2) Hypertension should be thoroughly investigated, and surgery should be performed for coarctation or proven renovascular hypertension.

(3) All patients should be regularly reassessed on a long-term basis (six-monthly) to allow the early detection of impaired renal function.

(4) Patients with proven glomerulonephritis should be given a course of corticosteroids. Steroids have been shown in some cases to improve renal function and to reverse the histological changes.[144]

7. SYMPTOMS OF A SYSTEMIC DISEASE

Aortic arteritis has rightly been described as a "great imitator"[7,67]. It may present with a myriad of non-specific "inflammatory" symptoms. In some cases these systemic symptoms may occur as an early manifestation of the disease, and form part of a "prepulseless" state.

There were 22 patients (10%) in this study who presented with non-specific systemic symptoms. These included fever; sweating;

skin rashes viz. erythema nodosum or pyoderma gangrenosum [31,159], fatigue; myalgia; weight loss; and arthralgia. Other symptoms in this category that have been described include pericarditis, pleural effusion, abdominal pain, anaemia, and tenderness of the main arterial trunks.

Many of these patients had "active" disease as indicated by a markedly elevated sedimentation rate and a rapidly progressive clinical course. It is possible that circulating immune complexes may be responsible for some of these symptoms, but this has not been verified. There is evidence that these systemic manifestations respond favourably to treatment with corticosteroids.[156,155].

8. OPHTHALMIC MANIFESTATIONS

Aortic arteritis was first recognised as a distinct clinical condition on the basis of the ophthalmic findings in a patient who also had a deficit in pulses. This patient was described at an ophthalmology congress in Japan in 1908[62]. Thus the link between eye disease and pulselessness was established.

The ophthalmic manifestations of aortic arteritis are proteàn, with involvement occuring from the optic nerve to the cornea. The essential underlying pathogenesis is ischaemia.

In the Cape Town study, expert ophthalmic opinion was sought in only 15% of the patients. Positive findings were present in less than a half of these, and included retinopathy, anterior and posterior uveitis and cataracts.

The usual symptoms include blurred vision, photophobia, ocular pain, visual field deficit and blindness. Amaurosis fugax is the commonest form of transient cerebral ischaemic attack described in Takayasu's disease.

The most important ophthalmic manifestation of the disease is the associated retinopathy. This reflects the effects of arteritis of the aortic arch, common carotid arteries and the ophthalmic arteries. Retinal changes secondary to hypertension are a common occurrence.

A classification proposed by Uyama and Asayama estimates the severity of the retinopathy:[10,68]

I	Dilatation of the small vessels
II	Microaneurysm formation
III	Arteriovenous anastomoses
IV	Ocular complications

The uveal tract may have the following pathology: iris atrophy, anterior and posterior synechiae, partial or complete occlusion

of the drainage angles with glaucoma, atrophy of the ciliary body, and atrophy of the entire choroid layer.

The other possible ophthalmic effects include: superficial keratitis; conjunctivitis; catarracts, reported in up to 40% of cases[68]; and optic atrophy.

The natural history of the ophthalmic pathology in aortic arteritis is that of progression with further ocular involvement[8]. The presence of ocular changes immediately implies a poor prognosis with respect to the patient's vision.

6. HYPERTENSION

1. INCIDENCE AND NATURAL HISTORY

Giffin in 1939 was the first to recognise hypertension as a clinical manifestation of aortic arteritis.[22] The clinical importance of hypertension was first noted by Ask-Upmark,[11] finding a 50% incidence in his series of aortic arteritis.

Hypertension was the commonest clinical presentation in this study, occurring in 168 patients (76%). This is the highest reported incidence of hypertension in aortic arteritis, and compares with Mexico 72%[70], Singapore 69% [21], China 64%[21] Sweden 48% [11], Soviet Union 54%. [18]

Renal artery stenosis (39%) and aortic coarctation (30%) were the most important causes of the hypertension. Another 17% of hypertensive patients had both pathologies. In 24 patients (14%) the pathogenesis was uncertain. These findings concur with the world experience in this condition.

Hypertension and its complications were responsible for 80% of the mortality in the current series. The most important sequelae included hypertensive heart disease with cardiac failure, ischaemic heart disease, stroke, chronic renal failure and ruptured aneurysm.

2. PATHOGENESIS

2.1 Renovascular hypertension

Renal artery stenosis causes hypertension via a renin-induced mechanism. Renin is a glycoprotein hormone (MW 42,000) secreted by cells of the afferent arterioles which form the juxtaglomerular apparatus of the kidney. Renin acts on angiotensinogen, an alpha 2 globulin synthesised in the liver and releases angiotensin I, a decapeptide. Converting enzyme splits 2 amino acids from the inactive angiotensin I to form the octapeptide, angiotensin II, a powerful pressor agent. Most of this conversion occurs during the passage of blood through the lungs, but converting enzyme is probably present in all endothelial cells. Angiotensin II also induces the secretion of aldosterone which has direct pressor effect on the vasomotor centre and causes sodium and water retention due to its effect on the renal tubules.

2.2 Aortic coarctation

The hypertension of coarctation of the aorta remains a poorly understood phenomenon.[48] 3 main theories have evolved to explain the pathogenesis. The earliest of these was the mechanical theory which suggested that hypertension proximal to the coarctation was a function of the high resistance to the left ventricle imposed by the narrowed segment. The neural theory proposes that hypertension results from a readjustment of the baroreceptors in the aortic arch, increasing the proximal pressure and therefore ensuring adequate flow to organs distal to the obstruction. There has been little evidence to support the neural theory.

The most important mechanism is the renin-angiotensin system. The narrowed aortic segment leads to renal underperfusion, with resultant stimulation of the renal pressor mechanisms. The available experimental evidence supports the latter theory. Scott and Bahnson[54] surgically created a coarctation, and established a group of hypertensive dogs. Transplanting one kidney above the coarctation and removing the contralateral kidney relieved the hypertension in the surviving animals.

2.3 Loss of elasticity in the aortic wall

In 1961 Ask-Upmark[11] suggested that the rigid inelastic aortic wall may contribute towards the hypertension in Takayasu's disease. The rigid calcified aorta is unable to dissipate the cardiac systolic pressures, resulting in a systemic hypertension which is then transmitted to the visceral end-points with resultant tissue damage. Furthermore, the loss of aortic elasticity results in abnormal flow dynamics and increased turbulence, contributing towards impaired tissue perfusion, superadded atherosclerosis of the vessels and aneurysmal dilatation.

2.4 Baroreceptor instability

This has been implicated due to the observed inadequate pressure responses occurring with postural changes in these patients[108]. It has also been considered that the baroreceptors may be affected by the disease process itself.

2.5 Cerebral ischaemia

The vasomotor centre, cardiac inhibitory centre and "pressor" areas of the medulla are largely responsible for the central control of blood pressure. Impaired cerebral perfusion and anoxia are finely detected by these centres, with resultant pressor responses mediated both hormonally and neurally. This results in enhanced cardiac contractility and increased peripheral resistance.

3. TREATMENT

3.1 Medical treatment

The hypertension in aortic arteritis is usually severe and is poorly controlled with medication. The hypertension usually begins in the 2nd or 3rd decade of life, and becomes progressively worse leading to major cardiac, renal and cerebrovascular complications which are usually responsible for the death of the patient.

There is only one study comparing prospectively medical and surgical treatment in renovascular hypertension, that of Hunt in 1973.[126] This study involved patients with fibrous dysplasia, atherosclerosis and arteritis, and showed long-term medical treatment to be inferior with respect to blood pressure control and to survival. Furthermore, there is increasing evidence that medical treatment may impair renal function owing to the added ischaemia occurring with the reduced perfusion pressure of the kidney.[122,123,124] The introduction of converting enzyme inhibitors was regarded as a major advance in the control of renovascular hypertension. However, these drugs

may aggravate renal failure, especially in patients with bilateral renal artery stenosis.[120,150)]

3.2 Surgery for aortic coarctation

Surgery remains the cornerstone of treatment for the aortic coarctation of Takayasu's disease, and should be undertaken for all surgically correctable lesions. The surgery is relatively simple consisting of a thoraco-abdominal bypass graft, [(24,25,26)] from normal proximal aorta (ascending aorta preferable)[(25)] to the abdominal aorta, with the diseased aorta left in situ. The most difficult aspects of the procedure concern the assessment of the distal extent of the disease, the possibility of mesenteric and renal artery involvement and the risk of post-operative intestinal ischaemia.[(3)]

Patients with this condition are usually young, with normal cardiorespiratory reserve, and tolerate the surgery very well. In the current study 15 patients underwent surgery for coarctation. Apart from one death in a high risk patient, the results of surgery were good, with the remaining patients all significantly improved following the procedure. These results are comparable with other studies.[(24,25,26,57,41,153)]

3.3 Renovascular hypertension : surgery and percutaneous angioplasty

The treatment of choice for renovascular hypertension in aortic arteritis is reconstructive vascular surgery. This not only provides adequate blood pressure control, but also may improve renal function in some patients.

There are 3 factors which limit the benefit of renovascular surgery in aortic arteritis:

(1) the frequent presence of segmental branch vessel disease, which may require a more complex surgical procedure.

(2) associated aortic arteritis, which may limit graft patency.

(3) the high incidence of bilateral disease.

Surgery should be undertaken only for proven renovascular hypertension, based on high renal vein renin levels, which are lateralising with a ratio of at least 1;6.

The surgical options include:

(1) aorta-renal bypass

(2) renal autotransplantation

Aorta-renal bypass is the choice procedure, and the main controversy concerns the graft material used. Expanded PTFE or saphenous vein are preferred to autogenous artery in view of possible involvement of the graft by the disease process. Venous grafts have however been shown to degenerate, especially when used in aortic arteritis.

Also controversial is the optimum site of the aortic anastomosis in aortarenal bypass surgery. It is certainly preferable that the anastomosis be made to normal aorta. The abdominal and descending thoracic aorta is often involved by arteritis in these cases, in which event the ascending aorta may be chosen for the anastomosis. However, a long-segment graft requires a thoraco-

abdominal operation, and has a significant risk of graft thrombosis. On the other hand, a short segment graft to diseased aorta may occlude due to progression of the arteritis. Therefore, the choice of procedure should be individualised, depending on the general condition of the patient and the severity of the aortic arteritis.

Renal autotransplantation is an "ex vivo" technique of revascularisation involving a distal branch vessel anastomosis to the renal artery, using the ipsilateral internal iliac artery and its divisions. The anastomosis is performed under magnification, with the kidney cold-perfused. The renal vein is anastomosed to the ipsilateral external iliac vein, and the kidney resited into the iliac fossa. This more complex procedure is reserved for patients with branch vessel disease.

The indications for nephrectomy have become more limited with the current emphasis on renal preservation. Previous criteria for nephrectomy based on function (20% function) and size (<9cm length) are no longer valid, especially with the evidence that vascular surgery may <u>improve</u> renal function.

There are 2 indications for nephrectomy:

(1) Segmental branch vessel disease, not suitable for reconstructive surgery, and not controlled on medical treatment.
(2) Atrophic scarred kidney which is renin-secreting, usually associated with renal artery occlusion.

Nephrectomy is a relatively simple procedure and has excellent results in selected cases [123,153]. The main risk is the possible subsequent involvement of the opposite side by the arteritis, with the risk of late-onset renal failure.[91]

In the current study, 17 patients (26%) had surgery for renovascular hypertension. 4 aorta-renal bypass grafts were performed. 2 had early thrombosis necessitating nephrectomy. The other 2 have been normotensive for at least 2 years. 2 patients underwent renal autotransplantation, and both remain normotensive at 4 years. 11 patients underwent nephrectomy, all of whom were significantly improved by surgery. This contrasts with Pokrovski's series[18] of 128 patients with hypertension, of whom 72(52%) had surgery (67 vascular surgery, 5 nephrectomy). In Lagneau's study in France [118] 75% had surgery. This discrepancy is partly accounted for by the diffuse nature of the disease seen in Cape Town, commonly with branch vessel involvement, and not suitable for surgery.

Most centres report 90% success following surgery, with $^{2}/_{3}$ of these cured, and $^{1}/_{3}$ significantly improved.[82,18] Pokrovski reports good long-term results in 92% of the 72 patients who had surgery.

The role of percutaneous transluminal angioplasty (PTA) in renovascular hypertension remains controversial. Introduced by Gruntzig in 1978, PTA has enjoyed widespread support, especially in the treatment of renal artery stenosis due to fibromuscular

dysplasia. There have been reports of PTA success in arteritis, with results similar to those in atherosclerosis viz. 67% cured or improved.[28,84,143] However, most series have shown disappointing results in arteritis. PTA was performed in 3 patients in this study and was found to be an unsatisfactory form of treatment for renal artery stenosis. The extensive medial fibrosis in the renal artery renders the vessel resistant to dilatation.

PTA is indicated only in non-orificial mainstem renal artery stenosis and should not be attempted for branch vessel disease. Unequivocal proof of renovascular hypertension should be established with lateralising renal vein renin ratios. The widespread use of PTA has led to increasing reports of complications, which include dissection, embolisation, and thrombosis. PTA should not be regarded as a preliminary procedure prior to surgery. Failed angioplasty usually makes surgery more difficult due to periarterial inflammation necessitating a more complex operation, involving the branch vessels.

7. CARDIAC DISEASE

103 patients (47%) developed cardiac complications of Aortic Arteritis. One third of the entire study (N=74, 34%) developed cardiac failure. Cardiac failure was responsible for 54% of the known deaths. The two commonest cardiac manifestations were hypertensive heart disease (30%) and valvular disease (22%), and 24 patients had both these pathologies. Other pathologies included ischaemic heart disease, pulmonary hypertension, cardiac aneurysm, and pericarditis.

1. HYPERTENSIVE HEART DISEASE

Hypertensive heart disease is a well-described feature of Aortic Arteritis. [87,38,90,128] In the early stages, the clinical findings consist of cardiomegaly in association with longstanding systemic hypertension. The chest radiograph confirms the presence of cardiomegaly, and the ECG shows features of left ventricular hypertrophy. In a study of patients with Takayasu's disease over the age of 40, Marooka [38] found that 92% had left ventricular hypertrophy and 82% had cardiomegaly.

In the later stages, ventricular dilatation occurs, often associated with left ventricular failure. Ischaemic heart disease may develop owing to coronary artery insufficiency and the increased nutritional requirements of the hypertrophied myocardium. Further complications that may occur include biventricular cardiac failure, arrhythmias, mitral and tricuspid valve incompetence, and mural thrombosis with embolisation.

A specific cardiomyopathy has been described in Takayasu's disease [90,150] with clinical, radiological and cardiographic features identical to advanced hypertensive heart disease. These patients develop cardiac failure which is non-hypertensive and non-valvular in origin. The histology of the myocardium consists of elastic and muscle fibre degeneration, and an infiltration of acute and chronic inflammatory cells. The prevalence of this cardiomyopathy in the Cape Town study could not be established. In the autopsies performed, this condition was not shown.

2. VALVULAR HEART DISEASE

48 Patients (22%) in this study had valvular heart disease. Aortic incompetence was the commonest pathology, occurring in 34 patients. 22 patients had mitral incompetence, 8 of whom also had aortic incompetence.

Aortic incompetence is the commonest valvular disorder seen in Takayasu's disease. It was first recognised as a feature of Takayasu's disease by Jervell in 1954 (cited in (1)). Aortic incompetence is also recognised in other forms of Aortic arteritis[148] viz. Giant cell arteritis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, syphilitic aortitis, Reiters syndrome and Behcet's syndrome.

The pathogenesis of aortic insufficiency remains controversial.[95,157] The two main causes are:

(1) arteritis of the valve itself

(2) aortic ring dilatation.

Other suggested causes include disunion of the commissures and changes in aortic compliance. The relative importance of these mechanisms is uncertain. In a review of 73 cases, Acar et al[95] showed that two-thirds of the cases with aortic incompetence had arteritis of the valves. However, other studies [116,5] suggest that the primary pathology is a dilatation of the valve ring. Morooka[116] evaluated the aortic valve ring angiographically in 70 patients with aortic incompetence. He showed a 100% incidence of valve ring dilatation. This occurs commonly in association with "dilating" disease of the ascending aorta.

The clinical presentation is nearly always in keeping with chronic aortic regurgitation. The symptoms are gradually progressive, and left ventricular failure due to myocardial dysfunction is the usual outcome. Cardiomegaly due to dilatation of the left ventricle is a hallmark of the condition.

In the Cape Town study, 3 patients underwent aortic valve replacement for intractable cardiac failure. 2 of these patients had simultaneous interposition grafting of the ascending aorta. The results of surgery, with a 4 year follow-up have been good. This has also been the experience at other centres [81,127,148]. The natural history of aortic incompetence and the results of surgery support <u>early</u> operative treatment in

Takayasu's disease. As in all patients with significant aortic incompetence, surgery is recommended when symptoms develop.

An acute severe aortic incompetence with left ventricular failure has been described in Takayasu's disease [148]. Early surgery is mandatory in these patients, and may be life-saving.

Mitral incompetence occurs secondary to left ventricular dilatation and cardiac failure. There is no evidence that the mitral valve is primarily involved in the arteritic process.

3. PULMONARY HYPERTENSION

Pulmonary hypertension was proven in 13 patients. This represents 11% of patients who underwent cardiac catheterisation studies. 5 of these patients had pulmonary arteritis and the remainder had pulmonary hypertension secondary to left ventricular failure. It is recognised that pulmonary hypertension in Takayasu's disease may occur via 3 mechanisms.[9]

(1) Pulmonary arteritis
(2) Left ventricular failure
(3) Combination of the above

Pulmonary arteritis is now recognised as a unique feature of Takayasu's disease. Recent Japanese publications [5,13] report a 50% incidence of pulmonary arteritis in Takayasu's disease. Cardiac catheterisation and pulmonary angiography is now regarded as a mandatory investigation in all cases of Takayasu's disease.

4. ISCHAEMIC HEART DISEASE

13 patients had clinical evidence of ischaemic heart disease. (9 angina pectoris, 4 proven myocardial infarcts) 2 patients died as a result of infarcts. Another 8 patients had asymptomatic coronary arteritis.

There have been several reports in the literature of coronary artery involvement in Takayasu's disease [14,70,72]. The autopsy study from Mexico [88] had the highest incidence of coronary artery disease (33% of 18 cases). However, in several large Asian series, coronary arteritis did not occur.

Coronary aneurysms are exceedingly rare, and apart from the 2 cases of Rose et al [14] are virtually undescribed. There were 4 cases in the Cape Town study. In the autopsy study of Rose [14] another interesting feature was shown: 3 of the cases had a distal arteritis of the coronary arteries with sparing of the orifices.

The true incidence of coronary arteritis has not been established. Associated atherosclerotic disease occurs frequently. Also, the myocardial hypertrophy of hypertensive heart disease predisposes to coronary artery insufficiency. Histologic proof of arteritis is essential to differentiate the pathology from atherosclerosis.

8. AORTIC ARTERITIS IN PREGNANCY

Aortic arteritis is classically a disease of young women of childbearing age. It is thus not surprising that the diagnosis is quite often first suspected at an ante-natal clinic. There is a distinct lack of literature on the subject of Aortitis and pregnancy.

There were 20 patients (9%) in the Cape Town study with Takayasu's disease detected in pregnancy. The patients were all hypertensive and the clue to the diagnosis in most cases was the associated deficit in pulses. Table 1 lists the main clinical problems encountered.

Table 1 Aortitis in Pregnancy	N = 20	
Hypertension	N = 20	(100%)
Abdominal aortic aneurysm	N = 5	(25%)
Cardiac failure	N = 2	(10%)
Intermittent claudication	N = 4	(20%)
Angina pectoris	N = 1	(Coronary steal to the descending aorta shown)
Transient cerebral ischaemic attacks	N = 2	(10%)
Renal failure (mild)	N = 1	(5%)
Raynauds phenomenon	N = 1	(5%)
Suspected intrauterine growth retardation (aortoiliac occlusive disease)	N = 2	(10%)

17 patients had normal vaginal deliveries of healthy babies. In some of these patients, labour was induced prior to term. There was one maternal death which occurred during the post-partum

period from a ruptured aortic aneurysm. 3 patients underwent early termination of pregnancy (T.O.P.). The indications for T.O.P. were severe hypertension (2 patients) and aortic aneurysm (1 patient).

The largest reported study of Aortic Arteritis in pregnancy is that of Ishikawa [74] describing 33 patients. Complications during pregnancy were noted in 60% of Japanese patients, primarily related to hypertension, cardiac failure and stroke. Pregnancy does not aggravate the inflammatory activity of the disease. The cortico-steroid hormonal secretion may even temporarily reduce the activity of the arteritis.[32,75] However, it is the cardiac and hypertensive complications of the disease that pose a threat to the mother and the baby. There are certain stresses imposed on the cardiovascular system in a normal pregnant woman. These include an increased cardiac output, stroke volume and pulse rate. These are direct consequences of the following physiological changes:

(1) the increased intravascular fluid volume in pregnancy
(2) the raised basal metabolic rate
(3) the increased pulmonary gaseous exchange
(4) the increased tissue oxygen requirements.

In the patient with aortic arteritis, who may have hypertensive heart disease, these added stresses on the cardiovascular system may lead to cardiac failure. There are two aspects to consider in the management of Aortic Arteritis in pregnancy.

1. There are 2 lives at risk, that of the mother and the fetus.
2. Aortic occlusive disease and aortic aneurysms should be considered separately. The complications of these pathologies differ, as do the treatment options.

Aortic occlusive disease is essentially a problem of the management of hypertension. These patients are nearly all hypertensive, due to either renal artery stenosis or aortic coarctation. The risk to the mother includes cardiac failure, stroke, eclampsia and abruptio placentae. With respect to the feto-placental unit, there are 2 possible effects. The aortic stenosis and coarctation may have a protective effect in that the systemic blood pressure in the distal aorta may be normal. Thus the fetus may be spared of the potential problems of ante-partum haemorrhage, premature labour or eclampsia. However, should the arteritis extend to involve the common iliac vessels, with stenosis of the internal iliac origins, there is a definite risk of placental insufficiency due to inadequate blood supply. This would result in intrauterine growth retardation of the fetus.[94] In some cases of severe aortic occlusive disease, a steal effect from the external iliac and major limb vessels may occur in order to maintain placental nutrition.

In the case of aortic occlusive disease and hypertension, the pregnancy should be managed in the usual fashion, according to the severity of the hypertension, and according to the risks to the mother and fetus. If the hypertension is severe and intractable, delivery of the baby should take place as soon as it is mature, probably by caesarian section. In some cases, the

severity of the hypertension may necessitate early termination of pregnancy.

Abdominal aortic aneurysm in pregnancy should be regarded as a major threat to the life of the mother and her baby. Abdominal aneurysms are at risk of rupture during pregnancy due to the following factors:

(1) direct pressure effect of the gravid uterus
(2) raised intra-abdominal pressure
(3) the commonly associated hypertension

The presence of an abdominal aortic aneurysm in pregnancy poses certain therapeutic dilemmas:

(1) the indications for urgent termination of pregnancy and aneurysm surgery.
(2) the method and timing of the delivery of the baby
(3) the timing of elective aneurysm surgery

The indications for urgent T.O.P. include:

(1) Symptomatic aneurysm
(2) Large aneurysm (> 6cm size)
(3) Associated severe hypertension

There are a number of unanswered questions concerning the delivery of the baby. Should a vaginal delivery be allowed, or should caesarean section be performed? Should delivery take place at term or as soon as the baby is mature? When should the elective aneurysm surgery be performed: during pregnancy, after

delivery or with simultaneous caesarean section? These are vexing problems which have not been addressed in the literature.

It is reasonable to surmise that the risk of aneurysm rupture is significantly increased during labour, due to the mechanical effects of the contracting uterus, and the changing intra-abdominal pressure. Similarly, laparotomy with caesarean section would also increase the risk of rupture owing to the proven release of collagenases and elastases that occurs with surgery.

It would be reasonable to recommend that the patient undergo caesarean section as soon as the baby is mature. Elective aneurysm surgery should be undertaken within a few weeks of delivery, as soon as the uterus has partially involuted, and when the possibility of post-partum sepsis has been entirely discounted.

In conclusion, the diagnosis of Aortic Arteritis is not an indication for termination of the pregnancy. The pregnancy itself does not aggravate the aortic arteritis. However, hypertension and possible cardiac sequelae should be carefully managed. Abdominal aortic aneurysm is a life-threatening condition in pregnancy. The options in management should be carefully considered in each patient according to the risk of rupture, the gestational age of the fetus and the wishes of the parents. These patients should all be managed in hospital for the duration of the pregnancy.

9. AETIOLOGY

The aetiology of nonspecific aortic arteritis remains controversial. The four main factors that have been implicated include:

(1) Genetics

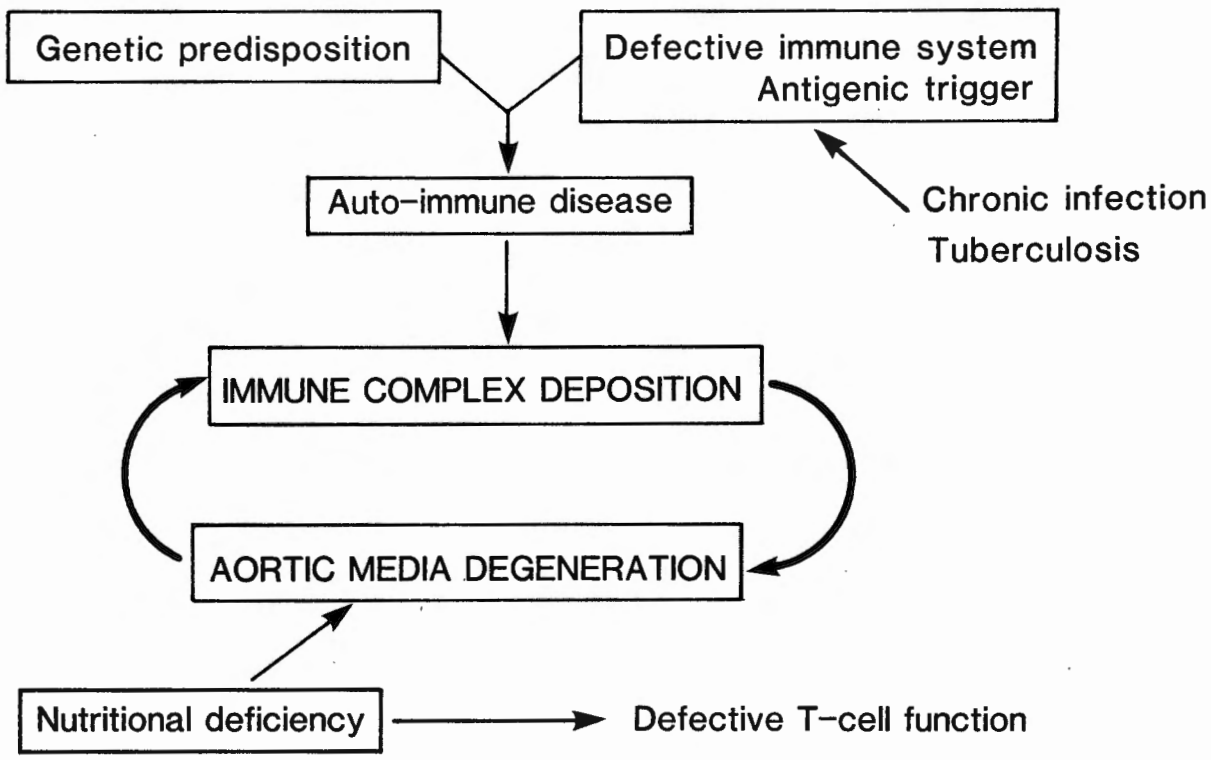
(2) Immunological factors

(3) Nutrition

(4) Chronic bowel infections

The possible contribution of these 4 factors is depicted in Fig. 1.

FIGURE 1.


Genetic predisposition
Defective immune system
Antigenic trigger
Auto-immune disease
Chronic infection
Tuberculosis
IMMUNE COMPLEX DEPOSITION
AORTIC MEDIA DEGENERATION
Nutritional deficiency
Defective T-cell function

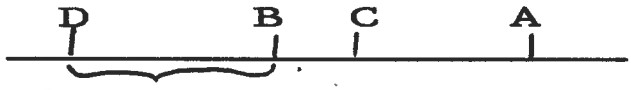
1. Genetic Factors

The genetic link with aortic arteritis was initially discovered by Numano and his colleagues in Japan.[92,130] In 1977 they encountered monozygotic Japanese identical twin sisters both of whom had aortic arteritis. A genetic survey of these twins and their family led to a study of Histocompatibility antigens with the postulation of genetic factors in the aetiology of this disease.[129] Their subsequent research is largely responsible for the current understanding of the genetic link with aortic arteritis. There is now unequivocal evidence that certain histocompatibility antigens are associated with this condition.[111,76,49] The most frequently associated antigens are HLA BW52[19,76] and the DW 12 antigen[78] which is a B cell antigen formerly called DHO. Their studies suggest that the genetic factors in Takayasu's disease are probably located at the B and D loci, and are closest to BW 52 and DW 12. These genes are considered to play a major role in determining the susceptibility to Takayasu's disease. Numano[49] et al have also shown that the presence of BW 52 and DW 12 tissue antigens in a patient with aortic arteritis, usually denotes a worse prognosis, with progression of disease and active inflammation.

An immune reactive gene has been identified, which is responsible for autoimmune processes. The entire region encompassing B and D loci on the HLA gene complex is postulated to contain genes governing immune responses. See Fig. 2.

Fig. 2 HLA Gene Complex

A single C6 chromosomal segment



Immune responses

governed by these genes

It is probably highly significant that both the BW 52 and DW 12 antigens are located near to the immune reactive gene, supporting the premise of an autoimmune disease, which is genetically determined. This would associate aortic arteritis with certain other autoimmune disease viz. Rheumatoid arthritis, ankylosing spondylitis, Hashimoto's disease, Addison's disease and pernicious anaemia. All of these conditions are considered to occur due to a genetically determined defect of the immune mechanism.

2. Immunological factors

The immune hypothesis for the aetiology of aortic arteritis is based on the following facts:

2.1 Immune complex deposition in the aorta.

Immuno-electrophoresis has demonstrated the presence of IgA and IgM complexes in the aortic media.[3,113,73] Circulating immune complexes and aortic antibodies have also been shown in up to 50% of patients. There is evidence that these cellular and humoral immune responses may cause damage to the aortic media.[14]

Could aortic arteritis be considered one of the immune complex diseases? Autologous antigens may be released from the aorta prior to tissue damage occurring. These antigens serve as immunogens, evoking an antibody response. Resultant immune complexes are deposited in the aortic media leading to tissue destruction.

Attractive as the theory may seem, the supporting evidence is inconclusive. Few studies have demonstrated the presence of complexes. Serum complement levels are usually normal. Diffuse small vessel vasculitis is absent. However, immune complexes have been shown on the glomerular basement membrane in active disease.[46,150]

2.2 Defective T lymphocyte function.

A qualitative T lymphocyte deficiency has been shown in aortic arteritis.[3] Nutritional deficiency and/or chronic infections may contribute to this functional defect, but this is uncertain.

2.3 The association with histocompatibility antigens BW52 and DW 12 which are located near to the immune reactive gene, responsible for autoimmune disease.

2.4 The association with other immune related diseases.[15,99] These conditions include Crohns disease, ulcerative colitis, glomerulonephritis, Stills disease and thyroiditis, and interstitial lung disease.[152]

2.5 The link with Tuberculosis

The relationship between aortic arteritis and tuberculosis was first documented by McKusick in 1962[131]. However, the role of tuberculosis in the aetiology of Takayasu's disease remains controversial.

The incidence of tuberculosis is variable:

Cape Town	20%
Japan	5 - 25% (Nakao's series[8]:25%)
Soviet Union	5 - 10%
Mexico	48%[70]

Tuberculosis may be regarded as a possible contributory factor in the pathogenesis of the disease. It may provide a chronic antigen trigger for an immune response, which, in the patient who is genetically predisposed and nutritionally depleted, leads to immune complex deposition in the aortic media, with resultant fragmentation and necrosis. However, this is merely speculative.

Several studies have shown a high percentage of +ve Mantoux tests eg. Sano:84%. But the Mantoux test is merely a non-specific test of cellular immunity, and positivity does not imply tuberculous infection. The histologic characteristics of tuberculous infection are not a feature of aortic arteritis. Also, there is no evidence of circulating antibodies to mycobacterial products occurring in Takayasu's arteritis.(112)

Both tuberculosis and aortic arteritis are diseases of the poorer socio-economic groups, occurring in patients with nutritional deficiency and are most commonly seen in poverty-stricken third world countries where hygiene is inadequate. Thus the link between these two conditions may be merely incidental.

3. Nutritional Deficiency

Nutritional deficiency is a frequent finding in patients with aortic arteritis, probably reflecting the lower socio-economic population which is prone to develop the condition. Although several studies have shown clinical evidence of nutritional deficiency,(3) no specific deficiency has been identified. It has been shown in experiments on monkeys that nutritional deficiencies cause fragmentation and degeneration of the elastic tissue of the aortic media.(132) Protein and vitamin C deficiency leads to inadequate collagen and elastin deposition in the aortic media, and results in defective cross-linkages between collagen and elastin fibres.

4. Chronic Bowel Infections

The incidence of chronic parasitic infections in patients with aortic arteritis is 30-70% in Japan and Asia.[3] Furthermore, certain chronic inflammatory bowel conditions are known to be associated with a defective T-cell function. Additional supportive evidence is that the immune complexes of aortic arteritis comprise IgA and IgM. These specific immunoglobulins are thought to be derived from the intestinal cells. However, chronic bowel infection was not a clinical feature in the Cape Town study.

In conclusion, non-specific aortic arteritis should probably be regarded as an auto-immune disease. The available genetic and immunological information on the subject would support this hypothesis. Further credence is given by other aspects of the disease, such as its natural history, the clinical presentation, the pathology and the response to treatment. The natural history of the condition is typical of an auto-immune disease. There are "active", "inactive" and "burnt out" phases of the disease. Multisystem involvement is common. The clinical presentation is also typical of autoimmune diseases: the female predominance; early age onset; familial characteristics; the non-specific symptoms such as fever, weight loss, malaise, arthralgia and skin rashes. The pathology may be diffuse or segmental, yet there is one target organ: the elastic layers in the aortic media. Finally, the disease responds to medical treatment in the

same way as other auto-immune conditions. Corticosteroids and cyclophosphamide lead to a reduced "activity" of the disease and may partly reverse the disease process.

10. PATHOLOGY

Takayasu's disease is an arteritis of the aorta and its major branches. The extent of the pathology is variable. It may occur in an isolated segment or in multiple segments of the aorta. There may be a diffuse arteritis involving the entire aorta, extending from the ascending aorta and aortic valve ring to the aortic bifurcation and common iliac arteries. The pathology occurs in the aortic media, and has the features of both an acute and chronic inflammatory process. The disease is confined to the major elastic arteries and the main target of the pathology is the elastic tissue within the aortic media. The pathological features, both macroscopic and microscopic support the hypothesis than non-specific arteritis is an auto-immune disease.

Macroscopically, the pathology may be indistinguishable from atherosclerosis. The gross findings consist of an indurated, thickened aortic wall. The periaortic tissue may be reactive and the adventitia may be inflamed. The pattern of the disease may be "dilating" or "occlusive" in nature. "Dilating" disease consists of aneurysms which may be single or multiple and usually occur in association with "occlusive" disease. Isolated "dilating disease" is rare. The aneurysms are fusiform and may rupture. Dissecting aneurysm is very rare in Takayasu's disease despite the 2 main predisposing factors for dissection being present in a high percentage of patients viz., destruction of the media and, associated systemic hypertension. Autopsy studies have led to speculation that in aortitis, well-developed scars in

the aortic wall either limit the spread of aortic dissection or prevent its occurrence by fusing the layers of the aorta.

The occlusions and stenoses of the major arteries occur due to the healing process in the aortic media. This healing by "secondary intention" leads to the production of large amounts of scar tissue with resultant contracture and deformity. Occlusion may also occur due to thrombosis of the artery.

Aortic arteritis that has been present for a minimum of 5 years may develop calcification of the aortic wall. Calcification typically involves the arch and descending aorta, and occurs in 10-25% of cases.[5] Significantly, the ascending aorta is spared of calcification, a feature that differentiates Takayasu's disease from other forms of arteritis, notably syphilitic aortitis.

A unique feature of this condition is the involvement of the pulmonary arteries by the disease. Pulmonary arteritis does not occur in other forms of aortic arteritis. Routine pulmonary angiography performed in several recently reported Japanese studies has shown a 50% incidence of pulmonary arteritis[5,109,13]. Usually the patients have no clinical features of respiratory disease, and the pulmonary function tests are normal. The arteritis may extend to involve the segmental pulmonary arteries, which also contain elastic tissue.[16] Pulmonary arteritis may occur irrespective of the degree of systemic involvement.

Histologically there is both acute and chronic inflammation of the aortic wall. Pokrovsky[2] has described 3 distinct pathological phases: acute, intermediate and chronic. A panarteritis occurs with infiltration of inflammatory cells into the adventitia and aortic media. These cells include polymorphonuclear leukocytes and mononuclear cells. The mononuclear cells comprise lymphocytes, plasma cells and histocytes. Giant cells may also occur as part of the inflammatory process. The main target of the disease process is the aortic media, more specifically the elastic tissue. Elastic von Giesen stains show a destruction of the elastic layers, especially the internal and external elastic laminae. There is necrosis of the smooth muscle cells in the aortic media. The vasa vasora are also involved, and may be surrounded by a cuff of inflammatory cells. Simultaneously there is a process of repair taking place. Neovascularisation occurs in the adventitia, media and intima, with the laying down of granulation tissue. This is followed by the more definitive healing by "secondary intention," with the formation of fibrous tissue. This healing process leads to the production of large amounts of scar tissue, with resultant deformity and contracture. Segments of the aortic wall with total medial destruction are especially prone to aneurysm formation.[14,146]

The intima is relatively spared by the disease process, although a degree of inflammation may occur, with neovascularisation and

repair. Intimal fibrous plaques are commonly seen throughout the aorta. Electron microscopy of the hyperplastic intima in aortic arteritis has shown that 2 cellular elements are responsible for the focal intimal growth: fibroblast-like cells producing type I collagen and cells ultrastructurally corresponding to smooth muscle cells producing type III collagen. Furthermore, there are many tiny capillaries located between these cells.(50) It is no longer considered that the intimal thickening is due to smooth muscle cell migration from the media. Rather, it is due to the hyperplasia of the capillary systems within the arterial wall, with the pericyte cells transforming into fibroblast-like cells.

The histological findings in Takayasu's disease are quite specific and differentiate the condition from other causes of aortic arteritis. The only two conditions with very similar histology are Giant cell arteritis and rheumatic mesaortitis.(14) However, Giant cell arteritis affects older patients and has an emphasis on small and medium-sized arteries with incidental aortic involvement. The aortitis of rheumatic fever may be histologically identical to Takayasu's disease. However, neither occlusion of major limb arteries nor aneurysm formation are features of rheumatic mesarteritis. Nonetheless, it is clear that the histological findings in aortitis should always be interpreted together with the angiography and the clinical setting.

The complications of the disease are responsible for secondary pathological effects which can occur in every system of the human

body. The two main complications responsible for these effects are:

(1) systemic hypertension

(2) visceral ischaemia

The aortic arteritis per se is seldom life-threatening. It is the effects of longstanding systemic hypertension and visceral ischaemia that account for the morbidity and mortality of this condition.

11. TREATMENT

There is no cure for aortic arteritis. The treatment is merely palliative and is directed at the control of symptoms, and the prevention of life-threatening complications. There is a dual therapeutic approach to aortic arteritis: Corticosteroids and vascular surgery. When implemented judiciously and early in the disease process, these therapeutic modalities are of undoubted benefit, with control of symptoms and prolongation of life.

Recent prospective studies[19,77,13] from Japan and North America have shown beyond doubt that corticosteroids are beneficial in patients with "active" aortitis. The controversies include the specific indications for treatment, the dosage and duration of therapy, and the effect on the natural history of the disease.

During the last 2 decades, extensive surgical experience in aortic arteritis has been acquired in Japan and the Soviet Union. Their results support surgical treatment of symptomatic patients with operable lesions. The role of surgery is becoming more clearly defined, and is considered in the following categories:

(1) Aortic arch and branches

(2) Descending and abdominal aortic surgery

(3) Renovascular surgery

The surgical treatment of hypertension has been discussed in chapter 6.

In Cape Town, 46 patients (21%) underwent vascular surgery, 62 (28%) had anti-tuberculous therapy, and only 25 patients (11%) received corticosteroids. Recent reports from Japan and the Soviet Union cite a much higher incidence of intervention both medical and surgical. (Table 1)

Table 1

	Cape Town	Japan (Kimoto)	Soviet Union (Pokrovsky)
Corticosteroids	11% (N=25)	60%	50%
Tuberculous treatment	28% (N=62)	10%	<5%
Vascular surgery	21% (N=46)	50% (N=67)	73% (N=8)

1. MEDICAL TREATMENT

A cure for aortic arteritis is not available. However, there is evidence that appropriate therapy may reduce the "activity" of the disease and prolong life. The optimal treatment programmes for the various manifestations of arteritis have not been defined. Adequately designed studies have been difficult to perform because of the diverse nature of the disease and the ill-defined prognostic parameters. Corticosteroids remain the mainstay of therapy, though immunosuppressive agents seem to be helpful in some patients.

The response to treatment is variable according to reports:

Lupi-Herrera [70]	1977 :	20%
Kimoto [79]	1967 :	62%
Shelhamer[19]	1985:	50%
Arabidze[33]	1985:	73%

There are only two published prospective trials on the use of corticosteroids in aortic arteritis: that of Shelhamer[19] (Bethesda, Maryland) and Hall[77] (Mayo Clinic). Although the numbers of cases were small, the trials were carefully planned and had control groups. Both showed definite benefit from the use of steroids in "active" disease. In the non-responders with "active" disease, about 50% were improved with cyclophosphamide treatment. In the Mayo Clinic study, steroids led to a return of pulses in 50% of cases. Steroids have also been shown to reduce the aortic wall thickening as shown on CT scan[142]. Recommended therapeutic dosage of Prednisone is 1mg/kg/day for 4 weeks, then gradually reduced.

Corticosteroid therapy has an important role in the preparation of patients for surgery.[155] Prior to surgery the "activity" of the disease should be reduced, and the sedimentation rate returned to normal. This is usually accomplished by a course of steroids.

Non-steroidal anti-inflammatory agents have been prescribed successfully in the control of systemic symptoms. Anti-tuberculous medication should be used only in proven tuberculosis. Long-term treatment with soluble aspirin is probably applicable in selected cases of aortic arteritis eg.

carotid arteritis, coronary arteritis and aortic arch disease. However, there is no scientific data[12] to support or refute the use of aspirin.

2. SURGERY

Reconstructive vascular surgery was performed in only 21% of cases in Cape Town, compared with the 50% in Tokyo[26] and 75% in Moscow[83]. This discrepancy is partly accounted for by the difference in the nature of the disease seen in Asia, where the pathology tends to involve the orifices of the main vessels. The diffuse pattern of disease with branch vessel involvement seen in Cape Town is less suitable for vascular surgery. Furthermore, many patients presented "late" and had severe cardiac complications which precluded surgery.

Vascular surgery was previously considered unsafe in aortic arteritis, with a risk of anastomotic disruption or aneurysm formation.[4,26,78] However, this has been shown to be fallacious, and there is no greater risk of anastomotic problems in Takayasu's disease than in atherosclerosis. Indeed, the results of surgery performed "early" in the disease process, on younger patients are usually excellent.[118,121,12,153]

Vascular surgery in aortitis usually comprises the insertion of a prosthetic graft either to bypass an occluded segment or to replace an aneurysm. Endarterectomy is <u>not</u> a surgical option in arteritis, as the pathology occurs in the <u>media</u> of the arteries

with relative sparing of the intima[42,85,107]. The long-term durability of venous grafts is doubtful, and degeneration has been reported.[118] The use of autogenous artery as a graft material carries the risk of the graft being involved by the arteritis.

The main indication for surgery in aortic arteritis is the treatment of hypertension. This has been discussed in Chapter 6. The other indications include ischaemia, (visceral, cerebral and limb ischaemia) and aneurysms.

3. AORTIC ARCH AND BRANCHES

The main indications for surgery in this category include:

(1) Common carotid artery occlusive disease which is symptomatic

(2) Aneurysms

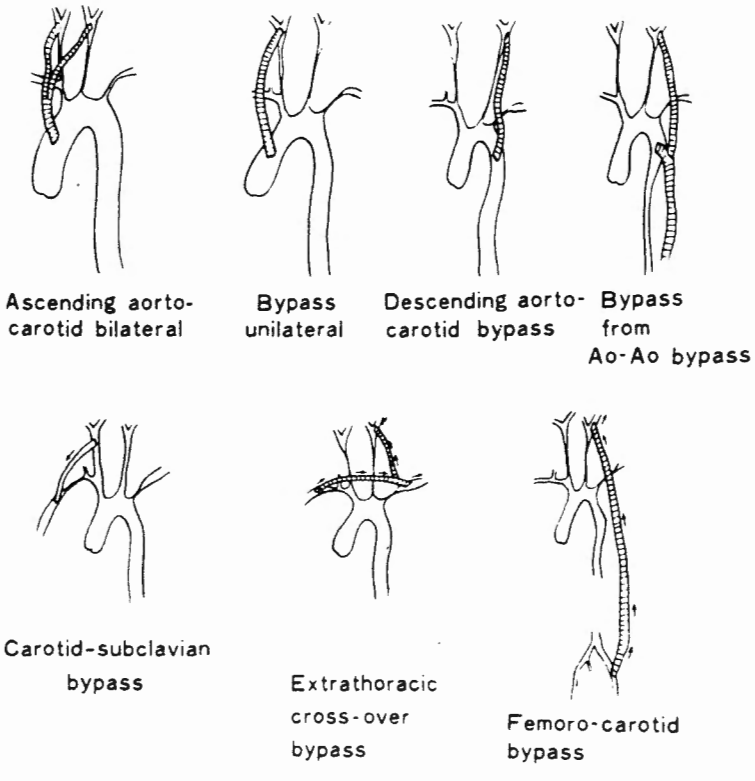
(3) Dilatation of the ascending aorta in association with aortic valve incompetence.

Arteritis of the carotid arteries is usually limited to the origin of the common carotid artery, with sparing of the carotid bifurcation. This distribution simplifies the surgical procedure, allowing easy access for the distal anastomosis of a bypass graft. Surgery for carotid occlusive disease should only be performed in symptomatic patients viz. transient ischaemic

attacks. Prophylactic surgery is not indicated for asymptomatic carotid stenosis, occlusion or bruits.

The surgical options for carotid disease include: (Fig. 1)

FIGURE 1.



(1) Carotid-subclavian/axillary bypass

(2) Aorta-carotid bypass. (Ascending or descending aorta)

(3) Extrathoracic axillo-axillary bypass graft, with a limb to the carotid artery. This is indicated in associated subclavian stenosis.

(4) Femoro-carotid bypass graft. This is warranted only in severe arteritis of the entire aortic arch.

During these procedures, cerebral perfusion should be maintained by the routine use of temporary shunts to the carotid artery.[153]

Aneurysms remain a major life-threatening problem in Takayasu's disease. Apart from the risk of rupture, aneurysms are an important source of emboli in aortic arteritis. Subclavian, common carotid and aortic arch aneurysms should be resected in all cases if technically possible and provided the patient is fit for surgery.

Aortic valve insufficiency is usually associated with both dilatation of the aortic valve ring and the ascending aorta. Valve replacement should be performed in patients with severe insufficiency complicated by cardiac failure. Simultaneous interposition grafting of the ascending aorta can be performed safely and with acceptable long-term results.[81,127,163] In Cape Town this procedure was performed successfully in 3 patients.

Occlusive lesions of the subclavian arteries are usually asymptomatic. Intermittent claudication of the upper limb may occur, but is seldom incapacitating. Owing to the adequate collateral circulation, limb-threatening ischaemia of the arm is rare, and surgery is seldom indicated.[36,29]

The results of several studies[36,47,56,43,44,118] have established the following guidelines for surgery to the aortic arch:

3.1 Surgery for carotid stenosis should be performed only in patients with symptoms of cerebral ischaemia, eg. T.I.A.S.

3.2 Subclavian revascularisation is seldom necessary because of spontaneous improvement of arm perfusion through collaterals.

3.3 Surgery is mandatory for all large and/or symptomatic aneurysms.

3.4 In order to reduce the risk of anastomotic problems, bypass grafts should, if possible, be anastomosed to arteries which are free of the disease process.

3.5 Extrathoracic revascularisation is usually the best therapeutic approach for branch occlusion of the aortic arch. Intrathoracic reconstruction is the choice method only for innominate lesions.

3.6 Unilateral cervical operations connecting the carotid and subclavian-axillary systems produce excellent long-term results, with acceptably low risks of operative mortality and neurological morbidity.

3.7 Larger cross-over bypass grafts eg. femoro-carotid bypass, should be viewed as compromise procedures, and are indicated only when the local or general condition of the patient preclude the safe performance of the standard operation.

4. DESCENDING AND ABDOMINAL AORTIC SURGERY

The indications for surgery are:

4.1 Hypertension due to a typical coarctation (see Chapter 6)

4.2 Aneurysms

4.3 Distal Aorto-iliac occlusive disease with Le Riche Syndrome

Abdominal aortic aneurysms are usually suprarenal in nature, and frequently have branch vessel involvement. In some cases the aneurysms are thoraco-abdominal. The surgery required for these complex aortic aneurysms is both technically difficult and hazardous. The major risks include:

(1) ischaemia to the spinal cord with possible paraplegia

(2) renal failure due to ischaemia and acute tubular necrosis.

(3) mesenteric ischaemia

These complications usually occur together with cardiorespiratory complications, lead to multi-organ failure and the death of the patient. Therefore surgery is undertaken only in the following cases:

(1) symptomatic aneurysms eg. pain or compression
(2) complicated aneurysms eg. leak or distal embolisation.
(3) large aneurysms (> 6cm)

Distal aortic occlusive arteritis is managed in identical fashion to atherosclerotic disease. The indications for surgery are:

(1) ischaemic lesions, eg. ulceration or gangrene
(2) ischaemic "rest" pain
(3) incapacitating claudication (relative indication only)

Aortic bifurcation arteritis and iliac arteritis has only recently been accepted as a manifestation of Takayasu's disease, despite an early description by Sen in 1963.[58] In the Cape Town series 30% (N=67) had bifurcation disease, and 21% (N=46) had common iliac arteritis. 6 patients underwent aortic surgery, all with good effect. The best surgical procedure is an aorta-bifemoral prosthetic graft. This is preferred to an aorta-bi-iliac graft in view of the possibility of progression of the disease to involve the iliac arteries. Splanchnic artery involvement in Takayasu's disease is common, and occurred in 41% (N=91) of the current series. However, intestinal ischaemia is

rare, and the consensus of opinion in the literature is that prophylactic visceral artery surgery is not indicated.[118,153,162]

12. OUTCOME AND MORTALITY

In view of the lack of prospective studies, the natural history and prognosis of aortic arteritis remain poorly understood and ill-defined. The scientific data available on this subject is provided mainly by the studies of Ishikawa from Japan.[9,12,13]

The following conclusions can be drawn from the results in the Cape Town study.

(1) Cardiac failure secondary to hypertensive heart disease was the commonest cause of death, accounting for 48% of the mortality in the series.

(2) The complications of hypertension were responsible for 80% of the known deaths. These complications included cardiac failure, renal failure, cerebrovascular disease, ischaemic heart disease, and ruptured aneurysm.

(3) Two-thirds of patients developed a "burnt out" inactive disease, with no evidence of progression of the arteritis. Follow-up data was available in only 40% of patients for a minimum of 5 years, and therefore definite conclusions cannot be drawn concerning the prognosis of the disease. However, the results suggest that the disease tends to fix at certain sites of the aorta at the outset of the illness. There is little evidence of spread or progression of the arteritis to other parts of the aorta. Furthermore, with the passage of time, in the majority of cases, there is a reduction in the "activity" of the disease.

(4) Prolonged survival can occur in this condition. This may be explained by

- inactivity of the disease after the initial onset
- sparing of the vessels supplying vital structures viz. coronary, cerebral and renal arteries.
- lack of complications in certain patients viz. hypertension, cardiac failure, enlarging aneurysm.

The results of the Cape Town study are similar to those reported from Japan, Singapore and the Soviet Union.[9,38,30,96,100,115] These studies emphasise that the prognosis and mortality are influenced primarily by the complications of the disease, viz. the cardiac, hypertensive and ischaemic sequelae of aortic arteritis. The mortality figures are comparable with those reported elsewhere (Table I).

Table I

	Mortality		Follow-up interval
Cape Town	N = 54	25%	1 - 25 years
Japan (Inada)[69]	N = 12	17%	1 - 21 years
Japan (Ishikawa)[13]	N = 15	16%	Mean 8.6 years
Japan (Marooka)[38]	N = 13	21%	Mean 6.6 years
Mexico (Lupi)[70]	N = 16	15%	1 - 15 years
Singapore (Teoh)[21]	N = 10	21%	1 - 18 years
Japan (Kimoto)[26]	N = 46	39%	1 - 24 years

Major contributions to the current understanding of the natural history of this disease have been made by Ishikawa,[9,12,13] from Kyoto, Japan. He has provided the only available prospective data on the subject. He has proposed a clinical classification

of aortic arteritis with special reference to natural history and prognosis (Table 2). This is based on the prospective evaluation of 95 patients over a period of 1 - 28 years.

Table 2

Type I Uncomplicated Takayasu's disease (irrespective of anatomical involvement)

Type II Single complication

The presence of 1 of the following complications:

(1) Takayasu's retinopathy

(2) Secondary hypertension

(3) Aortic regurgitation

(4) Aortic or arterial aneurysm

This type was further classified according to the severity of these complications into Type IIa (mild or moderate complications) and IIb (severe complications).

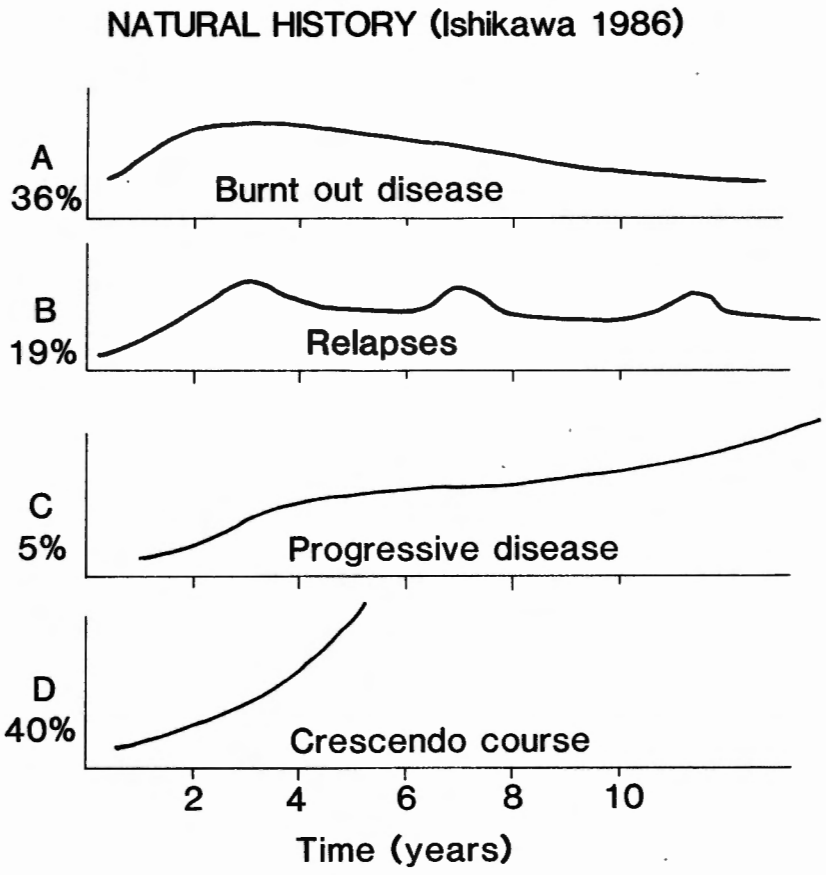
Type III Multiple complications

The mortality in Ishikawa's study corresponded closely with the Cape Town study. The commonest causes of death were cardiac failure, stroke, renal failure and ruptured aneurysm. There was a 10 year survival of 97% in Type I and IIa, and 58% in Type IIb and III.

Ishikawa[13] has defined 4 patterns of the course of the disease, based on the severity of the symptoms and signs which were graded (0-12) according to a scoring system. Fig. 1 shows these patterns with the incidences in Ishikawa's series. 12 out of the

15 deaths in his study were patients with patterns C and D. Ishikawa also maintains that certain patients with A or B patterns may progress to C or D if the diagnosis and treatment are delayed. (Fig. 1)

FIGURE 1.


NATURAL HISTORY (Ishikawa 1986)
A
36%
Burnt out disease
B
19%
Relapses
C
5%
Progressive disease
D
40%
Crescendo course
2
4
6
8
10
Time (years)

What are the prospects of improving the prognosis of patients with aortic arteritis? It is now becoming evident that an improved long-term outlook is possible, and that it depends on a strict adherence to 3 aspects of management.

(1) Early diagnosis and early detection of the complications.

(2) Early institution of treatment, both medical and surgical. Adequate control of the blood pressure and of cardiac failure is mandatory.

(3) Long-term follow-up. This should entail thorough clinical assessment, doppler pressure studies, biochemistry and sedimentation rate, performed six-monthly. Repeat angiography should be routinely performed, probably every two years. In this regard, intravenous digital subtraction angiography has been particularly successful.(145)

13. CONCLUSIONS AND FUTURE PERSPECTIVE

The Cape Town experience of aortic arteritis consists of 220 patients seen over a period of 36 years. All patients were extensively investigated, and pan-aortography was regarded as essential to the diagnosis. More than half the patients underwent cardiac catheterisation studies which included the measurement of cardiac pressures, assessment of myocardial function, and angiography of the coronary and pulmonary arteries. Detailed follow-up information was available in almost half of the patients for a minimum of 5 years, and several patients underwent repeat aortography. Histological proof of the diagnosis was obtained in 26% of the cases.

A "diffuse" pattern of disease was seen in Cape Town, with arteritis frequently involving the entire aorta. Branch vessel involvement was common and accounted for the high incidence of ischaemic complications involving the viscera, brain and limbs. A high incidence of aneurysms was noted which carried significant risk of rupture, thrombosis and distal embolisation. Compared with other studies, a high incidence of arteritis was detected at the following sites: renal arteries, subclavian, common carotid, coronary, mesenteric, aortic bifurcation, and common iliac arteries. "Dilating" disease predominated on the "right" side of the aortic arch, and associated aortic valve insufficiency was common.

Patients usually presented with "advanced" disease including serious complications of the condition and irreversible visceral damage. Hypertension was the commonest clinical presentation, and the sequelae of hypertension were responsible for 80% of the known deaths. Hypertension in pregnancy, seldom mentioned in the literature, was an important clinical presentation in Cape Town. Cardiac failure was the commonest complication of aortic arteritis. Hypertensive heart disease, and valvular insufficiency were equally responsible for the cardiac failure. One third of the entire study had cardiac failure at the time of presentation. The cardiac manifestations of aortic arteritis have never been studied in detail, with correlation of clinical, radiological, histological and autopsy findings. In this regard, many unanswered questions remain and the research opportunities are vast. For example, does a specific Takayasu cardio-myopathy exist? This has been neither proven nor refuted. Other common sequelae of aortic arteritis included stroke, ruptured aneurysm, renal failure, ischaemic heart disease and limb ischaemia.

The aetiology and pathogenesis of the condition remains obscure. Genetic and immunological factors are undoubtedly linked with the aetiology, and aortic arteritis should probably be regarded as an autoimmune disease. The pathogenetic link with tuberculosis is still uncertain. Takayasu's disease occurs in the nutritionally depleted lower socio-economic population, and the association with tuberculosis may be merely incidental. However, in some

patients tuberculosis may provide both an immunological "trigger" and a chronic immune stimulus which perpetuates the condition. Further studies should be directed at the genetic and immunological basis of the disease. Genetic and immunological markers should be sought after, to facilitate screening programmes, ante-natal testing, and early diagnosis. There is no curative treatment for aortic arteritis. The medical therapy is merely palliative and has the following intentions:

(1) control of hypertension
(2) reduction in the "activity" of the disease and halting of it's progression.
(3) treatment of cardiac failure
(4) prevention of thrombosis and microemboli

There is no doubt that corticosteroids are beneficial in patients with "active" disease. Treatment should be started early in the disease process, prior to the occurrence of complications. The dosage, duration of treatment and the specific indications for corticosteroids need to be clearly defined by means of prospective controlled studies. Such studies are difficult to perform in a rare condition with such a variable pathology and prognosis. The ideal of a specific drug to cure the disease seems highly improbable and is dependent on further elucidation of the aetiology and pathogenesis of the condition.

The role of surgery in aortic arteritis is becoming more clearly defined. The indications include:

(1) Hypertension (Renovascular or Coarctation)
(2) Aneurysms
(3) Cerebral, visceral, and limb ischaemia

(4) Aortic valve insufficiency with cardiac failure

Early surgical intervention in the appropriate clinical setting is mandatory to prevent life-threatening complications. Previously held fears of anastomotic disruption following surgery in aortitis have been shown to be unfounded. The patients are usually young, have no cardiorespiratory ailments, and tolerate surgery well. In the current series, surgery was found to be an effective treatment modality, in keeping with the Japanese and Soviet experience. The low percentage of operated patients is partly explained by the extensive disease pattern seen in Cape Town. Also, the "late" clinical presentation with severe cardiac failure and other complications precluded many patients from surgery.

Hypertension in aortic arteritis should be thoroughly investigated. Renal artery stenosis and coarctation should be surgically treated <u>early</u> in the disease process, prior to the development of hypertensive complications. Aneurysms should be resected if technically feasible owing to the definite risk of rupture, thrombosis or distal embolisation. Patients with common carotid artery disease and reversible ischaemia should undergo surgery urgently to prevent stroke. Aortic valve replacement can be safely performed in Takayasu's disease, and surgery should be performed early, prior to the development of irreversible myocardial damage.

The natural history of the disease is variable. The complications of the condition, rather than the aortitis itself,

are chiefly responsible for the morbidity and mortality. In this study, two-thirds of the patients developed "burnt out" disease, and some of these patients had a prolonged survival. The follow-up of these patients should be life-long, with annual visits to a special Arteritis clinic. Repeat angiography (I.V.D.S.A.) is essential to assess the progression of disease. Factors responsible for the varied prognosis in this condition need further clarification.

There is no doubt that the management of arteritis in Cape Town can be significantly improved. Emphasis on the following aspects of management would improve the overall prognosis of aortic arteritis:

(1) an improved "awareness" of the condition amongst medical practitioners and the general public to facilitate <u>early</u> diagnosis.

(2) management of all cases in one vascular unit under the auspices of a clinician who has a special interest in the disease. This co-ordinating clinician should be responsible for a multi-disciplinary approach to the treatment of the patients.

(3) "early" therapeutic intervention aimed at the <u>prevention</u> of the complications of the disease.

(4) institution of a follow-up clinic for the further assessment of patients. Regular visits to the clinic on a life-long basis is mandatory, and a clinical assistant should carry

the responsibility of tracing all defaulters. The establishment of such a clinic would undoubtedly lead to an overall improvement in patient care and in the prognosis. It will also provide a valuable source of information and facilitate further research.

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