THE PATHOLOGICAL ASPECTS OF HEART FAILURE IN THE NATAL AFRICAN

THESIS

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by

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CONTENTS

INTRODUCTION

The morbid anatomical changes of many diseases of the heart have been known for centuries. Useful knowledge, however, regarding correlation with clinical data, aetiological agents or processes, and an understanding of the physiological or haemodynamic changes which occur in heart failure, is a relatively recent acquisition.

While much has been achieved since the beginning of the century with regard to causative factors and the haemodynamic aspects of the different types of heart failure, it is of interest to note that its exact mechanism still remains obscure.

Hippocrates (460-370 B. C.), whose concepts swayed medical thought for many centuries, believed that the heart was not subject to disease (Moon 1927). Galen's (138-201 A. D.) concepts pertaining to the heart and circulation were almost entirely fallacious and yet, the near universal acceptance of his teaching is said to have prevailed for close on fourteen and a half centuries. The errors and omissions in his physiological concepts of the heart and circulation lay in his ignorance regarding the existence of the pulmonary, systemic and capillary circulations. From Galen to the late eighteenth century, while the development of the knowledge of the disease of the heart came slowly, certain important anatomical and physiological discoveries were made. These were to have a profound influence on the

future / ...

future recognition and understanding of cardiac pathology. During this period Ibn an Nafis (1210-1288) made the outstanding contribution of accurately describing the pulmonary circulation, but the credit for this discovery is usually accorded to the martyr Michael Servetus (1511-1553). According to Temkin, as quoted by Willius and Dry (1948), Servetus' conclusions regarding this aspect of the circulation, although coming at a much later date, were in fact original. It could not have been possible for Servetus to have known of this earlier work, either through word of mouth or by written document. The pulmonary circulation thus came to be discovered before the systemic and capillary circulations were known.

A long standing and bitter controversy has existed as to whether it was Andreas Cesalpino (1519-1603) or William Harvey (1578-1657) who first discovered the systemic circulation. Whatever the true facts may be there is no doubt that both Cesalpino and Harvey had a clear idea of the general circulation. In 1628 when Harvey described both the anatomy and general physiological concepts of the systemic and pulmonary circulations, he predicted the existence of a third, the capillary circulation. The latter was demonstrated in 1661 by Marcello Malpighi through the aid of the microscope.

Before the seventeenth century the knowledge of abnormalities of the heart was characterised by isolated observations, and no clear distinction was made between the functional and structural changes. Between the seventeenth and eighteenth centuries, writings on the subject became more systematized, but the rather fanciful concepts on which these were based did not change.

In the early nineteenth century the French school dominated in the field of medicine. Two great clinicians of this era were Jean Nicholas Corvisart (1755-1821) and Rene T.H. Laennec (1781-1826). These two led the advance in the expanding knowledge of the pathology of the heart. Amongst other contributions, Corvisart was the first to realise that an enlarged heart was a diseased heart, and to this day cardiac enlargement remains the cardinal objective sign of a diseased heart.

Laennec / . . .

Laennec in 1819 discovered the value of auscultation and the stethoscope. This discovery led towards a clearer correlation between clinical and pathological findings and a better definition of diseases of the heart.

However, prior to 1900 almost all classifications, discussions and writings about heart disease were concerned with structural and functional abnormalities. Little advance was made regarding their aetiology and pathogenesis. It was not until the early part of the twentieth century that an important milestone was added to the progress of cardiology, when the classification of heart disease began to acquire an aetiological basis. In June 1914, Richard Cabot read his paper entitled "The four common types of heart disease, an analysis of six hundred cases" before a section of the American Medical Association in Atlantic City. This paper was later published (1914) and the opening words read as follows:

> "To classify cases of diseases according to their pathogenic agent or process, and not solely by naming the region affected or the functions disturbed, is the ideal of scientific progress in medicine."

This trend soon became the general rule in the classification of diseases, and the interesting outcome of it was that certain types of diseases began to be recognised for which no cause could be found. Thus the term "idiopathic" made its appearance as a prefix every now and again. With regard to diseases of the heart it is only recently that certain types have been precisely defined. Pulmonary heart disease or chronic cor pulmonale, for instance, was in the past almost synonymous with chronic bronchitis and emphysema and earlier literature thus makes mention of the "Emphysema heart". It was, however, soon recognised that there were many other forms of chronic lung disease besides bronchitis and emphysema in which right ventricular enlargement and failure was the final outcome. Since certain lesions of the heart (e.g. mitral stenosis, congenital anomalies, chronic left ventricular failure) were found to cause right ventricular hypertrophy and failure, chronic cor pulmonale was variously defined and much confusion

followed /...

followed. It was only as recently as 1961 that a World Health Organisation Committee, appointed to sort out the confusion, put forward its report clearly defining cor pulmonale and offering a logical classification of its causes.

Even more recently the cardiomyopathies, with special dominance of two important idiopathic types in Africa, have come into prominence. Much interest and attention have been concentrated on these two forms of heart failure, and at present many research teams in different countries are working towards finding the cause or causes responsible for the production.

AIMS OF THE PRESENT THESIS

The purpose of this study is to investigate, from post-mortem material, the different aetiological types of heart disease which occur in the African population in Durban and its environs.

In order to achieve this it was necessary firstly to assess the overall incidence of deaths from heart failure among these people.

The literature on the subject is reviewed in order to compare the incidence, complications and mortality in the Natal African with African communities elsewhere in South Africa and in other parts of Africa. These findings are compared and contrasted also with those reported in other racial communities in order to see what significant differences and similarities exist in the pattern of heart disease between the various racial groups.

Special reference is made to right ventricular hypertrophy and failure in the African with the object of defining the aetiological factors involved and if possible offering some explanation for the mechanism whereby the right ventricle hypertrophies and finally fails.

PART I.

CHAPTER I

DEATHS CAUSED BY HEART FAILURE IN THE AFRICAN IN DURBAN

In the past two decades, although much has been said and written regarding heart failure in Africa, the main concern has been either the high incidence of heart failure of obscure origin or the rarity of coronary thrombosis in the indigenous population of the continent. There are but few reports in the literature which deal with the overall incidence of mortality from heart failure, as assessed from necropsy analysis. The field has been adequately covered in the Transvaal by Becker's (1946) analysis of cardiovascular diseases in the African and Coloured subjects in Johannesburg, and later by Siew (1958) in a comparative analysis of cardiovascular disease in the African, Coloured and White races on the Witwatersrand, but there have as yet been no adequate supplements of these works by similar studies from either Natal or other centres in the Republic. In fact, with a few exceptions, the continent as a whole lacks information of this nature.

It was thought necessary therefore, as a preliminary step, to assess the incidence of deaths caused by heart failure in the African population of Durban. For comparative purposes it was only possible to include post-mortem data on the Indians in Durban.

Becker (1946) from an analysis of 3,000 consecutive necropsies on African and Coloured patients found that while the lowest incidence (10%) of cardiovascular disease occurred during the first decade of life, there was a steady increase in frequency thereafter, reaching a peak of 90% in patients over sixty years of age. No difference in incidence between the two sexes was observed, and the author also remarked that there was no evidence of any particular racial susceptibility to cardiovascular disease among the African and Coloured people of South Africa. Becker recorded the incidence of cardiovascular disease among these subjects as being 46% and concluded that

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while cardiovascular disease in general was responsible for an all-age average incidence of 12% of all deaths in routine necropsies on African and Coloured patients, congestive heart failure accounted for 11% of all deaths.

Siew (1958) analysed necropsy statistics covering a period of twenty-one years (1936-1956 inclusive) and stated that the incidence of cardiovascular disease at necropsy was higher in the White races (41%) than in the African (25%) or the Coloured (31.8%) races. No difference was found in the sex incidence in any of the three racial groups.

From East Africa, Vint (1937), in a series of 1,000 consecutive post-mortems on African subjects, found the incidence of deaths due to disease of the cardiovascular system in general to be 5.6%. Davies (1948) considered congestive heart failure relatively common at Mulago Hospital, Uganda, with an incidence of 6.2% for all age groups in 3,705 necropsies. In 1,000 consecutive necropsies on African patients in Salisbury, Rhodesia, the incidence of cardiac disease was found to be 6.7% (Gelfand, 1957).

MATERIAL AND METHODS

This section represents a review of necropsy records, and the material studied consists of 9,898 consecutive routine post-mortems performed on African and Indian patients at King Edward VIII Hospital during the five year period June, 1958 to December, 1962. Medico-legal post-mortems are not included.

During the period under consideration necropsies were performed by various pathologists and every case was routinely studied by the usual histological methods. From July, 1959 a fair number of post-mortems were personally performed.

ANALYSIS / . . .

ANALYSIS OF MATERIAL

Population Sampled

The necropsy material for the survey was drawn from both King Edward VIII Hospital and its subsidiary hospital in Clairwood. These hospitals are situated in Durban and together serve the majority of the immediate African and Indian population of the city and its peri-urban areas. Through referral from district hospitals and clinics a small proportion of patients are drawn from many areas within the Province.

The African population attending these hospitals consists mainly of Zulus employed in industry as unskilled or semiskilled labour, in commerce as shop hands and messengers, and in domestic service. In comparison, only a very small number of doctors, nurses, school teachers and businessmen use these services. As in any large town or city in the Republic, the great majority are detribalised, living in an environment which is wholly westernised, and are therefore different from African communities in remoter parts of the continent.

The majority of Indian patients are mainly from the lower-middle and poorer classes and are therefore not representative of the Indian population of Durban as a whole.

Age and Sex Distribution of Patients Sampled

All age groups, with the exception of neo-natal deaths, have been included. It is relevant to mention that few African patients are able to state their age accurately and in many instances a rough estimate of age had been made on admission to hospital. Such estimates were based partly on appearances and partly on recollection of important events. Five patients whose ages were not stated have been excluded from the analysis.

The age and sex distribution of African subjects is shown in Table 1. It will be noted that more than half (59.1%) of all African necropsy subjects are below ten years of age. In fact the vast majority of patients

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falling into the group one month to nine years were under three years of age. Of the total number 54% were males and 46% were females.

TABLE I

AGE AND SEX DISTRIBUTION IN 9,069 CONSECUTIVE AFRICAN NECROPSIES

Age	Males		Females		Total	
Groups	No.	%	No.	%	No.	%
Under 9 yr	2854	58.2	2505	60.1	5359	59.1
10 - 19	107	2.2	118	2.8	225	2.5
20 - 29	205	4.2	255	6.1	460	5.1
30 - 39	385	7.9	333	8.0	718	7.9
40 - 49	479	9.8	263	6.3	742	8.2
50 - 59	383	7.8	279	6.7	662	7.3
60 - 69	299	6.1	267	6.4	566	6.2
70+	187	3.8	150	3.6	337	3.7
Total	4899	100.0	4170	100.0	9069	100.0

(Excluded are five cases in which ages were unknown)

TABLE II

AGE AND SEX DISTRIBUTION IN 829 CONSECUTIVE INDIAN NECROPSIES

Age	Males		Females		Total	
Groups	No.	%	No.	%	No.	%
Under 9 yr.	108	23.0	108	30.0	216	26.1
10 - 19	20	4.3	20	5.5	40	4.8
20 - 29	18	3.8	42	11.7	60	7.2
30 - 39	37	7.9	39	10.8	76	9.2
40 - 49	79	16.8	38	10.6	117	14.1
50 - 59	100	21.4	50	13.9	150	18.1
60 - 69	63	13.4	48	13.3	111	13.4
70+	44	9.4	15	4.2	59	7.1
Total	469	100.0	360	100.0	829	100.0

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The age and sex distribution of Indian cases is set out in Table II. Here it will be noted that just over one-quarter of the cases were under ten years of age.

Deaths Caused by Heart Failure

Cases falling into the above category included (i) congestive heart failure from any cause other than acute bacterial endocarditis, acute pericarditis associated with pneumonias and uraemia, and possible toxic myocarditis occurring with diphtheria, typhoid, pneumonia, etc., and, (ii) those in whom no evidence of congestive failure was found but death had been sudden and resulted from some form of heart disease, e.g. syphilitic heart disease, coronary thrombosis, etc.

Using the above criteria, in 9,069 consecutive African necropsies there were 690 (7.6%) cases in which heart failure was incriminated as the cause of death. Age and sex distribution is shown in Table III. The all-age average mortality from heart failure was found to be 7.4% in males and 7.8% in females.

In considering the incidence of such details with regard to age at time of death, the lowest percentage (1.7%) was shown during the first decade of life, and the highest (20.4%) during the second decade. Thereafter, apart from a slight fall in incidence, no definite trend is apparent and little variation is noted through all age groups.

The all-age average incidence for males was 22.4% and 20.3% for females. The lowest incidence (6.0%) was again observed during the first decade, and the highest (35.0%) in the second decade. A drop in incidence followed during the next two decades, but from the age of 40 a steady rise is shown. Although no difference in the sex incidence was noted in the African, the Indian showed a slight male preponderance from the 4th decade onwards.

Fig. I compares the incidence of mortality according to age in

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FIG. I

INCIDENCE OF HEART FAILURE IN RELATION TO AGE, SEX AND RACE

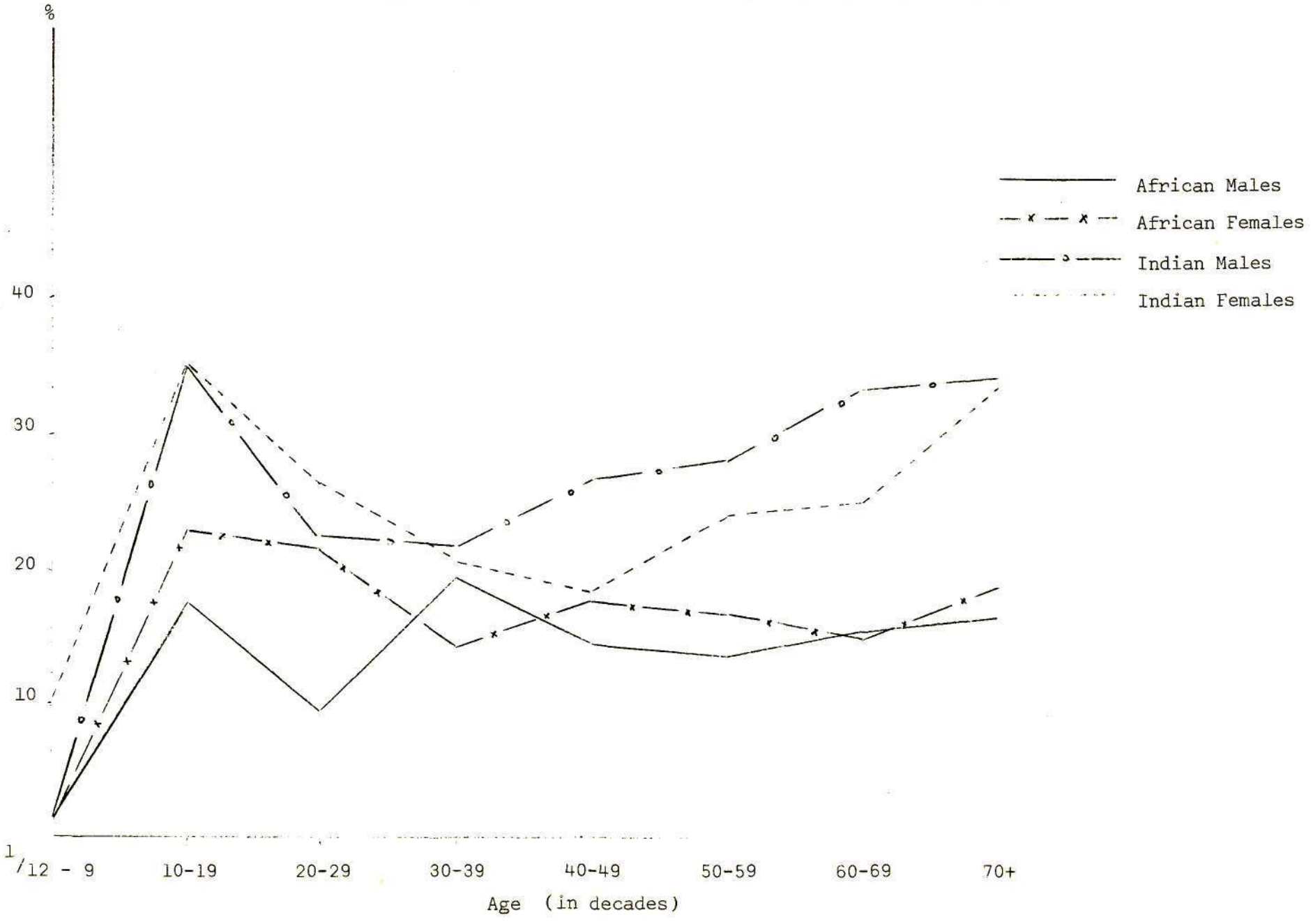

TABLE III

AGE AND SEX INCIDENCE OF 690 DEATHS FROM HEART FAILURE IN 9,069 CONSECUTIVE AFRICAN NECROPSIES

Age Groups Years	Total Male P.M.'s	Heart failure Deaths No.	%	Total Female P.M.'s	Heart failure Deaths No.	%	Total P.M.'s	Total deaths Heart failure No.	%
Under 9	2854	52	1.8	2505	37	1.5	5359	89	1.7
10 - 19	107	19	17.7	118	27	22.9	225	46	20.4
20 - 29	205	19	9.3	255	54	21.2	460	73	15.9
30 - 39	385	75	19.5	333	47	14.1	718	122	17.0
40 - 49	479	70	14.6	263	46	17.5	742	116	15.6
50 - 59	383	52	13.6	279	47	16.8	662	99	14.9
60 - 69	299	46	15.4	267	40	15.0	566	86	15.2
70+	187	31	16.6	150	28	18.7	337	59	17.5
Total	4899	364	7.4	4170	326	7.8	9069	690	7.6

Table IV shows the age and sex incidence of the 178 (21.5%) deaths from heart failure in 829 consecutive Indian necropsies.

TABLE IV

AGE AND SEX INCIDENCE OF 178 DEATHS FROM HEART FAILURE IN 829 CONSECUTIVE INDIAN NECROPSIES

Age Groups Years	Total Male P.M.'s	Heart failure Deaths No.	%	Total Female P.M.'s	Heart failure Deaths No.	%	Total P.M.'s	Total deaths Heart failure No.	%
Under 9	108	2	1.9	108	11	10.2	216	13	6.0
10 - 19	20	7	35.0	20	7	35.0	40	14	35.0
20 - 29	18	4	22.2	42	11	26.2	60	15	25.0
30 - 39	37	8	21.6	39	8	20.5	76	16	21.1
40 - 49	79	21	26.6	38	7	18.4	117	28	23.9
50 - 59	100	27	27.0	50	12	24.0	150	39	26.0
60 - 69	63	21	33.3	48	12	25.0	111	33	29.7
70+	44	15	34.1	15	5	33.3	59	20	33.9
Total	469	105	22.4	360	73	20.3	829	178	21.5

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TABLE V.

COMPARISON OF INCIDENCE OF DEATH FROM HEART FAILURE IN AFRICAN AND INDIAN SUBJECTS UNDER AND OVER 10 YEARS OF AGE

Age Groups Years	AFRICAN			INDIAN		
	Total Necropsies	Deaths from Heart Failure		Total Necropsies	Deaths from Heart Failure	
		No.	%		No.	%
Up to 9	5359	89	1.7	216	13	6.0
10 & over	3710	601	16.2	613	165	26.9
Total	9069	690	7.6	829	178	21.5

decades for both sexes and both race groups. African male and female deaths from heart failure are lower than those of the corresponding sexes in Indians, and also lower at all corresponding age groups.

The patient material sampled in the two races differs mainly in numbers included in the age group 1 month - 9 years. Table V shows that in subjects 10 years and over, although the difference (Africans 16.2%, Indians 26.9%) is less marked, the incidence of deaths from heart disease is still lower in the Africans.

DISCUSSION

It is extremely difficult to assess the incidence of a fatal disease in any given population. In order to obtain an accurate picture of deaths caused by disease of the heart for instance, one would require necropsy statistics based on all deaths in the population under consideration, over a lengthy period. Such statistical information is not available. Even if it were, it would still be subject to the criticism that necropsies are performed by many different pathologists who will certainly differ with regard to the diagnostic criteria used, and whose terminology is known to vary one from another. In addition, necropsies are performed on a highly selective group,

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and to what extent they reflect the general population is not known. The present survey need not even reflect the hospital incidence of mortality from heart failure, since not all deaths occurring within the hospital are investigated in the post-mortem room. Necropsy studies, nevertheless, are of immense value today despite these limitations, and while they lack exactness they remain the only means of confirming clinical evidence in the majority of cases and obtaining some picture, however crude, of the incidence of a fatal disease.

Before any comparison can be drawn with studies reported from elsewhere, allowances must be made for differences in patient material with regard to sex, age, and to some extent race, between this and other series. Of the necropsy subjects in the series analysed by Becker (1946) 73% were males and the bulk of his patients were between 20 - 50 years of age ; 11.2% were under 10 years of age. In the present study the sex variation is less marked (54% males and 46% females), and more than half our cases (59.1%) were under 10 years of age. In addition, Becker's figure of 11% (percentage deaths caused by congestive heart failure) included Coloured patients, and Siew (1958) has shown the incidence of cardiovascular disease in the Coloured (31.8%) to be slightly higher than that in the African (25%). It is therefore not surprising that the all-age average incidence obtained in the present series (7.6%) is lower than that reported by Becker.

While the overall incidence of heart failure in the African in Durban agrees with that reported by Davies (1948) and Gelfand (1957), it is unfortunate that details of their patient material with regard to age and sex are not known. The incidence of 5.6% for all deaths from cardiovascular disease in general, reported from East Africa (Vint 1937), appears to be lower than that of a similar race group in Durban.

Although the incidence of deaths due to heart failure is lower in the African for all age groups and for both sexes than in the Indian, the general pattern tends to be similar (Fig. I). In both races the lowest incidence was observed during the first decade and the highest in the second

decade / . . .

decade of life, with a slight fall in incidence thereafter. The very low incidence recorded during the first decade in Africans particularly, can be explained on the basis that in Durban a considerable number of deaths in children are caused by malnutrition and infection. It has been stated above that the majority of cases falling within this age group were under 3 years of age. Wainwright (1964) reported that 92% of all deaths in children under 3 years of age, at King Edward VIII Hospital, were found at necropsy to have been due to malnutrition and/or infection. The results obtained for this age group are therefore not comparable with figures reported in other populations, particularly those of white races in South Africa and most other countries.

The generally lower rate shown among Africans in the first three decades of life, in comparison with the Indian, may also be due to a higher death rate from infections and from malnutrition in the African. As shown in Tables I and II there are comparatively fewer deaths from all other causes in the African, during the second and third decades of life, and heart disease appears to be an important cause of mortality at these ages. On comparison this finding is similar to that observed among Indians.

The difference in incidence between the two races is least marked in the fourth decade of life, but thereafter the African does not show the same increase in incidence as the Indian. The most likely explanation for this appears to lie in the behaviour of atheromatosis in these two race groups. As mentioned, Becker (1946) reported that the incidence of cardiovascular disease in the African after the age of 60 was in the region of 90%, and that after the age of 40 some abnormality of the cardiovascular system was present in two-thirds of his cases. This, however, is not reflected in mortality statistics to the same degree. Becker (1946) concluded that the commonest cardiovascular lesion among the African and Coloured races was atheromatosis, and showed that its incidence increased with age. He concluded further, that while it was difficult to assess how far atheroma contributed towards a fatal outcome, only 0.4% of all deaths in his patients could be regarded as being the direct result of atheroma. Quoting the above

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author, ". . . . there are many instances too where atheroma has produced significant disease of the cardiovascular system but the fatal outcome was due to some other cause." Vint's (1937) findings were similar. However, Wainwright (1961) has shown that atheromatous involvement of the aorta and coronary vessels is of a lesser degree in the African than in both the Indian and White races.

Apart from the overall difference in incidence between African and Indian subjects, the Indian showed a slight male preponderance of deaths due to heart failure, while no sex difference was observed in the African. This trend among the Indians was noted regularly through all age groups after the third decade. Among Africans, although more female deaths from heart failure are noted in the second and third decades, no definite trend is apparent thereafter. While this may be a pattern of disease in the African, it is possible that it could be accounted for by errors in estimates of age.

Siew (1958) has shown that at necropsy the incidence of cardiovascular disease was lower in the African than in the Coloured and White races on the Witwatersrand. The present study indicates a lower incidence of deaths from heart failure in the African than in the Indian in Durban.

SUMMARY

The all age average incidence of deaths from heart failure in the African in Durban is almost 8%. This is lower than that observed for Indians (21.5%). After the age of 10 years the difference is less marked, but the African still shows by comparison a lower incidence.

The variations in incidence in the different race and age groups are discussed.

CHAPTER II

A COMPARATIVE REVIEW OF THE LITERATURE OF THE MAJOR CAUSES OF HEART DISEASE

Cardiovascular disease is at present a major cause of death and disability in adult life in many countries, and the aetiological types are known to vary not only between countries but also between communities and sexes within the same country (Puffer and Verhoestraete 1958). It has been suggested that such variations may be due either to differences in the terminology and classifications used in stating causes of death, or that they may in fact be true differences in the pattern of disease.

CORONARY HEART DISEASE

Wide differences in mortality from coronary heart disease have been reported amongst the white populations of countries on the same continent, e.g. France and Finland (W. H. O. 1956), and also in different regions of the same country, e.g. Finland (Keys et al. 1958) and the United States of America (Sauer 1962). Kent et al. (1958) demonstrated marked variations within the same section (Manhattan) of a city (New York City).

Although differences in the incidence of coronary artery disease have been reported in the white races of South Africa (Schwartz et al. 1958), extremes in mortality from this form of heart disease in the ethnic groups of the country are best illustrated by a comparison of its White and African populations (Vogelpoel and Schrire 1955; Schwartz et al. 1958; Reef and Isaacson 1962; Walter 1963; Seftel et al. 1963; Bradlow et al. 1964). Not only is this disease extremely common in the former, but its incidence is said to rank among the highest in the world (Bradlow et al. 1964). Death and disability from coronary atherosclerosis and myocardial infarction are, on the other hand, rare in the African in South Africa. Becker (1946) reported that atheroma was the most common of all cardiovascular lesions in

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the African, occurring in 27.5% of routine necropsies. As mentioned in the preceding chapter, this is not reflected in mortality statistics; Becker himself found it to be a direct cause of death in only a small percentage of cases in his series. From their comparative study, Higginson and Pepler (1954) concluded that while the incidence of atheromatosis may be high in Africans, they do not develop the same degree of aortic or coronary atheroma found in the White races.

Strong et al. (1959), from a necropsy study of aortic lesions in Bantu subjects up to the age of 40 years as compared with those of a similar group of White and Negro subjects in New Orleans, found that although fatty streaking of the aorta was comparable in all three groups, fibrous plaques were much less frequent in the Bantu than in the other two groups studied.

Laurie and Woods (1958) suggested that the African was not free from atheroma or its cerebral complications as stated by previous authors. Subsequently they (Laurie et al. 1960) reported that although acute cardiac infarction was uncommon, ischaemic myocardial fibrosis was often found in the African, frequently leading to 'cryptogenic' heart failure in these people.

Wainwright (1961), from his comparative study of the African, Indian and White races in Durban, came to the conclusion that the degree of atheromatous involvement of the aorta and coronary arteries is least in the African, intermediate in the Indian, and most marked in the White races.

While the reason or reasons for this difference cannot yet be explained, certain physiological racial pecularities have been shown to exist. Schlesinger (1940), from his injection studies of the coronary arteries, considered that inherited patterns of coronary artery distribution may be responsible for the familial and sex distribution of coronary heart disease. Brink (1949), using the Schlesinger technique, demonstrated that the majority of Bantu hearts belonged to the right coronary preponderance pattern, and that there was a significantly different anatomic pattern in the African heart, an extra branch of the left coronary, which he described and called the third primary division. This finding implied a better intercoronary

anastomosis/...

anastomosis in the African. Singer (1959) failed to demonstrate any significant difference in the anatomical distribution of the coronary arteries in the hearts of these subjects as compared with White and Coloured peoples. Laurie and Woods (1958) suggested that functionally inherited coronary anastomoses are present in the majority of hearts, and that these inherited patterns, while protecting some individuals against ischaemic heart disease, would modify the condition in others. Their claim that this applied to all races (Laurie 1959, Laurie and Woods 1959) has been refuted by Pepler and Meyer (1960) who, from a study of both African and European hearts, confirmed the presence of a better anastomotic blood supply in the African.

Differences in the serum cholesterol level have been shown to exist in the various racial groups. Bronte-Stewart et al. (1955) reported lower serum cholesterol and total serum lipid values in the African than in the Coloured or White races in South Africa. Brock and Gordon (1959) also found the mean serum cholesterol level to be higher in the Whites than in the Africans. A lower level in African subjects has also been reported by Higginson and Pepler (1954), and more recently by Joubert et al. (1961) in the urban Zulu adults of Natal. Similar results have been reported in Nigeria (Gordon 1958). Shaper and Jones (1959) found serum cholesterol levels to be lower in the African than in the Indian in Uganda. From their prison study of White and African volunteers, Antonis and Bersohn (1963) found the serum lipid patterns in the two races to be almost identical. On a diet containing 15% calories in the form of fat the pattern in both was that of the urban African population. After feeding diets containing 40% calories in the form of fats, the serum lipid patterns of both races were again similar, but correlated with that of the White population.

Several studies concerning blood coagulation in the African have been published. Gillman et al. (1957) reported high fibrinolysin levels in the African. Merscky et al. (1960) reported higher plasma levels of antihaemophilic globulin, and better prothrombin consumption, in the African than in the Whites. These authors also found lower plasma prothrombin and

serum / ...

serum factor VII levels in Africans, and noted that these subjects liberated more plasma thromboplastin and showed a faster fibrinolytic activity than did Whites.

Another difference is the presence of peculiar electrocardiographic patterns which, while abnormal for White races, appear to be compatible with normal health in the African (Grusin 1954; Powell 1959). Similar findings have also been reported from East Africa (Somers and Rankin 1962).

Conclusions

Except for Laurie and Woods, there is general agreement in the literature that complications of coronary artery disease are uncommon in the African, and that although the incidence of atheromatosis may be high in this population, the degree of involvement is less than that found in the other races in South Africa and in White and Negro populations in other continents. While certain physiological racial pecularities are known to exist in the various race groups and appear to correlate with the incidence of coronary heart disease in the different races, the precise mechanism of atherosclerosis still remains obscure. The inference that the African may have a diminished thrombotic tendency can only be speculative at this stage, since cerebral thrombosis is as common in the African as in the White population (Snyman 1962).

CARDIOMYOPATHY

Whereas morbidity and mortality from coronary heart disease is uncommon in the African by contrast with other races, a form of heart disease, of obscure aetiology, is commonly encountered in the African inhabitants of South Africa but is rarely seen in the other races. Since Bedford and Konstam (1946) first drew attention to a type of heart failure of unknown origin, in West and East African troops, numerous reports have appeared on idiopathic forms of heart disease in Africa. It is now generally believed that there are two forms of heart failure of obscure origin common in

Africa / ...

Africa. These occur mainly in the indigenous inhabitants, very infrequently in other races, and are rarely seen in Western countries.

Firstly, endomyocardial fibrosis as described by Davies (1948), Ball et al. (1954) and Williams et al (1954) in Uganda. The disease, however, is not confined to Uganda, but is known to occur in other tropical countries (Davies and Coles 1960). The pathological features of endomyocardial fibrosis, briefly, are characterised by deep scarring of the endocardium, often beginning at the apex of one or both ventricles and spreading along the inflow tract to involve the papillary muscles, chordae tendinae, and the posterior cusps of the atrio-ventricular valves. Males and females are equally affected, and the disease has been reported in patients of from 4 years to over 70 years of age. Embolic phenomenon is rarely observed in this form.

The second type, occurring mainly in South Africa, was described by Gillanders (1951), from Johannesburg, as 'Nutritional Heart Disease' and by Becker et al. (1953) also from Johannesburg as 'Cardiovascular Collagenosis with Parietal Endocardial Thrombosis'. Higginson et al. (1952) described the pathological features in hearts of patients presenting similarly to those recorded by Gillanders. From the published proceedings of a seminar held in the University of the Witwatersrand (1957) it is apparent that the above authors were in fact describing the same condition, but differed in regard to the possible causative processes involved. Much of the recent literature on this form of heart disease appears under the names of 'Cardiomyopathy' (Cosnett 1962; Powell and Wright 1965; Reid 1966), or 'Cryptogenic Heart Disease' (Higginson et al. 1960). The term cardiomyopathy will be used throughout this work.

The pathological features in cardiomyopathy consist of an enlarged heart with varying degrees of hypertrophy and dilatation of either one or both ventricles. Mural thrombi are frequently present, particularly in the right atrial appendage and left ventricle, and in contrast to endomyocardial fibrosis, embolic phenomena are frequent. Fibrosis of the

endocardium/...

endocardium is often patchy, rarely diffuse, and may be absent altogether. Valvular involvement is very rare. A slight male preponderance is reported (Higginson et al. 1960), and although the disease frequently affects adults a similar form of heart disease has been described in African children (Altman and Stein 1956).

Cardiomyopathy has been reported as occurring in Southern Rhodesia (Gelfand 1957, Baldachin 1963), and Edington and Jackson (1963) concluded that both endomyocardial fibrosis, similar to that described in Uganda, and cardiomyopathy as seen in South Africa, occur in Ibadan, Nigeria. Isolated cases of idiopathic cardiac hypertrophy, having features similar to those seen here, have also been reported from other parts of the world (Brigden 1957, Flynn and Mann 1946). The exact relationship of cardiomyopathy to postpartum or peripartum cardiomyopathy, as described by Seftel and Susser (1961) and Reid (1961), is not known. However, the type connected with pregnancy is known to have a better prognosis, with complete recovery in many cases, and fatal cases are reported to show pathological features similar to those not associated with pregnancy (Schwartz et al. 1958).

The aetiology of endomyocardial fibrosis and cardiomyopathy remains obscure. Whenever these two forms of heart disease have been critically compared (Thomas et al. 1954; Seminar Univ. of Wits. 1957) the conclusion has always been that they are two separate clinical and pathological entities. Davies and Coles (1960) concluded that "... the detailed distinctions between them are greater than their few similarities." However, Edington and Jackson (1963), while drawing no conclusion with regard to aetiology, considered that endomyocardial fibrosis and cardiomyopathy may be stages in one pathological process. They postulated that the myopathy in South Africa is more acute in type so that endomyocardial fibrosis is uncommon, whereas in Uganda the condition is more chronic, and as a result the endocardium is severely affected.

Gillanders (1951) noted that the diet of his patients was deficient

both / ...

both quantitatively and qualitatively, and found that, with the exception of cases of advanced disease, the majority improved when a well-balanced ward diet was used as the sole form of therapy. Patients maintained on deficient diets deteriorated, and furthermore, relapses readily occurred when the deficient home diet was substituted in those who had improved on the balanced diets. Similarly, relapses occurred when patients returned to their home environment and diet. The clinical picture thereafter was one of recurrent relapses until finally the disease became refractory to any form of therapy. Gillanders thus considered chronic malnutrition to be the possible aetiological factor responsible and therefore called the disease "Nutritional Heart Disease".

Becker et al. (1953), from a study of 40 cases showing changes similar to those described by Gillanders (1951) and Higginson et al. (1952), observed widespread focal involvement of connective tissue in most organs, but particularly in the heart. The histological picture closely resembled features present in 'diffuse collagen disease' but lacked characteristic lesions of rheumatic fever, periarteritis nodosa, lupus erythematosis, or diffuse scleroderma. They therefore called this type "Cardiovascular Collagenosis".

Abrahams (1959), from a study of heart failure in African subjects in Ibadan, finding Aschoff-like nodules in the endomyocardium and myocardium in addition to the features of endomyocardial fibrosis (as described in Uganda), suggested that the latter might represent an unusual expression of rheumatic fever, particularly in areas where the latter disease is uncommon in its typical form. Rheumatic heart disease in its usual form is said to be rare in Ibadan.

Subsequently Abrahams and Brigden (1961) reaffirmed this opinion, and added that factors such as anaemia, parasitic infestations and protein malnutrition combined with rheumatic fever, might produce endomyocardial fibrosis. While lesions resembling those of rheumatic fever have not been described in cases reported from Uganda, recent clinical and haemodynamic studies in Uganda show a similarity to the disease described in Nigeria (Shillingford and Somers 1961). However, rheumatic fever in its typical

form / ...

form does occur in Uganda (Shaper and Jones 1960).

Shaper (1966) reported a difference in the prevalence of endomyocardial fibrosis and rheumatic heart disease among the Baganda and Rwandan tribes living in the same areas in Uganda. While accepting the possibility that endomyocardial fibrosis may be a disorder similar to rheumatic heart disease in being a hypersensitivity response to some infection, he stated that even if the former were a response to streptococcal infection it was wiser not to state that endomyocardial fibrosis might be another form of rheumatic heart disease, since the rheumatic element is not evident in any of the published cases. Shaper suggests therefore that endomyocardial fibrosis is another form of hypersensitivity response to streptococci, and that an immunological factor such as malaria may alter the response in some to streptococcal infections.

Conclusions

There appear to be two distinct clinical and pathological types of heart disease of obscure origin, occurring commonly in the African inhabitants of the continent but rarely reported in the other races or in other parts of the world. Although endomyocardial fibrosis is common in Uganda, cardiomyopathy has not been observed. In South Africa and Southern Rhodesia cardiomyopathy is frequently encountered, but there have been no reports to suggest that endomyocardial fibrosis, as seen in Uganda, occurs in either of these countries.

In Nigeria conventional rheumatic heart disease is uncommon, so that endomyocardial fibrosis has been postulated to be an unusual expression of rheumatic fever. Yet conventional rheumatic heart disease is common both in Uganda, where endomyocardial fibrosis is prevalent, and in Southern Africa where it is rarely seen.

There also appear to be variants of cardiomyopathy which, while differing in regard to clinical course and prognosis, show similar pathological changes in the heart.

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The possibilities therefore are:

(1) that endomyocardial fibrosis and cardiomyopathy are different stages of a single pathological process, differing in reaction perhaps to local climatic and environmental factors, or to individual susceptibility and response to disease;

(2) that endomyocardial fibrosis and cardiomyopathy constitute two independent diseases, the different types of cardiomyopathy being stages in the one disease;

(3) that all types are separate disease entities, each based on an entirely different aetiological process or agent.

RHEUMATIC HEART DISEASE

Rheumatic Fever is a systemic, non-suppurative, inflammatory disease with a tendency to relapse. The basic lesion is a fibrinoid degeneration and necrosis of the ground substance and collagen tissue of many organs, but especially of the heart and joints. The disease, which is the commonest cause of acute inflammatory lesions in the heart, usually begins in young persons of either sex and may affect any race. It is, however, uncommon for rheumatic fever to occur after middle age.

Rheumatic Fever is often preceded by a Beta-haemolytic, group-A streptococcal infection of the upper respiratory tract, and is at present believed by most authorities to be a hypersensitivity phenomenon resulting from this infection. The disease is therefore likely to occur wherever group-A streptococcal sore throats are prevalent.

While the relative incidence of rheumatic heart disease varies greatly in different parts of the world rheumatic fever is apparently on the decline (White 1951). It remains, however, with hypertensive and coronary artery diseases, one of the three common types of heart disease.

Rheumatic heart disease has been shown to be common among the indigenous inhabitants in many parts of Africa (Heimann et al. 1929;

Becker / ...

Becker 1946; Schwartz et al. 1958,in South Africa; Galfand 1957, and Baldachin 1963,in Southern Rhodesia; Shaper and Williams 1960 in Uganda; Halim and Jacques 1961 in Sudan; Beet 1956 in Northern Nigeria).

Edington (1954) and Hawe (1954) considered rheumatic heart disease to be uncommon in Accra. In its typical form it is reported to be rare in Ibadan (Southern Rhodesia) where, if it occurs, it is said to present in the unusual form of endomyocardial fibrosis (Abrahams 1959; Abrahams and Brigden 1961).

Heimann et al. (1929) concluded that rheumatic heart disease was the most frequent form of cardiac disease among the non-Whites in South Africa and Schrire (1958), Schwartz et al. (1958) and Becker (1946) consider the relative incidence of chronic rheumatic heart disease to be comparable with that found in the White races in South Africa.

No unanimous opinion exists regarding the sex incidence of rheumatic fever. While Boyd (1963), Cappell (1964), and White (1951) agree on a higher incidence among females, Anderson (1966), Friedberg (1966) and Thompson and Cotton (1956) state that there is no significant sex predilection. Vakil (1949) from India, however contrary to opinion elsewhere, reported the incidence to be higher among males than females.

Becker (1946) found no difference in the sex incidence among the African and Coloured people of South Africa. Siew (1958) recorded rheumatic heart disease as being the commonest type of cardiac disease among African females, while in African males it was found to be the third commonest cause. Most other series elsewhere in Africa (Davies 1958; Shaper and Jones 1960; Beet 1956) contained fewer females because of a smaller female hospital population, making it impossible to draw any conclusions.

Anderson (1966), in the section on valvular deformities of the heart, states "...Among the diseases producing valvular deformities rheumatic fever is the commonest". According to Vint (1937) and Williams (1938) however, this is not true in East African countries (Uganda, Kenya and

Tanganyika), where syphilitic aortitis, with its complications involving the aortic valve, was reported to predominate. There is general agreement in the literature that the distribution of valvular involvement due to rheumatic fever in the African is similar to that reported in Western communities.

Cabot (1926), Campbell and Shackle (1932) and Clawson (1940) recorded mitral lesions as being commoner in females than in males, while the opposite was true for aortic lesions. Shaper and Williams (1960) recorded similar findings among the Africans in Uganda. Becker (1946) in South Africa found no difference in the sex incidence of either mitral or aortic valve involvement in rheumatic fever.

Davies (1948) reported that fewer cases of rheumatic valvular disease were encountered in the African after the age of 40 years than before this age. Similar observations in South Africa have led to the suggestion that the disease is probably more severe in this race, leading to death at an earlier age (Schrire 1958; Bradlow et al. 1964).

In Great Britain, Graham (1955) found that the fully developed picture of mitral stenosis rarely occurred before the 14th year. Rheumatic valvular disease is reported as not infrequently occurring at a much younger age in the African (Beet 1956; Shaper and Williams 1960; Halim and Jacques 1961). Sen et al. (1966) have shown that a large number of Indians in Bombay also present for mitral valvotomy at a much earlier age.

Superimposed bacterial endocarditis is a well-recognised complication of chronic rheumatic valvular disease. White (1951) records an incidence of 5%, whereas Becker (1946) in South Africa observed it in approximately 30% of all cases of rheumatic heart disease in African and Coloured subjects at necropsy.

Conclusions

Rheumatic heart disease is prevalent in most parts of Africa, and the distribution of valvular involvement with rheumatic fever is stated to be similar in the African to that found in Western communities. No

significant/...

significant sex difference in the incidence of rheumatic fever among Africans has been shown.

Rheumatic valvular disease is said to be more severe in the African, accounting for a smaller survival rate after the age of 40 years. Gross valvular deformities are frequently observed at an earlier age in the African, as in Indian subjects in India.

HYPERTENSIVE HEART DISEASE

Although hypertension has been classified in various ways it is customary to speak of:

(1) primary or essential hypertension - the underlying cause of which is not known, and

(2) secondary hypertension - the elevated blood pressure being associated with some lesion in the kidney, adrenal, thyroid, or pituitary. Renal hypertension is the commonest form of secondary hypertension, and is most frequently caused by glomerulonephritis both in its early and chronic stage, and by chronic pyelonephritis.

Congestive heart failure is an important cause of death in patients with hypertension. Clawson (1941) from an analysis of 2, 597 hypertensive patients who died as a result of cardiovascular disease, found that death was due to congestive heart failure in 43. 3%, to coronary heart disease in 36%, to cerebral haemorrhage and renal insufficiency in 20. 7%. Earlier, Murphy et al. (1932) had come to a similar conclusion from a study of 375 hypertensive subjects.

Becker (1946), in South Africa, found congestive heart failure to be the main cause of death in 114 African and Coloured subjects with primary hypertensive arteriosclerosis. Unlike White races, these subjects showed an extremely low incidence of coronary heart disease.

Hadfield and Garrod (1942) reported that the majority of cases of hypertensive arteriosclerosis occur in the age group 50 - 60, males being more frequently affected. This would apply to White communities in most parts of the world. While renal lesions can cause hypertension at all ages, they are the commonest cause of a raised blood pressure among younger individuals.

White (1961) stated that hypertension is universally common in the African and Negro races and may be the most common cause of heart disease in Africa. In South Africa, hypertension in the African has been shown to be at least as common as in the White races (Schwartz et al. 1958; Scotch et al. 1961; Ordman 1948), but it is reported to occur a decade earlier in the African (Uys 1956; Schwartz et al. 1958). Becker (1946) showed the frequency of hypertensive arteriosclerosis in the African and Coloured people to rise steadily with increasing age, reaching the maximum incidence in the sixth decade.

From the aetiological point of view, essential hypertension is the most frequent type encountered in the African in South Africa (Becker 1946; Isaacson and Kincaid-Smith 1962), and the impression is that malignant hypertension is commoner in Africans than in White races (Uys 1956). Seedat (1963) considered malignant hypertension to be a common disease among both Africans and Indians in Durban.

Hypertension is frequently encountered in the African inhabitants of Uganda (Williams 1941; Davies 1948), and according to Williams "...essential hypertension among the Africans is uncommon and its serious complications are quite rare". Hypertension secondary to renal disease is said to be more important in Uganda.

Becker (1946) reported that hypertensive heart disease was the commonest cause of congestive heart failure in the Bantu and Coloured peoples of South Africa and was responsible for one-third of all cases of congestive cardiac failure. Davies (1948) also found hypertensive heart disease to be the commonest cause of congestive heart failure among the Africans in

Uganda / ...

Uganda. While this finding is supported by other observers in Uganda (Davies 1948; Williams 1941; Shaper and Williams 1960), most investigators in South Africa (Schwartz et al. 1958; Higginson et al. 1960; Powell and Wright 1965; Adams and Wainwright 1958) have regarded it to be a less frequent cause of congestive heart failure than rheumatic heart disease, and Gelfand (1957) and Baldachin (1963) in Southern Rhodesia also found rheumatic heart disease to be the commoner cause of congestive cardiac failure in the African.

While Becker (1946) noted no difference in the sex incidence of the disease , Schwartz et al. (1958) considered hypertension in the African to be commoner among females than males.

Conclusions

Hypertension is common in the African population of Africa. A difference exists with regard to the aetiological types of hypertension as seen in Uganda and in South Africa. While it is reported as being often renal in origin in the former country, it is commonly essential in type in the latter. Just how accurate are these views is difficult to assess, Focal areas of scarring in the kidneys are very often observed at necropsy in our African patients. Such lesions frequently complicate benign nephrosclerosis, but difficulties are encountered not only in assessing the importance of these lesions in the production of hypertension, but also in attributing them to a definitely infective as opposed to a vascular origin.

Hypertension is said to manifest itself earlier in the African, and malignant hypertension is stated to be commoner in this race. Hypertensive heart disease is a frequent cause of congestive heart failure in African races and is shown in some series to be the commonest of all causes.

Cor pulmonale/...

COR PULMONALE

A review of this subject will be found in Part II.

SYPHILITIC HEART DISEASE

"Aortitis is one of the commonest of syphilitic lesions" (Boyd 1958) and occurs far more frequently in males than in females. The usual age of clinical manifestation is in the late forties, and it is reasonable to expect much older patients in necropsy series.

Syphilitic heart disease is dependent to a large extent on the aortitis and consists mainly of aortic incompetence following on syphilitic aortic valvulitis and/or pathological changes in the aortic valve ring, with dilatation of the latter. Thus aortic incompetence may occur in spite of the valve cusps remaining normal. Narrowing of the coronary orifices is also dependent on aortitis, and leads to ischaemic degeneration of myocardial fibres.

Two types of myocardial lesions have been described in syphilis:

(1) the gummatous form which may be localized or diffuse (Spain and Johannsen 1942) and

(2) active non-specific myocarditis, regarding which there is much dispute in the literature.

Warthin (1952) considered active syphilitic myocarditis to be common and reported 8 cases of sudden death which he attributed to an exacerbation of latent syphilitic myocarditis. The microscopic feature of the myocardium consisted of subacute infiltration by lymphocytes, plasma cells, monocytes, and a predominance of neutrophils. Completely healed myocarditis was represented by areas of interstitial fibrosis. Spirochaetes were found, particularly in those cases showing the more acute picture. This view has lost favour because of the failure of others (Martland 1940; Coombs 1930; and Shapir 1932) to demonstrate spirochaetes in heart muscle. In a study of 130 cases of syphilitic aortitis with incompetence of the aortic

valve / . . .

valve Shapir (1932) failed to demonstrate the presence of active or latent syphilitic myocarditis; on no occasion did he observe spirochaetes in the myocardium, but noted that coverslip preparations without tissue, prepared according to the Warthin-Starry method, often revealed artefacts which bore a remarkable resemblence to spirochaetes. He considered that fibrotic changes in the myocardium, even in the presence of perivascular infiltrations of lymphocytes and plasma cells, could be accounted for either by coronary ostial stenosis or coronary artery sclerosis. Anderson concludes that myocardial lesions in syphilis are rare (1966) and that syphilitic involvement of the pericardium occurs only as a result of spread of gummatous lesions from the myocardium.

Syphilitic heart disease is present throughout Africa and although its relative incidence varies in different parts of the continent, it still remains an important cause of heart failure in many African races (Heimann1929; Vint 1937; Williams 1938; Becker 1946; Davies 1948; Gelfand 1957; Siew 1958; Shaper and Williams 1960; Cosnett 1962; Baldachin 1963; Powell and Wright 1965). Vint (1937) attributed the greater proportion of deaths due to cardiovascular disease among Africans in East Africa to a syphilitic origin.

Williams (1938) from Uganda reported that syphilis was responsible for more than half the deaths from heart disease in the African. Because of this high incidence of syphilitic heart disease the author found the commonest valvular lesion from all causes to be aortic incompetence, which was also the most frequent effect of syphilitic cardiovascular disease on the heart in his series.

In South Africa, Heimann et al. (1929) found that approximately one-quarter of all cases of heart disease in urban Africans was caused by syphilis. Burton (1934) considered that it was probably less common in the more rural African population. Recent reports (Cosnett 1962; Powell and Wright 1965) show a lower but still significantly high incidence of heart disease from this cause in the African.

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The disease in South Africa is reported to be far less frequent in the White population than in the African races (Siew 1958). Cardiovascular syphilis is also stated to occur some 8 - 10 years earlier in the African or Negro than the usual average among White races (Williams 1938; Laws 1933; Hedley 1935).

Libman (1917) believed that the association between syphilitic heart disease and bacterial endocarditis was rare. Fulton and Levine (1932) supported this view of Libman, but others (Braunstein and Townsend 1940, Wright and Zeek 1940, and Rosenberg 1940) considered co-existing syphilis and bacterial endocarditis of the aortic valve to be more common than was generally believed. Koletsky (1942) cast some doubt upon syphilis as a predisposing cause stating that when bacterial endocarditis is associated with syphilitic valve disease, a combined rheumatic valve lesion is likely to be also present.

Williams (1938) found this association to be rare in his cases of syphilitic heart disease amongst Africans in Uganda, but Siew (1958) in South Africa found subacute bacterial endocarditis to be not uncommonly associated with syphilitic valve lesion in her series.

Besides causing congestive heart failure, cardiovascular syphilis is reported to be a frequent cause of sudden death in the African in South Africa (Elliot 1953) and in Uganda (Diavies 1948). As stated by Davies (1948), "... it is to the African what coronary atheroma and coronary obstruction are to the European ".

Conclusions

The literature shows syphilis in the African, in contrast to other races, to be a significant cause of heart disease in many parts of the Continent including South Africa. Syphilitic aortitis, with its complications of the aortic valve and the coronary ostia, still accounts for a large number of deaths from congestive heart failure as well as sudden deaths from acute coronary insufficiency among this population. Controversy still exists regarding the

possibility / ...

possibility of subacute bacterial endocarditis complicating syphilitic aortic valvulitis.

PERICARDITIS

Pericarditis refers to an inflammation of the visceral and/or parietal layers of the pericardium. The various aetiological types of pericarditis in any population will be determined by the prevalence within it of those diseases which may also affect the pericardium.

Schrire (1958) from Cape Town and Siew (1958) from Johannesburg reported that pericarditis, while a common form of heart disease in the African, is rare in the White races in South Africa. When present, it was usually tuberculous in origin, and males were affected more frequently than females; the peak age in the African was stated to be between 30 and 49. Gelfand (1957) and Baldachin (1963) in Southern Rhodesia also found pericarditis to be frequently tuberculous in aetiology in African patients. Pyogenic pericarditis is reported as being infrequent in the African (Schrire 1958).

When congestive heart failure supervenes, it results either from cardiac tamponade or constriction, the mechanism in both being an interference with the diastolic filling of the heart. The recognition of the constrictive variety at necropsy is not possible and the diagnosis is only made on correlation with the clinical findings.

Amoebic colitis and amoebic liver abscess are frequently encountered in the African in Natal, but amoebic pericarditis is relatively rare. MacLeod et al. (1966) reported that while more than 500 patients are treated annually at King Edward VIII Hospital, Durban, for amoebic liver abscess, less than 2% of these develop amoebic pericarditis. Of those who develop the condition the majority are males, and the peak age is between 20 - 40. Two types were described which the authors termed presuppurative and

suppurative/...

suppurative, the latter being a progression of the former.

In most series in South Africa (Becker 1946; Cosnett 1962; Powell and Wright 1965; Higginson et al. 1960) pericarditis is shown to be less frequently the cause of congestive cardiac failure than are rheumatic heart disease, hypertensive heart disease, cardiomyopathy, cor pulmonale, or syphilitic heart disease.

Conclusions

Pericarditis remains one of the six major causes of congestive heart failure in the African population of South Africa. It is usually tuberculous in origin and less frequently of amoebic or pyogenic aetiology.

RARER CAUSES OF HEART DISEASE

IDIOPATHIC AORTITIS. Isaacson et al. (1959) described an idiopathic form of aortitis occurring in young African children and adolescents. Subsequent reports (Isaacson 1961; Isaacson and Schnier 1961) stressed the predilection of this disease for young African subjects, particularly females. Hypertension is usually present because of the increased tendency towards involvement of the renal arteries. Investigations revealed no known aetiological agent or process, and it has been suggested by the above authors that the lesion probably belongs to the pulseless disease/giant-cell arteritis group of diseases.

Other rarer, causes of heart disease in the African include THYROTOXIC heart disease and OBSTRUCTIVE CARDIOMYOPATHY. While BERI-BERI heart disease is reported to be common in the Cape Coloured cummunity (Schrire and Gant 1959), it is supposedly rare among the African population of the country.

CHAPTER III

MAJOR AETIOLOGICAL TYPES OF HEART FAILURE IN THE AFRICAN IN DURBAN

MATERIAL AND METHODS

Material for this study includes routine necropsy and histological records of 877 consecutive deaths from heart failure in African and Indian subjects at King Edward VIII Hospital during the period January 1958 - December 1962. The criteria determining their inclusion in this series are as outlined in the preceding chapter:

(1) Sudden cardiac death:- those in whom no evidence of congestive failure was found but death had been sudden and resulted from some form of heart disease, and

(2) Congestive heart failure:- congestive heart failure from any cause other than acute bacterial endocarditis, acute pericarditis associated with pneumonias and uraemia, and possible toxic myocarditis occurring with diphtheria, typhoid, pneumonia etc.

ANALYSIS OF MATERIAL

1. Sudden cardiac deaths

In 9,069 consecutive necropsies, performed on African patients, there were 6 sudden cardiac deaths. The age, sex, and aetiological types of heart disease in these 6 patients are summarized in Table I.

Syphilitic aortitis is thus the commonest cause of acute heart failure in the African in this series, males in the sixth decade of life being most frequently affected. For comparison, in 829 consecutive Indian post-mortems there were 5 cases of acute heart failure, the age, sex, and aetiology being shown in Table II.

TABLE I /...

TABLE I

AGE, SEX, AND AETIOLOGICAL FACTORS IN 6 CASES OF SUDDEN CARDIAC DEATH IN AFRICAN PATIENTS

Race	Sex	Age	Cause
A	M	60	Syphilitic aortitis with narrowing of the coronary ostia.
A	M	53	Syphilitic aortitis with narrowing of the coronary ostia.
A	M	60	Syphilitic aortitis with narrowing of coronary ostia plus coronary artery embolism from vegetations on the aortic valves.
A	F	53	
A	M	34	Coronary atheroma and myocardial infarction.
A	F	30	Rheumatic valvular disease (mitral stenosis).

TABLE II

AGE, SEX, AND AETIOLOGICAL FACTORS IN 5 CASES OF SUDDEN CARDIAC DEATH IN INDIAN PATIENTS

Race	Sex	Age	Cause
I	M	52	Coronary atheroma and myocardial infarct.
I	M	57	Coronary atheroma and myocardial infarct.
I	M	50	Coronary atheroma and myocardial infarct.
I	M	44	Coronary atheroma and myocardial infarct
I	F	45	Coronary atheroma, myocardial infarction with rupture of wall of left ventricle.

By contrast with the African, coronary atheroma accounts for all 5 acute cardiac deaths amongst Indian subjects.

DISCUSSION/...

Discussion

Although these results do not reflect the true incidence of acute heart failure on account of legal formality attached to sudden deaths, they nevertheless do reveal interesting differences in the aetiological processes responsible for such deaths in the African as compared with the Indian in Durban.

Coronary artery and hypertensive diseases, in predominantly White American communities, are reported as being the most frequent of all causes of unexpected, sudden, natural deaths (Maitland 1940; Helpern and Rabson 1945; Rabson and Helpern 1948). Males are particularly affected, and the majority of all cases sampled by Maitland (1940) were between the ages of 40 - 65. Helpern and Rabson (1945), while recording coronary artery disease as the major aetiological factor among all diseases of the heart and aorta responsible for sudden deaths, placed syphilitic aortitis second and valvular diseases third in order of frequency. Rabson (1950) recorded disease of the heart and aorta as occupying first place among all causes of sudden natural deaths at and after the ages of 35 - 39 years.

The results here show that coronary artery disease, which features so predominently in White pathology in South Africa and in many other parts of the world, is also the most frequent cause of acute heart failure in the Indian population, but much less so among the African races in Durban.

Obstruction of the coronary ostia by syphilitic involvement of the aorta is the main cause of an acute cardiac death among Africans in agreement with the findings of Williams (1938) and Davies (1948) in Uganda, and Elliot (1953) in South Africa. Although extensive atheroma may occur in association with syphilitic aortitis (Williams 1938) this was not considered an important factor contributing towards the suddenness of death in these patients. Because obstruction takes place at the coronary ostia, death occurs rapidly and usually follows on sudden exertion, excitement, or alcohol. The myocardium in such instances may show no evidence of infarction, this being

so / . . .

so in the present series.

With regard to age, the patients included here are older than the majority of Williams' (1938) cases, but it must be appreciated that the above author referred to age at onset of symptoms, while this work reflects age at death. Males preponderated in this series, in keeping with the general opinion that syphilitic aortitis is more frequent among males.

It is of interest to note that in 2 of the 4 cases of acute deaths from syphilitic aortic-cardiac disease, although ostial narrowing was present, the final episode was the result of an embolus impacting in a narrowed coronary ostium. The source of embolism was, in both cases, bacterial vegetations on the aortic valves. While this contrasts with the findings of Libman (1917), Fulton and Levine (1932), Williams (1938), and Koletsky (1942), it is in agreement with those of Braunstein and Townsend (1940), Rosenberg (1940), Wright and Zeek (1940), and Siew (1958) and supports the view that the association between syphilitic aortic valve disease and subacute bacterial endocarditis is not as rare as is believed. Such association when present may enhance the risk of sudden death from coronary embolism.

2. Congestive heart failure

In African as in Indian subjects this was the commonest type of heart failure encountered at necropsy. During the five year necropsy survey period 684 African and 173 Indians died as a result of congestive heart failure. The relative incidence of the aetiological types encountered in the two race groups is shown in Table III.

This reveals 6 major aetiological types of heart disease occurring in the African in Durban, accounting for 80% of all deaths from congestive heart failure in these subjects. In contrast, four main aetiological types occur in the Indian and together are responsible for 80% of all deaths from congestive heart failure in this group.

TABLE III / . . .

TABLE III

AETIOLOGICAL TYPES OF CONGESTIVE HEART FAILURE:
684 AFRICAN AND 173 INDIAN CONSECUTIVE CASES
OF C. C. F. IN ROUTINE NECROPSIES

Aetiological type of Heart Disease	Africans		Indians	
	No.	%	No.	%
Rheumatic	147	21.5	40	23.1
Hypertensive	129	18.9	40	23.1
Cardiomyopathy	108	15.8	1	0.6
Cor Pulmonale	82	12.0	19	11.0
Syphilitic	33	4.8	1	0.6
Pericarditis Tuberculous	33	4.8	1	0.6
Non-Tuberculous	19	2.8	0	-
Coronary	15	2.2	45	26.0
Congenital	48	7.0	7	4.0
Senile (Multiple causes)	20	2.9	5	2.8
Miscellaneous	31	4.5	7	4.1
Undiagnosed	19	2.8	7	4.1
TOTAL	684	100.0	173	100.0

While marked differences appear in the relative incidence of cardiomyopathy, pericarditis, syphilitic heart disease and coronary heart disease in the two racial groups, no significant differences are apparent when the less common causes of heart failure are considered.

In an appreciable number of older subjects (65 years and over),of both races, multiple causes for the development of congestive heart failure were present in the same patient, and no single cause could be incriminated as being the most important. Such cases have therefore been listed separately under the heading 'Senile (Multiple causes)', the incidence proving much the same in both the African and the Indian.

The miscellaneous group included anaemia (6 Africans and 4 Indians; viral myocarditis, occurring mainly in children (19 Africans and 2 Indians); suppurative myocarditis (1 Indian); mycotic aneurysm of mitral valve (1 African); eclampsia (2 Africans); myocardial infarction due to embolism

of / . . .

of coronary artery in an otherwise normal heart or aorta (3 Africans).

In a fair number of cases of both races no cause was apparent either at necropsy or on histological examination. Included in this category were 2.8% of African and 4.1% of Indian deaths from congestive heart failure.

Table IV shows comparative clinical and necropsy figures from four series of cases elsewhere in Africa (Davies 1948; Galfand 1957; Shaper and Williams 1960; Baldachin 1963) and five series from South Africa (Becker 1946; Schwartz et al. 1958; Higginson et al. 1960; Cosnett 1962; Powell and Wright 1965) together with those quoted for the United Kingdom by Wood (1956). The latter are used in substitution for figures in relation to White races, since no comparative figures for South African Whites are available.

As evident from Table IV the present series of African necropsies show rheumatic heart disease to be the commonest cause of congestive heart failure, with hypertensive heart disease occupying second place, and cardiomyopathy third position. Cor pulmonale, pericarditis, and syphilitic heart disease follow in order of frequency. Although general agreement exists among the majority of clinical and necropsy studies regarding the chief causes of congestive heart failure in the African population of South Africa, variations appear in respect of the relative incidence of the different aetiological types.

Rheumatic heart disease, though not shown as the most frequent cause of congestive heart failure in some other series, nevertheless appears as one of the three most common causes of heart failure in the African. Whereas the necropsy incidence of this disease is by comparison extremely low in Uganda (Davies 1948), a comparatively higher incidence is seen in Bulawayo (Baldachin 1963).

Hypertensive heart disease, as a cause of congestive heart failure, is common throughout Africa. Although most series do not show this to be the most frequent cause as reported by Becker (1946), it is nonetheless obvious from both clinical and necropsy studies that the disease is less common among

LURE IN THE AFRICAN

ll & ght lfr. al) 65	NECROPSY SERIES				
	Present Series (African)	Becker (S.Afr. Tvl) 1946	Davies (Uganda) 1948	Higginson et al. (S. Afr. Tvl.) 1960	Present Series (Indian)
70	694	332	229	537	173
.0	21.5	23.5	3.4	32.4	23.1
.0	18.9	28.6	31.0	18.6	23.1
.0	15.8		-	14.9	0.6
	-	-	9.6	-	-
.0	12.0	10.0	3.9	15.6	11.0
.0	7.6		3.5	4.8	0.6
.0	4.8	16.9	20.9	6.1	0.6
	2.2	1.5	4.3	2.2	26.0
	7.0	1.8		2.2	4.0
.0	2.9	-		-	2.8
.0	4.5	6.3		3.0	4.1
-	2.8	4.0	5.1	-	4.1

the African inhabitants of South Africa than in those of Uganda.

There is almost general disagreement among the various investigators in South Africa as regards the relative incidence of cardiomyopathy among the African. Higginson et al. (1960) from a necropsy study, and Cosnett (1962) from clinical evidence, regarded cardiomyopathy to be less frequent than cor pulmonale, placing it fourth in line of causes of congestive cardiac failure. Yet, the clinical reports of Schwartz et al. (1958) and Powell and Wright (1965) show cardiomyopathy as the most important cause of heart failure among the Africans in South Africa. A disparity in the incidence of the disease is also observed in reports from Southern Rhodesia (Gelfand 1957; Baldachin 1963). Becker (1946), however, makes no mention of cardiomyopathy, his work having been published before the concept of this disease was defined.

Cor pulmonale is apparently common in the African in South Africa, where its incidence is shown in the various series to be of the order of 10% - 16% of all cases of congestive heart failure. These percentages are higher than those quoted elsewhere in Africa and higher also than that reported by Wood (1956) for central London.

Except for the low percentage quoted by Schwartz et al. (1958), syphilitic heart disease is an important cause of congestive cardiac failure throughout Africa. In contrast to most other series, pericarditis is shown in the present study to be a more common cause of heart failure in the African than is syphilitic heart disease. During the course of this study it was noted that clinically pericarditis was more often misdiagnosed as cardiomyopathy than vice versa. This factor may account for a higher incidence of syphilitic heart disease in comparison with pericarditis in certain clinical series.

The figures obtained for Indians in Durban bear a close similarity to those reported by Wood (1956). The high incidence of coronary heart disease and the low incidence or absence of cardiomyopathy, pericarditis, syphilitic heart disease and endomyocardial fibrosis among Indian and Whites

in these studies contrast with the findings amongst Africans in this and other series.

SUMMARY AND CONCLUSIONS

In contrast to the findings for Indians and those reported for White races, syphilitic heart disease is the main cause of a sudden cardiac death among African patients. Subacute bacterial endocarditis may complicate syphilitic aortic valve disease, and embolization from such vegetations may be responsible for the suddenness of death in some such cases.

Congestive heart failure is the commonest form of cardiac decompensation encountered in the African at necropsy. Whereas coronary heart disease, rheumatic heart disease, hypertensive heart disease, and cor pulmonale are the four main causes for congestive cardiac failure among the Indian and White races in South Africa, the African shows six major causes which in order of frequency are rheumatic heart disease, hypertensive heart disease, cardiomyopathy, cor pulmonale, pericarditis, and syphilitic heart disease.

The chief difference regarding aetiology is observed in the low incidence of coronary heart disease, and the increased frequency with which infective conditions are encountered among Africans in contrast to the other two race groups. However, cardiomyopathy, pericarditis, and syphilitic heart disease together account for almost as many deaths from congestive cardiac failure in the African as does coronary heart disease in the other racial groups.

Apart from minor variations the pattern of heart disease in the African in South Africa is similar to that reported in African communities in other parts of the continent, apart from the occurrence of endomyocardial fibrosis in certain countries where cardiomyopathy does not occur.

CHAPTER IV

RHEUMATIC HEART DISEASE IN THE AFRICAN IN DURBAN

In 9,069 consecutive routine necropsies performed on African subjects, rheumatic heart disease accounted for 147 of 684 deaths following on congestive heart failure. This indicated an incidence of 21.5% in all cases of congestive heart failure and 1.6% in all deaths.

In 829 consecutive routine post-mortems on Indians, rheumatic heart disease was responsible for 40 of 173 deaths resulting from congestive heart failure. Thus 23.1% of all cases of congestive heart failure and 4.8% of all deaths among Indians were caused by the cardiac complications of rheumatic fever.

Age Incidence

Table I shows the age incidence of congestive heart failure from rheumatic heart disease in 147 Africans and 40 Indian patients as observed at necropsy.

It is evident from Table I that congestive heart failure from rheumatic heart disease attains its highest level of incidence in the African during the second decade, constituting in this age group 13.3% of all routine necropsies and 65.2% of all cases of congestive heart failure among Africans. In this respect a similarity is shown in results obtained from Indian subjects, although a difference is apparent in the rate of decline of rheumatic heart disease with increasing age in the two groups.

Table I also shows a significant number of Africans with rheumatic heart disease to have died as a result of congestive heart failure after the age of 40 years.

TABLE I /...

TABLE I

AGE INCIDENCE OF C. C. F. DUE TO RHEUMATIC HEART DISEASE IN AFRICANS AND INDIANS (% AMONG ROUTINE NECROPSIES AND % AMONG C. C. F. CASES)

Age Groups	AFRICANS			INDIANS		
	No. with R. H. D.	% of Routine P. M.'s	% of C. C. F. cases	No. with R. H. D.	% of Routine P. M.'s	% of C. C. F. cases
Under 9 yrs.	13	0.2	14.6	4	1.9	30.8
10 - 19	30	13.3	65.2	12	30.0	85.7
20 - 29	30	6.5	41.1	12	20.0	80.0
30 - 39	23	3.2	19.2	5	6.6	31.3
40 - 49	25	3.4	21.6	3	2.6	11.5
50 - 59	15	2.3	15.5	2	1.3	5.6
60 - 69	10	1.8	11.9	2	1.8	6.1
70+	1	0.3	1.7	0	-	-
Total	147	1.6	21.5	40	4.8	23.1

TABLE II

SEX INCIDENCE OF C. C. F. CAUSED BY RHEUMATIC HEART DISEASE IN AFRICANS (% INCIDENCE AMONG ROUTINE NECROPSIES AND C. C. F. CASES)

Age Groups	MALES			FEMALES		
	No. with R. H. D.	% of Routine P. M.'s	% of C. C. F. cases	No. with R. H. D.	% of Routine P. M.'s	% of C. C. F. cases
Under 9 yrs.	7	0.2	13.5	6	0.2	16.2
10 - 19	9	8.4	47.4	21	17.8	77.8
20 - 29	8	3.9	42.1	22	8.6	40.7
30 - 39	11	2.9	14.9	12	3.6	26.1
40 - 49	15	3.1	21.4	10	3.8	21.7
50 - 59	4	1.0	7.8	11	3.9	23.9
60 - 69	3	1.0	6.8	7	2.6	17.5
70+	0	-	-	1	0.7	3.6
Total	57	1.2	15.8	90	2.2	27.8

Sex / ...

TABLE III

SEX INCIDENCE OF C. C. F. CAUSED BY RHEUMATIC HEART DISEASE IN INDIAN NECROPSIES (% INCIDENCE AMONG ROUTINE NECROPSIES AND C. C. F CASES)

Age Groups	MALES			FEMALES		
	No. with R. H. D.	% of Routine P. M. 's	% of C. C. F. cases	No. with R. H. D.	% of Routine P. M. 's	% of C. C. F cases
Under 9 yrs.	0	0	0	4	3.7	36.4
10 - 19	5	25.0	71.4	7	35.0	100.0
20 - 29	4	22.2	100.0	8	19.0	72.7
30 - 39	2	5.4	25.0	3	7.7	37.5
40 - 49	3	3.8	15.0	0	-	-
50 - 59	1	1.0	4.2	1	2.0	8.3
60 - 69	2	3.2	9.5	0	-	-
70+	0	-	-	0	-	-
Total	17	3.6	16.8	23	6.4	31.9

TABLE IV

SEX INCIDENCE OF C. C. F. CAUSED BY RHEUMATIC HEART DISEASE IN INDIANS BELOW AND OVER 30 YEARS

	MALES			FEMALES		
	No. with R. H. D.	Total C. C. F. cases	% of C. C. F. cases	No. with R. H. D.	Total C. C. F. cases	% of C. C. F. cases
Under 29 yr.	9	13	69.3	19	29	65.4
Over 30 yr.	8	88	9.1	4	43	9.3
Total	17	101	16.8	23	72	31.9

Sex incidence

Table II shows the sex incidence of congestive heart failure caused by rheumatic heart disease in African necropsies. A female preponderance

is / . . .

is apparent not only in the overall sex incidence but also at each age group, with the exception of the third decade. This sex difference has been shown to be significant.

Table III shows comparable figures from Indian necropsies.

Although the gross percentage shows an apparent female preponderance this is not statistically significant, being explained by the age distribution of cases of congestive heart failure in Indian males and females. (Table IV).

Valvular lesions in rheumatic heart disease

The valvular lesions encountered at necropsy in 147 African subjects with congestive heart failure following on rheumatic fever are summarized in Table V.

TABLE V

RHEUMATIC VALVULAR LESIONS IN AFRICAN NECROPSIES

	Females	Males	Total No.	%
Mitral alone	48 (58.5%)	15 (31.3%)	63	42.9
Mitral and Aortic	19 (23.2%)	16 (33.3%)	35	23.8
Aortic alone	11 (13.4%)	16 (33.3%)	27	18.4
Mitral, Aortic & Tricuspid	2	1	3	2.0
Mitral & Tricuspid	1	0	1	0.7
Aortic & Tricuspid	1	0	1	0.7
Total	82	48	130	88.5

The pattern of rheumatic valvular disease in the African does not differ significantly from that reported elsewhere. While females show a greater tendency towards involvement of the mitral valve, in the male the

aortic /...

aortic valves seem to be equally vulnerable with the mitral.

Of the 147 African patients with rheumatic heart disease 130 showed a significant degree of valvular deformity of which 9 were below 15 years of age. In the absence of active carditis, severe valvular deformity accounted for death from congestive heart failure in 7 of these 9 patients. For comparison, of 37 Indian patients with rheumatic valvular disease 3 were under 15 years of age. Active carditis was noted in 29 of the 147 cases of rheumatic heart disease and all except 2 patients were under 30 years of age. Pericarditis was observed in 8 patients and was associated with active carditis.

Superimposed bacterial endocarditis was present in 30 of the 147 cases of rheumatic heart disease, the aortic valve being involved in 15, the mitral in 9, both aortic and mitral together in 5, and aortic and tricuspid together in 1 patient. Subacute bacterial endocarditis was the common form encountered, acute bacterial endocarditis being noted on one occasion only.

DISCUSSION

Rheumatic heart disease is shown, at necropsy, to be the most frequent cause of congestive heart failure in the African populace in Durban, accounting for 21.5% of all deaths from congestive cardiac failure. While this contrasts with the necropsy findings of Becker (1946), who recorded hypertensive heart disease as being the commonest cause of such failure in the African and Coloured people in Johannesburg, it is in agreement with those of an earlier investigation by Heimann et al. (1929). This finding is also contrary to the clinical observations of Schwartz et al. (1958) from Johannesburg, and Powell and Wright (1965) from Durban, that cardiomyopathy is the major cause of congestive heart failure in the African.

Although the relative incidence of rheumatic heart disease in the African appears to vary very slightly within South Africa, the disease is

comparatively/...

comparatively less frequent in Uganda but more common in Bulawayo, Southern Rhodesia.

With regard to age, deaths from congestive heart failure following rheumatic heart disease attain the highest level of incidence among Africans in the second decade, and a steady decline is noted thereafter. While among Indians the age group with the highest incidence is similar, a significant drop is noted only after the third decade. This high incidence in the second decade correlates with the findings of Becker (1946) and Beet (1955) in Africans and also with White (1951) in Americans.

It is of interest to note that a fair percentage (34.7%) of African patients with rheumatic heart disease, dying from congestive heart failure, were 40 years or over in age. This contrasts with the findings of Davies (1948), Schrire (1958), and those reported by Bradlow et al. (1964), and repudiates the view that rheumatic heart disease is rare in African patients over 40 years of age. The present series, in fact, shows a smaller percentage (45%) of African subjects with rheumatic heart disease to have died from congestive heart failure before the age of 40 years than Indians (82.5%).

Although fully developed valvular lesions were encountered among African subjects below the age of 15 years, this finding was in no way peculiar to the African, similar lesions being observed among Indian patients of corresponding age.

There was a definite female preponderance in the African in contrast to an equal sex distribution in the Indian. Becker (1946), however, found no significant difference in the incidence of the disease in African males and females, nor in the incidence of mitral and aortic lesions in these subjects. The present series, in agreement with the findings of Clawson (1940) and Shaper and Williams (1960), shows mitral lesions to be more common in females and aortic lesions more common in males.

Active carditis and pericarditis, as in most other series, were the

commonest /...

commonest cause of congestive heart failure during the first and early part of the second decade.

Superimposed bacterial endocarditis (almost always subacute in type) occurred in 20.4% of all cases with rheumatic heart disease, the aortic valve being more commonly affected than the mitral. The high incidence of subacute bacterial endocarditis observed here correlates with that reported by Becker (1946) in the African in Johannesburg.

SUMMARY

Rheumatic heart disease is found to be the commonest cause of congestive heart failure in the African in Durban. The various effects of rheumatic fever on the heart in the African are discussed and compared with reported findings in South Africa and elsewhere.

CHAPTER V

HYPERTENSIVE HEART DISEASE IN THE AFRICAN IN DURBAN

During the period under survey, in 9,069 consecutive routine necropsies performed on African patients, there were 684 deaths from congestive heart failure, and of these 129 were the result of hypertensive heart disease. This indicates an all-age average necropsy incidence of 1.4% and an incidence of 18.9% of all deaths from congestive heart failure.

Age incidence

The age incidence of hypertensive congestive heart failure in 129 African patients is summarized in Table I.

The lowest incidence of congestive heart failure from hypertension occurs in individuals under 30 years of age. Thereafter, although a rise in incidence is noted, this does not take the form of a steady increase with advancment of age, but shows two peaks, one during the fourth decade and another, the highest, during the seventh decade.

Table II shows the age distribution of primary and secondary types of hypertension in 129 African patients in whom death resulted from hypertensive congestive cardiac failure.

Primary hypertension in the African accounted for 63.5% of all deaths from hypertensive heart failure. Of 63 patients with benign hypertension, 58 (92.1%) were 40 years of age or over, and more than half (36) were between 50 - 69. There were 34 females and 29 males with benign nephrosclerosis in this series, and no significant sex difference was noted. Malignant termination of benign hypertension was recorded in 4 instances. Primary malignant nephrosclerosis was detected in 19 patients (8 females, 11 males) with congestive heart failure, and uraemia was often also present. Of these 19 patients, 16 were between 30 - 50 years of age.

There were 43 cases of secondary hypertension (24 females, 19 males) in this series, indicating an incidence of 33.3% of all cases of

hypertensive/...

hypertensive congestive heart failure. Hypertension secondary to acquired renal disease was noted in 30.9% of all cases. Less frequent causes were congenital polycystic kidneys (2 cases) and pheochromocytoma (1 case). Of patients with secondary hypertension 60% were below 40 years of age, a third being in the fourth decade of life. The high incidence of congestive heart failure from hypertension during the fourth decade (Table II) is thus explained by the prevalence of secondary hypertension during this period. Malignant termination occurred in 2 patients with secondary hypertension, and in both instances followed chronic pyelonephritis.

For comparison, in 829 consecutive necropsies performed on Indian subjects there were 173 deaths from congestive heart failure. Hypertension was incriminated as the cause of such failure in 40 cases. Thus hypertensive heart disease accounted for 4.8% of all necropsies and 23.1% of all deaths from congestive heart failure in Indian subjects in Durban. Of these 40 hypertensive patients, 35 were found to have primary hypertension, 29 in the benign form and 6 malignant in type. Malignant termination of benign nephrosclerosis was observed in one instance. The majority of patients with benign hypertension (93.1%) were 40 years or over in age, and, as among Africans, no significant sex difference was apparent. Hypertension secondary to renal disease was present in 5 patients

TABLE I

AGE INCIDENCE OF HYPERTENSIVE C.C.F. IN AFRICANS

(% AMONG ROUTINE NECROPSIES AND % AMONG C.C.F. CASES

Age Group	No. with Hypertensive Heart Disease	% of Routine Necropsies	% of C.C.F. Cases
Under 30	12	0.2	5.8
30 - 39	27	3.8	22.5
40 - 49	18	2.4	15.5
50 - 59	29	4.4	29.9
60 - 69	27	4.8	32.1
70	16	4.7	27.1
Total	129	1.4	18.9

TABLE II /...

TABLE II

AGE DISTRIBUTION OF PRIMARY AND SECONDARY HYPERTENSION IN 129 AFRICAN DEATHS FROM HYPERTENSIVE C. C. F.

Types of Hypertension	Under 29	30-39	40-49	50-59	60-69	70+	Total No.	Total %
A. Primary								
1. Benign Hypertension	0	5	9	18	18	13	63	48.8
2. Malignant Hypertension	1	4	5	7	1	1	19	14.7
B. Secondary								
1. Renal								
Acute Glomerulonephritis	8	2	0	1	2	0	13	10.0
Chronic Glomerulonephritis	2	3	2	1	1	0	9	7.0
Chronic Pyelonephritis	1	8	1	2	4	2	18	13.9
2. Congenital								
Polycystic Kidneys	0	1	0	0	1	0	2	1.6
3. Endocrinal								
Pheochromocytoma	0	1	0	0	0	0	1	0.8
C. Unclassified	0	3	1	0	0	0	4	3.2
Total	12	27	18	29	27	16	129	100.0

DISCUSSION

Hypertension is the second most frequent cause of deaths from congestive heart failure in the African in Durban and has been shown to be responsible for 18. 9% of all cases of congestive cardiac failure. This correlates closely with the findings of Higginson et al. (1960), and also with the clinical observations of Cosnett (1962) in South Africa and Baldachin (1963) in Southern Rhodesia, although differing from those of Becker (1946). The incidence of congestive heart failure from hypertension is only slightly lower in the African than in the Indian.

Congestive heart failure from hypertension is lowest in the first three decades and thereafter, contrary to the findings of Becker (1946), does not show a steady rise with increasing age. There are two peaks, the

first / . . .

first, in the fourth decade, being related to renal hypertension. The second, beginning in the sixth decade and showing the highest incidence of hypertensive congestive heart failure in the seventh decade, is accounted for by the prevalence of benign hypertension and, to a lesser extent chronic pyelonephritis, in the later years of life. Thus, while both primary and secondary hypertension occur in the African in Durban, essential hypertension is the more frequent in this race group, being present in its benign form in 48.8%, and in the malignant form in 14.7%, of all cases with hypertensive congestive heart disease. These findings are supported by Becker (1946) and Isaacson and Kincaid-Smith (1962). The greater proportion of patients with benign hypertension (92.1%) were 40-plus in age, and as mentioned, the maximum incidence for this type was noted in the seventh decade. This is a decade later than the highest incidence reported by Becker (1946), but it is difficult to draw conclusions regarding such a difference since the age is often merely an estimate in the African and may thus be far from accurate. In agreement with Becker (1946), but in contrast to Schwartz et al. (1958), no significant difference was apparent in sex incidence of benign hypertension in these subjects.

Uraemia commonly accompanied heart failure in patients with primary malignant hypertension and should be considered an important additional factor in the cause of death. It has been the author's experience that in those cases developing congestive heart failure the renal vessels frequently show hyperplasia or productive endarteritis as the main, and often the sole feature, of malignant nephrosclerosis, and that necrotizing arteriolitis is conspicuously absent. In contrast, those dying from renal failure and uraemia without developing congestive heart failure usually show both productive endarteritis and necrotizing arteriolitis occurring concurrently. It is possible that early treatment, with subsequent longer survival, may be responsible for this difference in the histological picture of malignant nephrosclerosis.

The incidence of malignant hypertension in the African is similar

to / . . .

to that found in the Indian, and in both races there is a tendency for males to be affected more frequently. This correlates with the findings of Seedat (1963). The age at death in the majority of patients was between 30 - 50, thus falling within the reported age range for malignant hypertension.

Four African subjects with benign nephrosclerosis were observed to terminate in a malignant phase. Vascular changes described in malignant nephrosclerosis were also noted in 2 cases of chronic pyelonephritis. Thus in 25 cases of malignant hypertension with congestive cardiac failure, chronic pyelonephritis was observed in only 2 instances (8%). This is in contrast to the necropsy findings of Heptinstall (1953) and the clinico-pathological study of Kincaid-Smith et al. (1958), whose estimates of the proportion of malignant hypertension due to chronic pyelonephritis, in Britain, were of the order of 16% and 21% respectively, and also to the 30% incidence of chronic pyelonephritis as a cause of severe and malignant hypertension reported from Uganda (Somers 1960). These differences are possibly due to the criteria accepted for the diagnosis of chronic pyelonephritis. While hypertension due to chronic pyelonephritis was found to be responsible for congestive heart failure in 13.9% of all hypertensive subjects in this series, focal lesions simulating chronic pyelonephritis were often observed in both African and Indian patients with essential benign nephrosclerosis. The significance of this association is not yet known.

SUMMARY

Hypertension was found to be the second most common cause of congestive heart failure in African subjects in Durban. The various aetiological types occurring in this population have been described and discussed. Two peaks in incidence of hypertensive heart failure were encountered. The first, occurring in the fourth decade of life, was related to the high incidence of hypertension secondary to renal disease, and the second, apparent in the seventh decade, was due mainly to essential hypertension.

Malignant hypertension was usually primary, being far less frequently secondary to renal disease.

CHAPTER VI

CARDIOMYOPATHY AND COR PULMONALE IN THE AFRICAN IN DURBAN

CARDIOMYOPATHY

During the five year period under survey in 9,069 consecutive routine necropsies performed on African patients, cardiomyopathy accounted for 108 of 684 (or 15.8%) deaths from congestive cardiac failure. By contrast, in 829 Indian necropsies, with 173 deaths from congestive cardiac failure, cardiomyopathy was suspected on one occasion only.

Age and sex incidence

Table I shows the age and sex incidence of cardiomyopathy in 108 African subjects.

TABLE I

AGE AND SEX INCIDENCE OF CARDIOMYOPATHY IN 108 AFRICAN PATIENTS AT NECROPSY

Age Groups	MALES			FEMALES		
	No. with Cardio-myopathy	% of Routine Necropsies	% of CCF Cases	No. with Cardio-myopathy	% of Routine Necropsies	% of CCF Cases
Under 30	4	0.13	4.4	6	0.21	5.1
30 - 39	19	4.9	25.7	8	2.4	17.4
40 - 49	16	3.3	22.9	9	3.4	19.6
50 - 59	13	3.4	25.5	12	4.3	26.1
60 - 69	9	3.0	20.5	7	2.6	17.5
70+	1	0.5	3.2	4	2.7	14.3
Total	62	1.3	17.2	46	1.1	14.2

Although/...

Although the disease occurs at all age groups as shown in Table I it most commonly occurs from the age of 30 years onwards, and little variation in incidence is found in the latter decades. This is true for both sexes. There is also no significant sex difference in the incidence of cardiomyopathy in the African.

The clinical and pathological diagnosis of cardiomyopathy is one fraught with difficulties, especially in view of the frequent occurrence of right ventricular hypertrophy. Hence a detailed account of investigations on such cases will be considered in Part II of this work.

COR PULMONALE

During the period January, 1958 - December, 1962, in 9,069 consecutive routine necropsies performed on African subjects at the King Edward VIII Hospital in Durban, 684 deaths were caused by congestive heart failure. Of these 82 (12.0%) were due to right ventricular failure from causes other than rheumatic valvular disease, congenital heart disease, and right ventricular failure following on left ventricular failure. Of these 82 cases of right ventricular failure, 56 (68.3%) were males and 26 (31.7%) were females. The sex difference was found to be of no significance statistically.

In a series of 829 consecutive routine necropsies on Indian patients, in which there were 173 cases from congestive heart failure, 11% of deaths from such failure were recorded as being right ventricular in type. Thus no significant racial difference is shown to exist.

Acute cor pulmonale

Among African patients, there were 5 cases (2 males, 3 females) of acute cor pulmonale, all of which were caused either by embolism or thrombosis involving the pulmonary arterial tree. In one female patient the disease followed childbirth. In the other 4 (2 males, 2 females), no precipitating cause was found. The incidence of acute cor pulmonale among African cases

of / . . .

of congestive cardiac failure was thus 0.7%.

Chronic cor pulmonale and right ventricular failure

There were 77 (11.3%) cases of chronic cor pulmonale or right ventricular failure of unknown aetiology among African patients during the five year survey period. Table II summarises the age distribution of right ventricular failure, as regards known and unknown causes, in 77 African subjects as observed in routine necropsies.

TABLE II

AGE DISTRIBUTION AND CAUSE AMONG 77 AFRICAN SUBJECTS WITH CHRONIC RIGHT VENTRICULAR FAILURE

	Under 20	20-30	30-39	40-49	50-59	60-69	70+	Total No.	Total %
Chronic Emphysema	-	1	2	5	5	5	3	21	27.3
Chronic Bronchitis and Emphysema	-	-	-	-	1	1	-	2	2.6
Pulmonary Fibrosis	-	4	6	10	3	-	1	24	31.1
Silico-tuberculosis	-	-	-	-	-	1	1	2	2.6
Bronchiectasis	-	-	2	-	1	1	2	6	7.8
Carcinoma of Lung	-	-	-	-	-	1	-	1	1.3
Congenital Cysts	1	1	-	-	-	-	-	2	2.6
Primary Pulmonary Hypertension	-	-	1	-	-	-	-	1	1.3
Pulmonary Embolic Disease (chronic and recurrent	-	-	-	-	-	-	-	-	-
Unknown	1	1	-	8	2	3	3	18	23.4
Total	2	7	11	23	12	12	10	77	100.0

Right ventricular failure is observed in all age groups after the second decade but almost 90% of patients were 30 years and over.

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The common causes recorded in the production of such failure are pulmonary fibrosis (31.1%), chronic emphysema (29.9%), and bronchiectasis (7.8%). One case was considered to be a primary pulmonary hypertension. No case of chronic thromboembolic cor pulmonale was diagnosed during the five year survey period. In 23.4% of all cases of chronic right ventricular failure, the aetiology was undetermined.

DISCUSSION

In the voluminous literature dealing with cor pulmonale the incidence would seemingly vary considerably in different parts of the world, but this may in part be due to the lack of clarity as to what is meant by this term. Only as recently as 1960 the World Health Organisation appointed a committee to sort out the confusion regarding cor pulmonale.

It is also a well known fact that the ordinary routine post-mortem procedures are grossly inadequate in the investigation of cor pulmonale. The presence, extent and type of emphysema, and the abnormalities of the pulmonary vascular systems demand special methods of investigation such as whole lung sections and pulmonary angiography. As we have seen the aetiology of almost one-quarter of the cases in the present series was not determined.

For this reason it was thought necessary to conduct an investigation of a series of cases with right ventricular hypertrophy and failure other than those associated with chronic left ventricular failure, mitral stenosis and congenital anomalies of the heart, occurring in the African in Durban, to ascertain the precise aetiological factors involved in the production of cor pulmonale in this population. (See Part II).

CHAPTER VII

PERICARDITIS AND SYPHILITIC HEART DISEASE IN THE AFRICAN IN DURBAN

PERICARDITIS

This group includes all cases presenting with signs of congestive cardiac failure resulting from large pericardial effusions or constrictive pericarditis. Pericarditis associated with uraemia, acute pneumonias, or active rheumatic carditis have been excluded.

Using the above criteria, during the five year period (January, 1958 - December, 1962) under survey, pericarditis was found to be responsible for 52 of 684 deaths resulting from congestive heart failure among African subjects in Durban. In contrast, during the same period, only one in 173 deaths from congestive cardiac failure among Indians was attributed to pericardial disease.

Table I summarizes the sex and age incidence of congestive cardiac failure of pericardial origin in 52 Africans as seen at necropsy.

No significant sex difference is apparent in the incidence of pericardial disease in the African. In males, although the disease was found at all ages, 70% of the cases occurred between 30 - 59 years. There was no age predilection among African females. The various aetiological types of pericardial disease encountered in the African are summarized in Table II.

It is evident from Table II that 63.5% of all cases of pericardial disease in this series were of tuberculous origin. Of the 33 subjects with tuberculous pericarditis, 18 were males and 15 females, indicating no significant difference in sex incidence. The disease was observed at all age groups, but half the total number of patients with tuberculous pericarditis were between 30 - 49 years of age. It was commonly serofibrinous, haemorrhagic or granulomatous in type, the chronic constrictive variety being observed in only four patients.

TABLE I /...

TABLE I

AGE AND SEX INCIDENCE OF C. C. F. CAUSED BY PERICARDIAL DISEASE IN AFRICANS (% C. C. F. IN ROUTINE NECROPSIES)

Age Groups	MALES No. with Pericardial Disease	MALES % of C. C. F. Cases	FEMALES No. with Pericardial Disease	FEMALES % of C. C. F. Cases
Under 19	5	7.0	0	0
20 - 29	1	5.3	5	9.3
30 - 39	10	13.5	3	6.5
40 - 49	6	8.6	6	13.0
50 - 59	5	9.8	2	4.3
60 - 69	1	2.3	4	10.0
70+	2	6.5	2	10.0
Total	30	8.3	22	6.8

TABLE II

AGE DISTRIBUTION AND AETIOLOGICAL TYPES OF PERICARDIAL DISEASE IN AFRICANS

Causes	Under 20	20-29	30-39	40-49	50-59	60-69	70+	Total No.	Total %
Tuberculous	2	3	6	8	7	5	2	33	63.5
Amoebic	2	1	5	4	-	-	-	12	23.1
Rheumatic	-	1	-	-	-	-	-	1	1.9
Pyogenic	1	-	-	-	-	-	-	1	1.9
Primary Tumours	-	-	1	-	-	-	1	2	3.8
Unclassified	-	1	1	-	-	-	1	3	5.8
Total	5	6	13	12	7	5	4	52	100.0

Amoebic pericarditis, related to a left lobe amoebic liver abscess, accounted for 23.1% of all cases of congestive heart failure from pericardial disease. Of the 12 cases observed, the majority (10) were males. This was to be expected, since amoebic liver abscess is commoner in males than females.

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The pericarditis was commonly of the "suppurative" type, due to rupture of the abscess through the diaphragm. In a few cases there was a haemorrhagic serofibrinous pericarditis, this phase preceding actual rupture of the subphrenic abscess. Three patients showed evidence of constrictive pericarditis. The histological picture of the pericardium in these consisted of a non-specific chronic inflammatory reaction with granulation tissue formation. Amoebae were not observed in any instance.

Chronic constrictive rheumatic pericarditis was observed in a single case, a male aged 21 years, and one case of pyogenic pericarditis was encountered in an infant aged 18 months. Of the 3 cases (1 male, 2 females) in which aetiology was undetermined, one was serofibrinous, the other two of the chronic constrictive type. These may have been of tuberculous aetiology. There were two cases of primary tumours of the pericardium, a haemangiosarcoma with a large haemorrhagic effusion, and a fibroma.

DISCUSSION

Pericarditis is the fifth commonest cause of congestive heart failure in African subjects in Durban, being responsible for 7.6% of all deaths from such failure, in contrast to the very low incidence (0.6%) found among Indians, in Durban, and also to that reported in White races in South Africa. The finding that pericarditis remains an important factor in the production of heart disease in the African is in accord with the opinions of others in South Africa (Becker 1946; Siew 1958; Schrire 1958; Powell and Wright 1965) and also with the findings of Gelfand (1957) in Southern Rhodesia.

Pericarditis in the African in Durban has been observed to be mainly tuberculous in origin, and, as found by Schrire (1958), the peak age limits are between 30 - 49 years. However, no significant sex difference was noted in the incidence of tuberculous pericarditis in this series. Most of the cases were in the active phase of the disease.

Although amoebic pericarditis is said to be rare in comparison with

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the large number of cases of amoebiasis seen among Africans in Durban, it nevertheless is the most important cause, after tuberculosis, of congestive heart failure due to pericarditis in this population. Clinically it can closely mimic tuberculous pericarditis. At necropsy it was also the commonest "suppurative" or purulent variety encountered, pyogenic pericarditis being relatively uncommon among Africans (Schrire 1958). Necropsy findings here confirm the clinical evidence of MacLeod et al. (1966), that amoebic pericarditis occurs more frequently in males, the peak age being between 20 - 40 .

Support is also given to the observation of Lamont and Pooler (1958) and MacLeod et al. (1966), that amoebic pericarditis may go on to constriction. Wilmot (1962) suggested that secondary bacterial infection may be the important factor producing constriction in such cases, but subsequent experience appears to indicate that bacterial infection is not essential (MacLeod in press). Only with a drop in the incidence of tuberculosis and amoebiasis as infections among Africans will pericarditis become an infrequent cause of heart failure in these people .

SUMMARY

Pericarditis is still a common cause of heart disease in the African in Durban, and when present is more often tuberculous in aetiology. Amoebic pericarditis, although rare relative to the incidence of amoebiasis, is the second commonest type of pericardial disease producing congestive cardiac failure whereas pyogenic pericarditis is an uncommon cause of heart failure.

SYPHILITIC HEART DISEASE

In the present series of 9, 069 consecutive routine post-mortems

performed/. . .

performed on Africans, there were 684 deaths from congestive heart failure, of which 33 were syphilitic in origin. By comparison, one case was encountered in 829 Indian necropsies, with 173 deaths from congestive cardiac failure.

TABLE III

AGE AND SEX INCIDENCE OF C. C. F. FROM SYPHILITIC HEART DISEASE IN AFRICANS

(% AMONG C. C. F. CASES)

Age Groups	MALES No. with Syphilitic Heart Disease	MALES % Among C. C. F. Cases	FEMALES No. with Syphilitic Heart Disease	FEMALES % Among C. C. F. Cases
Under 30	2	2.2	3	2.5
30 - 39	9	12.2	2	2.2
40 - 49	2	2.9	3	6.5
50 - 59	1	2.0	2	4.3
60 - 69	5	11.4	1	2.5
70+	2	6.5	1	3.6
Total	21	5.8	12	3.7

TABLE IV

TYPES OF CARDIAC LESIONS ENCOUNTERED AT NECROPSY IN 33 CASES OF SYPHILITIC HEART DISEASE IN AFRICANS

	Under 30	30-39	40-49	50-59	60-69	70+	Total No.	Total %
Aortic incompetence with or without ostial narrowing	4	11	4	2	4	2	27	81.8
Coronary ostial narrowing (without A.I.)	0	0	1	1	2	1	5	15.2
Gumma	1	0	0	0	0	0	1	3.0
Chronic myocarditis	0	0	0	0	0	0	0	0
Total	5	11	5	3	6	3	33	100.0

Table III shows the sex and age incidence of congestive heart failure from syphilitic heart disease in 33 African patients, and Table IV the types of cardiac lesions found at necropsy.

In the present series, in addition to the 33 cases of congestive heart failure, 4 sudden deaths were caused by syphilitis. In these 37 cases superimposed subacute bacterial endocarditis was observed in 5 instances, indicating an incidence of 13.5%.

DISCUSSION

It has been shown that 4.8% of all cases of congestive heart failure among Africans are syphilitic in origin. The disease is clearly much more common than in the Indian population in Durban (0.6%), or among White races as judged by reports from the literature.

Although syphilitic aortitis is generally accepted as being more common in males, no significant sex difference in the incidence of congestive heart failure from cardiovascular syphilis was apparent among Africans in this series. As observed by Williams (1938) in Uganda and Laws (1933) and Hedley (1935) in the Negro population in the United States of America, a significant number of African patients die from syphilitic heart disease at an earlier age than that reported for White races. One-third of the patients in this series died during the fourth decade of life. Thus, as suggested by Williams (1938), little value can be attached to age in distinguishing syphilitic heart disease from rheumatic valvular disease in African subjects.

Aortic incompetence and narrowing of the coronary ostia are seen to be the major lesions. Gummatous involvement of the myocardium, as reported in the literature, is rare in the African in Durban, being observed on one occasion only. Diffuse syphilitic myocarditis, as described by Warthin (1925), was not observed, and all fibrotic lesions in the myocardium were attributed to vascular changes associated with stenosis of the coronary ostia.

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The association of subacute bacterial endocarditis and syphilitic aortic valve disease is, as mentioned earlier, not as rare as commonly believed. An incidence of 13.5% in this series is considered to be significant.

SUMMARY

Syphilis still remains an important factor in the production of heart failure in the African in Durban. Aortic incompetence, with or without coronary ostial narrowing, is the common effect of aortic syphilis on the heart. Death from syphilitic heart disease occurs at an earlier age in the African and the disease is found to be a frequent cause of sudden death in these subjects. Subacute bacterial endocarditis is not rare in association with syphilitic valvular disease in the African at necropsy. It is doubted whether active syphilitic myocarditis really exists as an entity.

PART II

CHAPTER I

RIGHT VENTRICULAR HYPERTROPHY AND FAILURE IN AFRICAN SUBJECTS IN DURBAN

PURPOSE

This study was undertaken in an attempt to determine the cause of right ventricular hypertrophy and failure in African patients since routine necropsy and histological techniques had failed to provide the answer in a large number of cases.

While the occurrence of chronic right ventricular failure is clearly evident on routine post-mortem examination, the cause for such failure remains unknown in almost one-quarter of all cases coming to necropsy. Although causes such as emphysema and pulmonary vascular disease may be suspected at necropsy, confirmatory evidence is often necessary before definite conclusions can be drawn. Such evidence is sometimes lacking even with the additional aid of microscopy, since one is limited to the number of slides that can possibly be examined in any individual case. Thus the extent and anatomical distribution of diseases such as emphysema and pulmonary thrombo-embolism cannot be assessed with a sufficient degree of accuracy from the routine methods employed at necropsy. In some cases, parenchymal and vascular disease occur together, or parenchymal pathology of more than one type may be present concurrently, so that eventual right ventricular strain and failure is dependent not on any one factor but possibly on the cumulative effect of several lesions. It was necessary therefore to include additional methods such as pulmonary arteriography and whole lung sections, so that a more complete picture of the disease process or processes might be obtained.

Although right ventricular hypertrophy in the presence of mild to moderate dilatation is easily recognisable at necropsy, difficulties arise with lesser degrees of hypertrophy. This is particularly so in cardiomyopathy,

where / ...

where although both ventricles are usually involved it is difficult at necropsy to assess with any degree of accuracy whether hypertrophy involves both these chambers equally or one preponderantly. In order to confirm ventricular hypertrophy and establish which of the two ventricles was predominantly enlarged, additional methods for studying cardiac enlargement became necessary.

MATERIAL AND METHODS

For this purpose it was necessary to investigate all cases showing either exclusive or predominant right ventricular hypertrophy and failure. Right ventricular hypertrophy due to mitral disease was excluded but cardiomyopathy was included because of the frequency with which predominant right ventricular hypertrophy was suspected at necropsy.

Thus thirty consecutive cases of cor pulmonale and thirty-five consecutive cases of cardiomyopathy, on which post-mortems were performed during the period April, 1964 to February, 1966, were studied. These included African patients of both sexes of ten years of age and over. Cases were investigated in the following way:

(a) Necropsy examination

At necropsy particular attention was paid to the state of the heart and lungs. The heart was examined for hypertrophy and dilatation of its chambers, and all abnormalities of the pericardium, myocardium and endocardium were recorded. Intramural thrombi were specially sought and their location noted.

The lungs were examined for pleural thickening and adhesions between the lung and thoracic cage, and diaphragm. One lung was sectioned and examined at necropsy for parenchymal and/or vascular disease, the type and extent of abnormality being recorded. The lung least damaged during

removal

removal was reserved for further investigation.

With few exceptions, in the earlier cases, the pelvic veins and those of the lower extremities, including calf veins, were examined for venous thrombosis.

(b) Assessment of ventricular hypertrophy

Total heart weights are routinely recorded in all cases. Ventricular hypertrophy was assessed by the following two methods:

i. Measurement of thickness of ventricular wall. The free walls of the right and left ventricles were measured at standard sites, the right ventricle being regarded as hypertrophic when this measurement exceeded 5 mm. (Zeek 1942), and the left when the measurement was greater than 13 mm.(Scott et al. 1955). Before such measurements can be meaningful it is important to know whether or not dilatation of the chamber is present. A dilated chamber with these dimensions must be hypertrophied, whereas a contracted chamber which exceeds them is not necessarily hypertrophic. Because there is no accurate method for the assessment of degrees of dilatation, the results of such measurements must be treated with some reserve. When a lesser degree of hypertrophy of a ventricle is present, dilatation may mask this slight hypertrophy. In the course of this study it soon became apparent that the results obtained by this method, even though recommended and widely used by others, were often difficult to interpret. Because of these deficiencies this method was abandoned in favour of;

ii. Separate ventricular weights. To achieve this the free wall and infundibulum of the right ventricle was dissected from the rest of the heart and the weight taken as representing that of the right ventricle. The free wall of the left ventricle, together with the septum, represented left ventricular weight. The method employed for the separation of the ventricles was that described by Keen (1955), except that the heart valves were not removed.

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It was necessary to have control values for comparative purposes, and to this end 53 normal hearts from African subjects, 20 years of age and over, were dissected and weighed in a similar manner. These were obtained from patients dying sudden traumatic deaths and were correlated with both height and body weight. The normal weight of the free wall and infundibulum of the right ventricle was found to be 66.3 Gms. (SD 7.7), and that of the septum and left ventricle to be 160.5 Gms. (SD 22.49). The normal LV/RV ratio was assessed as 2.48 Gms. (SD 0.21). The values obtained correlate well with those of a similar study by Fulton et al. (1952).

This method is a time-consuming procedure, but the results obtained not only clearly showed the presence or absence of ventricular hypertrophy, but also indicated which of the two ventricles was exclusively or predominantly enlarged, irrespective of the degree of dilatation.

(c) Histological examination.

This entailed a study of sections of relevant organs, stained by the ordinary haematoxylin and eosin method. Sections from the heart and lungs were in addition stained with Weigert's elastic stain for the purpose of studying structural changes involving the endocardium and lung vasculature, and with Toluidine Blue for endocardial changes. The findings relating to pulmonary vasculature are based on the criteria as laid down by Brenner (1935) and as accepted by most modern workers in this field. Histological study of the pulmonary arteries was performed on both the injected and non-injected lung. It soon became apparent,however, that the picture obtained in the injected lungs was erroneous, on account of the marked distension of such vessels with the radio-opaque medium which caused distension of the lumina and thinning of the walls. There was thus absolutely no correlation between the findings in the injected and non-injected lung.

Histochemical/...

(d) Histochemical methods

These were employed on myocardial tissue in the hope of finding a constant change which would distinguish cardiomyopathy clearly from other forms of heart disease. Such methods included:

(1) Staining for the enzyme succinic dehydrogenase after the method outlined by Nachlas et al. (1957), as cited by Pearse (1960).

(2) Staining for the enzyme DPN diaphorase after the method described by Nachlas et al. (1958).

(3) Perl's prussian blue reaction for ferric acids.

(4) Sudan-red stains for fat.

Methods for alkaline phosphatase (Gomori,as cited by Pearse 1960) and acid phosphatase (Gomori,as cited by Pearse 1960) were also tried. The former was not found of value because only trace quantities of alkaline phosphatase were present in myocardial tissue. The latter failed completely, presumably because the substrate was unsuitable although this substrate gave satisfactory results when used for renal tissue.

(e) Pulmonary arteriography

The method employed was that described by Short (1956), and the radio-opaque medium consisted of a barium sulphate suspension of 80% micropaque and 3% gelatine. The ideal medium for this purpose is one which, while filling the smallest arterioles, does not cross the capillary bed. The micropaque-gelatine medium satisfied these requirements.

After removal at necropsy and prior to injection the lungs were refrigerated for 48 - 72 hours.

It was noted that maximum inflation prior to injection was of great value in ridding the lungs of excess fluid and loosely attached antemortem thrombi which escaped via the pulmonary vessels. The lungs were then deflated and the radio-opaque medium injected at a pressure of 50 - 80 mm. Hg. Following injection the lung was again fully inflated and positioned on a 12" x 10" casette fitted with Fast Tungstate screens and Ilford Red Seal film.

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The film was exposed at 34 KV, 25 mA for 0.1 sec. at a distance of 48" for lateral views. A Watson mobile 100 mA unit was used and the films were developed manually in Planocop 1 : 1 for $1\frac{1}{2}$ minutes at 74°F. The resultant film was reasonably satisfactory, but there was room for improvement in contrast to enhance detail. The later series was exposed to Ilfex Non-screen film placed in a cardboard casette and inserted into a perspex film box which supported the lung. The Ilfex film was exposed at 64 KV, 25mA for 0.1 sec. at a distance of 20" for lateral views. These were developed in Planocop 1 : 1 for $2\frac{1}{4}$ minutes at 74°F., the increased time compensating for increased thickness of the emulsion of non-screen films. These showed a marked improvement of definition as compared with the screen-film technique.

In every case histological sections from the injected lungs were examined to confirm full distension of the pulmonary arteries before conclusions were drawn from the arteriograms (see Figs. 1 & 2, Plate I). Satisfactory injection, as according to Short (1956), meant a thinning of the arterial wall in relation to the size of the lumen, and smoothing-out of the normally deeply crenated elastic coat. Filling defects observed on arteriograms were investigated by gross dissection and histological examination.

Pulmonary arteriography proved to be of immense value in the study of right heart failure in establishing the level and extent of loss of vascular territory. Arteriograms were particularly helpful in assessing the number, size and distribution of pulmonary thrombo-emboli and in giving some indication as to the degree of reduction of pulmonary arterial capacity resulting from embolization

(f) Whole lung sections

These were prepared from the lungs on which arteriography was performed, and the method used was that described by Gough and Wentworth (1949). Whole lung sections proved to be of great value in the study of

emphysema/...

emphysema as regards the anatomic distribution and extent of parenchymal destruction. The collapse of emphysematous spaces in fresh necropsy lungs distorts the anatomic location of emphysema in relation to lobules and masks the true extent of parenchymal damage. Fixation of the lung in the expanded position is essential also for the recognition of the more serious centrilobular form of emphysema.

This work is presented in two parts, the first dealing with cor pulmonale, and the second with right ventricular enlargement in cardiomyopathy.

CHAPTER II

COR PULMONALE : A REVIEW OF THE LITERATURE

(A) IN GENERAL

The heart in cor pulmonale

The gross anatomical changes occurring in the heart in response to chronic pulmonary disease, especially emphysema, have been known for more than a century.

As cited by Parkinson and Hoyle in 1937, Senac (1783); Louis (1830); and Laennec (1846) are said to have remarked on the enlargement of the heart in asthmatics and in patients with emphysema. Sibson in 1848 described marked right ventricular enlargement of the heart found at necropsies performed on persons with emphysema who had died in congestive heart failure. Although Laennec had noted the biventricular nature of cardiac enlargement, this point was most strongly emphasized by Gardiner, who stated that he had not observed marked enlargement of the right heart without concurrent enlargement of the left.

In the latter half of the 19th century the bilateral nature of cardiac enlargement was mentioned by a number of writers, and left ventricular enlargement was believed by many to be due to associated chronic nephritis, chronic myocarditis, or atheroma, which were said frequently to occur together with emphysema.

The majority of the more recent necropsy studies (Kountz et al. 1936; Nemet and Roseblatt, 1937; Scott and Garvin, 1941; Spain and Handler, 1946; Zimmerman and Ryan, 1951; Walzer and Frost, 1954; Phillips, 1958; Padamavati and Joshi, 1946) of cor pulmonale show concomitant left ventricular enlargement of varying degrees in a significant number of cases of chronic cor pulmonale. Kountz et al. (1936) considered the cause of left ventricular enlargement to be unknown in their cases and made no mention of associated systemic hypertension. Parkinson and Hoyle

(1937) /...

(1937) maintained that hypertension could not be excluded as a cause of the left ventricular hypertrophy in such patients.

More recently, Michelson (1960) reviewed the evidence on ventricular hypertrophy in pulmonary disease and, adding data of his own, found that the thickness of the walls of the two ventricles varied from case to case at necropsy. Although, on an average, the increase in size as judged by the degree of thickness was approximately equal in the two ventricles, a consideration of such increase in terms of percentage showed the change to be greater in the right ventricle. He pointed out that an increase of about 3mm. while causing a 100% increase in the right ventricle, shows only about a 30% increase in the left ventricle. Michelson concluded that there was no way of knowing whether the absolute or relative change was important physiologically.

Altschule (1962), in his review of the studies of others (Cudkowitz, Fritts et al. and Nakamura), found that the left ventricle is also under strain and can enlarge in such cases. These deductions followed on studies in which simultaneous output measurements of the ventricles were undertaken. The majority of patients studied had bronchiectasis and silicosis, and a few had other types of fibrosing lung disease. Control patients, with one exception, showed that the left and right ventricular outputs did not differ by more than plus or minus 10% of the mean value. In patients with fibrosing lung disease, particularly bronchiectasis, the left ventricular output was significantly greater than that of the right. Only occasionally did patients with other forms of lung disease show such circulatory disturbances. These anatomical and physiological data would seem to indicate that the diagnosis of cor pulmonale does not imply strain solely, or even predominantly, on the right ventricle.

Following on the above, it has been postulated that the development of shunts from bronchial arteries to pulmonary arteries and veins, such as occur in fibrosing lung diseases, may increase considerably the flow into, and consequently the work of, the left ventricle (Altschule 1962). In this manner pulmonary heart disease places a great burden on the right ventricle because

of / . . .

of increased pressure and on the left ventricle as a result of increased flow. Rushmer (1958) claims to have shown that while the burden imposed by pressure loads is poorly tolerated by the right ventricle, the left ventricle sustains a pressure load more effectively than it does an increase in output.

Pulmonary hypertension in cor pulmonale.

In 1840 Budd described the reduction of the capillary circulation in emphysematous lungs. This curtailment of the pulmonary capillary bed was considered to lead to obstruction of the circulation through the pulmonary arteries and finally to oedema. Isaakssohn in 1871 described the widespread narrowing with subsequent thrombosis, rupture and atrophy of the capillaries in emphysematous lungs. This formed the anatomical basis for all subsequent opinion regarding cardiac involvement in emphysema. However, a few authors (Delafield 1884-5, 1886; Hoffman 1903; and Laubry and Routier 1922) questioned the importance of these changes as a cause of cardiac enlargement.

Parkinson and Hoyle (1937) quote several authors as having described, prior to 1930, sclerosis of the smaller pulmonary arteries in association with chronic lung disease, including emphysema and chronic bronchitis and emphysema, but there were many others who made no mention of such associated vascular changes in descriptions of the histology of the lungs in emphysema. Karsner (1933), however, considered emphysema the most important factor in the development of pulmonary arteriosclerosis.

More recent authors, in describing the histological changes occurring in the pulmonary vessels, have based their findings on the criteria outlined by Brenner (1935), but the structural alterations in the pulmonary vessels however remain a subject of much controversy. Parker (1940) noted the presence of vascular changes in 80% of 32 cases but found no correlation between such cases and right ventricular hypertrophy. He considered that arteriosclerotic changes in the small pulmonary arteries and arterioles in diffuse lung disease were the result rather than the cause of pulmonary hypertension. Arteriosclerotic changes in the small branches of the pulmonary arteries are also found in cases of

pulmonary/...

pulmonary thrombo-embolism (O'Neal and Thomas 1955; Barnard 1954a), and have been produced experimentally in animals by injecting fibrin emboli intravenously (Barnard 1954b; Harrison 1948).

McKeown (1952), in a necropsy study of 111 cases of chronic lung disease (including many different aetiological types), found marked vascular lesions to be uncommon even in the advanced cases, and observed that the incidence of severe vascular lesions was little different in emphysema with or without right ventricular hypertrophy and in controls. From a review of current views she concluded that the cause of right ventricular failure in some cases of emphysema was not to be found in the pulmonary vessels. Kernen et al. (1958), from a necropsy study of 125 patients with diffuse pulmonary emphysema and 54 controls, concluded that in the development of pulmonary hypertension vascular changes were a less important cause than either anoxia of shunting of blood from higher pressure bronchial arteries to pulmonary arteries.

From post-mortem angiographic studies of emphysematous lungs Junghanss (1959) stated that although there was a reduction in the capillary bed, there was still sufficient vasculature remaining to prevent cor pulmonale in diffuse "senile" emphysema. In the centrilobular type the emphysematous spaces caused distortion of the distal parts of vessels, resulting in increased pulmonary vascular resistance and cor pulmonale. Dunnill(1961), from injection-radiography-histology studies of the pulmonary vasculature in 44 emphysematous lungs, considered intimal fibrosis, destruction of the vascular bed, and thrombo-embolism to be of minor importance. The raised peripheral vascular resistance was due to vascular deformity and to pressure of emphysematous spaces on adjacent arteries. Precapillary anastomosis was an additional factor in bronchiectasis.

However, from a clinico-pathological study of 91 patients with chronic lung disease James and Thomas (1963) concluded that organic stenosis of small pulmonary arteries and arterioles was present in some cases of emphysema, and that this probably contributed towards pulmonary

hypertension/...

hypertension in these subjects. Hicken et al. (1965) have described the pulmonary arterioles in cases of emphysema, especially the centrilobular form, as showing a distinct circular media in all cases with right ventricular hypertrophy, and suggested that this might be the organic basis for the increased peripheral vascular resistance in emphysema. The presence of abnormal longitudinal muscle fibres internal to the inner elastic lamella, found in arterioles and arteries, was not considered to be related to pulmonary hypertension. According to Mitchell (1962), thrombo-embolism may occasionally cause cor pulmonale in emphysema.

von Euler and Liljestrand (1946) made the observation that hypoxia could cause a rise in pulmonary blood pressure in animals and in man, the mechanism being a reflex vasoconstriction of the pulmonary arteries. Evans (1946) concluded that while pulmonary hypertension results from both a diminution of the capillary bed and anoxic pulmonary vasoconstriction, the latter appears to be the more important. Motley et al. (1947) also found hypoxia to produce a considerable rise in pulmonary blood pressure. A number of experiments have since shown hypoxia to be an important cause of pulmonary hypertension (Dirken and Heemstra 1948; Lewis and Gorlin 1952; Peters and Roos 1952; Yu et al. 1953). The fact that cor pulmonale resulting from intercurrent bronchopulmonary infection can be reversed with treatment (Harvey et al. 1951, 1953), suggests that functional disturbances of the pulmonary vasculature are more important than the structural changes.

Friedberg (1966) considers that hypoxia in emphysema follows perfusion of hypoventilated portions of the lung, and that although the significance of shunts is not known they may also contribute to hypoxia.

Although the exact mechanism whereby chronic lung disease produces heart failure is still not perfectly understood, it can now be confidently stated that the process is not simply the result of a reduction in number of the pulmonary capillaries and/or structural alterations in the arteries and arterioles with consequent increased resistance in the pulmonary circulation.

Circulatory/...

Circulatory haemodynamics in cor pulmonale

The circulatory haemodynamics in cor pulmonale appear to be very different from those in most other forms of heart disease. Bloomfield et al. (1946); Riley et al. (1948); and Ferrer and Harvey (1959) have shown that the cardiac output in patients with chronic bronchitis and emphysema does not decrease once right ventricular failure develops, but remains normal or may be higher than normal. The cardiac output, if raised during failure, usually returns to normal levels with recovery from failure.

Oedema in cor pulmonale

A slightly raised jugular venous pressure in chronic lung disease does not necessarily indicate heart failure (Wood 1956), and oedema has been observed in patients with severe anoxia in whom the heart was of normal size, or only slightly enlarged (Fulton 1953). That oedema and a raised jugular venous pressure may develop in the absence of right ventricular failure is further supported by the work of Mounsey et al. (1952) who measured the right ventricular systolic pressure in 8 patients with so-called "congestive failure" due to chronic lung disease and found that the pressure was only slightly elevated in 4 patients. Simpson (1959) reported that in some emphysematous patients who were hypoxic, hypercapnaic and oedematous, the oedema failed to respond to the usual diuretic measures but regressed spontaneously.

Because of these observations, Campbell and Short (1960) suggested that some mechanism other than heart failure might be responsible for the development of oedema in chronic cor pulmonale. While not discarding the sequence pulmonary hypertension ------ right ventricular hypertrophy ------ right ventricular failure ------ venous engorgement ------ oedema, they suggested that this might be an uncommon cause of oedema in cor pulmonale. These authors, from their own personal observations and those of others, noted a relationship between respiratory acidosis and oedema in cor pulmonale, and postulated a mechanism for oedema production on the basis of respiratory dysfunction and acidosis. They advanced the idea that

a / . . .

a raised blood PCO_2 was followed by an increase in the amount of carbonic acid formed in the renal tubular cells; the hydrogen ions excreted into the tubules were then exchanged for sodium ions which pass, together with the bicarbonate ions, into the blood, thereby increasing the reabsorption of "bicarbonate-bound base". With the development of oedema in emphysema, the compliance of the lungs is reduced, and the non-elastic resistance increased. This leads to further hypoventilation by increasing the work of breathing, and thus results in the establishment of a "self-aggravating cycle".

Ellis (1961) suggested that the diffuse enlargement of the kidneys in chronic cor pulmonale was a form of work hypertrophy, developing to compensate for chronic respiratory acidosis.

Several authors (Green and Dundee 1952; Latts et al. 1956; Flint and Warrack 1958; Ellis 1961) have commented on the association between peptic ulceration and chronic cor pulmonale. Latts et al. (1956) suggested that the association might be explained on the basis of respiratory acidosis and a high acid output by the parietal cells of the stomach. They concluded that although the exact relationship between hypersecretion of gastric hydrochloric acid and peptic ulceration is not known, the existence of an association between the two is widely recognised.

(B) IN SOUTH AFRICA AND SOME OTHER PARTS OF THE CONTINENT

White (1961) stated that cor pulmonale was quite frequent in many countries in Africa and was largely due to fibrotic changes in the lungs secondary to infection, and to emphysema. Rarely, it was caused by bilharziasis.

Becker (1946), while stating that cor pulmonale was an important cause of congestive heart failure in the African and Coloured subjects in South Africa, made no comment regarding the aetiological aspects of the disease.

Gelfand (1957), in Southern Rhodesia, suggested that chronic cor pulmonale was probably of equal incidence in the Bantu and European, and that chronic bronchitis or advanced silicosis might be responsible in some. He also commented that although cor pulmonale due to bilharziasis might be common in Egypt, it was certainly not frequent in the endemic areas in Rhodesia and South Africa.

Siew (1958) in South Africa found the incidence for Whites (5.5%) to be higher than that (2.2%) for Africans, chronic bronchitis and emphysema, present together as a rule being the commonest cause of cor pulmonale in both African and White races and also in both sexes. Tuberculosis and silicosis, together or separately, constituted the second most important cause among African and European males. Whereas tuberculosis alone accounted for this in African females, kyphoscoliosis was the second commonest cause in White females. While the next most important cause among European males and females was carcinoma of the lung, bronchiectasis was found to be the most important factor in African males and females. Only 2% of all White races with cor pulmonale showed evidence of bronchiectasis. Bilharzia was a rare cause. Causes such as obliterative pulmonary arteriolitis and repeated pulmonary embolism were uncommon in White races and were not observed in African subjects. Siew also noted that African patients had a wider age range for cor pulmonale (males 40 - 60, females 20 - 60) than the White races, the majority of whom were in the 60+ age group.

Gelfand (1957) remarked,"It is an interesting observation that the African rarely develops acute cor pulmonale". This correlated with the supposedly extremely low incidence of peripheral venous thrombosis in the African. Idiopathic thrombophlebitis, especially of the femoral vein, has been reported in the African (Fisher 1941; Gelfand 1946), but pulmonary embolism is said to be extremely rare in this condition. Schrire (1960), from a clinical study of heart disease, stated that "pulmonary embolism requiring electrocardiographic investigation was not encountered in the Bantu in this series".

Contrary/...

Contrary to the above findings, Turner (1962), reporting on 16 cases of pulmonary heart disease among the Africans in Mombasa, found acute cor pulmonale resulting from massive pulmonary embolism in 2 patients and one case with thrombo-embolic obliterative pulmonary hypertension.

The relative incidence of cor pulmonale in most series in South Africa (Becker 1946; Powell and Wright 1965; Higginson et al. 1960; Cosnett 1962) is found to vary from about 10 - 16%. In Rhodesia the reported incidence (Gelfand 1957; Baldachin 1963) is lower and varies between 4 - 5%, while figures from Uganda are extremely low. Clinical studies in Uganda give an incidence of 0.28% (Shaper and Williams 1960), but a necropsy investigation (Davies 1948) reveals a 4% incidence.

The figures quoted for South Africa are also higher than that (5.0%) reported for central London, England (Wood 1956). However, Flint (1954), in the northern industrial city of Sheffield, found that in all patients with congestive heart failure 40% of males and 8.5% of females had cor pulmonale, chronic bronchitis and emphysema being by far the commonest cause.

Definitions and Classification

Lewis (1933) defined heart failure as a inability on the part of the heart to maintain an adequate circulation. This may apply when the burden of excessive work is imposed on either one or both ventricles simultaneously. Consequently, terms such as right ventricular failure, left ventricular failure and biventricular failure came into usage, and the term congestive heart failure has been used to describe both right ventricular and biventricular failures (Wood 1956). Failure of both ventricles may occur ab initio or the failure of one ventricle may lead to the failure of the other.

The commonest cause of right ventricular enlargement and failure is chronic left ventricular failure. It also occurs in response to cardiac or pulmonary disorders which result either in obstruction to flow out of the right ventricle or through the pulmonary circulation, or to an increase in the volume of blood within the right ventricle.

Once /...

Once it became apparent that certain chronic diseases of the lungs could produce a secondary effect on the heart, terms such as cor pulmonale and pulmonary heart disease came into usage. This was in keeping with the tendency to divide heart disease according to aetiology. Distinction was soon made between the acute (McGinn and White 1935), subacute (Brill and Robertson 1937; Greenspan 1934), and chronic forms of cor pulmonale.

The term acute cor pulmonale is applied when a rapid dilatation of the right heart occurs, secondary to acute pulmonary hypertension. By far the commonest cause of acute pulmonary hypertension is a massive sudden occlusion of the pulmonary circulation. Such sudden massive obstruction of the lesser circulation occurs, in the vast majority of cases, as a result of extensive pulmonary embolism, commonly originating in the leg veins (White 1951). Patients suffering acute pulmonale from this cause either die rapidly or recover if they survive long enough for the clot to retract and so relieve the obstruction. Acute cor pulmonale can also develop as a result of acute compression of the lungs, as occurs in valvar pneumothorax (Hudson 1965), sudden increase in herniation of abdominal viscera through the diaphragm (McGinn and Spear 1941), and acute spontaneous mediastinal emphysema (Klein 1947).

Subacute cor pulmonale refers to a progressive, intermittent obstruction of the pulmonary arteries occurring over a period of several months (Schrire 1963), and follows either pulmonary thrombo-embolism (Brill and Robertson 1937; Wood 1956), or embolism of neoplastic tissue in the lung vessels and perivascular lymphatics with widespread arterial thrombosis (Greenspan 1934; Storstein 1951).

In the past, chronic cor pulmonale was almost synonymous with chronic bronchitis and emphysema ("the emphysema heart") because in certain countries like Great Britain this was the most frequent type observed, and much of the earlier literature was thus confined to this single cause. As the recognised aetiological factors (other than the existence of chronic pulmonary disease) giving rise to right ventricular enlargement and failure

multiplied/...

multiplied, e.g. chronic left ventricular failure, mitral stenosis, certain congenital anomalies of the heart, much confusion arose regarding the precise definition of the term chronic cor pulmonale. As a result, as recently as 1960, a committee of experts of the World Health Organisation met to try to solve the difficulty. In 1961 their conclusions appeared in a report (WHO, 1961), and chronic cor pulmonale was defined as "hypertrophy of the right ventricle resulting from diseases affecting the function and/or structure of the lungs, except when these pulmonary alterations are the result of diseases that primarily affect the left side of the heart or of congenital heart disease". This definition thus excludes lung changes resulting from mitral stenosis, left ventricular failure, and congenital anomalies of the heart, but still includes conditions such as "primary" or thrombo-embolic pulmonary hypertension. Their recommended classification of chronic cor pulmonale is as follows:-

1. Diseases primarily affecting air passages, lungs and alveoli:
   - 1.1 Chronic bronchitis with generalised airway obstruction, with or without emphysema.
   - 1.2 Bronchial asthma.
   - 1.3 Emphysema without bronchitis and asthma.
   - 1.4 Pulmonary fibrosis, with or without emphysema, due to tuberculosis, pneumoconiosis, bronchiectasis, other pulmonary infections, radiation, and muco-viscoidosis.
   - 1.5 Pulmonary granulomata and infiltrations due to sarcoidosis, chronic diffuse interstitial fibrosis, berylliosis, eosinophilic granuloma or histiocytosis, malignant infiltration, scleroderma, disseminated lupus erythematosis, dermatomyositis, and alveolar microlithiasis.
   - 1.6 Pulmonary resection.
   - 1.7 Congenital cystic disease of the lungs.
   - 1.8 High altitude hypoxia.
2. Diseases primarily affecting movements of the thoracic cage:
   - 2.1 Kyphoscoliosis and other thoracic deformities.

2.2 / . . .

2.2 Thoracoplasty.

2.3 Pleural fibrosis.

2.4 Chronic neuromuscular weakness e.g. poliomyelitis.

2.5 Obesity with alveolar hypoventilation.

2.6 Idiopathic alveolar hypoventilation.

3. Diseases primarily affecting pulmonary vasculature:

3.1 Arterial wall (a) primary pulmonary hypertension
(b) polyarteritis nodosa
(c) other arteritis.

3.2 Thrombotic disorders (a) primary pulmonary thrombosis
(b) sickle cell anaemia.

3.3 Embolism (a) from outside lungs
(b) schistosomiasis
(c) malignant embolism
(d) other embolism.

3.4 Pressure on main pulmonary arteries and veins by mediastinal tumours, aneurysm, granulomata, or fibrosis.

It was also recommended that the right ventricle be regarded as hypertrophied if the outflow tract measured over 5mm. in thickness, and that emphysema be described with regard to its anatomic distribution as observed after formalin fixation of post-mortem lungs in their distended state.

CHAPTER III

FIBROSING LUNG DISEASE AS A CAUSE OF CHRONIC COR PULMONALE IN THE AFRICAN

Widespread pulmonary fibrosis can be caused by irritants (pneumoconiosis, lipid pneumonia), infections (tuberculosis and other pulmonary infections), bronchiectasis, radiation, and mucoviscoidosis. It is also a feature of the Hamman-Rich syndrome, and may frequently occur in scleroderma, dermatomyositis, polyarteritis nodosa, systemic lupus erythematosis, rheumatoid arthritis, and interstitial pneumonia. In some cases the cause is obscure (WHO.1961, Hudson 1965).

As commented on by Wainwright (1964), infective conditions, particularly tuberculosis and amoebiasis, are still common in the African in Durban. In populations in which tuberculosis is still prevalent it is an important factor in the development of bronchiectasis.

Impairment of pulmonary function in chronic pulmonary disease is dependent on several factors. Basically these include the extent of fibrosis, the degree of emphysema, and the state of the bronchial tree (Theodcs 1954). Right ventricular hypertrophy and failure follow when extensive damage to the lung parenchyma and vasculature occur. Ventilatory defects result not only from widespread parenchymal damage but also from restrictions caused by extensive fibrotic thickening of the pleura (Bromberg and Robin 1963). The development of pulmonary hypertension is dependent both on a reduction of the pulmonary vascular bed and on vasoconstriction resulting from hypoxia. Dunnill (1961) emphasized the presence of bronchopulmonary shunts as an added factor in the development of cor pulmonale in bronchiectasis.

ANALYSIS /...

ANALYSIS AND MATERIAL

In a series of 30 consecutive cases of cor pulmonale in African patients investigated at necropsy chronic fibrosing lung was incriminated as a cause of the right ventricular hypertrophy and failure in 13. Among these 30 cases there were 2 examples of acute cor pulmonale while the rest were either the subacute or chronic forms of right ventricular strain and failure. Thus 46.4% of all the more chronic forms of cor pulmonale followed on chronic fibrosing lung disease and its complications, and this proved to be the most common cause of such failure encountered, at necropsy, in African subjects. Included in this category are 4 patients with bronchiectasis.

Of the 13 cases discussed here, 9 were males and 4 were females. Their ages varied from 26 years to 70 years, 9 being under 50 years. The average age was 52.1 years. The relevant necropsy findings in these 13 cases are summarised in Table I. It is evident from Table I that the most important single factor contributing towards pulmonary fibrosis in this series was tuberculosis, being incriminated in 10 of the 13 patients studied. In the remaining 3 cases, (one case of pulmonary fibrosis and emphysema, and 2 cases of bronchiectiasis) the aetiology remains unknown.

When present, tuberculosis was either fibrocaseous in type, or consisted of widespread healed fibrotic lesions. Tuberculosis causing bronchiectiasis was observed in 2 patients.

All cases listed in Table I showed bilateral pulmonary involvement. Although the degree of pulmonary parenchymal loss and fibrosis varied greatly, 12 of these 13 cases showed in addition gross pleural thickening and extensive adhesions between lung and chest cage and/or diaphragm. Furthermore, emphysema was observed in 8 of 10 cases where this was looked for (Fig. 2, Plate II). In Cases 2, 3 and 4 whole lung sections were damaged during removal at necropsy, and no comment regarding emphysema is therefore possible in these 3 patients.

Histological /...

llowing on Fibrosing Lung Disease

ry Findings	Aetiology
ons between lungs and thoracic cage.	Tuberculosis
diaphragm	Tuberculosis
and thoracic cage and diaphragm.	Tuberculosis
and thoracic cage and diaphragm.	Tuberculosis
ions between lungs, thoracic cage	Tuberculosis
	Unknown
and emphysema.	Tuberculosis
ulmonary arterial thrombo-embolism.	Tuberculosis
ions between lungs and diaphragm.	Tuberculosis
lungs.	Unknown
Emphysema of contralateral lung.	Unknown
and middle lobe. Emphysema.	Tuberculosis
Emphysema of contralateral lung. e and diaphragm.	Tuberculosis

Histological examination of the lungs in these cases, in addition to confirming gross naked-eye changes, revealed structural alterations of the pulmonary arteries. Such changes consisted of (1) intimal proliferation with narrowing of the lumen of muscular arteries and bronchial arteries, the latter particularly in cases of bronchiectasis (Fig. 6, Plate II); (2) an additional layer of longitudinal muscle fibres with elastic tissue hyperplasia in the intima of both the larger and smaller muscular arteries (Fig 3, Plate II); (3) the presence of muscularized vessels below 100 μ in diameter (Fig. 2, Plate II); (4) fresh and organising thrombotic occlusions of the pulmonary arteries (Fig. 5, Plate II).

Thrombo-embolic occlusions, while involving vessels of all sizes, are rarely widespread, being extensive in one case (Case 8) only. A source for embolization was found in the calf veins in 6 patients showing pulmonary thrombo-embolism, including that with extensive involvement. In 3 patients in whom thrombotic occlusions of a few pulmonary arteries were present no source for embolization was found at necropsy. Thus local thrombosis and embolization may be a factor in explaining the thrombotic occlusions found in the pulmonary arteries of cases with chronic disease.

Angiograms showed loss of normal pulmonary arterial pattern with distortion in the areas where extensive fibrosis was present (Fig. 1, Plate II). Thrombotic occlusions involving secondary branches were sometimes observed and accounted for large filling defects in the pulmonary arterial tree. In some cases loss of pulmonary arterioles, simulating the pruned-tree effect, was observed. When present the latter change was always generalised and not related solely to areas of scarring. Sub-pleural bronchopulmonary anastomoses were frequently observed.

The heart, in all cases of chronic fibrosing lung disease with cor pulmonale, showed right ventricular hypertrophy and dilatation. As shown in Table I, the total heart weights were not markedly increased, all except 4 being below 400 Gms.

Table II shows the results obtained when cardiac hypertrophy was

assessed /...

assessed by measuring the greatest thickness of the free wall of the right and left ventricles in 6 patients.

TABLE II

MEASUREMENT OF THICKNESS OF VENTRICULAR WALLS IN 6 CASES OF FIBROSING LUNG DISEASE AND CHRONIC COR PULMONALE IN AFRICANS

Case No.	Sex	Age	Total Heart Weight (Gms)	RV thickness (mm)	LV thickness (mm)
1	M	56	270	6	12
2	M	60	450	7	16
3	M	58	500	10	16
4	F	36	330	6	14
12	M	32	450	7	18
13	F	65	340	6	13

TABLE III

SEPARATE VENTRICULAR WEIGHTS AND LV/RV RATIO IN 5 CASES OF FIBROSING LUNG DISEASE WITH COR PULMONALE IN AFRICANS

Case No.	Sex	Age	Total Heart Weight (Gms)	RV (Gms)	LV (Gms)	LV/RV
5	M	54	350	108	131	1.21
6	F	70	370	104	135	1.29
9	F	65	370	105	126	1.20
10	M	26	350	82	145	1.76
11	M	33	470	164	166	1.01

While right ventricular thickness exceeded 5 mm. in all cases shown in Table II, 4 patients showed a left ventricular thickness of over 13 mm.

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Left ventricular hypertrophy however, while queried in Case 3, was not suspected in any of the other 5 cases on macroscopic examination.

Table III shows separate ventricular weights and LV/RV ratios in 5 cases of fibrosing lung disease and cor pulmonale.

The right ventricular weights were above the normal values for Africans (66.3, SD 7.7), in all 5 instances. The left ventricular weights were within the normal range (160.5, SD 22.49) in all patients. The LV/RV value was below normal in every case (2.48, SD).21). These results indicate exclusive right ventricular hypertrophy in cases where cor pulmonale followed on fibrosing lung disease. Bronchiectasis was present in Cases 10 and 11, and both these show exclusive right ventricular hypertrophy.

DISCUSSION

Tuberculosis, in countries where it is still prevalent, is recognised as an important aetiological factor in the development of both pulmonary fibrosis and bronchiectasis, and consequently plays a significant role in the incidence of cor pulmonale within such populations. In Great Britain the incidence of chronic cor pulmonale is known to have fallen significantly since tuberculosis as an infection has been controlled and reduced to an uncommon disease among its population. In Africa, in contrast to most Western countries, infections as a whole remain a major cause of morbidity and mortality among the indigenous people in many parts of the continent. It is not surprising therefore that chronic infective pulmonary disease, particularly pulmonary tuberculosis, and its complications should be found to be the most common cause of cor pulmonale among African subjects in and around Durban; tuberculosis by itself being responsible for over a third of all cases of the more chronic forms of cor pulmonale encountered in this study. Although the above finding differs from the views of both Siew (1958) and Schrire (1960), who regard chronic bronchitis and emphysema as the usual aetiological factors responsible for cor pulmonale in the African, it supports the comment

by / . . .

by White (1961) that fibrotic lung disease secondary to infection is largely responsible for the development of this form of heart failure among this race group in Africa. As shown in the present series, the complication of cor pulmonale arising from pulmonary changes caused by tuberculosis can occur in young subjects, and this probably explains the wider age range obtained by Siew (1958) for cor pulmonale in Africans as compared with Whites.

The development of right ventricular strain and failure in cases of chronic pulmonary tuberculosis does not appear to be related solely to pulmonary parenchymal damage by fibrosis. Associated fibrotic thickening of the pleura and adhesions between lung, chest cage and diaphragm were always present and must surely have interfered with movements of the thoracic cage and consequently with ventilation. Significant emphysema was often also present. A reduction in the pulmonary vascular bed in these cases besides being related to areas of scarring and emphysema was also found to be due to pulmonary arterial thrombo-embolism. The latter, however, was rarely extensive, but its effect on an already reduced pulmonary arterial tree must be considered significant. Structural changes in the small pulmonary arteries, similar to those described in emphysema and some cases of cardiomyopathy were found. While such changes may be secondary to the presence of emphysema, one cannot exclude the possibility of their being secondary to pulmonary hypertension. It follows therefore that more than one factor is responsible for the development of cor pulmonale in cases of chronic pulmonary tuberculosis. Besides the curtailment of the pulmonary arterial tree, ventilatory defects and hypoxia result from damage to the lung parenchyma and from restriction caused by extensive pleural fibrosis and adhesions between lungs, chest cage and diaphragm, emphysema being a further contributory cause. That such additional factors play an important role in the production of cor pulmonale in cases of fibrosing lung disease secondary to tuberculosis correlates with the views of Bromberg and Robin (1963).

In three of the 13 cases investigated the aetiology of the pulmonary

pathology/...

pathology was not ascertained. These included one case of pulmonary fibrosis with emphysema, and 2 cases of bronchiectasis.

The absence of pneumoconiosis as a cause of cor pulmonale is explained by the fact that all such cases are now diverted to the district surgeon for necropsy and relevant organs are forwarded to the Pneumoconiosis Bureau of South Africa. As a result, no comment is possible on the role of pneumoconiosis in the development of cor pulmonale in the African in Durban.

The heart in cases of pulmonary fibrosis with cor pulmonale was usually below 400 Gms. in weight, indicating mild to moderate enlargement. The two methods employed in studying cardiac enlargement, while showing negligible variation in regard to hypertrophy of the right ventricle, gave conflicting results regarding the state of the left ventricle. As reported by others also (Kountz et al. 1936; Nemet and Roseblatt 1937; Scott and Garvin 1941; Spain and Handler 1946; Zimmerman and Ryan 1951; Walzer and Frost 1954; Phillips 1958; Padmavati and Joshi 1964), measurements of the thickness of the free walls of the ventricles frequently yielded values indicative of left ventricular hypertrophy, but separate ventricular weights, where these were assayed, always showed pure right ventricular hypertrophy. It is therefore reasonable to conclude that, while bronchopulmonary shunting with consequent hypoxia and diastolic overload of the left ventricle, due to the bronchial veins draining into both atria (Altschule 1962), may occur in fibrosing lung disease, results show that in this series the left ventricular overload is relatively unimportant on account of there being pure right ventricular hypertrophy. In bronchiectasis, where shunting is said to be most significant (Dunhill 1962), no increase above normal weight for the left ventricle was found in the 2 cases in which separate ventricular weighing was performed. Case 11 in fact showed gross right ventricular hypertrophy with a weight approaching that of the normal left ventricle (plus septum) and a LV/RV ratio of close to unity, but a normal weight value for the left ventricle. It is also of interest that the left ventricle was not markedly dilated in any of

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of the cases investigated in this series, and erroneous results on measurement of its free wall are believed to have resulted from inadequate dilatation of this chamber, since it has been stressed that for this method to be of any value a chamber should be adequately dilated.

The findings with regard to the heart in cases of fibrosing lung disease with cor pulmonale thus show neither hypertrophy nor gross dilatation of the left ventricle, which must therefore be considered unaffected under such circumstances.

SUMMARY

1. Fibrotic lung disease, secondary especially to tuberculosis, was found at necropsy to be the commonest cause of chronic cor pulmonale among African subjects in Durban and its environs.

2. The pathogenesis of right ventricular strain and failure in such cases has been discussed.

3. Cardiac enlargement in these conditions is described and discussed.

It has been shown that hypertrophy involves the right ventricle exclusively.

CHAPTER IV

THROMBO-EMBOLIC COR PULMONALE IN THE AFRICAN

Pulmonary thrombo-embolic disease may lead to acute, subacute, or chronic cor pulmonale, and while it is a common cause of the acute type it is a relatively infrequent aetiologic factor in the production of chronic cor pulmonale. However, of the many possible causes of obliterative pulmonary hypertension it has been suggested (Goodwin 1960), that pulmonary thrombo-embolism is probably the commonest.

While the occurence of pulmonary thrombo-embolism is not infrequent in the chronically bedridden, especially those with severe heart disease and with malignancy, it has also been found to occur in active, previously healthy young persons for reasons as yet unknown (Goodwin et al. 1963). The latter thus form a group quite distinct from the former in whom the pathogenesis is understandable.

As early as 1928, Ljundhahl (as cited by Friedberg 1966 and Wilhelmsen et al. 1963) indicated that there was a chronic form of pulmonary heart disease which followed on chronic pulmonary emboli, and he concluded that these resulted from recurrent embolism as opposed to local pulmonary arterial thrombosis.

Belt (1939a) stated that cor pulmonale resulted from organisation of emboli with subsequent obliteration of a large part of the arterial tree. He described 4 cases of recurrent embolization involving the pulmonary arteries and occurring over a period of from 3 months to 6 years. Carroll (1950) reported 5 cases of chronic cor pulmonale resulting from obstruction of the pulmonary arteries, of which 4 were believed to be embolic in origin and one to have resulted from local thrombosis. Petch (1951) emphasized that chronic failure could follow recurrent pulmonary embolization, and Erhner et al. (1959) recorded the occurrences of chronic cor pulmonale following thrombo-embolism in 3 previously healthy young men who also

showed/...

showed evidence of peripheral venous thrombosis. Larger series of cases of thrombo-embolic cor pulmonale have recently been reported by Owen et al. (1953); Thompson and Hamilton (1962); Goodwin et al. (1963); and Wilhelmsen et al.(1963).

Regarding the clinico-pathological picture in pulmonary thrombo-embolism, there appear to be two quite distinct forms. In the one, occlusion occurs in the large pulmonary arteries, is associated with pulmonary vascular or cardiac disease, and an obvious source for embolization is usually present. In the second type, occlusion involves the arterioles and muscular arteries, and such patients show clinical evidence of progressive pulmonary hypertension without obvious cause. However, larger arteries may be obstructed in the absence of heart disease. It has been suggested that larger emboli may come from the leg veins, and that thrombosis in the small pelvic radicles may give rise to emboli of microscopic size (Goodwin et al. 1963).

As regards pathogenesis, evidence favours the view that pulmonary vascular obstruction is embolic in origin in the vast majority of cases, and that cor pulmonale results from recurrent episodes of pulmonary embolization (Belt 1939b; Owen et al. 1953; O'Neal and Thompson 1955; Thompson and Hamilton 1962; Wilhelmsen et al. 1963).

Although evidence favours the mechanical block theory with resistance to flow, a consequent drop in cardiac output and strain on the right heart as important factors resulting from pulmonary embolization, disagreement exists with regard to the vasoconstrictive factor in relation to smaller emboli. The extent of damage to the pulmonary vascular bed, necessary to cause severe circulatory disturbance has been shown experimentally to be over 65% of its cross-sectional area; a cut-off of more that 85% results in death (Friedberg 1966). Wood (1952) considered that two-thirds of the lung vasculature had to be destroyed before pulmonary hypertension was likely to occur.

Fineberg and Wigger (1936) observed that lesser degrees of

obstruction/...

obstruction could lead to an increase in the pulmonary vascular resistance with a rise in right ventricular and pulmonary arterial pressures. From experimental evidence Daley et al. (1951) and Knisely et al. (1957) considered reflex vasoconstriction did not occur with small pulmonary emboli. However, Hyman et al. (1964) found that shock, pulmonary hypertension, and right ventricular strain may follow small vessel embolization shown at necropsy to involve less than 50% of the cross-sectional area of the pulmonary arteries. It was considered therefore that the remainder of the pulmonary bed must have been diminished by active reflex vasoconstriction. This view is supported by the more recent experimental studies of Williams (1956); Gootman et al. (1962); and Vitolo et al. (1965).

The possibility of a pulmono-coronary reflex operating at times in instances of small emboli has been suggested by de Takats et al. (1939). They suggested deaths in such patients to be due to autonomic reflexes causing spasm of the unobstructed pulmonary vessels, or to a reflex vasoconstriction of the coronary arteries mediated by the vagus nerve.

ANALYSIS OF MATERIAL

Although clinical distinction is made between the acute, subacute and chronic forms of thrombo-embolic cor pulmonale it is not easy to distinguish between the latter two forms at necropsy on account of the similar pathological features present in both. Clinical separation into subacute and chronic types is based largely on the duration of heart failure, and such evidence was not always available from case histories. Hence all instances of thrombo-embolic cor pulmonale with evidence of pure or predominant right ventricular hypertrophy and chronic passive venous congestion of the organs will be referred to as cor pulmonale from chronic recurrent pulmonary thrombo-embolism. The diagnosis of acute cor pulmonale was made at necropsy in those cases showing recent pulmonary thrombo-embolism, marked dilatation of the right side of the heart without

exclusive/...

exclusive or preponderant hypertrophy of the right ventricle, and signs of acute congestion of the viscera.

In 30 consecutive cases of cor pulmonale investigated in this series, 9 were thrombo-embolic in origin. Of these 9 patients, 5 were females and 4 males, and their ages ranged from 19 to 70 years. Six were in the 40-plus group, and the remaining 3 patients were 19 years, 33 years, and 35 years of age.

Acute thrombo-embolic cor pulmonale was encountered on two occasions, while the remaining 7 cases showed the more chronic form of right heart failure resulting from recurrent episodes of pulmonary thrombo-embolism. Table I summarises the relevant necropsy findings in these 9 cases.

As observed in Table I the total heart weights in cases of thrombo-embolic cor pulmonale, even those with recurrent episodes of pulmonary thrombo-embolism, showed little increase, being below 400 Gms. in all except one instance (Case 7). In the first 4 cases ventricular hypertrophy was assessed by measuring the greatest thickness of the free wall of the right and the left ventricles (Table II).

These results show the right ventricle to be hyperthropic in the 2 cases where cor pulmonale followed on recurrent pulmonary thrombo-embolic disease, and this correlates with the impression gained by naked-eye examination of these hearts.

Hypertrophy of the left ventricle is evident by measurement in 3 cases. While this could be explained on the basis of systemic hypertension in Case 2, no explanation for such was apparent in the other two cases. On macroscopic examination of the specimen,however, left ventricular hypertrophy was not suspected.

In the remaining 5 cases, hypertrophy was assessed by weighing the ventricles separately. Ventricular weights and LV/RV ratios in these further cases of recurrent pulmonary thrombo-embolism are shown in Table III.

Table I./...

›r Emboli	Other Disease	Cause of Death
ɪimb and ɪmined.	Nil apparent.	Acute Cor Pulmonale
ɔeal, and	Carcinoma of Bladder	Acute Cor Pulmonale
.ng into throm- ɹeg veins	Posteriorly placed (R) lobe amoebic liver abscess	Chronic Cor Pulmonale
Leg nil.	As above	As above
ɪ.	Nil apparent	As above
.iteal	Malnutrition and Cachexia.	As above
›elvic	Nil apparent.	As above
.eft	Nil other than local- ized apical T.B.	As above
.	Amoebic liver abscess plus cerebral cysticercosis	As above

TABLE II

MEASUREMENT OF VENTRICULAR WALL THICKNESS IN 4 CASES WITH PULMONARY THROMBO-EMBOLIC COR PULMONALE

Case	Sex	Age	Total heart Weight (Gms)	RV thickness (mm)	LV thickness (mm)	Cause of death
1	F	50	355	4	12	Acute cor pulmonale
2	M	70	350	3	20	Acute cor pulmonale
3	M	70	350	7	14	Chronic cor pulmonale
4	M	35	380	7	15	Chronic cor pulmonale

TABLE III

SEPARATE VENTRICULAR WEIGHTS AND LV/RV RATIO IN 5 CASES WITH PULMONARY THROMBO-EMBOLIC COR PULMONALE

Case	Sex	Age	Total heart Weight (Gms)	RV Weight (Gms)	LV Weight (Gms)	$\frac{LV}{RV}$	Cause of death
5	F	65	370	98	145	1.48	Chronic cor pulmonale
6	M	40	250	61	92	1.51	"
7	F	50	440	105	213	2.02	"
8	F	19	360	101	146	1.46	"
9	F	33	350	101	126	1.26	"

An obvious increase in right ventricular weight (normal mean 66.3 Gms. SD 7.7) is evident in 4 of the 5 cases shown in Table III. In the one patient (Case 6) where this is not apparent, both total heart weight and left ventricular weight are well below normal and the body weighed only 39.1 kilograms. In view of these findings and a LV/RV ratio of 1.51 (normal 2.48), the right ventricle can in this case also be considered predominantly, if not exclusively, enlarged although weighing 61 Gms.

Left ventricular weights were within or below normal range (160.5 Gms. SD 22.49) in all except Case 7. Here the only blood pressure reading (130/90) was taken during failure but both kidneys showed features

suggestive/...

suggestive of chronic focal pyelonephritis, so that systemic hypertension could not be excluded. Nevertheless, the LV/RV ratio was below the normal value, as in all other cases.

Histological examination of the heart revealed no abnormality other than hypertrophy of the muscle fibres where this was suspected.

The lungs at necropsy, in all 9 cases, showed extensive involvement of the pulmonary tree by thrombo-emboli. Although lung infarction was not observed in the two patients in whom death resulted from acute thrombo-embolic cor pulmonale, 5 of the 7 patients with recurrent pulmonary thrombo-embolism showed evidence of recent infarction. In every case arteries of both lungs were involved, and in 8, multiple intrapulmonary branches of varying sizes were affected. Table IV illustrates the distribution of the thrombo-emboli in pulmonary arteries.

In all 9 cases, elastic arteries were affected at one or other level. Similarly, muscular arteries were involved in all instances. Arteriolar involvement was demonstrated by histological examination in 5 patients and was found to be extensive in 1 case (Case 3).

Arteriography was performed on the one lung of 4 patients with thrombo-embolic cor pulmonale showing evidence of right ventricular hypertrophy and failure. In all 4 instances the arteriogram showed large filling defects caused by obstruction of either secondary or tertiary branches of the pulmonary artery (Fig. 1 - 3, Plate III). Areas or segments not affected by thrombo-emboli showed a normal arterial and arteriolar pattern. These arteriograms, together with the knowledge that the contralateral lung was also involved, must suggest a considerable reduction in the total pulmonary arterial bed.

Recent haemorrhagic infarction of the lung was present in 5 of the 9 cases of thrombo-embolic cor pulmonale investigated in this series (Figs. 1 - 3, Plate III). All 5 were examples of recurrent pulmonary thrombo-embolism. Evidence of healed infarction was noted in one of the 5 plus another case. Thus 6 of the 7 patients with cor pulmonale from

recurrent/...

recurrent episodes of pulmonary thrombo-embolism can be said to have suffered lung infarction at some stage of the disease. Abscess formation from secondary infection of the infarcted areas was observed in one patient. On further examination of these lungs after arteriography, thrombo-embolic obstruction were noted distal to those stopping flow of the radio-opaque medium, and these also varied as regards degree of organisation.

Parenchymal pulmonary disease other than that caused by thrombo-embolism was observed in one case and was tuberculous in aetiology (Table I). Whole lung sections, prepared in 5 of the 7 cases of recurrent pulmonary thrombo-embolism with right ventricular hypertrophy and failure, failed to demonstrate diffuse emphysema. Bullous emphysema was seen in two instances.

TABLE IV

LOCALIZATION OF THROMBO-EMBOLI IN THE PULMONARY ARTERIES IN 9 CASES

Type of Vessel Affected		No. of Cases Involved
A.	Elastic Arteries	
	Main Trunk	0
	Left and right main branches	1
	Secondary branches	4
	Tertiary branches	8
B.	Muscular Arteries	9
C.	Arterioles	5 (sparsely distributed in 4 cases)

Histological examination in all cases confirmed the presence of antemortem thrombi (Fig. 4, Plate III), and showed that besides a variation in size, the thrombo-emboli also varied widely as regards age. In the two patients in whom death resulted from acute cor pulmonale the lesions were mainly recent in origin and organisation, although occasionally observed,

was/...

was not a feature and pulmonary infarction was absent.

In all 7 cases of chronic recurrent pulmonary thrombo-embolism both recent and organising lesions were present, and thrombi within any particular age group were multiple. While degrees of organisation varied (Fig. 4 - 5, Plate III), completely organised lesions were infrequent in this group. It was therefore apparent from histological examination that while several thrombo-embolic episodes must have occurred in these 7 patients, the course was relatively rapid.

A source for embolization was present in 8 of the 9 patients in this series, of which 6 had thrombi in the veins draining the lower extremities. In those with venous thrombosis of the lower limbs the deep calf veins were most frequently involved. In the only instance where the source of embolism is unknown the pelvic veins and those of the lower limbs had not been examined at necropsy.

The unusual association of amoebic liver abscess and thrombosis of the inferior vena cava was observed in 2 patients. In both cases the liver abscess was placed posteriorly and a communication between the abscess and the inferior vena cava was established at necropsy. One of the two cases included here (Case 3) has been resported previously (Kallichurum 1966). Intramural thrombosis of the right heart was observed in one case, but a further source for embolization was found in the hepatic vein and inferior vena cava in this patient (see Plate IV for illustrations). In all suspected cases of venous thrombosis histology confirmed the presence of antemortem thrombi. Both fresh and organising thrombi were found, and all instances of venous thrombosis of the lower limbs were classified as examples of phlebothrombosis.

Sufficient disease from other causes was present in 5 subjects including 2 of the 3 patients under 40 years of age. In one patient, a localised apical tuberculous lesion was present but was considered an unlikely factor in producing peripheral venous thrombosis. In 4 patients no cause for peripheral venous thrombosis was apparent at necropsy.

DISCUSSION/...

DISCUSSION

In contrast to the generally accepted views regarding peripheral venous thrombosis and pulmonary embolism in African subjects, the findings here show pulmonary thrombo-embolic disease with right ventricular strain and failure to be a relatively common cause of cor pulmonale in this population. In 30 consecutive cases of cor pulmonale investigated in this series, there were 2 instances of acute right ventricular failure and both were thrombo-embolic in aetiology. Of the remaining 28 cases of the more chronic forms of cor pulmonale 7 (25%) were thrombo-embolic in origin, making this disease the second most common cause (after fibrosing lung diseases) of cor pulmonale in the African at necropsy. This finding supports the view of Turner (1962) that thrombo-embolic cor pulmonale is probably not as rare in the African as is generally believed. Although the more chronic form of thrombo-embolic cor pulmonale was encountered in this study more frequently than the acute variety, it is possible that this may not be a true reflection of the incidence of these types, since acute cor pulmonale may easily be missed at necropsy unless the pathologist is alert to its possible presence.

In patients with the more chronic form of cor pulmonale, while the great variation shown in the age of emboli in individual cases implies the occurrence of repeated episodes, the infrequency of completely organised thrombo-emboli nevertheless suggests a somewhat rapid course, measured in months rather than in years. It is possible therefore that this group of patients (with the exception of Case 3, where completely organised lesions were common) represents chiefly the subacute variety of thrombo-embolic cor pulmonale. A more rapid fatal course is further supported by the minor increase in the total heart weights in these patients. As shown, such weights were commonly below 400 Gms. These patients therefore differ from those reported in Owen et al. (1953), in whom marked right ventricular hypertrophy and well organised pulmonary lesions were frequent, suggesting a longer course, measured probably in years rather than in weeks or months. In the 12 cases of thrombo-embolic cor pulmonale reported by the above authors the

total / ...

total heart weights were above 400 Gms. in 7 cases and over 500 Gms. in 4 cases.

The main pathological type of pulmonary thrombo-embolic disease observed in this series of cases is one in which fairly large pulmonary arteries (secondary and tertiary branches), as opposed to those of microscopic size (muscular pulmonary arteries and arterioles), are affected. The fact that such large vessels were often involved probably explains the frequency with which infarction was observed in this group of cases. Both Owen et al. (1953) and Thompson and Hamilton (1962) commented on the infrequent occurrence of extensive infarction in their cases. It is possible that in those cases where the disease extends over a longer period, with longer intervals between embolic showers, there is time for an adequate collateral circulation to be established, whereas with rapidly repeated episodes of pulmonary thrombo-embolism this is not possible and infarction will follow.

Because a source for embolization was found in all except the one case where a search for it was unfortunately omitted, it is reasonable to assume that the pathogenesis is embolic as opposed to multiple autochthonous pulmonary arterial thrombosis.

Goodwin et al. (1963), have suggested that large pulmonary emboli probably come from the veins draining the lower limbs, and that the smaller pelvic radicles give rise to emboli of microscopic size which lodge in the muscular arteries and arterioles. Hunter et al. (1941), have commented on the surprisingly large size of the thrombi situated in the deep veins of the legs, and these authors also reported that major pulmonary arteries could sometimes be obstructed by emboli originating in the calf veins. In the present series, although emboli to large pulmonary arteries were found to have originated in the deep calf veins, smaller muscular pulmonary arteries (100 - 1000 μ in diameter) were frequently involved in addition to the larger vessels. This correlates with the findings of Owen et al. (1953), the pathological picture differing, as mentioned, only as regards the rapidity with which recurrent episodes of embolization occurred and the time lapse between obstruction and the

supervention/...

supervention of cor pulmonale.

A predisposing cause for venous thrombosis in the form of severe illness from diseases other than that involving the cardiovascular system was present in just over half the cases in this series. In 4 patients no such factor was apparent at necropsy and the pathogenesis of peripheral venous thrombosis in these cases cannot be explained. While advancing age, relative inactivity and lack of muscle tone as suggested by McCartney (1945) may be important factors contributing towards the development of venous thrombosis, the reason for its occurence in healthy young individuals remains obscure.

Perhaps the most interesting point with regard to other diseases associated with venous thrombosis and pulmonary embolism, wth subsequent cor pulmonale, in this series, is the relationship to hepatic amoebiasis. In both patients (Cases 3 and 4) described here, necropsy revealed the presence of an amoebic liver abscess, posteriorly situated, and associated with thrombosis of the inferior vena cava. In Case 4 the initial site of thrombosis formation was in the inferior vena cava and the abscess communicated with this vessel through a small perforation. The primary site of thrombosis in Case 3 was the right hepatic vein, the process extending from here to involve the inferior vena cava. The final outcome in both cases was recurrent obstruction to the pulmonary arterial tree by emboli, with subsequent right ventricular hypertrophy and failure.

Three cases of amoebic liver abscess with inferior vena cava thrombosis (including Case 3 in this series) have previously been reported (Kallichurum 1966). In 2 of these, extensive pulmonary thrombo-embolic disease and subsequent cor pulmonale were noted. Case 4 in this series is a further such example, encountered more recently.

Both intestinal amoebiasis and its hepatic complication in the form of an abscess are fairly common infective conditions among the African population in and around Durban. Thrombosis of the small veins often accounts for the nutmeg appearance seen around an amoebic liver abscess, but

major/...

major veins are said to be rarely involved (Wilmot 1962). Thrombosis of the inferior vena cava in a case of amoebic liver abscess has been described by Gordin (1937), and Hare and Ritchey (1946) reported thrombosis involving the portal and hepatic veins in association with amoebic liver abscess. In neither report was mention made of pulmonary embolization.

The occurence of inferior vena cava thrombosis in such cases appears to be related particularly to posteriorly situated liver abscesses, and often a communication can be found at necropsy between the abscess and the inferior vena cava, unless of course the thrombotic process involves this vessel by extending along the hepatic veins.

It is of interest to note that although thrombosis of the inferior vena cava may have been massive, the emboli were multiple and involved the smaller vessels episodically. It is reasonable to assume that thrombi in such infective circumstances are friable and fragment readily. This may also be so, however, in instances of phlebothrombosis involving the peripheral veins (Belt 1939a).

With reference to cardiac enlargement in the group of cases described in this series, dilatation without hypertrophy was present in the 2 cases of acute thrombo-embolic cor pulmonale. In Case 2 it is possible that dilatation may have masked lesser degrees of hypertrophy due not to pulmonary thrombo-embolism but to associated systemic hypertension with left ventricular hypertrophy.

In the more chronic forms hypertrophy of the right ventricle was present according to either of the 2 methods used to assess this. In the evaluation of the left ventricle, however, difficulties were encountered when wall thickness was used as a method of measuring hypertrophy. The results obtained were contrary to those found on macroscopic examination of the gross specimen, and erred always on the side of hypertrophy. Differential ventricular weights, however, undertaken in 5 cases, showed no increase in left ventricular weight above the normal values obtained for African subjects. Thus, while chronic failure of one ventricle may lead to failure of the other,

and / ...

and while the occurrence of pulmonary shunts may increase the diastolic burden of the left ventricle, the results obtained in this study do not reveal evidence of chronic left ventricular strain. A relatively small heart with exclusive right ventricular hypertrophy appears to be the rule, exceptions occurring when cardiovascular disease from other causes co-exists.

The finding of pulmonary thrombo-embolic disease as an important aetiological factor in the development of cor pulmonale in African subjects is in strong contrast to all previous opinion regarding venous thrombo-embolism in this race group. While such disparity may be explained by the protean clinical and pathological manifestations of the disease, the question naturally arises, is venous thrombo-embolism on the increase? That this may be so in Western societies is suspected by many, but the position in regard to the African is difficult to assess on account of the lack of previous studies of this nature. However, because of this rather surprising result it seemed essential to obtain some estimate of the general necropsy incidence of peripheral venous thrombosis and pulmonary embolism in the African, purely from the point of view of confirming these findings. Such a study was undertaken concurrently, and the results obtained are given and discussed in the following chapter.

SUMMARY

1. Thrombo-embolic cor pulmonale was found to be the second commonest cause of cor pulmonale among African subjects in Durban,

2. While this was the only cause for acute cor pulmonale it was found to account for 25% of all more chronic forms of cor pulmonale among Africans.

3. The aetiological role of amoebic liver abscess in the development of pulmonary thrombo-embolism and subsequent cor pulmonale has been described and discussed.

4. The pathological type of pulmonary thrombo-embolism encountered here and the associated pathological state of the heart have been described and discussed.

CHAPTER V

VENOUS THROMBO-EMBOLISM IN THE AFRICAN

Venous thrombo-embolism is a disorder which increases in incidence with advancing age and affects most commonly the chronically bedridden and seriously ill. Rarely it may occur in the young ambulatory person, for reasons as yet unknown.

The chief hazard of venous thrombosis is pulmonary embolism, and the catastrophic results of pulmonary emboli have been known for decades. More recently a recurrent form of pulmonary embolism, consisting of showers of small emboli terminating in chronic right heart failure, has come into prominence. It was with regard to this latter aspect of venous thrombo-embolism that the present study was undertaken. The aim was to re-evaluate the incidence of venous thrombo-embolism in the African population in which the occurrence of this phenomenon has hitherto been believed to be very infrequent.

Since the turn of the century a great deal of interest and attention has been accorded to thrombo-embolism, and the literature accumulated on the subject is enormous. In a critical review De Bakey (1954) has pointed out how inconsistencies, conflicting findings and incompatible statistics keynote all phases of this condition. Many factors contribute to this state of confusion, but a lack of knowledge of the precise aetiological factors involved and the protean clinical manifestations of venous thrombosis have been considered most important.

Although the doctrine of thrombo-embolism was propounded by Virchow in 1846, the greater part of all early writings and discussions pertaining to this subject are found in surgical literature. It was not long before it became evident, however, that this complication also followed accidental trauma and occurred in pregnancy and the puerperium. It is now known that thrombo-embolism is not just a surgical or obstetrical

problem/...

problem, but occurs with equal if not greater frequency in medical conditions. Published figures on its occurrence after medical and surgical conditions show a considerable variation. This variation must, as is realised by many, be dependent upon the hospital population from which these figures are derived. Gross differences in the number of admissions to either the medical or surgical services would account for an appreciable variation in the incidence of a particular complication when expressed as a percentage against the total number of admissions.

In the opinion of Virchow (1846), and of many others since, the pelvic and thigh veins were regarded as sites for thrombus formation, and fatal emboli were thought to originate in these vessels. It was also believed that the pale primary thrombus gradually obstructed a vessel and that the red "coagulation thrombus" arose in that end of the vessel which was peripheral to the primary thrombus. Frykholm (1940) credits Denecke (1929) and Olow (1930) with being among the first to suggest that the deep veins of the sole of the foot and the calf were the initial sites of thrombus formation. Homans in 1934, from clinical and morbid anatomical observations, emphasized the importance of the deep veins of the legs as sites for the origin of thrombi. It seems likely that Rossle (1937) undertook his investigation of veins draining the lower extremities in order to test the validity of such clinical evidence. From his necropsy dissections he demonstrated thrombi in the calf veins in 27.1% of patients investigated. While concomitant thrombosis of the femoral vein was frequent (43%), only a small number showed evidence of femoral vein thrombosis in the absence of thrombosed calf veins. From this work Rossle concluded that, although thrombi formed more frequently in the deep veins of the leg, they rarely gave rise to fatal emboli but that fatal emboli resulted from propagation of such thrombi into the femoral veins.

The validity of Rossle's (1937) findings were confirmed by most subsequent workers (Neumann 1938; Putzer 1939; Frykholm 1940; Hunter et al. 1941; Bauer 1946; Ochsner 1948; Wilson 1949; Eisendorf 1949). Neumann (1938) commented on the frequency with which the plantar veins were

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also involved. Putzer's work stressed the high incidence of calf vein thrombosis in medical cases, while Hunter et al. (1941), commented on the surprisingly large number and size of thrombi in calf muscle veins.

Whereas the above authors considered that a thrombus does not begin in the femoral vein unless it is an extension from a thrombus in the deep veins, and that the process continues upwards with the blood flow and not, as was assumed formerly, in a retrograde direction from the femoral vein, others (McLachlin and Patterson 1951; Ingraham 1942) were of the opinion that the majority of thrombi arise in the thigh and/or pelvic veins.

The frequency with which leg vein thrombosis has been diagnosed clinically varies greatly (4 - 20%) in the experience of different authors (Belt 1934; Robertson 1938; Barker 1941; Crutcher and Daniel 1948; Ochsner and De Bakey 1951). The generally low percentages obtained however, stress the difficulties encountered in the clinical recognition of calf vein thrombosis.

Estimates of the incidence of pulmonary embolism, in general autopsy series range from 5 - 14% (Parker and Smith 1958).

The high rate of pulmonary embolism in cardiac patients has been well documented (Kinsey and White 1940; McCartney 1945; Moran 1950; Short 1951'52; Byrne 1960; Herman et al. 1961). This disorder is said to occur about three times more frequently in patients with heart disease than in non-cardiac patients, in all decades except the first (McCartney 1945). While Short (1952) found the incidence in patients with heart disease to be in the region of 10%, both Kinsey and White (1940) and Moran (1950) reported the incidence of pulmonary embolism in such patients as being around 30% and 48% respectively. Byrne and O'Neil (1952) considered pulmonary emboli in cardiac patients to have come from the leg veins more frequently than from the right heart.

The prognosis of pulmonary embolism in patients with heart disease is very poor, and is even worse when cardiac decompensation is present.

Morton/...

(Morton et al. 1947; Carlotti et al. 1947; Short 1952; White 1951; Wood 1956).

Ochsner (1948) is of the opinion that one should differentiate between phlebothrombosis and thrombophlebitis because the latter, since it occurs as a sequel to inflammatory changes in the vein wall, produces a more firmly adherent clot which is unlikely to embolize. In phlebothrombosis on the other hand, the thrombus, because it arises as a result of stasis and altered coaguability, is loosely attached and pulmonary embolism is likely to occur. Others (Allen et al. 1946) do not attempt a separation, while some feel that such differentiation may be misleading and dangerous (Fine and Starr 1945), or that little is to be gained thereby (Veal and Hudson 1948).

Ochsner and De Bakey (1951) found that thrombi-embolism occurred less frequently in the Negro patients as compared with White patients. A racial difference has always been suspected in Africa, and venous thrombosis has been considered an uncommon disorder in the African patient (Gelfand 1957). It followed therefore that pulmonary embolism was also an infrequent finding in this group, except when it complicated heart failure due to cardiomyopathy.

Because of the supposedly rare occurrence of venous thrombosis and pulmonary embolism in post-operative African and Indian patients in Durban, Franz et al. (1961) investigated the plasma fibrinolytic activity in African, Indian and White subjects, and concluded that while the plasma fibrinolytic activity was twice as high in healthy African controls as it was in White and Indian controls, the plasma fibrinogin levels were the same in all 3 groups. These authors also commented on the extremely low necropsy incidence of this disorder as reflected in the records of this hospital (King Edward VIII Hospital, Durban) during the six year period (1953-1958) of their survey. It must be appreciated, however, that the veins of the lower limbs are not examined routinely and that dissection of the deep veins of the calf are only rarely performed.

In order to assess the occurence of venous thrombo-embolism in this group it was necessary to investigate the problem on the lines followed by

earlier/...

earlier workers. Attention was paid to the veins of the lower extremities because of the major role they play in the incidence of this condition in the White races, and also because the clinically silent nature of this disorder is better appreciated to-day, so that lack of symptoms and physical signs in the lower limbs does not necessarily exclude the presence of venous thrombosis.

MATERIALS AND METHODS

The material for this study was obtained from consecutive routine necropsies performed on African patients of both sexes, of 10 years of age and over. Similar material was obtained from Indian post-mortems for comparative purposes. The majority of patients (314) studied were in-patients of King Edward VIII and Clairwood Hospitals, coming to post-mortem during the period February, 1964 to June 1965; of these 49 were medico-legal cases consisting mainly of acute traumatic deaths, and a few other acute deaths following upon possible poisoning.

In addition to routine post-mortem examination the soleus and gastrocnemius muscles were removed from both lower limbs in every case. Removal of these muscles was accomplished by a medial incision extending from the Achilles tendon to just above the knee joint. The muscles were then dissected from the posterior aspect of the leg bones and detached high enough to include as much as possilbe of the popliteal vein. The posterior tibial veins were also dissected down to their small branches. The specimens were labelled and fixed for 3 - 4 days in trays containing 10% formol saline. The calf muscles were then sliced transversely at intervals of approximately 1 cm. and macroscopic observations recorded in each case. In every instance where venous thrombus was present, several blocks of tissue were taken for microscopic examination. The superficial femoral vein was examined in situ on both sides, and the findings recorded. Veins of the feet were not examined. On this basis a total of 363 African and Indian patients were investigated for leg vein thrombosis.

In / . . .

In 343 of these both lungs were also reserved after routine post-mortem examination, and were labelled and fixed in 10% formol saline. The pulmonary arteries and their branches were examined for thrombi at the same time as the calf muscles were sectioned. This was achieved firstly by opening the larger vessels as far as was possible and then making thin sections of less than $\frac{1}{2}$ cm. for smaller thrombi. It was found easier to feel rather than visualise thrombi in very small vessels. Again, in all instances where thrombi were suspected, blocks were taken for microscopic examination.

All blocks of tissue were sectioned at 5μ thickness and stained with haematoxylin and eosin, and lung sections were also stained by Weigert's elastic stain. These sections were studied for distinction between antemortem and post-mortem thrombi, size of vessel involved, presence or absence of organisation of thrombi, and for the presence or absence of any inflammatory infiltrate in the vessel wall. Those cases where a pulmonary arteritis was found in addition to thrombi (all such cases being associated with infections of the lung) were excluded.

The race and sex distribution of the total number of cases investigated is shown in Table I.

TABLE I

RACE AND SEX DISTRIBUTION OF PATIENTS STUDIED

Race	Male	Female	Total
African	189	94	283
Indian	52	28	80
Total	241	122	363

ANALYSIS OF CASES

This analysis is based on two inter-related studies: (1) venous thrombosis

thrombosis, and (2) pulmonary thrombo-embolism as found at necropsy. Since primary pulmonary arterial thrombosis is known to occur, and one cannot always be absolutely certain as to whether a bland antemortem thrombus present in the pulmonary arterial tree was local in origin or was the result of embolization, the term pulmonary thrombo-embolism has been used.

Besides the division into racial groups, the cases studied were further subdivided into four main groups, viz. medical, post-operative, traumatic, and post-partum. The majority of patients (84.3%) investigated were classified as medical and included in this group were patients from medical and surgical wards on whom no surgery was performed; Also included here are 6 medico-legal cases suspected of dying either from poisoning or from causes undetermined. The post-operative group (2.7% of total) consisted of all patients having undergone major surgery. Included here are one Indian and two African patients who suffered extensive pelvic and abdominal trauma in whom surgical intervention was necessary. The traumatic group (11.3% of total) included injured patients on whom no major surgery was performed. The majority of these were cases of head injuries, stab wounds, and multiple limb fractures, who arrived dead or died soon after admission to hospital. The post-partum group, comparatively a very small group (1.7% of total) included mostly cases of abortion with one case of rupture of the uterus.

VENOUS THROMBOSIS OF THE LOWER EXTREMITIES

Of a total of 363 African and Indian patients in whom deep veins of the thighs and legs were specially examined, thrombosis was observed in 141 (38.8%). The incidence of this disorder in the 4 major divisions of medical service is shown in Table II. Medical cases were separated into cardiac and non-cardiac patients, the former group including cases of congestive heart failure in both race groups. Venous thrombosis in the lower limbs occurred most frequently in cardiac subjects.

Table II/...

TABLE II

INCIDENCE OF VENOUS THROMBOSIS AND PULMONARY THROMBO-EMBOLISM IN THE AFRICAN AND INDIAN AT NECROPSY

	Venous Thrombosis				Pulmonary Thrombo-Embolism			
	African	Indian	African	Indian	African	Indian	African	Indian
	No.	No.	No. %	No. %	No.	No.	No. %	No. %
Medical								
Cardiac	42	10	27(64.3)	5(50.0)	38	10	19(50.0)	4(40.0)
Non-cardiac	209	45	77(36.7)	18(40.0)	193	45	42(21.2)	13(28.9)
Post-operative	7	3	3(42.9)	1(33.3)	7	4	3(42.9)	2(66.6)
Traumatic	22	19	6(27.3)	4(21.1)	22	19	7(31.8)	5(26.3)
Post-partum	3	3	0 (0)	0 (0)	3	3	0 (0)	1(33.3)
Total	283	80	113 (39.9)	28 (35.0)	263	80	71 (27.0)	25 (31.3)

Post-operative African patients followed next, but if one were to exclude the 2 African and 1 Indian patient suffering severe pelvic and abdominal trauma necessitating surgery, the incidence in the African would be 20.0% and in the Indian 0%. The medical non-cardiac group, the largest group studied, showed a significantly high incidence in both the African and the Indian. The lowest incidence occurred in the post-partum group, which was, in comparison, the smallest group investigated. No significant racial difference is observed in the overall incidence of venous thrombosis in the African and Indian.

Table III shows the sex incidence of venous thrombosis in the two racial groups studied. As is evident from Table III there is no appreciable difference between African and Indian males, or African and Indian females, in the incidence of this disorder.

Fig. (I) shows the age incidence of venous thrombosis in the African.

TABLE III/...

FIG. I

INCIDENCE OF VENOUS THROMBOSIS AND PULMONARY THROMBO-EMBOLISM IN THE AFRICAN

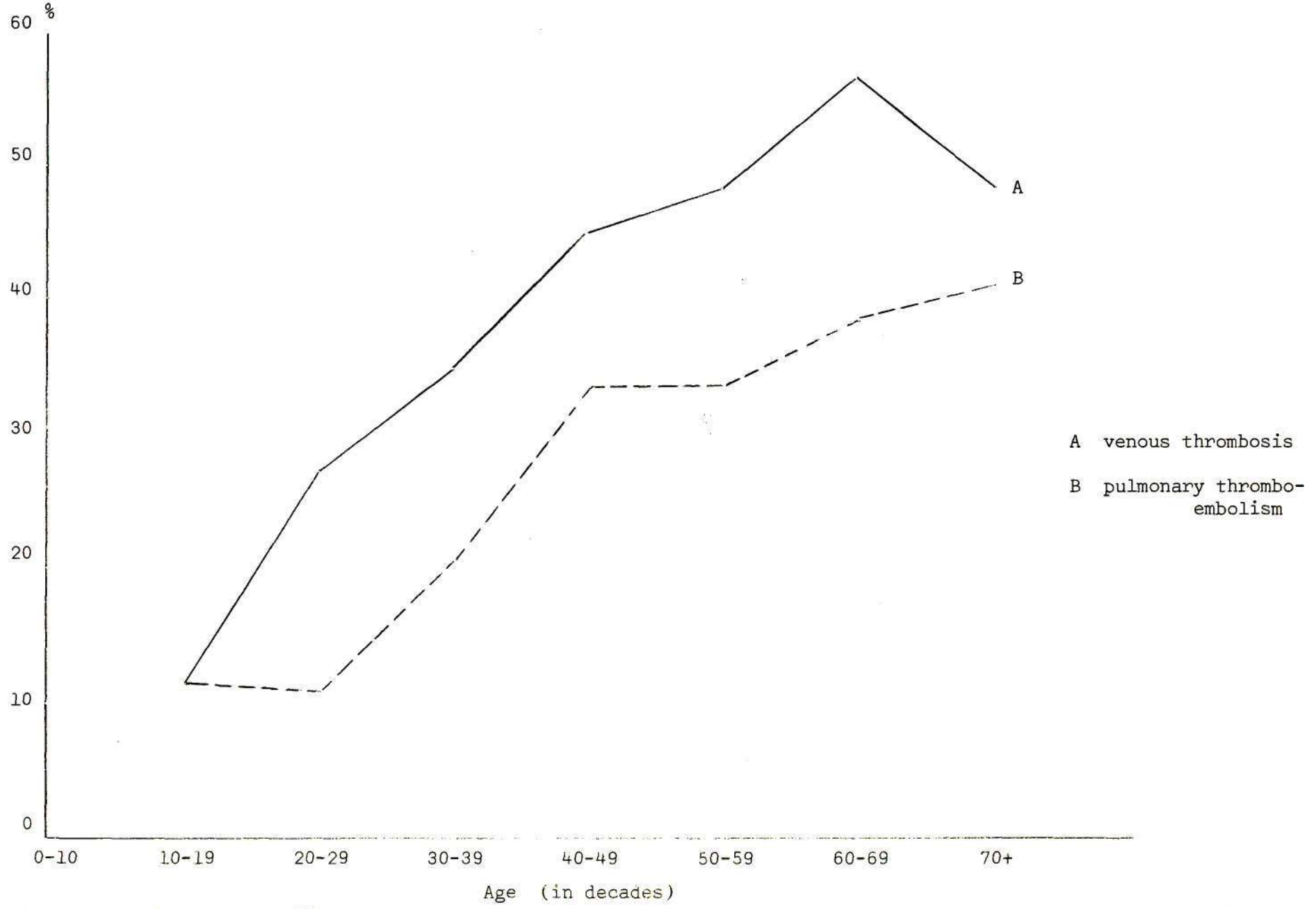

TABLE III

SEX INCIDENCE OF VENOUS THROMBOSIS
COMPARISON BETWEEN AFRICANS (283)
AND INDIANS (80)

Race	MALES			FEMALES		
	Total No.	Ven. Thrombosis No.	%	Total No.	Ven. Thrombosis No.	%
African	189	69	36.0	94	44	46.8
Indian	52	15	28.8	28	13	46.4
Total	241	84	34.9	122	57	46.7

TABLE IV

THROMBOSIS IN VARIOUS VEINS DRAINING THE LOWER
LIMBS IN 113 AFRICANS AND 28 INDIANS AT NECROPSY

	THIGH VEINS				CALF VEINS			
	Femoral		Popliteal		Post. Tibial		Soleal and Gastrocnemius	
	African	Indian	African	Indian	African	Indian	African	Indian
Limbs:								
Right	1	0	9	3	17	2	17	5
Left	1	0	14	4	27	5	24	5
Both	4	1	9	4	31	10	56	11
Total	6	1	32	11	75	17	97	21
Percentage	(5.3%)	(3.6%)	(28.3%)	(39.3%)	(66.6%)	(60.7%)	(85.8%)	(75.0%)

Whereas thrombosis of the veins draining the lower limbs was observed in all age groups (in decades), it was found to increase with advancing age. The drop in incidence in the 70+ group may be explained by the smaller number of patients of this age group included in the present series.

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The combinations of veins or groups of veins affected by thrombosis were found to vary considerably and often to differ in the two lower limbs of the same patient. Thrombi, however, were most frequently observed in the deep veins of the calf (Fig. 1 and 2, Plate V), were often bilateral, and the left leg was slightly more often involved.

The distribution of thrombi within the veins of the lower extremities in the African and Indian is summarised in Table IV.

As apparent from Table IV, the deep veins of the calf (soleal, gastrocnemius, and posterior tibials) were more often affected than any of the other veins or groups of veins examined, and of these the soleal veins were most commonly involved. Of the thigh veins examined, the popliteals contained thrombi more frequently than did the femorals, but the incidence of popiteal vein thrombosis was significantly lower than that of thrombosis in the deep veins of the calf. In only 3 of the 141 positive cases were the thigh veins affected without concomitant involvement of the calf veins.

The majority of thrombi examined were of recent origin (Fig. 3, Plate V). In 38 cases (29 Africans and 9 Indians) varying degrees of organisation were observed (Fig. 4, Plate V). Thus, while venous thrombosis was present in 38.8% of the total number coming to necropsy, in 10.5% of all cases investigated this was definitely not a terminal event.

Thrombi within femoral veins measured between 10 - 15 mm. in diameter, while those in the popliteal veins ranged from 7 - 10 mm. Thrombi situated within the calf muscles were usually numerous (Fig. 1, Plate V), and varied in size from 2 - 15 mm. in diameter, the majority being between 3 - 10 mm. in diameter.

Venous thrombosis of the lower limbs in this series was almost always classified as phlebothrombosis. Thromboplebitis was encountered on two occasions only.

TABLE V/...

TABLE V

SEX INCIDENCE OF PULMONARY THROMBO-EMBOLISM

COMPARISON BETWEEN AFRICANS (263) AND INDIANS (80)

	M A L E S			F E M A L E S		
Race	Total Number	No. +ve PE/T	%	Total Number	No. +ve PE/T	%
African	176	44	25.0	87	27	31.0
Indian	52	12	23.1	28	13	46.4
Total	228	56	24.6	115	40	34.8

TABLE VI

THROMBO-EMBOLISM IN THE VARIOUS BRANCHES OF

THE PULMONARY ARTERIAL TREE IN 71 AFRICANS

AND 25 INDIANS AT NECROPSY

Lung involved and Total patients	Main branch of Pulmonary artery alone		Main branch plus smaller branches		Smaller branches alone	
	African	Indian	African	Indian	African	Indian
Lungs:						
Right	3	2	0	0	5	4
Left	1	0	1	0	5	1
Both	2	0	8	6	46	12
Total patients	6	2	9	6	56	17
Percentage	(8.4%)	(8%)	(12.7%)	(24%)	(78.9%)	(68%)

PULMONARY THROMBO-EMBOLISM

The incidence of venous thrombosis and pulmonary thrombo-embolism in African and Indian necropsy subjects is shown in Table II. No significant racial difference was found in the incidence of pulmonary thrombo-

embolism/...

embolism. The highest incidence of pulmonary thrombo-embolism in Africans occurred in patients with heart disease. The frequency of this disorder was found to exceed that of venous thrombosis of the lower limbs in the traumatic group in both races, and in the post-operative group among Indians. In 18 African and 7 Indian patients with pulmonary thrombo-embolism venous thrombosis of the lower extremities was either absent or insignificant. In these the source was considered likely to have been sites other than the veins of the lower limbs e.g. pelvic veins, right heart, inferior vena cava, etc., or pulmonary arterial thrombi may have arisen locally.

Infarction was observed in 9 Africans and 1 Indian. In the majority (8) infarcts were of recent origin, being older and related to previous embolism in the other 2 cases. Abscess formation was found in 2 of the 10 cases of infarction of the lungs.

Table V shows the sex incidence of pulmonary thrombo-embolism in African and Indian subjects.

No significant differences are apparent between the corresponding sexes of the two race groups studied. As shown in Fig. (1), the incidence of pulmonary thrombo-embolism increases with advancing age and parallels the age incidence of venous thrombosis.

The morphology of pulmonary arterial thrombi recorded in these cases was divided into 3 main groups: (i) where a thrombus blocked one or both branches of the pulmonary artery; (ii) where a large thrombus was present in one or both main arteries with concomitant involvement of segmental and more peripheral branches; (iii) where thrombi were present in the segmental and peripheral arteries only. Thrombi in the pulmonary arteries were commonly multiple, the lower lobes were frequently involved, and usually both lungs were affected.

Table VI shows the frequency with which the various branches of the pulmonary arterial tree were involved according to the above grouping. No significant difference in the distribution of pulmonary thrombo-emboli was

observed/...

observed in the two races studied. The segmental and peripheral branches alone were most commonly involved. Next in order of frequency was concomitant involvement of one or both main branches and smaller branches, while involvement of the main branches alone was least frequent.

In 15 patients (10 Africans, 5 Indians) thrombi were found in the segmental and/or more peripheral arteries of the one lung only. Of these 7 showed evidence of multiple pulmonary emboli in one lung while the other was apparently unaffected. In the remaining 8 involvement was negligible.

The great majority of thrombi-emboli present in the pulmonary arteries were of recent origin (Fig. 5, Plate V). Varying degrees of organisation (Fig. 6, Plate V), were found in 19 cases (13 Africans, 6 Indians). However, in 15 of these cases fresh occlusions were present in addition to those undergoing organisation.

The size of thrombo-emboli found in the pulmonary arteries varied from 1 - 15 mm. in diameter. Large thrombi measuring 10 - 15 mm. in diameter were found in the main branches of the pulmonary artery, while those in the more peripheral branches were between 1 - 6mm. in diameter.

In all except one case occluding thrombi were found to be bland in nature.

DISCUSSION

Observations at necropsy and their confirmation by histological examination have shown that, contrary to clinical evidence, the occurrence of peripheral venous thrombosis and pulmonary thrombo-embolism is not uncommon in the African. A comparison of their occurrence among African and Indian hospital patients, coming to necropsy, has shown no appreciable difference in incidence. In both races thrombosis was observed most frequently in the calf veins, was more often bilateral, and was not suspected clinically in the great majority. When thrombi were found in the

pulmonary/ . . .

pulmonary arterial tree, they were commonly multiple and showed a definite tendency towards involvement of the vessels of the lower lobes. Frequently both lungs were affected, and again in a large percentage of cases, clinical evidence of pulmonary embolism was lacking.

Considerable disagreement still exists regarding the sites of origin of pulmonary emboli although many authors have tried to clarify this point by necropsy studies of various types. It must be borne in mind, however, that these studies have unfortunately differed widely in patient populations as regards age, sex, and disease state, and also in the extent of venous dissection, all of which must have a bearing on the experience and interpretations of findings of the different authors.

Important sites for primary thrombus formation are the leg veins, femoral and iliac veins, pelvic veins, inferior vena cava, arm veins, and the right side of the heart. Although the reprted frequency with which the above sites are involved has varied, it is now believed that pulmonary emboli most often originate in the veins of the lower extremities (Hampton and Castleman 1940; Cohn and Walsh 1946; Ravdin and Kirby 1951; Byrne and O'Neil 1952; Short 1952). In the present series venous thrombosis of the lower extremities could have accounted for 74.6% and 72% of all cases of pulmonary embolism in the African and Indian respectively. These findings, while showing the incidence of venous thrombo-embolism in the African to be similar to that in the Indian, are in agreement with those of earlier authors (Rossle 1937; Neumann 1938; Putzer 1939; Frykholm 1940), in that venous thrombosis in the lower extremities most frequently affects the deep veins of the calf. This contrasts with the observations of Ingraham (1942) and McLachlin and Patterson (1951) that the pelvic and thigh veins are the usual sources for pulmonary emboli. The finding that the soleal veins were the most commonly involved of calf veins confirms the observations of Hunter et al. (1941).

Measurements of larger thrombi within the calf muscle veins also correlated with the findings of Hunter et al. (1941) and supported their view that fatal pulmonary emboli can and do arise in these veins. It has been the

experience/...

experience here that the left leg is slightly more frequently involved.

When one considers the occurrence of thrombo-embolism in the various age groups (Fig. 1) it is evident that while thrombosis and embolism occur in all groups, there is a definite tendency towards a higher incidence as age advances. In the present series almost 50% of African patients, 40 years of age and over, showed evidence of venous thrombosis at necropsy. With increasing age many diseases favouring the production of venous thrombo-embolism are encountered, but disease of the heart, particularly when decompensation is present, appear to be the most important single predisposing factor in this study.

The frequency with which leg vein thrombosis has been recognised clinically varies from 4% to 20% in the different series. Of the 141 patients with venous thrombosis shown here, the condition was suspected clincially in 2 instances and was diagnosed with certainty in another 3. Pulmonary embolism or infarction was also infrequently diagnosed clinically, being suspected on 5 occasions and diagnosed with surety in another 6 cases.

While the overall incidence of pulmonary thrombo-embolism was found to be 28.0% in 343 patients investigated, the patterns of distribution of occluding thrombi and the degree of arterial involvement varied widely. However, it was usual for multiple smaller pulmonary arteries to be involved. The incidence of 28.0% is high, but it should be appreciated that this includes even solitary emboli in the central and peripheral portions of the lungs in addition to those involving major branches. Twenty-three patients (15 Africans, 8 Indians) were found to have thrombus obstructing, either completely or partially, one or both main branches of the pulmonary artery. In 16 (10 Africans, 6 Indians) both main arteries were blocked. In no case was involvement of the main stem of the pulmonary artery observed. Of the group with smaller thrombi, 7 patients (6 Africans, 1 Indian) were observed to have a significant number of segmental and/or more peripheral branches of one lung occluded by thrombi, while the contra-lateral lung appeared unaffected. The only explanation for this is that a large, friable

thrombus/...

thrombus must have lodged temporarily in the one main branch of the pulmonary artery, then broken up and passed into smaller branches centrally and peripherally. Gorham (1961), in his extensive study of pulmonary embolism, makes mention of this phenomenon and adds that its occurrence is very rare and that in such circumstances recovery is likely. It is possible that of the two cases reported recently by Sautter et al. (1964) as examples of complete resolution of massive pulmonary embolus, one may fall into this category.

In 20 patients (17 Africans, 3 Indians) significant numbers of thrombi were observed in segmental and smaller branches of both lungs. Without the aid of angiography, however, it is impossible to comment with any degree of accuracy on the true extent of vascular obstruction. Of the remaining 46 cases, a solitary thrombus involving a segmental or smaller artery was found in 8 patients, while the rest (38) showed evidence of multiple but less significant affection of both lungs. Whereas the latter degree of arterial obstruction may not be fatal, it is reasonable to assume that it could place an added burden on an already embarrassed heart.

While both observations on patients and experimental evidence in animals (Knisely et al. 1957; Williams 1956) support the mechanical theory and agree that obstructive embolus in the main pulmonary stem or in either one or both major branches must be present to be fatal, there is no unanimous opinion regarding the effects of multiple, smaller emboli. Reflex vasospasm may be an important factor here, but will not be considered in this paper.

Measurements of venous thrombi in calf veins (2 - 15 mm. in diameter) and those in the pulmonary arterial tree (1 - 15 mm. in diameter) do suggest that the majority of the latter could have arisen in the deep veins of the legs, and are therefore examples of pulmonary embolism as opposed to primary arterial thrombosis.

The incidence of venous thrombo-embolism was significant in the post-operative group, but negligible in the post-partum group. It must be appreciated, however, that these two groups contain comparatively fewer

patients/...

patients, and the findings may therefore not be truly representative. Its frequency in the traumatic group is significantly high. The incidence of pulmonary involvement here exceeded that of venous thrombosis (Table II), thereby suggesting sources other than leg veins, or possible local thrombus formation.

The medical group was the largest of all groups investigated, and the occurrence of this disorder in these patients was common. On separation into cardiac and non-cardiac patients, the former showed the highest incidence of both venous thrombosis and pulmonary embolism in African patients (Table II). Whereas a difference of opinion exists regarding the source of emboli in cardiac patients, it should be appreciated that in many instances incomplete search in the veins of the lower limbs was carried out, or that thrombi were found both in the right heart and in the leg veins. In the present series, 64.3% of African and 50% of Indian patients with congestive heart failure were found to have venous thrombosis of the lower extremities, and the incidence of pulmonary embolism/thrombosis in this group is also high, being 50% in African and 40% in Indian patients. Infarction was noted in 10 of 96 patients with pulmonary arterial obstruction caused by thrombus. Congestive heart failure was present in 8 of the 10 patients showing pulmonary infarction. Abscess formation was noted in 2 instances and was believed in both to result from secondary infection of a bland infarct.

While it is agreed that other sources for embolization, particularly the right side of the heart, may also have been present in these patients, it is nevertheless obvious that the incidence of venous thrombosis of the lower extremities in patients with cardiac decompensation is extremely high.

The fact that the majority of cases were classified as phlebothrombosis indicates that at necropsy thrombophlebitis is the rarer of the two conditions in the African as in the Indian. Because of the very few cases of thrombophlebitis encountered here it is impossible to draw any conclusions regarding the likelihood or otherwise of embolization in such patients.

SUMMARY/...

SUMMARY

1. Necropsy evidence has shown venous thrombosis in the African to be very much more common than is presently believed. While the overall incidence of this disorder in African subjects of 10 years and over in age was found to be in the order of 40%, the highest incidence occurred in patients with congestive heart failure.

2. Venous thrombosis of the lower limbs involved particularly the deep veins of the calf, and such thrombi were sometimes large enough to give rise to fatal pulmonary embolism. Pulmonary emboli were usually multiple and more frequently involved the smaller intrapulmonary branches of the pulmonary artery.

CHAPTER VI

EMPHYSEMA AND CHRONIC BRONCHITIS AS A CAUSE OF CHRONIC COR PULMONALE IN THE AFRICAN

Over the past 15 years our understanding of emphysema has progressed beyond the simple concept of alveolar hyperventilation called diffuse vesicular emphysema. At present emphysema is defined in anatomic terms and two such definitions are available. A Ciba symposium (1959) defined emphysema as "a condition of the lung characterised by increase beyond the normal in the size of the air spaces distal to the terminal bronchiole either from dilatation or destruction of their walls". The World Health Organisation (1961) limited its definition to enlargement of air spaces, distal to the terminal bronchioles, accompanied by destruction; enlargement without destruction being termed "over inflation". The latter definition thus excluded terms such as compensatory emphysema and diffuse acute obstructive emphysema. Criticism has been levelled against both these definitions, the first in that it presupposes an accurate knowledge of the normal size of an air space which as yet has not been established conclusively, and the second because it fails to define destruction.

While many varieties of emphysema are found in both acute and chronic forms, the chronic generalised types are the more important as a cause of heart disease. A clearer understanding of the anatomy in emphysema began with Gough's (1952) description of "two fundamentally different types of emphysema". These two forms are now known as centrilobular and panlobular emphysema. The latter terminology was introduced by Wyatt (1959) in substitution for Gough's 'generalised emphysema'.

Centrilobular emphysema is primarily a destructive lesion involving the central tissue of the lung lobules around the respiratory bronchioles. The latter consequently enlarge and become confluent, forming emphysematous spaces towards the centre of lobules. Although the lesions in centrilobular emphysema are diffuse, they are said to be more

common/...

common and more severe in the upper zones of the lungs (Thurlbeck 1963), and the degree of involvement within individual lobules and between lobules is also said to vary. Pigment is usually present in relation to the emphysematous spaces and is stated by Pratt et al (1963) to be secondary to emphysema. However, pigment is often present in this site in the absence of emphysema (Anderson 1966). Inflammation of the distal bronchioles is always found in centrilobular emphysema, and narrowing of these together with the bronchioles supplying the emphysematous spaces is reported to be common (Leopold and Gough 1957; McLean 1958). Whereas McLean (1958) emphasized the occurrence of narrowing and obliteration of the bronchioles with trapping of air, Leopold and Gough (1957) found that no correlation existed between the degree of narrowing and the size of emphysematous spaces. These authors concluded that narrowing of the bronchioles did not necessarily result in the development of centrilobular emphysema. Pratt et al. (1961) noted that although narrowing was present, complete obstruction of the bronchioles did not occur.

Panlobular emphysema is also a destructive process and implies demonstrable involvement of the whole acinus or lobule with extensive loss of lung parenchyma. Although such emphysematous process may involve any part of the lung it is said to show a tendency towards more frequent affection of the anterior basal segment, tip of lingula, and middle lobe (Snider et al. 1962; Thurlbeck 1963). It is rare for panlobular emphysema to be uniformly distributed, and inflammation and distortion of the bronchioles is not a prominent feature as compared with the finding in centrilobular emphysema.

The two forms frequently occur together, particularly with the more severe grades of emphysema. While most observers agree with Gough's view that they represent two fundamentally different varieties of emphysema with one or more common pathogenic factors, a few are of the opinion that panlobular emphysema represents the end stage of centrilobular emphysema (Heard 1959).

In most series (Leopold and Gough 1957; Wyatt et al. 1961, 1962; Thurlbeck 1963),

panlobular/...

panlobular emphysema has been found to be less frequent than the centrilobular type, but the difference is slight.

Centrilobular emphysema affects males particularly, and also occurs at a younger age (Leopold and Gough 1957; Thurlbeck 1963). Panlobular emphysema appears to be the commoner type in females, but both forms affect males far more commonly than females (Sweet el al. 1961; Wyatt el al. 1961; Snider et al. 1962).

Conclusive evidence concerning the aetiology and pathogenesis of chronic generalised emphysema is lacking, and views relating to primary vascular disease or destruction of alveolar elastic tissue are not now acceptable. The three leading theories are those of Spain and Kaufmann (1953); Leopold and Gough (1957); and McLean (1958). While opinion regarding the mechanics involved in the production of emphysema may differ, the three theories share a common belief in the role of chronic bronchitis in emphysema. In Britain the term emphysema is taken to include also the effects of chronic bronchitis. This is not so in the United States of America, and disagreement exists as to whether the disease is identical in these two countries (Friedberg 1966).

Thurlbeck (1963) has pointed out how difficult it is to assess the necropsy incidence of emphysema in a population. Nevertheless, with newer methods of study, emphysema has been found to be more common than was previously believed. In Britain, deaths caused by emphysema are said to be twice as many as those resulting from carcinoma of the lung. Emphysema is also the commonest cause of cor pulmonale in Britain, being responsible for nine-tenths of all cases which, in turn, account for 5 - 10 % of all cardiac disease (British Medical Journal 1959). In industrial areas the incidence is even higher (Flint 1954; Stuart-Harris et al. 1959).

The relationship between emphysema and cor pulmonale is now regarded as a complex one. McKeown (1952) found structural changes in the pulmonary vessels in emphysematous lungs to be often insufficient to account for cor pulmonale in cases where right ventricular hypertrophy was

found/...

found. The observation that pulmonary hypertension resulting from bronchopulmonary infection is reversible in such cases also suggests that disturbances in function in the pulmonary arterial tree are more important than structural changes. Although thrombo-embolism has sometimes been incriminated in the development of cor pulmonale in emphysema, it is generally believed to be of little consequence, as is the shunting of deoxygenated blood into the left atrium.

The presence or absence of chronic bronchitis in emphysema now appears to be of importance. Scadding (1963) differentiates between cases with or without bronchitis in describing the clinical types commonly known in Britain as the "blue bloaters" and the "pink puffers". The former always give a history of long-continued chronic bronchitis, are cyanosed, hypoxic and oedematous, and right ventricular failure occurs episodically. At necropsy emphysema may not be a prominent feature in these patients. The "pink puffer" however, has no preceding history of chronic bronchitis and, although hypoxic, is not cyanosed, and right ventricular failure if it occurs is usually terminal. At necropsy these patients often show a considerable degree of emphysema.

Available evidence now strongly suggests that pulmonary hypertension is more likely to be dependent on disturbances in blood-gas tension than on the type and severity of emphysema.

ANALYSIS OF MATERIAL

Emphysema with or without chronic bronchitis was incriminated as the cause of chronic cor pulmonale in 6 of 30 consecutive cases of cor pulmonale encountered in this series. On excluding the 2 cases of the acute variety, the above factor or factors were responsible for 21.4% of all the more chronic forms of this disorder among Africans and proved the third commonest aetiological process responsible for the development of cor pulmonale in these subjects.

The/ ...

The relevant necropsy findings in these 6 patients are summarised in Table I.

TABLE I

NECROPSY FINDINGS IN 6 CASES OF CHRONIC COR PULMONALE FOLLOWING EMPHYSEMA WITH OR WITHOUT CHRONIC BRONCHITIS

Case No.	Sex	Age	Total heart Weight (Gms)	Type of Emphysema	Associated Chronic Bronchitis	Structural Vascular Changes
*1	M	42	520	Centrilobular	+	+
2	M	40	540	Panlobular	+	+
3	M	44	380	Centrilobular and Panlobular	+	+
4	M	60	290	Panlobular	-	-
5	F	60	460	Centrilobular and Panlobular	+	+
6	M	56	470	Centrilobular and Panlobular	+	+

*(associated mitral stenosis)

As seen in Table I all except one patient were males. The ages ranged from 40 - 60 years, with an average of 50.3 years.

Emphysema with chronic bronchitis occurred more frequently than did emphysema without chronic bronchitis. Using the whole lung section technique to study emphysema, concurrent centrilobular (Fig. 6, Plate VI) and panlobular involvement (Fig. 5, Plate VI), was encountered more frequently than either type in its pure form (Fig. 3, Plate VI).

Histological study of the pulmonary arteries was undertaken in the non-injected lung in every case, and varying degrees of structural alterations were seen in 5 of the 6 cases investigated. The vascular changes observed involved particularly the small pulmonary arteries (muscular pulmonary

arteries/...

arteries and arterioles), and these 5 cases collectively revealed every type of vascular alteration described by Hicken et al. (1965), in their cases of emphysema. These are shown in Plate VII and may be compared with those of the above authors. Muscular arteries showing no hypertrophy of the circular muscle fibres, but revealing a layer of longitudinal muscle in the intima with elastic tissue hyperplasia, were observed in all 5 cases (Fig. 1 Plate VII), being the most frequent type of vascular change encountered in sections. Although muscular arteries of all sizes were involved, such change was particularly marked in vessels measuring 100-300μ in diameter (Fig. 2, Plate VII). In two cases longitudinal muscle fibres external to the outer elastic lamina were found, but such vessels were extremely infrequent.(Fig. 4, Plate VII).

Pulmonary arteries below 100μ in diameter showing a distinct circular muscle layer, with and without a thick layer of longitudinal muscle, separated by elastic fibres, in the intima, were observed in four cases (Fig. 3, Plate VII). Vessels of this type were frequent in one case only. In the other 3 they were observed only after careful search in many sections made from several blocks taken from different areas of the lung. Hicken et al. (1965) referred to these as muscularized arterioles. Intimal fibrosis devoid of elastic tissue was noted in all 5 cases (Fig. 6, Plate VII), to varying degrees, and was thought to be of significant degree in one case.

Angiograms in some of these cases showed loss of abhorization, indicating arteriolar loss (Fig. 1, Plate VI), and some dilatation of the segmental branches. In others there was little or no change in the more peripheral small branches (Fig. 2, Plate VI). Bronchopulmonary subpleural communications were observed in some (Fig. 3, Plate VI), and thrombotic occlusions (Fig. 5, Plate VII), although frequent, were seldom widespread.

The total heart weights ranged from 290 - 540 Gms. with 4 of the 6 cases showing a total heart weight of over 400 Gms. Ventricular hypertrophy was assessed by measurements of wall thickness in 3 cases. The results obtained are shown in Table II.

Table II/...

TABLE II

MEASUREMENT OF WALL THICKNESS IN 3 CASES OF CHRONIC COR PULMONALE FOLLOWING EMPHYSEMA WITH OR WITHOUT BRONCHITIS

Case No.	Sex	Age	Total heart Weight (Gms)	RV thickness (mm)	LV thickness (mm)
1	M	42	520	0.7	1.4
2	M	40	540	0.8	1.5
3.	M	44	380	0.6	1.3

In all 3 cases right ventricular wall thickness was above 0.5 mm. indicating hypertrophy. This was in keeping with naked eye impressions. In the first two cases in Table II measurements obtained for the left ventricle are indicative of mild hypertrophy. This finding did not correlate with the macroscopic appearance of the left ventricle.

Separate ventricular weighing was undertaken in three cases and the results obtained are shown in Table III.

TABLE III

SEPARATE VENTRICULAR WEIGHTS IN 3 CASES OF CHRONIC COR PULMONALE FOLLOWING ON EMPHYSEMA WITH OR WITHOUT BRONCHITIS

Case No.	Sex	Age	Total heart Weight (Gms)	RV Weight (Gms)	LV Weight (Gms)	LV/RV
4	M	60	290	58	116	2.0
5	F	60	460	119	172	1.44
6	M	56	470	140	174	1.24

A definite increase in right ventricular weight above normal

value /...

value (66.3 Gms., S.D. 7.7) is observed in two cases. In Case 4, a right ventricular weight of 58 Gms. must be correlated with a total heart weight of 290 Gms. and a body weight of only 47.2 Kilograms. The left ventricle in this patient weighed 116 Gms. being well below average normal value (160.5 Gms., S.D. 22.49). The LV/RV ratio of 2.0 (mean 2.48, S.D. 0.21) is, however, indicative of slight right ventricular hypertrophy. It is of interest to note that in this patient associated chronic bronchitis was not observed.

In all three cases the weight of the left ventricle was within normal limits, and the LV/RV ratio well below normal, indicating exclusive hypertrophy of the right ventricle. Thus, as in cases of fibrosing lung disease, the left ventricle showed no evidence of prolonged strain or of undue dilatation at necropsy, and can be taken as normal.

DISCUSSION

Emphysema with or without associated chronic bronchitis, in contrast to being the most important aetiological factor in the production of cor pulmonale in countries such as Britain, is found at necropsy to be the third commonest cause of the more chronic varieties of cor pulmonale in the African in Durban. The incidence of this disease as a cause of cor pulmonale in the African thus appears to be overstressed. Fibrotic lung disease, secondary particularly to tuberculosis, and pulmonary thrombo-embolism were found to be the more common causes of cor pulmonale in this series. Although emphysema was often also a feature in cases of fibrosing lung disease, it was regarded as being secondary to the fibrosis and not the initial change leading to the development of cor pulmonale.

A comparison of the incidence of emphysema and chronic bronchitis as a cause of cor pulmonale in the different racial groups in Durban or elsewhere in South Africa is not possible on account of lack of comparative data. Although a difference exists between the climatic and

environmental/..

environmental conditions in Britain and South Africa, and while the climate here can be said to be less conducive to the development of chronic bronchitis and emphysema, a lack of data of acceptable quality makes it impossible to estimate comparative incidence in populations living under different environmental conditions. As is realised by other workers in this field, estimates of the necropsy incidence of emphysema, in which the lungs were not inflated prior to being studied, may be erroneous and as such are not acceptable to-day.

With regard to the type of emphysema seen here, the mixed picture (centrilobular and panlobular involvement) was observed far more frequently on examination of whole lung sections than either variety in its pure form. From this study it is not possible to say whether these cases were a progression of centrilobular emphysema or were in fact the mixed variety. Nonetheless, centrilobular involvement frequently occurred in the upper zones, whereas the panlobular involvement was observed more commonly in the lower zones.

It is not possible to comment with any degree of accuracy on the severity of emphysema in these cases since only the one lung was inflated. From examination of the inflated lung it can be said that the degree of emphysema varied from surprisingly mild to gross involvement. It was also noted that single whole lung sections were inadequate for study since the anatomic type and severity of the lesions varied tremendously at different levels.

Associated chronic bronchitis was frequent in this series. How this would correlate with the clinical picture is not known, since none of these patients was subjected to catheterization or blood gas analysis.

Pulmonary vascular alterations were present in 5 of the 6 cases studied, and changes similar to those described by Hicken et al. (1965) were observed. The question remains, however, as to whether such changes lead to pulmonary hypertension or are in fact secondary to such hypertension. Vascular alterations of a similar type were also present in

cases / ...

cases of fibrosing lung disease, and, as will be shown later, were to occur in certain cases of cardiomyopathy as well.

Hicken et al. (1965) have postulated that muscularization of arterioles may be the basis of pulmonary hypertension in emphysema. Such lesions were, however, rarely extensive in this series, being noted only after examination of multiple sections. Although these may be muscularized arterioles, one cannot definitely exclude the possibility of their being contracted small muscular arteries. In one case of emphysema with right ventricular hypertrophy and failure in this series, no structural vascular alterations were found. It is therefore possible that, in this case at least, some cause other than structural alterations in the pulmonary vessels must have been responsible for pulmonary hypertension and subsequent right ventricular strain and failure. Pulmonary infection was not observed in this patient, but was thought to have been the immediate cause of right ventricular failure in one other case in this series.

While thrombi in the pulmonary arteries were often present, thrombo-embolism of significant degree was found in only one of the six cases studied.

It seems likely therefore that structural alterations in the pulmonary arteries, in a significant number of cases of emphysema, are of insufficient degree to account for pulmonary hypertension. This is in agreement with the observations of McKeown (1952) and Kernen et al. (1958). Although vessels below 100μ in diameter with a distinct circular muscle media were present in four of the six cases investigated, the infrequency with which such lesions were observed in the majority of cases in this series, fails to support the view of Hicken et al. (1965), that muscularization of arterioles form the organic basis for the increased pulmonary vascular resistance in emphysema.

The heart in such cases showed evidence of exclusive right ventricular hypertrophy in every case where separate ventricular weighing was undertaken. Values indicative of left ventricular hypertrophy on

measurement/..

measurement of the free wall of this ventricle were thought to be erroneous on account of the chamber having been inadequately dilated. It is unlikely therefore that the left ventricle suffered any significant and prolonged excess in its diastolic volume as a result of bronchial shunting.

SUMMARY

1. Emphysema with or without chronic bronchitis is found to be the third commonest cause, at necropsy, of the more chronic varieties of cor pulmonale in the African in Durban.

2. With regard to the morphological type, emphysema was usually mixed, showing both centrilobular and panlobular involvement, and chronic bronchitis was often associated.

3. The structural alterations observed in the pulmonary arteries in these cases are described and discussed.

4. All cases in which separate ventricular weighing was undertaken showed evidence of exclusive right ventricular hypertrophy.

CHAPTER VII

BILHARZIAL COR PULMONALE IN THE AFRICAN

Although it had long been known that bilharzial ova may be found in the lungs, it was only after Shaw and Ghareeb had published their work in 1938 that both the frequency and importance of the pulmonary complications of bilharzia became apparent. These authors demonstrated pulmonary involvement in 33% of all cases of bilharzia in Egypt, and found that in 2% pulmonary bilharziasis was the immediate cause of death through the mechanism of right ventricular failure.

Pulmonary complications may occur following infection with either S. haematobium or S. mansoni. On account of the vesical veins draining into the internal iliac veins detached ova can readily embolize to the lungs. However, before the ova of S. mansoni can reach the lungs hepatic cirrhosis with the establishment of a collateral circulation is necessary. Shaw and Ghareeb (1938) noted that although ova of S. haematobium were commonly found in the lungs, arterial lesions more often followed S. mansoni involvement of the lungs. The explanation offered for this was that pulmonary involvement with S. mansoni, unlike that with S. haematobium, almost always occurred in association with hepatic cirrhosis and severe somatic lesions, indicating a massive infestation. ..."It is only, then, at a comparatively late stage of the disease that conditions are favourable for pulmonary infection, which will tend to be massive and therefore productive of arterial lesions".

Bhagwandeen (1964) has shown Durban to be an endemic area for bilharziasis. In a study of S. haematobium and S. mansoni infection among the African and Indian populations in Durban this author demonstrated their respective incidence to be of the order of 30% and 10%.

In the present series of 30 cases of cor pulmonale, bilharziasis was incriminated as a cause in a single instance, an African male aged 8 years.

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A Case of Bilharzial Cor Pulmonale:

Necropsy findings. At post-mortem gross generalised oedema, a small ascites, pleural and pericardial effusions were found. The heart weighed 300 Gms. and showed marked right ventricular and right atrial hypertrophy. The left ventricle appeared normal in size. The heart valves were normal and there was no evidence of intra-cardiac thrombi. Except for infarction of the left lower lobe, the lungs appeared normal. Pulmonary arteriography, performed on both lungs, revealed obstruction at the level of the segmental arteries of both lungs, with filling defects peripheral to these (Fig. 1, Plate XI).

On dissection, the main trunk of the pulmonary artery was dilated and mild atheroma of the trunk and main branches was observed. The obstruction of segmental branches was proved to have been due to antemortem thrombi. Peripheral venous thrombosis of the lower limbs was sought but not found.

Bilharzial involvement of the bladder, sigmoid colon and rectum was present. Bilharzial granulations were also noted over the peritoneum in the recto-vesical pouch. Squash-preparations from the large bowel revealed ova of S. mansoni, while those from the bladder revealed ova of S. haematobium (Fig. 2, Plate XI). A mixed infection in this patient was thus established.

The liver showed a nutmeg pattern with tubercle-like structures scattered throughout the organ. Early bilharzial cirrhosis with centrilobular necrosis due to intense congestion was suspected. The spleen was of normal size and showed no abnormality beyond congestion.

Microscopic examination confirmed the presence of vesical and colonic bilharziasis. The liver sections revealed severe centrilobular congestion with necrosis and confirmed the suspicion of early bilharzial cirrhosis. Numerous tubercles, some rather large and necrotic, were observed. The myocardium and spleen showed no evidence of bilharzial involvement.

Histological sections from the lungs showed the presence of

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parenchymatous pseudotubercles lying in close proximity to small pulmonary arteries (Fig. 3, Plate XI). Bilharzial ova were present in some of these lesions, being either calcified or occupied by foreign body giant cells (Fig. 4, Plate XI). Identification of the ova as regards species was not possible on account of their distortion. Apart from these granulomata marked vascular changes were seen in the form of obliterative endarteriolitis, with organising thrombi in arterioles; diffuse intimal thickening of arterioles not directly related to ova was also observed (Fig. 5, Plate XI). The muscular arteries showed medial thickening and also some adventitial thickening. Finally, numerous angeiomatoid lesions (Fig. 6, Plate XI), were seen, indicating, as suggested by Heath and Edwards (1958), a severe chronic pulmonary hypertension.

DISCUSSION

A variety of vascular lesions, including thrombosis of the main pulmonary arteries, have been described by Shaw and Ghareeb (1938) and Cavalcanti et al. (1962). Such lesions consist of proliferative arteritis and intimal thickening of elastic arteries; intravascular granulomata, thrombosis, necrotizing arteritis, angeiomatoid lesions, intimal proliferation and medial and adventitial thickening of muscular arteries; intravascular granulomata, and obliterative lesions of arterioles. Diffuse intimal thickening of arterioles unrelated to ova is possibly due, as suggested, to allergic reaction. Other lesions include parenchymal granulomata, focal fibrosis and pleural thickening.

Factors concerned in the production of right ventricular hypertrophy and failure are said to be mechanical due to obstruction of the pulmonary arteries by ova and worms, allergic, and vasoconstrictive (Cavalcanti et al. 1962). Magalhaes Filho (1959) is cited by Cavalcanti et al. (1962) as having shown that the passage of ova through the lungs of mice previously infected produce acute arteritis with an intense allergic reaction. Zaky et al.

(1962) /...

(1962), as a result of catheter studies on patients with pulmonary bilharziasis, demonstrated bronchopulmonary as well as splenic shunts, and postulated that such shunts, plus repeated showers of ova in the lungs, contributed towards cor pulmonale in bilharziasis.

Angeiomatoid lesions are known to occur in other forms of pulmonary hypertension. While Shaw and Ghareeb (1938) thought they were enormously dilated capillaries escaped from a canalizing vessel through a lesion in the media, recent workers (Brewer 1955, and Wagenvoort 1959), have suggested that they are probably greatly dilated arterioles which arise from small arteries proximal to the obstruction and eventually join the alveolar capillaries, producing a new route to the latter.

SUMMARY

A case of bilharzial cor pulmonale resulting from a mixed (S. haematobium and S. mansoni) infection has been described. Experience from this and two more recent cases leads one to stress the lack of obvious naked-eye lesions and apparent normality of the lung at necropsy. Furthermore, there may be areas of the lung microscopically devoid of lesions, so that random sections might result in the diagnosis being missed. It does seem coincidental that these examples of pulmonary bilharziasis should have been found since the start of this intensive investigation, so that it is possible that cases have been missed in the past and that the syndrome is more common than suspected. An alternative possibility is that the disease is becoming more widespread and infection more severe.

PRIMARY PULMONARY HYPERTENSION IN THE AFRICAN

Brenner (1935) defined primary pulmonary arteriosclerosis and stated that it was a rare condition. The diagnosis of this disease at

necropsy/...

necropsy, as evidenced by right ventricular hypertrophy, is suggested when no aetiological factor either in the form of heart disease, lung disease, or pulmonary emboli, can be found.

Pulmonary vascular lesions may or may not be present, and those without structural alterations in the vessels have been designated idiopathic right ventricular hypertrophy by De Navasquez et al. (1940). Similar cases have been reported by East (1940) and Armstrong (1940).

Nevertheless in the majority of cases vascular lesions have been recorded, consisting of hypertrophy of the media, focal intimal proliferation and fibrosis of the muscular arteries. The larger arteries show mainly atheromatous changes. Although fibrous tissue may appear totally to exclude the lumen, a narrow rough channel is usually seen. Local dilatation of the smallest muscular arteries is uncommon, but thrombosis usually occurs at this site and later organises and recanalizes (Harris and Heath 1962).

The aetiology of primary pulmonary hypertension is not known. The disease is reported as occurring at any age, and is stated to be far more common among females than males (Evans et al. 1957). Rosenberg (1964) reported that in a series of 23 patients in whom a clinical diagnosis of primary pulmonary hypertension was made 9 died and were examined at necropsy. In six of these 9 patients a post-mortem diagnosis of thrombo-embolic pulmonary disease was made. A similar experience had been reported by Evans et al. (1957), and Dexter et al. (1960). The latter concluded that unless recurrent pulmonary embolism is conclusively excluded, the diagnosis of primary pulmonary hypertension is unjustified.

Gilmore and Evans (1946) considered the endarteritis to be the result of the medial deficiency, possibly aggravated by transient hypertension due to coughing. Ultimately a vicious circle is established and pulmonary hypertension becomes permanent.

Because of the high incidence of polythelia in persons with this disease, and the presence of aplasia and hypoplasia of the media of the lung arteries, Evans (1959) considered a congenital or genetic origin. An

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inherited abnormality was also suggested by Coleman et al. (1959), who found primary pulmonary hypertension in three siblings.

Farrar (1963) postulated that in some cases of primary pulmonary hypertension with occlusive vascular changes, vasospasm might be the initial disturbance, and that organised and recanalized thrombi arose locally as a result of antemortem vasoconstriction and were not embolic in origin.

In this series of cor pulmonale in Africans there was one case of possible primary pulmonary hypertension, occurring in a 12-year old boy. The diagnosis was made at necropsy on account of marked right ventricular hypertrophy and failure for which no cause could be found in either the heart or the lungs, and no obvious source for pulmonary embolization was observed. There was no evidence of polythelia. Apart from signs of chronic passive venous congestion of the organs no other disease process was apparent. Unfortunately pulmonary angiography was impossible in this case as the lungs had been damaged during opening of the thoracic cage.

Lung histology revealed atheromatous change in the elastic arteries; medial hypertrophy, intimal proliferation, and intimal fibrosis of the muscular arteries, and "muscularization of arterioles" were also observed. Again the possibility of these being contracted muscular arteries cannot be excluded. Although obvious thrombi was not observed in the pulmonary arteries, focal intimal proliferation suggestive of organizing thrombi was sometimes seen.

SUMMARY

Primary pulmonary hypertension is a rare cause of right ventricular hypertrophy and failure in the African, as also in the other races.

CHAPTER VIII

CARDIOMYOPATHY IN THE AFRICAN

Cardiomyopathy has been included in this study because of the frequency with which preponderant right ventricular hypertrophy was suspected in such hearts at necropsy. Higginson et al. (1960), in describing the heart in cardiomyopathy at necropsy, commented that it was usual for hypertrophy to be generalised with equal involvement of all chambers, only a few of their cases showing predominant right-sided hypertrophy. In a previous report Higginson and his co-workers (1952) had mentioned one such example in a series of 12 cases. In a series of 90 cases Becker (1963) encountered 2 patients with isolated right ventricular endomyocardial fibrosis and mural thrombi, of which one showed hypertrophy and dilatation of the right ventricle and dilatation only of the left ventricle. This author found predominant left ventricular hypertrophy to be far commoner than that of the right ventricle. Reid (1966), in a study pertaining to the muscle fibre of the heart in cardiomyopathy among Africans in Durban, found the thickness of the free wall of the right ventricle to be significantly greater than normal while similar measurements for the left ventricle revealed no significant change from normal. The right ventricle also showed a greater total muscle fibre width as compared with controls, but no significant change in total fibre width was noted in the wall of the left ventricle. The proportionate increase in weight of the two ventricles, however, was much the same. From this work Reid (1966) postulated that "a major cause accounting for change in weight must be an increase in the length of fibres of the ventricles without change in their number", and suggested that the enlargement of the right ventricle might be secondary to left ventricular failure. While the inference of a lengthwise hypertrophy may be a possibility, it must be remembered that the width of the cardiac muscle fibres in decompensated hearts will be interfered with by dilatation of a chamber which causes the fibres to become elongated and consequently narrowed. This is particularly so in cardiomyopathy hearts, where dilatation is so often marked.

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On the clinical front Powell and Wright (1965) reported that patients with cardiomyopathy can present with predominant right-sided heart failure, making differentiation of these from cor pulmonale difficult. However, these authorsfound such cases to be very infrequent in their series.

In view of the findings of others, and the impression at necropsy that predominant right ventricular enlargement is more common than hitherto believed, it was necessary to study a series of consecutive cases of cardiomyopathy on lines similar to those followed in investigating cor pulmonale. It was felt that in this way other known causes of right ventricular hypertrophy would be excluded and some estimate of incidence of predominance of this chamber in cardiomyopathy obtained; at the same time it was hoped that some idea of the possible underlying causes might come to light.

ANALYSIS OF MATERIAL

These results are based on the necropsy findings in a series of 35 consecutive cases of cardiomyopathy in African subjects. The diagnosis of cardiomyopathy at necropsy has been based on the exclusion of coronary heart disease, hypertension, valvular disease, and cor pulmonale as causes of the heart failure. Cardiomegaly from dilatation and /or hypertrophy (the former in excess of the latter), endocardial sclerosis, and mural thrombi, were taken as positive evidence of its presence. Excluded from this series are three cases in which cardiomyopathy was believed to have co-existed with other forms of heart disease. These included one instance where tuberculous pericarditis was also present, and two patients in whom associated rheumatic valvular disease was strongly suspected.

This series was made up of 24 males and 11 females. The youngest patient was 16 years of age and the oldest 68; there were 3 in the second decade, 7 in the third, 6 in the fourth, 7 in the fifth, 8 in the sixth, and 4 were over 60 years of age.

The heart in cardiomyopathy.

Macroscopic examination: All 35 patients included in this study died as a result of congestive heart failure. The heart was enlarged in all cases, being both hypertrophied and dilated. Table I shows the total heart weights in these 35 cases. Comparable statistics as given by Higginson et al. (1960) are also included in this table.

TABLE I

TOTAL HEART WEIGHTS IN CASES OF CARDIOMYOPATHY

Total Heart Weight (Gms)	Present series 35 cases		Higginson et al. (1960) 78 cases	
	No.	%	No.	%
300-400	4	11.4	13	16.7
400-500	11	31.4	24	30.1
500-600	17	48.6	28	35.9
600-700	2	5.7	11	14.1
700+	1	2.9	2	2.1

As evident in both series in Table I the majority of cardiomyopathy hearts showed a moderate increase in weight.

While bi ventricular involvement was clearly obvious at necropsy, it was often very difficult on account of the dilatation to assess, naked-eye, which of the two ventricles was more hypertrophied.

Ventricular hypertrophy was therefore assessed by means of the two methods described. Because dilatation was always present, and because it varied in degree from case to case, estimates of hypertrophy by measuring the thickness of the free walls of the ventricles was found to be of little value in showing which of the two ventricles was predominantly enlarged. Unequal dilatation of the chambers, if present, would also give erroneous results. Table II shows the results obtained on measurement of the free walls of the two ventricles in 17 cases of cardiomyopathy.

TABLE II/...

TABLE II

MEASUREMENTS OF VENTRICULAR WALL THICKNESS IN 17 CARDIOMYOPATHY HEARTS

Case	Total heart weights (Gms)	LV thickness (mm)	RV thickness (mm)
1	430	15	5
2	450	18	6
3	320	22	4
4	390	16	5
5	630	25	8
6	650	17	8
7	550	11	4
8	580	20	5
9	530	25	9
10	550	19	9
11	430	22	14
12	460	20	9
13	510	12	5
14	580	20	10
15	530	17	5
16	350	16	5
17	530	18	10

As evident from Table II, there appears to be little if any correlation between total heart weights and ventricular wall thickness. Two cases in the above Table, although showing total heart weights of over 500 Gms. on measurement yielded normal values of wall thickness for both ventricles.

In a further 18 consecutive cases of cardiomyopathy, ventricular hypertrophy was estimated by use of the method entailing separate ventricular weighing. Table III shows the results obtained.

As evident in Table III the right ventricle shows an increase in weight above normal in all 18 instances. Whereas exclusive right ventricular hypertrophy is apparent in three cases (Case 20, 26 and 35, Table II), biventricular enlargement with right ventricular predominance is present in 9 cases. Equal enlargement is observed in 5 cases, and only 1 case shows left ventricular predominance.

TABLE III/...

TABLE III

SEPARATE VENTRICULAR WEIGHTS IN 18 CASES OF CARDIOMYOPATHY

Case	Total heart Weights(Gms)	LV weight (Gms)	RV weight (Gms)	$\frac{LV}{RV}$
18	550	277	124	2.23
19	500	214	132	1.62
20	420	179	102	1.75
21	450	240	97	2.47
22	580	280	127	2.20
23	420	200	134	1.49
24	450	244	104	2.35
25	560	265	149	1 79
26	360	169	105	1.61
27	530	247	118	2.09
28	480	228	110	2.07
29	500	233	101	2.31
30	400	198	102	1.94
31	530	323	99	3.26
32	570	246	135	1.82
33	1000	520	212	2.45
34	580	200	118	1.69
*35	470	183	120	1.52

* + diffuse emphysema

Normal LV weight = 160.5 (S. D. 22.49). RV weight = 66.3(S. D. 7.7)
LV/RV = 2.48(S. D. 0.21)

Table III may be compared with similar tables in cor pulmonale, where exclusive right ventricular hypertrophy was noted, and Table IV where separate ventricular weights in 6 cases of hypertensive heart failure, showing predominant left ventricular hypertrophy, are given.

Other gross morbid anatomical features correlated closely with descriptions of Higginson et al. (1960); Becker et al. (1953); Becker (1963). In 11 hearts no significant changes other than hypertrophy, dilatation, and in some, small patches of endocardial sclerosis, were seen. Intraluminal thrombi were observed in 24 of the 35 hearts studied. These were most frequently found in the right atrial appendage and the second commonest site was the apical region of the left ventricle. However, no chamber was immune

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to mural thrombus formation. Embolic phenomenon occurred in 14 patients and Table V shows the organs involved and the frequency with which they were affected.

TABLE IV

SEPARATE VENTRICULAR WEIGHTS IN 6 CASES OF CONGESTIVE CARDIAC FAILURE DUE TO HYPERTENSION

Total heart Weights (Gms)	LV Weight (Gms)	RV Weight (Gms)	$\frac{LV}{RV}$
500	267	97	2.75
510	305	86	3.54
590	345	91	3.79
520	280	92	3.04
570	343	100	3.43
400	215	65	3.30

TABLE V

EMBOLIC PHENOMENON IN 14 CASES OF CARDIOMYOPATHY

Organs	No. of Cases
Lungs	11
Kidneys	5
Spleen	3
Myocardium	1
Brain	1

The lungs were most frequently involved, and a double source for embolization (right heart and leg veins) was present in 4 cases. In two patients with cardiomyopathy in whom extensive pulmonary thrombo-embolism and infarction were found, the right heart showed no thrombi and the source was found at necropsy in the deep veins of the legs. In patients showing either myocardial or cerebral infarction, significant arterial disease was excluded

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and the opinion was that in both, these were embolic in origin.

Sclerotic thickening of the endocardium when present was most marked in the right atrium and apical region of the left ventricle and, in agreement with Higginson et al. (1952) and Higginson et al. (1960), is believed to have been the end result of thrombus organisation.

The sequence of primary mucinous endocardial degeneration followed by fibrinoid necrosis and later thrombosis, as described by Becker et al. (1953), was not demonstrated in this series. Small areas of mucinous degeneration were often noted in the endocardium but only in relation to mural thrombi, and were thought to be possibly secondary to the anoxia or thrombus formation. In no instance was endocardial fibrosis of the degree described in Uganda observed, nor were valvular lesions noted.

Histological study in cases with endocardial sclerosis revealed the thickening to be fibroelastic in nature, and a mild cellular infiltrate of lymphocytes and plasma cells was sometimes present. Microscopic examination was suggestive of hypertrophy on account of the prominence of nuclei rather than obvious increase in the width of fibres; this was considered due possibly to elongation and thinning of the fibres from dilatation of the chambers. Fibre hypertrophy was by comparison more obvious in the right ventricle than in the left. In many hearts the myofibrils were widely separated, and thus intercellular oedema could not be excluded. If such oedema were present it must play some part in the increase in heart weight in cardiomyopathy. Just how much of the weight increase is due to oedema has not been assessed in this study, but nevertheless it justifies consideration in assessing heart weights.

Scarring of the myocardium was sometimes observed, and in the majority such scars consisted of small foci of fibrosis, though occasionally larger ones (Figs. 5 and 6, Plate ~~VIII~~ IX) were noted. Myocardial scars were usually situated in the inner third-half of the wall, and larger scars, in this series, were seen only in the wall of the left ventricle involving either the apical region, posterior wall, or anterior wall. It is the opinion of the

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author that larger scars arose from organisation of small infarcts, the latter being embolic in origin. This supports the clinical opinion of Cosnett and Pudifin (1964) that myocardial infarction may complicate some cases of cardiomyopathy.

The histochemistry of the myocardium in cardiomyopathy.

The ordinary histological methods of study show no specific feature whereby cardiomyopathy may be distinguished from some other types of heart disease, and its diagnosis still rests to a large extent on the exclusion of all known causes. For this reason certain histochemical investigations were undertaken in the hope of finding some feature which would distinguish cardiomyopathy from other cardiac diseases. As mentioned, some of the histochemical methods tried gave unsuitable results when myocardial tissue was used. Hence only histochemical findings relating to successful staining for succinic dehydrogenase, DPN diaphorase, haemosiderin and fat will be discussed here.

The literature contains very little information pertaining to histochemistry of the myocardium in African cardiomyopathy. Pearse's (1964) work on histochemistry and electron microscopy of the myocardium was undertaken in cases of obstructive cardiomyopathy, which is an entirely different condition from African cardiomyopathy.

Higginson et al. (1952) found little iron in the heart muscle in cases of African cardiomyopathy and concluded that haemosiderosis per se could not be the cause of heart failure in these cases.

Kobernick et al. (1963) reported diminished succinic dehydrogenase activity in the myocardium from a case of idiopathic cardiomegaly and suggested that the diminution of this enzyme might have been responsible for the cardiac failure in their case, since succinic dehydrogenase occupies a key position in the tricarboxylic acid cycle which is a major source for the production of ATP necessary for muscle contraction. These authors also suggested that cardiac hypertrophy could conceivably be stimulated by a chemical energy deficiency.

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The material used in this survey was derived from the cases summarised in Table VI.

TABLE VI

DIFFERENT AETIOLOGICAL TYPES OF HEART DISEASE USED FOR HISTOCHEMICAL STUDY

Types of Heart Disease	No. of Cases
Cardiomyopathy	15
Rheumatic	14
Hypertensive	12
Cor Pulmonale	9
Syphilitic	8
Viral Myocarditis	2
Total	60

Results:

1. Succinic dehydrogenase and DPN diaphorase activity in the myocardium; Staining for these enzymes in the heart muscle in cases of cardiomyopathy indicated that their activity in the majority of fibres was normal. In some small areas there was either a diminution (Figs. 1 and 2, Plate VIII) in or complete absence (Fig. 3, Plate VIII) of these enzymes. Such decrease or lack, although frequent, was not always present in cases of cardiomyopathy and was by no means specific to such cases; similar observations were recorded in cases of rheumatic and viral myocarditis, and in a few cases of hypertensive heart disease.

2. Stainable Iron in the Myocardium.

Staining for haemosiderin in the myocardium in cardiomyopathy showed either negligible amounts or complete absence of the pigment. In no case in this series was haemosiderin present to the degree described in some cases of haemochromatosis, and the picture observed in cardiomyopathy differed in no way /...

way from that observed in other aetiological forms of heart disease in the African.

3. Stainable Fat in the Myocardium;

In a few cases of cardiomyopathy focal areas of fatty change of the myofibrils were observed. Similar areas, however, were also observed in a small number of patients investigated in each of the different types of heart disease shown in Table I.

The lungs in cardiomyopathy.

While a fair number of published works relating to the structural changes of the heart in cardiomyopathy are available, little mention has so far been made of the lungs in this condition. Because of this omission, and also on account of the findings in this series regarding predominant right ventricular hypertrophy in hearts of patients succumbing to congestive heart failure in cardiomyopathy, it became necessary to study the lungs more closely.

The salient points noted on gross examination of such lungs at necropsy were, firstly, that although pulmonary oedema was always present, the effects of chronic passive venous congestion were usually absent or mild and secondly, the frequency with which pulmonary thrombo-embolism and infarction occurred. As mentioned previously, the lungs were the organs most frequently affected by thrombo-embolism in cardiomyopathy, and a double source for embolization was sometimes present. Pulmonary embolization and infarction when present were often sufficiently extensive to have been the immediate cause of death in a significant number of patients in whom this complication had occurred.

The picture obtained on pulmonary arteriography depended to a large extent on the presence or absence of pulmonary thrombo-embolism, and on the degree of right ventricular predominance. Figs. 1 - 4, Plate IX, show the patterns observed on pulmonary arteriography in cases of cardiomyopathy with pulmonary thrombo-embolism. It will be noted that the picture closely resembles those obtained in cases of primary thrombo-embolic lung disease.

While/...

While any-sized vessel can be involved, occlusion of the large arteries such as the segmental branches with consequent pulmonary infarction were commonly observed. Fig. 4, Plate IX shows the presence of a liquifying and infected infarct, close to the pleural surface. Pulmonary arteriography in some patients dying from congestive cardiac failure due to cardiomyopathy, but not showing significant pulmonary embolization and/or infarction, revealed marked narrowing in the calibre of the intrapulmonary arteries of all sizes, and loss of peripheral arborization was also observed (Fig. 1 - 2, Plate IX). Such changes were not restricted to cases with right ventricular predominance, nor were they common in cardiomyopathy, being observed in only 4 of the 17 cases on whom post-mortem arteriography was undertaken. These 4 included two cases of predominant right ventricular hypertrophy, one with equal enlargement of the ventricles and one with left ventricular predominance.

Whole lung sections were made in 32 of the 35 cases investigated, and while localized emphysema secondary to small scars was often noted, significant generalised emphysema was found to co-exist with cardiomyopathy in one case only.

Unilateral pyogenic empyema was noted in 3 patients at necropsy, and in all 3 was suspected to have originated as a result of liquifaction, infection, and finally rupture into the pleural cavity of infarcts situated close to the pleural surface.

Histological examination of the lungs, while confirming many of the naked-eye findings, revealed structural alterations in the pulmonary arteries in a large number of cases of cardiomyopathy. Certain changes were particularly common in cases showing narrowing and loss of peripheral vessels on angiography. The vascular changes consisted of:-

1. Pulmonary thrombo-embolism varying from fresh occlusions to those showing different stages in organisation and completely organised lesions. The latter always took the form of fibro-elastic thickening of the intima. Fig. 1 and 2, Plate X show late and intermediate stage of organisation within the muscular pulmonary arteries. Fresh and organising emboli

were/...

were found in 11 patients, and completely organised lesions in another 4 cases. Right ventricular predominance could have been caused by recurrent thrombo-embolism in 2 of the 18 patients investigated by arteriography.

2. An additional longitudinal muscle layer, with elastic tissue hyperplasia, in the intima of muscular pulmonary arteries, accounting for an increase in wall thickness of these vessels (Figs. 5 and 6, Plate X) was seen in 26 patients. Although in many cases such lesions were fairly frequently observed, a few showed involvement of isolated vessels only. This was the commonest of all structural changes in the pulmonary arteries, but is in no way confined to cardiomyopathy, being present also in emphysema and occurring in some cases of hypertensive heart disease dying from congestive cardiac failure.

3. Vessels below 100μ in diameter showing a distinct circular muscle layer with a double elastic lamina (Fig. 4, Plate X) was the third most common lesion observed. Whereas such lesions were frequent in the contra-lateral lung of those showing marked narrowing of the pulmonary arteries on arteriography (4 Cases), careful search in multiple sections often revealed a few such vessels in cases not showing the above arteriogram pattern. The question which arises is whether these are muscularized pulmonary arterioles, or contracted small pulmonary arteries.

4. Vessels below 100μ while showing distinct circular muscle layers with double elastic laminae, sometimes showed an additional longitudinal layer, with elastic tissue hyperplasia, in the intima (Fig. 3, Plate X). This was the least common of the vascular changes, being observed in 8 cases, but was particularly marked in only one case, in which other causes for right ventricular hypertrophy, including emphysema, were excluded.

Similar arterial changes have been described in emphysema, and the same difficulties as regards pathogenesis arise here. Do these changes cause pulmonary hypertension and subsequent right ventricular hypertrophy, or are they in fact secondary to the pulmonary hypertension initiated by some other cause?

Discussion/...

DISCUSSION

Whereas the cause of cardiomyopathy remains obscure, a number of possibilities have been suggested.

Clinical and necropsy findings exclude the possibility of cardiomyopathy, as seen in South Africa, being secondary to diseases such as anaemia, cor pulmonale, glycogen-storage disease, amyloidosis, toxoplasmosis, scleroderma, disseminated lupus erythematosis, carcinoid syndrome, chronic liver abscess, or severe infective myocarditis, and fail to support the view of Laurie et al. (1960) that it represents a form of ischaemic heart disease dependent on coronary atherosclerosis. The role of siderosis in cardiomyopathy is questionable, since stainable iron in the myocardium, in both the present series and in that of Higginson et al.(1952), was found to be either negligible or totally absent. Histochemical investigation of the enzymes succinic dehydrogenase and DPN diaphorase, while showing a diminished or complete lack of activity in some fibres, was in no way specific to cardiomyopathy, similar changes being observed also in cases of rheumatic and viral myocarditis.

That chronic malnutrition may be responsible for the production of this disease has been suggested by Gillanders (1951), who emphasized the frequency with which relapse occurred when patients returned home. The lack of obvious signs of malnutrition in a fair number of patients in this series makes this seem an unlikely cause. Grusin (1957) described the rapid response to thiamine of certain cases of acute heart failure among African patients. However, cardiomyopathy similar to that seen here does not appear to be common in the Far East, where a large number of cases of acute beri-beri heart disease are seen.

Reid (1966) was able to produce pathological changes similar to those observed in cardiomyopathy in rats by feeding them on a diet deficient in tryptophan. The only criticism of this work is that rats may develop a form of myocarditis spontaneously (Wainwright 1967), and this throws doubt on the significance of results based on necrotic or fibrotic changes in the hearts of these animals.

Becker /...

Becker et al. (1953) suggested that the primary lesion in cardiomyopathy lay in the endocardium. The sequence described by these workers was , however, not demonstrable in the present series, or in that of Higginson et al. (1960).

Brigden (1957) regards alcoholic cardiomyopathy as an entity, and while there is a close similarity between African cardiomyopathy and the findings in alcoholic heart disease as recently reviewed by Brigden and Robinson (1964), the position of alcoholism is difficult to assess in necropsy studies. Powell and Wright (1965) were, however, unable to incriminate alcoholism as a cause in any of their cases of cardiomyopathy in the African.

While it has been shown in this study, in agreement with the general view, that biventricular involvement of the heart is found in cardiomyopathy, the results obtained regarding the frequency with which right ventricular predominance occurs contrasts sharply with the necropsy findings of the other investigators. It must be remembered, however, that with the exception of Reid (1966) separate ventricular weighing, which would give a more accurate assessment of ventricular enlargement, was not undertaken in the necropsy studies of others (Higginson et al. 1952; Higginson et al. 1960; Becker et al. 1953). Although Becker (1963) mentions separate ventricular weighing, his figures are not available for comparison.

Reid (1966) found right ventricular wall thickness, as measured in situ at necropsy, to be significantly greater than normal in contrast to similar measurements for the left ventricle, but noted no difference in the proportionate increase in the weights of the two ventricles. In the present series, although values above 5 mm. for the free wall of the right ventricle were found, almost half the total number of hearts on which this measurement was made failed to show a right ventricular wall thickness greater than 5 mm. Hypertrophy of this chamber was nevertheless not excluded but was believed to have been masked in every case by its extreme dilatation. Similarly, in some cases, measurement of the free walls of both ventricles fell within the normal range in spite of the total heart weights being significantly increased (Table II).

While/...

While the results of separate ventricular weighing, in this series, show exclusive right ventricular hypertrophy to be uncommon in cardiomyopathy, biventricular hypertrophy with right ventricular preponderance was found to be the most frequent form of cardiac hypertrophy in such hearts. Equal involvement of the two ventricles was the second most common type of enlargement encountered. Left ventricular predominance was least frequently noted, and no instance of exclusive ventricular hypertrophy was found. These observations do not agree with those of Higginson et al. (1960) and Reid (1966) that the ventricles are usually equally hypertrophied, nor with Becker's (1963) finding of frequent left ventricular predominance in cardiomyopathy.

The infrequency with which exclusive right-sided hypertrophy is found may explain the clinical findings of Powell and Wright (1965) regarding the infrequency with which right-sided failure simulating *cor pulmonale* occurs in cardiomyopathy.

It is, nevertheless, usual for these patients to present with peripheral oedema early in the disease. If both ventricles are not affected simultaneously by failure, the early appearance of oedema must at least suggest early involvement of the right side of the heart. Under such circumstances it would be unlikely for right ventricular hypertrophy to be secondary to long-standing left ventricular failure. The absence of exclusive left ventricular hypertrophy, together with the infrequency with which left ventricular predominance (in cases where both ventricles were involved) occurred, rather suggest that left ventricular hypertrophy may be secondary to right ventricular failure. This, however, is believed to be unlikely.

The finding of structural alterations in the muscular pulmonary arteries in a large number of cases of cardiomyopathy in the present series is in no way specific, being observed in at least 3 types of heart failure, including congestive heart failure due to hypertension.

Although fresh pulmonary emboli and infarcts were frequent, and often of such degree as to be the immediate cause of death, chronic pulmonary

thrombo/...

thrombo-embolism of an extent sufficient to cause right ventricular predominance was suspected in only 2 of 18 cases investigated by arteriography. Other vascular changes, observed particularly in the small pulmonary arteries, were identical to those found in emphysema, thereby indicating that such lesions are not confined to emphysema. Hicken et al. (1965) suggest that muscularisation of the pulmonary arterioles may be responsible for the pulmonary hypertension with subsequent right ventricular hypertrophy and failure in emphysema. In the majority of cases of cardiomyopathy, however, as in some cases of emphysema, such alterations were found to be of insufficient extent to account for the right ventricular hypertrophy. Pulmonary arteriograms in some cases of cardiomyopathy show a marked narrowing of the arteries at all levels, and muscularized vessels below 100μ in diameter were especially frequent in the contralateral lungs of cases showing this pattern. The possibility that these vessels may be contracted small muscular pulmonary arteries cannot be excluded.

In view of these findings it is suggested that the cause of pulmonary hypertension in cardiomyopathy may lie in some factor other than structural changes in the pulmonary arteries, and that the alterations observed are secondary to the increased pulmonary arterial pressure. The fact that the picture of pulmonary hypertension was not always present on arteriography, although right ventricular preponderance was common, might suggest that some factor such as pulmonary vasoconstriction, episodic in type rather than sustained, could be responsible, and that pulmonary hypertension might be reversible, as in emphysema, until irreversible vascular changes develop.

If right ventricular hypertrophy in cardiomyopathy is to be explained on the basis of pulmonary hypertension alone following on episodes of generalised pulmonary arterial vasoconstriction, enlargement of the left ventricle can be said to be due to increased shunting of blood via the bronchial vessels, with a possible diastolic overload of the left ventricle as a result of the distal bronchial veins draining into the left atrium.

This, however, seems unlikely because it fails to explain the lesions

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so frequently observed in the left ventricle in cardiomyopathy. It is highly probable that some form of damage to the myocardium occurs concurrently with pulmonary vasoconstriction, the latter accounting for the frequency with which right ventricular predominance occurs.

Whereas no positive evidence regarding the aetiology of cardiomyopathy emerges from this study, it is postulated that the cause may lie in some form of exogenous toxin which acts as an arterial vasoconstrictor affecting not only the arteries to the lungs but also those of other organs in the body. The African in these parts is known to resort to the herbal 'remedies' of the inyanga, which he may inhale, swallow, or administer by way of an enema. That some such remedies may be toxic has long been suspected on account of the frequency with which acute, diffuse centrilobular necrosis of the liver and acute renal tubular necrosis are encountered among this population at necropsy. It is suggested, therefore, that the high recurrence rate of heart failure among patients with cardiomyopathy, after discharge from hospital, may be related to a resumption of some form of noxious practice peculiar to the African, rather than to a return to a deficient diet as implied by Gillanders (1951).

5-hydroxytryptamine has been implicated in the aetiology of endomyocardial fibrosis on account of the high content of this substance in plantain which is eaten by the people of Uganda (Arnott 1959; Crawford 1963). This hypothesis, however, does not explain why the lesions in endomyocardial fibrosis commonly occur in the left ventricle, since 5-hydroxytryptamine does not reach the left side of the heart. It is similarly unlikely to be the cause of our cases of cardiomyopathy, in which endocardial lesions are less severe and valvular lesions are never encountered.

The cardiac lesions in cardiomyopathy could be explained on the basis of anoxia resulting from coronary vasoconstriction. This would explain not only why myocardial scars in cardiomyopathy are often restricted to the inner half/third of the wall of a ventricle, but also the mucinous degeneration, fibrinoid necrosis and haemorrhages of the endocardium observed by Becker (1963) in cases of so-called acute mural endocardial disease. The formation

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of mural thrombi would thus be secondary to anoxic damage to the endocardium.

SUMMARY

1. The morbid anatomy, histopathology, and certain histochemical findings, together with post-mortem pulmonary arteriography, in 35 consecutive cases of cardiomyopathy are described and discussed.

2. In view of the results obtained it is suggested that the possible aetiological factor responsible for this form of heart disease may be an exogenous toxin which acts as an arterial vasoconstrictor, both in the lung and systemic circulations.

RÉSUMÉ

The aims and objects of this work, as outlined in the introduction, were to assess the necropsy incidence of deaths due to heart failure in the African in Durban, to assess the necropsy incidence of the various aetiological types of heart failure with particular reference to right ventricular hypertrophy and failure, and to compare and contrast the incidence, complications, morbidity and mortality of heart disease in the Natal African with the same in other African and racial groups, both in South African and elsewhere. Many of the points emerging from this work merely confirm what has long been known, but others refute previous concepts.

The all-age average necropsy incidence of deaths from heart failure in the African in Durban is of the order of 8%. This percentage does not, unfortunately, lend itself to straight comparison with most other series because of the high infant mortality shown in the present study. However, in considering deaths due to heart failure in the 10-plus age groups, the African still shows a lower mortality from heart disease in comparison with figures obtained for Indians or those reported for the Coloured and White races in South Africa.

There are six major causes of heart disease in the African, which in order of frequency are, rheumatic heart disease, hypertensive heart disease, cardiomyopathy, cor pulmonale, pericarditis, and syphilitic heart disease. While little difference is apparent in the incidence of rheumatic and hypertensive heart disease, and possibly cor pulmonale, among the various races, cardiomyopathy, pericarditis and syphilitic heart disease are far more important causes of heart failure in the African by contrast with the other racial groups in South Africa. Although coronary artery disease is by comparison very uncommon in the African, cardiomyopathy, pericarditis, and syphilitic heart disease together claim as many deaths from heart failure in these people as does coronary heart disease among the Indian and White races in the Republic. Except for minor variations in the incidence of certain aetiological types, and the geographical distribution of endomyocardial fibrosis and

cardiomyopathy/..

cardiomyopathy, the general pattern of heart disease among the Africans in Natal appears to be similar to that reported from other Provinces in South Africa and most other countries on the continent.

Rheumatic heart disease is responsible for 21.5% of all deaths from congestive heart failure in the African in Durban. The immediate and the late cardiac complications of rheumatic fever in the Durban African are, on the whole, found to be no different from those reported in Western communities. The findings in this study therefore refute the view that rheumatic heart disease is infrequent in the African after the age of 40 years, and failed to support the suggestion that the disease affects them more severely or that death from rheumatic heart disease occurs at an earlier age in this race. While it is agreed that severe valvular deformity in young African subjects (under 15 years of age) occurs comparatively more frequently, it must be stated that this is in no way peculiar to the African, similar lesions being observed in Indian subjects of corresponding age.

Hypertensive heart disease is common among the African in Durban, accounting among them for 18.9% of all deaths from congestive heart failure. While both essential and secondary forms of hypertension occur in the local indigenous population, the former appears to be more common, with a peak incidence in the seventh decade of life. Secondary hypertension, mostly renal in origin, is an important cause of hypertensive congestive cardiac failure in the fourth decade. The wide variations in the type of hypertension reported from the different regions in Africa, and the doubt existing as regards the significance of focal lesions in the kidneys, point towards the need for generally accepted criteria in the diagnosis of renal hypertension, particularly with regard to chronic phylonephritis.

Cardiomyopathy claims 15.8% of all deaths from congestive heart failure in the local African population. While many of the pathological changes occurring in the heart in this disease were found to be similar to those of other investigators, certain features, relating to cardiac hypertrophy and structural alterations in the pulmonary vessels, have been especially

investigated/...

investigated and results obtained in this series of cases show that whereas pure right ventricular hypertrophy is uncommon in cardiomyopathy biventricular hypertrophy with predominance of the right ventricle is the most frequent form of cardiac enlargement in such cases. Equal hypertrophy of the ventricles is the next common form of enlargement; left ventricular predominance is by far the least frequent, and no case of exclusive left ventricular hypertrophy was encountered.

Although structural alterations in the pulmonary arteries, indicating pulmonary arterial hypertension, were observed in a large number of cases investigated, such changes were in no way specific to cardiomyopathy, since similar changes were observed in cor pulmonale due to emphysema and also in some cases of hypertensive congestive heart failure. Structural alterations in the small muscular pulmonary arteries and arterioles were also identical with those found in emphysema. Whereas fresh pulmonary emboli and infarcts were frequently encountered and were often of such degree as to be the immediate cause of death, chronic pulmonary thrombo-embolism of an extent sufficient to have been the cause of right ventricular predominance was seldom found.

It is suggested that the cause of the pulmonary hypertension and certain pathological changes in the heart in cardiomyopathy may lie in some form of exogenous toxin, possibly related to the practice of herbal medication among the African people, which acts as an arterial vasoconstrictor in both the pulmonary and systemic circulations. This would suggest that the arterial changes observed in the lungs are probably the result and not the cause of pulmonary hypertension.

The incidence of cor pulmonale as a cause of congestive heart failure among the African in Durban is of the order of 12%. It has been shown that almost one quarter of all cases of right ventricular failure remains undiagnosed, as regards aetiology, at routine necropsy. The latter finding pointed towards the need for an investigation of the causes of right ventricular failure in the African. Such a study was undertaken and special methods of investigation

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were used as aids towards a more conclusive diagnosis. This study showed fibrosing lung disease, due particularly to the late complications of pulmonary tuberculosis, to be the most important cause in the production of chronic cor pulmonale in the African in Durban. The development of cor pulmonale in such cases depends not only on the presence of pulmonary parenchymal damage by fibrosis, but also on the associated pleural thickening, adhesions between chest cage and diaphragm, emphysema, and the curtailment of the pulmonary arterial bed. In this series, all cases of fibrosing lung disease with cor pulmonale investigated for cardiac hypertrophy by means of separate weighing of the ventricles, showed evidence of pure right ventricular enlargement, indicating no significant chronic burden on the left ventricle of a diastolic overload through bronchial shunting.

Thrombo-embolic cor pulmonale, hitherto believed to be rare in the African, emerges as the most important cause of acute cor pulmonale and the second most common cause of the more chronic varieties of the disease. The usual pathological type of pulmonary thrombo-embolic disease observed in this study is one in which fairly large pulmonary arteries, as opposed to those of microscopic size, were involved and in consequence infarction was frequent. The lack of completely organised lesions, and the relatively small increase in total heart weights (majority below 400 Gms) suggest a rapid course in these cases, measured in months rather than in years. The usual source for pulmonary emboli was found to be the veins draining the lower limbs, particularly the deep calf veins. Whereas a predisposing factor for the development of venous thrombosis was found in just over half the number of cases investigated, in 44% of all cases of thrombo-embolic cor pulmonale in this study no cause was found at necropsy for the peripheral venous thrombosis. Of the predisposing causes encountered a posteriorly placed amoebic liver abscess emerges as an interesting aetiologic factor in the development of thrombo-embolic cor pulmonale because of its ability to produce hepatic vein and inferior vena caval thrombosis.

Emphysema, usually in association with chronic bronchitis, was found to be the third most common cause of chronic cor pulmonale among

Africans/...

Africans in Durban, and was encountered mainly in its mixed form (centrilobular and panlobular). Although structural alterations in the pulmonary arteries were noted in a significant number these were sometimes of insufficient degree to be the cause of pulmonary hypertension, thereby suggesting some other factor in the production of a raised pulmonary arterial pressure. Results of separate ventricular weighing in these cases show exclusive right ventricular hypertrophy, again indicating strain solely on the right ventricle.

Bilharzial cor pulmonale, although one of the rarer causes of cor pulmonale in the African in this series, is suspected to be probably more frequent than hitherto believed. The lack of obvious macroscopic changes in the lungs of such cases is stressed, and while this may account for omissions in diagnosis, a sudden recent increase in the incidence of bilharzial cor pulmonale might also suggest that the disease is becoming more severe.

Primary pulmonary hypertension as a cause of cor pulmonale in the African is rare, being suspected in only one case in this series.

In keeping with the generally high incidence of infective diseases in the African, pericarditis as a complication of tuberculosis and hepatic amoebiasis, and the cardiac complications of syphilitic aortitis still occupy major positions among the causes of congestive heart failure in this population; together accounting for 12.4% of all deaths from congestive heart failure. Tuberculosis and amoebiasis are important not only in the production of pericarditis, but, as mentioned, also play an important part in the development of cor pulmonale. Syphilitic heart disease, besides being a significant factor in the production of congestive heart failure, is the most important cause of a sudden cardiac death in the African.

In conclusion it may be said that while little can be achieved with regard to the control of diseases for which no cause has as yet been found, the elimination of infective conditions such as tuberculosis, amoebiasis and syphilis will result in a significant drop in the incidence of death and disability from heart failure in the African in Natal.

PLATE I

Fig. (1) Normal arteriogram of the right lung

Fig. (2) Injected lung. Muscular pulmonary artery showing attenuation of its wall and stretching of the elastic laminae
Weigert's Elastic x 60

Fig. (3) Non-injected lung. Normal muscular pulmonary artery with deeply crenated elastic laminae
Weigert's Elastic x 150

Fig. (4) Non-injected lung. Normal pulmonary arteriole whose wall consists of a single elastic lamina
Weigert's Elastic x 500

PLATE II

Fig. (1) Fibrosing lung disease, pulmonary hypertension. Right pulmonary arteriogram. In addition to filling defects there is distortion of the pulmonary arterial bed, particularly in the upper lobe of the lung. Pleural thickening also apparent.

Fig. (2) Fibrosing lung disease. Whole lung section of same lung as shown in Fig. (1) revealing generalised emphysema

Fig. (3) Fibrosing lung disease. Lung section showing small muscular pulmonary artery with an additional layer of longitudinal muscle and elastic tissue hyperplasia in the intima
Weigert's Elastic x 500

Fig. (4) Fibrosing lung disease. Lung section showing a vessel below 100μ in diameter with a distinct circular muscle layer between inner and outer elastic laminae
Weigert's Elastic x 500

Fig. (5) Fibrosing lung disease. Lung section showing a muscular pulmonary artery with eccentric intimal fibrosis resulting from organization of a thrombus
Weigert's Elastic x 60

Fig. (6) Bronchiectasis. Lung section revealing a bronchial artery with a markedly thickened muscular wall and a narrow lumen
H & E x 150

PLATE III

Fig. (1) Recurrent pulmonary thrombo-embolism, cor pulmonale. Left pulmonary arteriogram. Filling defects from thrombotic occlusion of large arteries. Some filling of finer vessels related to unaffected segmental arteries. Infarction of lower half of lower lobe.

Fig. (2) Recurrent pulmonary thrombo-embolism, cor pulmonale. Left pulmonary arteriogram. There is generalised depletion of the finer branches due to occlusion of segmental and lobular arteries.

Fig. (3) Recurrent pulmonary thrombo-embolism, cor pulmonale. Left pulmonary arteriogram. Almost generalised depletion of finer branches due to occlusion of segmental and/or lobular branches. Large infarct of the lower lobe.

Fig. (4) Acute thrombo-embolic cor pulmonale. Fresh ante-mortem thrombi in an elastic artery and a small muscular artery
Lung section H & E x 25

Fig. (5) Recurrent pulmonary thrombo-embolism, cor pulmonale. Organizing thrombus in a large elastic artery
Lung section
Weigert's Elastic x 25

Fig. (6) Recurrent pulmonary thrombo-embolism, cor pulmonale. Muscular arteries with organizing thrombi
Lung section
Weigert's Elastic x 60

PLATE IV

Fig. (1) Amoebic liver abscess, recurrent pulmonary emboli, cor pulmonale. Thrombus of right hepatic vein extending into the inferior vena cava.

Fig. (2) Amoebic liver abscess, recurrent pulmonary emboli, cor pulmonale. Section from edge of liver abscess showing amoebae (arrow)
H & E x 400

Fig. (3) Amoebic liver abscess, recurrent pulmonary emboli, cor pulmonale. Lung section showing variation in the size of emboli
H & E x 150

Fig. (4) Amoebic liver abscess, recurrent pulmonary emboli, cor pulmonale. Lung section showing organization of thrombi in small muscular arteries
H & E x 320

Fig. (5) Amoebic liver abscess, recurrent pulmonary emboli, cor pulmonale. Lung section with well organized lesion in a small artery, bearing a close resemblance to arteriosclerosis
H & E x 230

PLATE V

Fig. (1) Venous thrombo-embolism. Multiple thrombosed veins within the calf muscles.

Fig. (2) Venous thrombo-embolism. Large thrombus involving a deep calf vein.

Fig. (3) Venous thrombo-embolism. Photomicrograph showing a fresh ante-mortem thrombus in a deep calf vein
H & E x 60

Fig. (4) Venous thrombo-embolism. Photomicrograph showing an organizing thrombus in a deep calf vein
H & E x 25

Fig. (5) Venous thrombo-embolism. Lung section showing early organization of a thrombus within an elastic pulmonary artery
H & E x 25

Fig. (6) Venous thrombo-embolism. Lung section showing an organizing thrombus in a small muscular artery
H & E x 150

PLATE VIII

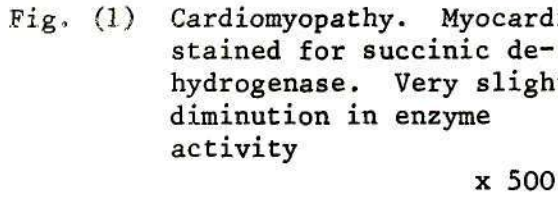

Fig. (1) Cardiomyopathy. Myocardium stained for succinic dehydrogenase. Very slight diminution in enzyme activity
x 500

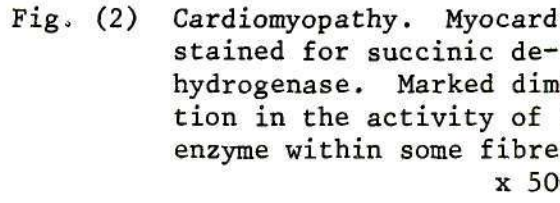

Fig. (2) Cardiomyopathy. Myocardium stained for succinic dehydrogenase. Marked diminution in the activity of the enzyme within some fibres
x 500

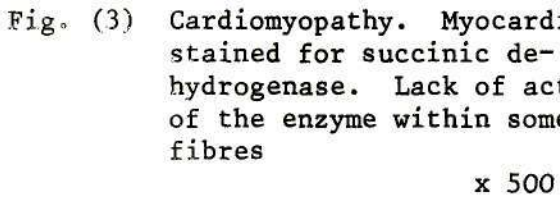

Fig. (3) Cardiomyopathy. Myocardium stained for succinic dehydrogenase. Lack of activity of the enzyme within some fibres
x 500

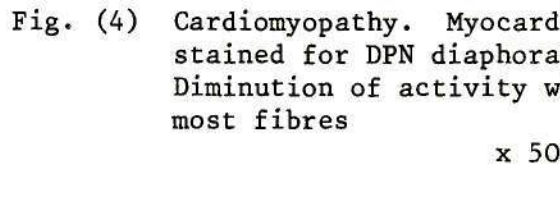

Fig. (4) Cardiomyopathy. Myocardium stained for DPN diaphorase. Diminution of activity within most fibres
x 500

PLATE IX

Fig. (1) Cardiomyopathy with right ventricular predominance. Right pulmonary arteriogram. There is a generalised narrowing of all-sized pulmonary arteries with lack of filling of the arterioles, particularly in the lower lobes.

Fig. (2) Cardiomyopathy with left ventricular predominance. Right pulmonary arteriogram. Generalised diminution of the finest branches.

Fig. (3) Cardiomyopathy with equal enlargement of the ventricles. Right pulmonary arteriogram. Large filling defects due to thrombo-embolic obstructions of segmental arteries. Normal arteriolar filling in relation to unaffected vessels. Infarction in lower lobe.

Fig. (4) Cardiomyopathy with right ventricular predominance. Left pulmonary arteriogram. In addition to large filling defects there is liquifaction, with abscess formation, of infarcted areas close to the pleural surface.

Fig. (5) Cardiomyopathy. Section of myocardium from left ventricle showing scarring of the inner third
H & E x 60

Fig. (6) Cardiomyopathy. Section of myocardium (left ventricle) showing a large area of scarring. Explained on the basis of coronary artery embolism → infarction → organization
H & E x 60

PLATE X

Fig. (1) Cardiomyopathy. Lung section showing intimal scarring of small muscular arteries
Weigert's Elastic x 60

Fig. (2) Cardiomyopathy. Lung section showing intimal scarring of small muscular arteries
Weigert's Elastic x 25

Fig. (3) Cardiomyopathy. Lung section revealing a vessel below 100μ in diameter with a distinct circular muscle layer, and in addition a longitudinal muscle layer and elastic tissue hyperplasia in the intima
Weigert's Elastic x 500

Fig. (4) Cardiomyopathy. Lung section showing vessels below 100μ in diameter with a distinct circular muscle layer with inner and outer elastic laminae
Weigert's Elastic x 500

Fig. (5) Cardiomyopathy. Small muscular artery (below 300μ in diameter) showing an additional layer of longitudinal muscle and elastic tissue hyperplasia in the intima
Weigert's Elastic x 500

Fig. (6) Cardiomyopathy. Large muscular artery showing features similar to those described in Fig. (5) above
Weigert's Elastic x 150

PLATE XI

Fig. (1) Pulmonary bilharziasis, cor pulmonale. Right pulmonary arteriogram. Filling defects caused by thrombotic occlusion of the segmental branches of the pulmonary artery. Infarction of the lower lobe.

Fig. (2) Pulmonary bilharziasis, cor pulmonale.
Above: Postmortem squash-preparation of bladder mucosa revealing ovum of S. haematobium (lateral spine).
Below: Postmortem squash-preparation of rectal mucosa revealing ova of S. mansoni (terminal spines).

Fig. (3) Pulmonary bilharziasis, cor pulmonale. Lung section showing parenchymal pseudotubercles
H & E x 60

Fig. (4) Pulmonary bilharziasis, cor pulmonale. Lung section showing pseudotubercle with a giant-cell in the centre, containing a distorted ovum.
H & E x 150

Fig. (5) Pulmonary bilharziasis, cor pulmonale. Pulmonary arteriole not related to ova but showing intimal thickening
H & E x 500

Fig. (6) Pulmonary bilharziasis, cor pulmonale. Lung section showing intravascular pseudotubercle surrounded by dilated, thin-walled vessels giving rise to the so-called angeiomatoid lesion
H & E x 150

APPENDIX

NORMAL HEART WEIGHTS : 53 AFRICAN CONTROLS

Age	Sex	Body Wt. (Kilos.)	Height	Total Heart Wt. (Gms.)	R.V. (Gms.)	L.V. (Gms.)	L.V./R.V.
21	M	50.5	5'6"	265	61	148	2.43
22	M	55.9	5'6"	260	61	144	2.36
30	M	54.5	5'6"	300	66	167	2.53
21	M	65.5	5'8"	395	72	182	2.53
60	M	63.6	5'3"	350	65	171	2.63
36	M	65.5	5'11"	325	71	167	2.37
35	M	55.0	5'6"	290	61	141	2.31
45	M	58.6	5'9"	290	61	139	2.28
28	M	55.5	5'9"	286	57	140	2.46
42	M	45.5	5'7"	240	52	125	2.40
36	M	81.8	6'0"	350	76	200	2.63
35	M	51.8	5'4"	267	60	145	2.42
20	M	40.9	5'2"	230	55	135	2.45
36	M	73.2	5'5"	310	70	162	2.31
36	M	63.6	5'10"	325	65	213	3.28
40	M	58.6	5'9"	297	72	167	2.32
35	M	68.2	5'11"	350	87	203	2.33
28	M	57.7	5'7"	280	70	165	2.36
28	M	59.1	6'0"	287	70	168	2.40
36	M	61.4	5'8"	302	71	175	2.46
45	M	75.5	5'11"	292	66	159	2.41
40	M	46.4	5'6"	290	60	148	2.47
50	M	63.6	5'8"	310	68	166	2.44

Age	Sex	Body Wt. (Kilos.)	Height	Total Heart Wt. (Gms.)	R.V. (Gms.)	L.V. (Gms.)	L.V./R.V.
30	M	58.1	5'10"	280	65	160	2.46
28	M	65.5	5'8"	325	65	166	2.55
20	M	71.4	5'10"	325	65	178	2.74
30	M	59.1	5'9"	336	76	177	2.33
35	M	59.1	5'6"	305	67	165	2.46
56	M	62.7	5'7"	320	71	175	2.46
22	M	64.1	5'6"	305	70	164	2.34
50	M	51.4	5'7"	300	65	163	2.51
26	M	61.8	5'6"	305	68	163	2.40
30	F	73.2	5'4"	290	60	144	2.40
43	F	39.1	5'5"	200	47	115	2.45
56	F	70.9	5'5"	215	44	110	2.50
50	F	71.4	5'6"	265	60	148	2.47
50	F	52.7	5'5"	240	54	121	2.22
50	M	69.1	5'6"	265	65	149	2.29
30	M	52.7	5'6"	310	67	170	2.54
36	M	63.6	5'10"	325	61	217	3.56
32	M	54.0	5'10"	275	62	145	2.34
40	M	54.5	5'5"	315	64	159	2.48
30	M	57.2	5'6"	280	62	152	2.45
56	F	47.7	5'4"	285	58	147	2.53
54	M	48.6	5'6"	310	71	177	2.49
37	M	52.2	5'6"	310	71	175	2.46
50	F	67.1	5'5"	295	61	158	2.59
30	M	73.1	5'10"	350	84	208	2.48
28	F	73.1	5'7"	300	58	138	2.38

Age	Sex	Body Wt. (Kilos.)	Height	Total Heart Wt. (Gms.)	R.V. (Gms.)	L.V. (Gms.)	L.V./R.V.
28	F	45.9	5'8"	290	65	165	2.54
40	M	46.3	5'4"	250	60	138	2.30
39	M	48.1	5'8"	300	68	174	2.56
54	F	67.7	5'6"	275	62	154	2.48
					Mean = 66.3	Mean = 160.5	Mean = 2.48
					S.D. = 7.7	S.D. = 22.49	S.D. = 0.21

For body weight and
total heart weight $r = 41 \pm 11$

For body height and
total heart weight $r = 46 \pm 11$

A C K N O W L E D G E M E N T S

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