Pathology of the heart in the tenth decade

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SYNOPSIS The pathology of the heart was studied in 60 patients dying in their tenth decade in a general hospital. The severity of coronary atherosclerosis and the incidence of ischaemic heart disease was lower than in younger geriatric patients. The incidence of minor 'aging' changes was similar to that in younger patients with the exception of mitral valve atheroma where the increase with aging continued into the tenth decade. Marked nodular thickening of the tricuspid valve was seen only in males. Over half the systolic murmurs heard were associated with mitral valve abnormalities and not with aortic valve changes. Multiple cardiac pathology was more frequent than in younger patients but its association with failure was much less striking. It is concluded that resistance to the development of coronary atherosclerosis and to failure being precipitated by the multiple minor cardiac abnormalities associated with aging are important factors in attaining extreme longevity.

As cardiovascular disease is the main cause of death in adults, the hearts of patients with exceptionally long life spans are of considerable interest. Survival into the tenth decade is still relatively uncommon and few pathological studies have been made on such people. The largest group consists of 40 nonagenarians from a south London geriatric research unit (Howell, 1963; 1964 a and b); McKeown's (1965) Belfast series included only 19 cases over 90 years. The present communication describes and discusses the cardiac findings in 60 patients in their tenth decade dying in a large general hospital.

CLINICAL FINDINGS

There were 26 males and 34 females, aged between 90 and 98 years at death (Table I). Almost three-quarters of these patients had been in normal rhythms: auricular fibrillation was the commonest abnormality (17%) and other abnormalities included multiple extrasystoles and complete heart block. Hypertension appeared relatively uncommon (10%), only one male and five females having readings of 200/100 mm Hg or above. Heart murmurs were heard in 31% of the males and 44% of females. These were almost all systolic, of variable characteristics, and no correlation between the site, intensity, and conduction described clinically and the subsequent pathological findings could be

TABLE I
CLINICAL FINDINGS

	Males	Females	Total
<i>Rhythm</i>			
Regular	18 (70%)	27 (80%)	45 (75%)
Fibrillating	7 (27%)	3 (9%)	10 (17%)
Multiple extrasystoles	0	2	2
Flutter	0	1	1
Complete atrioventricular block	1	1	2
<i>Cardiac Failure</i>			
200/100 mm Hg or higher	11 (42%)	14 (41%)	25 (41%)
	1	5	6 (10%)
<i>Heart Sounds</i>			
Systolic murmur	8	15	23
Diastolic murmur	2	1	3
	{ (31%) }		{ (44%) }
<i>Electrocardiograph Findings</i>			
Non-contributory	1	4	5
Suggesting ischaemia	2	0	2
Left ventricular hypertrophy	1	2	3
Complete atrioventricular block	1	1	2
Right bundle branch block	1	2	3
Wandering pacemaker	0	1	1
Myocardial damage? cause	1	0	1

established. Cardiac failure was present in 40% of cases. Recent electrocardiograms were available for 17 patients, and the abnormalities found included myocardial infarction, probable ischaemia, left ventricular hypertrophy, complete and bundle branch blocks, wandering pacemaker, and non-specific myocardial damage.

PATHOLOGY

ATHEROMA AND ISCHAEMIC HEART DISEASE Coronary atherosclerosis was sufficiently uniform for a rough

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quantitative assessment in 58 hearts, and was graded as slight in 36%, moderate in 35%, and marked in only 29% (Table II). This is in contrast to Howell's (1964a) finding of marked coronary atheroma in 60% of 13 males and 27 females and slight in only 17.5%. In the present series atherosclerosis was less severe in the females; 41% showed slight narrowing and only 18% marked narrowing compared with 27% and 42% respectively in the males. The severity of coronary and aortic atheroma was similar in almost two-thirds of cases; coronary disease was noticeably more marked than aortic in 8%, and aortic atherosclerosis than coronary in 30%. There was no significant difference between the sexes in this respect.

TABLE II
ATHEROSCLEROSIS AND MYOCARDIAL CHANGES

	Males	Females	Total
	26	34	60
<i>Coronary atherosclerosis</i>			
Slight	7 (27%)	14 (41%)	21 (36%)
Moderate	8 (31%)	12 (35%)	20 (35%)
Marked	11 (42%)	6 (18%)	17 (29%)
<i>Myocardial fibrosis/infarcts with moderate or marked coronary disease</i>	9 (35%)	10 (34%)	19 (31%)
<i>Interstitial/paravascular fibrosis with slight coronary narrowing only</i>	1	5 (17%)	6 (10%)
<i>Senile cardiac amyloidosis</i>	16 (62%)	14 (41%)	30 (50%)
<i>Hypertrophy of myocardium (over 400 g)</i>	9 (35%)	6 (18%)	15 (25%)
<i>Atrophy of myocardium (under 300 g)</i>	2 (8%)	12 (36%)	14 (23%)

Ischaemic myocardial changes were present in 19 cases (31%). Two of the 20 hearts with moderate coronary disease had healed infarcts, four patchy focal fibrosis, and one a fine diffuse fibrosis. Of the 11 males with marked coronary atherosclerosis, three had no apparent gross or microscopic fibrosis; all six females in this group had severe ischaemic changes which included two recent infarcts, both associated with a thrombotic occlusion and one of which had ruptured, and a ventricular aneurysm. Although 12 of the cases with ischaemic lesions had been in failure, death was attributed to ischaemic heart disease in only five and the remaining seven had been free from cardiac symptoms. In Howell's (1963) series death was attributed to coronary disease in 30% of cases, but equally severe lesions were also observed in patients dying of other causes. A decrease in the incidence of ischaemic heart changes in extreme old age has been noted previously in a smaller group of nonagenarians (Pomerance, 1965) and a similar fall was reported by

McKeown (1965) in the ninth decade; there were no examples of ischaemic heart disease in her 19 cases in the tenth decade.

OTHER MYOCARDIAL FINDINGS Table II summarizes this information.

HYPERTROPHY AND ATROPHY Hearts weighed between 300 and 400 g in 31 (51%) patients. Although the total number of patients with larger or smaller hearts was approximately equal, 12 of the 14 (23%) with hearts less than 300 g were female, while nine of the 15 (25%) with hearts weighing over 400 g were male. Marked divergences from these weights were uncommon; only three hearts weighed less than 250 g and two over 500 g. The smallest heart (200 g) was from a woman dying of carcinoma of the gall bladder; the largest (540 g), from a woman dying of left ventricular failure with calcified aortic stenosis and ischaemic heart disease. Ischaemic heart disease was present in five of the patients with hypertrophied hearts, in four with hypertension; both these conditions in one; and rheumatic mitral disease and cirrhosis of the liver in one patient each. Compared with the 40% incidence in the group as a whole, the cases with small hearts included a lower proportion with failure (28%) and those with large hearts a higher proportion (53%). This finding agrees with Sonnek's (1954) that the small heart is less likely to fail. A conspicuously brown myocardium (brown atrophy) was noted in only three hearts, one of which was from a patient in failure. Only one weighed less than 300 g.

Cardiomyopathy Fibrosis in an elderly heart is usually attributed to atherosclerosis, even in the absence of appropriate coronary disease. Kline, Kline, and Saphir (1963), however, differentiated between ischaemic and non-arteriosclerotic myocardial changes and showed that the latter were not uncommon in persons over 70 years. In the present series six patients with minimal coronary atherosclerosis had patches of interstitial or paravascular fibrosis and were therefore most appropriately classified as cardiomyopathy (*British Medical Journal*, 1963).

Senile cardiac amyloidosis The incidence of this condition continued to increase with age (Pomerance, 1966b) and it was present in 62% of male and 41% of female nonagenarians; in four of the female cases deposits were minimal.

VALVULAR FINDINGS These are set out in Table III.

Calcific aortic stenosis Jokipii (1963) has stated that this is the most common valvular disease in the elderly, and Bedford and Caird (1960) found 13

TABLE III
VALVULAR CHANGES

	Males	Females	Total
	26	34	60
Mitral Valve			
Endocarditis—chronic rheumatic	1	2	3
bacterial	1	2	3
thrombotic	1	2	3
acute necrotising	—	1	1
		(overlying calcification)	
Non-specific scarring and chronic inflammatory changes	1	1	2
Mucoid degeneration	7 (25%)	5 (15%)	12 (20%)
Ring calcification	9 (35%)	22 (65%)	31 (52%)
Nodular thickening			
Slight (normal)	9 (35%)	9 (27%)	18 (30%)
Moderate	8 (31%)	14 (41%)	22 (37%)
Marked	4 (15%)	7 (20%)	11 (18%)
Not assessable	5 (19%)	4 (12%)	9 (15%)
Atheroma			
Slight	2 (8%)	2 (6%)	4 (7%)
Moderate	14 (53%)	14 (41%)	28 (47%)
Marked	8 (31%)	13 (38%)	21 (35%)
Not assessable	2 (8%)	5 (15%)	7 (11%)
Aortic Valve			
Calcification	9 (33%)	11 (33%)	20 (33%)
Commissural adhesion	10 (39%)	11 (33%)	21 (35%)
Broadened commissures	2	0	2
Fenestration	7 (28%)	5 (15%)	12 (20%)
Thrombotic endocarditis	1	1	2
Tricuspid Valve			
Nodular thickening			
None (normal)	6 (23%)	18 (53%)	24 (40%)
Slight	6 (23%)	10 (29%)	16 (27%)
Moderate	8 (31%)	4 (12%)	12 (20%)
Marked	6 (23%)	2 (6%)	8 (13%)
Scarring and fibrosis	2	0	2
Ulceration	4	1	5
Pulmonary Valve			
Nodules (morganii)	10 (40%)	11 (33%)	
Fenestration	1	2	

cases in their 28 patients over 90 years with valvular heart disease. Although macroscopic calcification was present in the valve fibrosa in almost one third of the 60 nonagenarians from this hospital and in Howell's (1964a) 40 cases, this was severe enough to cause stenosis in only one case, and there were no examples of calcification with commissural fusion in either series.

Rheumatic mitral disease The existence of this condition in old age is now well recognized. Cases in the tenth decade were reported by Howell and Piggot (1951), by Jokipii and Heino (1963), and by Bedford and Caird (1960). In the present series, mitral stenosis of rheumatic type was seen in three patients, a man of 92 and two women aged 90 and 92 respectively. The cusps were greatly thickened, opaque and distorted with commissural fusion and short thick chordae tendineae but no valve calcification. One woman and the man had complete heart block.

FIG. 1. Opened left side of heart showing a pedunculated vegetation on the anterior cusp of the mitral valve (from a woman aged 91 dying of congestive cardiac failure and carcinoma of stomach). $\times 1\frac{1}{2}$ approximately.

FIG. 2. Photomicrograph showing thrombotic vegetation attached to a mitral valve endocardium (from a woman aged 93 dying of bronchopneumonia and cardiac failure). Elastic Van Gieson. $\times 30$.

Other forms of endocarditis Non-bacterial (thrombotic) endocarditis (Figs. 1 and 2) was present on the anterior mitral cusps of three patients with

otherwise normal valves and on the aortic valve of the male with rheumatic heart disease. Bacterial endocarditis was seen in three cases, all involving the posterior mitral cusp. In the male the chordae tendineae were necrotic and a less severe infection was present in the apposing cusp surface. In the females, the endocarditis was only apparent on microscopy, having developed in areas of valvulitis over mitral ring calcification. Minor degrees of non-specific scarring and distortion and minor microscopic post-inflammatory changes were seen in the mitral valve of one patient of each sex, and two other males showed thickening and distortion of the anterior tricuspid leaflets, with thick adherent chordae tendineae. The pathogenesis of these lesions has already been discussed (Pomerance, 1965, 1967a) and, as with non-arteriosclerotic myocardial fibrosis, was thought to result from non-specific inflammatory changes which may occur in Cocksackie (Smith, 1967), upper respiratory tract, and similar relatively minor infections of undiagnosed origin (*Lancet*, 1967).

Mitral ring calcification Although the incidence of this condition increases with age the pathogenesis cannot be attributed to involutional changes alone (Pomerance, 1967a and b; McKeown, 1965). Realization of its clinical significance is comparatively recent (Korn, DeSanctis, and Sell, 1962) and few pathological studies are available. It was noted in 20% of Howell's (1964a) nonagenarian group and was present in 52% of the present series. It was almost twice as frequent in females (65%) as in males (35%) and tended to be more severe. Massive calcification with spikes of calcareous material distorting the posterior cusp was seen in only two males but in nine females. Two females showed

FIG. 3. Posterior wall of left atrium and ventricle showing haemorrhagic discoloration over irregular mitral ring calcification which is distorting the posterior cusp (from a woman aged 93 with rheumatoid arthritis, dying of acute bronchitis and bronchopneumonia). $\times 1\frac{1}{2}$ approximately.

haemorrhagic necrotizing valvulitis in relation to calcified masses (Fig. 3); in one, severe acute inflammatory changes extended for several millimetres into the surrounding myocardium. Bacterial infection of inflamed valves had also occurred in two cases. Mitral incompetence was demonstrated by marked left atrial dilatation in one case and a 'jet' lesion on the posterior atrial wall in another, and systolic murmurs had been noted in all patients in whom the heart sounds had been clearly audible.

MISCELLANEOUS MINOR FINDINGS Mild or moderate 'ballooning' (mucoid degeneration) occurred in 20% of posterior mitral cusps but no severe examples of this change were seen.

Nodular thickening was present to some degree at the line of apposition of all anterior mitral cusps, but was marked ('senile' sclerosis) in only 18%. Lipoid plaques were also present on the ventricular surface of this cusp in all cases, and to a marked degree in 35%. There was little quantitative difference between the sexes. The incidence of calcification, commissural adhesions, and fenestration of semi-lunar valves was also similar but tricuspid changes were more frequent in males, only six (23%) having normal thin, translucent cusps, compared with 18 (53%) of females. Six males (23%) showed nodular thickening of this valve; post-inflammatory changes were present in two; and small superficial ulcers were superimposed on the thickened plaques in four cases. These 'aging' changes have already been fully discussed (Pomerance, 1966a; 1967a and b).

MULTIPLE PATHOLOGY Multiple lesions increase in frequency with age (Howell, 1964a). This is true in the heart as well as in the body as a whole, and there is a striking difference in the incidence of multiple cardiac pathology in elderly patients with and without cardiac failure (Pomerance, 1965). Although the proportion of hearts with multiple abnormalities was higher in the tenth decade, this difference was much smaller than in younger patients; 87% of hearts from cases of failure showed multiple pathology, but so did 48% of those from patients without clinical cardiac disease.

CARDIAC MURMURS AND PATHOLOGICAL FINDINGS Systolic murmurs had been heard in 15 females and eight males. Six, all in females, were described as aortic ejection type, the remainder as 'apical' or 'mitral'. Two aortic murmurs were associated with severe degenerative aortic cusp calcification, one showed minimal aortic and mitral ring calcification but marked mitral nodular thickening, and in two others the aortic cusps were normal but the mitral

valve ring was heavily calcified; in the sixth case the only valvular abnormality was minimal aortic commissural adhesions, but the patient had been hypertensive (250/100 mm Hg) and also showed slight aneurysmal dilatation of the membranous interventricular septum. The findings in the males with 'mitral' or apical systolic murmurs were mitral ring calcification, mild aortic cusp calcification, post-inflammatory distortion of the tricuspid and mitral valve in one case each, slight mitral and aortic calcification, and mitral ring calcification with posterior cusp 'ballooning' also in one case each, and 'ballooning' (*ie* mucoid degeneration of the mitral valve) alone in two cases. In the females, mitral ring calcification was found in four cases, rheumatic mitral stenosis and ring calcification, mitral thrombotic endocarditis and aortic cusp calcification, thrombotic endocarditis and mitral ring calcification, and mitral ring calcification with 'ballooning' in one case each. One patient had no cardiac abnormality but a blood pressure of 220/120 mm Hg.

COMMENT

Relatively little is known of the pathology of extreme old age and any studies on patients in the tenth decade are therefore of considerable academic interest, and may help to dispel such common misconceptions as the association of brown atrophy with aging. Their main value, however, is in the identification of factors which may have contributed to the unusually long life span, and in this context two findings in the present group were relevant: the low incidence of ischaemic heart disease and the decreased association of multiple pathology with failure, compared with younger groups.

The presence of ischaemic heart disease in less than one third of patients in the tenth decade confirmed the falling incidence in extreme old age previously noted in smaller series (Pomerance, 1965; McKeown, 1965) and contradicts the widely held view that geriatric heart disease is synonymous with ischaemic heart disease. However, the theory of Russek, Zohman, Doerner, Russek, and White (1951) that absence of severe coronary atherosclerosis might be a prerequisite to the attainment of old age was not confirmed either; severe coronary

changes were present in 29% of hearts. The continuing increase in mitral valve atheroma independently of coronary disease was also of interest, indicating that intimal lipid changes continue to progress with age. This suggests that the relative freedom from coronary atherosclerosis resulted from resistance to development of complicated atheroma lesions rather than from biochemical factors influencing lipid metabolism.

The decreased association between multiplicity of pathology and failure was more unexpected than the fall in ischaemic heart disease. In younger geriatric patients multiple pathology was five times as frequent in failure cases (Pomerance, 1965); the incidence increased with age, but although this increase continued in the tenth decade, the multiple pathology was only about twice as frequent in the failure cases in this age group.

It seems, therefore, that the hearts of people with unusually long life spans show not only unusual resistance to ischaemic changes but also an exceptional capacity to tolerate the other increasing and multiple cardiac abnormalities of aging, without failure. Studies on factors associated with the absence of coronary disease in the elderly (Brown and Ritzmann, 1967) and the well known familial pattern of longevity suggest that this resistance to atherosclerosis and failure is likely to be genetically determined.

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