ASYMPTOMATIC DISEASE OF CORONARY ARTERIES IN YOUNG MEN

BY

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Epidemiological and pathological studies of atherosclerosis have recently received impetus through the agency of the World Health Organization. This work, together with the majority of the previous literature, is largely concerned with overt disease and death from coronary heart disease; there is a comparative dearth of information on the prevalence of occult affection of the coronary arteries, the study of which cannot be divorced from that of ischaemic heart disease (Strong and McGill, 1962). So as to eliminate any possible adverse effects of unrelated disease on the health of the coronary arteries, the basic extent of symptomless atheroma must be sought in supposedly healthy persons killed accidentally rather than in hospital populations; most of the relevant reports have therefore emanated from military medicine.

Mönckeberg (1915a, 1915b, 1916) appears to have been the first to explore this field. His three series include 167 combatant troops compared with 136 men exempt from war service, all of whom were killed either in action or accidentally; atherosclerosis was discovered in 50.9% of the combatants and in 63.2% of the non-combatants, the potentiating effect of age being demonstrated in both groups—even so, 44.5% of soldiers under the age of 30 were found to be affected to some extent. This study must surely have been followed up, but the next apposite reference that I discovered is that Enos, Holmes, and Beyer (1953). These authors made a strictly comparable study of American soldiers killed in action in Korea. Narrowing of one or more coronary arteries resulting in more than 50% restriction was found in 12.3% of 300 cases, the average age of the men being 22.1 years. In civilian life, Spain and Bradess (1959) reported their findings in 166 white men aged 31–60 who were killed accidentally; they confirmed the presence of widespread asymptomatic coronary atheroma, although completely normal arteries were discovered even in a proportion of their oldest subjects. Strong and McGill (1962) also studied accidental death and concluded that it was impossible to divide American white males into those having and not having coronary atherosclerosis after the age of 20 years—the only distinction lay in the severity of disease.

The activities of the Joint Committee on Aviation Pathology (Brody, 1957) have in recent years focused attention on the occurrence of pre-existing disease in aircrew—possibly the most highly physically selected group available—who were killed while flying, and numerous articles have been published from the United States of America dealing in general terms with coronary arterial disease in the context of aircraft accident pathology (Townsend, 1957; Berry and Stembridge, 1958; Silliphant and Stembridge, 1958; Townsend and Stembridge, 1958; Townsend and Davidson, 1961). Specific studies of occult coronary arterial disease in American aircrew have been reported from the Armed Forces Institute of Pathology (Glantz and Stembridge, 1959; Townsend and Glantz, 1959; Rigal, Lovell, and Townsend, 1960; Catherman, Davidson, and Townsend, 1962). Depending primarily on the age-group involved and secondarily on the method of examination, these various authors have assessed the incidence of restrictive disease as from 14% in the age-group 20–24 to 32% marked sclerosis—that is, more than

75% restriction—in the age-group 40–49 years. Comparable British series of aircrew fatalities have been reported (Mason, 1959, 1962; Stevens, 1961, 1962), but the articles have been of a limited distribution. It is also noted that the problem has been considered by the Soviet Air Force (Koldovski, Novak, and Vorel, 1961); this article has been seen only in abstract form.

It therefore seemed appropriate to collect and publish the British data in more readily available form so that valid comparisons of the occurrence of asymptomatic coronary arterial disease in physically fit young men on both sides of the Atlantic could be made. The significance in aviation of discovered arterial disease could be threefold. Firstly, it might be shown to be a disease state directly related to the stresses of professional aviation. Secondly, it might be shown to be a significant cause of unexplained aircraft accidents; this possibility is not considered in detail in this paper. Thirdly, it could be no more than a marker of the incidence of atherosclerosis throughout the population.

Materials and Methods

All the coronary arteries examined were obtained from British males within the age limits of 17 and 42 years at last birthday. There are five groups of person involved.

1. *R.A.F. Aircrew.*—Except that all persons known to be of foreign extraction have been excluded—a restriction which applies to all groups—these are unselected deaths resulting from aircraft accidents. No distinction has been made between pilots and other aircrew, as previous experience (Mason, 1962) has shown the subgroups to be homogeneous in the present context. The fact that all were killed in peacetime operational flying indicates that there was no clinical evidence of disease at the time of death.

2. *R.N. Aircrew.*—These were selected as above, but the group as a whole is rather younger.

3. *Other Professional Aircrew.*—These are civilians holding a commercial flying licence whose livelihood depended on aviation and who were killed in flying accidents. The vast majority were pilots, but a few other crew members are included; stewards are excluded. The aircraft involved range from small club trainers to global airliners.

4. *Private Pilots.*—This small group consists of persons holding or training for a private pilot's licence killed in aircraft accidents. They have been isolated as they cannot be included in the controls, but are also unlikely to have sustained any significant flying stress.

5. *Controls.*—These are persons killed accidentally who had no connexion with regular flying. Most of these specimens have been kindly provided by coroners' pathologists in Great Britain and come from traffic accidents and the like; suicides have been excluded. A few passengers killed in aircraft accidents have been included where this was justifiable, and there are a number of Army personnel killed in action. Whole hearts were available in most cases and the methods of preparation and examination were the same as those used for aircrew. It is apparent that, overall, the possibility of complete physical fitness at the time of death is less in this group than in the others.

Groups 1, 2, and 3 have been combined under the title of "All Professional Aircrew."

The method of examination has not extended beyond routine post-mortem technique. The coronary arteries

were sectioned transversely, often after fixation of the whole heart. The most severely affected portion was retained for histological examination from the left (main left and anterior descending branch combined), left circumflex, and main right arteries.

The selected blocks were stained by haematoxylin and eosin and a purely subjective assessment of the degree of restriction was made under low-power magnification. The protocol is open to criticism on the grounds of oversimplification; this, however, is deliberate, as it is felt that any series which may need to be compared with a general study performed outside a research establishment must be examined within the limitations likely to apply to a busy pathologist working in a routine laboratory.

An equally simple classification of findings has been adopted (Mason, 1959): grade 0, normal arteries; grade 1, atheromatous plaquing leading to 50% restriction or less; grade 2, atheromatous plaquing leading to more than 50% restriction; and grade 3, atheromatous plaquing with degenerative changes (thrombosis, vascularization, or calcification). Each grade has been further divided into upper (+) and lower (−) limits, grade 0+ representing minimal intimal thickening of no more than technical interest. Grade 1− represents the lowest degree of disease clearly acceptable as such when viewed microscopically, while grade 1+ corresponds with macroscopically manifest atheroma. Individual cases have been assigned to the maximum grade discovered in any of the three arteries examined.

It is emphasized that this form of examination takes no account of the total distribution of atheroma in the coronary tree. Moreover, the assessments must be regarded as an absolute maximum. In this respect the series is less comparable with that of Glantz and Stembridge (1959), who regarded their results as probably indicating a lower level of disease than actually existed, than it is with that of Catherman *et al.* (1962), who showed an apparent increase in disease incidence and severity when they examined whole hearts. Neither the present series nor those reported by the American authors can be said to have been examined "blind"; in the circumstances of accident investigation it is inevitable that the observer is aware of the source of his material.

The extent of the present study is detailed in Table I. The total group consists of 275 persons; there are 180 professional aircrew and 90 control cases. The failure to examine all three main arteries in 85 cases stems from the whole heart not being available owing either to traumatic fragmentation or to the forwarding of incomplete specimens from outside laboratories in cases not seen personally by me.

TABLE I.—Extent of Study

No. of Arteries Examined	R.A.F. Aircrew	R.N. Aircrew	Other Professional Aircrew	Private Pilots	Control Group	Total
1	22	5	1	0	4	32
2	32	3	3	1	14	53
3	78	24	12	4	72	190
Total cases	132	32	16	5	90	275

Results

The overall results of this examination are summarized in Table II. Taking the professional airmen as a whole, exactly one-quarter have coronary atheroma of potentially significant degree (more than 50% restriction in at least one point) while 40% show macroscopic disease. The comparable figures in the controls are 16.7% and 25.6% respectively and in the total combined groups 21.9% and 34.5%. At first glance there appears to be a possibly significant difference between the R.N. aircrew and any other grouping and between the control group and any other aircrew group except the Royal Navy. In fact, the groups are not strictly comparable in age. For example, 56 out of 132 R.A.F. cases lie in the age-group 25–33 years as against 13 out of 90 controls, while in no Royal Naval case was the subject aged more than 33 years. When the groups are standardized for age there is no significant difference either in the occurrence or in the severity of disease.

The effect of age is shown in Table III. Even within the relatively limited age-groups under consideration there is a significant association between age and severity of disease ($P < 0.001$) in any aircrew group and in the controls. It is, however, noteworthy that, although potentially significant disease begins to appear at approximately 20 years of age, there will still be some persons with completely normal arteries even up to the age of 40; in this respect the results differ from those of Strong and McGill (1962) but are similar to those of Glantz and Stembridge (1959) and of Spain and Bradess (1959).

Myocardial fibrosis has not been found in any routine sections taken from the interventricular septum.

Discussion

The primary purpose in preparing this study was to assess the role of aviation itself in the aetiology of coronary arterial disease which appeared with great frequency in routine post-mortem examinations performed after fatal aircraft accidents. The figures presented show no significant differences between aircrew and control cases either in the occurrence of macroscopic disease or in potenti-

TABLE II.—Incidence of Disease

Grade of Disease	R.A.F. Aircrew (132)		R.N. Aircrew (32)		All Professional Aircrew (180)		Controls (90)		Total Group (275)	
	No.	% of Group	No.	% of Group	No.	% of Group	No.	% of Group	No.	% of Group
0-	22	52	6	14	28	68	20	45	50	117
0+	30		8		40		25		67	
1-	29	43	7	14	40	67	22	30	63	98
1+	14		7		27		8		35	
2-	15	22	1	2	17	28	3	6	20	34
2+	7		1		11		3		14	
3-	9	15	1	2	10	17	6	9	16	26
3+	6		1		7		3		10	
% showing macroscopic disease	38.6 (28.0)*		34.4 (12.5)		40 (25.0)		25.6 (16.7)		34.5 (21.9)	
Average age	28.6		24.8		28.3		26.3		27.3	
Age limits	19-42		18-33		18-42		17-42		17-42	

* Figures in parentheses = % showing more than 50% occlusion.

TABLE III.—Effect of Age

Age	Grade of Disease									% Showing	
	0—	0+	1—	1+	2—	2+	3—	3+	Total	Macroscopic Disease	More than 50% Occlusion
<i>Total Group</i>											
17-18	1	2	4	—	—	—	—	—	7	14.1	5.1
19-21	14	16	9	1	—	—	—	—	41		
22-24	12	13	14	8	—	2	—	—	51		
25-27	3	14	11	7	3	—	3	2	43	35.9	19.1
28-30	7	8	5	6	3	1	1	—	31		
31-33	2	4	3	2	2	—	1	1	15		
34-36	2	2	7	4	5	4	3	3	30	62.5	50.0
37-39	6	2	1	1	1	3	4	3	21		
40-42	—	1	3	3	3	1	1	1	13		
Unknown	3	5	6	3	2	3	1	—	23		
Total	50	67	63	35	20	14	16	10	275		
<i>All Professional Aircrew</i>											
17-18	1	—	—	—	—	—	—	—	1	17.3	5.8
19-21	8	7	5	1	—	—	—	—	21		
22-24	7	7	8	5	—	2	1	—	30		
25-27	—	9	11	6	3	—	2	2	33	40.0	21.3
28-30	7	7	4	6	3	1	1	—	29		
31-33	1	3	3	2	2	—	1	1	13		
34-36	2	2	5	2	4	3	2	3	23	64.3	52.4
37-39	2	1	1	1	1	1	2	1	10		
40-42	—	1	1	2	3	1	1	—	9		
Unknown	—	3	2	2	1	3	—	—	11		
Total	28	40	40	27	17	11	10	7	180		
<i>Controls</i>											
17-18	—	2	4	—	—	—	—	—	6	11.1	4.4
19-21	6	9	4	—	1	—	—	—	20		
22-24	5	4	6	3	—	—	1	—	19		
25-27	2	5	1	1	—	—	1	—	9	15.4	7.7
28-30	—	1	—	—	—	—	—	—	2		
31-33	1	1	—	—	—	—	—	—	2		
34-36	—	—	1	2	1	1	1	—	6	65.0	50.0
37-39	3	1	—	—	—	2	2	2	10		
40-42	—	2	2	1	—	—	—	1	4		
Unknown	3	2	4	1	1	—	1	—	12		
Total	20	25	22	8	3	3	6	3	90		

ally significant restriction of the lumen. The proposition that coronary atherosclerosis and total hours flown are directly related has been considered elsewhere (Mason, 1962); although a significant association was shown, it was strongly supposed that the relationship rested on the equivalent effect of age on both the severity of disease and flying experience. The very similar effect of age in both aircrew and controls demonstrated in the present series firmly supports the previous supposition. Although a study of premature traumatic death is a poor substitute for a follow-up until natural death, it is concluded that there is no association between aviation and coronary atherosclerosis and that there is no suggestion of an occupational disease state. Similar conclusions were reached by Rigal *et al.* (1960) and by Koldovski *et al.* (1961) studying helicopter pilots; the latter authors nevertheless believed that the degree of atherosclerosis in jet aircraft pilots was comparable to that of men 15 years older in the general population. In the present series of 164 R.A.F. and R.N. aircrew 77% were killed in jet aircraft and 71% of these were pilots.

It is generally accepted that sudden death from pure coronary atherosclerosis without thrombosis is a real entity (Levy and Bruenn, 1936; Yater, Welsh, Stapleton, and Clark, 1951; Spain and Bradess, 1959; Crawford, Dexter, and Teare, 1961); there is some evidence that completely unheralded fatal occlusion is rather more common in the younger age-groups (Meessen, 1944; Yater *et al.*, 1951; Schimert, 1960); and French and Dock (1944) believed that death from only a single occlusive lesion was perhaps more frequent in young men than in the older groups. The results here reported and those from similar series there-

fore merit consideration regarding their interpretation in cases of sudden unexplained death in young adults, an interpretation which is far more difficult if the death is masked by accidental trauma. Most authors who have specifically considered this problem (Townsend and Stembridge, 1958; Glantz and Stembridge, 1959; Enderle, Kettenmeyer, Rillaert, and Evard, 1959; Mason, 1959; Rigal *et al.*, 1960; Jackson, 1962; Stevens, 1962) have commented on the need for caution in ascribing accidents to coronary atherosclerosis. The very extent of potentially significant disease here disclosed supports this opinion and adds weight to the view of Morris and Dale (1955) that many are susceptible but few suffer or, as put by Weiss (1940), that underlying organic disease of a vital organ found at necropsy may be compatible with good function and not be the cause of death.

While it is not intended to discuss the role of coronary atherosclerosis in accident causation in detail, the atherosclerotic disease described in this general series broadly differs from that causing death in men of a similar age-group in that, in the latter, there is far more extensive disease and myocardial fibrosis is very common. The absence of myocardial fibrosis has been most obvious in the present series and contrasts markedly with the results reported from America (Glantz and Stembridge, 1959; Catherman *et al.*, 1962); no explanation, other than a possible difference in interpretation, can be adduced for this discrepancy.

The similarity of findings in aircrew and control cases here presented strongly suggests that the whole group constitutes a fair sample of the British male population within the age-group 17-42 years. A simple comparison of the present series with those previously published (Table IV) shows that the occurrence of occult coronary arterial disease is comparable in British and American personnel, the effect of age being critical. There is no doubt that similar results can be obtained in other white populations (Hannah, 1958), and a recent article evaluating almost

TABLE IV.—Occurrence Per Cent.* of Asymptomatic Coronary Atherosclerosis in Accidental Death

Grade of Disease	Catherman <i>et al.</i> (1962) (Aviators)	Glantz and Stembridge (1959) (Aviators)	Stevens (1961) (Aviators)	Present Series		Enos <i>et al.</i> (1953) (Soldiers)	Rigal <i>et al.</i> (1960) (Controls)
				Aviators	Controls		
0	24	30	34.5	38	50	58.4	36
1	38	49	43	37	33	29.3	46
2 and 3	38	21	22.5	25	17	12.3	18
Average age	30	28	—	28.3	26.3	22.1	25
Total in series	96	222	190	180	90	300	167

* Other authors' figures have been reduced to conform so far as possible to the system of grading used in this series.

identical techniques shows that coronary atherosclerosis may be widely disseminated among Asiatics (Wig, Malhotra, Chitkara, and Gupta, 1962). Notwithstanding the results of Morris and Dale (1955), it can be accepted that atherosclerosis is an invariable precursor of fatal cardiac infarction (Simpson, 1939; French and Dock, 1944; Spain and Bradess, 1959; Crawford *et al.*, 1961; Catherman *et al.*, 1962; Strong and McGill, 1962). The conclusion is thus indicated that epidemiological reviews aimed at eliciting the aetiology of the latter could, as suggested by Strong and McGill (1962), be based on the former condition, particularly as it affects younger age-groups.

Thus there may well be a case for a widely based epidemiological study of traumatic deaths which would

compare the degree of atherosclerosis discovered at necropsy with the previous socio-economic, dietary, and other possibly relevant history. It is not, however, suggested that this would do any more than clarify one aspect of the problem. Indeed, Reid (personal communication) has pointed out that the contrast between the similar frequency of asymptomatic coronary atherosclerosis in British and American aircrews shown here and the dissimilar morbidity in the R.A.F. and U.S.A.F. in terms of hospital admissions for the treatment of coronary heart disease is in itself suggestive evidence that factors other than the underlying atherosclerosis are of importance in the production of fatal cardiac ischaemia.

Summary

The incidence of asymptomatic coronary atherosclerosis in young adults has been assessed in a study of accidental deaths. Two major groupings—professional aircrew and controls—have been delineated.

In the whole group of 275 men of mean age 27.3 years significant luminal restriction of one or more coronary arteries was demonstrated in 21.9% ; macroscopic disease was present in 34.5%. The profound effect of age on the incidence of disease was shown in all subgroups.

When standardized for age, there was no significant difference in the disease state in aircrew and controls. It is concluded that aviation itself has no direct adverse effect on the health of the coronary arteries.

The findings underline the need for a cautious interpretation of coronary arterial disease as an aetiological factor in accident causation.

The results are compared with those obtained in other similar series and a marked correlation is noted. It is concluded that coronary atherosclerosis is widely distributed in young adults throughout the world.

It is suggested that an epidemiological study of accidental death might be of value in elucidating the aetiological factors leading to coronary atherosclerosis which is at least partly responsible for cardiac infarction.

I am indebted to all those coroners' pathologists who have assisted in this investigation both in their particular attention to aircrew fatalities and in providing specimens for the control series. Particular thanks for interest and encouragement are

given to Air Vice-Marshal Sir Aubrey Rumball and Air Commodore W. P. Stamm, the R.A.F. senior consultants in medicine and pathology respectively. Professor D. D. Reid and Mr. P. Wiggan have been good enough to examine the results statistically. The Director-General of Medical Services, Royal Air Force, has kindly given permission for publication of this paper.

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INCIDENCE OF UNSUSPECTED CHRONIC GLAUCOMA IN A POPULATION SAMPLE AT OXFORD

BY

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Chronic open-angle glaucoma is defined as "a composite congeries of pathological conditions which have the common feature that their clinical manifestations are to a greater or lesser extent dominated by an increase in the intraocular pressure and its consequences" (Duke-Elder, 1940).

Recent mass-screening measurement of intraocular pressures, on random samples of the population over the age of 45 years, have been undertaken in the United States. These have suggested that between 3 and 4% of this population have abnormally raised intraocular pressure at the first test (Wolfer and Sherman, 1954). In these surveys the ophthalmologists used a Schiøtz tonometer, an instrument

commonly employed for routine measurement of intraocular pressure (tonometry). In further investigations, on those individuals found to have raised intraocular pressure, they employed tests designed to measure the outflow of aqueous humour from the anterior chamber (tonography) and/or to provoke an abnormal rise of the intraocular pressure—for example, water-drinking test (water-loading). If open-angle glaucoma be defined as consisting essentially of raised intraocular pressure, together with poor outflow of aqueous humour which can be aggravated by "provocative" tests—for example, water-drinking test—then 1.5 to 2% of the tested populations over the age of 45 had early open-angle glaucoma. At this stage patients do