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

not necessarily show cupping of the optic disk or visual-field loss.

The validity of the American figures was uncertain because only a small number of those found to have raised intraocular pressure at the first examination returned for further investigation. It was possible that raised intraocular pressure and poor aqueous outflow in these individuals was caused by an irrelevant environmental factor. No follow-up studies were undertaken, so it was not established that cupping of the disk and field loss would inevitably follow.

Leydhecker *et al.* (1958) did a similar mass-screening test in Bonn, Germany, establishing that unsuspected glaucoma was not peculiar to the United States. He found an incidence of early open-angle glaucoma of 2% in Bonn.

Goldmann (1959) has suggested that in open-angle glaucoma raised intraocular pressure over a period of 15 to 20 years is a prerequisite for cupping of the optic disk. Applying this to the results of mass screening, it appears that at any one time 1.5 to 3% of the population over 45 years of age are in this "transition" phase. This is thought to be of significance in the prevention of blindness. Glaucoma is responsible for 14% of the blind population in England and Wales (Sorsby, 1950). If the disease can be identified before cupping of the disk becomes manifest (given a "latent" period of 15 to 20 years), then adequate treatment at an early stage should prevent the onset of visual-field loss and eventual blindness. Tonometry with a Schiøtz tonometer is a simple test, often done by trained nursing staff in eye hospitals. It would not be difficult for the general practitioner to perform routine tonometry on patients over 45 years of age, in the same way as beaumanometry.

Present Investigation

It seemed important to establish whether a similar "transition" group existed in this country; therefore the present survey was organized. The American and German surveys had been confined to the population over 45 years of age. We took the opportunity of examining the population in all age-groups from 10 years upwards, and also of noting the colour of the iris.

Our sample was obtained from patients attending various out-patient departments at the Radcliffe Infirmary and associated hospitals in Oxford who did not have any complaints referable to their eyes. Patients for admission as in-patients, acutely ill persons, and patients attending the eye hospital were excluded. The total number screened was 2,000. They were recruited in such a way as to obtain approximately equal numbers of each sex and age group. Detailed figures are given in Tables I and II.

Method

The screening test was tonometry, using a standardized weighted Schiøtz tonometer and carried out by one of us

TABLE I.—Source of Persons Included in the Survey

Out-patient Department	No. of Patients
Medical	485 (24%)
Ear, nose, and throat	575 (29%)
Physical medicine	244 (12%)
Littlemore hospital (psychiatric)	239 (12%)
Geriatric—Cowley Road and Rivermead hospitals	233 (12%)
Army and Air Force (young adults)	224 (11%)
Total	2,000 (100%)

TABLE II.—Age and Sex Distribution of 2,000 Persons Tested

Age in decades	1	2	3	4	5	6	7	8	9+
No. tested	—	204	303	257	272	355	267	212	130

Sex: male 1,012; female 988.

(D. S.). The patient was placed on a couch and the corneae were anaesthetized with guttae novesine 0.4%. One reading was taken using a 5.5-g. weight. An intraocular pressure of 20.6 mm. Hg (a tonometer scale reading of 4) or over was regarded as requiring further investigation. Where the reading was in the vicinity of 20.6 mm. Hg it was repeated with a 5.5-g. weight, a 7.5-g. weight, and applanation tonometry in order to diminish, so far as was possible, any bias around the critical tension. A doubtful reading was repeated with both a 5.5-g. and a 7.5-g. weight, making any necessary correction for scleral rigidity. The iris colour was noted at the same time.

Funduscopy.—The optic disks were examined in each case. If the cup looked suspicious a central field examination was done.

Applanation Tonometry.—Measurement of the ocular tension was repeated with a Goldmann applanation tonometer, which is thought to give a more accurate reading than the Schiøtz tonometer.

Tonography.—A tonometer with a 5.5-g. weight is kept on the cornea for four minutes and the tension simultaneously recorded by a galvanometric recorder. During this time intraocular pressure falls, and the amount it falls is an indication of the facility of aqueous outflow from the eye. For this investigation a Mueller electronic tonometer was used with a Honeywell-Brown recorder. With this measurement the "coefficient of aqueous outflow" (C) is read from Friedenwald's (1957) nomograms. The C value expresses the aqueous outflow in cubic microlitres per minute per millimetre of mercury pressure gradient.

Po/C Value.—The Po value is the initial intraocular pressure in mm. Hg before starting tonography, using both Schiøtz reading and applanation reading ("corrected" Po/C value). The C value is the facility of aqueous humour outflow. The value Po/C relates the intraocular pressure to aqueous outflow, and in the normal eye is less than 125. Where necessary, corrections were made for scleral rigidity.

Water-drinking Test.—After the drinking of 1 litre of water the intraocular pressure of a normal eye may rise by not more than 6 mm. Hg Schiøtz. Anything more than a 6 mm. rise is abnormal.

Tonography after Water-drinking.—Where the previous tests gave doubtful results, tonography was done half an hour after 1 litre of water was drunk. The normal eye can deal with this water load by increasing aqueous outflow—that is, the C value rises. In the glaucomatous eye it may not. The Po/C value derived from this test relates the tension after water-drinking with the aqueous outflow after water-drinking. In normal eyes it is less than 200.

Tension Curve (In-patients).—Those cases giving inconclusive results were admitted to hospital and a 48-hour "tension curve" was plotted, recording the intraocular pressure every four hours. This provides two sets of information: first, the intraocular pressure may be raised at any time of day or night; second, the normal diurnal variation of intraocular pressure may be increased from 4 to 8 mm. Hg or more.

Gonioscopy.—Examination of the angle of the anterior chamber. This has a normal appearance in most cases of open-angle glaucoma, and by definition is open, whether wide or narrow.

Results

Optic disks were found to be within normal limits in the 91 patients who returned for further investigation.

Intraocular Pressure

Of the 2,000 persons screened, 120 had an intraocular pressure at screening of more than 20.6 mm. Hg (the mean value for the series was 16.27 mm. Hg). These were recalled and investigated, 91 returning for further tests. They were divided into four categories according to results (Table III).

TABLE III.—Results of Tests for Intraocular Pressure and Aqueous Outflow on Patients Recalled

Category	No. of Cases		Definite, Suspicious, and Doubtful Cases Expressed as Percentage of Population Tested	
	Total	Aged Over 45	Total (2,000)	Aged Over 45 (1,092)
Definite glaucoma ..	18	17	0.9	1.5
Suspicious cases ..	6	6	0.3	0.5
Doubtful ..	12	12	0.6	1.1
No glaucoma ..	55	48	—	—
Total ..	91	83	1.8	3.1

1. *Definite "Early Glaucoma."*—These persons had an intraocular pressure of 24.4 mm. Hg or more measured with the Schiøtz tonometer on at least three separate occasions, and over 20 mm. Hg with the aplanation tonometer. The tonography value was less than 0.10, or the Po/C value was greater than 125, and either the water-drinking test was positive or the Po/C value after drinking water was greater than 200. There were 18 patients (10 males, 8 females) in this group.

2. *Suspicious Cases.*—These were cases where the intraocular pressure was found to be raised, as in group 1, but there were fewer than two positive "provocative" tests (tonography, Po/C value, water-drinking test, Po/C value after drinking water). Alternatively, there were cases in which the intraocular pressure was found to be raised but on fewer than three separate occasions, and in these two out of the four provocative tests were positive. There were six patients (four males, two females) in this group.

3. *Doubtful Cases.*—In these the intraocular pressure was within normal limits on repeating the tonometry, and only one provocative test out of the four was positive (either a tonography value of less than 0.10 or a positive water-drinking test). Twelve cases fell into this group.

4. *No Glaucoma.*—These were patients in whom, apart from one tonometer reading above 20.6 mm. Hg at the screening test no evidence of glaucoma was found. These patients were asked to present themselves for a check at yearly intervals. There were 55 cases (2.7%) in this group.

In assessing these results we dealt with numbers of persons rather than numbers of eyes. Individuals were classified according to the state of the worse eye. Hence a "definite glaucoma" may have had definite glaucoma (within the criteria for diagnosis used in this paper) in one eye while the other eye was "suspicious." The clinical status of both eyes of each individual is summarized in

TABLE IV.—Summary of Clinical Status of Two Eyes in Cases with Definite Glaucoma

Cases with Definite Glaucoma	No. of Cases	Percentage with Definite Glaucoma	Percentage of Total Sample
Definite glaucoma in both eyes	12	66.7	0.60
" " " " one eye, suspicious in one eye	2	11.1	0.10
Definite glaucoma in one eye, doubtful in one eye	1	5.6	0.05
Definite glaucoma in one eye, no glaucoma in one eye	3	16.7	0.15
Total ..	18	100	0.9

Tables IV and V. All the doubtful cases were doubtful in both eyes.

The iris colour is shown in Table VI.

TABLE V.—Summary of Clinical Status of Two Eyes in Suspicious Cases

Suspicious Cases	No. of Cases	Percentage of Suspicious Cases	Percentage of Total Sample
Suspicious in both eyes ..	2	33.3	0.10
" " " " one eye, doubtful in one eye ..	3	50.0	0.15
Suspicious in one eye, no glaucoma in one eye ..	1	16.7	0.05
Total ..	6	100	0.30

TABLE VI.—Distribution of Different Coloured Irises in Total Sample, and in Cases of Definite and Suspicious Glaucoma

Colour	Total Sample		Cases of Definite and Suspicious Glaucoma	
	No.	%	No.	%
Blue ..	1,159	58	19	79
Green ..	282	14	3	12.5
Brown ..	559	28	2	8.5
Total ..	2,000	100	24	100

Discussion

The findings in this survey agree closely with those of American authors and of Leydhecker *et al.* in Germany. From this survey one may conclude that at least 1.5% of the population over 45 years of age in Oxford and probably in the country as a whole have early chronic open-angle glaucoma as defined for the purpose of this survey, presumably discovered at a stage prior to cupping of the optic disk and visual-field loss. Table IV shows that in those cases diagnosed as definite glaucoma the disease was bilateral in two-thirds of cases, even at this early stage. Only one person below the age of 45 years was found to have raised intraocular pressures with poor outflow. This was a man aged 32 with malignant hypertension. He was the only patient in our survey with this disease. The screening technique that we have used allowed us to recognize only those cases of ocular hypertension that happened to have raised tensions at the moment of screening. It is possible that cases of early open-angle glaucoma were missed, so that our figures reflect the minimum incidence.

Our diagnosis of "early open-angle glaucoma" is open to some criticism. By the generally accepted definition, cupping of the optic disk and visual-field loss are essential. It is widely accepted that cupping is the result of chronic hypertension. Goldmann (1959) has calculated that it may take 15 to 20 years of ocular hypertension to produce cupping; it can thus be argued that these individuals are cases in the "transition" phase between the onset of raised ocular tension and cupping of the optic disk. Nevertheless, it has not been shown that cupping of the disk and field loss occur in untreated cases of this category; only a long-term follow-up can establish this. Moreover, it is not certain whether these persons are a separate group from the general population or merely at the extreme end of what is a physiological rise of intraocular pressure with age. At present, therefore, it is probably better to refer to these cases as "pre-glaucoma" rather than "early open-angle glaucoma" until it can be established that they do develop cupping of the disk and visual-field loss. One criticism of this terminology is that "pre-glaucoma" suggests a specific group distinct from the normal population, but our statistical analysis suggests that it may be so, and the evidence for this will be presented in another paper.

It is intended to follow up the cases considered to be definite, suspicious, or doubtful glaucoma, together with a random sample of those in whom no glaucoma was found, as a long-term project in the glaucoma clinic conducted by one of us (J. P. F. L.) at the Oxford Eye Hospital.

Iris colour was recorded in each patient in the survey. The results are shown in Table VI. These suggest that the colour distribution is similar in the two groups—that is, the total sample and the cases of glaucoma, although there are fewer brown eyes in the latter. This is not a significant finding, because most of our brown-eyed persons happened to be in the younger age-groups.

Summary

A survey of the intraocular pressures of a random sample of 2,000 of the population at Oxford, including all decades from 10 years of age, was undertaken. Persons with an intraocular pressure of over 20.6 mm. Hg at the first examination were subjected to aqueous-outflow studies. These results are presented and the following points made: (a) 0.9% of the total sample had raised intraocular pressure and abnormal outflow resistance; (b) 1.5% of the persons over 45 years of age fell into this group; (c) this group has been labelled "pre-glaucoma," which is regarded as a

better description at the present time than "early open-angle glaucoma"; (d) in a further 0.5% of the persons over 45 years one was led to suspect glaucoma, and in a further 1.1% the diagnosis was in doubt; (e) the importance was stressed of routine measurement of the intraocular pressure, using a Schiøtz tonometer in individuals over the age of 45 years—this simple test could be carried out by the general practitioner.

We are grateful to our colleagues at the Radcliffe Infirmary and at Littlemore, Cowley Road, and Rivermead Hospitals who allowed us access to their clinics; also to our colleagues in the R.A.M.C., the R.A.F., and the U.S.A.F. for allowing us to examine recruits. It is a pleasure to thank Dr. A. Pirie for constant encouragement and useful criticism. We are indebted to Mr. David Hewitt for handling the statistical analyses.

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GLUCOSE-6-PHOSPHATE DEHYDROGENASE ACTIVITY LEVELS IN ENZYME-DEFICIENT GREEK INDIVIDUALS*

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A deficiency of the red-cell enzyme glucose-6-phosphate dehydrogenase (G.-6-P.D.) is considered to be responsible for many drug-induced haemolytic anaemias (Dern *et al.*, 1954; Beutler, 1959). This erythrocyte lesion is hereditary; it is transmitted through a sex-linked gene with intermediate dominance in the female (Childs *et al.*, 1958). Haemolytic reactions due to primaquine are the prototype of this group of anaemias, and have been described first in negroes; hence the term "primaquine sensitivity" (Dern *et al.*, 1954).

The presence of the same enzyme deficiency in individuals with favism justified the inclusion of the latter among this category of haemolytic anaemias (Szeinberg *et al.*, 1957; Larizza *et al.*, 1958; Zannos-Mariolea and Kattamis, 1961). The similarity of the erythrocyte defect, both in favism and in primaquine sensitivity, was proved further by the crucial experiment of Larizza *et al.* (1958)—that is, the induction of haemolysis after administration of primaquine to an individual with a past history of favism.

Recent findings have shown, however, that in Caucasians—among whom favism is mainly observed—G.-6-P.D. deficiency is more severe than in negroes (Marks and Gross, 1959), affecting not only the old red cells but also the young erythrocyte population, the liver, platelets, and white cells (Ramot *et al.*, 1959; Marks *et al.*, 1959). The clinical significance of the latter findings is at present unknown.

Data on G.-6-P.D.-activity levels in enzyme-deficient Greek individuals are very limited. They were obtained

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from Americans of Greek extraction and showed a marked decrease of enzyme activity similar to that observed in other Caucasians (Childs and Zinkham, 1959).

The purpose of this study is to determine G.-6-P.D. activity in Greek individuals with the enzyme deficiency. To this end, subjects with favism or a past history of favism were chosen. In addition, G.-6-P.D.-deficient male individuals who had never experienced any symptoms of haemolytic anaemia were included in this study. Findings in mothers of the above subjects are reported as well.

Enzyme-activity levels in G.-6-P.D.-deficient infants with a history of severe neonatal jaundice unrelated to blood-group incompatibility or drug exposure are presented separately. Similar babies have been described first by Smith and Vella (1960) in Singapore and later by Italian (Panizon, 1960) and Greek authors (Doxiadis *et al.*, 1961; Zannos-Mariolea *et al.*, 1962; Fessas *et al.*, 1962); they have not been observed so far in negroes. The pathogenesis of their jaundice remains unexplained.

Levels of enzyme activity in these neonates have not been reported from Greece so far.

A correlation between biochemical findings and clinical reactions has also been attempted.

Material

The material of this study consists of the following groups:

Group I.—Forty normal children and adults, all males, used as controls.