BLOOD GROUPS OF MINERS WITH COAL-WORKERS' PNEUMOCONIOSIS AND BRONCHITIS

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An unexpected finding in a survey of a random sample of men from the Rhondda Fach valley in South Wales suggested an association between blood group A and coal-workers' pneumoconiosis. A further and larger sample of 1,250 miners and ex-miners from the same area, covering the same age range of 35 to 64 years, was chosen at random from the population in order to verify this finding. Each man was radiographed and questioned on his history and symptoms of chronic respiratory disease, and samples of blood and of saliva were obtained. The chest radiographs were classified according to the 1953 International Classification of Pneumoconiosis, and ABO and Rhesus blood groups and the secretor status were determined.

No convincing association between ABO or Rhesus blood groups or secretor status and either pneumoconiosis or respiratory symptoms associated with bronchitis was found. If an association between the blood groups and pneumoconiosis in fact existed, it would manifest itself as an effect on the response to exposure to dust. Future investigations should therefore be concerned with variations in the dose-response relation rather than with variations in the prevalence of pneumoconiosis.

During the analysis of the results of a field survey in 1958 in the Rhondda Fach, an excess of blood group A and a corresponding deficiency of blood group O were found among miners and ex-miners with pneumoconiosis (Table 1). The random sample of 600 persons consisted of equal numbers of miners and ex-miners and of non-miners divided into three decennial groups in the age range 35 to 64 years (Higgins and Cochrane, 1961; Kilpatrick and Hardisty, 1961). The only publication on blood group frequency in pneumoconiosis is that of Kuroda (referred to by Winkler, 1943), who found blood group B predominant in Japanese miners with silicosis.

This paper describes our studies in 1961 of a larger sample of miners and ex-miners in relation to pneumoconiosis and to bronchitis.

Methods

A sample of 1,250 miners and ex-miners was drawn from the population of the Rhondda Fach (defined by private census in the summer of 1958) by random numbers.

Details of the samples, the largest that could be studied in the time available, are given in Table 2.

All subjects were seen by appointment and samples of blood and saliva were obtained. A questionnaire similar to that approved in 1960 by the Medical Research Council's Bronchitis Committee was completed. "Chronic bronchitis" was defined as a persistent cough with sputum for some part of the day for at least three months together with one or more "chest illnesses". "Chest illness" was defined as one sufficiently severe to keep a man off work for a week or more with cough and sputum or an increase in these symptoms if they were usually present. The grades of breathlessness were those advocated by Fletcher (1952).

A 14 × 14 in. (35.56 × 35.56 cm.) postero-anterior radiograph was taken of the chest and classified according to the International Classification (I.L.O., 1953). To avoid variation between observers, all questionnaires were completed, and all chest films were read by the same observer.

Blood grouping was performed using clotted blood samples; these were tested the day after collection. The methods used were those described in the Medical Research Council's Memorandum on ABO and Rh grouping (1958) and by Drummond (1961).

TABLE 1
BLOOD GROUPS A, B, AND O, ACCORDING TO AGE, OCCUPATION, AND X-RAY CATEGORY OF
PNEUMOCONIOSIS: RANDOM SAMPLE OF NON-MINERS, MINERS, AND EX-MINERS SEEN IN 1958

Age Group	Occupation	X-ray Category	Blood Groups				
			O	A	B	AB	Total
35-44	Non-miners Miners and ex-miners	—	42 (47.7)*	32 (36.4)	10 (11.4)	4 (4.5)	88 (100.0)
		O	16 (44.4)	15 (41.7)	4 (11.1)	1 (2.8)	36 (100.0)
		Simple pneumoconiosis	15 (35.7)	23 (54.8)	3 (7.1)	1 (2.4)	42 (100.0)
		P.M.F.	3 (37.5)	3 (37.5)	2 (25.0)	0 (0.0)	8 (100.0)
		Total: Miners and ex-miners	34 (39.5)	41 (47.7)	9 (10.5)	2 (2.3)	86 (100.0)
45-54	Non-miners Miners and ex-miners	—	37 (42.0)	42 (47.7)	5 (5.7)	4 (4.5)	88 (99.9)
		O	16 (59.3)	10 (37.0)	1 (3.7)	0 (0.0)	27 (100.0)
		Simple pneumoconiosis	15 (36.6)	22 (53.7)	3 (7.3)	1 (2.4)	41 (100.0)
		P.M.F.	5 (18.5)	14 (51.9)	6 (22.2)	2 (7.4)	27 (100.0)
		Total: Miners and ex-miners	36 (37.9)	46 (48.4)	10 (10.5)	3 (3.2)	95 (100.0)
55-64	Non-miners Miners and ex-miners	—	47 (54.7)	28 (32.6)	4 (4.7)	7 (8.1)	86 (100.0)
		O	11 (44.0)	11 (44.0)	1 (4.0)	2 (8.0)	25 (100.0)
		Simple pneumoconiosis	15 (37.5)	19 (47.5)	4 (10.0)	2 (5.0)	40 (100.0)
		P.M.F.	3 (30.0)	17 (56.7)	3 (10.0)	1 (3.3)	30 (100.0)
		Total: Miners and ex-miners	35 (36.8)	47 (49.5)	8 (8.4)	5 (5.3)	95 (100.0)
All ages	Non-miners Miners and ex-miners	—	126 (48.1)	102 (38.9)	19 (7.3)	15 (5.7)	262 (100.0)
		O	43 (48.9)	36 (40.9)	6 (6.8)	3 (3.4)	88 (100.0)
		Simple pneumoconiosis	45 (36.6)	64 (52.0)	10 (8.1)	4 (3.2)	123 (99.9)
		P.M.F.	17 (26.2)	34 (52.3)	11 (16.9)	3 (4.6)	65 (100.0)
		Total: Miners and ex-miners	105 (38.0)	134 (48.6)	27 (9.8)	10 (3.6)	276 (100.0)

*Percentages in parentheses.

TABLE 2
RANDOM SAMPLES OF MINERS AND EX-MINERS STRATIFIED BY AGE

Age Group	No. in Population at Census*	No. Sampled	Excluded	Left Area	Dead	Refused	Examined	No. in Group after Correcting Ages
35-44	1,137	500 (100.0)†	5 (1.0)	27 (5.4)	1 (0.2)	27 (5.4)	440 (88.0)	440
45-54	1,263	250 (100.0)	1 (0.4)	9 (3.6)	10 (4.0)	23 (9.2)	207 (82.8)	210
55-64	1,168	500 (100.0)	2 (0.4)	8 (1.6)	39 (7.8)	57 (7.4)	414 (82.8)	411
Total	3,568	1,250 (100.0)	8 (0.6)	44 (3.5)	50 (4.0)	87 (7.0)	1,061 (84.9)	1,061

*Date of census, June 1, 1958.

†Percentages are given in parentheses.

ABO Grouping.—Cells were tested with A, B, and O grouping sera. Sera were tested against A and B cells and for irregular antibodies, *e.g.* anti-Rh agglutinins. Tests were done to ensure that weakly reacting A agglutinin (A_3 , *etc.*) in group A or AB bloods did not escape detection. In bloods initially typed as group B, the cells were further tested with group O serum having strong anti-A and which had been absorbed of its anti-B agglutinin. The sera of bloods typed initially as B were also tested with A_1 and A_2 cells.

Rh Typing.—Cells were tested with two anti-D sera and those giving negative reactions were further tested with anti-C, D, and E sera. The D^u antigen was tested for by the indirect anti-globulin test after treatment of the cells with potent anti-D serum known to react with the D^u antigen. Bloods classified as D-negative were those giving negative reactions with anti-D and anti- D^u sera. D-negative bloods comprise those which lack the C and E antigens or which contain one or other, or both, of these antigens.

Saliva Tests.—All salivas were tested independently by two observers for A, B, and H substances. Anti-H extracted from seeds of *Ulex europaea* was used. One

observer used a single tube technique with suitably diluted antisera. The other observer titrated the salivas. Any discrepancies between the results obtained were checked by repeating the tests if necessary on fresh specimens of saliva.

Results

Coal-workers' Pneumoconiosis.—Table 3 shows the prevalence of the various categories of pneumoconiosis in the sample. The proportion of men with pneumoconiosis was lower in this sample than in the previous one (Higgins and Cochrane, 1961). It seems probable that this is due to observer variation in film classification because in the present study all the radiographs were read by I.T.T.H. whereas in the previous sample all the radiographs were read by Professor A. L. Cochrane. At that time we commented that we had expected to find roughly equal numbers of miners and ex-miners with and without pneumoconiosis, whereas we had in fact found a deficiency of men with normal radiographs. The present findings are more in line with our earlier expectations.

TABLE 3
PREVALENCE OF PNEUMOCONIOSIS IN THE SAMPLE

Age Group	Radiological Category			
	No Pneumoconiosis	Simple Pneumoconiosis	P.M.F.	Total
35-44	259 (58.9)*	144 (32.7)	37 (8.4)	440 (100.0)
45-54	103 (49.0)	56 (26.7)	51 (24.3)	210 (100.0)
55-64	178 (43.3)	132 (32.1)	101 (24.6)	411 (100.0)
Total	540 (50.9)	332 (31.3)	189 (17.8)	1,061 (100.0)

*Percentages are given in parentheses

TABLE 4
A, B, O, AND RHESUS BLOOD GROUPS AND SECRETOR STATUS BY AGE AND RADIOLOGICAL CATEGORY OF PNEUMOCONIOSIS

Age Group	Radiological Category	A, B, O Blood Group					Rhesus Group Positive	Secretor Status Positive
		O	A	B	AB	Total		
35-44	O	108 (41.7)	118 (45.6)	22 (8.5)	11 (4.2)	259 (100.0)	227 (87.6)	194 (74.9)
	Simple pneumoconiosis	65 (45.1)	57 (39.1)	16 (11.1)	6 (4.2)	144 (100.0)	112 (77.8)	96 (66.7)
	P.M.F.	14 (37.8)	17 (45.9)	6 (16.2)	0 (0.0)	37 (99.9)	33 (89.2)	26 (72.2)*
	Total	187 (42.5)	192 (43.6)	44 (10.0)	17 (3.9)	440 (100.0)	372 (84.5)	316 (72.0)*
45-54	O	53 (51.5)	31 (30.1)	14 (13.6)	5 (4.9)	103 (100.1)	81 (78.6)	78 (75.7)
	Simple pneumoconiosis	23 (41.1)	24 (42.9)	6 (10.7)	3 (5.4)	56 (100.1)	48 (85.7)	40 (71.4)
	P.M.F.	19 (37.3)	25 (49.0)	5 (9.8)	2 (3.9)	51 (100.0)	49 (96.1)	40 (78.4)
	Total	95 (45.2)	80 (38.1)	25 (11.9)	10 (4.8)	210 (100.0)	178 (84.8)	158 (75.2)
55-64	O	79 (44.4)	72 (40.4)	22 (12.4)	5 (2.8)	178 (100.0)	142 (79.8)	134 (75.3)
	Simple pneumoconiosis	50 (37.9)	61 (46.2)	14 (10.6)	7 (5.3)	132 (100.1)	106 (80.3)	98 (74.8)*
	P.M.F.	49 (48.5)	39 (38.6)	8 (7.9)	5 (5.0)	101 (100.0)	82 (81.2)	71 (70.3)
	Total	178 (43.3)	172 (41.8)	44 (10.7)	17 (4.1)	411 (99.9)	330 (80.3)	303 (73.9)*
Total	O	240 (44.4)	221 (40.9)	58 (10.7)	21 (3.9)	540 (99.9)	450 (83.3)	406 (75.2)
	Simple pneumoconiosis	138 (41.6)	142 (42.8)	36 (10.8)	16 (4.8)	332 (100.0)	266 (80.1)	234 (70.7)*
	P.M.F.	82 (43.4)	81 (42.9)	19 (10.1)	7 (3.7)	189 (100.1)	164 (86.8)	137 (72.9)*
	Total	460 (43.4)	444 (41.8)	113 (10.7)	44 (4.2)	1061 (100.1)	880 (82.9)	777 (73.4)*

*In two cases samples of saliva were not obtained.

Table 4 shows the frequency of ABO and Rhesus blood groups according to age and radiological category. When all age groups are considered together, the frequencies of groups O and A are found to be 44.4 and 40.9% in the men without pneumoconiosis and 42.2 and 42.8% in those with pneumoconiosis. The differences between these percentages are quite insignificant. When individual age groups are considered separately there is again no suggestion of an increased frequency of blood group A among miners with pneumoconiosis. Only in the 45-54 group (the smallest) are there differences in the blood group frequency that are at all suggestive. Here there is a deficiency of group A and a corresponding excess of group O among the miners without pneumoconiosis, a result that is in accordance with the findings of the earlier survey. Indeed, the differences between the three age groups in this survey approach a significant level ($\chi^2 = 5.12$ with two degrees of freedom, $0.10 > p > 0.05$).

The proportions of Rh positive subjects among the men with pneumoconiosis and the men without vary

significantly between the three age groups. Among the men aged 35 to 44 the proportion of Rh positive subjects is somewhat lower when pneumoconiosis was diagnosed than when it was not; among those aged 45 to 54 the proportions are reversed, to an extent which in isolation appears significant ($0.02 > p > 0.01$); among the men aged 55 to 64 there is no apparent difference. This variation between age groups is unlikely to be due to chance ($\chi^2 = 10.18$ for two degrees of freedom, $0.01 > p > 0.001$).

Respiratory Symptoms and Bronchitis.—Table 5 shows the prevalence of respiratory symptoms in the sample according to age and radiological category of pneumoconiosis. As age advances, symptoms in each category become more frequent. There is a clear relation in this sample between respiratory symptoms and the radiological category of pneumoconiosis. In each group the men with simple pneumoconiosis had a higher prevalence of symptoms than those without though the difference is sometimes small, and those with P.M.F. recorded an even higher prevalence. An

TABLE 5
PREVALENCE OF RESPIRATORY SYMPTOMS AND "CHRONIC BRONCHITIS" ACCORDING TO AGE
AND RADIOLOGICAL CATEGORY OF PNEUMOCONIOSIS

Age Group	Radiological Category of Pneumoconiosis	No. ¹	Cough	Sputum	Cough and Sputum	Chest Illness ²			Breathlessness ³		"Chronic ⁴ Bronchitis"
						Once	More than Once	Total	Grades 2 and Over	Grades 3 and Over	
35-44	O	259	109 (42.1)	106 (40.9)	80 (30.9)	24 (9.3)	18 (6.9)	42 (16.2)	47 (18.1)	21 (8.1)	25 (9.7)
	Simple pneumoconiosis	144	72 (50.0)	71 (49.3)	57 (39.6)	14 (9.7)	15 (10.4)	29 (20.1)	54 (37.5)	16 (11.1)	18 (12.5)
	P.M.F.	37	22 (61.1)	24 (66.7)	21 (58.3)	3 (8.3)	8 (22.2)	11 (30.5)	15 (41.7)	7 (19.4)	8 (22.2)
	Total	440	203 (46.2)	201 (45.8)	158 (36.0)	41 (9.3)	41 (9.3)	82 (18.7)	116 (26.4)	44 (10.0)	51 (11.6)
45-54	O	103	50 (48.5)	53 (51.5)	42 (40.8)	8 (7.8)	17 (16.5)	25 (24.3)	37 (35.9)	12 (11.7)	16 (15.5)
	Simple pneumoconiosis	56	37 (66.1)	36 (64.3)	28 (50.0)	5 (8.9)	9 (16.1)	14 (25.0)	29 (51.8)	10 (17.9)	13 (23.2)
	P.M.F.	51	35 (68.6)	34 (66.7)	29 (56.9)	11 (21.6)	9 (17.6)	20 (39.2)	33 (64.7)	12 (23.5)	16 (31.4)
	Total	210	122 (58.1)	123 (58.6)	99 (47.1)	24 (11.4)	35 (16.7)	59 (28.1)	99 (47.1)	34 (16.2)	45 (21.4)
55-64	O	178	107 (60.1)	93 (52.2)	79 (44.4)	12 (6.9)	32 (18.3)	44 (25.1)	78 (43.8)	46 (25.8)	32 (18.2)
	Simple pneumoconiosis	132	78 (60.0)	75 (57.7)	63 (48.5)	10 (7.7)	26 (20.0)	36 (27.7)	71 (54.6)	45 (34.6)	29 (22.3)
	P.M.F.	101	70 (70.0)	69 (69.0)	61 (61.0)	14 (14.1)	27 (27.3)	41 (41.4)	68 (68.7)	41 (41.4)	29 (29.3)
	Total	411	255 (62.5)	237 (58.1)	203 (49.8)	36 (8.9)	85 (21.0)	121 (30.0)	217 (53.3)	132 (32.4)	90 (22.2)

¹In one man aged 35-44 with P.M.F., and two men with simple pneumoconiosis and one man with P.M.F. aged 55-64, respiratory symptoms were not recorded.

²In three men category O and one man with P.M.F. aged 55-64 chest illness was not recorded.

³In one man with P.M.F. aged 55-64 breathlessness was not recorded.

⁴In two men category O and one man with P.M.F. aged 55-64 "chronic bronchitis" was not recorded.

TABLE 6
RESPIRATORY SYMPTOMS AND "CHRONIC BRONCHITIS" ACCORDING TO AGE AND BLOOD GROUP

Age Group	Blood Group	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"
						Once	More than Once	Total	Grades 2 and over	Grades 3 and over	
35-44	O	187	86 (46.0)	91 (48.7)	71 (38.0)	17 (9.1)	18 (9.6)	35 (18.7)	53 (28.3)	22 (11.8)	23 (12.3)
	A	192	84 (44.0)	82 (42.9)	61 (31.9)	15 (7.9)	15 (7.9)	30 (15.7)	47 (24.6)	18 (9.4)	19 (9.9)
	B	44	24 (54.5)	20 (45.5)	19 (43.2)	7 (15.9)	6 (13.6)	13 (29.5)	24 (54.5)	3 (6.8)	6 (13.6)
	AB	17	9 (52.9)	8 (47.1)	7 (41.2)	2 (11.8)	2 (11.8)	4 (23.5)	3 (11.8)	1 (5.9)	3 (17.6)
	Total	440	203 (46.2)	201 (45.8)	158 (36.0)	41 (9.3)	41 (9.3)	82 (18.7)	116 (26.4)	44 (10.0)	51 (11.6)
45-54	O	95	53 (55.8)	61 (63.1)	44 (46.3)	9 (9.5)	22 (23.2)	31 (32.6)	47 (49.5)	18 (18.9)	24 (25.3)
	A	80	46 (57.5)	43 (53.8)	37 (46.3)	12 (15.0)	9 (11.3)	21 (26.3)	37 (46.3)	14 (17.5)	16 (20.0)
	B	25	17 (68.0)	16 (64.0)	15 (60.0)	3 (12.0)	3 (12.0)	6 (24.0)	12 (48.0)	1 (4.0)	4 (16.0)
	AB	10	6 (60.0)	3 (30.0)	3 (30.0)	0 (0.0)	1 (10.0)	1 (10.0)	3 (30.0)	1 (10.0)	1 (10.0)
	Total	210	122 (58.1)	123 (58.6)	99 (47.1)	24 (11.4)	35 (16.7)	59 (28.1)	99 (47.1)	34 (16.2)	45 (21.4)
55-64	O	178	110 (62.1)	101 (57.1)	88 (49.7)	13 (7.4)	33 (18.9)	46 (26.3)	90 (50.8)	52 (29.4)	29 (16.5)
	A	172	109 (63.7)	104 (60.8)	87 (50.9)	17 (10.1)	37 (21.9)	54 (32.0)	95 (55.6)	64 (37.4)	44 (26.0)
	B	44	27 (62.8)	21 (48.8)	20 (46.5)	4 (9.3)	12 (27.9)	16 (37.2)	23 (54.8)	11 (26.2)	13 (30.2)
	AB	17	9 (52.9)	11 (64.7)	8 (47.1)	2 (11.8)	3 (17.6)	5 (29.4)	9 (52.9)	5 (29.4)	4 (23.5)
	Total	411	255 (62.5)	237 (58.1)	203 (49.8)	36 (8.9)	85 (21.0)	121 (30.0)	217 (53.3)	132 (32.4)	90 (22.2)
35-64	O	460	249 (54.2)	253 (55.1)	203 (44.2)	39 (8.5)	73 (16.0)	112 (24.5)	190 (41.4)	92 (20.0)	76 (16.6)
	A	444	239 (54.1)	229 (51.8)	185 (41.9)	44 (10.0)	61 (13.9)	105 (23.9)	179 (40.5)	96 (21.7)	79 (18.0)
	B	113	68 (60.7)	57 (50.9)	54 (48.2)	14 (12.5)	21 (18.8)	35 (31.3)	49 (44.1)	15 (13.5)	23 (20.5)
	AB	44	24 (54.5)	22 (50.0)	18 (40.9)	4 (9.1)	6 (13.6)	10 (22.7)	14 (31.8)	7 (15.9)	8 (18.2)
	Total	1,061	580 (54.9)	561 (53.1)	460 (43.5)	101 (9.6)	161 (15.3)	262 (24.9)	432 (40.9)	210 (19.9)	186 (17.6)

increasing prevalence of respiratory symptoms with increasing radiological category of pneumoconiosis was noted by Rogan, Ashford, Chapman, Duffield, Fay, and Rae (1961) when the findings in six British collieries surveyed by the National Coal Board were combined.

Table 6 shows the prevalence of respiratory symptoms and "chronic bronchitis" according to age and

blood group. There is no evidence of any association between symptoms and blood group. This agrees with the observations of Lewis and Woods (1961), who studied the blood groups in six respiratory disorders in patients referred to the Brompton Hospital. They found no evidence of any association between blood group and cases diagnosed as bronchitis and emphysema.

TABLE 7
PREVALENCE OF SYMPTOMS ACCORDING TO AGE AND SECRETOR STATUS

Age Group	Secretor Status	No.	Cough	Sputum	Cough and Sputum	Chest Illness			Breathlessness		"Chronic Bronchitis"
						Once	More than Once	Total	Grades 2 and Over	Grades 3 and Over	
35-44	Positive	316	147 (46.5)	147 (46.5)	115 (36.4)	30 (9.5)	33 (10.4)	63 (19.9)	87 (27.5)	34 (10.8)	38 (12.0)
	Negative	123	56 (45.5)	54 (43.9)	43 (35.0)	11 (8.9)	8 (6.5)	19 (15.4)	29 (23.6)	10 (8.1)	13 (10.6)
45-54	Positive	158	90 (57.0)	93 (58.9)	73 (46.2)	21 (13.3)	27 (17.1)	48 (30.4)	79 (50.0)	25 (15.8)	36 (22.8)
	Negative	52	32 (61.5)	30 (57.7)	26 (50.0)	3 (5.7)	8 (15.4)	11 (21.4)	20 (38.5)	9 (17.3)	9 (17.3)
55-64	Positive	303	196 (65.1)	177 (58.8)	153 (50.8)	27 (9.1)	62 (20.9)	89 (30.0)	156 (52.0)	91 (30.3)	68 (22.8)
	Negative	107	59 (55.1)	60 (56.1)	50 (46.7)	9 (8.4)	23 (21.5)	32 (29.9)	61 (57.0)	41 (38.3)	22 (20.6)
Total	Positive	777	433 (55.9)	417 (53.8)	341 (44.0)	78 (10.1)	122 (15.8)	200 (25.9)	322 (41.5)	150 (19.4)	142 (18.4)
	Negative	282	147 (52.1)	144 (51.1)	119 (42.2)	23 (8.2)	39 (13.8)	62 (22.0)	110 (39.0)	60 (21.3)	44 (15.6)

TABLE 8
BLOOD GROUP FREQUENCIES ACCORDING TO RADIOLOGICAL CATEGORY IN THE 1958 AND 1961 SAMPLES

Radiological Category	Year	Blood Group				
		O	A	B	AB	Total
O	1958	43 (48.9)	36 (40.9)	6 (6.8)	3 (3.4)	88 (100.0)
	1961	240 (44.4)	221 (40.9)	58 (10.7)	21 (3.9)	540 (99.9)
Pneumoconiosis	1958	62 (33.0)	98 (52.1)	21 (11.2)	7 (3.7)	188 (100.0)
	1961	220 (42.2)	223 (42.8)	55 (10.6)	23 (4.4)	521 (100.0)
Total	1958	105 (38.0)	134 (48.6)	27 (9.8)	10 (3.6)	276 (100.0)
	1961	460 (43.4)	444 (41.8)	113 (10.7)	44 (4.1)	1,061 (100.0)

Table 7 indicates that secretor status also appears to be unimportant in this respect. The age standardized prevalence of respiratory symptoms is the same in both secretor-positive and secretor-negative groups.

Discussion

The impression of an association between blood groups O and A and pneumoconiosis suggested by the small sample drawn in 1958 has not been strongly supported by the larger sample, drawn from virtually the same population, in 1961. Table 8 brings the relevant results together. The excess of group A in men with pneumoconiosis (and a corresponding deficiency of group O) is still present but is extremely small, and the combined evidence from the two samples only attains the 10% level of significance. There is no convincing evidence of heterogeneity of the two samples ($p \approx 0.08$), so it appears that the play of chance may well have been responsible for the differences between them.

Associations between characteristics observed in samples in which many such characteristics have been recorded will appear, by chance, with a frequency larger than that suggested by a single test of significance. If it were known how many pairs of characteristics had been examined for association, the chance frequency could be calculated; in practice,

the suggestion of Fraser Roberts (1955) that a significance level of 1/1,000 should be demanded in blood group work before an association is accepted provides a reasonable safeguard.

When the hypothesis of a particular kind of association has been formed by inspection of sample data not specifically collected with this hypothesis in mind, it is well not to accept the result of a conventional test of significance but to explore the hypothesis by means of a new sample, as we have done in this case with the suggested association between pneumoconiosis and the O/A ratio. In the new sample we have now found apparent evidence of heterogeneity in the relation of pneumoconiosis to Rh positivity. It is clear that further studies are necessary before this can be accepted.

It is of some interest to consider what form of association would be expected if there were a connexion between pneumoconiosis and the blood groups. The very extensive evidence that the prevalence of pneumoconiosis can be related to exposure to dust by some form of dose-response curve (Fay and Ashford, 1961) suggests that any effect of the blood group would be in modifying the shape of this curve, the speed of radiological response to dust inhalation, rather than in producing similar differences in prevalence among men of all ages, of widely differing dust exposures. Unless the blood group in some way determines the dust exposure of an

individual, which seems unlikely, one would expect differences in prevalence to be small among young men, to increase with age (and thus dust exposure), remaining large or perhaps diminishing again among the oldest men. Alternatively, it may be the risk of massive fibrosis associated with a given degree of simple pneumoconiosis which depends on the blood group. It may therefore be better in future studies to attempt to distinguish the dose-response curves of groups of men of different blood groups rather than to proceed with further studies of prevalence unrelated to dust exposure.

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