ABO blood groups in patients with gastric carcinoma associated with pernicious anaemia

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SUMMARY Comparison of the ABO blood groups of patients with all forms of gastric cancer and of those with gastric cancer preceded by pernicious anaemia has shown no differences between them. This finding supports the concept that blood group has a single effect associated with an underlying factor predisposing to either disease.

Both gastric cancer and pernicious anaemia are found more frequently in people of blood group A than in those of the remaining blood groups (Aird, Bentall, and Roberts, 1953; Roberts, 1957).

Patients with pernicious anaemia have in addition an increased susceptibility to gastric cancer and it has been claimed that those individuals who develop pernicious anaemia and gastric cancer successively are much more likely to be of blood group A than those who have either condition alone (Hoskins, Loux, Britten, and Zamcheck, 1965). It has therefore been suggested that liability to gastric cancer may involve two pathways, one associated with blood group A, gastric atrophy, and pernicious anaemia, and the other associated neither with blood group A nor with gastric atrophy. To re-examine this thesis we have compared the ABO blood groups of patients who have developed pernicious anaemia and gastric cancer with those of unselected patients with all forms of gastric cancer.

Method

Information had previously been collected about the causes of illness and death in a large number of patients with pernicious anaemia during an investigation of a possible association between treatment for pernicious anaemia and subsequent liability to leukaemia (Blackburn, Callender, Dacie, Doll, Girdwood, Mollin, Saracci, Stafford, Thompson, Varadi, and Wetherley-Mein, 1968). The blood groups of 29 of the patients known to have developed gastric cancer were determined by reference to the case notes. This group was augmented by the

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collection of further information about 50 patients known to have had pernicious anaemia followed by gastric cancer who had been seen at various centres in the United Kingdom and Denmark. Details of a final group of 12 patients seen in Denmark and Scotland were obtained by reference to published work (Köster, Sindrup, and Sele, 1955; Shearman, Finlayson, Wilson, and Samson, 1966). Details of the numbers and sources of all patients are given in Table I. The ABO blood groups of these patients were then compared with those of unselected patients with gastric cancer diagnosed in the same geographical areas. The diagnosis of gastric cancer was based upon operative, histological, or postmortem evidence, and the criteria for diagnosis of pernicious anaemia included the presence of a megaloblastic anaemia responding to treatment with vitamin B₁₂.

	<i>Pernicious Anaemia Survey and Other Published Data</i>	<i>Additional Patients</i>	<i>Total</i>
<i>United Kingdom</i>			
Oxford & Reading	12 ¹	13	25
London	5 ¹	4	9
Nottingham & Sheffield	3 ¹	3	6
Newcastle	2 ¹	1	3
Edinburgh	10 ^{1,2}	0	10
<i>Denmark</i>			
Copenhagen	9 ³	29	38
			91

Table I *Sources and numbers of patients with gastric cancer and pernicious anaemia*

¹Blackburn *et al* (1968)

²Details of three patients given by Shearman *et al*, remainder by Blackburn *et al* (1968)

³Köster *et al* (1955)

associated with a histamine-fast achlorhydria. In addition vitamin B₁₂ concentrations and tests of absorption were examined in some patients and were found to be unduly low.

Results

Table II gives details of the ABO blood groups in the 91 patients with pernicious anaemia plus gastric cancer and in the control unselected cancer patients. Analysis is complicated because the proportion of healthy individuals of each blood group varies widely from one geographical area to another. Thus the percentage of people of group A tends to be higher in southern England and in Denmark than in Scotland. These differences are reflected in the ABO blood group distributions found in unselected gastric cancer patients because in any one area the relative incidence of gastric cancer in individuals of group A and in those of groups O, B, and AB compared with healthy controls tends to remain constant at 1:20:1 irrespective of overall incidence. In the present study direct comparisons would therefore have best been made separately in each geographical area for pernicious anaemia plus cancer patients and unselected gastric cancer

patients and the results combined, for instance by Woolf's (1955) method.

This procedure was impracticable because of the small numbers of patients with pernicious anaemia plus gastric cancer in some of the areas. However, even without such an analysis it can be seen from Table II that there was no evidence to suggest that the ABO blood group distributions of the pernicious anaemia plus cancer patients and the cancer controls differed materially. Just over 45% of the pernicious anaemia plus cancer patients in the United Kingdom were of blood group A, a proportion which was lower than in three of the five control groups. Furthermore, the proportions of patients of blood group A were slightly higher in the Copenhagen gastric cancer control group than in the pernicious anaemia plus cancer group, the percentages being 48.7 and 42.1 respectively.

Discussion

These results have failed to confirm that patients of blood group A who have pernicious anaemia are more liable subsequently to develop gastric cancer than those of groups O, B, or AB (Hoskins *et al*, 1965). By ordinary standards in investigations of

Source	Pernicious Anaemia and Gastric Cancer Group				Total
	Blood Group				
	A	O	B	AB	
<i>United Kingdom</i>					
Oxford & Reading	11	11	3	0	25
London	4	5	0	0	9
Nottingham & Sheffield	2	1	1	2	6
Newcastle	0	3	0	0	3
Edinburgh	7	2	1	0	10
Total	24	22	5	2	53
	(45.3 %)	(41.5 %)	(9.4 %)	(3.8 %)	
<i>Denmark</i>					
Copenhagen	16	12	8	2	38
	(42.1 %)	(31.5 %)	(21.1 %)	(5.2 %)	
<i>Gastric cancer only</i>					
<i>United Kingdom</i>					
Oxford & Reading ¹	186	144	32	16	378
	(49.2 %)	(38.1 %)	(8.5 %)	(4.2 %)	
London ²	617	578	106	39	1,340
	(46.0 %)	(43.1 %)	(7.9 %)	(2.9 %)	
Nottingham & Sheffield ³	73	60	11	6	150
	(48.7 %)	(40.0 %)	(7.3 %)	(6.0 %)	
Newcastle ⁴	44	44	12	1	101
	(44.0 %)	(44.0 %)	(11.9 %)	(1.0 %)	
Scotland ⁵	174	245	46	13	478
	(36.4 %)	(51.2 %)	(9.6 %)	(2.7 %)	
<i>Denmark</i>					
Copenhagen ⁴	854	673	172	65	1,764
	(48.7 %)	(38.2 %)	(9.8 %)	(3.9 %)	

Table II ABO blood groups of patients with pernicious anaemia plus gastric cancer and with gastric cancer alone

¹New data. Oxford Record Linkage Survey (1962-67).

²Aird *et al* (1953).

³New data. Cases diagnosed in Nottingham 1967-69.

⁴Mosbech (1958).

associations between ABO blood groups and disease the present group of pernicious anaemia plus gastric cancer patients is not large. However, this combination of diseases, though well recognized, is relatively uncommon, and the total group is nearly three times as large as that upon which the claim of a particular association between group A and pernicious anaemia plus gastric cancer was based.

The present results are unlikely to have been affected by bias in collecting data. The diagnoses of pernicious anaemia and gastric cancer were only accepted if based upon clear conventional criteria; furthermore, examination of the blood groups of patients with gastric cancer in whom diagnoses of previous pernicious anaemia seemed insecure showed no evidence of an unduly high proportion of individuals of group A.

Since an additional group A effect on liability to gastric cancer cannot be detected in those who already have pernicious anaemia, it seems probable that the blood group has a single effect upon an underlying factor predisposing to either disease, probably related in some way to gastric atrophy. This view is supported first by the accumulated evidence which suggests that the relative incidence of pernicious anaemia or of gastric cancer in individuals of group A compared with those of group O is the same at approximately 1:20:1 (McConnell, 1966). Furthermore, this ratio has been found to vary little if at all from areas where gastric cancer is common, such as Japan, to those where it is rarer, such as the USA (Segi, Fujisaku, Kurihara, and Moniwa, 1957; Buckwalter, Wohlwend, Colter, Tidrick, and Knowler, 1957). If ABO blood group substances protected the mucosa directly by their presence in the secretions then it would be expected first that ABH non-secretors would, in general, be particularly liable to gastric cancer and pernicious anaemia, and secondly that no ABO blood group effect would be detectable in non-secretors. The weight of the evidence suggests, however, that neither disease is associated with non-secretion of ABH (McConnell, 1966) and, at least for gastric cancer, that the proportions of patients of groups O, B, and AB are to be the same in secretors and non-secretors (Doll and Langman, unpublished observations).

Differences have been detected in the serum and mucosal concentrations of intestinal alkaline phosphatase in healthy people of groups A and groups O and B (Arfors, Beckman, and Lundin, 1963; Bamford, Harris, Luffman, Robson, and Cleghorn, 1965; Shreffler, 1965; Langman, Constantinopoulos,

and Bouchier, 1968). Furthermore, it has been claimed that liability to gastric cancer is associated with small intestinal metaplasia of the gastric epithelium (Morson, 1955). However, it seems unlikely that a link between intestinal metaplasia and alkaline phosphatase formation could in some way be responsible for the ABO blood group effect in liability to gastric cancer because the amount of the intestinal isoenzyme present in the mucosa and secretions is strongly affected by an individual's secretor status. The basic reasons for the relationship between blood group A and liability to gastric cancer therefore remains obscure.

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