The above body of data provided excellent material whereby the degree of correlation between the responses of infants to two very dissimilar antigens could be calculated.

Calculations with combined and separate groups in both cases give a correlation coefficient r of <0.1 and P of >0.4. (Since the distribution of responses to both antigens is log normal all calculations were made on logs of titres.) This signifies a complete absence of relationship between the human infant's responsiveness to diphtheria toxoid and to the agglutinogen of *H. pertussis* vaccine.

Summary

Two similar groups of urban infants (Barking, Essex) aged from 2 to 5 months inclusive at time of first injection were immunized against diphtheria and whooping-cough in different ways: (*a*) A course of three injections of *combined* prophylactic (W.D.P.—red). (*b*) A separate course of five injections: the course of three injections of suspended pertussis vaccine (Glaxo) preceding that of two doses of diphtheria prophylactic P.T.A.P. All injections were made at monthly intervals, each child was bled at 15 months of age, and the sera were assayed for their diphtheria antitoxin and *H. pertussis* agglutination titres.

Three doses of the combined prophylactic—W.D.P. (red)—gave significantly higher antitoxin titres than those previously reported for two doses of A.P.T. It is noteworthy that the very young infants inoculated with the combined prophylactic gave higher antitoxin titres than somewhat older ones given A.P.T. Two doses of P.T.A.P., however, gave the highest figures.

Although whooping-cough vaccines of different manufacture and *H. pertussis* content were used in the two groups the titres obtained were of the same order, and showed no significant difference.

No correlation was found between the responses of individuals to the diphtheria toxoid and the *H. pertussis* agglutinogen.

We gratefully acknowledge the help of other medical officers who assisted with the injections, and that of the health visitors in persuading parents to include their children in the research, as well as for the important part they are playing in the clinical follow-up. We have received invaluable assistance from Mr. Brian in the collection of blood specimens, and a considerable amount of clerical assistance from Mrs. Joan Saul. Thanks are also due to Mrs. Ann Watts for her help in the serum titrations.

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The Department of Public Health of the Territory of Papua and New Guinea published last May the first number of the *Papua and New Guinea Medical Journal*. It is to appear quarterly. The Director of the Department, J. T. GUNTHER, explains in his foreword: "The journal is intended to keep all our varied grades of medical personnel abreast of world progress in the prevention and treatment of the disease pattern of the Territory, to promote medical research locally into these diseases, and to facilitate an exchange of ideas between officers who are otherwise geographically isolated." The first issue includes original articles, extracts from current literature, clinical notes, and book reviews.

THE RELATIONSHIP OF THE ABO BLOOD GROUPS TO DUODENAL AND GASTRIC ULCERATION

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This investigation concerns the distribution of the ABO blood groups in 1,665 duodenal and gastric ulcer patients drawn from three Liverpool Hospitals. It was prompted by the recent paper by Aird *et al.* (1954) in which they showed a greatly increased incidence of blood Group O in 3,011 patients with peptic ulcer from London, Manchester, and Newcastle. The higher frequency of Group O in their series was more marked in duodenal than in gastric ulcer, but the difference between the two sites was not significant on the numbers available. Their overall finding was that persons of Group O are about 35% more likely to develop peptic ulceration than are persons of the other groups.

Collection of Data

The three Liverpool hospitals in which the survey was carried out were the Liverpool Royal Infirmary (374 beds), the David Lewis Northern Hospital (208 beds), and Broadgreen Hospital (657 beds). The first two of these belong to the teaching group and the third to the Regional Board.

The Royal Infirmary ulcer cases were obtained by two of us (W. H. E. and J. C. W.) from an examination of the disease index and operating theatre record books between the years 1948 and 1954. The total number of patients (5,109) who had been blood-grouped in the hospital during 1949–54 inclusive was also recorded.

In the David Lewis Northern Hospital the same two members of the team (W. H. E. and J. C. W.) first extracted from the pathological records the names of the 3,257 patients who, irrespective of diagnosis, had been blood-grouped during the years 1948–54. From this source and from the disease index the case sheets of all patients diagnosed as having had duodenal or gastric ulceration were obtained.

In Broadgreen Hospital two of us (J. W. E. and W. K. C.) scrutinized the pathological records and from them extracted the case sheets of the 8,706 patients who had been blood-grouped during the years 1948–54. From this total were obtained the notes of all the ulcer patients.

Criteria of Diagnosis and Classification of Material

In all three hospitals the diagnosis of ulceration had to be supported either by macroscopical evidence—operation findings, gastroscopy report, or necropsy material—or by a definite positive radiological opinion. Those diagnosed macroscopically are recorded separately from those in which the diagnosis was only radiological. There were very few of the latter except at Broadgreen Hospital, which, as a regional hospital, admits many emergency cases of haemat-

emesis requiring transfusion but not necessarily surgery. Those cases in which it was not possible to decide whether the ulcer was in the stomach or duodenum are recorded separately, as are those in which both duodenal and gastric ulcers were present. Gastric ulcers associated with hiatus hernia were excluded. The material, therefore, in the three hospitals was classified as follows and subdivided according to sex and blood groups :

I. Duodenal ulcers ; macroscopical evidence.
II. Duodenal ulcers ; definite radiological diagnosis.
III. Gastric ulcers ; macroscopical evidence.
IV. Gastric ulcers ; definite radiological diagnosis.
V. Ulcers—site uncertain, mainly " juxtapyloric."
VI. Duodenal and gastric ulcers occurring in the same patient.

Selection of Controls

It is always a difficult matter to make valid comparisons between the blood-group frequencies of a group of people and the population from which they are drawn. In the present investigation two independent sets of controls have been used, and by comparing these one can judge how much confidence may be placed in them as estimates of the group frequency in the populations from which the ulcer patients came.

The first set of controls was obtained by recording the frequency of the ABO blood groups among the patients of the three hospitals, excluding those with ulcer (Table I).

TABLE I.—*Frequency of the ABO Blood Groups Among the Hospital Patients Other Than Those with Ulcer*

Hospital	O	A	B	AB	Total
R.I.	2,251	1,837	444	131	4,663
Northern ..	1,387	1,097	286	66	2,836
Broadgreen ..	3,889	3,081	720	188	7,878

There are two possible major sources of error in controls of this nature : (1) The frequencies among the patients in the hospital may not be the same as in the general population because of associations between certain of the blood groups and specific diseases (Aird *et al.*, 1954). (2) The patients with the particular disease being investigated may not come from exactly the same areas as the rest of the hospital patients.

The second set of controls was obtained from data supplied by the Nuffield Blood Group Centre, using donors being grouped for the first time. This procedure eliminates the first of the sources of error mentioned above, but difficulties arise because in the present study there is a significant heterogeneity ($\chi^2_6 = 21.25$, $P < 0.01$) in the blood-group frequencies between the several areas from which two of the hospitals draw their patients. Only Broadgreen Hospital obtains virtually all its ulcer patients from within one area. Consequently, in constructing controls it is necessary to take into account the estimated frequencies of the blood groups in the various areas, together with the proportions of patients taken from each area (Table II). This makes it difficult

TABLE II.—*Blood Groups of Donors in Different Areas and the Proportion of Patients Taken from these Areas by the Three Hospitals*

	Liverpool Postal District	S.W. Lancashire	West Cheshire	North Wales	Elsewhere in U.K.
No. of donors:					
O	1,398	1,208	483	358	—
A	1,148	1,020	467	304	—
B	259	192	121	77	—
AB	83	55	41	19	—
Total	2,888	2,475	1,112	758	—
Proportion of patients taken:					
Royal Infirmary ..	74%	7%	7%	8%	4%
Northern Hospital	52%	13%	18%	9%	8%
Broadgreen Hospital (excluding thoracic unit) ..	100% approx.	—	—	—	—

to calculate a standard error for the controls, for comparison with the ulcer patients. However, if there is no significant difference between these controls taken at their face value and a sample with which they are being compared, then there will be no significant difference between the controls and the other group if the standard error of the controls is taken into account, because this will reduce and not increase the χ^2 value. It is only when the χ^2 is above the significance level that difficulty arises. In the three hospitals there is no significant difference between the two types of control (Table III), and consequently the controls taken from the

TABLE III.—*Tests of Significance of Difference Between the Ratio O:A:B+AB in Total Groupings (Excluding Ulcer Patients) and Blood Donor Controls*

Hospital	χ^2 for Heterogeneity D. of F. = 2	Probability
R.I.	< 1·09	> 0·5
Northern	< 3·53	> 0·1
Broadgreen ..	0·80	> 0·5

hospitals have been used for comparisons with the ulcer patients because the numbers are large and do not suffer from the defect of the blood-donor controls.

In all the analyses of the data the B and AB blood groups have been taken together. This has been necessary because both these groups have low frequencies and many of the samples to be compared are small.

Results

The basic data are shown in Table IV. The chief findings are as follows.

1. In all three hospitals there is a highly significant increase in the frequency of Group O in the duodenal ulcer patients compared with the controls (Table V).

TABLE IV.—*Basic Data*

Type of Ulcer	Men				Women			
	O	A	B	AB	O	A	B	AB
I. Duodenal ulcer (macroscopical):								
Royal Infirmary ..	156	67	20	11	13	6	2	—
Northern Hospital	131	62	18	8	13	10	3	—
Broadgreen ,,	160	94	13	10	32	24	6	1
Total ..	447	223	51	29	58	40	11	1
II. Duodenal ulcer (radiological):								
Royal Infirmary ..	8	1	1	—	—	1	—	—
Northern Hospital	10	11	4	1	6	—	2	—
Broadgreen ,,	74	21	15	3	28	10	2	1
Total ..	92	33	20	4	34	11	4	1
III. Gastric ulcer (macroscopical):								
Royal Infirmary ..	49	29	10	1	9	10	—	—
Northern Hospital	16	16	7	3	11	11	—	1
Broadgreen ,,	64	67	11	3	36	18	3	2
Total ..	129	112	28	7	56	39	3	3
IV. Gastric ulcer (radiological):								
Royal Infirmary ..	4	1	—	—	—	—	—	—
Northern Hospital	2	—	—	—	3	3	—	—
Broadgreen ,,	11	17	2	1	10	7	—	—
Total ..	17	18	2	1	13	10	—	—
V. Ulcers of uncertain site:								
Royal Infirmary ..	16	8	4	1	2	1	2	—
Northern Hospital	19	23	2	2	6	4	1	—
Broadgreen ,,	27	15	2	2	7	4	1	1
Total ..	62	46	8	5	15	9	4	1
VI. Cases with both gastric and duodenal ulcers:								
Royal Infirmary ..	5	2	2	1	2	1	—	—
Northern Hospital	8	1	—	—	1	1	1	—
Broadgreen ,,	13	5	1	—	1	3	—	—
Total ..	26	8	3	1	4	5	1	—

The data in groups V and VI have not been included in the analyses, the main purpose of which has been to distinguish between duodenal and gastric ulcers.

TABLE V.—*Significance of the Comparison Between the O:A:B +AB Ratios of Duodenal Ulcer Patients and Controls*

Hospital	Comparison	χ^2 for Heterogeneity D. of F. = 2	Probability
R.I. ..	Duodenal ulcer, macroscopical—hospital controls	20·31	< 0·001
Northern ..	,, ,, ,,	9·61	< 0·01
Broadgreen	,, ,, ,,	7·02	< 0·05
,, ..	Duodenal ulcer, radiological—hospital controls	23·27	< 0·001

TABLE VI.—*Significance of the Comparison Between the O:A:B +AB Ratios of Gastric Ulcer Patients and Controls*

Hospital	Comparison	χ^2 for Heterogeneity D. of F. = 2	Probability
R.I. ..	Gastric ulcer—hospital controls	2·05	> 0·3
Northern ..	,, ,, ,, ,,	0 88	> 0·5
Broadgreen	,, ,, ,, ,,	2·83	> 0·2
		$\chi^2_6 = 5·76$	> 0·3

TABLE VII.—*Significance of the Comparison Between the O:A:B +AB Ratios of Duodenal and Gastric Ulcer Patients*

Hospital	Comparison	χ^2 for Heterogeneity D. of F. = 2	Probability
R.I. ..	Duodenal ulcer (macroscopical) —gastric ulcer (macroscopical)	3·43	> 0·1
Northern ..	,, ,, ,, ,,	6·17	< 0·05
Broadgreen	,, ,, ,, ,,	3·01	> 0·2
		$\chi^2_6 = 12·61$	< 0·05
Broadgreen	Duodenal ulcer (radiological)—gastric ulcer (radiological)	16·71	< 0·001
		$\chi^2_8 = 29·32$	< 0·001

2. In all three hospitals there is no significant difference between the blood-group frequencies of patients with gastric ulcer compared with the controls (Table VI).

3. When the blood groups of duodenal ulcer patients are compared with those of gastric ulcer patients there is a significantly higher frequency of Group O among people with duodenal ulceration (Table VII).

4. If our macroscopically diagnosed ulcer patients are combined with those of Aird *et al.* a highly significant difference is found in the blood-group frequencies between duodenal and gastric ulcer patients, leaving little doubt that there is a real difference between the diseases (Table VIII).

TABLE VIII.—*Tests of Significance for the Ratio A/(A+O) Combining the New Data with those of Aird et al.* (1954)

Comparison	Weighted Mean Difference %	χ^2 for Difference D. of F. = 1	Probability	χ^2 for Heterogeneity of Areas D. of F. = 5	Probability
Gastric ulcer—duodenal ulcer	+5·61	10·68	< 0·01	4·55	> 0·3
Gastric ulcer♂—gastric ulcer♀	+4·10	1·93	> 0·1	7·32	> 0·1
Duodenal ulcer♂—duodenal ulcer♀	−2·97	1·07	> 0·3	0·93	> 0·95
Gastric ulcer—controls	−3·99	7·89	< 0·01	6·45	> 0·2
Duodenal ulcer—controls	−9·69	92·74	< 0·001	7·59	> 0·1

Analysis of Results

Sex.—Because of the small number of female patients it seemed desirable to pool the data from the two sexes if this were possible. Consequently, where the samples were large enough a comparison was made between the frequencies of the blood groups in the two sexes, and although one of the differences was significant at the 5% level (Table IX) the sum-total of evidence did not suggest that there is a real difference—a finding which is in agreement with that of Aird *et al.* (1954).

TABLE IX.—*Significance of the Comparison Between the O:A:B +AB Ratios of Male and Female Ulcer Patients*

Hospital	Disease	Comparison	χ^2 for Heterogeneity D. of F. = 2	Probability
Broadgreen	Macroscopically diagnosed duodenal ulcer	Male—female	1·16	> 0·5
,,	Radiologically diagnosed duodenal ulcer	,, ,,	2·18	> 0·3
,,	Radiologically and macroscopically diagnosed gastric ulcer	,, ,,	6·82	< 0·05

Duodenal Ulcer.—The duodenal ulcer cases are divided into two groups—those diagnosed by operation or at necropsy (macroscopical diagnosis) and those diagnosed from definite radiological evidence. When the data from Broadgreen Hospital for these two groups were compared a highly significant difference between them was found ($\chi^2_2 = 11.54$) (Table X). The difference, if it is real and not due to chance, is difficult to account for, as the frequency of Group O is higher in the radiologically diagnosed patients than in the operation cases. A similar comparison could not be made between patients in the Royal Infirmary because of a shortage of data for the radiological group. A comparison between the two groups in the David Lewis Northern Hospital showed no significant differences. However, because of the discrepancy found in the Broadgreen Hospital data the two groups were kept separate in the subsequent analysis. A comparison of the frequencies of the blood groups among macroscopically diagnosed duodenal ulcer patients and the hospital controls gives at the Royal Infirmary a χ^2_2 of 20.31, at the David Lewis Northern Hospital a χ^2_2 of 9.61, and at Broadgreen Hospital a χ^2_2 of 7.02 (Table V). A comparison between the radiologically diagnosed patients at Broadgreen Hospital and hospital controls gives a χ^2_2 of 23.27, showing that in all the data there is a difference between the duodenal ulcer patients and the controls, with a higher frequency of Group O among the duodenal ulcer patients.

TABLE X.—*Significance of the Comparison of the O:A:B+AB Ratios of Macroscopically and Radiologically Diagnosed Ulcers*

Hospital	Disease	Comparison	χ^2 for Heterogeneity D. of F. = 2	Probability
Northern	Duodenal ulcer	Macroscopical—radiological	2·58	> 0·2
Broadgreen	,, ,,	,,	11·54	< 0·01
,,	Gastric ,,	,,	1·27	> 0·5

Gastric Ulcer.—In the data from Broadgreen Hospital there is no significant difference between the frequency of the blood groups among patients diagnosed at operation or necropsy and those diagnosed radiologically. Moreover, there is none between either of these groups of patients and the hospital controls (Table VI). The data for the Royal Infirmary and the David Lewis Northern Hospital also show no difference in the blood-group frequencies of the gastric ulcer patients and the hospital controls.

Comparison Between Duodenal and Gastric Ulcer.—Because of the significant difference between the two groups of duodenal ulcer patients at Broadgreen Hospital separate comparisons between radiologically and macroscopically diagnosed patients were made. There is a highly significant difference between the frequency of the blood groups in radiologically diagnosed duodenal ulcer and gastric ulcer patients, with the frequency of Group O higher in the duodenal ulcer group (Table VII). Among the macroscopically diagnosed duodenal ulcer patients at Broadgreen Hospital there is also a higher frequency of Group O than among the corresponding gastric ulcer patients, although the difference is not significant. The same tendency holds good at the Royal Infirmary, but again the difference is not significant. However, at the David Lewis Northern Hospital there is a significant difference, and again the frequency of Group O is higher among the duodenal ulcer patients. Summing

the χ^2 for the macroscopically diagnosed patients we obtained χ^2_6 of 12.61. This difference is significant at the 5% level. If the radiologically diagnosed Broadgreen data is also used a χ^2 of 29.32 with 8 degrees of freedom is obtained, showing heterogeneity between the duodenal and gastric ulcer groups. Moreover, the frequency of Group O is always higher among the duodenal ulcer group.

Combination of Present Data with those of Aird et al.

Aird *et al.* (1954) analysed their data in such a way that as new information is obtained it can be combined with theirs. Their most important comparisons from the point of view of the present investigation are those for the A/(A+O) ratio for different groups of people, and their results give the weighted mean differences per cent., a χ^2 for this difference, and a χ^2 for heterogeneity between the areas (Aird *et al.*, 1954, Table IX). In Table VIII will be found the same comparisons as those made by Aird *et al.*, together with the comparison between the A/(A+O) ratio for duodenal ulcer patients compared with controls, which was not given by them. In constructing this table the data given in the present paper were combined with the previous data, and only ulcers that had been diagnosed macroscopically were used for the comparisons, because previous data did not include radiologically diagnosed ulcers.

The results given in Table VIII are fully consistent with previous findings, there being no significant heterogeneity between different areas for any of the comparisons made. There is still no significant difference in the A/(A+O) ratio between the sexes in patients with gastric ulcer or duodenal ulcer. There is a highly significant difference between duodenal ulcer and the controls, leaving no doubt that the frequency of Group O among duodenal ulcer patients is much higher than in the general population from which the patients came. There is still a significant difference between gastric ulcer and the controls, although the χ^2 has been reduced. Aird *et al.* (1954) did not find a significant difference between gastric ulcer and duodenal ulcer, although their data did suggest that there might be a real difference between them. The addition of the present data makes the difference highly significant, leaving little doubt that there is a real difference between them.

Table XI shows the blood-group percentages of the macroscopically diagnosed ulcers and of the controls, weighted to make them comparable with those of Aird

TABLE XI.—*Percentage Group Frequencies*

	Duodenal Ulcers	Controls	% Inc. or Dec. on Controls	Gastric Ulcers	Controls	% Inc. or Dec. on Controls
Aird *et al.*	1,351 cases			1,015 cases		
O ..	56·62	47·11	+20·2	53·01	46·89	+13·1
A ..	33·28	40·86	−18·6	37·04	41·13	−9·9
B ..	7·62	9·00	−15·3	7·59	8·94	−15·1
AB ..	2·49	3·02	−17·5	2·36	3·04	−22·4
Liverpool data:	860 cases			377 cases		
O ..	58·72	48·89	+20·1	49·07	48·97	+0·2
A ..	30·58	39·08	−21·8	40·05	39·12	+2·4
B ..	7·21	9·53	−24·3	8·22	9·41	−12·6
AB ..	3·49	2·50	+39·6	2·65	2·50	+6·0

et al., 1954. It will be seen that the percentage increase of Group O in the duodenal ulcer patients over that of the controls is remarkably similar in the two series. In our series the figures for Group AB are so small that the comparison between them and those of Aird *et al.* means very little.

Discussion

The finding of a significant difference between the frequency of Group O in duodenal and gastric ulcer lends support to the view that they are two different conditions. Up to the present this view has been based on the differences in sex ratio, age incidence, precipitating factors, gastric acidity levels, and clinical course, and on the evidence produced by Doll and Kellock (1951), suggesting that they are probably inherited independently.

The nature of the relationship of blood Group O to duodenal ulcer is unknown, but a consideration of three other associations between blood groups and disease suggests a possible explanation. Firstly, in carcinoma of the stomach there is a higher frequency of Group A than among controls (Aird *et al.*, 1953); secondly, a high Group A frequency has been found among young diabetics (McConnell, 1955); and, thirdly, in 457 cases of pernicious anaemia Buchanan and Higley (1921) reported a higher incidence of Group A than in other conditions which they investigated. A feature common to all these diseases is an abnormal level of gastric acidity, and it seems possible that the ABO genes may in some way modify the amount of hydrochloric acid which an individual can secrete.

It has been suggested that the associations found between the ABO genes and diseases are not of a causal nature, but are the result of incomplete miscegenation. While the evidence on the whole seems against this view, we are carrying out investigations at the present time to determine the relationship of the blood groups to duodenal ulcer within families, and this should solve the problem.

Summary

The distribution of the ABO blood groups in 1,665 ulcer patients from three Liverpool hospitals has been investigated.

Compared with controls there is a much higher frequency of Group O among patients with duodenal ulceration.

The blood-group distribution of patients with gastric ulcer is not significantly different from that of the controls.

A comparison of duodenal and gastric ulcer patients showed a significant difference in the frequency of their blood groups. This difference was also found when the present data were combined with those of Aird *et al.* (1954).

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ADDENDUM.—Since submitting this paper (March, 1955) our views on a possible relationship between the ABO groups and the level of gastric acidity have altered. This is because of an investigation which we have been making into the ABO secretor status of duodenal ulcer patients compared with controls. The preliminary results suggest an abnormally high incidence of non-secretors among those affected. If this finding is confirmed it would lend support to the suggestion by Aird *et al.* (1954) that the ABO antigens may exercise a protective action on the gastro-duodenal mucosa. The full data will be the subject of another paper.

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