

cancer of the bronchus. We have no data for cancer of the stomach. Making a number of comparisons, including a variety of further subdivisions, and also of additions, only one barely significant difference emerges. It was noted that in both sexes and in all three areas patients of group A with gastric ulcer were older than patients of group O. Simple addition of the figures gave a difference of 1.64 years, 2.05 times its standard error. Simple addition is not adequate, but, using a method of weighting analogous to that used for the group comparisons, the result was unchanged. This difference, however, is only one arbitrarily selected out of many, and there is no confirmation in the figures for duodenal ulcer, nor in those of groups B and AB. The conclusion is, therefore, that, both in the disease which shows blood-group associations—peptic ulcer—and in the three giving a negative result, there is no evidence on these numbers of any difference in mean age between patients of the four groups. Table X shows mean ages with their standard errors for the most important subdivisions.

Summary

Data are presented on the ABO blood-group frequencies amongst 3,011 patients with peptic ulcer, mainly those who have required treatment by transfusion and/or operation, 2,599 with cancer of the colon and rectum, 998 with cancer of the bronchus, and 1,017 with cancer of the breast.

Compared with controls from the general population of the areas sampled, patients suffering from peptic ulcer show an increased incidence of group O and a correspondingly lower incidence of the other three groups. The difference is a large one. If our series is typical, persons of group O are about 35% more likely to develop peptic ulceration than are persons of the other groups.

The ABO frequencies shown by the three cancers do not differ significantly from the population controls. These three negative results serve as a test of the appropriateness of using population controls for hospital patients.

On the numbers available, there is no indication of any difference in ABO frequencies between gastric and duodenal ulcer.

In none of the diseases is there any significant difference in sex proportion or in age between patients of the four blood groups.

Patients suffering from the four diseases do not differ significantly in the proportion who are Rhesus negative, the overall value being close to the expectation in the general population.

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ABO BLOOD GROUPS AND TOXAEMIA OF PREGNANCY

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The advantages and disadvantages of belonging to one or other ABO blood group are being slowly established. Aird, Bentall, and Roberts (1953) have shown the disadvantage of group A in cancer of the stomach, and Aird *et al.* (1954) that of group O for peptic ulcers. There was an excess of group A children dying under 2 years of age from bronchopneumonia (Struthers, 1951); and fertility and abortions (Waterhouse and Hogben, 1947; Allan, 1953) also show differing incidence in the various blood groups. It occurred to one of us (L. A. P.) that toxæmic and non-toxæmic patients could be compared in this respect in relatively large numbers from existing obstetric records.

Material

The investigation was carried out on 3,813 consecutive admissions to Perivale Maternity Hospital between March, 1951, and April, 1954. Primigravidae are booked in order of their application for admission, to the extent of available beds, and constituted almost half the admissions. Multiparae are admitted on medical, obstetrical, and social grounds only. Dr. J. R. E. Richardson, of the King Edward Memorial Hospital, Ealing, has been responsible for the routine grouping of all patients.

A patient was regarded as toxæmic if she possessed two of the following signs: (1) a blood pressure of 140/90 or

over, after the 28th week of pregnancy; (2) the presence of clinical oedema, or a weight gain of more than 1 lb. (450 g.) a week during the same period; (3) the presence of albuminuria in a catheter specimen, not due to infection. These criteria eliminate those few chronic hypertensive patients who did not develop "superadded toxæmia" by showing oedema or albuminuria. The others (the majority) are included. No case of chronic nephritis was admitted during the period studied. Only two patients developed oedema and albuminuria without a hypertension of 140/90.

A few cases of abortion were omitted, together with some for whom the records were incomplete. The total omitted was 162, leaving 3,651 acceptable records.

These records are included in a larger compilation of 10,000 pregnant women made by Dr. J. R. E. Richardson, who has kindly allowed us to use his figures.

Results

The distribution of groups in our series of 3,651 cases and in Dr. Richardson's larger series proved very similar to those of Discombe and Meyer's (1952) 10,000 pregnant women drawn from an area of Middlesex adjacent to our own (Table I). All three series agree very closely. Com-

TABLE I.—Group Frequencies in Totals of Pregnant Women

Group	Present Series		Richardson's Series		Discombe and Meyer's Series	
	No.	%	No.	%	No.	%
O	1,706	46.73	4,579	45.79	4,578	45.78
A	1,545	42.32	4,238	42.38	4,219	42.19
B	297	8.13	866	8.66	890	8.90
AB	103	2.82	317	3.17	313	3.13
Total ..	3,651		10,000		10,000	

paring our series and Richardson's larger series with that of Discombe and Meyer, χ^2 for three degrees of freedom was respectively 3.17 and 0.40.

There is a marked preponderance of group O in the toxæmic patients (Table II). Comparing the relative proportions of group O and the other groups taken together, for toxæmic and non-toxæmic patients the difference is highly

TABLE II.—Group Frequencies in Toxæmic and Non-toxæmic Patients

Group	Non-toxæmic Patients		Toxæmic Patients		% Increase or Decrease of Toxæmic Patients Over Non-toxæmic Patients
	No.	%	No.	%	
O	1,416	45.5	290	53.6	+18
A	1,342	43.2	203	37.5	-13
B	263	8.5	34	6.3	-26
AB	89	2.9	14	2.6	-10
Total	3,110		541		

significant (χ^2 , with Yates's correction, is 11.75). Comparing the proportions of groups O and A only, χ^2 is 9.09—again significant—and a comparison of group O against B, despite the fact that the number of the latter is small, gives a χ^2 of 5.35.

It was thought important to find whether these differences were predominantly due to primigravidae or to multiparæ, but no such effect was found (χ^2 for three degrees of freedom

TABLE III.—Group Frequencies by Parity in Toxæmic Patients

Group	Primigravidae		Multigravidae	
	No.	%	No.	%
O	146	51.8	144	55.6
A	106	37.6	97	37.5
B	22	7.8	12	4.6
AB	8	2.8	6	2.3
Total	282		259	

is 2.67). As stated above, the total admissions over the period studied comprised primigravidae and multiparæ in almost equal numbers. Table III does not show the expected preponderance of primigravidae in toxæmic patients, but it must be remembered that the multiparæ were a group selected for hospital confinement.

Discussion

This increased proportion of group O patients developing toxæmia of pregnancy, with the increased risk of foetal loss that toxæmia implies, is interesting from many points of view. If proved typical it must be remembered when considering stabilizing mechanisms for maintaining the distribution of blood groups. It might prove to account in part for the shortage of A children from the mating of O mothers with A fathers, shown by Waterhouse and Hogben (1947).

The problem arises whether the association might be due in some way to ABO incompatibility between foetus and mother. Harvey Smith (1945) found that mothers carrying a heterospecific foetus (that is, a foetus bearing a blood-group antigen of the ABO system absent from the maternal red cells) showed distinct evidence of iso-immunization in the second half of pregnancy, and in most cases the rise in antibody titre persisted into the puerperium. He did not mention whether his subjects suffered from toxæmia or not. This effect was shown only when the babies were secretors of group-specific substance (and could therefore presumably transmit antigen through the placenta, without the actual passage of foetal red cells). Group O mothers have a greater chance than those of other groups of bearing a heterospecific foetus. In a population with group frequencies such as those shown in Table I, about 32% of O mothers will bear a heterospecific foetus, as against about 6% for A mothers.

Dienst (1905) made the surprising statement that "eclampsia is nothing but a transfusion of incompatible blood of the child into the mother's circulation as a result of a communication between the two." He abandoned this idea (Dienst, 1908) for what seem rather inadequate reasons, but it was resurrected and elaborated by McQuarrie (1923) and Ottenberg (1923). It was then severely criticized by Allen (1926) and again passed into oblivion. With further interest, however, in iso-immunization and its association with foetal loss, Schwartz and Levine (1943), Browne (1944), and Harvey Smith (1945) have all suggested that further work on the association of ABO blood groups and toxæmia is necessary. Perhaps their advice should be taken and the situation reassessed.

In some cases certain of the features of toxæmia might conceivably be explained by a variety of antigen-antibody reaction, either in the blood or in the walls of the smaller vessels of the mother. Most of the toxæmic phenomena are essentially vascular. Oedema, albuminuria, anuria and oliguria, hepatic and cerebral changes, have been thought to be associated with vascular damage, and toxæmic hypertension is humoral, not neurogenic, in mechanism (Kellar and Sutherland, 1941). Placental insufficiency has been demonstrated by many ingenious methods, and is thought to be due to some interference with the maternal blood supply. No existing theory of the aetiology of toxæmia known to us can explain the appearance of eclampsia or a continued rise in blood pressure in the puerperium, but Harvey Smith and Dienst found the rise in antibodies to persist at least until the fourth day of the puerperium (although their observations at that time were few).

It is obvious that this mechanism is not a factor in many cases of toxæmia. For instance, our figures show 14 toxæmic patients belong to group AB who cannot have carried heterospecific foetuses as defined by Levine (1946). Dr. Richardson has kindly looked up records of 33 toxæmic rhesus-negative mothers, and finds that only four children were heterospecific, and two possibly heterospecific. It would, moreover, need more armchair ingenuity than we possess to explain the known hormonal changes in toxæmia.

But it should be possible to prove or disprove whether this mechanism is a factor in some cases of toxæmia, and further work is planned.

There is another way of looking at this problem. Browne and Dodds (1939) showed that about 50% of toxæmic patients were left with a residual hypertension. They were at that time using a blood pressure of 130/70 as a criterion for both conditions. Other workers, using higher blood pressures as criteria, have shown proportionately similar results. Nevertheless, Isehour, Kuder, and Dill (1942) have shown no increased incidence of hypertension (140/90) in parous rather than in nulliparous patients, and conclude that hypertension following toxæmia occurs in those patients who would have developed it in any case. Perhaps, however, toxæmia in the other group—those not destined to develop permanent hypertension—could be due to a mechanism peculiar to pregnancy such as we have postulated. It would be interesting to know the group distributions in chronic hypertension.

Any discussion on this subject must remain highly speculative; nevertheless, if these empirical findings are confirmed in other series some explanation must be sought.

Summary

The distribution of blood groups in 3,651 admissions to a maternity hospital has been studied. These admissions included 541 patients suffering from toxæmia of pregnancy.

As compared with the non-toxæmic patients, the toxæmic patients showed a significant excess of women of group O.

Some possible implications are discussed.

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Professor A. B. SEMPLE, medical officer of health of Liverpool, in his annual report for 1953 remarks that there was some disquiet about the standard of food hygiene in Liverpool, and that detailed inspection suggested that co-operation was not being maintained by some managements and by personnel employed in some food establishments. "Day-to-day cleanliness was not carried out satisfactorily and many employees were careless in their habits, and the absence of soap, towels, and hot water made things worse. Large accumulations of dirt were found as well as major infestations of rodents and pests." Eventually legal action was taken against the managements of eight bakehouses and eleven cafés. All were found guilty, 15 of the 19 defendants pleading guilty in court.

BLOOD GROUPS IN CARCINOMA OF THE LUNG

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This inquiry into the distribution of the ABO and rhesus blood groups in carcinoma of the lung was prompted by the recent paper by Aird and his colleagues (1953); they found a statistically significant association between cancer of the stomach and blood group A, suggesting that there may be some factor in the disease which is inherited. In lung cancer, on the other hand, a great deal of new work stresses the environment, and there is good evidence of a connexion between this carcinoma and cigarette smoking (Wynder and Graham, 1950; Doll and Hill, 1952; McConnell *et al.*, 1952). On a *priori* grounds an external factor such as tobacco is likely to account for the recent rapid increase in the incidence of carcinoma of the lung, since a mutant gene could not possibly have spread through the population in such a short space of time. Nevertheless, a large number of people who smoke heavily do not develop the disease, and as many as 40.5% of the cancer patients of Doll and Hill (1952) had smoked less than the equivalent of 16 cigarettes a day. Experiments with mice suggest that some strains are more susceptible than others to carcinogens, and it may be that in man part of the population has an inborn tendency to cancer. It therefore appeared worth while investigating the blood groups of cases of cancer of the lung to see if these provided any support for the presence of an inherited factor.

Sources of Material

The 777 patients with cancer of the lung which form the basis of this paper were all drawn from the records of the Liverpool Thoracic Surgical Unit. During the years 1944–53 about 2,000 cases of lung cancer were diagnosed by the unit, and all the histologically proved cases which had been blood-grouped have been included in this series. The histological proof of the disease was from biopsy of the growth, operation specimens, or post-mortem material.

In other surveys of this nature blood-groupings done before 1948 have not been included, on the ground that the standard of technique was not uniformly good up to then. This series includes ABO cases from 1944 onwards, as it is felt that the standard of grouping was high enough throughout and the majority of the earlier cases which were grouped were operated upon and received blood transfusions. The rhesus groupings date from 1949.

As a control, the blood-group distribution amongst 1,000 blood donors of the Liverpool Regional Blood Transfusion Service has been used. In order to avoid any bias due to people who know that they are rhesus negative and therefore volunteer as blood donors, only those being grouped for the first time were included. Samples were drawn over the whole area covered by the Blood Transfusion Service—that is, from North Wales, West Cheshire, and West Lancashire; this is the same area from which the Regional Thoracic