Progress report

ABO blood groups and gastrointestinal function

Since the discovery by Aird and his colleagues of the association between blood group A and gastric cancer,1 there have been many similar claims for other diseases. However, it has often transpired that these claims were unjustified and the publication of such conflicting reports has tended to make the study of associations between ABO blood groups and disease a somewhat unfashionable pastime.

Most of the claims of associations which have proved well founded have related to upper gastrointestinal conditions; these have included the association between blood group A and pernicious anaemia3 and salivary tumours,4 as well as gastric cancer5 and the association between gastric and duodenal ulcers and blood group O.6, 7 In addition, it has been shown that the inability to secrete the ABH blood groups substances in the gastrointestinal mucus, a genetically determined characteristic, is associated with ulcer.8, 9, 10

The causes of these relationships are unknown, but simple protective actions of the ABO(H) blood group substances in the mucus seem unlikely, because in non-secretors these mucopolysaccharides are replaced in equal amounts by Lewis substance. Furthermore, it appears that there is no association between ABH non-secretion and gastric cancer.5, 11 The fact that the gastrointestinal mucosa contains large amounts of blood-group mucopolysaccharides12, 13, 14 has emphasized, however, that they may still have a local effect. A natural hypothesis in view of the association of group O with ulcer and group A with gastric cancer has been to relate the effects of the blood group to acid secretion. Early work suggested that acid secretion did tend to be slightly greater in individuals of group O than of group A,15, 16 but the observed differences in the comparatively elderly subjects could have been due to gastric atrophy which might have been more severe in those of group A than of group O. Studies of younger, healthy individuals have given uncertain results: in one investigation there was a very slightly higher acid output in group O subjects than in group A,17 as measured by serum pepsinogen concentrations, but the difference could well have been due to chance; in a second secretory activity was found to be markedly greater in those of group O than of group A,18 and in a third no difference was found.19 However, the concept of a difference in secretory potential between groups O and A is likely to be oversimplified for it ignores the fact that in ulcer the main difference is between group O and A plus B, whilst in cancer and pernicious anaemia it is between groups O plus B and A. A further point to be considered is that the association between group O and ulcer has been found to be particularly obvious in those who have had symptoms of haematemesis or melaena and may well be nonexistent in those with pain or obstruction.20, 21, 22

An extra dimension was added to the problem by the discovery that an isoenzyme of alkaline phosphatase, which can be identified as of small-intestinal origin by its electrophoretic,23 biochemical,24 and immunological
properties,\textsuperscript{25} appeared in the serum in amounts which varied according to the individual's ABO blood group.\textsuperscript{26} These observations have been confirmed and extended to show that the small intestinal fraction can only be detected in very small amounts, if at all, in the serum of non-secretors, whatever their ABO blood group. But in secretors it can be distinguished progressively more often in the serum of those of groups A, AB, and O or B, the last two blood groups having equal effects on its appearance.\textsuperscript{27, 28, 29, 30}

It therefore became natural to enquire as to whether these patterns could be related to the known associations with disease, for instance with gastric cancer. Simple comparisons of serum isoenzyme patterns in healthy individuals and with those with disease could not, however, be made for diet seemed also to influence the appearance of the intestinal isoenzyme in the serum. In particular, the feeding of fat seemed to be the stimulus to the appearance of intestinal alkaline phosphatase in the serum, provided the individual had the appropriate ABO blood group and secretor status.\textsuperscript{31, 32, 33} These studies agreed well with independent observations showing that the administration of fat but not protein or carbohydrate markedly increased the alkaline phosphatase content of human thoracic duct lymph.\textsuperscript{34} A logical extension to those studies was to determine whether fat handling itself was influenced by ABO blood groups and secretor status. Analysis of the results of serum cholesterol determinations in healthy blood donors and in population samples has shown that concentrations tended to be slightly higher in individuals of group A than in those of groups O or B\textsuperscript{35, 36} and that they were slightly, but significantly, higher in individuals with red cells which were Lewis a positive (equivalent to ABH non-secretors).\textsuperscript{36} Thus there was an inverse correlation between the ABO associated factors for serum cholesterol and serum intestinal alkaline phosphatase. The associated variations of the ABO group in serum cholesterol detected were small but could be of importance in the aetiology of coronary heart disease. This condition is known to be determined in part by familial, and probably genetic factors,\textsuperscript{37} one of the most compelling pieces of evidence in favour of this view being the stronger tendency for both of like twin pairs compared with unlike twins to develop the disease once one has been affected.\textsuperscript{38} In addition, it has been shown that a higher proportion of patients of group A can be found amongst those with coronary heart disease than in controls,\textsuperscript{39, 40} matching with the finding of slightly raised concentrations of serum cholesterol in individuals of this blood group and emphasizing the possible importance of intestinal factors in the control of serum cholesterol concentrations.

The strongest association between the ABO blood groups and disease yet to be clearly demonstrated has been for venous thromboembolism where a deficit of group O individuals was detected during a drug surveillance programme which, during confirmatory studies, was shown to be most obvious in women taking oral contraceptive agents and of intermediate degree in those who were pregnant or puerperal.\textsuperscript{41} This situation could be the reverse of the group O excess noted for bleeding duodenal ulcer and may be related to the unexplained finding that plasma factor VIII concentrations tend to be slightly lower in individuals of group O than in those of groups A, B, and AB.\textsuperscript{42}

In general terms, therefore, it is possible to suggest two patterns of disease: one in which the findings in group O contrast with those in groups A, B, and AB such as duodenal ulcer haemorrhage and venous thromboembolism, and the other in which group A contrasts with groups O and B and (possibly) AB with gastric cancer, pernicious anaemia, and salivary tumours as examples. Further evidence is required, particularly on the importance of secretor status and on the relationships of the ABO blood groups with clotting factors and intestinal fat handling, in order to make the picture clearer.
References


