It is apparent that the application of an antibacterial cream to the anterior nares is the best method of reducing colonization in newborn infants. Gould (1955), using an antibiotic cream, reduced the carriage rate in adults to 25%, but the use of an antibiotic likely to produce resistant strains is a disadvantage. Baker and Christie (1959) used neomycin drops in infants with good clearance, and this antibiotic has the advantage of not adversely affecting the general sensitivity patterns although resistance to neomycin itself has been described (Quie *et al.*, 1960). We have used a combination of neomycin and chlorhexidine, with a reduction in nasal carriage rate to 18% in babies and 3.5% in mothers and a marked reduction in the infection rate. No harmful effects were noted during the trial, and *in vitro* observations have not shown any resistance to neomycin when it is combined in this manner with chlorhexidine (K. G. Green, personal communication, 1960).

The recent work of Gillespie *et al.* (1958), Simpson *et al.* (1960), and Corner *et al.* (1960), using hexachlorophane dusting powder, suggests that a combination of both methods might be of further benefit, and such a trial is now in progress.

**Summary**

A trial of combined neomycin/chlorhexidine nasal cream ("naseptin") was carried out in an attempt to reduce nasal colonization by staphylococci in newborn infants and mothers in a maternity hospital.

There was a definite reduction of nasal colonization in both groups.

The incidence of infections both in hospital and in the two-months period after discharge was appreciably reduced, more particularly in the group who were not nasal carriers of staphylococci.

The majority of the staphylococci that were phage-typed belonged to group I.

It is suggested that daily use of nasal cream combined with regular powdering with an antiseptic dusting powder might produce a further fall in colonization and infection in the newborn period.

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# SECRETION OF ABH ANTIGENS IN PEPTIC ULCERATION AND GASTRIC CARCINOMA*

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Various hypotheses have been proposed to explain the association of the ABO blood groups with disease processes. Best-established are the association with peptic ulceration characterized by an increased group O frequency and that for gastric carcinoma characterized by an increased group A frequency (Buckwalter *et al.*, 1958). Perhaps the most plausible explanation for the associations with peptic ulceration and gastric carcinoma is that the mucopolysaccharide ABH blood-group substances which are secreted into the gastro-intestinal tract protect the mucous membrane against ulcerogenic and carcinogenic agents (Aird *et al.*, 1954). This is a report of a study of secretion of mucopolysaccharide blood-group substance in peptic ulcer and gastric carcinoma patients.

## Materials and Methods

Since 1956 peptic ulcer and gastric carcinoma patients admitted to the University of Iowa and Iowa City Veterans Administration hospitals have provided clinical material for this study. The diagnoses have been established on morphological grounds in all patients with gastric carcinoma and in two-thirds of those with peptic ulcer; and in the remainder on the basis of a typical history with positive upper gastro-intestinal *x*-ray studies. Blood and saliva samples and relevant history have been obtained for each patient. A qualitative determination of the ABH substance in saliva has been done, employing the isohaemagglutination test, using anti-H substance prepared from seeds of *Ulex europaeus*, and A and B antisera. Controls have been provided by a random sample of hospital personnel and patients with diagnoses other than those being studied. The differences between the secretor and non-secretor percentages of the patients and the controls have been examined for statistical significance by the chi-square ($\chi^2$) method.

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## Results

The raw data are recorded in Table I. Controls, and duodenal ulcer, gastric ulcer, and gastric carcinoma patients are subdivided by blood group, secretor status, and sex. Blood groups A and AB are further divided into $A_1$, $A_2$, $A_1B$, $A_2B$. The results of the statistical analysis of these data are recorded in Table II. The results of only those comparisons are given which are of importance in evaluating the findings. Blood groups B and AB are combined in the analyses. The smallness of the numbers of patients in these categories makes their analysis as separate groups meaningless. Observe that the controls and various patient categories are examined for heterogeneity. Some heterogeneity is present in the female controls, but is not significant.

Secretor status of the patients is compared with that of controls. A significant increase in non-secretion is found in duodenal ulcer patients when they are compared with controls ($P<0.001$). When the secretor status of duodenal ulcer patients of the different blood groups is examined, note that those with blood group A ($A_1$, $A_2$) compared with controls of blood group A show a statistically significant increase in non-secretion ($\chi^2=10.364$; $P<0.01$). Of less statistical significance were the differences between duodenal ulcer patients of group O and the O controls ($\chi^2=6.272$; $P<0.02$), $A_1$, $A_1B$ patients and controls ($\chi^2=6.438$; $P<0.02$), and $A_2$, $A_2B$ patients and controls ($\chi^2=3.565$; $P<0.10$). Observe that the secretor status of gastric ulcer and gastric carcinoma patients did not differ significantly from that of the controls.

TABLE I.—*Secretor and Blood-group Status of Patients and Controls*

| | Total Patients | Blood Group % | Secretors M | Secretors F | Secretors Total | Secretors % | Non-secretors M | Non-secretors F | Non-secretors Total | Non-secretors % |
|---|---|---|---|---|---|---|---|---|---|---|
| *Controls* | | | | | | | | | | |
| O | 563 | 44·65 | 250 | 197 | 447 | 79·40 | 69 | 47 | 116 | 20·60 |
| A | 512 | 40·60 | 233 | 154 | 387 | 75·59 | 75 | 50 | 125 | 24·41 |
| $A_1$ | 424 | 33·62 | 195 | 127 | 322 | 75·94 | 54 | 48 | 102 | 24·06 |
| $A_2$ | 88 | 6·98 | 38 | 27 | 65 | 73·86 | 21 | 2 | 23 | 26·14 |
| B | 144 | 11·42 | 66 | 41 | 107 | 74·31 | 19 | 18 | 37 | 25·69 |
| AB | 42 | 3·33 | 20 | 10 | 30 | 71·43 | 7 | 5 | 12 | 28·57 |
| $A_1B$ | 31 | 2·46 | 13 | 9 | 22 | 70·97 | 6 | 3 | 9 | 29·03 |
| $A_2B$ | 11 | 0·87 | 7 | 1 | 8 | 72·73 | 1 | 2 | 3 | 27·27 |
| Total | 1,261 | 100·00 | 569 | 402 | 971 | 77·00 | 170 | 120 | 290 | 23·00 |
| *Duodenal Ulcer* | | | | | | | | | | |
| O | 257 | 53·65 | 156 | 28 | 184 | 71·60 | 62 | 11 | 73 | 28·40 |
| A | 163 | 34·03 | 83 | 19 | 102 | 62·58 | 44 | 17 | 61 | 37·42 |
| $A_1$ | 140 | 29·23 | 75 | 15 | 90 | 64·29 | 37 | 13 | 50 | 35·71 |
| $A_2$ | 23 | 4·80 | 8 | 4 | 12 | 52·17 | 7 | 4 | 11 | 47·83 |
| B | 44 | 9·18 | 22 | 7 | 29 | 65·91 | 13 | 2 | 15 | 34·09 |
| AB | 15 | 3·13 | 8 | 3 | 11 | 73·33 | 3 | 1 | 4 | 26·67 |
| $A_1B$ | 10 | 2·09 | 4 | 3 | 7 | 70·00 | 2 | 1 | 3 | 30·00 |
| $A_2B$ | 5 | 1·04 | 4 | 0 | 4 | 80·00 | 1 | 0 | 1 | 20·00 |
| Total | 479 | 99·99 | 269 | 57 | 326 | 68·06 | 122 | 31 | 153 | 31·94 |
| *Gastric Ulcer* | | | | | | | | | | |
| O | 104 | 56·52 | 57 | 18 | 75 | 72·12 | 23 | 6 | 29 | 27·88 |
| A | 54 | 29·35 | 35 | 6 | 41 | 75·93 | 10 | 3 | 13 | 24·07 |
| $A_1$ | 43 | 23·37 | 28 | 5 | 33 | 76·74 | 7 | 3 | 10 | 23·24 |
| $A_2$ | 11 | 5·98 | 7 | 1 | 8 | 72·73 | 3 | 0 | 3 | 27·27 |
| B | 19 | 10·33 | 13 | 3 | 16 | 84·21 | 2 | 1 | 3 | 15·79 |
| AB | 7 | 3·80 | 4 | 1 | 5 | 71·43 | 2 | 0 | 2 | 28·57 |
| $A_1B$ | 3 | 1·63 | 2 | 0 | 2 | 66·67 | 1 | 0 | 1 | 33·33 |
| $A_2B$ | 4 | 2·17 | 2 | 1 | 3 | 75·00 | 1 | 0 | 1 | 25·00 |
| Total | 184 | 100·00 | 109 | 28 | 137 | 74·46 | 37 | 10 | 47 | 25·54 |
| *Gastric Carcinoma* | | | | | | | | | | |
| O | 43 | 36·44 | 26 | 8 | 34 | 79·07 | 9 | 0 | 9 | 20·93 |
| A | 61 | 51·69 | 29 | 18 | 47 | 77·05 | 7 | 7 | 14 | 22·95 |
| $A_1$ | 54 | 45·76 | 25 | 17 | 42 | 77·78 | 5 | 7 | 12 | 22·22 |
| $A_2$ | 7 | 5·93 | 4 | 1 | 5 | 71·43 | 2 | 0 | 2 | 28·57 |
| B | 10 | 8·47 | 5 | 3 | 8 | 80·00 | 2 | 0 | 2 | 20·00 |
| AB | 4 | 3·39 | 2 | 1 | 3 | 75·00 | 1 | 0 | 1 | 25·00 |
| $A_1B$ | 4 | 3·39 | 2 | 1 | 3 | 75·00 | 1 | 0 | 1 | 25·00 |
| $A_2B$ | 0 | 0·00 | 0 | 0 | 0 | 00·00 | 0 | 0 | 0 | 00·00 |
| Total | 118 | 99·99 | 62 | 30 | 92 | 77·97 | 19 | 7 | 26 | 22·03 |

In Table III the secretor status of patients with duodenal ulcer and gastric ulcer is examined as related to severity of the disease process. The five clinical groups into which the patients are divided are described in the first column. No evidence of heterogeneity was found in these data ($0.10<P$) for both duodenal and gastric ulcer.

TABLE II.—*Statistical Analysis of the Data*

| Groups | $\chi^2$ | |
|---|---|---|
| *Controls:* | | |
| Males O×A×(B+AB) | 0·578 | 0·10<P |
| Females O×A×(B+AB) | 4·875 | 0·05<P<0·10 |
| Males×females | 0·0 | 0·10<P |
| $A_1A_1B \times A_2A_2B$ | 0·267 | 0·10<P |
| *Duodenal ulcer:* | | |
| Males O×A×(B+AB) | 1·764 | 0·10<P |
| Females O×A×(B+AB) | 3·290 | 0·10<P |
| Males×females | 0·577 | 0·10<P |
| $A_1A_1B \times A_2A_2B$ | 0·737 | 0·10<P |
| Patients×controls | 14·585 | P<0·001 |
| ,, O× ,, O | 6·272 | 0·01<P<0·02 |
| ,, A× ,, A | 10·364 | 0·001<P<0·01 |
| ,, B+AB×controls B+AB | 1·012 | 0·10<P |
| ,, $A_1A_1B$× ,, $A_1A_1B$ | 6·438 | 0·01<P<0·02 |
| ,, $A_2A_2B$× ,, $A_2A_2B$ | 3·565 | 0·05<P<0·10 |
| ,, A,B,AB× ,, A,B,AB | 10·746 | 0·001<P<0·01 |
| *Gastric ulcer:* | | |
| Males O×A×(B+AB) | 1·317 | 0·10<P |
| Females O×A×(B×AB) | 0·0 | 0·10<P |
| Males×females | 0·0 | 0·10<P |
| $A_1A_1B \times A_2A_2B$ | 0·0 | 0·10<P |
| Patients×controls | 0·557 | 0·10<P |
| ,, O× ,, O | 2·386 | 0·10<P |
| ,, A× ,, A | 0·0 | 0·10<P |
| ,, B+AB×controls B+AB | 0·896 | 0·10<P |
| ,, $A_1A_1B$× ,, $A_1A_1B$ | 0·0 | 0·10<P |
| ,, $A_2A_2B$× ,, $A_2A_2B$ | 0·0 | 0·10<P |
| *Gastric carcinoma:* | | |
| Males O×A×(B+AB) | 1·380 | 0·10<P |
| Females O×A×(B+AB) | 3·476 | 0·10<P |
| Males×females | 0·231 | 0·10<P |
| $A_1A_1B \times A_2A_2B$ | 1·355 | 0·10<P |
| Patients×controls | 0·061 | 0·10<P |
| ,, O×controls O | 0·0 | 0·10<P |
| ,, A× ,, A | 0·099 | 0·10<P |
| ,, B+AB×controls B+AB | 0·378 | 0·10<P |
| ,, $A_1A_1B$× ,, $A_1A_1B$ | 0·106 | 0·10<P |
| ,, $A_2A_2B$× ,, $A_2A_2B$ | 0·0 | 0·10<P |

TABLE III.—*Secretor Status Related to Severity of Disease*

| | Duodenal Ulcer S. | Duodenal Ulcer % | Duodenal Ulcer N.S. | Duodenal Ulcer % | Gastric Ulcer S. | Gastric Ulcer % | Gastric Ulcer N.S. | Gastric Ulcer % |
|---|---|---|---|---|---|---|---|---|
| Medical therapy; good response | 84 | 64·62 | 46 | 35·38 | 33 | 78·57 | 9 | 21·43 |
| Medical therapy; poor response | 81 | 72·32 | 31 | 27·68 | 11 | 55·00 | 9 | 45·00 |
| Surgical therapy; good response | 101 | 66·45 | 51 | 33·55 | 37 | 74·00 | 13 | 26·00 |
| Surgical therapy; poor response | 47 | 71·21 | 19 | 28·79 | 13 | 59·09 | 9 | 40·91 |
| Surgical therapy; poor response after more than one operation | 6 | 60·00 | 4 | 40·00 | 0 | 0·00 | 0 | 0·00 |
| Total | 319 | 67·87 | 151 | 32·13 | 94 | 70·15 | 40 | 29·85 |

S.=Secretor. N.S.=Non-secretor.

## Discussion

When the differences between the ABO blood-group percentages of the 479 duodenal ulcer, 184 gastric ulcer, and 118 gastric carcinoma patients included in this study are compared with the blood-group percentages of the 1,261 controls for this study, the differences for gastric ulcer and gastric carcinoma patients from the controls are found to be greater than those for duodenal ulcer patients. However, when the statistical significance of these differences is examined we obtain the following: duodenal ulcer ($\chi^2=13.624$; $P<0.01$), gastric ulcer ($\chi^2=10.432$; $P<0.02$), gastric carcinoma ($\chi^2=5.680$; $0.10<P$). The blood-group percentage differences in the gastric ulcer and gastric carcinoma patients are also greater than those previously

found in much larger groups of patients (Buckwalter *et al.*, 1958). These discrepancies between the size of the blood-group percentage differences and the levels of statistical significance emphasize the need for large numbers of patients in these investigations if statistically valid conclusions are to be obtained, and illustrate how overemphasis of differences in the blood-group frequencies might lead to erroneous conclusions.

The suggestion of heterogeneity in the female controls, female duodenal ulcer patients, and female gastric carcinoma patients is not statistically significant. It seems probable, supported by the findings of Clarke *et al.* (1956), that these apparent differences are related to the volume of the data and may disappear if sufficient data are obtained.

This study confirms the increased percentage of non-secretors among patients with duodenal ulcer and the absence of any increase of non-secretion in gastric ulcer patients as reported by Clarke *et al.* (1959). However, as indicated before, and contrary to Clarke *et al.* (1955), a statistically significant increase in the frequency of blood group O in gastric ulcer patients was found similar to that found in the previous study. Also, an excess of group O was found in the propositi of both gastric ulcer and duodenal ulcer patients when the propositi were compared with their siblings (Van Scoy and Buckwalter, in preparation). Therefore, results of sibship and blood-group frequency studies are similar for gastric and duodenal ulcer, while the results of secretor studies differ for these two disease processes. This contradiction may be real or specious, and awaits the accumulation of more data for proper interpretation.

The secretion findings in the duodenal ulcer patients are consistent with the hypothesis that the mucopolysaccharide blood-group substances, by coating the gastro-intestinal mucosa, protect it against ulceration, and therefore could explain the association of blood group and duodenal ulcer. Our results suggest that most important is whether or not any ABH blood-group substances are secreted. Clarke *et al.* (1959), using fucose as an index of the mucopolysaccharide blood-group substance content in saliva, found evidence that the total content of the blood-group substances (ABH and $Le^a$) did not differ significantly between duodenal ulcer patients and their controls. This suggests that the secretor effect is related to ABH mucopolysaccharides rather than being a non-specific polysaccharide effect. Evidence against the hypothesis of ABH secretion as an explanation for the blood-group findings in patients with gastric ulcer and gastric carcinoma is provided by the close agreement of the secretor/non-secretor percentages of these patients with the controls.

Aird (1955) suggested that blood-group substances might vary in their ability to confer protection on the gastro-intestinal mucosa, with H substance offering less protection and A and B substances more protection. This would account for the increased frequency of blood group O in duodenal ulcer patients, since persons of group O secrete only H substance. It would also lead one to expect a lower frequency of ulcer in secretors of groups A, B, and AB, and, conversely, a higher percentage of non-secretors in ulcer patients of blood groups A, B, and AB.

Our findings of a higher percentage of non-secretion in duodenal ulcer patients of group A than in those of group O support the concept of a group specific association. Clarke *et al.* (1955) found the highest non-secretor percentages in duodenal ulcer patients of blood group O, while Wallace *et al.* (1958) found the highest non-secretion percentage in patients of groups A, B, and AB. However, the data indicate that the association of duodenal ulceration to the overall non-type-specific ABH secretion is statistically much stronger, and therefore probably more important.

It is probable that duodenal ulcer is not a single disease entity. If this is true, increasing numbers of factors will be discovered which play parts in the aetiology and pathogenesis of duodenal ulcers. The secretion of mucopolysaccharide blood-group substances through a mechanical, immunological, or some other mechanism may be one of the factors. It is possible that these investigations will also help resolve the questions concerning the relationship between duodenal and gastric ulcer.

No indication was found of a correlation between the severity of the disease process and secretor status. It is possible that secreted mucopolysaccharide blood-group substances form only an initial protective barrier against ulceration. Once this barrier has been bridged, the secretor may not differ from the non-secretor.

The only finding of statistical significance when groups A and AB were subdivided into groups $A_1$, $A_2$, and $A_1B$, $A_2B$ was when duodenal ulcer patients were compared with the controls. The statistically increased rate of non-secretion in $A_1$, $A_1B$ patients simply reflects the increased non-secretion percentage in all group A patients.

## Conclusions

A statistically significant increase in non-secretors of mucopolysaccharide blood-group substances was found in patients with duodenal ulcer compared with controls.

In addition to the increase in non-secretion in patients of all ABO blood groups, a secondary association characterized by the highest non-secretion rate in group A patients was noted.

No association of secretor status to severity of duodenal ulcer was found.

The percentages of non-secretors in gastric ulcer and gastric carcinoma patients do not differ significantly from the controls.

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