Frequencies of Secretors and Non-secretors of ABH Group Substances among 1,000 Alcoholic Patients

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Summary: The ABO blood group and secretor status of 1,000 alcoholic patients has been determined. The patients were drawn from large alcoholic units in the London area together with several small units, including rehabilitation centres, and 127 were from Aberdeen.

The findings have been compared with appropriate controls which take into account the ethnic origin of the patients in the series. A striking disturbance of the secretor/non-secretor ratio among group A patients compared with the controls is observed. There is an increase in group A non-secretors, which is almost exactly balanced by a loss of group A secretors so that the overall frequency of the group A phenotype is not disturbed. It is difficult to find an acceptable explanation for these results.

Introduction

The antigens A, B, and H of the ABO blood group system are not confined to the red cells but are found in a soluble form in the body fluids. Not all individuals, however, secrete their corresponding ABH substances. A proportion are non-secretors—that is, their fluids are free from or contain only trace amounts of A, B, or H group specific substances. In the English population this figure is about 23%. It is considered that the secretion of group-specific substances is controlled by a pair of allelomorphous genes, *Se* and *se*. Three types of individual are therefore possible—*SeSe*, *Sese*, and *sese*. The first two are secretors and the third is a non-secretor.

There is an association between the secretion of ABH blood group substances and the Lewis blood group system in that individuals whose red cells type as *Le* (*a+b-*) fall into the non-secretor category while those whose red cells are *Le* (*a-b+*) are secretors. There are therefore available two independent tests for secretor status: (a) a test on a body fluid, usually saliva, and (b) a test for the Lewis type of the red cells. A small proportion of the population (about 6%) have red cells which type as *Le* (*a-b-*) and these are either secretors or non-secretors. Their secretor status has to be determined on their body fluids.

In 1967 we reported an increase in the incidence of non-secretors of ABH blood group substances among alcoholic patients compared with the controls (Camps and Dodd, 1967). By the time 318 patients had been investigated it was seen that an increase in the number of patients who were both group A and non-secretor was largely responsible for the total increase found.

It was therefore decided to continue the investigation until 1,000 patients had been examined. These patients were drawn from three large alcoholic units in the London area, together with several smaller units, including rehabilitation centres. In addition 127 patients were from Scottish units in Aberdeen, for the collection of which we are indebted to the kindness of Dr. Colin McCance, of the Cornhill Hospital, Aberdeen.

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Materials and Methods

Saliva Samples.—From each patient 1–2 ml. of saliva was collected. As soon as possible after collection these were placed in a boiling-water bath for 15 minutes to destroy enzymes which might interfere with the activity of the blood group substances. They were then diluted one in two with normal saline and stored frozen at -20° C. until required.

Antisera.—Most of the antisera used throughout the investigation were kindly supplied by Dr. R. A. Zeitlin, of the South London Regional Transfusion Centre. Specially selected anti-A and anti-B sera were used for the inhibition tests on saliva samples. H was detected by means of anti-H from *Ulex europaeus*. Anti-*Le^a* and anti-*Le^b* typing tests were placed in a cold-water bath at a constant temperature of 15° C. *Dolichos biflorus* was used by a tile method to distinguish between subgroups *A₁* and *A₂*.

The determination of ABO groups and Lewis types was carried out by well-recognized blood grouping techniques. The ABH content of the saliva samples was determined by a screening inhibition technique against suitably diluted anti-A, anti-B, and anti-H.

Results

Table I shows the distribution of secretors and non-secretors within the various ABO groups of the 1,000 alcoholic patients tested. The overall percentage of non-secretors irrespective of their ABO group is 32.7. If this is compared with the usual figure of 22.7% given for non-secretors of European origin

TABLE I.—ABO Groups and Secretor Status of 1,000 Alcoholic Patients

	Group A	Group O	Group B and AB	ABO Group Unknown
Total No.	380	475	130	15
Secretors	235	333	99	4
Non-secretors	144	141	31	11
Unknown secretor type	1	1	0	0
% non-secretors in each ABO group	37.9	29.7	23.8	73.4

(Race and Sanger, 1968) there is an increase of 10%. Although this is not emphasized in the literature there is, however, considerable variation between the frequencies of non-secretors in different parts of the British Isles. Of the 1,000 patients described here, 404 were English, 178 Irish, and 264 Scottish. The 154 "other" alcoholics included some Welsh and others predominantly British whose exact ethnic origin was not recorded. It was therefore considered necessary to compile our own controls by visiting various parts of the British Isles. The English controls comprised 486 individuals from the staffs of the North London and South London Regional Transfusion centres and members of the staff of the London Hospital. The 981 Irish controls were obtained from blood donors from the Blood Transfusion Centres of Dublin and Belfast. The 554 Scottish controls were blood donors from Aberdeen. These gave us figures for secretor/non-secretor frequencies for comparison with the alcoholic patients. The distribution of ABO groups among Scottish and Irish controls was derived from three large published series because the call-up of donors at the various centres was not random for these groups (Hart, 1944; Kopeć, 1956; Hackett and Dawson, 1958).

Table I also shows the distribution of non-secretor frequencies among the various ABO groups of the total number of patients tested. The group A non-secretors outstrip those of group O by 8.2%. The 15 patients whose ABO group is unknown are those from whom only saliva samples were obtained.

An analysis of the results, taking into account the different ethnic groups within the British Isles, shows the same trend (Table II). There is a striking increase of group A non-

TABLE II.—Secretor Status Within the ABO Groups for Different Parts of the British Isles

	Group A		Group O		Group B and AB	
	Total No.	% Non-secretors	Total No.	% Non-secretors	Total No.	% Non-secretors
English alcoholics ..	167	35.9	185	26.5	51	27.5
English controls ..	150	24.0	157	25.5	36	16.6
Irish alcoholics ..	61	42.6	93	27.9	22	31.8
Irish controls ..	289	30.4	534	32.6	153	27.2
Scottish alcoholics ..	95	43.2	137	38.7	32	21.9
Scottish controls ..	208	29.3	272	31.6	67	25.4
Other alcoholics ..	57	29.8	60	21.6	25	13.6
Total alcoholics ..	380	37.9	475	29.7	130	23.8

secretors compared with the controls. The English group show an increase of 11.9%, the Irish 12.2%, and the Scottish 13.9%. Group O individuals show an increase in non-secretors of 7.1% among Scottish patients, while the Irish in fact show a decrease of 4.7% and the English an increase of 1% compared with appropriate controls.

Tests for the statistical significance of the results shown in Table II were made as follows: χ^2 values (1 d.f.) were obtained for group A secretor/non-secretor frequencies in each ethnic group and the results were combined, making allowance for the direction of the differences found between alcoholics and controls, and giving $0.00001 < P < 0.0001$. A similar calculation from the data for group O secretor/non-secretor frequencies showed $P > 0.30$.

TABLE III.—Comparison Between Expected and Observed Frequencies of ABO and Secretor Types for the Total Series

ABO Group and Secretor Status	Expected Frequencies Compiled from Controls	Observed Alcoholics
A secretors	276	235
A non-secretors	100	144
O secretors	343	333
O non-secretors	140	141
AB + B secretors	97	99
AB + B non-secretors	27	31
Unknown ABO group secretors	4	4
Unknown ABO group non-secretors	17	11
Unknown secretor status		2
Total	1,000	1,000

Table III makes a comparison between the expected and observed frequencies of ABO and secretor types within the whole series. This enables the relative frequencies of the various groups to be studied.

The "expected" numbers in Table III were calculated from the control data on ABO and secretor status distribution separately for each ethnic group, and taking into account the number of alcoholic patients of each ethnic group—that is, 404 English, 178 Irish, and 264 Scottish (Table IV). In dealing with the 154 "other" patients mentioned above as being mostly British of unknown ethnic origin, it was assumed that the proportions of the various ethnic groups among these would be similar to those found in the 846 patients whose ethnic origin was known.

The largest increase over the corresponding controls is again found in the group A non-secretors. In addition, this method of analysis shows that the corresponding decrease of secretors, instead of being equally distributed throughout all ABO groups as might be expected, is almost entirely confined to group A.

There is therefore no overall increase in the frequency of group A compared with the controls (see Table III).

Table IV divides the patients according to ethnic origin but shows the ABO group and secretor status as percentages of the total number of patients within each ethnic group. In this table groups B and AB are not included in the analysis owing to insufficient numbers. This table also gives the same information in respect of the largest individual units. Thus whatever the method of breakdown of the series the same general pattern is observed.

TABLE IV.—Blood Group Distribution and Secretor Status Analysed According to Ethnic Origin and Alcoholic Units

Type of Comparison	Category	No. of Alcoholics	Observed and Expected	Group A		Group O	
				% Non-secretors	% Secretors	% Non-secretors	% Secretors
Ethnic	English	404	O	14.9	26.4	12.1	37.4
			E	10.1	31.7	11.8	34.6
	Irish	178	O	14.6	19.7	14.6	37.6
			E	10.3	23.4	17.0	35.8
	Scottish	264	O	15.5	20.4	20.2	31.8
			E	10.5	25.3	16.2	35.1
Units	1	305	O	17.0	25.6	10.1	37.4
			E	10.2	29.0	13.7	35.0
	2	118	O	10.6*	17.7	18.6	30.1
			E	10.2	26.8	14.9	35.2
	3	198	O	11.1	21.8	15.1	35.9
			E	10.3	28.8	13.9	34.9
	Aberdeen	127	O	16.5	19.7	18.1	32.3
			E	10.3	25.1	16.1	35.1

* Recent testing of patients of unknown ABO group increases this figure to 14.8.

When the distribution of ABO groups among the patients in the series is compared with appropriate controls there is marked similarity between them; see Table III, where the differences in secretor/non-secretor ratios, particularly of group A, between patients and controls have not affected the overall group A frequency.

The series included 744 men, 194 women, while the sex was not recorded in 62. The distribution of ABO groups was essentially the same in both sexes. The overall percentage of non-secretors among the men is 35, whereas that for women is 28.8. A larger series of women would be required before any firm conclusion about sex differences could be drawn.

In view of the work of Clarke *et al.* (1956), who noted that the incidence of duodenal ulcer is more common among non-secretors than among secretors, a record was kept of any history of ulcers, either peptic or duodenal, among the patients in the present series. A total of 143 patients had suffered from ulcers of one type or the other. The exclusion of these from the counts did not alter the pattern of results observed: 37.4% of group A, 28.2% of group O, and 25.2% of group B and AB patients were non-secretors (cf. Table II) when the patients with ulcers were omitted from the series.

Discussion

The term "alcoholic" is ill defined and almost certainly includes compulsive drinkers of more than one kind and even heavy drinkers who strictly should not be included as alcoholic under any classification. The patients in this series were selected merely on the ground that they were found attending well-known alcoholic units or rehabilitation centres. Samples from 60 individuals collected at an annual congress of Alcoholics Anonymous have also been included. It is therefore all the more striking that such a marked disturbance of secretor/non-secretor frequencies, largely in group A, should emerge.

As mentioned above, it was not always possible to test consecutive patients attending the units. Some were lost from the series because they were unable to stay the course and had left the unit before it was possible to sample them. This may have had some bearing on the pattern of results obtained.

That there is indeed a relation between a large intake of alcohol and the secretion of ABH blood group substances

would seem to be supported by the consistency of the pattern of results shown by either the series as a whole or after division according to ethnic origin, or after analysis within single alcoholic units. The general pattern of an increase of group A non-secretors among the alcoholic patients and a corresponding decrease of group A secretors is maintained.

Moreover, when the patients are divided according to ethnic origin the group A secretor/non-secretor frequencies found in each ethnic group vary in such a way as to maintain about the same differential between alcoholics of a particular ethnic group and their appropriate controls. This is well shown by the percentages of non-secretors (see Table II).

There is at the present time good evidence for a number of associations between blood groups and various diseases, particularly of the alimentary tract. These have been reviewed by Roberts (1959).

Various explanations of an association between alcoholism and ABO groups and secretor status come to mind: for example, a genetically determined predisposition to the disease or the existence of an enzyme or enzymes associated with the metabolism of alcohol varying with ABO group and secretor status (cf. the association between intestinal alkaline phosphatase and ABO blood groups described by Arfors *et al.*, 1963). Such theories, however, would not be consistent with the finding of an *almost exact balance* between the increase in A non-secretors and the loss of A secretors in the series investigated.

Such a balance points to a direct effect of alcohol on the secretor status of an individual as a cause of the disturbed secretor/non-secretor distribution. Though from most points of view this would appear to be an unacceptable theory it would best fit the experimental findings. It would require that a certain number of genetically constituted group A secretors become phenotypically non-secretors through the constant imbibition of alcohol. One difficulty is the fact that the disturbed secretor/non-secretor frequency does not apparently involve group B. In addition, whatever effect the alcohol might be supposed to exert would have to be at least moderately permanent, since most of the patients were "dry" at the time of testing. Under the experimental conditions of the tests in the series no intermediate forms difficult to categorize either as secretors or as non-secretors were encountered. Moreover,

since all the non-secretor alcoholic patients have the expected red cell Lewis type—that is, they are mainly Le(a+b−) and none are Le(a−b+)—it would have to be postulated that the prolonged intake of alcohol affected the uptake of Lewis antigens by the red cells as well as the secretion of group-specific substances by the salivary glands.

Family studies might offer one solution to the problem, since the production of secretor children from the mating of a group A non-secretor alcoholic with a non-secretor spouse (of any ABO group) would be very interesting indeed.

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Spontaneous Decrease in Gastric Secretory Response to Humoral Stimuli

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Summary: The gastric response to pentagastrin was studied over a period of seven months in a healthy 25-year-old man without symptoms or history of gastrointestinal disease. An abrupt impairment of the gastric response to several stimulants was observed one month after starting the tests. Periodic testing since that time has shown no reversion to the type of response seen during the initial period of testing. A second subject with proved chronic duodenal ulceration presented an identical change in pattern of gastric response to stimulants.

This study suggests that such a variation in the response to gastric stimulation in a subject with a normal stomach should be borne in mind when interpreting results of gastric secretory studies.

Introduction

Pentagastrin has been used to stimulate secretion of acid by continuous intravenous infusion (Wormsley *et al.*, 1966; Multicentre Pilot Study, 1967), subcutaneous injection (Makhlof *et al.*, 1966; Wormsley *et al.*, 1967), and intramuscular injection (Johnston and Jepson, 1967), and also as snuff (Wormsley, 1968; Jepson *et al.*, 1968).

This study had been planned to investigate the dose-response of a normal human stomach to gastric stimuli and to examine the effect on this response of gastric secretory inhibitors. After the first few tests, however, there was a pronounced reduction in the gastric response to all stimulants

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