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Some laboratory correlates of drinking habits

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SUMMARY The effect of drinking habits on the frequency distributions of eight biochemical or haematological test results was studied in 7915 patients attending a multiphasic health testing centre.

Increasing incidences of abnormal results with increasing alcohol intake, at levels of alcohol intake habitual for a large proportion of the population, were found for plasma gamma-glutamyl transpeptidase, triglycerides and uric acid, and for erythrocyte mean corpuscular volume. Of four frequently used liver function tests, aspartate aminotransferase, alkaline phosphatase, bilirubin, and albumin, only aspartate aminotransferase was strongly affected by drinking habits.

These findings have relevance for the detection of individuals whose drinking habits are harmful to them, and for the interpretation of 'profile' results.

It is well known that alcohol intake is associated with a number of metabolic changes and with overt clinical disease, and the association between alcohol and abnormalities in certain biochemical and haematological test results has been shown by Rosalki and Rau (1972) and by other workers (Rollason *et al.*, 1972; Olin *et al.*, 1973; Spencer-Peet *et al.*, 1973; Ostrander *et al.*, 1974; Unger and Johnson, 1974; Wu *et al.*, 1974; Patel and O'Gorman, 1975).

Most studies on this subject have compared groups of 'normal' people (some of whom may be quite heavy drinkers) with patients who are suffering from the clinical and social effects of their drinking —termed 'alcoholics'. We were interested in the effect of different levels of drinking on the results of biochemical tests in the context of a multiphasic health testing programme, in which those attending answer a questionnaire on their health, medical history, and social habits and undergo a number of physiological, biochemical, and haematological tests. This study has been undertaken both to determine the degree of abnormality which may be accounted for by the admitted alcohol intake alone, without seeking other causes, and to detect those individuals whose alcohol intake is producing metabolic changes which may later lead to clinical disease.

Subjects and methods

The subjects were 7915 consecutive patients (4562 men and 3353 women) attending the Medicheck centre in Sydney. They were adults of all ages with a median age of 46 for the men and 45 for the women. They attended after referral from a medical practitioner, but a survey of patient attitudes to Medicheck (Rawson, 1975) has shown that in approximately 60% of referrals the suggestion of attendance came from the patient rather than from the referring doctor. No detailed analysis of social class has been made, but the survey cited showed that incomes were higher than the Australian average.

Blood was taken after fasting since the previous evening, and the subjects then answered about 150 questions related to their medical history, present subjective assessment of health, presence of symptoms, and social habits including alcohol consumption. The questions relating to alcohol are shown in Table 1.

Table 1 *Questions relating to alcohol intake*

In the past year, how often did you drink alcohol?
Every day or most days .....
A couple of times a week .....
Once every week or two .....
Very rarely .....
How many drinks (wine, whisky, beer, cocktails, etc) did you usually have on each drinking day in the past year?
Total of nine drinks a day or more .....
Six to eight drinks a day .....
Three to five drinks a day .....
Two drinks or less a day .....

Results for seven biochemical tests and one haematological test were abstracted from the data held on computer file and related to the stated alcohol intake for both frequency and amount. Significance of association was assessed by the chi-square test (Bradford Hill, 1971).

Results for men and women have been treated

separately throughout. Uric acid, alkaline phosphatase, bilirubin, and albumin were measured on a Technicon SMA 12/60 using standard Technicon methods. Mean corpuscular volume (MCV) was measured on a Coulter S counter. Gamma-glutamyl transpeptidase (GGT) and aspartate aminotransferase (AsT, previously known as GOT) were measured by reaction rate (Karmen, 1955; Szasz, 1969) and triglycerides by an enzymatic method (Bucolo and David, 1973). Results were considered abnormal if they fulfilled the following criteria: GGT greater than 40 IU/l at 30° (men) or 30 IU/l at 30° (women); MCV greater than 90 fl (men) or 92 fl (women); uric acid greater than 440 μmol/l (7.4 mg/100 ml); triglycerides greater than 2.49 mmol/l (220 mg/100 ml); AsT greater than 25 IU/l at 30°; alkaline phosphatase greater than 90 IU/l at 37° (men) or 80 IU/l at 37° (women), and albumin less than 40 g/l.

These limits are to some extent arbitrary and were chosen to illustrate the increasing incidence of 'abnormality' with increasing alcohol intake rather than as reference ranges for clinical use. Statistical analysis was done on the actual distribution of results and not just on these normal/abnormal criteria.

Results

The incidence of abnormality for these eight tests is shown in Tables 2 and 3 in relation to frequency and extent of drinking respectively.

Histograms of the results for GGT, MCV, triglycerides, and uric acid, which showed the most notable effects, are given in Figures 1 to 4.

Discussion

This work relies on the subject's own declaration of alcohol intake and is therefore subject to human errors, or deceptions, but the vast majority attended Medicheck of their own free will and not at the request of present or prospective employers, so their answers were probably honest. In any case, inaccurate answers would obscure a trend rather than reveal one that was not truly present.

Four tests, GGT, MCV, uric acid, and triglycerides, showed a strong change in distribution of results with increasing alcohol intake. Of four widely used liver function tests, AsT, alkaline phosphatase, bilirubin, and albumin, only AsT showed a strong

Table 2 *Effect of frequency of drinking: percentage of results outside normal range*

Frequency	*GGT*	*MCV*	*Uric acid*	*Triglyceride*	*AsT*	*Alk. Phos.*	*Bilirubin*	*Albumin*
Men								
Every day or most days	25·5	21·1	25·5	12·6	9·3	4·5	3·6	0·5
Twice a week	10·9	6·9	13·7	6·4	3·8	2·1	3·6	0·4
Once each week or two weeks	6·9	2·5	12·1	7·5	1·8	2·9	3·5	0·6
Very rarely	6·6	0	4·7	4·5	0	5·6	6·5	0
P (χ^2 test)	<0·001	<0·001	<0·001	<0·001	<0·001	NS	NS	NS
Women								
Every day or most days	13·5	14·3	3·0	2·6	3·3	5·6	2·5	1·5
Twice a week	7·8	6·7	1·3	1·5	2·5	3·3	3·3	0·6
Once each week or two weeks	6·5	4·1	1·7	1·0	2·9	2·9	2·3	0·2
Very rarely	6·4	3·9	3·2	4·3	5·5	4·0	1·5	3·9
P (χ^2 test)	<0·001	<0·001	NS	NS	(<0·001)*	NS	NS	NS

*Statistically significant, but expected trend not found

Table 3 *Effect of number of drinks: percentage of results outside normal range*

No. of drinks	*GGT*	*MCV*	*Uric acid*	*Triglyceride*	*AsT*	*Alk. Phos.*	*Bilirubin*	*Albumin*
Men								
9 or more	44·1	34·9	37·9	19·9	22·7	7·0	4·6	0·4
6-8	29·2	22·7	29·4	13·8	10·1	5·2	2·8	1·7
3-5	16·4	12·8	18·6	9·7	5·5	3·2	3·8	0·2
1-2	9·1	5·8	11·9	6·0	2·4	2·6	3·7	0·2
P (χ^2 test)	<0·001	<0·001	<0·001	<0·001	<0·001	<0·001	NS	<0·001
Women								
9 or more	27·7	15·8	0	10·5	11·1	22·0	0	5·9
6-8	26·5	18·7	3·7	6·9	3·7	6·3	1·2	1·2
3-5	14·8	15·6	3·8	2·1	3·5	5·7	2·5	1·0
1 or 2	6·4	5·8	1·5	1·6	2·8	3·2	2·8	1·1
P (χ^2 test)	<0·001	<0·001	NS	<0·001	<0·001	<0·001	NS	<0·001

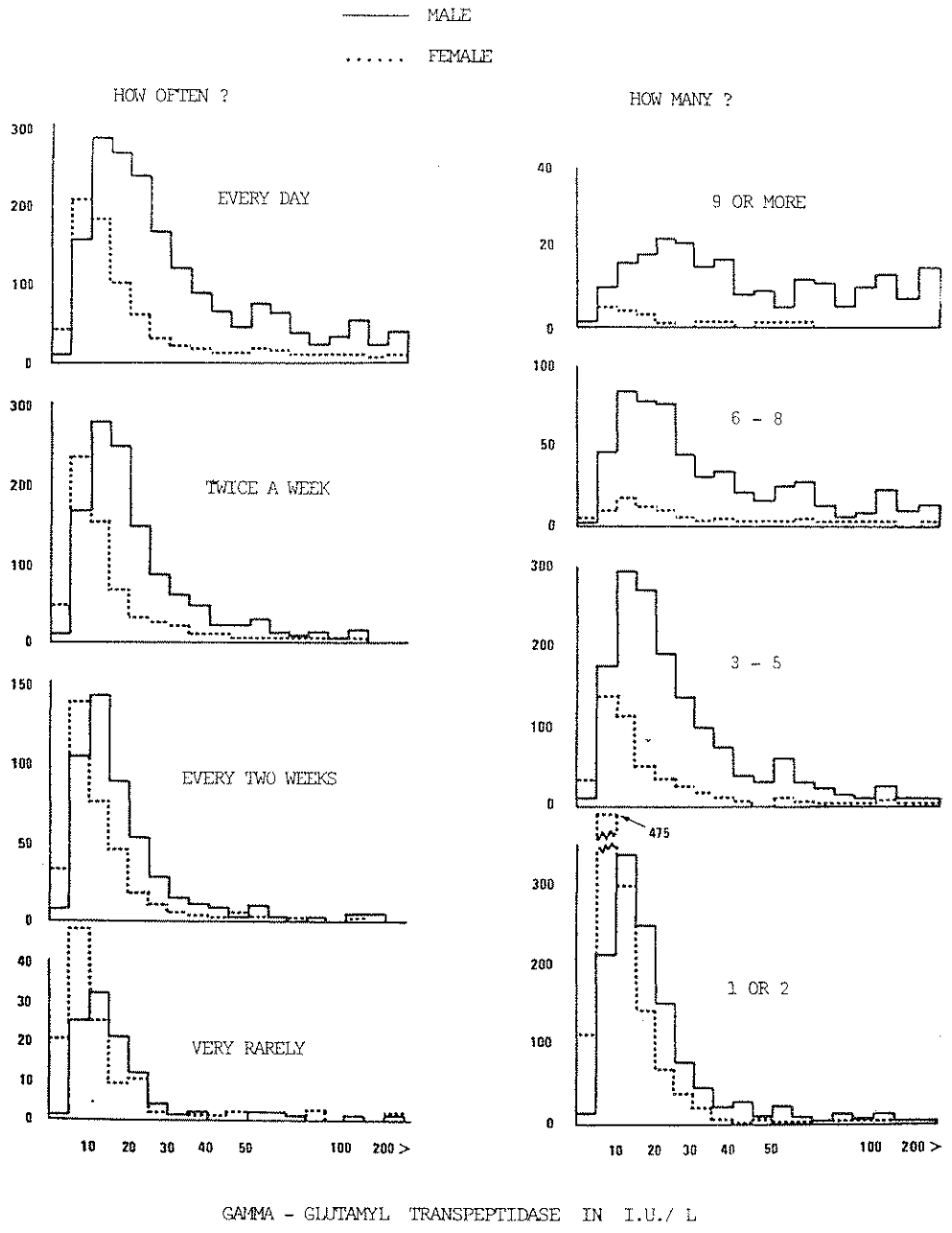

Fig. 1 *Frequency distributions for plasma gamma- glutamyl transpeptidase, grouped according to frequency and extent of alcohol intake.*

trend, and even then it was not abnormal in the heavy drinking groups as frequently as the other four tests. Abnormality of AsT, therefore, appears to indicate a later effect of drinking than GGT, MCV, or triglycerides and is a less useful measurement of subclinical liver damage. The trend towards increasing incidence of abnormality was more marked in relation to the number of drinks taken than to the frequency of drinking. This was to be expected since there were a large number of people who drank every day or most days, and many of them must have had only a small number of drinks on each occasion. The number stating that they had nine or more drinks on each drinking day was much less. These people might well correspond to the group described as 'alcoholics' in previous

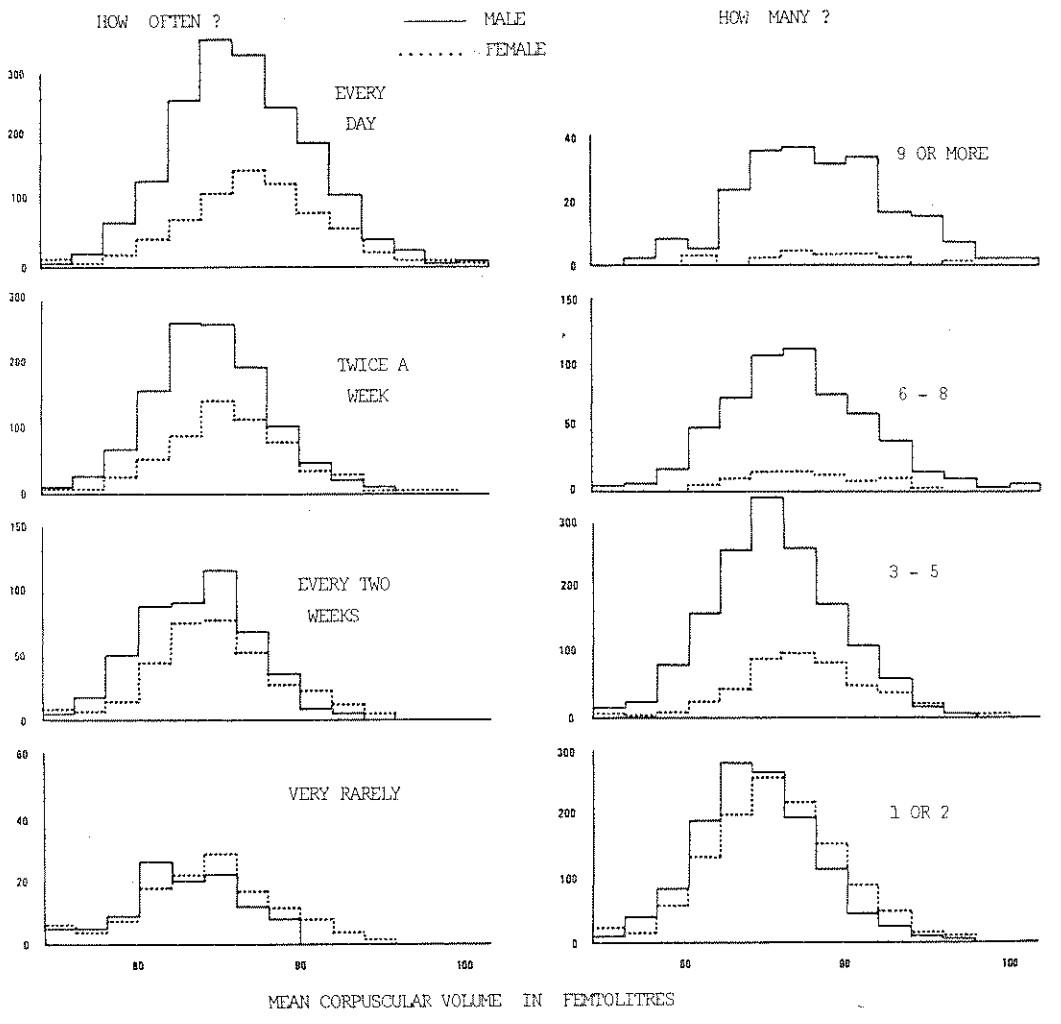

Fig. 2 *Frequency distributions for erythrocyte mean corpuscular volume, grouped according to frequency and extent of alcohol intake.*

papers, and the incidence of abnormalities is similar to that reported for 'alcoholics'.

Differences were noted between men and women not only in the 'normal' ranges in the low alcohol group but also in the response of the incidence of abnormalities to alcohol intake. For a given frequency or degree of drinking, men showed more abnormalities than women. This could be due to a more accurate assessment of drinking habits from women than from men, or to the greater dissociation between frequent and heavy drinking in women, or to true differences in biochemical responses to alcohol. The difference between men and women is particularly marked with uric acid. It is well known that the normal range for uric acid is higher in men than in women, but while uric acid levels are related strongly to alcohol consumption in men there is no significant association in women.

The frequency distribution of many biochemical tests, and indeed other measurements in the total population, often deviates from the Gaussian distribution, and this can be seen for many of the tests studied here. However, the distributions become much more Gaussian when a factor producing abnormality, in this case alcohol, is excluded. This can be seen most clearly for GGT (Fig. 1).

The mechanism by which alcohol produces these changes is not clear. In the case of GGT it may well be similar to the increase caused by hepatic microsomal enzyme-inducing drugs, which raise the plasma GGT (Rosalki *et al.*, 1971; Whitfield *et al.*, 1973). Association between increased GGT and raised triglycerides has been reported (Martin *et al.*, 1975), and it was suggested that the increase in triglycerides was also related to enzyme induction.

The increase in MCV has been ascribed to folate

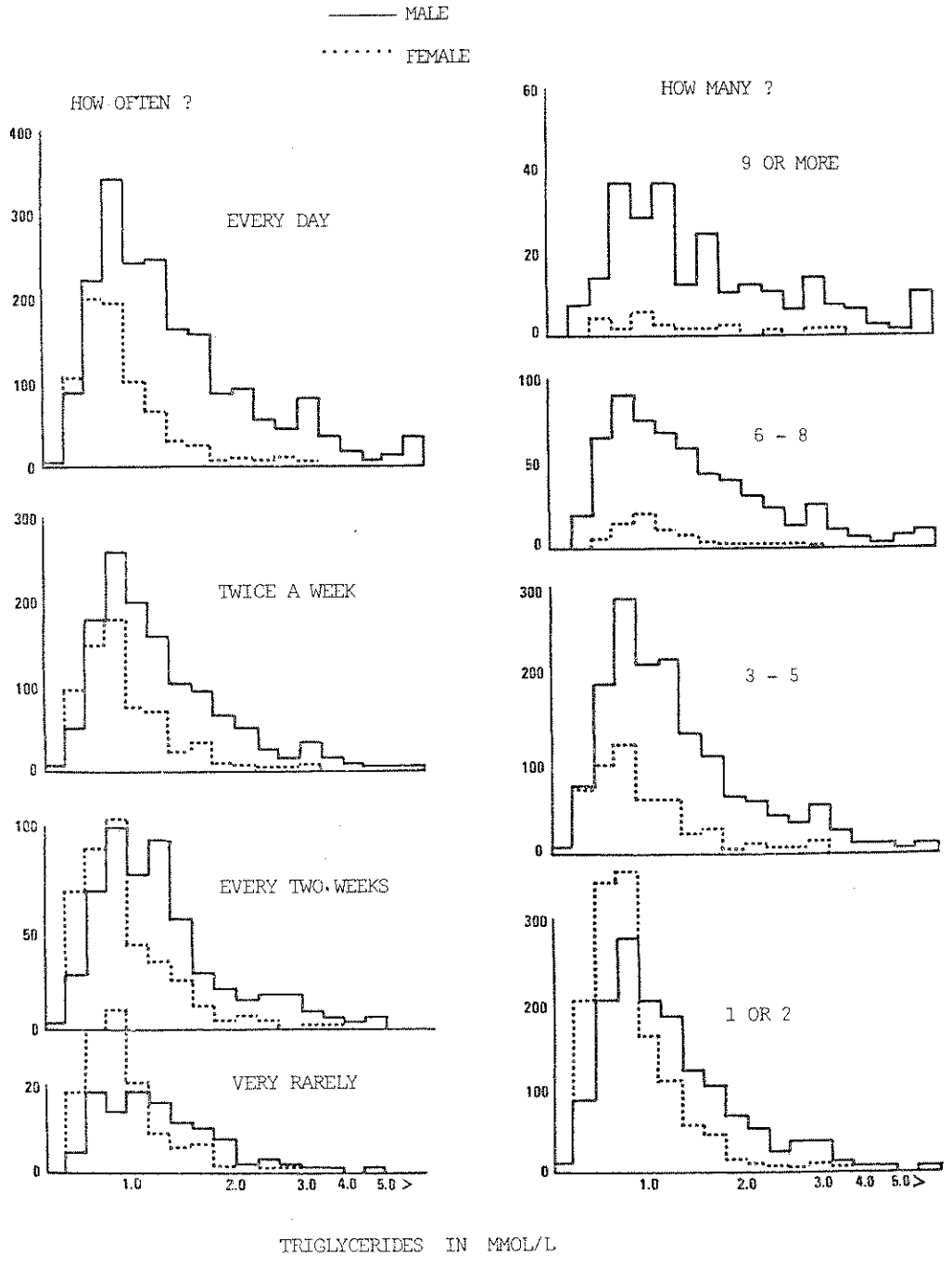

Fig. 3 *Frequency distributions for plasma triglycerides, grouped according to frequency and extent of alcohol intake.*

deficiency but folate supplementation does not abolish the macrocytosis in the face of continuing high alcohol intake (Wu *et al.*, 1974). It is thought that there is some direct effect of ethanol on red cell development. The increase in uric acid is due to decreased urinary excretion, probably caused by interference with tubular secretion by lactate (Lieber *et al.*, 1962). Why this should occur in men but not in women is not clear, and this finding must cast doubt on this explanation.

Elevation of plasma triglycerides in association with high alcohol intake is said to be due to increased

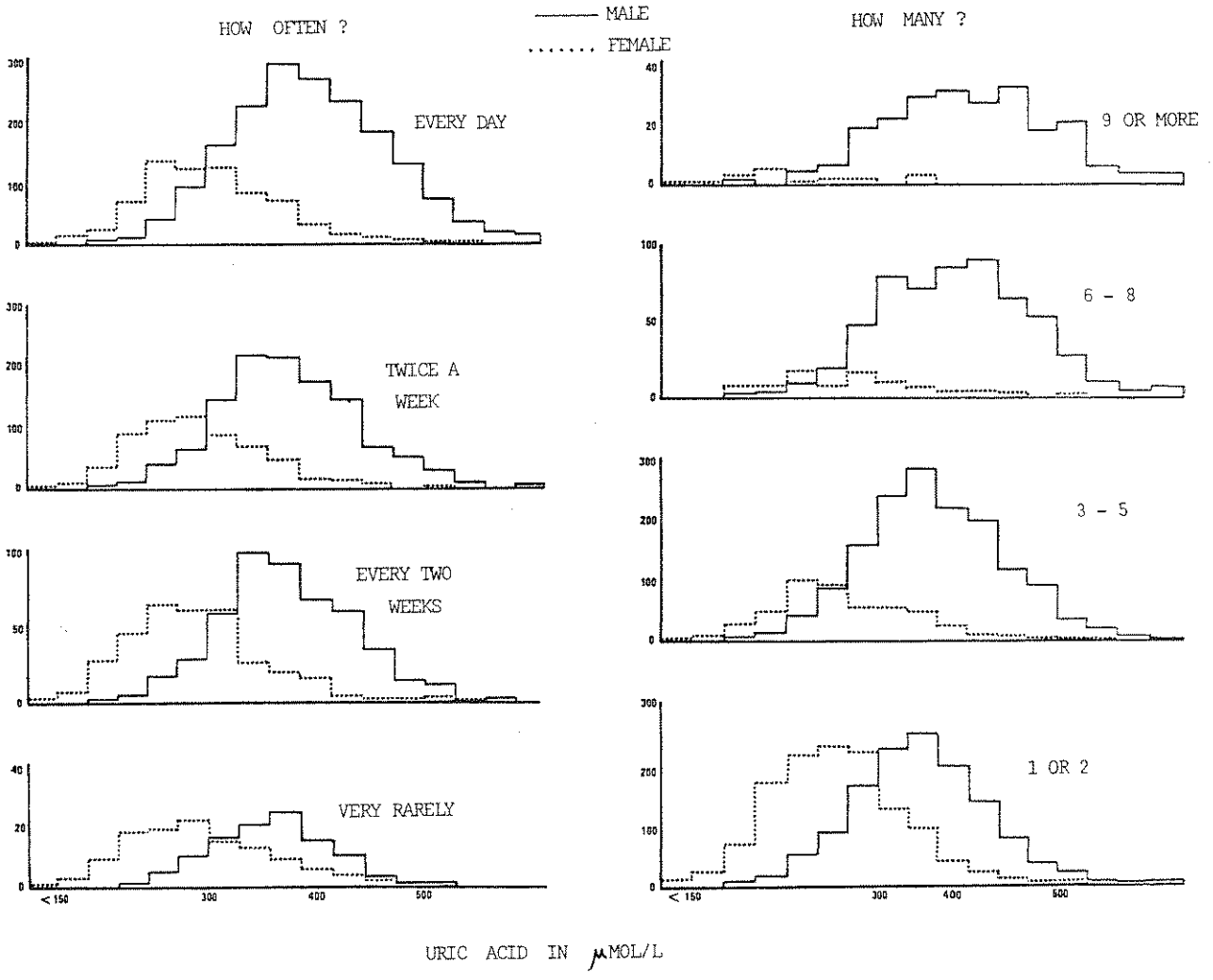

Fig. 4 *Frequency distributions for plasma uric acid, grouped according to frequency and extent of alcohol intake.*

production of pre-β lipoprotein by the liver (Chait *et al.*, 1972), and the increase in aspartate aminotransferase is presumably due to increased permeability of the hepatocyte membrane to this enzyme.

These results could have a predictive value, both in indicating those people who are taking large amounts of alcohol but who are not willing to admit it, and possibly in predicting those drinkers who are on the way to clinical disease. The former possibility could be enhanced by discriminant function or similar techniques, and the latter will require a prospective study of the progress of patients with similar drinking habits but differing biochemical results. We hope to extend our work into these two areas.

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