injections were documented. Control groups consisted of blood donors, hospital inpatients with cardiac and respiratory disease, and chronic alcoholics without liver disease.

Sera were examined for hepatitis B surface antigen (HBsAg), anti-HBc, and anti-HBs by radioimmunoassay (Ausria II, Corab, and Ausab, Abbott Laboratories) and reported as positive or negative compared with standard controls. Sera were also examined for antibodies to 12 common infective agents—namely, influenza A and B, adenovirus, *Mycoplasma pneumoniae*, psittacosis, *Coxiella burnetii*, herpes simplex, cytomegalovirus, varicella zoster, mumps, and measles by complement fixation test and rubella by haemagglutination-inhibition test. All sera were examined without knowledge of the clinical diagnosis. Statistical analysis was by χ^2 test and, where appropriate, by Fisher and Yates's exact test.

All sera gave negative test results for HBsAg. The positive hepatitis B virus antibody results are recorded in the table. Significant differences between patients and controls were confined to those patients with alcoholic cirrhosis. Hepatitis B virus antibodies were found in 28 (34%) of the 82 patients with alcoholic cirrhosis ($p<0.0001$) and in 18 (47%) of the 38 with portal hypertension, 11 (44%) of the 25 who died within 6 months, 13 (42%) of the 31 with hepatic encephalopathy, and 13 (32%) of the 41 with ascites. Among patients with alcoholic cirrhosis hepatitis B virus antibodies were equally common in those whose liver biopsy appearances were diagnostic of active alcoholic liver disease (25 of the 73 patients) and in those with inactive cirrhosis (3 of the 9 patients). There was no significant difference between the patients with alcoholic cirrhosis and the remaining patients with liver disease in respect of previous blood transfusion, jaundice, the finding of tattoos, or social class, and no patients admitted to parenteral drug abuse. The distribution of hepatitis B virus antibodies between men (21 of the 56 patients) and women (7 of the 26 patients) with alcoholic cirrhosis was not significantly different.

There was no significant increase in the prevalence of antibodies to the 12 common infective agents in patients with alcoholic liver disease. In patients with chronic active hepatitis and cryptogenic cirrhosis, however, there was a significant rise in antibody titres to measles and the patients with cryptogenic cirrhosis also had raised antibody titres to rubella, observations which have previously been described.[3]

Comment

The high prevalence of serum antibodies to hepatitis B virus antigens in alcoholic cirrhosis has been confirmed in this survey and shown to be more common in advanced cirrhosis. Anti-HBc and anti-HBs were often both present, a response characteristic of previous hepatitis B virus infection.[1] The failure to show abnormal antibody titres against other common infective agents in alcoholic cirrhosis indicates the specificity of this response.

Factors which may be associated with an increased prevalence of serum hepatitis B virus antibodies are increasing age, male sex, foreign domicile, lower social class, exposure to infective serum, male homosexuality,[4] and institutional life. Sexual histories were not taken from our patients but homosexuality would seem to be an unlikely explanation for our results. None of the above factors can explain our findings in alcoholic cirrhosis.

The incidence of liver disease among chronic alcoholics is variable. While the development of liver disease is related to both the volume of alcohol consumed and the duration of intake, the overall prevalence of cirrhosis in alcoholics remains between 10 and 15%.[5] Other factors are therefore important. Host factors may determine susceptibility, as alcoholic hepatitis appears to develop more quickly in women, and alcoholic cirrhosis may be associated with HLA-B8.[5] Nevertheless, other genetic or environmental factors, as yet unidentified, may also be important in the progression to chronic liver disease in the alcoholic. Previous hepatitis B virus infection could be such a risk factor, selecting a population of chronic alcoholics who are then susceptible to alcohol-induced hepatic damage. More evidence, however, is required before establishing a pathogenic relation between the hepatitis B virus and chronic alcoholic liver disease.

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Androgens, oestrogens, and coronary heart disease

To test the hypothesis that testosterone may be a risk factor for coronary heart disease[1] we compared serum androgen and oestrogen concentrations in men with a history of myocardial infarction and in matched controls.

Patients, methods, and results

In a population-based case-control study 50 middle-aged men who had had a myocardial infarction five months to 11 years before (median 57 months) were each matched with a control man of the same age and marital state working in the same factory and known to be free of coronary heart disease.[2] Information on other coronary risk factors including cholesterol and blood pressure, weight, height, and smoking history were obtained from a recent screening examination.

Two blood samples were taken from each subject 15 minutes apart between 9 and 11 am and the serum frozen to −20°C on the same day. Measurements on pooled samples from the two venepunctures were made by radioimmunoassay using validated and published methods. At the time of the study 15 men were taking a beta-blocking drug (three together with clofibrate), 12 clofibrate (three in combination with beta-blockers), and four various other drugs.

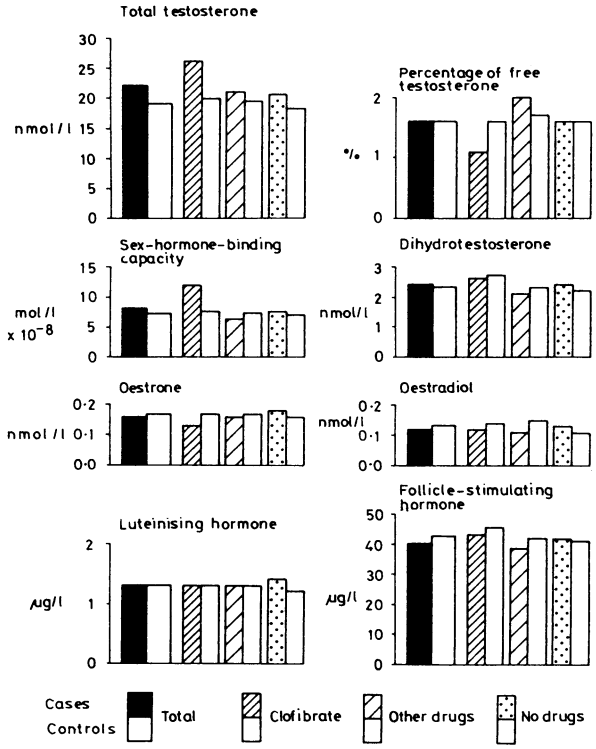
The figure compares hormone concentrations according to drugs being taken with the concentrations in matched controls. The 12 men taking

Hepatitis B antibodies in patients with chronic liver disease and in controls

Group	Diagnosis	No of patients	No of women	Mean age (years)	No of patients with: Anti-HBc alone	Anti-HBs alone	Both anti-HBc and anti-HBs	Total No (%) of patients with hepatitis B antibodies
1	Alcoholic steatosis	33	10	49	1	2	2	5 (15)
2	Alcoholic hepatitis	46	20	50	0	3	3	6 (13)
3	Alcoholic cirrhosis	44	16	55	0	2	8	10 (23)
4	Alcoholic cirrhosis and portal hypertension	38	10	56	1	5	12	18 (47)
5	Chronic alcoholism (no liver disease)	31	5	49	0	0	3	3 (10)
6	Primary biliary cirrhosis	34	32	57	0	1	5	6 (18)
7	Chronic active hepatitis	28	20	50	1	0	3	4 (14)
8	Cryptogenic cirrhosis	18	10	54	0	0	2	2 (11)
9	Haemochromatosis	9	0	52	0	0	0	0 (0)
10	Hospital inpatients, matched for 3 and 4	82	26	55	0	2	2	4 (5)
11	Blood donors, matched for 3 and 4	82	26	55	0	0	3	3 (4)
12	Hospital inpatients, matched for 6	34	32	57	0	1	2	3 (9)

Total hepatitis B virus antibodies: 3 *v* 10 $p<0.005$; 4 *v* 10 $p<0.0001$; 6 *v* 12 $p>0.1$; 3 and 4 *v* 1 and 2 $p<0.01$; 4 *v* 3 $p<0.025$. Remainder (1, 2, 5, 7, 8, 9)—no significant difference from 10.

clofibrate showed an increase in sex-hormone-binding capacity (11·9 and $7·5 \times 10^{-8}$ mol/l in cases and controls respectively) and a decrease in the percentage of testosterone circulating free in the unbound state (1·1% and 1·6% respectively), both differences being statistically significant ($p<0·05$). Though total testosterone was higher and oestrone and oestradiol lower in those taking clofibrate than in their controls, the differences were not significant. Comparison of men not taking medication with their matched controls showed a non-significant increase in total testosterone, oestrone, and oestradiol. When the hormone concentrations were put into a multiple



Hormone concentrations in cases, grouped according to current drug treatment, compared with their matched control pairs. Numbers of pairs (total=50): clofibrate, 12; other drugs, 16; no drugs, 22. (One value missing for each of % free testosterone, sex-hormone-binding capacity, oestradiol, luteinising hormone and follicle-stimulating hormone; 11 values missing for oestrone; 16 values missing for dihydrotestosterone.)

Conversion: SI to traditional units—Testosterone: 1 nmol/l ≈ 28·8 ng/100 ml. Oestrone: 1 nmol/l ≈ 27 ng/100 ml. Dihydrotestosterone: 1 nmol/l ≈ 29 ng/100 ml. Oestradiol: 1 nmol/l ≈ 27·2 ng/100 ml.

linear regression model (to examine case-control differences while taking account of the effect of drugs and other risk factors for coronary heart disease) testosterone was a better discriminator between cases and controls ($t=1·78$; $p<0·10$) than either oestrone or oestradiol, but none of these hormonal differences were statistically significant.

Comment

Although the patients in this study were survivors of myocardial infarction and may thus have been somewhat unrepresentative of all men with coronary heart disease, they were particularly well matched with the controls: the members of each pair were working in the same factory, were of the same age and marital state, and had blood taken at the same time of day under identical conditions. A major effect of clofibrate on sex hormones had not, however, been anticipated and seriously influenced the case-control comparisons. The primary mechanism is probably an increase in sex-hormone-binding globulin, which reduces the proportion of testosterone circulating in the free unbound state, an effect which mimics the known influence of clofibrate on thyroid hormone metabolism, where it has been shown to increase thyroxine-binding globulin and decrease the percentage of free thyroxine.[3]

Our results do not show any significant excess of sex hormone concentrations in men with coronary heart disease and suggest that if there is a difference it is probably on the testosterone rather than the oestrogen side: we do not confirm reports of much higher plasma oestrogen concentrations in men with coronary heart disease than in controls.[4 5]

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Fetal macrosomia and maternal diabetic control in pregnancy

Infants of diabetic mothers tend to have more adipose tissue than normal at birth, and the associated macrosomia is an important complication of diabetic pregnancy. Subcutaneous fat as assessed by neonatal skinfold thickness correlates with maternal blood glucose concentrations in the third trimester of pregnancy,[1] but the contribution of maternal hyperglycaemia earlier in pregnancy is uncertain.

To determine the possible role of maternal hyperglycaemia at earlier stages of pregnancy in subsequent fetal macrosomia we correlated maternal glycosylated haemoglobin (HbA_1) and blood glucose concentrations measured in all three trimesters of pregnancy with the neonatal birth weight and skinfold thickness.

Methods and results

We studied 43 insulin-dependent diabetics. All delivered normal live healthy babies at 36-38 weeks' gestation. HbA_1 was measured blind and in duplicate[2] on presentation to the antenatal clinic, at delivery, and usually at one other time during pregnancy. Gestational age was divided into three periods—namely, 14 weeks and under, 15-27 weeks, and 28 weeks and over. When HbA_1 concentration had been measured more than once in a single period the mean value was taken. Random blood glucose concentrations were measured in all patients as outpatients at intervals of two to four weeks throughout pregnancy. After routine admission to hospital at 30-34 weeks preprandial blood glucose concentration was measured twice weekly. Birth weight was recorded and the birthweight ratio calculated as the ratio between the birth weight and the 50th percentile weight for that gestational age.[3] Skinfold thickness was measured using a Holtain skin callipers within 12-36 hours of delivery.[2] The sum of the readings from the biceps, triceps, subscapular, and sacroiliac sites on the left and right was recorded. Statistical analysis was made using Pearson's regression analysis. Values of $p<0·05$ were accepted as significant.

Concentrations of HbA_1 fell from 9·6 ± SD 2·0% in the first trimester to 8·8 ± 1·5% in the second and 7·9 ± 1·3% in the third ($p<0·001$ between first and third trimesters, $p<0·02$ between second and third trimesters). HbA_1 concentrations at delivery and during the third trimester were correlated with the mean inpatient blood glucose concentration between 32 and 38 weeks' gestation ($r=0·32$, $p<0·05$). The neonatal total skinfold thickness correlated with the mean HbA_1 concentrations in the third trimester ($r=0·52$,