immunofluorescence (IF). Focal segmental glomerulonephritis with fibrinoid necrosis but varying glomerular IF may also be seen in other forms of glomerulonephritis, such as Goodpasture's syndrome (linear IgG), subacute bacterial endocarditis (IgG, C3, Clq), SLE (all immunoglobulins and C3, C4, Clq), Henoch-Schönlein purpura (mesangial IgA), and IgA nephritis (mesangial IgA). Although we did not look for soluble antigen-antibody complexes or cryoglobulins, such complexes have been implicated in this type of renal disease.⁸⁻⁹ Rheumatoid factor was present in one of our patients, possibly as an indirect marker of circulating immune complexes. The reported incidence of rheumatoid factor in relapsing polychondritis is 18%.¹

Since 1971 we have treated 28 cases of rapidly progressive crescentic glomerulonephritis with quadruple therapy of prednisolone, azathioprine, anticoagulants, and dipyridamole.¹⁰ In case 1 the GFR improved with treatment from 15 to 28 ml/min and the patient's renal function remained steady for at least two years. In case 2 the patient initially appeared to respond to treatment, with a rise in GFR from 3.5 to 19 ml/min and a steady renal function for 12 months, but died in renal failure after two years.

Acute symptoms have a variable response to oral steroids but

can usually be controlled. Only one death with severe azotaemia has previously been reported. The patient also had scleroderma, and renal histology showed the changes of malignant hypertension.⁶ In relapsing polychondritis associated with rapidly progressive crescentic glomerulonephritis aggressive treatment may be lifesaving.

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Growth hormone, prolactin, and corticosteroid responses to insulin hypoglycaemia in alcoholics

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Summary and conclusions

Plasma growth hormone (GH), prolactin, and corticosteroid responses to insulin-induced hypoglycaemia were studied in 24 men with progressive alcoholism who had been abstinent for two to seven days. Ten normal healthy subjects (five men, five women) served as controls for comparing GH and prolactin responses, while cortisol responses were studied in a further six male controls. Blood samples were taken at intervals after an injection of soluble insulin (0.1 U/kg body weight). All patients developed adequate hypoglycaemia (blood glucose <2.2 mmol/l (<39.6 mg/100 ml)) and nine had impaired GH responses (peak concentration <10 mU/l). Prolactin concentrations fell or remained unchanged in nine patients, eight of whom also had impaired GH responses. In seven patients corticosteroid concentra-

tions decreased from basal concentrations, and six of these patients had impaired GH responses. All three hormone responses were impaired in several patients, and significant correlations were found between the GH and prolactin responses at 45 and 60 minutes. GH response was not correlated with age, duration of drinking, duration of alcoholism, or admitted alcohol intake. GH responses were significantly lower in patients who had the most severe withdrawal symptoms. Our observations of impaired stress responses in some recently abstinent alcoholics may have important implications for the management of alcohol withdrawal syndrome.

Introduction

Chronic alcohol consumption has several important effects on the endocrine system.¹ In particular, some alcoholics have an impaired cortisol response to oral alcohol and hypoglycaemia,² and shortly after withdrawal of alcohol some may also have an impaired growth-hormone (GH) response to hypoglycaemia.³ We decided to extend these studies by investigating GH, prolactin, and corticosteroid responses to insulin-induced hypoglycaemia in a larger group of patients. Relations between the hormone responses and relevant features of the patient's clinical history were also examined.

Patients

Twenty-four men with progressive alcoholism (mean age 45 years; range 25-65) were investigated two to seven days after they had stopped drinking. All had given informed consent to the study. Only patients with symptoms of physical dependence on alcohol were studied, patients with hepatic cirrhosis, hypokalaemia, or

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jaundice being excluded. Liver function tests performed on admission included measurement of serum transaminases and γ -glutamyltranspeptidase in 24 and 16 patients respectively (table I). The results showed biochemical evidence of liver damage in several patients and were consistent with the history of alcohol abuse. GH and prolactin responses were also studied in 10 normal healthy controls (five men, five women) with a mean age of 42 years (range 32-51). Cortisol response was studied in six male control subjects with a mean age of 38 years (range 23-51).

TABLE I—Results of liver function tests in 24 alcoholics

Case No	Serum alanine transaminase (IU/l; normal range 12-40)	Serum aspartate transaminase (IU/l; normal range 8-47)	γ -glutamyltranspeptidase (IU/l; normal up to 45)
1	25	12	35
2	22	32	42
3	38	26	69
4	27	25	55
5	38	52	55
6	39	64	51
7	30	27	37
8	93	106	45
9	21	23	74
10	65	164	NA
11	10	12	49
12	61	84	79
13	20	21	NA
14	17	31	35
15	36	33	21
16	21	48	79
17	54	74	NA
18	54	54	NA
19	74	118	NA
20	94	40	36
21	15	29	NA
22	30	37	NA
23	33	38	NA
24	144	199	123

NA = Result not available.

Methods

Clinical features of alcoholism were assessed independently from a standard questionnaire, which was given when the patients no longer had signs or symptoms of alcohol withdrawal. The information was corroborated by a relative when possible. Severity of withdrawal symptoms was estimated on the basis of an objective rating scale: (0) no symptoms; (1) tremor, insomnia, autonomic nervous system manifestations; (2) delirium tremens.

Blood samples were withdrawn from a cannula in an antecubital vein before and 10, 20, 25, 30, 35, 40, 45, and 60 minutes after an injection of soluble insulin (0.1 U/kg body weight) via the cannula. A 4-ml portion of each blood sample was deproteinised by addition to 5 ml 10% perchloric acid, and the remainder added to a heparinised container. The deproteinised samples were analysed for glucose (glucose oxidase method).⁴ Plasma samples were analysed by radioimmunoassay techniques for GH⁵ and prolactin.⁶ Plasma 11-hydroxycorticosteroids were estimated by fluorometry.⁷

Results

All patients had consumed relatively large amounts of alcohol regularly for years, and none had a history of alcoholism of less than two years. Eleven had been admitted to hospital more than once previously for alcoholism (table II).

Basal blood glucose concentrations were similar in the patients and controls (table III). The minimum concentration after the insulin injection showed that all patients developed adequate hypoglycaemia (blood glucose < 2.2 mmol/l (< 39.6 mg/100 ml)).

Basal GH concentrations were generally lower in the patients than in the controls (table III). Nine of the patients had an inadequate GH response, with a peak concentration less than 10 mU/l.

Basal prolactin concentrations were similar in the patients and controls. In nine patients the prolactin concentrations fell or remained unchanged, and eight of these patients had impaired GH responses (table III). In the 14 remaining patients prolactin concentrations rose at least slightly.

Plasma corticosteroids—In 13 patients and all the controls the basal corticosteroid concentrations increased by more than 200 nmol/l (7.25 μ g/100 ml). In four patients plasma corticosteroids increased

by less than 200 nmol/l, and in the seven remaining patients plasma corticosteroids decreased from basal concentrations. Six of the patients whose corticosteroid concentrations decreased had impaired GH responses.

Relation between GH, prolactin, and corticosteroid responses—To see whether all three hormone responses were impaired in some patients the increase or decrease from basal concentrations of GH at 45 and 60 minutes was correlated with the corresponding change in prolactin and corticosteroid concentrations (table IV). The only significant correlation found was between the GH and prolactin responses at 45 and 60 minutes.

Relation between GH response and features in clinical history—The increase or decrease from basal concentrations of GH at 45 and

TABLE II—Clinical history of 24 alcoholics

Case No	Age (Years)	No of previous admissions for alcoholism	Years of regular alcohol consumption	Years of alcoholism	Admitted alcohol intake (g/week)	Withdrawal symptoms (Score*)
1	33	10	10	5	1260	0
2	34	4	15	15	1568	1
3	50	2	30	6	1470	1
4	44	1	25	2	3360	2
5	52	0	30	5	1680	0
6	38	0	20	15	2499	1
7	42	0	20	2	2457	0
8	42	0	15	3	1680	1
9	53	10	30	13	3276	0
10	41	1	20	12	1313	0
11	39	5	20	7	3665	1
12	46	2	30	22	3266	2
13	41	3	25	14	1638	1
14	48	0	30	10	1680	0
15	30	6	12	3	1736	0
16	52	1	30	20	2457	2
17	25	0	8	3	1229	0
18	48	1	20	8	2205	1
19	65	0	40	20	1680	2
20	47	0	30	7	2310	1
21	50	6	30	15	1628	0
22	50	8	20	5	3360	1
23	49	2	30	4	1680	1
24	53	0	35	10	—	2

*0 = No symptoms; 1 = tremor, insomnia, autonomic nervous system manifestations; 2 = delirium tremens.

Increase or decrease from basal concentrations (mU/l) of growth hormone (GH) and prolactin 60 minutes after injection of insulin (0.1 U/kg body weight) in 24 alcoholics with differing scores for severity of withdrawal symptoms (see footnote to table II).

TABLE III—Basal concentrations of blood glucose, plasma growth hormone (GH), plasma prolactin, and plasma corticosteroids; minimum concentration of blood glucose; and concentrations of GH, prolactin, and corticosteroids at 45 and 60 minutes after injections of insulin in 24 alcoholics. Concentrations in controls given for comparison

Case No	Blood glucose (mmol/l)		Plasma GH (mU/l)			Plasma prolactin (mU/l)			Plasma corticosteroids (nmol/l)		
	At rest	Minimum	At rest	At 45 min	At 60 min	At rest	At 45 min	At 60 min	At rest	At 45 min	At 60 min
1	4.68	1.47	2.6	60.4	25.2	120	600	360	489	908	756
2	5.4	1.4	4.2	88.6	89.0	300	1580	1620	345	566	649
3	5.8	2.0	2.0	55.0	41.6	160	120	120	541	1065	1228
4	5.0	0.8	2.8	4.8	3.6	180	160	160	472	574	519
5	4.4	1.8	0.2	69.4	71.0	120	600	400	613	519	439
6	4.6	1.0	8.2	33.2	65.4	160	360	300	445	745	552
7	5.6	0.8	0.5	21.0	19.9	160	700	580	414	657	668
8	4.8	1.4	2.5	0.4	0.6	60	30	20	439	163	179
9	5.4	1.0	4.2	95.8	81.4	360	650	900	345	317	436
10	4.2	1.2	0.2	21.2	19.1	160	240	200	444	693	707
11	4.2	1.1	1.8	72.6	53.8	180	1640	1740	235	400	502
12	6.3	1.6	0.2	0.2	0.2	160	120	100	800	259	287
13	5.9	1.4	0.4	31.8	44.8	120	140	140	502	1041	894
14	6.0	1.8	2.1	3.6	5.8	120	120	80	469	914	527
15	5.8	1.3	0.4	89.2	135.2	200	200	240	474	500	500
16	4.5	1.0	0.8	3.0	2.4	120	100	90	469	524	745
17	6.5	1.4	0.2	0.2	0.4	240	140	140	497	497	392
18	6.1	1.1	0.7	12.7	24.0	100	160	240	524	635	607
19	6.8	1.2	2.8	5.3	1.8	360	360	340	381	351	323
20	5.0	1.5	0.4	1.6	1.4	660	720	800	287	179	157
21	4.7	1.1	2.4	15.6	27.0	240	850	850	337	585	773
22	4.5	1.7	4.8	20.8	39.0	280	400	460	442	657	668
23	4.5	1.0	0.8	63.2	89.4	100	420	620	226	580	276
24	5.9	1.6	0.6	1.2	8.0	240	180	100	745	489	444
Control values:											
Mean	4.2	1.2	7.8	71.4	78.6	207	520	530	453	894	767
Range	4.4-4.8	1.1-1.5	4.2-10.4	26.2-96.0	68.0-96.3	140-360	200-825	245-820	392-485	695-945	680-860

Conversion: SI to traditional units—Blood glucose: 1 mmol/l $\approx$ 18 mg/100 ml. Plasma cortisol: 1 nmol/l $\approx$ 0.04 μ g/100 ml.

TABLE IV—Relation between increase or decrease from basal concentrations of growth hormone (GH), prolactin, and corticosteroids at 45 and 60 minutes after injection of insulin (0.1 U/kg body weight) in 24 alcoholics

Time (min)	Increase or decrease from basal concentrations		Correlation coefficient	Significance
	Y	X		
45	GH	Prolactin	0.571	P < 0.005
	GH	Corticosteroids	0.279	NS
60	GH	Prolactin	0.447	P < 0.01
	GH	Corticosteroids	0.203	NS

NS = Not significant.

60 minutes was correlated with age, duration of drinking, duration of alcoholism, and admitted alcohol intake. In no case was a significant correlation found. The concentrations of the various hormones at 45 and 60 minutes were grouped according to the patient's score for withdrawal symptoms. GH concentrations in patients with a score of 2 were significantly lower than in those with scores of 0 and 1 at 45 minutes ($P < 0.014$ and $P < 0.008$ respectively) and 60 minutes ($P < 0.024$ and $P < 0.002$ respectively) (see fig). The difference between the GH concentrations at both times in those who scored 0 and 1 was not significant. Patients with scores of 2 had lower prolactin concentrations than those who scored 0 and 1 at 45 and 60 minutes, but the difference was not significant at the 5% level. There was no significant difference between plasma corticosteroid concentrations for any of the withdrawal score groups at either 45 or 60 minutes.

Discussion

Our results confirm that GH responses are impaired in some alcoholics.³⁻⁵ All the patients developed adequate hypoglycaemia for the GH response (blood glucose < 2.2 mmol/l) and nine had impaired GH responses. Prolactin concentrations decreased from basal concentrations in eight of the patients with impaired GH responses. In seven patients corticosteroid concentrations decreased, and six of them had an impaired GH response. Our observation that some alcoholics have an impaired corticosteroid response to hypoglycaemia is consistent with other findings.^{2,3} In patients who had impaired responses of all three hormones the release of these hormones may have been generally depressed.

Impaired release of all three hormones might have been shown by a significant positive correlation between the three responses in the patients. Significant correlations were found between the prolactin and GH responses at 45 and 60 minutes. Nevertheless, prolactin responses were relatively small and variable, and a greater degree of hypoglycaemia may be required for a more consistent response.⁹ Although the correlation between the GH and corticosteroid responses was not significant, individual differences in adrenal responsiveness or timing of corticotrophin release may exist. The results suggest that both GH and prolactin responses were reduced in some patients, but further investigation of corticotrophin responses is required to determine whether the responses of all three hormones are impaired.

The most consistent abnormality in our patients was an impaired GH response. We found no significant correlation between GH response and any feature in the clinical history. GH responses vary with age,¹⁰ but such a relation would probably not have been apparent in our study, since age differences were relatively small and some of our patients had impaired responses. If the impaired GH response was related to chronic alcohol consumption, then factors such as duration of drinking problem and admitted alcohol intake might have been significantly related to it, but we found no evidence of this.

The GH responses in the five patients with the most severe withdrawal symptoms were impaired, suggesting that this effect may be apparent only when alcohol is withdrawn. Wright *et al*¹¹ investigated hypothalamic-pituitary function in alcoholics and reported that the GH response to insulin hypoglycaemia was normal. Nevertheless, their patients were drinking up to the time of investigation and had not experienced alcohol withdrawal. An impaired GH response to insulin hypoglycaemia has been reported in a single abstinent alcoholic, but normal responsiveness returned when the patient was reinvestigated.⁸ Abstinence or withdrawal of alcohol from the alcoholic may be required to show an impaired GH response.

Withdrawal symptoms indicate alcohol dependence, but the mechanisms concerned in the development of alcohol withdrawal syndrome are not fully understood.¹² Our observation of impaired stress responses in recently abstinent alcoholics requires further investigation as it may have important implications for the management of alcohol withdrawal syndrome.

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Epidemiology and clinical significance of cervical erosion in women attending a family planning clinic

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Summary and conclusions

Women attending a family planning clinic were studied to determine the relation between cervical erosion and clinical and social characteristics. The appearance of the cervix was recorded without knowledge of the women's symptoms.

The prevalence of erosion increased with parity but, when the effects of other factors were controlled, decreased in women aged 35 and over. Erosion was significantly more common in women taking the "pill" and less common in women using barrier methods of contraception than in others. There was considerable variation between doctors in the reporting of erosion. No association was found between erosion and postcoital bleeding, dyspareunia, backache, or dysuria. There was a significant but modest association between erosion and vaginal discharge and a suggestion that erosion may sometimes be associated with nocturia and frequency of micturition. Vaginal flora was similar in women with and without erosion.

Cervical erosion should not be regarded as pathological in asymptomatic women, nor should it be assumed necessarily to be the cause of symptoms in women with genitourinary complaints.

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Introduction

Cervical erosion is one of the most common reasons for hospital admission of women aged 15-44 years. It accounts for about 5000 admissions a year in Scotland¹ and 30 000 admissions a year in England and Wales.² In addition an unknown number of women with erosions are treated as outpatients. The term erosion is misleading, since there is no loss of surface tissue from the cervix^{3,4}: the lesion consists of a zone of columnar epithelium on the vaginal portion of the cervix in place of the stratified, squamous epithelium normally found below the external os.

Cervical erosion is a common finding on routine pelvic examination during the fertile years,^{5,6} but whether it should be treated or ignored remains controversial. Many doctors refer for specialist treatment only those women in whom the erosion is associated with genitourinary symptoms. Even in these patients, however, it is not certain that the lesion causes the symptoms, since similar symptoms also occur in women with a normal cervix. Uncertainty about the clinical significance of cervical erosion results in substantial variation in its management. For example, Philip⁷ recommended that most erosions in non-puerperal women should be treated, whereas Townsend⁸ thought that treatment should be reserved for selected, symptomatic cases. This leads to uncertainty about the need to refer women with erosion for specialist care—in one study⁹ the rate of referral for treatment of erosion varied seventeenfold among different family planning clinics.

Because cervical erosion is so common and its clinical significance often obscure we undertook a study to describe the characteristics of women with erosion and determine the relation between genitourinary symptoms and erosion. Clinical signs were recorded "blind"—that is, without knowledge of the women's symptoms.

Patients and methods

The study was conducted from October 1975 to March 1977 in the family planning centre at Edinburgh. Patients included were either new attenders or attenders who had not been seen for at least six months. In an attempt to standardise the recognition and description of erosions the seven participating clinic doctors received instruction from a consultant gynaecologist (JDOL).

Each patient was asked to participate in a survey of "common symp-