(which in our patient failed to rise with LHRH values). Patients with no chromosome abnormality and an HCG-secreting tumour may have gynecomastia and an appearance in testicular specimens at biopsy that mimics Klinefelter's syndrome¹; they too have normal testosterone values and suppressed FSH values.⁵ We suggest that karyotyping should be performed on all patients with choriocarcinoma to determine the prevalence of the association of XXY aneuploidy and this tumour, since other data may be misleading.

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Hypoglycaemia in insulin-dependent diabetic drivers

The possibility of hypoglycaemia occurring in insulin-dependent diabetics while driving is well recognised,¹ and a recent case of this type prompted us to study the problem further. A 50-year-old experienced insulin-taking driver was called out suddenly just before his evening meal. His regular source of dextrose was kept in his jacket, which in his haste had been left behind in the house. Severe hypoglycaemia ensued, but fortunately he was able to stop his car without mishap.

Patients, methods, and results

We selected at random 157 insulin-dependent diabetics (age 17-65 years) from patients attending outpatient diabetic clinics in Manchester and Sheffield. Each patient was interviewed by the same person (BC). The questionnaire contained a mixture of questions designed to establish early in the interview whether the patient was a driver. A full account of each

patient's symptoms of hypoglycaemia was then taken, with particular reference to premonitory symptoms. Precipitating factors such as exercise, emotion, late meals, and alcohol were identified. Patients were then asked where they kept carbohydrate in the event of hypoglycaemia occurring and whether such material was kept permanently in their vehicles. Finally, the patients were asked if they had ever experienced symptoms of hypoglycaemia while driving. No attempt was made to estimate the frequency of this event in any particular case.

In three cases (two men, one woman) it was not possible to ascertain whether carbohydrate material was kept in the vehicle. From the table it may be seen that a much higher proportion of the male diabetic population were drivers (79% of men, compared with 37% of women). Furthermore, 49% of men drivers experienced hypoglycaemia while driving, whereas only 19% of women drivers did so. The presence of any of the patient's premonitory symptoms was taken to indicate that hypoglycaemia was occurring. The table shows that over half of both men and women drivers failed to maintain a permanent energy source in their vehicles.

Comment

Estimates show that about 150 000 diabetics in Great Britain are potential drivers.² Under the Road Traffic Act 1974 diabetes is not a disqualifying disability, although it is recommended that patients requiring insulin should not drive heavy goods vehicles or public service vehicles. Hypoglycaemia may occur suddenly during driving, even in well-stabilised diabetics. Insulin is regarded as a drug under the Road Traffic Act 1962, and a driver with symptoms of hypoglycaemia may be charged with driving while under the influence of drugs. Patients must therefore be advised that if they have any early symptoms they should stop the car and move to the back seat to take their sugar, because it is illegal to be in charge of even a stationary vehicle if under the influence of a drug. Our results indicate that hypoglycaemia while driving is commoner than might be supposed; nevertheless, a more important finding may be that less than 50% of diabetic drivers keep carbohydrate material permanently in their vehicles, although the British Diabetic Association leaflet on the diabetic driver states that carbohydrate should be kept in the car. It is unsafe to depend on material carried in bags or clothes, which may easily be left behind. In addition, road conditions may be such as to prevent drivers from stopping quickly should hypoglycaemia occur. We suggest, therefore, that the education of diabetic drivers to these hazards should be undertaken by all those responsible for their medical care.

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Requests for reprints should be addressed to Dr Ward.

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Patients, prevalence of hypoglycaemia while driving, and maintenance of permanent energy source in vehicle

	Men	Women	Total
Number of patients interviewed	86	71	157
No (%) of drivers	68 (79.0)	26 (36.6)	94 (59.8)
Mean ($\pm$ 1 SD) age of drivers	41.8 $\pm$ 18.08	34.1 $\pm$ 13.20	39.7 $\pm$ 17.28
Mean ($\pm$ 1 SD) duration of diabetes (years)	14.8 $\pm$ 10.69	10.3 $\pm$ 6.32	13.5 $\pm$ 9.88
No (%) of drivers experiencing symptoms of hypoglycaemia while driving	33 (48.5)	5 (19.2)	38 (40.4)
No (%) of drivers who keep permanent energy sources in their vehicles (91 drivers; 66 men, 25 women)	32 (48.5)	12 (48.0)	44 (48.3)

Finger wrinkling after immersion in water

Wrinkling of the skin over the pulp of the fingers after prolonged immersion in water has been suggested as a test of sympathetic function.^{1,2} Since autonomic fibres are carried in the peripheral nerves, by extension skin wrinkling may also be regarded as a measure of the integrity of the peripheral nerves.³ The physiology of this normal mechanism has been reviewed by Braham *et al.*¹ The simplicity of this innocuous bedside test of autonomic function requires an assessment of its reliability.

Subjects, methods, and results

We examined 54 normal people (30 women, 24 men) aged from 40 to 60 years; 27 of these were hospital staff or relatives of patients and 27 were patients in hospital being treated for a variety of non-neurological conditions. No individual was found to have or give a history of neurological disease. We were careful to exclude all patients being treated with drugs that are known to be potential causes of peripheral neuropathy such as nitrofurantoin, isoniazid, and phenytoin. Patients suffering from illnesses that may be associated with peripheral neuropathy such as malignancy of any sort were also excluded. No subject had a family history of diabetes and all had normal fasting blood sugar concentrations. No severely ill patient was included in our study. All patients gave informed consent to the procedure.

Testing was carried out by seating the person comfortably and immersing one hand in warm water (40-45°C). The hand was examined before immersion, when all pits or creases resembling wrinkles in the pulps of all the fingers were noted; examination was repeated after 20 minutes of immersion.

We found a gradation between abundant wrinkling of the skin of all five fingers and mild wrinkling of only one finger. Results were tabulated as: (a) where wrinkling could be observed in one or more fingers; and (b) where fingers emerged from immersion flat and often a little swollen.

We observed wrinkling in 38 individuals, but there was no apparent wrinkling in 16. There was no difference between the sexes.

Comment

The fact that some of the normal subjects examined developed extensive creasing of the skin of the fingers while others did so to only a modest extent is probably within the bounds of normal biological variation. The finding that stands out is that nearly one-third of these normal people showed no wrinkling of their fingers at all. It seems safe to say that sympathetic function is preserved if finger wrinkling after immersion in water is observed, but if the fingers emerge smooth it cannot be assumed that there is a lesion to the autonomic supply or to the peripheral nerves of the hand. This high proportion of false-positives limits the usefulness of this test.

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Comparison of two combination chemotherapy regimens in advanced colorectal cancer

Methylchloroethyl-cyclohexyl-nitrosourea (methyl CCNU) and 5-fluorouracil reportedly gave a 47% response rate in colorectal cancer.¹ We have therefore examined whether adding a further agent (vincristine or mitomycin C) would prove more effective for response and survival.

Patients, methods, and results

Patients—Thirty-one consecutive patients, who had not been treated with chemotherapy and had histological confirmation of adenocarcinoma of the colorectum, were entered into the trial. Fifteen patients were given regimen A and 13 regimen B. Three patients were excluded from analysis because of violations of protocol. The patients were aged between 33 and 73 years (median 57). There were 20 men and nine women.

Disease sites—Patients with pretreatment disease sites included all those

with local or residual disease, 24 with hepatic metastases, eight with intra-abdominal lymphadenopathy, three with lung metastases, and seven with involvement of other sites.

Pretreatment evaluation included some or all of the following: measurement of the tumour at laparotomy, CT scan of abdomen, liver function tests, ultrasonic examination of abdomen, isotope liver scan, and testing for carcinoembryonic antigen.

Assessment—Follow-up procedures for response included evaluating clinical state of patients and repeating pretreatment tests.

Treatment programme—Regimen A: methyl CCNU 150 mg/m² given by mouth on day 1, then 5-fluorouracil 10 mg/kg/day given intravenously on days 1-5; vincristine 1.5 mg/m² (maximum 2 mg) given intravenously on day 1. Regimen B: methyl CCNU 150 mg/m² given by mouth on day 1, then 5-fluorouracil 10 mg/kg/day given intravenously on days 1-5; mitomycin C 25 ng/m² given intravenously on days 1-5. Both regimens were repeated at six-weekly intervals. If there was evidence of myelosuppression the doses, time intervals, or both were adjusted. Most patients were treated as out-patients. Chemotherapy was continued until death or until other forms of management such as operation or radiotherapy were indicated for palliation.

Survival from diagnosis in two groups of patients with colorectal cancer taking different regimens.

There was one complete response and two partial responses. The median survival for both regimens was five months from onset of treatment and 17 and 14 months from diagnosis for regimens A and B respectively. The figure shows the survival curves. Nausea and vomiting were noted in most patients after day 1. These were attributed to methyl CCNU. Leucopenia and thrombocytopenia were noted but these were reversible. Neurotoxicity with vincristine was noted occasionally as areflexia or paraesthesiae.

Comment

Chemotherapy with 5-fluorouracil, methyl CCNU, vincristine, and mitomycin C has been used before for treating advanced colorectal cancer.^{1,2} We have attempted to compare two combinations of these agents, with particular emphasis on survival. Neither combination affected the natural progression of advanced colorectal cancer. This is in keeping with the results of other similar studies.³⁻⁵

Future trials of chemotherapy should therefore include a control group given no chemotherapy. Furthermore, the effects of single agents should now be more carefully assessed before embarking on combination chemotherapy that may be more toxic but has so far proved no more effective.

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