As retinal changes usually precede the development of diabetic nephropathy, in the five patients with proteinuria but without retinopathy (three positive and two negative for chlorpropamide-alcohol flushing) the proteinuria may possibly have been due to other causes. If these cases are excluded the difference between the groups positive and negative for flushing becomes greater (1/191 (0·5%) *v* 12/100 (12%).

AHB is and RDGL was supported by the MRC.
Requests for reprints should be sent to Dr D A Pyke, Diabetic Department, King's College Hospital, London SE5 9RS.

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(*Accepted 21 November 1980*)

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Chlorpropamide-alcohol flushing and microangiopathy in insulin-dependent diabetes

Patients with non-insulin-dependent diabetes often show facial flushing after drinking alcohol when taking chlorpropamide (chlorpropamide-alcohol flushing).[1 2] We found that patients who show this reaction have a decreased frequency of retinopathy[3] and proteinuria[4] compared with those who do not.

In view of the association between chlorpropamide-alcohol flushing and diminished risk of microangiopathy in non-insulin-dependent diabetics we wondered whether the same was true for insulin-dependent diabetics. We therefore examined the frequency of chlorpropamide-alcohol flushing in an unselected group of insulin-dependent diabetics (group 1) and two selected groups of patients with (group 2) and without (group 3) microangiopathic complications.

Patients, methods, and results

The criterion for insulin dependence was that the patient had been taking insulin from the first few weeks after diagnosis or had shown appreciable ketonuria. In group 1 the general frequency of chlorpropamide-alcohol flushing in insulin-dependent diabetics was studied by testing patients chosen at random from our diabetic clinic. Group 2 comprised patients who had developed severe microangiopathic complications within 10 years of the diagnosis of diabetes—namely, maculopathy with visual deterioration, proliferative retinopathy, or any form of retinopathy with persistent proteinuria. Group 3 comprised patients who, after more than 15 years of diabetes, showed no diabetic complications. The mean ages of the patients (±SD) at diagnosis of diabetes in groups 2 and 3 were 23 ± 15 and 22 ± 14 years respectively. The mean durations of diabetes were 22 ± 8·5 and 26·6 ± 8·6 years respectively.

Each patient was given a placebo to take on the first day of the test and then 40 ml of sherry 12 hours later. On the second day chlorpropamide 250 mg was given and the sherry again taken 12 hours later. The patient was not aware that a placebo was being used. Patients were asked to report any unusual sensation in the face within 45 minutes of consuming the alcohol. Results were analysed by the χ^2 test.

Of the 125 unselected patients in group 1, 20 (16%) showed chlorpropamide-alcohol flushing. A further five patients flushed with both placebo and chlorpropamide and were excluded. Of the 72 patients with severe complications (group 2), six (8%) showed chlorpropamide-alcohol flushing. None showed flushing with the placebo tablet. Of the 117 patients with no complications (group 3), 33 (28%) showed chlorpropamide-alcohol flushing. A further three also flushed with placebo and were excluded. The difference in the frequency of chlorpropamide-alcohol flushing between groups 2 and 3 was significant ($p < 0.01$), as was the difference between groups 3 and 1 ($p < 0.02$). The difference in frequency between group 1 and 2 did not reach significance.

Comment

In view of the relatively low frequency of chlorpropamide-alcohol flushing in insulin-dependent diabetics—16% in this series—the design of this study was different from that in our previous studies in non-insulin-dependent diabetics.[3 4] We thought that the best way to establish differences in the frequency of chlorpropamide-alcohol flushing between insulin-dependent diabetics with and without complications was to look at groups selected from each extreme—namely, those in whom severe microangiopathy had developed in the early years after diagnosis and those with no complications after many years of diabetes. There was a distinct difference in the incidence of flushing between the two groups (9% *v* 28%); the frequency in the unselected group lay between these two extremes (16%). Thus, as in non-insulin-dependent diabetics,[3] chlorpropamide-alcohol flushing in insulin-dependent diabetics seems to be associated with a decreased frequency of microangiopathy, though the association is not so striking. We have not yet done any family studies of chlorpropamide-alcohol flushing in insulin-dependent diabetics so we do not know whether it is an inherited feature in such patients, as we think it is in non-insulin-dependent diabetics,[2 3] and thus whether there is an inherited component to the development of diabetic retinopathy in insulin-dependent diabetes.

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[1] FitzGerald MG, Gaddie R, Malins JM, O'Sullivan DJ. Alcohol sensitivity in diabetics receiving chlorpropamide. *Diabetes* 1962;**11**:40-3.
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(*Accepted 21 November 1980*)

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Group R streptococcal meningitis (Streptococcus suis type II): a new industrial disease?

Four cases of meningitis due to group R streptococci occurring in men working with pigs or pork products have been described in England. I report a fifth case and suggest that this infection should be classed as an industrial disease.

Case report

A 61-year-old meat inspector was referred to this hospital in coma. Six days earlier he had inspected a consignment of pig carcasses, which were subsequently condemned. He had not accidently cut himself during this inspection, and no routine bacteriological cultures had been taken from the carcasses. Four days later he developed a sore throat with fever and shivering, which resolved within 36 hours. The day before referral he had noticed pain at the base of his back, followed 12 hours later by a gradual onset of headache, vomiting, and difficulty in hearing. From this time his level of consciousness steadily deteriorated.

On admission he was comatose, restless, with pronounced nuchal rigidity, and a fever of 40°C. There was no sign of cutaneous infection, and examination of fauces and external ears showed no abnormality. Appearances on funduscopy were normal, and there were no abnormal focal neurological signs. Lumbar puncture showed turbid cerebrospinal fluid under raised pressure; microscopical examination showed 18×10^3 white blood cells/μl (95% polymorphs) with 36 red blood cells/μl, and abundant Gram-positive cocci. Cerebrospinal fluid protein concentration was 4 g/l and glucose was undetectable. Treatment was immediately started with ampicillin, 200 mg/kg/day, given as 4 g six-hourly intravenously. Twenty-four hours later benzylpenicillin, three megaunits six-hourly intravenously, was added when

cultures of the cerebrospinal fluid and blood grew a β-haemolytic streptococcus not identifiable as a member of Lancefield group A, B, C, D, or G. Sensitivity plates subsequently showed the organism to be fully sensitive in vitro to both the drugs administered. Within 48 hours of this treatment the patient's fever had resolved, and after six days of gradual improvement he regained consciousness. As soon as he was well enough to concentrate, however, he complained of tinnitus, dizziness, and deafness in both ears. Intravenous antibiotics were stopped after 10 days and phenoxymethylpenicillin, 1·5 g four times daily, with probenecid, 500 mg three times daily, were given for a further five weeks. The patient was discharged after three weeks in hospital; since then he has suffered no recurrence of meningitis but remains disabled by dizziness, unsteadiness of gait, and deafness of his right ear.

The division of hospital infection (streptococcal reference) at the Public Health Service Laboratory, Colindale, identified his isolates from blood cultures and cerebrospinal fluid as *Streptococcus* group R (*Str suis* type II).

Comment

Group R streptococci were identified as a cause of septicaemic infections of pigs in 1959,[1] and nine years later three cases of human infection, two of meningitis and one of fatal septicaemia, were caused by this organism in Denmark.[2] In 1975 Zanen and Engel described ten cases of human meningitis due to group R streptococci which had occurred since 1968 in Holland[3]; of these, nine worked in the meat trade with pigs or pig carcasses (the other being a housewife), and of nine who recovered on antibiotic treatment five suffered permanent deafness and vertigo.

The first case of meningitis due to group R streptococci in England and Wales was recorded in a pork-pie factory worker in 1976,[4] and this was followed by a further case in a man with the same occupation[5]; both patients suffered residual deafness and vertigo. Wright (unpublished observations, Communicable Diseases Surveillance Centre) has described two more cases of infection occurring in pork handlers in Britain and has drawn attention to the almost invariable occupational association between humans handling pigs or pork products and group R streptococcal infections.

The case I have described highlights the occupational association with pigs in this rare disease, and in view of the disabling sequelae recorded in most cases, suggests that group R streptococcal infection in humans should be classed as an industrial disease; this could enable those who are incapacitated by the sequelae to benefit from industrial compensation.

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(*Accepted 18 November 1980*)

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Strongyloides stercoralis infection in renal transplant recipients

Strongyloides stercoralis infection is endemic in tropical and subtropical regions. A host may remain infected but asymptomatic with this nematode for more than three decades.[1] Overwhelming infection with *S stercoralis* may occur in immunosuppressed hosts,[2] including renal transplant recipients.[3 4] We report two such infections in Guyanese recipients of transplants. At the time these patients developed symptoms of *S stercoralis* infection the immunosuppressive regimen for acute rejection in this unit was as follows: an increase in oral prednisolone to 200 mg daily, reducing by 50 mg steps every five days until the dose was 50 mg daily, after which it was reduced slowly to a minimum dose of 15 mg daily. Azathioprine was used at maximum tolerated dose. From our experience we now recommend prophylactic preoperative treatment against *S stercoralis* in transplant recipients who come from, or who have lived in, tropical or subtropical regions.

Case reports

Case 1—A 30-year-old man visited Guyana seven years before he received a cadaveric transplant. On the eighth postoperative day acute rejection occurred and he was treated successfully. Renal function deteriorated again, and on day 63 he received two single doses of 1 g methylprednisolone. On day 81 he developed dyspnoea, cyanosis, and haemoptysis, with widespread crepitations in the lungs. Chest radiography showed an alveolar infiltrate initially interpreted as pulmonary oedema. Larvae of *S stercoralis* were found in sputum and gastric aspirate. There was no eosinophilia. Thiabendazole 25 mg/kg body weight for 14 days cleared the larvae from his sputum and he made a good recovery. Creatinine clearance was 79 ml/minute. On day 157 he was readmitted with fever and apparent acute rejection. He was treated with 2 g methylprednisolone and prednisolone 100 mg daily for five days. Graft nephrectomy was performed on day 170 because of cortical necrosis. Immunosuppression was withdrawn. On day 175 he became severely dyspnoeic with massive haemoptysis. Chest radiography showed prominent alveolar infiltrate similar to the previous episode. *S stercoralis* larvae were again recovered from his sputum and gastric aspirate. Thiabendazole was started, but he died on day 179. Histological examination showed a single larva lying within an alveolus.

Case 2—A 37-year-old man with a history of pulmonary sarcoidosis had last visited Guyana 15 years before he received a kidney transplant. After operation he remained oliguric and on the fifth day was treated for presumed acute rejection. On day 30 he developed a cough with white frothy sputum, and a chest radiograph showed residual sarcoid changes. Sputum contained larvae of *S stercoralis*. There was no eosinophilia. He was treated with thiabendazole 25 mg/kg twice daily for 10 days and then prophylactically with three-day courses of thiabendazole monthly for six months. He had remained well four and a half years later.

Comment

Clinical infection with *S stercoralis* was closely related to high-dose prednisolone treatment in both patients. Respiratory distress mimicking pulmonary oedema is a common presentation.[2 3 4] Eosinophilia was not present in either patient before or after transplantation. Eosinophilia may be absent in infected individuals or as a result of therapeutic immunosuppression.[4] The first patient showed that conventional doses of thiabendazole in an immunosuppressed patient are insufficient to eradicate the nematode. The correct duration of treatment is arbitrary, but should be monitored by examination of concentrated stool samples for larvae.

S stercoralis infection in a transplant recipient is usually diagnosed when respiratory failure has developed and is fatal.[3 4] We now recommend prophylactic treatment of transplant recipients who come from endemic areas even if routine investigation does not show chronic infection. We adopted this policy in a third Guyanese patient, who developed no features suggestive of *S stercoralis* infection 12 months after transplantation, though larvae were never recovered from his stools.

We thank Dr Roland Davies for his help in investigating these patients.

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(*Accepted 9 December 1980*)

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