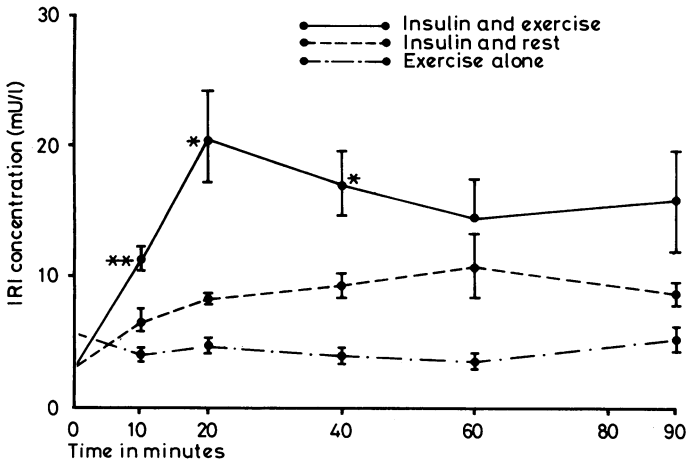
and (c) injection of 10 IU of mono-component insulin followed by exercise. All injections of insulin were given subcutaneously on the anterior aspect of the right thigh. The subjects were exercised intermittently for 60 minutes on a bicycle ergometer. During the last 30 minutes of the "exercise" experiments the subjects were rested. On the "rest" days the subjects sat in deep armchairs for the entire 90 minutes after the injection of insulin. Insulin concentrations in serum were measured by radioimmunoassay (using a kit from the Radiochemical Centre, Amersham). Glucose concentrations were measured by an autoanalyser.

Exercise alone induced an initial fall in blood glucose concentration by 15 to 20%; this fall was not associated with any significant alteration in serum IRI concentration. Exercise alone did not induce any consistent change in IRI concentrations at any stage (figure). In the resting subject insulin concentration became maximal 60 minutes after the injection. The blood glucose concentration did not alter significantly. When the injection of insulin was followed by exercise, serum IRI concentration increased sharply at 10 minutes and achieved a maximum at 20 minutes; the peak IRI concentration was twice as high as that achieved when the subjects were rested after the insulin injection. After exercise, the IRI concentration was significantly higher throughout the experimental period of 90 minutes.



Effect of exercise on immunoreactive insulin (IRI) concentration in four normal subjects (mean ± SE). The fifth patient was overweight and hyperinsulinaemic but the effect of exercise in her was similar.

*P<0·05.**P<0·01.

Discussion

The fact that serial IRI concentrations were much higher after exercise than those associated with rest must mean that exercise increases the rate and the magnitude of insulin absorption from subcutaneous tissue. Since exercise alone did not alter serial IRI concentration significantly, increased endogenous secretion cannot account for our observations. This difference was maintained at 90 minutes; this would imply that the effect of exercise may outlast the duration of exercise. Such an increase in absorption of insulin from subcutaneous tissue after exercise provides an obvious and a more satisfactory explanation for exercise-induced hypoglycaemia in insulin-dependent diabetics than some other circulating hypoglycaemic factor.[3]

No significant hypoglycaemia was observed in any of the subjects; this is probably the result of a combination of a small insulin dose; switching off of endogenous insulin secretion; and the release of glucagon, catecholamines, and cortisol. In diabetic patients who lack an adequate B-cell reserve much larger doses of insulin are used and when after exercise a large bolus of insulin is absorbed into the circulation little is achieved by switching off the limited endogenous secretion of insulin. These patients thus have only their glucagon and catecholamine secretion to protect them from hypoglycaemia.

The mechanism underlying the enhanced absorption of insulin from subcutaneous tissue is probably through an increase in blood flow in the injected limb. Binder[4] measured the absorption of insulin after an intramuscular injection and concomitantly measured the local blood flow; in a group of 12 patients he studied no correlation between insulin absorption and local blood flow was found. Binder did not, however, measure the effect of an increase in local blood flow on insulin absorption in the same person. On the other hand, Binder[4] showed quite convincingly that the rate of insulin absorption is not altered by increasing the skin temperature.

Exercise thus augments the rate and magnitude of insulin absorption from subcutaneous tissue and this effect may play an important part in the pathogenesis of exercise-induced hypoglycaemia in the insulin-dependent diabetic patient. Exercise does not probably alter the requirement of insulin to the same extent as it enhances the bioavailability of subcutaneously injected insulin. It would be of interest to investigate the possibility that patients may be protected from exercise-induced hypoglycaemia by injecting insulin into those parts of the body which are not likely to be exercised or to study the effect of such drugs as would prevent exercise-induced enhancement of insulin absorption.

We thank Mrs A Winsbury for secretarial help.

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Remission of psoriasis during haemodialysis

Increased epidermal cell proliferation is a characteristic feature of psoriasis. The factors responsible may derive from the epidermis, dermis, or blood. We present here evidence that the factors involved are blood-borne. Two patients with chronic renal failure and psoriasis noticed complete clearing of their skin lesions during treatment with haemodialysis.

Case reports

Case 1—A 57-year-old man developed psoriasis at the age of 25. Six years later he presented with back pain and was shown to have polycystic disease of the kidneys. During the years leading up to end-stage renal failure he had noticed some seasonal fluctuation in the extent of his psoriasis; otherwise it had been chronic and stable. In November 1975, just before starting haemodialysis, his psoriasis was extensive on the trunk, elbows, knees, and scalp. Within eight weeks of treatment with dialysis his psoriasis cleared. He continued on dialysis and in October 1977 his psoriasis was confined to two tiny papules in the scalp.

Case 2—A 50-year-old man developed psoriasis on the elbows and knees in 1949 and progressively lesions of the scalp in 1960 and on the legs and trunk in early 1971. In November 1971 he presented with ankle oedema and the diagnosis of chronic proliferative glomerulonephritis was established; his renal function rapidly deteriorated and haemodialysis was instituted. Within three weeks of starting dialysis his widespread and extensive psoriasis vanished. In April 1974 he had a cadaver renal transplant and was started on immunosuppressive treatment with prednisolone 40 mg and azathioprine 150 mg daily. Three weeks later he was taken off dialysis. The first sign of recurrence of his psoriasis, mild disease of the scalp and trunk, occurred three weeks after dialysis was stopped. One year later, after gradual reduction of immunosuppressive treatment to prednisolone 15 mg and azathioprine 150 mg daily, his psoriasis relapsed further with moderately severe disease of the scalp, discoid lesions on the trunk, and guttate papules on the limbs.

Comment

Remission of psoriasis during haemodialysis was first reported in 1976.[1] The patient described had chronic renal failure and psoriasis; the psoriasis was cleared for the first time within two weeks of starting haemodialysis; remission was maintained throughout 12 months' dialysis, and for a further 11 months after successful renal transplantation and the introduction of immunosuppressive treatment; a trivial relapse then finally occurred when the patient fractured a tibia.[2]

All three patients now described had psoriasis responsive to haemodialysis. The beneficial effect of this treatment is unlikely to be due to coincidence. While McEvoy and Kelly noted that their patient relapsed 11 months after the withdrawal of dialysis, our second patient had psoriasis that reappeared promptly after dialysis was stopped and at a time when immunosuppressive treatment would have been expected to maintain a remission. The delay in the appearance of more extensive psoriasis in case 2 and the ultimate relapse in the patient of McEvoy and Kelly was probably due to and dependent upon the reduction of immunosuppressive treatment required after transplantation.

Studies on ^{14}C-thymidine incorporation in DNA of transforming lymphocytes suggest that haemodialysis causes a loss of factors from normal and uraemic plasma that are essential for DNA synthesis.[3] These changes are independent of any lymphopenia caused by dialysis. Similar blood-borne factors responsible for epidermal DNA synthesis may exist and would explain our observations in psoriasis.

We thank Sister Arnold, Ryehill Hospital, Newcastle upon Tyne, who noted the phenomenon and drew our attention to it; Dr R Elliot, Professor D N S Kerr, and Professor S Shuster for advice and permission to report the cases; and Mrs Hogben for secretarial help.

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Effects of naloxone on auditory hallucinations

Recent work suggests that naturally occurring endorphins and opiate receptors in the brain have a role in the pathogenesis of some symptoms of schizophrenia.[1-3] Terenius *et al*[2] showed an increased endorphin content in the cerebrospinal fluid of chronic schizophrenics during an active phase of the illness, and Gunne *et al*[3] have shown that auditory hallucinations could be abolished in schizophrenic patients by the administration of naloxone, a pure morphine antagonist.

We describe a schizophrenic patient with severe auditory hallucinations which responded to treatment with naloxone, though they had previously been relieved by self-administered morphine and heroin.

Case report

A 28-year-old woman had a 10-year history of psychiatric illness. She presented initially with mutism, and first complained of auditory hallucinations in 1969. These consisted of voices speaking to her and discussing her. Later she complained of confusion in her thoughts, difficulty in apprehending what was said to her, indefinable panic, and specific fear of the voices. She appeared tense, expressionless, silent, and immobile. She reported reasonable control over the hallucinations on flupenthixol decanoate 80 mg weekly with thioridazone 100 mg at night, though the hallucinations continued to vary in intensity and disruptiveness.

She had first abused drugs in 1970—chiefly opiates, but also amphetamines and lysergide. Her psychotic symptoms seemed least troublesome when she used opiates regularly, and she completed a diploma course in sociology while a registered addict. She took opiates to relieve her symptoms, and said that the voices disappeared almost immediately after an intravenous injection of heroin. These effects wore off within a few hours of the injection.

Trial—In a single-blind procedure 0·4 mg naloxone or isotonic saline was injected intravenously on three separate occasions when her auditory hallucinations were most troublesome. The effects on her hallucinations were monitored every five minutes for the first 20 minutes, and every 10 minutes for a further three hours by asking her to report on their intensity. Five minutes after intravenous naloxone the patient reported that her hallucinations were less intense; at 15 minutes they had disappeared and she became mildly euphoric. The mood elevation lasted for two hours, and the hallucinations had returned to their usual intensity after three hours. The time course of these changes closely followed that reported by the patients after taking morphine or heroin, and was similar to that shown by Gunne *et al*.[3] No effects were observed after isotonic saline, there was no alteration in mood, and her hallucinations were totally unaffected.

Comment

The effects of naloxone reported here are important because the immediacy of the clinical response might suggest a direct effect on the psychopathological processes of auditory hallucinations. This contrasts sharply with the known effects of neuroleptic drugs, which take much longer to produce clear-cut effects on psychotic symptoms.

Comfort[4] has suggested that morphine-like drugs may be the only effective anti-psychotic for some patients. Our patient was not a typical schizophrenic, and no general conclusions can be drawn about schizophrenia. Nevertheless, the comparable effects of morphine and naloxone on her symptoms suggest that drugs with a high affinity for opiate receptors could be developed as an effective means of controlling hallucinations in schizophrenia, and that intravenous naloxone could be used as a short-term emergency measure in patients with distressing hallucinations. These observations may also have important implications for the role of endorphins and opiate receptors in the pathogenesis of auditory hallucinations in schizophrenia, as both morphine and naloxone may act as competitive inhibitors of an endorphin fraction possibly present in excess in such patients.

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Mid-trimester septic abortion and Escherichia coli septicaemia in a copper IUCD user

Reports of septic abortion in association with intrauterine contraceptive devices (IUCDs) have been mainly a North American phenomenon in which the Dalkon shield has principally figured. Nevertheless, in Great Britain figures do not show an increase in septic abortion in IUCD users and certainly do not single out the Dalkon shield.[1] We report a case of septic mid-trimester abortion and septicaemia in a Gravigard (copper 7) user.

Case report

A 25-year-old nulliparous woman was admitted with a five-day history of slight vaginal bleeding after an episode of 13 weeks' amenorrhoea. A Gravigard IUCD had been fitted in 1976. The uterus was compatible in size with a gestation of 16 weeks and an ultrasonic scan reported a pregnancy of 15 weeks' gestation. She was treated as having a threatened abortion and discharged on the following day. There was no fever during her admission. She was readmitted one week later in the early hours with a 24-hour history of heavy vaginal bleeding and fever. Her temperature was 39°C. Blood and a high vaginal swab were sent for culture and the IUCD was removed. She was started on co-trimoxazole (Septrin) and metronidazole (Flagyl). She aborted spontaneously a normal-looking fetus and placenta 36 hours later, at which time her temperature was 38°C. Cultures were taken from the placenta.