(Dawson, 1954), and secreting islet cell tumours of the pancreas are not a common phenomenon. Therefore it would seem that the coexistence of both diseases would not be a mere coincidence. Though this case is, to our knowledge, the first of this kind reported, the possibility may be raised that in a certain number of cases of tuberous sclerosis the "epilepsy" may be caused by an insulin-secreting pancreatic tumour. An appropriate clinical investigation, followed by surgery, may relieve the patients of one of the aggravating symptoms of the disease.

The possibility of involvement of the pancreas in some cases of tuberous sclerosis was raised by Pagenstecher (1955). He reported that an elder brother of a patient with tuberous sclerosis died suddenly at the age of 21 while serving in the Navy. The primary pathological diagnosis at necropsy was acute pancreatic necrosis, and the necropsy report read, in part: "The pancreas is normal in size. It is soft to the point of liquefaction, especially in the body. It is markedly hyperaemic, with hyperaemia not extending past the capsule. Some lobules are preserved. There is no evidence of calculi of the ducts." The author speculates on the possibility that a sudden change in a hypothetical (tubero-sclerotic) lesion, like rupture of a cyst or obstruction of a small duct, could have caused the acute necrosis, while the quick digestion of the tissues by the pancreatic enzymes destroyed all histological traces of the causative mechanism.

It should also be mentioned that van der Hoeve (1933) reported the occurrence of pancreatic cysts in von Recklinghausen's disease, which shows a close relationship to tuberous sclerosis (Lillie, 1954; Wechsler, 1958).

Summary

A case of tuberous sclerosis, marked by frequent epileptiform seizures, associated with spontaneous hypoglycaemia, is described. The patient was operated on and an islet-cell adenoma of the pancreas was removed. Elevated insulin activity in the serum was found. Since the operation the patient has been free from seizures. The possibility of a pancreatic tumour as an aetiological factor of the epileptiform seizures in some cases of tuberous sclerosis is discussed.

We are particularly indebted to Dr. J. Groen, of the Medical School in Jerusalem, for the determination of the insulin content of the serum and the tumour, and to Dr. H. Winnik, of the Psychiatric Hospital Talbieh in Jerusalem, for putting the case records at our disposal. We also wish to express sincere thanks to Mrs. Kaye Norton for producing the illustrations.

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PROCHLORPERAZINE AND IRRADIATION SICKNESS

BY

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A trial is described in which prochlorperazine is compared with pyridoxine and an inert tablet for the relief of side-effects due to therapeutic irradiation.

Prochlorperazine ("stemetil") is a brand of 1-[3-(3-chloro-10-phenothiazinyl)propyl] - 4 - methylpiperazine. This drug is one of the many new anti-emetic preparations now available. It resembles chlorpromazine in its range of pharmacological action, differing, however, in that it is several times more effective as an anti-emetic, but less active in reducing conditioned and instinctive reflex activity and in enhancing the activity of hypnotics and analgesics.

The most distressing side-effects associated with therapeutic irradiation are nausea and vomiting rather than any local reaction at the site of treatment. Anorexia and lassitude may accompany the symptoms of nausea and vomiting, or may occur alone.

Until recently the drug most commonly used in the control of these side-effects was pyridoxine (vitamin B₆), and some authorities have claimed relief of symptoms in a large percentage of cases (Shorvon, 1949; Ellis and Stoll, 1952; Stoll, 1957).

With the advent of a number of anti-emetic drugs having a primarily central action on the "vomiting centre," the suppression of the side-effects of irradiation has become easier.

Stoll (1957) compared a number of these drugs with pyridoxine and discussed their mode of action in the treatment of irradiation sickness. Prochlorperazine was not included in this trial. The use of prochlorperazine has been investigated in the control of vomiting due to a number of unrelated causes (Gray, 1957), and has been compared with chlorpromazine and other drugs in the suppression of artificially induced vomiting in experimental animals (Ducrot and Koetschet, 1956; Boyd, 1957). Ducrot and Koetschet (1956) found that prochlorperazine was four times more effective than chlorpromazine and superior to any of the other drugs used.

As pyridoxine was found to be relatively ineffective in reducing irradiation sickness, a trial series of patients were given 10 mg. of prochlorperazine orally thrice daily before meals prior to the first exposure to irradiation, and were maintained on this dosage throughout their treatment. Of 12 patients on this regime, only one vomited and one developed slight nausea. It was decided to compare the efficacy of prochlorperazine with that of pyridoxine and an inert tablet.

Method.—For uniformity, two tablets of the particular drug were given three times a day before meals. This gave a total daily dose of 30 mg. of prochlorperazine, 60 mg. of pyridoxine, or six inert tablets. The tablets were made up in anonymity, being labelled: A, B, and C; the only person knowing which was which being the pharmacist. Patients were selected

at random, the only discrimination being that those considered unlikely to develop symptoms were excluded. At the onset of nausea or vomiting, tablets A, B, or C, 2 t.d.s., a.c., were prescribed. If after 48 hours there was no relief, in the best interests of the patient prochlorperazine, 10 mg., t.d.s., a.c., was substituted for the unknown tablets. The effect of the tablets on anorexia and lassitude was also noted.

Results

Observations were made of 57 patients who were expected to suffer side-effects from therapeutic irradiation; 12 did not develop symptoms. The results of treating the remaining 45 during the first 48 hours are shown in Table I.

From these figures: $\chi^2 = 12.4$. D.F. = 4. $P < 0.02$. A probability of this order is significant.

The 20 patients showing only partial or no improvement were changed to prochlorperazine after 48 hours. In 11 cases the symptoms were completely relieved. There was some improvement in five cases, but in the remaining four there was no improvement. Two of these had, of course, already had prochlorperazine. These resistant cases were finally improved by giving a combination of prochlorperazine and chlorpromazine, but in two cases having a marked psychical element phenobarbitone had also to be given.

TABLE I.—Effect of Prochlorperazine, Pyridoxine, and Inert Tablets on Nausea and Vomiting in 45 Patients Receiving Therapeutic Irradiation

Drug	No. of Cases	Complete Alleviation	Partial Improvement	No Improvement
A (inert) ..	15	5	4	6
B (prochlorperazine) ..	16	14	2	Nil
C (pyridoxine) ..	14	6	5	3

TABLE II.—Analysis of Effect of Prochlorperazine, Pyridoxine, and Inert Tablets on Alleviating Side-effects of Irradiation, Including Anorexia and Lassitude

Drug:	B Prochlorperazine	C Pyridoxine	A Inert Tablets
Total No. of cases treated	34	14	15
Cases improved	25 (73.5%)	5 (36%)	6 (40%)
Complete relief of all symptoms ..	5 (15%)	4 (29%)	2 (13%)
Lassitude present ..	18 (53%)	2 (14%)	2 (13%)
Mild anorexia present ..	14 (41%)	2 (14%)	Nil
Marked anorexia present ..	6 (18%)	Nil	3 (20%)
Mild nausea present ..	4 (12%)	2 (14%)	2 (13%)

Toxicity

In the dosage used (30 mg. a day) prochlorperazine is remarkably free from toxic effects. In higher doses it may cause slight drowsiness and interference with accommodation (Gray, 1957), and in doses of more than 60 mg. a day confusion, dizziness, and fainting have been reported (Friend and McLemore, 1957). The manufacturers describe more bizarre forms of toxic effects occasionally encountered with very large doses, but none of these occurred in the trial described.

In this series it is difficult to evaluate whether any drowsiness encountered was due to the drug used or to the effects of irradiation. Apart from the occurrence of slight drowsiness in a small number of cases, there was no evidence of any undesirable constitutional side-effects in any of the patients treated.

Regular blood examinations showed no appreciable change in the cell count that could not be attributed to irradiation except in one case. This was a female patient aged 72 receiving post-operative irradiation following a

local mastectomy for carcinoma of the breast. The total white-cell count dropped to 1,200 after one week of irradiation and treatment with prochlorperazine. After about two weeks at this level there was a gradual return to normal, in spite of continuing both the irradiation and the prochlorperazine.

No other toxic effects were encountered.

Summary and Conclusions

In a controlled trial involving 45 patients receiving therapeutic irradiation, prochlorperazine has been found significantly more effective in relieving radiation sickness than pyridoxine or inert tablets.

The following conclusions may be drawn from the small series described: (1) Prochlorperazine is more effective in relieving the toxic symptoms of irradiation than pyridoxine or an inert tablet. (2) In the dosage of prochlorperazine used (10 mg. t.d.s.) there were no material side-effects; marked drowsiness as occurs with so many other anti-emetic drugs was not seen. (3) For maximum benefit it is best to begin giving prochlorperazine with the first exposure to irradiation, or at least as soon as possible after the onset of symptoms.

I thank Dr. I. Churchill Davidson for allowing me to conduct this trial on his patients and for his helpful suggestions and criticisms.

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Preliminary Communications

"Debricin": A New Agent for Wound Debridement

The presence of necrotic tissue in an open wound is an obstacle to healing. Infection persists, granulations are slow to appear, and epithelization is delayed. For small and superficial sloughs, routine treatment with local antiseptics and rest for the affected part usually provide sufficient help for the natural reparative processes to allow healing to occur within a reasonably short period of time. When a slough is of greater extent in depth or size, healing by this means is slow and may extend over many weeks, and it may also prevent the early application of a skin graft in suitable cases. For this reason, surgical excision of deep and extensive sloughs is often preferred, and may be combined with immediate skin-grafting.

Another way of tackling this problem is to rely on one of a variety of enzymatic preparations, application of which accelerates the removal of necrotic tissue and sloughs, which are broken up by proteolytic digestion; thus the period of healing or of wound preparation prior to a plastic procedure is greatly shortened. This approach has been investigated by others. Morani (1953) reported great improvement in six cases of chronic sloughing lesions using a trypsin preparation. A mixture of trypsin and chymotrypsin was used by Reiser, Roettig, and Curtis (1953), who found very rapid clearance of sloughs in similar lesions. Prueter, Stein,