may cause confusion, particularly with inexperienced staff, so we prefer the occultest tablet test for ward use, in spite of its greater sensitivity, which will presumably produce a higher incidence of false-positive results. If this test is used on specimens from patients on a normal diet, weakly positive results are of doubtful significance, but positive results are probably significant, and strongly positive results are highly significant.

Summary

A modification of the orthotolidine test for faecal occult blood is described. It may be used when the patient is on a normal diet, provided foods containing particularly large amounts of blood—for example, liver—are excluded. The test is much less sensitive than the standard orthotolidine test. Strongly positive results are significant, but false-positive and weakly positive results may be expected in up to about 10% of cases.

The occultest tablet test is suggested as a suitable alternative, particularly for ward use.

My thanks are due to Dr. H. Loewenthal, senior pathologist, for his advice and encouragement; to the medical and nursing staff of the Enfield Hospital Group who assisted in the collection of the specimens; and to Messrs. Ames (London) Ltd. for the supply of hematest tablets.

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INDICATIONS FOR USE OF IPRONIAZID IN PSYCHIATRIC PRACTICE

BY

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Iproniazid (" marsilid "; 1-*iso*nicotinyl-2-*iso*propylhydrazine phosphate) is a derivative of isoniazid and was originally introduced because of its similar activity on tubercle bacilli. In the early clinical trials of iproniazid in pulmonary tuberculosis, using doses of 300 mg. daily, increased appetite associated with large gains in weight was noticed, accompanied in a proportion of patients by mood changes which sometimes developed into frank psychosis. These changes were reversible on stopping the drug (Kamman *et al.*, 1953; Crane, 1956).

The mechanism of this reaction is at present not fully understood, but it is thought to arise from the action of iproniazid as an inhibitor of monoamine oxidase. Iproniazid in animal experiments has been shown to produce an elevation of the 5-hydroxytryptamine (serotonin) level in the brain, and, if injected into rabbits over two to three days, to lead to a state of excitement.

These findings have aroused interest in the effect of iproniazid on depressive and allied affective states in man, and a number of papers have been published and a symposium was held in New York in November, 1957, on the use of iproniazid in psychiatric diseases. It seems to be generally agreed that iproniazid is of value in the treatment of depressive illness, but claims have been made that as many as 75% of patients do as well, if not better, with it than with electric convulsion therapy (Kline, 1957). Electric convulsion therapy is widely used in the treatment of depression at the present time, and such claims, if confirmed, would obviously have far-reaching effects. A pilot trial has therefore been undertaken in this department to determine its value in depressive and allied psychiatric disorders.

Method

So far 131 cases have been treated with iproniazid. They comprise 99 depressions, 24 anxiety states, 6 obsessional states, and 2 cases of anorexia nervosa. Cases were at first unselected, but as the indications for the use of iproniazid became known the tendency was to choose those most likely to be helped. Both in-patients and out-patients were treated, but the majority were out-patients, these being seen once a week for the first month and then at progressively longer intervals.

Each patient was started on 150 mg. (three tablets) daily, in three divided doses, but was warned to reduce the drug to 100 mg. daily if side-effects developed, and to stop altogether if these continued. This daily dosage was continued for four weeks, and then reduced by 50 mg. at intervals of a month, until either the patient was off the drug completely or symptoms of depression again began to be experienced. If this happened the daily dosage of iproniazid was increased by 50 mg. weekly until the patient was symptom-free, and maintained for a further month before again being reduced.

The results are shown in the Table.

Results of Treatment

Type of Patient	No.	Recovered	Improved	No Effect	Worse (Agitation and Tension Increased)
Depression with weight loss	67	15	22	21	9
" without weight loss	32	—	1	13	18
Anxiety state	24	—	—	—	24
Obsessional states	6	—	—	6	—
Anorexia nervosa	2	—	—	2	—

Discussion

Iproniazid was found to be of value in the treatment of certain patients showing symptoms of mild depression associated with loss in weight. There was a time-lag of between 7 and 10 days after starting the treatment before improvement was noticed, the patient then reporting that he had an increased appetite, a sense of " couldn't care less," and more energy. Some of these mild depressive illnesses had continued for several years, adversely affecting work capacity and family happiness. Amphetamine and its derivatives had had an immediate but short-lived uplifting effect. E.C.T. had caused temporary or partial improvement only. The natural course of the illness is to progress to full recovery, and this makes the interpretation of any treatment of depressive illness particularly difficult.

Many of the patients in this trial had been ill for over a year, and may therefore have been remitting naturally. None the less, iproniazid undoubtedly helped some to improve, and this was confirmed by the return of symptoms that sometimes occurred when the drug was reduced or stopped. The advantage of iproniazid over amphetamine or E.C.T. in this type of depression is that improvement appears to be maintained as long as the drug is given in adequate dosage. It thus seems possible that the course of some of these mild but obstinate depressive illnesses associated with loss of weight, which in these trials included both manic-depressive and involutional groups, may be shortened by treatment with iproniazid. Severe depressions, however, were not helped and depressive states associated with agitation were often made worse, and E.C.T. was usually

needed without delay. Two such patients, treated with iproniazid, had to be admitted to hospital hurriedly because of fear of suicide.

It is interesting to note that only one patient who complained of depression but had lost no weight was improved by iproniazid, and that a number of others stated that their symptoms were made worse. This is in contrast with the much better results in those who had lost weight. It was also noticed that E.C.T., either previous or subsequent to treatment with iproniazid, also tended to aggravate the symptoms of some of those patients who had lost no weight and were made worse by iproniazid. It is possible that an underlying chronic state of tension was present in many of these patients, and this may be why they felt worse with both treatments. Iproniazid certainly caused obvious anxiety states to flare up in a remarkable way after two or three days of treatment, and, in fact, a trial of 150 mg. of iproniazid daily for three days was often useful in differentiating between a tension state and a true depression; patients complained of intense anxiety, weakness, palpitations, and an increase in phobias, but if treatment was continued long enough a number did notice increasing appetite.

Obsessional states, like anxiety states, were not helped, and two cases of anorexia nervosa, given iproniazid to the limit of tolerance, failed to increase their weight and noticed no change in appetite on out-patient treatment.

Side-effects.—These depended largely upon the dosage, and occurred increasingly when 150 mg. or more of iproniazid a day was given. Constipation, impotence, decreased need of sleep, dryness of mouth, and blurring of vision were all reported. These are common symptoms in depression, but seemed to be caused by the drug, since they disappeared on stopping it; and they would sometimes be seen despite improvement in successful cases. Six patients had symptoms of postural hypotension, such as sudden dizziness and vertigo on standing, and two patients actually had attacks of fainting until they stopped the drug. Systolic blood pressure showed a drop of only 10–20 mm. from normal, but patients were free from side-effects at the time of measurement. An interesting side-effect was noticed in patients receiving modified insulin. Those who had previously had 20 or more units of soluble insulin without hypoglycaemic reactions began, two or three days after starting iproniazid, to become drowsy and difficult to arouse. One woman at first sight seemed to have lapsed into coma, but there was no sweating, and blood-sugar estimates were within normal limits.

Conclusion

Iproniazid is of value in the treatment of mild depression associated with loss of weight, and will often lead to a dramatic improvement in suitable cases. It is of no use in severe depression, and may be dangerous if given to agitated patients, for whom electric convulsion therapy is usually needed without delay. Indiscriminate use of iproniazid by practitioners is therefore to be avoided, but in carefully selected cases it is well worth a trial.

I thank Dr. William Sargant for his encouragement and advice, and Dr. Mary Briggs, of Roche Products, for a generous supply of marsilid.

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The St. Marylebone Operatic Society has presented £118 to the National Society for Cancer Relief as a result of two performances of *The Mikado* at the St. Pancras Town Hall last January. The Society will be presenting *The Gondoliers* in September and the proceeds will again be devoted to the National Society for Cancer Relief.

Medical Memorandum

Calcinosis Universalis

Atkinson and Parkes Weber (1938) divided cases of calcinosis into two main groups—one in which the deposits of calcareous material are confined to the skin and subjacent tissues, and which they termed "calcinosis circumscripta," and a second or universal type, "calcinosis universalis," in which the distribution is more widespread and the degree of severity of the lesions varies greatly. The skin, muscle, tendon fascia, and nerves may be involved. Although both forms are similar pathologically, they differ clinically in their prognosis. Death has occurred in the first variety, but it is in the second form that this outcome is the invariable rule, although many years may pass before the patient finally succumbs.

The first authentic case of calcinosis was reported by Teissier in 1876, but the condition was first reported by Holländer as occurring in 1654. In 1902 Hutchinson described the first case in the English literature. The rarity of the condition justifies the publication of the following case.

CASE REPORT

A married woman was first seen in July, 1943, at the age of 58. Apart from "rheumatism" at 18, she had never had a day's illness until 1937, when, in her 52nd year, she began to suffer from burning pain in the thumb and second finger of her right hand. The pain, which was constant, was aggravated by manual activity and radiated upwards on the volar aspect of the forearm towards the elbow. Within a matter of weeks all fingers of the right hand were affected, and corresponding symptoms had appeared on the left side, but the pain remained localized to the fingers. Walking was no longer a pleasure because of a feeling of heaviness in the feet, while even the slightest exertion caused fatigue. Some months later intense itching of the skin of the upper chest was noted, accompanied by a glossiness of the skin, which persisted after disappearance of the itch a few weeks later. During this period her nails had become brittle and the tips of her fingers bulbous.

Within five months of the onset of the first symptoms, hard white nodules had appeared deep in the pulp of the fingers. These nodules gradually worked towards the surface, causing intense pain due to a local inflammatory reaction. When the overlying skin broke down, the hard central core was discharged, with immediate relief of pain, after which healing took place uninterruptedly. About this time larger masses were seen to have formed over the left patella and right shin, and on the lateral aspects of both heels. While some of these accumulations continued to increase in size gradually, others remained unchanged for months. As these calcareous tumours increased in size and number there was a corresponding loss of weight and of physical vigour.

When first seen, she was a healthy-looking woman of 58, of average height and nutrition, in whom the skin of the face, arms, and legs showed a dark pigmentation. The finger-nails were short and brittle, and the terminal phalanges bulbous and somewhat truncated. Widely scattered in and under the skin of the hands, elbows, legs, and feet were

Calcium Excretion

	Total Calcium Intake	Urinary Output	Output in Faeces	Retained
First 3-day period	2·1 g.	199 mg.	1·2 g.	0·7 g.
Second ,, ,, ...	2·1 g.	107 mg.	1·18 g.	0·8 g.