diagnosis may be confused by the excessive phosphate excretion that may occasionally be found in multiple myelomatosis, associated usually with the excretion of myeloma globulin.

FIG. 1.—Relation between plasma inorganic phosphate and rate of urinary phosphate excretion. Control cases. (Herbert, 1951.) ● Miscellaneous disease without renal damage or disturbance of acid-base balance. ○ Non-metabolic diseases of bone. The area within which these points fall defines the normal limits indicated by the two straight lines.

FIG. 2.—Relation between plasma inorganic phosphate and rate of urinary phosphate excretion. Hyperparathyroidism and hypoparathyroidism. (Herbert, 1951.) ● Hyperparathyroidism, untreated. ○ Hyperparathyroidism, post-operative. + Hypoparathyroidism. The continuous lines represent the normal limits as in Fig. 1. The dotted lines connect consecutive data on individual cases, in the sequence indicated by the arrows.

In the absence of complicating features, we placed great reliance upon the relationship of the rate of urinary phosphate excretion to the plasma phosphate level. The normal relationship is shown (Fig. 1) and compared with that found in primary hyperparathyroidism (Fig. 2). Figs. 1 and 2 show that a urinary phosphate excretion of 0.4 mg. a minute falls outside normal limits when the plasma phosphate level is 2 mg. per 100 ml.

Since the diagrams were originally published (Herbert, 1951), phosphate excretions in a number of patients suffering from hyperparathyroidism have been investigated. No unexpected results were found (Herbert, 1956, personal communication).

It would appear from our experience, and that of McGeown and Montgomery (1956), that the interpretation of

urinary phosphate excretions can be difficult. They are not necessarily an index of parathyroid activity, even in the apparently uncomplicated case.

The presence of anaemia did not influence the diagnosis. It occurs in most patients suffering from myelomatosis, but in primary hyperparathyroidism, fibrosis and cyst formation may also be associated with anaemia and leucopenia.

Post-operatively, protein (80 mg. per 100 ml.) appeared in the urine, but the heat test for Bence Jones protein was negative. The proteinuria was transient. A 24-hour urine specimen collected 10 days after operation was examined for protein concentration with a view to investigation of its electrophoretic mobility, but it contained less than 10 mg. of protein per 100 ml.

The biochemical estimations illustrate the manner in which multiple myelomatosis may occasionally simulate hyperparathyroidism. The examination of a sternal-marrow aspirate might have revealed the true diagnosis, and this investigation should be made if a diagnosis of multiple myelomatosis is at all likely.

Summary

A case of multiple myelomatosis is reported, presenting many of the features of hyperparathyroidism. The absence of serum protein changes and proteinuria led to an erroneous diagnosis of parathyroid adenoma. A possible diagnosis of bony metastases from a carcinoma of the thyroid had also to be considered.

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PROPANTHELINE BROMIDE IN PRIMARY DYSMENORRHOEA

BY

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Primary dysmenorrhoea is such a common condition and causes such invalidism that any treatment which promises relief to even some patients deserves investigation. Secondary dysmenorrhoea due to disease of the pelvic organs does not come within the scope of this investigation. In investigating any form of treatment it is essential that the effects of suggestion should be eliminated so far as possible by giving dummy tablets to alternate patients in a control series.

A trial of propantheline bromide ("pro-banthine") was made on these lines. Methanthelinium, then propantheline, were introduced as anticholinergic drugs for treatment of various conditions in which spasm was believed to play a part. Propantheline bromide is used extensively in the treatment of gastric and duodenal ulcers. It has also been used successfully for treatment of spasmodic conditions of the various components of the renal tract. It therefore seemed likely that it would be of value in the treatment of primary dysmenorrhoea.

Malkin (1955), in a preliminary report based on three cases in which methanthelinium was used, felt that the results justified further investigation. Ainsworth (1955) published a most favourable report in which propantheline was used: out of 36 cases all but two obtained

complete relief. His cases were taken from general practice and included at least one patient of 32 and one of 37 years. Propantheline bromide has fewer side-effects than methanthelinium, but is otherwise similar.

Clinical Trial

Before beginning the trial with a control series it was decided to try propantheline bromide in the dosage recommended by Ainsworth so that any side-effects, contraindications, or indications for varying the dosage might be discovered. It is the result of this preliminary trial that is reported here.

Dosage.—The routine described by Ainsworth was followed. This consisted of 45 mg. on the night before the period began. The following day one tablet of 15 mg. was taken at intervals of four hours, with a further 30 mg. at night. Some patients were unable to predict which was the night before the period; these patients spread out the initial dose over the first twelve hours if they were at work, or took 45 mg. as the initial dose if at home.

The ages of the 30 patients were between 15 and 29 years. All were unmarried, and, so far as was known, none had been pregnant.

Previous Treatment.—*Analgesics*: All the patients had been treated with a variety of drugs with varying degrees of relief. *Suppression of ovulation*: Three patients had been treated by suppression of ovulation by the administration of oestrogen in various forms. All three had obtained relief from treatment until it had been stopped owing to reluctance to continue hormone therapy indefinitely in young women. *Dilatation of the cervix*: Four patients had undergone the operation of dilatation of the cervix without permanent relief.

Results

The results are very disappointing. No patient obtained complete relief. Few of the patients admitted to experiencing any diminution of the pain. Most of them complained of some dryness of the mouth, but this was not so unpleasant as to prevent them from using the tablets during two or three consecutive periods. After a trial for two or three periods none of the patients wished to continue the use of propantheline for the relief of her dysmenorrhoea. A few patients agreed to try a larger dosage, but had to stop taking the tablets on the first day owing to the unpleasant side-effects. One patient obtained relief from pain by taking four 15-mg. tablets the night before the period began, and two 15-mg. tablets every three hours on the first day of the period. This dosage produced so much dryness of the mouth, with inability to keep her eyes focused on her typing, that she was unable to do any work. Several patients complained of constipation with marked dyschezia.

Subsequent Treatment.—Two patients were treated by dilatation of the cervix, and this gave relief for at least the two subsequent periods. Five patients obtained relief from pain by the use of oestrogen to suppress ovulation. One of the five had previously obtained relief from this form of treatment. The remaining patients returned to the use of common analgesics.

In view of the failure of propantheline bromide to relieve dysmenorrhoea in these patients the trial as planned with a control series and dummy tablets was not carried out.

Conclusion

The conclusion is that propantheline bromide is of no value in the treatment of primary dysmenorrhoea.

My thanks are due to Mr. A. F. Clift and Mr. J. C. Miller for permission to treat their patients, and to Messrs. Searle for generous supplies of pro-banthine and for help with the literature.

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Medical Memoranda

Acute Systemic Reaction to Acetarsol

Acetarsol (3-acetylamino-4-hydroxyphenylarsonic acid) in pessary form is commonly used in the treatment of vaginitis due to *Trichomonas vaginalis* and *Candida albicans* infections. On occasion these pessaries have caused local skin reactions, affecting the vulva and inner aspects of the thighs and presenting as a contact dermatitis, the condition clearing up on stopping treatment. More severe reactions affecting the skin have been described. Peck (1954) reported a case of generalized maculo-papular eruption following four weeks' treatment of a vaginal discharge, two 4-gr. (220-mg.) acetarsol pessaries having been inserted nightly. This skin reaction deteriorated in spite of antihistamine preparations, and an acute exfoliative dermatitis developed. Campbell (1937), Orchard (1951), and Long (1937) have described somewhat similar skin reactions.

More severe systemic reactions affecting other organs have rarely occurred, although Crosswell (1951) described a case of angioneurotic oedema and jaundice after treatment with acetarsol pessaries. In the following case a widespread systemic reaction followed the use of acetarsol pessaries.

CASE HISTORY

A woman aged 23 was admitted to hospital in a state of collapse, mentally confused, and complaining of severe abdominal pain. She gave a history of seven days' duration, beginning with vague symptoms of anorexia, some nausea, and general debility. Two days later she developed a headache and generalized aches and pains, which persisted, to be followed in a further two days by vomiting, and simultaneously a rash appeared on the arms; the next day this became generalized and was described as rubella by her doctor. The vomiting persisted, and was said to contain a brownish material. A slight rectal and vaginal discharge of a brownish colour was also present. On the day before admission she complained that her arms and legs were cold at times. She was reported to have been mentally confused. For three weeks before admission she had been treating a vaginal discharge with acetarsol, inserting two 4-gr. (220-mg.) pessaries night and morning, as directed.

She had had two mild attacks of jaundice as a child; the latter of these she remembers as being a very mild illness, keeping her from school for one week. She has one child, a boy of 14 months; pregnancy and labour were normal.

The patient, a well-nourished woman, was admitted in a moribund condition. Her hands and feet were cold and cyanosed and her arms and legs were tense, swollen, and erythematous. The redness of the skin of the limbs contrasted vividly with the deep cyanosis of the hands and feet. A diffuse purpuric type of rash was present on the trunk. The abdomen was tender all over, with marked guarding below the umbilicus. The tongue was dry and coated. The respirations were shallow and rapid, but no abnormal signs were present in the chest. The radial pulse was not palpable, and the blood pressure could not be recorded. The heart sounds were soft and rapid but regular. No abnormal signs were found in the nervous system, but the patient was dull, lethargic, and unable to remember exactly the course of her illness.

These findings were compatible with a severe state of shock associated with suprarenal failure, and accordingly she was given 200 mg. of cortisone orally and 5 min. (0.3 ml.) of adrenaline hourly for three hours. The cortisone was continued over a period of six days in doses of 200, 150, 100, 75, 50, and 25 mg. respectively. Intravenous fluids were given for three days, the choice of fluid being according to the serum electrolytes. On the fourth day the patient was able to retain fluid by mouth, and on the fifth day she had some light food. A high-protein, high-carbohydrate, low-fat diet was given, supplemented by vitamins, methionine 25 mg. daily, and iron orally. This diet was maintained