Prognosis.—Our first patient is of interest because of the long survival period. A significant feature of septal perforation is that death does not occur immediately: Edmondson and Hoxie (1942) found an average period of survival of 7.4 days. In the series of Sanders *et al.* (1956) 13% (12 patients) lived from two months to several years.

Treatment.—The general principles of treatment are based on the knowledge that the efficiency of the heart in which septal perforation has occurred has already been impaired by coronary atherosclerosis followed by myocardial infarction. The left-to-right shunt, with increased blood-flow and raised pressure in the pulmonary circulation, throws an extra strain on the ventricles, and leads to heart failure. In our first two cases the administration of digitalis was of benefit, and diuretics were of considerable help. In Case 1, after a few weeks, there was a loss of response to mercurial diuretics: chlorothiazide with potassium supplements had an immediate beneficial effect.

Summary

Three cases of ventricular septal perforation are described. The diagnosis should be considered when a patient with an acute myocardial infarction suddenly deteriorates and develops a loud blowing pansystolic murmur between the left sternal edge and apex in the fourth and fifth left intercostal spaces. Dye-dilution curves in two cases showed the presence of a left-to-right shunt.

We thank Professor J. McMichael for his advice and encouragement, Dr. D. Emslie-Smith for the phonocardiograms, and Miss E. Mason for the photographs.

REFERENCES

Briggs, J. F., and Holt, J. (1954). *Amer. Heart J.*, **47**, 926.
Cooley, D. A., Belmonte, B. A., Zeis, L. B., and Schnur, S. (1957). *Surgery*, **41**, 930.
Diaz-Rivera, R. S., and Miller, A. J. (1948). *Amer. Heart J.*, **35**, 126.
Edmondson, H. A., and Hoxie, H. J. (1942). Ibid., **24**, 719.
Gottsegen, G., Szám, I., Romoda, T., and Matheides, P. (1957). *Acta med. scand.*, **158**, 157.
Latham, P. M. (1846). *Lectures on Clinical Medicine, Comprising Diseases of the Heart*, 2nd ed., **2**, 168. Longman, London.
Maher, J. F., Mallory, G. K., and Laurenzi, G. A. (1956). *New Engl. J. Med.*, **255**, 1.
Muller, O., Humerfelt, S., Rasmussen, H., and Storstein, O. (1950). *Acta cardiol. (Brux.)*, **5**, 633.
Oakley, C., Taylor, S., Wilcken, D., Hollman, A., Goodwin, J. F., and Shillingford, J. (1960). *Brit. Heart J.*, **22**, 533.
Oblath, R. W., Levinson, D. C., and Griffith, G. C. (1952). *J. Amer. med. Ass.*, **149**, 1276.
Romanoff, H., and Cooley, D. A. (1960). *Israel med. J.*, **19**, 103.
Sanders, R. J., Kern, W. H., and Blount, S. G. (1956). *Amer. Heart J.*, **51**, 736.
Schlappi, J. C., and Landale, D. G. (1954). Ibid., **47**, 432.
Shickman, M. D., Fields, J., Pearce, M..L. (1959). *Arch. int. Med.*, **103**, 140.
Swan, H. J. C., and Wood, E. H. (1957). *Proc. Mayo Clin.*, **32**, 486.
Wood, F. C., and Livezey, M. M. (1942). *Amer. Heart J.*, **24**, 807.
Zucker, R., Leibowitz, S., Brody, H., and Sussman, R. M. (1952). *Arch. intern. Med.*, **89**, 899.

About one child in every 600 born in this country is a mongol, and the National Association for Mental Health has published a booklet, *A Letter to Parents of a Mongol Baby*, prepared by a children's specialist, which will be of help to those concerned with what, how, and when to tell the parents that their child suffers from this condition. (N.A.M.H., 39 Queen Anne Street, London W.1, price 1s. 3d.)

EXPERIMENTAL AND CLINICAL OBSERVATIONS ON POLDINE IN TREATMENT OF DUODENAL ULCER

BY

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The gastric secretion of acid by a patient with duodenal ulcer in response to a glucose test meal is about halved if an effective dose of poldine methosulphate (" nacton ") is taken beforehand (Douthwaite and Hunt, 1958). The drug also reduces gastric secretion of acid in response to a large dose of histamine (R. Seidelin, 1960, personal communication). These observations, made under strictly controlled experimental conditions, suggest that the drug might be useful in the treatment of duodenal ulcer. To investigate this possibility, the effect of the drug on the acidity of gastric contents has been investigated under the conditions of clinical use, and the drug has been subjected to a small controlled therapeutic trial.

Experimental Observations

Observations are reported on 16 patients with an uncomplicated radiologically proved duodenal ulcer. All were admitted to hospital, they were allowed up, and drugs other than poldine and sedatives were withheld unless stated otherwise. The individual dose of poldine for each patient was found by giving increasing doses until side-effects appeared. The initial dose given was 7.5 mg. daily, divided into three doses, or 12.5 mg., divided into five doses, and the total dose was increased by 7.5 or 12.5 mg. each day. If the first side-effects to appear were trivial the dose was further increased until definite side-effects developed. The dose just below that producing uncomfortable side-effects was defined as the " optimum " dose.

On the days of the test, samples of gastric contents were withdrawn every hour, on the hour, for 24 hours through a fine naso-gastric tube placed radiologically so that the aspiration holes lay in the likely position of the gastric antrum. The *p*H of the samples was measured with a sealed glass electrode. Doses of the drug, food, and drinks were given immediately after a sample was withdrawn.

Gastric Acidity of Patients Taking Gastric-type Diet

The effect of different doses of poldine was studied under these conditions in 16 patients. Observations made on a control day without poldine were compared with observations made on days when the drug was given. The control observations were made first in 13 patients and last in three patients. Four patients were studied while the dose of poldine was being increased and at a time when they were experiencing no side-effects from the drug; two patients were studied on one day at daily doses of 30 and 40 mg. respectively, the other two patients were studied on two days at daily doses of 30 and 60 mg., 30 and 90 mg., respectively. Of 10 patients taking the drug in the optimum dose, nine received five daily doses and the other patient three daily doses. Four of these patients had received the drug continuously in the optimum dose for periods of 1, 4, 9, and 12 days respectively before the test. The results in these four

patients did not differ from those in patients who began the optimum dose (found by previous trial) on the day of the test. Three patients were studied at a time when they were experiencing severe side-effects from the drug. The results from all the patients are combined in Figs. 1 and 2. Each section of the histogram in Fig. 1 shows the total number of samples in a particular *p*H range on the control day and on the day when the drug was given. Fig. 2 shows the mean acidity on an arithmetic scale at each hour of the day. It is clear that in patients taking a ward gastric-type diet, poldine did not affect the acidity of the gastric contents whether given in a dose insufficient to produce side-effects, in the optimum dose, or in a dose producing side-effects too severe to be tolerated as a maintenance treatment.

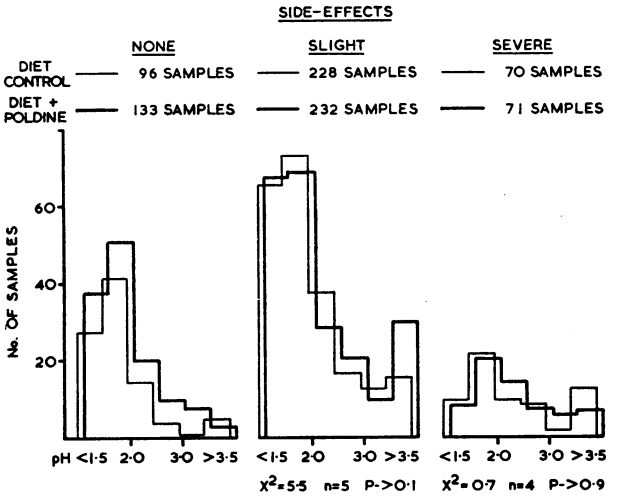

FIG. 1.—Number of samples in different *p*H ranges on the day when poldine was given compared to the control day. No difference between the two days is apparent even when poldine was given in a dose large enough to produce severe side-effects. Differences between the distribution of the samples have been assessed by the χ^2 test except in the series with no side-effects, where two observations at different doses of poldine were made in two of the four patients (n=5, unless the number of samples in any range was small, when two adjacent ranges were combined).

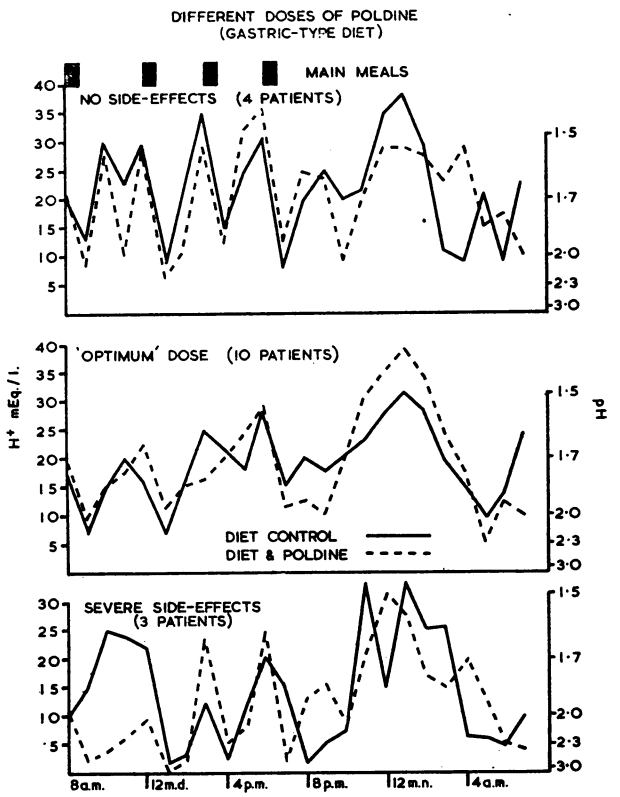

FIG. 2.—Mean acidity at each hour of the day on the day when poldine was given compared with the control day.

Gastric Acidity Under Special Dietary Conditions

Some other antisecretory drugs have been shown to lower gastric acidity, as measured by the sampling technique, when patients take hourly drinks of a milk–cream mixture without other food. The effect of poldine under these conditions has been compared with the effect when the same patients took a standard diet. Four patients were each studied during four 24-hour periods: hourly milk–cream drinks, with and without poldine; and on the diet, with and without poldine. The order of these 24-hour periods was varied from patient to patient in a latin-square pattern. Details of the method employed and the standard diet used are described elsewhere (Bingle and Lennard-Jones, 1960). Poldine was given in the optimum dose, five times daily. The

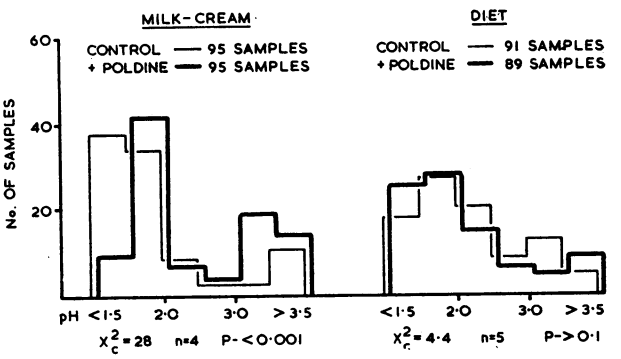

FIG. 3.—Distribution of samples in different *p*H ranges when patients took poldine in the "optimum" dose with hourly milk–cream drinks and with a standard bland diet. There was a significant (P<0.001) reduction in the proportion of samples *p*H<1.5 when patients took poldine with milk–cream drinks.

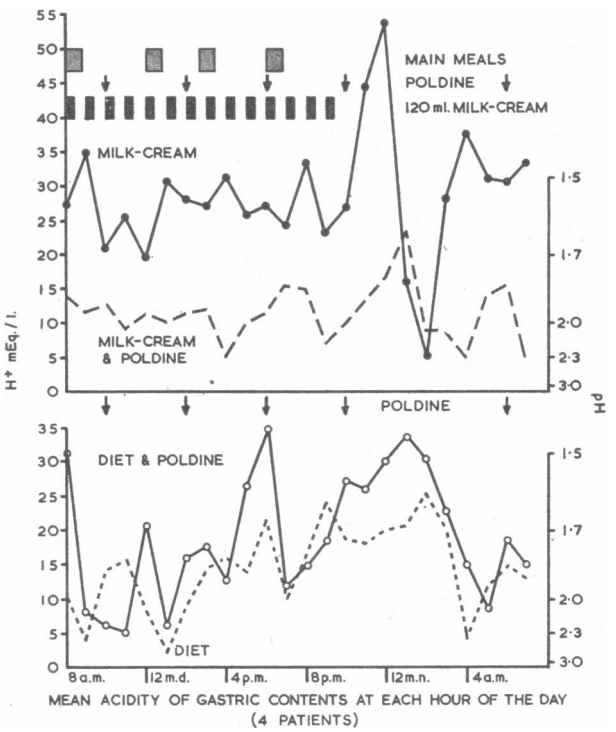

FIG. 4.—Mean acidity at each hour of the day when poldine was given with milk–cream drinks and with diet.

results, depicted in Figs. 3 and 4, show that there was a significant ($P<0.001$) reduction in the number of very acid samples, below *p*H 1.5, when milk–cream drinks were taken with poldine and a corresponding reduction in the mean acidity throughout the day. There was no suggestion of reduced acidity when the same patients took the diet.

Observations on Gastric Emptying at Night

By giving two charcoal tablets at 10 p.m. and observing the presence or absence of charcoal in subsequent samples it is possible to gain some information about gastric emptying. The accuracy of the method is limited by the apparent tendency of the charcoal to sediment, so that it may not appear in samples early during the night, and by the difficulty of determining the end-point. In this study the end-point has been taken as the last sample containing much charcoal, although traces of charcoal may appear in several subsequent samples. The results of 15 observations in eight patients are shown in Fig. 5. It will be seen that charcoal generally persisted longer when poldine was taken in the optimum dose. The mean time was 3.4 hours on the control day and 6.1 hours when the drug was taken; the difference of 2.7 hours is significant ($P<0.001$).

Gastric Acidity in Patients Taking a Standard Diet and Alkali

A drug which reduces gastric secretion, gastric motility, or both is likely to increase the effectiveness of alkali given by mouth. This has been investigated in three patients by giving them repeated small doses of alkali—enough to reduce gastric acidity a little—and then adding poldine to see if acidity was reduced further. The dose of tab. mag. trisil. co., sucked between meals from 7 a.m. to 9 p.m., which was just sufficient slightly to reduce gastric acidity, was found for each patient by preliminary experiment. After control observations had been made, the effect of adding poldine to this regime in optimum dose, five times daily, was studied. The same patients were also given a large dose of alkali at 10 p.m. to see if poldine prolonged its effect. The results are shown in Figs. 6, 7, and 8.

During the day, between 7 a.m. and 9 p.m., poldine apparently augmented the effect of the alkali, but there is nothing to suggest that poldine prolonged the effect of the dose of alkali given at bedtime.

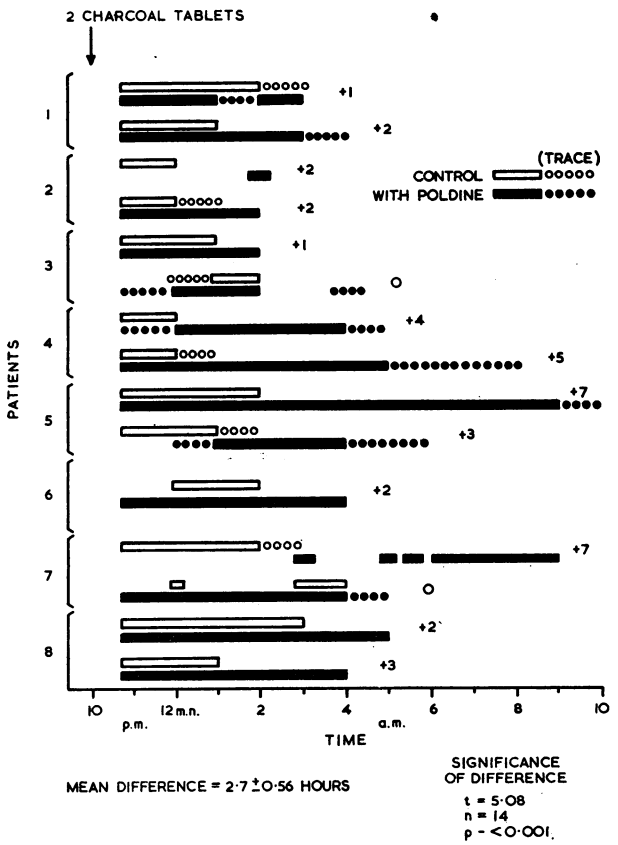

FIG. 5.—Diagram showing times at which charcoal was present in nocturnal samples after two charcoal tablets had been given at 10 p.m. 15 observations in eight patients. Charcoal persisted significantly ($P<0.001$) longer when poldine was given in optimum dose than when poldine was not given.

A Controlled Therapeutic Trial

To be clinically useful a new remedy for duodenal ulcer should succeed where simpler measures have failed. For this reason the patients selected for this trial were those in whom simple measures had either failed to control the pain from the ulcer or had failed to prevent frequent exacerbations of pain.

Design of the Trial

A double-blind trial was planned but proved unworkable in practice, since the active tablet gave rise to marked side-effects but the placebo did not. Patients

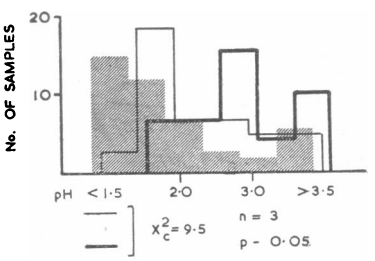

FIG. 6.—Number of samples in different *p*H ranges between 7 a.m. and 9 p.m. when patients took a standard diet (shaded area), the diet with a regular antacid (thin line), and diet with a combination of antacid and poldine in optimum dose (thick line). Poldine apparently augmented the effect of the antacid.

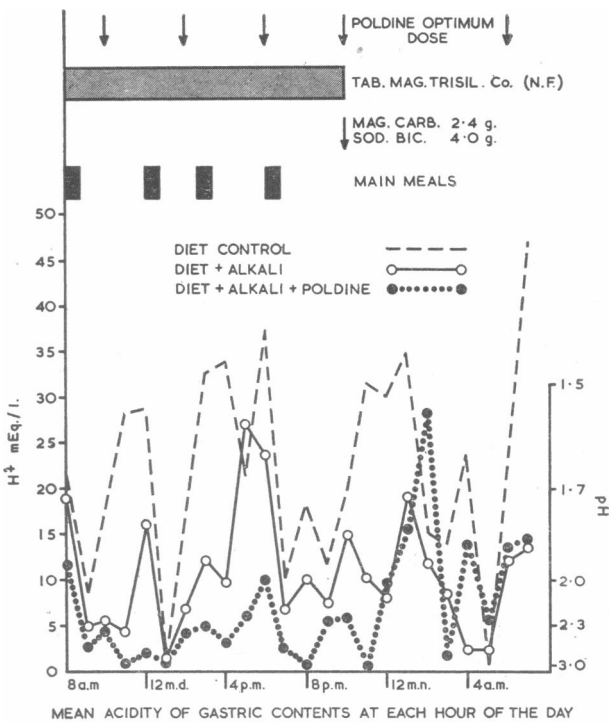

FIG. 7.—Mean acidity at each hour of the day with diet alone, diet and antacid, and diet with a combination of antacid and poldine in optimum dose.

in whom a recent barium-meal examination showed a duodenal-ulcer crater without delayed gastric emptying, and who were regarded as suitable because simple treatment had failed, were invited to enter a trial of two new remedies for their ulcer. Details about the 11 patients who completed the trial are set out in Table I. The two drugs used were poldine and an identical control tablet. The patients were given much personal attention and advised about alteration of their mode of life if this seemed necessary. In addition to the treatment under trial, alkalis were given to control pain, and sedatives were given if indicated. The trial lasted six months, and each trial tablet was given for three months, so that every patient who completed the trial acted as his own control; the order in which the treatments were given was randomized. The patients were warned that the trial would initially involve weekly visits to the clinic while the correct dose of the drug was being found and that the trial involved treatment for three months with the correct dose of each of the two drugs.

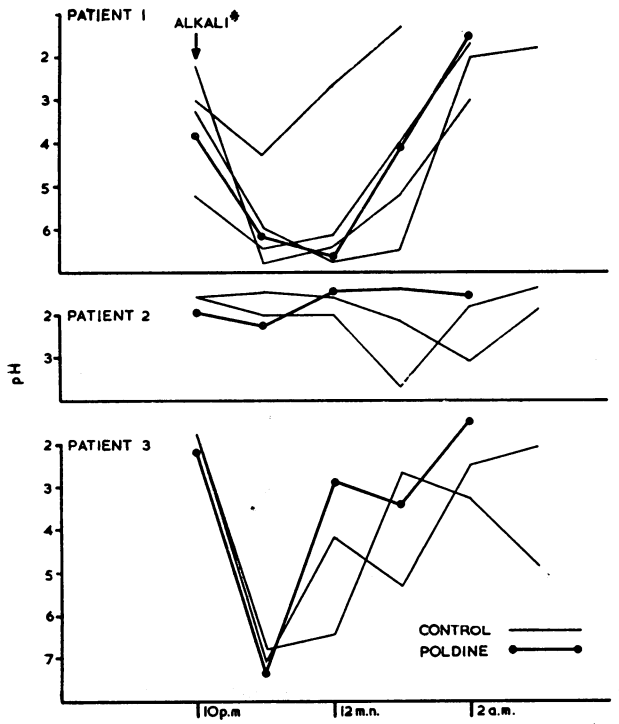

FIG. 8.—*p*H of nocturnal gastric samples in three patients after doses of alkali (mag. carb. 2.4 g. and sod. bicarb. 4 g.) at 10 p.m. with and without poldine in optimum dose.

The drugs were given in a dose of 7.5 mg. daily, divided into three doses, for the first week. Thereafter patients were seen weekly, and at each visit the daily dose was raised by increments of 7.5 mg. and later of 15 mg. daily until side-effects appeared or until a maximum of 60 mg. daily was reached. When the optimum dose or, if no side-effects appeared, 60 mg. daily was reached the trial began. The dose often needed slight alteration from visit to visit; it was increased if tolerance developed, or lowered if side-effects became severe. Table I shows that all the patients given the control tablet took 60 mg. daily, while no patient could take more than 45 mg. daily of the active tablet.

Assessment of Results

The results of treatment were judged by the following criteria:

Pain.—An effective drug should rapidly relieve pain and prevent its recurrence. Two changes were therefore noted: improvement of severe symptoms present at the beginning of treatment and the recurrence of severe symptoms during treatment.

Time Off Work on Account of Ulcer Dyspepsia.—Absence of whole days only was noted.

Barium-meal Findings.—A barium-meal examination was performed at the end of each treatment. The radiologist examined only the duodenum so as to reduce irradiation, and he reported on the presence or absence of an ulcer crater. Previous attempts to measure the size of the crater proved unreliable (C. F. Hutton, 1958, personal communication).

Patients' Preference.—Patients who completed treatment with both remedies were asked which they thought was the better.

Results

A summary of the results is shown in Table II. Eleven patients, out of 18 who entered the trial, completed treatment for three months with both active and placebo tablets. Four patients defaulted—two after the first out-patient visit, one after the third visit, and one during a severe exacerbation of pain two months after entering the trial. Three patients required admission to hospital before the trial was completed—two because of failure to control the ulcer dyspepsia as an out-patient and one for incidental illness.

The two treatments gave similar results by all the criteria used. Perhaps the most significant finding is that an exacerbation of symptoms occurred with equal frequency whether patients were receiving optimum doses of poldine or the placebo. The trial was deliberately undertaken, using alkalis for relief of pain

TABLE I.—*Details of Patients who Completed the Trial*

Case No.	Age	Sex	Length of History	First Treatment	Control			Poldine		
					Dose (mg. day)	Side-effects	Result	Dose (mg. day)	Side-effects	Result
1	34	M	2 years	B	60	None	Exacerbation	45	Dry mouth	Exacerbation
2	25	M	5 ,,	B	60	,,	Well	30	,, ,, hesitancy, constipation	,,
3	39	M	8 ,,	A	60	Dry mouth	Exacerbation	30	,, ,,	Well
4	54	M	1½ ,,	A	40–60	"Upset him"	,,	30	Dry mouth	Failed to control pain
5	37	M	1½ ,,	B	60	None	,,	15	,, ,,	Well
6	49	F	13 ,,	A	30–60	Dry mouth	Well	15	,, ,,	,,
7	25	M	8 ,,	B	60	None	Initial symptoms controlled	22·5	Very severe* hesitancy and constipation	Exacerbation
8	41	F	8 ,,	A	60	,,	Well	12	Dry mouth	,,
9	39	M	2 ,,	B	60	,,	Exacerbation	45	,, ,, hesitancy	Initial symptoms controlled
10	49	M	8 ,,	B	60	,,	,,	30–45	,, ,, blurred vision	Well
11	54	F	14 ,,	A	60	,,	Well	45	Dry mouth, hesitancy, constipation	Exacerbation

* See text for details (Case III).

only, this being the common practice. The experimental evidence already presented suggests that poldine might be beneficial if used in conjunction with large doses of alkali; this possibility has not been investigated.

TABLE II.—*Results of Treatment*

	Control	Poldine
Treatment Completed		
No. of patients	11	11
Relief of initial symptoms* within six weeks	1	1
Failure to relieve ,, six weeks	0	1
Exacerbation during treatment	6	5
Lost time from work	4	2
Ulcer crater demonstrated at end of treatment	7	9
Patients' preference (without preference = 2)	5	4
Treatment Incomplete		
Failure to control symptoms Admitted to hospital	1	1
Other illness Admitted to hospital	0	1
Defaulted	2	2

* Most patients were symptom-free when the trials began and only three patients were suffering pain at this time.

Observations on Side-Effects, Tolerance, and Cumulation

During the course of this study the optimum dose of poldine has been established in 14 women and 22 men.

A wide range of tolerance to the drug was noted, as shown in Table III. The side-effects complained of were those of parasympathetic inhibition, the commonest

TABLE III.—*Number of Patients for Whom the Optimum Dose of Poldine was Established in Different Dose Ranges*

Dose range (mg./day)	<10	11–20	21–30	31–50	51–75	76–100	>100
No. of patients	3	3	10	10	7	2	1

being dry mouth (26), hesitancy of urination (17), constipation (12), and blurred vision (11). Other complaints were headache (3), exacerbation of ulcer dyspepsia (3), heartburn (2), stuffy nose (2), and sore eyes (2). Dryness of the mouth was the first, or among the first, of the side-effects to appear as the dose of the drug was increased in 24 patients. The urinary symptoms were often severe; they occurred in 6 women and 11 men. Several patients developed extreme slowness in passing water, with painful distension of the bladder; complete retention did not occur. The need for caution in giving poldine to elderly men is illustrated by the following case:

Case I.—A man of 74, known to have had a duodenal ulcer for 20 years, was given a single dose of poldine, 2 mg. He complained of inability to pass water during the next six hours. Previously he had noticed slight hesitancy in starting to pass urine but had no other urinary symptoms. He was able to take large doses of propantheline without trouble.

The development of tolerance to the drug was noted in four patients, and cumulation of the drug was noted in two patients. On two occasions these effects led to unpleasant reactions:

Case II.—A man of 24 took increasing doses of poldine without side-effects until a dose of 15 mg. five times daily was reached, when he noticed slight hesitancy of micturition. The drug was stopped, and 10 days later he received two doses of 15 mg. four hours apart. Immediately after the second dose he felt very dizzy and ill, with stuffy nose, headache, and total inability to read. An exacerbation of ulcer dyspepsia began on this day. After beginning with small doses again he was able to take two 15-mg. doses as before without side-effects.

Case III.—A man of 25 noticed constipation at a daily dose of 30 mg.; at 37.5 mg. severe dryness of the mouth and hesitancy of micturition developed. The dose was reduced, and he was treated with 22.5 mg. daily for six weeks without side-effects. At the end of this time he became constipated, and developed lower abdominal pain and extreme difficulty in passing urine. He stopped taking the drug and the urinary symptoms cleared over two days. An exacerbation of ulcer dyspepsia began after this episode. In retrospect it seems likely that constipation allowed cumulation of the drug.

Discussion

Contrary to expectation the results described do not support the hypothesis that poldine used alone is a beneficial treatment for duodenal ulcer. The apparent potentiation of the effect of alkali by poldine was not pursued further, since better results than those found with the combined treatment can be obtained by using a different regime of sucked antacid tablets without poldine (Lennard-Jones, 1960). A similar discrepancy between the reduction of acid secretion obtained with poldine under experimental conditions (Douthwaite and Hunt, 1958; Seidelin, 1960, personal communication) and the failure of the drug to reduce the acidity of gastric contents when patients take food has been observed with other drugs. For example, atropine reduces basal secretion of acid (Sun *et al.*, 1955) and the acid secretory response to a large dose of histamine (Clark *et al.*, 1960), yet atropine does not reduce the acidity of gastric contents when patients take food (Nicol, 1939; Thomson, 1958). A difference between results found under experimental conditions and results found under the conditions of clinical use can be cited for hexamethonium (Kay and Smith, 1951; Rowlands *et al.*, 1952), methanthelinium (Atkinson, 1954), penthienate bromide ("monodral") (Kirsner and Palmer, 1953; Thomson, 1958), and a long-acting form of propantheline bromide (Sun *et al.*, 1955; Kasich and Argyros, 1958; Bingle and Lennard-Jones, 1960).

There are two possible reasons why poldine and the other drugs reduce secretion under certain conditions but do not reduce gastric acidity when patients take food. Firstly, food is a powerful and natural stimulant to acid secretion; and, secondly, the acidity of the gastric contents depends on a number of factors besides acid secretion. Kay and Smith (1951) made the significant observation that hexamethonium decreases spontaneous gastric secretion but does not diminish acid secretion in response to meat extract. Observations on the effect of drugs made under basal conditions, therefore, may give little or no indication of the effect of the drug upon stimulated secretion. It is thought that the glucose test meal, used in the testing of poldine, stimulates gastric secretion mainly by distending the stomach, but this is only part of the stimulus applied during a normal meal. Food not only stimulates acid secretion but also buffers the acid produced. The acidity of the gastric contents depends on the time since food was last taken, on the nature and consistency of the food, on the amount of acid secreted, and on the rate at which food and acid leave the stomach. Most gastric antisecretory drugs tend to slow gastric emptying as well as reducing acid secretion; both factors influence gastric acidity (Rowlands *et al.*, 1952).

Controlled therapeutic trials in duodenal ulcer are difficult and time-consuming because of the remittent nature of the disease. It would be helpful if gastric antisecretory drugs could be assessed for a likely

therapeutic effect by a reliable experimental screening procedure before a controlled trial is considered. The gastric sampling technique under conditions as close as possible to those in which the drug is used clinically seems to offer such a method. Theoretically, the samples should be withdrawn from the duodenal bulb, but this is difficult technically. A tube placed in this position tends to move back into the stomach or on into the duodenum, and close radiographic control is needed. In practice, gastric sampling is probably adequate, since there is good evidence that gastric acidity parallels acidity in the duodenal bulb (Lopusniak and Berk, 1948; Atkinson and Henley, 1955). The difference, described here and elsewhere (Bingle and Lennard-Jones, 1960), between results obtained when patients take milk–cream drinks and take diet emphasizes the necessity of testing drugs under the actual conditions of use.

Summary

Poldine methosulphate, even in doses large enough to produce severe side-effects, did not reduce the acidity of the gastric contents of patients with duodenal ulcer taking a bland diet.

Gastric acidity was reduced by poldine under special conditions when patients took hourly drinks of milk–cream without other food.

Poldine apparently augmented the effect of a regime of regular antacid by day but did not prolong the effect of a dose of alkali at bedtime.

No therapeutic benefit from poldine in duodenal ulcer was demonstrated in a small controlled trial.

The relevance of these observations to the testing of other antisecretory drugs is discussed.

I thank Dr. E. N. Rowlands for much helpful advice; Miss P. Wilcox (in receipt of a grant from the Medical Research Council) for her assistance with the *p*H determinations; Dr. C. Hutton for performing barium-meal examinations; and Dr. Richard Doll for advice about the design of the therapeutic trial. I thank Dr. F. Avery Jones, Dr. K. E. Harris, Dr. J. C. Hawkesley, Dr. T. D. Kellock, Dr. E. E. Pochin, and Dr. J. F. Stokes for allowing me to study patients under their care. The dietetic departments at the Central Middlesex Hospital and University College Hospital gave much assistance by arranging the special diets. I thank Mr. V. K. Asta and Mrs. I. M. Prentice for the diagrams. C. L. Bencard Ltd. kindly supplied the "nacton" and control tablets used in this study.

REFERENCES

Atkinson, M. (1954). *Gastroenterology*, **26**, 288.
—— and Henley, K. S. (1955). *Clin. Sci.*, **14**, 1.
Bingle, J. P., and Lennard-Jones, J. E. (1960). *Gut*, **1**, 337.
Clark, C. G., Curnow, V. J., Murray, J. G., Stephens, F. O., and Wyllie, J. H. (1960). *J. Physiol. (Lond.)*, **153**, 61P.
Douthwaite, A. H., and Hunt, J. N. (1958). *Brit. med. J.*, **1**, 1030.
Kasich, A. M., and Argyros, T. G. (1958). *Gastroenterology*, **34**, 232.
Kay, A. W., and Smith, A. N. (1951). Ibid., **18**, 503.
Kirsner, J. B., and Palmer, W. L. (1953). *J. Amer. med. Ass.*, **151**, 798.
Lennard-Jones, J. E. (1960). *Postgrad. med. J.*, **36**, 722.
Lopusniak, M. S., and Berk, J. E. (1948). *Gastroenterology*, **11**, 891.
Nicol, B. M. (1939). *Lancet*, **2**, 881.
Rowlands, E. N., Wolff, H. H., and Atkinson, M. (1952). Ibid., **2**, 1154.
Sun, D. C. H., Shay, H., and Ciminera, J. L. (1955). *J. Amer. med. Ass.*, **158**, 713.
Thomson, T. J. (1958). *Clin. Sci.*, **17**, 701.

The Central Youth Employment Service has published a revised illustrated booklet, *Radiographer*, in the "Choice of Careers" series. (No. 41, H.M.S.O., price 1s. net.)

CLINICAL EVALUATION OF POLDINE METHOSULPHATE

BY

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AND

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Assessment of the therapeutic effectiveness of an anticholinergic drug in duodenal ulcer requires experimental demonstration of substantial inhibition of human gastric secretion, confirmation of antisecretory potency under ordinary dietary conditions, and demonstration of the ability of the drug to abolish or alleviate ulcer symptoms when used on a long-term basis. The large and growing number of drugs available in this category suggests that an antisecretory drug of undoubted benefit in the treatment of duodenal ulcer has not yet been found; indeed, the real clinical value of prolonged therapy of this type has been held in question (*British Medical Journal*, 1955). Poldine methosulphate ("nacton") has been described as a selective inhibitor of gastric secretion and has been reported on favourably by Douthwaite *et al.* (1957) and Douthwaite and Hunt (1958). They studied the effect of poldine on the volume and acid content of gastric juice and observed that acid output could usually be reduced by half without troublesome side-effects appearing.

In the present investigation the clinical value of poldine has been studied by use of the following procedures: (1) inhibition of insulin-stimulated gastric juice; (2) electrometric testing of gastric juice *p*H at two dosage levels during a 24-hour period while on normal diet; and (3) long-term "double-blind" clinical trial on out-patients. All patients had radiologically proved duodenal ulcer.

Materials and Methods

Effect on Insulin-stimulated Gastric Secretion

In six fasting male patients a small-bore stomach tube was passed and the stomach emptied by hand suction. Thereafter the patient was positioned on the left side and continuous supervised mechanical aspiration was applied at a negative pressure of 5 to 10 mm. Hg. Gastric juice aspirated for the first 15 minutes was defined as the control sample. Soluble insulin 15 units intravenously was then given and gastric juice obtained for the next 45 minutes was discarded. Juice collected in the ensuing 15-minute period represented the insulin-stimulated juice, and the free-acid content of this specimen as well as of the control sample was estimated. Several days later the test was repeated, giving poldine 1 mg. intramuscularly immediately before the 15-minute collection of insulin-stimulated juice. Between the tests no treatment had been given other than modification of the diet when necessary. One patient vomited on taking his first meal after completion of the test, and this was attributed to gastric atonicity induced by poldine. A second patient felt nauseated but did not vomit. The gastric juice was titrated against N/10 NaOH using Töpfer's double indicator, and the results were expressed in milliequivalents of hydrochloric acid.

Twenty-four-hour Test of Gastric Juice pH

A Ryle tube was passed into the stomach by the nasal route in seven male patients. The tube remained in