must have had an Ms chromosome, and the one who supplied the Ns chromosome to the children must have been MsNs. To account for the MS+ child the other parent must have been MSMs. Thus the genotypes of the S-positive children must be MSMs and MSNs respectively. The patient's husband is MsMs, and their son, who is MsNs, got Ms from his father and Ns from his mother.

This family does not open up any possibilities of detecting cross overs between the MN and Ss loci, but 123 families have now been investigated without the detection of a cross-over (Race, Sanger, Lawler, and Bertinshaw, 1949). This fact and, even more strongly, the maintenance in the general population of an uneven distribution of S and s with respect to M and N, show that crossovers must be very rare and the linkage between the loci must be comparable in closeness to that between the C, D, and E loci on the Rh chromosome. When it was found that the antibody was probably of spontaneous origin it was thought that its occurrence might be genetically determined. The sera of the patient's three S-negative siblings were therefore examined for anti-S, but none was found.

Summary

A summary of previous work on the occurrence of anti-S in human serum is given. Eight of the nine known examples other than the present one appear to be the results of immunization, and seven of them contain some form of anti-Rh.

A case is described in which anti-S seems to have occurred spontaneously and was discovered in a direct-matching test in preparation for a transfusion. The serum from this case has proved to be a valuable testing reagent for the S factor.

Addendum

While this paper was in the press the serum from a fatal transfusion reaction case was referred to the M.R.C. Blood Group Reference Laboratory; it was confirmed that it contained anti-S and no other abnormal antibody.

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The Hampstead Health Institute, which the London County Council is considering acquiring for conversion into a health centre under the National Health Service, is a large 22-roomed house in an overcrowded district of Kilburn. It was founded in 1911 by the late Mr. Thomas Hancock Nunn, and is supported by private subscription and by the rent received from certain subtenants. It runs two social clubs and an old people's club, and dances are occasionally held, and in addition it houses the local Citizens' Advice Bureau, Poor Man's Lawyer, S.S.A.F.A. and H.S.A. branch offices, and the Hampstead Association for Moral Welfare Work. An L.C.C. maternity and child-welfare clinic is open four full days a week. Dental, aural, and ophthalmic clinics are held regularly, and classes for breathing exercises and for squint meet once a week. The Minor Ailments Centre of the Institute is open every day, with a doctor present every Wednesday.

THE EFFECTS OF HEXAMETHONIUM BROMIDE ON THE STOMACH

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The following is an account of a study of the action of hexamethonium bromide (C6) on gastric secretion and motility which was undertaken in the light of a paper by Kay and Smith (1950). Working with patients suffering from duodenal ulcer, they found that a closely similar compound, hexamethonium iodide, inhibited the spontaneous secretion of hydrochloric acid to the point of achlorhydria. They also showed that the compound inhibited the secretion of acid which normally occurs in insulin-induced hypoglycaemia but did not affect that produced by histamine. They noted, too, that the drug induced a prolonged inhibition of gastric motility.

For the purposes of our investigation it was decided to use two routine and commonly practised tests—the barium meal and the gruel test-meal. These tests were chosen, first, because of the value for comparative purposes of assessing the properties of new compounds by previously tried methods; secondly, because both these tests afforded an opportunity of studying the action of C6 on the full rather than the empty stomach, in contrast to the work of Kay and Smith; and lastly, because most of the subjects employed were old cases who well knew the routine tests, and in whom undue apprehension would therefore be avoided. This was considered to be important, as the marked inhibitory effects that strong emotions exert on gastric motility should be eliminated so far as possible.

Effect on Gastric Motility

Ten patients were chosen. Nine were males with clinical and radiological evidence of duodenal ulcer, and one was a female without such evidence; their ages ranged from 16 to 56 years. They were bed patients, and some had previously been treated with L-hyoscyamine sulphate and alkaline powders, but in no case were these drugs given within 12 hours of the tests. On the day before the trial a test dose of 50 mg. of C6 was given intramuscularly and the patient was observed in the supine and erect positions so that hyper-reactors could be excluded from the subsequent experiments.

Gastric motility and emptying time were assessed radiologically by means of barium meals. The patients, having fasted for at least 12 hours, were given about three-quarters of a pint (426 ml.) of barium meal to swallow. They were screened during the actual swallowing of the meal, kept under observation until it had entered the duodenum, and subsequently re-examined radiologically in half an hour and, if this was indicated, thereafter at hourly intervals. In the intervals between being screened the patients sat in chairs; but the actual x-ray films were taken with the subjects in the erect position unless they felt faint. The points that were particularly noticed during the examination were gastric tone, as revealed by the shape and peristalsis of the

FIG. 1.—Case 10. Control: appearance of the stomach immediately after the swallowing of a barium meal.

stomach, and emptying time, as shown by the measurement of the interval before the first appearance of the meal in the duodenum and the appearance of the stomach in the half-hour and subsequent films.

All the subjects were first given control barium meals, and nine out of the ten were shown to have highly motile stomachs with active peristalsis and a consequent rapid appearance of barium in the duodenum (see Table).

FIG. 2.—Case 10. Control: half an hour after the barium meal, showing almost complete gastric emptying, the meal being distributed throughout the jejunum.

Time Intervals Between the Taking of a Barium Meal and its Observed Entry into the Duodenum

Case No.	Control	C6
2	4 minutes	10 minutes
4	Immediate	10 "
5	4 minutes	5 "
8	Immediate	20 "
9	"	30 "
1, 3, 6, 7, 10 ..	{ Differences between control and C6 too small for assessment	

The timing is approximate only, because of the impracticability of keeping the subjects under continuous screening.

After half an hour nine of the ten stomachs had emptied themselves of about four-fifths or more of their contents, the tenth being half emptied, and the barium was distributed throughout the jejunum, having traversed the duodenum, leaving it nearly void of radio-opaque material (Figs. 1 and 2).

Three days later seven of the subjects were given 100 mg. of C6 intramuscularly half an hour before receiving a barium meal. No obvious difference was noted in the shape of the stomachs immediately after taking the meal; but there was some diminution in peristalsis, which was by no means completely inhibited, however (Fig. 3). In five cases there was, too, a notable prolongation of the interval between the taking of the barium and its apparent entry into the duodenum (see Table).

The half-hour films differed remarkably from the controls. In no case had the stomach emptied itself of more than about a quarter of its contents. The portion of the meal that had passed through the sphincter was almost completely confined to the duodenum and the beginning of the jejunum, which on screening appeared as immobile dilated segments of bowel, so loaded with barium that the normal mucosal pattern was obliterated (Figs. 4, 5, and 6). Subsequent x-ray films revealed that this state of affairs persisted for varying periods of up to six hours.

Seven of the subjects were given repeated doses of 100 mg. of C6 four times daily at four-hourly intervals for a period of seven days, after which the barium meal was repeated. All seven reacted in a manner similar to that already described. But a close study of the films of

FIG. 3.—Case 10. 100 mg. of C6 given: half-hour film, showing delayed gastric emptying, and the confinement of barium to the first and second parts of the duodenum. Although there is delay in emptying, gastric peristalsis is present.

this series revealed that in four cases the inhibitory effect was not so marked as it had been after the initial experimental dose, though in only one subject was this difference notable.

Effect of C6 on Gastric Secretion

In this investigation routine gruel test-meals were given as controls to patients who had fasted 12 hours or more ; and three days later these tests were repeated half an hour after the administration of 100 mg. of C6 intramuscularly. The test was performed on seven subjects suffering from duodenal ulcer. Six of these had high-climbing acid curves which were only slightly lowered after the administration of C6 (Fig. 7). In only one subject was the C6 followed by achlorhydria, and here the control meal had shown a low acid curve initially (Fig. 8). Emptying times were found to be slightly prolonged, but these results were not comparable to those obtained with the barium meals and were assessed less accurately.

Side-effects of C6

The most disabling side-effects were those consequent upon a loss in vascular tone. Of the ten subjects, six fainted while standing erect drinking their barium meals, and the others felt faint. These sensations were relieved when the patient sat down or when the x-ray table was tilted to an angle of about 30 degrees to the horizontal. In addition, three patients were rejected from the trial because of their vigorous reaction to a 50-mg. test dose. The onset of syncope was associated with a weakening and sometimes complete obliteration of the radial pulse, and was accompanied by tachycardia.

FIG. 4.—Case 9. Control: half-hour film, showing greater part of meal in small intestine.

FIG. 5.—Case 9. 100 mg. of C6: half-hour film. Note the retention of barium in stomach and duodenum.

Comparative readings of the blood pressures of eight patients were taken in supine and erect positions, with and without C6. In no case was there significant alteration of the supine blood pressure when this was taken three-quarters of an hour after a single injection of 100 mg. of C6. But in all cases in which an attempt was made to estimate the blood pressure in the erect position syncope ensued or threatened to ensue.

All the patients noted transitory defects of visual accommodation, and six felt dryness of the mouth developing about 20 minutes after the administration of C6 ; in addition four complained of a burning sensation in the eyes. Those patients who were in a position

FIG. 6.—Case 9. Same as in Fig. 5, two hours later. The meal is held back in the duodenum and jejunum.

to make the comparison agreed that visual symptoms and dryness of the mouth were not so pronounced as when they had been taking L-hyoscyamine sulphate

FIG. 7.—Average test-meal values of seven patients with and without C6. Case 7 (Fig. 8) was not included in this series.

FIG. 8.—Case 7. Gruel-test-meal curves with and without C6, demonstrating the production of achlorhydria. This was the only case in the series showing such an effect.

or belladonna. Of those who were treated with C6 for a week two complained of occasional abdominal discomfort and nausea. This discomfort took the form of a bloated sensation and anorexia.

In general all the other side-reactions became less marked towards the end of the course of treatment, though standing still in the erect position, as for the estimation of blood pressure or for screening, still caused faintness.

Discussion

Kay and Smith found complete inhibition of peristalsis for periods of up to four hours. They were, however, studying the empty stomach and not, as here, the loaded one; and this may explain also the fact that we found the free and total gastric acid levels little altered, while they noted a marked lowering of free acid in the resting stomach and a modified response to insulin but not to histamine. It may be that we were primarily measuring hormonal rather than vagal induced acid secretion, and that the exact effect of C6 depends on the extent to which the vagal factor is involved in the total secretory response to gruel in any particular case. Their results show that C6 might be beneficial in suppressing spontaneous gastric secretion.

There are, however, the following possible drawbacks to its therapeutic use. First, in all the subjects of our experiments vasomotor side-effects of the drug when given in doses of 100 mg. intramuscularly were incapacitating enough to make it unsuitable for ambulant patients. Secondly, after continued use C6 might lose some of its potency as an agent which inhibits gastric and intestinal motility. Finally, the effect on a duodenal ulcer of an artificial duodenal ileus produced by C6 cannot be predicted with certainty; for while diminished peristalsis and relaxation of the bowel wall might well have a beneficial effect, distension of the duodenum would probably be harmful. The dangers of an association of duodenal ileus with ulcer were pointed out by Hurst, Rowlands, Jones, and Ryle (1926), who described

two such ulcers which perforated and three others which remained resistant to medical treatment.

Although the ileus artificially induced by C6 lacks the organic obstructive element of the naturally occurring condition, it is difficult to be certain that the barium meal arrested by C6 in the upper part of the jejunum is not itself acting as an obstruction. Measurements of intraduodenal pressure should decide this point.

In general the disadvantages of C6 discussed above come into operation only when the subject is ambulant and taking food; thus its potentialities would seem to be strongest for bed patients and for use at night.

The experiments were not in the nature of a therapeutic trial, all the patients being without symptoms at the time of the tests, and receiving orthodox treatment.

Summary

C6 given in doses of 100 mg. intramuscularly to 10 patients was found to delay the onset of gastric emptying of a barium meal for periods of up to 30 minutes, and completion of emptying till the sixth hour.

Gastric peristalsis was diminished but not completely inhibited, and there was no change in the shape of the stomach. The small gut (particularly the duodenum and upper jejunum) was revealed to be dilated and immobile for periods of up to six hours after the drug was given.

Gastric secretion, as revealed by the gruel test-meal, was only slightly altered by C6. The patients in this trial were found to be much more susceptible to the unpleasant side-effects of the drug than those reported by Kay and Smith, perhaps because they were bed patients.

The properties which C6 possesses suggest that the drug may be of therapeutic value in the treatment of gastric and duodenal ulcer, particularly in bed patients and at night.

We acknowledge with thanks the helpful co-operation of Dr. T. H. Hills, director of the Department of Diagnostic Radiology, Guy's Hospital, and his colleagues. We express our thanks also to Messrs. May & Baker Ltd. for the supplies of hexamethonium.

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At a meeting of the Zoological Society of London on December 12 last Dr. L. Harrison Matthews showed slides and a film to illustrate the account of an expedition to the island of Ramsey to study the process of lactation in the grey seal during September and October, 1950. An adult female seal was captured by means of a special net, and was kept in captivity with her baby for fifteen days. Daily weighings of mother and young were made, specimens of milk were taken for analysis, and information on the breeding and nursing habits of the seals was collected. The average daily gain in weight of the pup was 3.3 lb., the weight increasing from 43 lb. on the third day after birth to 92 lb. on the eighteenth (the birth weight of the grey seal is about 30 lb.). The average daily loss in weight of the mother was 6.3 lb. during the same period, her weight decreasing from 371 lb. to 276 lb., a total loss of 95 lb. Adult and pup occasionally drank small amounts (undetermined) of water, both fresh and salt, but the mother did not feed during the nursing period. Daily weighings of a number of pups at liberty showed that the growth rate of the captive pup was not affected by the conditions of captivity. Analysis of the milk (undertaken by Dr. I. R. Rowland) showed over 67% solids with over 53% fats. The captive pup was weaned on the eighteenth day after birth, and left the beach on the thirtieth after it had completed the moult of its natal coat. Both adult and pup were surprisingly docile in captivity.