The Advancement of Dermatology

With regard to the specialty itself, and to those who practise it, the lack of a Diploma in Dermatology is a serious handicap to the advancement of the subject. Holders of special diplomas are essentially men whose competence has been assessed by others than their own teachers. Even allowing for the faults inherent in an examination system, one usually finds that the majority of men who have achieved a difficult diploma are men of worth. In these highly competitive days when most specialties in medicine and surgery have their diplomas, there is considerable danger lest the poorer quality of man is attracted to a specialty which demands no particular hall-mark of intensive effort. The establishment of a diploma would not benefit only the diplomates—it would tend to standardize, and thus to improve, the nomenclature of our subject, to crystallize our views on therapy, and very materially to increase the standards of teaching of dermatology.

It is desirable that we should develop much greater facilities than at present exist for research. At the present time, when the methods of research are becoming more and more specialized and the technicalities of mathematical assessment are becoming increasingly important, there is danger lest we be outstripped in research in our own specialty by scientists who have had little or no dermatological training. There are problems of preventive dermatology which must be solved—problems in rehabilitation which must be met. In these fields we can make rapid progress, particularly if we collaborate with our colleagues in physical medicine, pharmacology, chemistry, and psychology.

Points Relevant to the Army

Finally there are three points relevant to the Army to which I must refer. When the time comes for us to shed the bright panoply of war the measure of our success—or failure—in our present effort will be the effect which our work has had in influencing the military medical strategy of the future. Very sincerely do we hope that we will have succeeded in ensuring three matters:

1. That in times of peace dermatology is not swamped by venereology, and that a permanent cadre, small though it will be, of medical officers will keep alight the torch of dermatology.
2. That from the outset of any future campaign it will be remembered that skin diseases are a vital cause of inefficiency and that full provision will be made both at home and abroad for dermatological services, proportionate in size and efficiency to the problems which will assuredly arise.
3. That, with the help of the Matron-in-Chief, the British soldier suffering from a cutaneous disease receives treatment in wards in which the nursing is supervised by sisters.

We, the dermatologists in the Army, owe much to many officers of high and low rank who have helped to smooth our way; it would be an impossible task to name them all, as one would like to do; but to three officers of the higher executive we are greatly indebted—first, to the Director-General, Army Medical Services (Lieut.-Gen. Sir Alexander Hood), who has always appreciated the significance of our work, and done much both at home and abroad to ensure that our contribution to the war effort was utilized to the full; secondly, to the Director of Hygiene, Major-Gen. D. T. Richardson, who has given daily attention to our problems, and on whose staff I had the honour to serve; and, thirdly, to the Consultant in Venereology (Brigadier T. E. Osmond), who, with General Richardson, was largely responsible for ensuring that dermatology and venereology went their separate but harmonious ways, and that we too had the full recognition of War Office representation.

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PEPSIN INACTIVATION IN ULCER THERAPY

BY

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The treatment of peptic ulcer is largely based on methods designed to neutralize the free HCl of gastric juice, so it is important to understand, first, what degree of neutralization is required, and, secondly, how successful modern treatment is in achieving this end. Neutralization is commonly thought to mean complete neutralization to pH 7, but in practice this is very difficult to produce, and dangerous owing to the considerable risk of alkalosis.

In order to understand the purpose of neutralization of gastric free acid it must be realized that its chief function is to create the required medium for the action of the proteolytic enzyme pepsin, which initiates digestion of proteins. The activity of pepsin is greatest at pH 1-2—the value in pure gastric juice—and this activity is abolished probably at pH 3.5 and certainly at pH 5 (Hollander, 1939). Now the normal gastric mucosa is resistant to digestion by its own gastric juice, but an ulcerated gastric mucosa, and probably also the intact mucosa of the small intestine, are susceptible to peptic digestion when the required pH is present, as has often been demonstrated in experimental work on ulcer production. This has recently been well shown by Schiffrin and Warren (1942), who perfused loops of cat's small intestine (including duodenum) for 12 hours with N/10 HCl, which damaged the mucosa very little, but when pepsin was added to the perfusing fluid extensive ulceration, bleeding, and perforations of the gut were seen. It was further shown that at pH 2.24 pepsin had no such effects and that the maximum destruction occurred at pH 1.10. Similar effects on the gastric mucosa were obtained in chronic experiments when the stomach was perfused through a fistula. From these experiments in cats it is seen that even N/10 HCl has little harmful action *per se*, and that relatively slight neutralization is necessary to reduce peptic activity. There is certainly no evidence to show that a pH of 3-4 is by itself capable of damaging an intact or ulcerated mucosa in animals or man, and pH values of over 4 would appear to be unnecessary in counteracting the activity of pepsin.

The common method of measuring the acidity of gastric juice is to determine the volume of N/10 NaOH required to neutralize 100 c.cm. of gastric contents, using Toepfer's reagent, which changes colour at pH 3-4, to measure "free acid," and phenolphthalein, which becomes coloured at pH 8-10, to measure "total acid"; other indicators are occasionally employed. Toepfer's reagent is not very accurate with opaque fluids, but it does indicate a pH change at about the desired value, and the pH of the sample can be roughly estimated from the amount of N/10 NaOH required to change the colour. If the sample does not give a red colour to Toepfer's reagent it may be assumed that peptic activity is negligible. Total acid values give no useful information.

pH values of gastric contents have also been studied by electrometric determinations on samples aspirated from the stomach—a much more accurate technique than the indicator methods; and recently the preparation of electrodes suitable for direct insertion into the stomach has provided a method for continuous recording of pH *in situ*.

Our purpose in this paper is to emphasize that inactivation of pepsin is the aim of peptic ulcer therapy and that this is obtained by neutralization to pH 3.5-4, and we shall consider how effective the usual method of treatment by milk and antacids is in fulfilling this aim.

Effects of Milk on Free HCl in Gastric Juice

Milk is the basis of the dietetic treatment of peptic ulcer, so its actions are very important. Freezer, Gibson, and Matthews (1928) showed that milk can neutralize an equal

volume of 0.3% HCl to pH 4, so the amount of milk in an ulcer diet would theoretically deal with the total quantity of acid secreted daily, provided the milk is given at the right times. Hurst (1928) noted that milk neutralized more effectively than carbohydrate feeds, and that hourly feeds were more effective than two-hourly. We have made observations on ulcer patients in whom a Ryle's tube, introduced via the nose,

FIG. 1.—Patient No. 1: 10 oz. of milk two-hourly.

FIG. 2.—Patient No. 2: 10 oz. of milk two-hourly.

FIG. 3.—Patient No. 3: 10 oz. of milk two-hourly.

FIG. 4.—Patient No. 1: 10 oz. of milk hourly.

FIG. 5.—Patient No. 1: Continuous-drip milk.

was retained for several days, and samples of gastric contents were removed hourly, day and night, just before a feed. Free acid values were determined, using Toepfer's reagent as indicator.

10 oz. of Milk Two-hourly.—There are considerable individual variations in response to milk, and Figs. 1, 2, and 3 show free acid values in 3 patients with gastric ulcer, which radiographs and gastroscopy showed to be of similar size and location, when 10 oz. of milk was given two-hourly.

10 oz. of Milk Hourly.—The patient whose response to 10 oz. of milk two-hourly is shown in Fig. 1 showed complete neutralization of free HCl on hourly feeds of 10 oz. of milk (Fig. 4). Other patients have shown proportional reductions of free acid levels.

Continuous-drip Milk (6 Pints in 24 Hours).—This method of administration was introduced by Winkelstein (1933), and has the great advantage of being effective by night as well as by day. Fig. 5 illustrates this point in the same patient as above. The obvious disadvantage of this procedure is the continuous presence of the tube in the stomach, but we have found that if the tube is passed intranasally and removed every other day for cleaning the discomfort is reduced to a minimum. Breuhaus and Eyerly (1941) found that 3 oz. of milk half-hourly raised the pH to 2.4–2.9 and was superior to magnesium trisilicate, $\text{Al}(\text{OH})_3$, and NaHCO_3 , given in doses which were roughly equal to milk in neutralizing capacity *in vitro*. Cornell, Hollander, and Winkelstein (1942) have shown that a continuous NaHCO_3 -milk drip keeps the pH of gastric contents about 4 (control pH 1.2–1.5) and is somewhat better than continuous $\text{Al}(\text{OH})_3$ drip, which produces a pH of about 3.5. Wosika (1938) has suggested that powdered skimmed-milk tablets are more effective than liquid milk or cream.

Mode of Neutralizing Action of Milk

Milk contains several substances which may influence gastric secretion. The fat is probably the most powerful constituent, and its inhibitory effect on gastric secretion has been frequently confirmed since the original observations of Ewald and Boas (1886). Fat inhibits gastric movements and secretion when it reaches the duodenum, and fatty acids are far more active than the fats from which they are derived (Card, 1941). It has been demonstrated by Ivy (1937) that the action of fats is due to the liberation in the intestinal mucosa of a substance called enterogastrone, which in turn inhibits the movements and secretion of the stomach. Sugars in high concentrations also inhibit gastric secretion and mobility, and it has been shown by Day and Komarov (1939) that glucose acts partly after absorption by a central action due to the rise of blood sugar, and partly by a peripheral, probably osmotic, action. We have found that glucose, cane sugar, and lactose inhibit gastric secretion in man, but the effective concentration of the last-named is about 12.5% as against the 4% present in milk, so it is unlikely that the neutralizing action of milk owes much to its lactose content.

Proteins of course act as buffering agents, but some proteins can stimulate gastric secretion, probably through their breakdown products. We found that 20 g. of egg albumen hourly greatly increased free acid secretion in man, but Matzner, Windwer, Gawron, and Sobel (1941) showed that gelatin reduced the free acid response to histamine. Levy and Siler (1942) have found that a solution of amino-acids obtained by hydrolysis of casein (amigen) maintained the pH of gastric contents above 3.5 for half an hour after oral administration to normal subjects. The calcium present in milk will also neutralize free HCl.

Thus the inhibitory effect of milk is due partly to depression of secretion and partly to neutralization, and if given in quantities greater than 5 oz. hourly milk is undoubtedly an efficient therapeutic neutralizing agent; but in most cases something more will be required to raise the pH to 4, so antacids must now be considered.

Gastric Antacids

Antacids are almost invariably used to supplement the neutralizing action of milk. Their efficiency has been tested by measuring their neutralization of free HCl *in vitro*, but more useful information can be obtained by studying the reaction of gastric contents after oral administration of antacids. Direct electrometric measurements of pH are more informative than indicator studies, and have been used by Kirsner and Palmer (1940) and Breuhaus and Eyerly (1941) on aspirated samples of gastric contents, and by Flexner and Kniazuk (1941) and Breuhaus and Eyerly (1941) in the study of gastric pH *in situ*, in the dog and man respectively. In this way all grades of neutralization may be accurately measured, and continuous recording is possible with the electrodes in the stomach.

Kirsner and Palmer (1940) and Kirsner (1941) recorded the pH of aspirated gastric samples at hourly intervals in patients with healing duodenal ulcer who were given hourly feeds of milk and cream plus antacids hourly midway between the milk feeds. The gastric contents were aspirated just before each feed—i.e., half an hour after the antacid was given. They found that milk and cream feeds alone (3 oz. total volume, made up of equal parts) had no effect after one hour, although others have found that larger volumes or more frequent feeds were very effective, as described above. A general diet raised the pH somewhat.

A number of antacids in various doses, and atropine, were tested. 2 g. CaCO_3 hourly raised the pH from 1.75 to 4.35, 2 g. magnesium carbonate from pH 1.9 to 5.1, 2 g. magnesium trisilicate from pH 1.95 to 2.57, 2 g. $\text{Ca}_3(\text{PO}_4)_2$ from pH 1.75 to 2.61, 2 g. $\text{Mg}_3(\text{PO}_4)_2$ from pH 1.65 to 3.06, and 30 c.cm. (1 fl. oz.) $\text{Al}(\text{OH})_3$ from pH 1.9 to 3.0. Atropine enhanced the action of CaCO_3 but had little effect on the other drugs.

The order of efficiency of drugs acting alone in equal (2-g.) doses was: (1) calcium carbonate; (2) magnesium carbonate; (3) tribasic magnesium phosphate; (4) tribasic calcium phosphate; (5) magnesium trisilicate. 30 c.cm. (1 fl. oz.) of 5% colloidal aluminium hydroxide is probably little inferior to calcium and magnesium carbonates.

Breuhaus and Eyerly (1941) studied the effects of antacids in man by recording the intragastric pH at 5-minute intervals for two hours. $\text{Ca}_3(\text{PO}_4)_2$, $\text{Mg}_3(\text{PO}_4)_2$, and CaCO_3 in doses of 1–1.3 g. raised the pH more effectively than 1.3 g. of NaHCO_3 , 10 c.cm. of colloidal $\text{Al}(\text{OH})_3$, or 0.65 g. of $\text{Mg}_2\text{Si}_2\text{O}_8$, and the effects were not necessarily proportional to the neutralizing capacity *in vitro*. This was particularly well shown when mucin was compared with the tribasic powders or CaCO_3 : 10 g. of mucin *in vitro* neutralized as much acid as 1 g. CaCO_3 or $\text{Mg}_3(\text{PO}_4)_2$, but in the stomach mucin was much less efficient than either of the salts. This was probably due to the inadequate distribution of the mucin in the stomach—obviously a question of prime importance. It was also shown that 90 c.cm. of milk half-hourly was inferior only to the tribasic powders and CaCO_3 .

Bennett and Gill (1939) have demonstrated the efficiency of colloidal aluminium hydroxide in patients with peptic ulcer (see Fig. 6). Suggestions have also been made by Schiffrin and

FIG. 6.—Milk plus aluminium hydroxide (Bennett and Gill, 1939).

Komarov (1941) that aluminium hydroxide and phosphate inactivate pepsin even at pH 1–2, but their work has been criticized on technical grounds by Schoch and Fogelson (1942).

It is unlikely that methods of treatment in which two-hourly milk feeds are given, with antacids halfway between, would be as efficient in neutralizing free HCl as the hourly administrations of Kirsner and Palmer; so a pH of 4 will probably not be reached for very long, and at night there will be no neutralization on either regime. Since the majority of peptic ulcers heal readily it may well be that complete inactivation of pepsin is unnecessary and that a pH of 2–3 will cause sufficient reduction of proteolytic activity. We do not know the answer to this question, but if an ulcer does not heal it is important to determine free HCl or pH levels of gastric contents to see how much neutralization has occurred. We have seen cases in which free acid levels increased when antacids were added to a two-hourly milk-feed regime, and such patients would probably require continuous drips of milk or colloidal $\text{Al}(\text{OH})_3$ to control free HCl levels adequately.

Summary

The immediate aim of peptic ulcer therapy is to inactivate the pepsin of gastric juice by raising the pH of gastric contents to 3.5–4. Neutralization to pH 7 is unnecessary, and may easily produce alkalosis.

Milk, magnesium carbonate, calcium carbonate, tribasic magnesium and calcium phosphates, colloidal aluminium hydroxide, and magnesium trisilicate are the most efficient and safe neutralizing agents.

Our own observations were made on patients in the Courtauld Research Ward of the Middlesex Hospital before the war, and we are grateful to Dr. T. Izod Bennett for permission to study his patients. We should like to thank Prof. Samson Wright for his advice and criticism.

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A PRECISION METHOD OF CEPHALOMETRY AND PELVIMETRY

BY

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No method of cephalometry in common use hitherto can claim to be a method of precision. Each is based upon a preliminary estimate (not upon exact measurement) of the height of the "greatest circular section" of the skull above the film. Measurements based upon estimates can never be consistently accurate. The essential features of the various methods are as follows:

Reece (1935) palpates the head, makes allowance for the thickness of the abdominal wall, and adds 2 in. to the tube-skull distance. Thoms (1927) estimates the height and inclination of the occipito-frontal diameter with the patient in the supine position, and after exposure of the film makes another exposure with a perforated lead strip placed above the couch at the height and in the plane of the occipito-frontal diameter. Rowden (1935) measures the foetal skull with the patient in the sitting position, using cephalic scale strips placed at the estimated level of the foetal skull. Walton (1931) and McDonogh (1935) take lateral views of the patient lying either prone or supine with lead marks or a graduated lead rule at right angles to the couch in order to determine the height of the skull above the film. Roberts (1935) examines the patient in the prone position without using a Potter-Bucky diaphragm, and measures the suboccipito-bregmatic diameter on the basis that at term the true diameter of $3\frac{1}{4}$ in. results in a film diameter of 4 in. Chassar Moir (1941) uses a lateral view with the tube at 5-ft. distance and with a scale interposed at the mid-plane of the pelvis. He claims that this gives a fairly accurate guide to the size of the foetal head in about 75% of cases.

It is obvious that in all these methods there is a margin of possible error. For instance, the thickness of the abdominal wall can be estimated but it cannot be measured. The taking of a lateral film in breech cases does not definitely establish the depth of the foetal skull, as the foetus may have moved in the interval between the exposure of the A.-P. and lateral views. A serious disadvantage of these methods is that they require the whole-time supervision of a radiologist. No radiologist should be expected to take the responsibility of calculating the size of a foetal skull from factors not estimated by him personally. These are some of the reasons why