been established. Treatment is principally that of the underlying condition and has often been instituted before the neural complication makes its appearance. Surgical decompression or, in appropriate cases, irradiation alone is urgent in any of these conditions in which spinal cord compression occurs. Even in the case of secondary carcinomatous deposits these measures may provide rewarding palliation if instituted early enough. The spectre of the potentially treatable solitary intracerebral secondary remains, despite the well-recognized fact that its occurrence in post-mortem material declines in proportion to the thickness of the brain slices examined. The removal of a bronchial carcinoma has not been shown to result in improvement in the non-infiltrative polyneuropathies, but has been followed by regression of cerebellar degeneration. Oral steroids have been reported to relieve the distressing paraesthesiae and even the motor and sensory deficits in a very small number of these cases.

Metabolic disturbances due to the production of hormone analogues by bronchial carcinoma may respond to relatively simple palliative measures, making the terminal stages of this disease less intolerable. Hypercalcaemia, may cause a syndrome indistinguishable from that seen in parathyroid hyperfunction in which muscle cramps and weakness of limb girdles and trunk give rise to difficulty getting out of a chair and a waddling lordotic gait yet brisk tendon reflexes; this may be relieved with oral steroids. Irradiation of an inoperable tumor which is producing a corticotrophin-like substance may relieve, for a short period, the disabling myopathy due to adrenal hypercorticism.

*(This article will be concluded next week with a review of the neurological complications of disorders of connective tissue and endocrine glands.)*

# TODAY'S DRUGS

## Antacids

*With the help of expert contributors we print in this section notes on drugs in current use.*

Antacids are drugs which neutralize or reduce the acidity of the gastric contents. The digestive properties of gastric juice are mainly due to pepsin. The function of gastric acid is considered to be the maintenance of an optimal *p*H for the action of pepsin (1·5-3·5). Pepsin has very little activity at *p*H 4·0 and none at *p*H 5·0. Acid and pepsin are secreted in response to stimuli from the parasympathetic nervous system and from the hormone gastrin, which is released from the gastric antrum in response to a number of stimuli, including a fall in gastric acidity.

Our knowledge of the aetiology of peptic ulceration is still very incomplete. Modern opinion accepts the importance of acid secretion, but a number of other factors contribute to the susceptibility of the gastric and duodenal mucosa to the irritative and erosive effect of gastric juice. In fact, acid secretion may be normal or low in some patients with peptic ulceration—which emphasizes the importance of mucosal resistance. Aspirin, alcohol, and bile acids can all alter the physiological properties of the gastric mucosa and may predispose to erosion or ulceration. Relatively little is known, however, of the factors which affect mucosal resistance, and so treatment has mainly been directed at reducing gastric acidity. There is no doubt that antacids relieve the pain of peptic ulceration.

### Pharmacology

The gastric juice normally contains approximately 0·5% hydrochloric acid, and about 1,500 ml. is secreted over 24 hours. Most of the available drugs have little effect on the volume of gastric secretion, but theoretically it is relatively simple to neutralize the hydrochloric acid. The ideal antacid should effectively neutralize the acid and have a prolonged action in the stomach without producing a systemic alkalosis or other unwanted effects.

All the common gastric antacids are weak bases, and all indirectly suppress the activity of pepsin when given in sufficient doses to elevate the *p*H above 4. Aluminium hydroxide has a direct effect of inhibiting pepsin as well. No harmful effects appear to result from the suppression of the activity of pepsin, since protein digestion proceeds in the intestinal tract. The secretion of gastric juice and the output of hydrochloric acid is in fact increased by the presence of an antacid in the stomach;[1] this effect is particularly marked in patients with duodenal ulcers. The "acid rebound" is probably due to gastrin release, and it explains the need for continuous antacids if a high intragastric *p*H is to be maintained. Calcium salts have recently been shown to produce marked acid rebound.[2]

Antacids can be considered as absorbable or non-absorbable; some also *adsorb* acid in addition to simple neutralization. *Sodium bicarbonate* is a constituent of a large number of proprietary antacid mixtures. It is highly soluble and rapidly effective in reducing the pain of peptic ulceration; for the same reason it has a short duration of action. The released carbon dioxide causes eructation of gas, which gives a sensation of relief to some patients. Even if given in doses which only partly or intermittently neutralize gastric acid, sodium bicarbonate can alter the *p*H of the extracellular fluid, producing a metabolic alkalosis and an alkaline urine. This may be particularly harmful if calcium is being taken (as milk) in excess when chronic hypercalcaemia, metastatic calcification, and uraemia may result—the milk-alkali syndrome.[3] In conditions in which sodium retention occurs sodium bicarbonate can contribute to oedema and must, therefore, be avoided.

*Magnesium hydroxide* is practically insoluble and does not produce systemic effects. It is not effective until it has been converted to magnesium chloride by the action of gastric acid; hence it has a slower onset and a longer duration of action than sodium bicarbonate. The soluble but unabsorbed magnesium ion accounts for its laxative action, which is shared by all the compounds containing magnesium. Calcium salts, which tend to constipate, are often given in combination with magnesium salts to offset this effect. A small proportion of magnesium ions is absorbed, but this is unimportant unless there is renal impairment.

*Calcium carbonate* is also an effective antacid. It is of low solubility and tends to precipitate in the intestine to form insoluble calcium soaps in combination with fatty acids. A small fraction of the calcium ions may be absorbed and may similarly result in the milk-alkali syndrome if excess quantities of milk are being taken, but this is more often a complication of the use of sodium bicarbonate. However, an acute reversible form with hypercalcaemia and uraemia may follow the use of calcium carbonate alone.[4]

*Magnesium trisilicate* reacts with gastric acid to form magnesium chloride and hydrated silicic acid, which has a gelatinous consistency. The mixture is a good adsorbent, at least *in vitro*, and it is superior to aluminium hydroxide in this respect.[5] It has a prolonged action, but its slow onset is a disadvantage since after a single dose the stomach may have emptied before appreciable relief is obtained.

*Aluminium hydroxide* preparations contain hydrated aluminium oxide, which reacts with gastric acid to form aluminium chloride. The effect of aluminium hydroxide is attributed to both antacid and adsorbent properties. The onset of action is slow but more rapid than that of magnesium trisilicate. All aluminium salts are highly insoluble and therefore do not cause an alkalosis. They form complexes with protein and phosphates, inhibit pepsin, and also stimulate mucous secretion; they may also complex tetracyclines and atropine and markedly reduce their absorption. Excessive use of compounds containing aluminium can occasionally cause weakness due to hypophosphataemia.[6]

## Therapeutic Use

Antacids are effective in relieving the pain of uncomplicated peptic ulceration, and this is the main indication for their use; they have not been shown to speed healing or delay recurrences. They are also effective in relieving the pain of peptic oesophagitis. It follows that antacids are less effective in simple gastritis, in which acid secretion is usually diminished.

None of the available antacids is ideal. They all have a relatively short action, and in ordinary doses cannot neutralize the 30-80 m.Eq. of acid that are produced each hour. It has been found that 60 g. of sodium bicarbonate per day in a milk drip is necessary to maintain the gastric *p*H above 4·0 in patients with gastric ulceration, but considerably more than this is often required in patients with duodenal ulceration. Calcium carbonate is chemically probably the most suitable preparation. Hourly doses of 4 g. given with milk are capable of maintaining the gastric *p*H above 4·0.[7] There is also some evidence that in patients with duodenal ulceration calcium carbonate is more effective and its action is considerably prolonged if it is taken one hour after a meal.[8] Aluminium hydroxide appears to be equally effective in relieving symptoms, but hourly doses of 30 ml. given with milk do not raise the *p*H above 3·4.[7] There is little possibility of maintaining such intensive therapy during the night unless a continuous intragastric drip is employed. There is no evidence that this treatment has any influence on the rate of healing of gastric ulcers.[9] Milk containing 20 g. sodium bicarbonate per litre has been found the most effective mixture for reducing gastric acidity in patients with duodenal ulceration, but its value in promoting healing has not been established.[10]

Liquid preparations, or powders mixed with water, are generally more effective than antacids in tablet form because of the more complete interaction with hydrochloric acid in the stomach.[11] There are a large number of other proprietary and non-proprietary antacid preparations, but none seems to offer any particular advantage over those mentioned. There is no place for large doses of highly absorbable antacids such as sodium bicarbonate.

An alternative method of providing prolonged neutralization of the gastric contents is by the use of antacid tablets such as "Nulacin or "Prodexin." If these tablets are sucked continuously between meals a *p*H of approximately 3·0 can be maintained.[12]

## Unwanted Effects

Disturbances of bowel function are commonly associated with the use of antacids but can be avoided by the use of combinations of drugs with opposing effects.

Systemic alkalosis usually occurs only after the use of large doses of absorbable antacids such as sodium bicarbonate; it may be precipitated by coincident vomiting or renal impairment. The milk-alkali syndrome may occasionally result from the continued intake of sodium bicarbonate or less frequently calcium carbonate together with excess calcium as milk. Calcium carbonate alone may be the cause of an acute reversible form. Other unwanted effects are rare.

## Conclusion

Antacids relieve the pain which is associated with peptic ulceration, but there is no evidence that their use influences the rate of healing.[13] If symptoms are pronounced, antacids such as calcium carbonate or aluminium hydroxide may need to be given at frequent, probably hourly, intervals or antacid tablets should be sucked continuously between meals. A continuous intragastric milk drip with added alkali is occasionally required to relieve pain. Apart from these circumstances, antacids should be used intermittently only when pain occurs; there is little value in their prophylactic use.

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