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Drugs in the Treatment of Peptic Ulcer and Hypersecretion

By

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IN the treatment of peptic ulcer, drugs usually affect only the symptoms. These are caused chiefly by increased secretion of gastric juice. The reason is that in the ulcer cavity gastric juice causes an increased production of histamine-like substance. This substance stimulates secretion and finally leads to hypertrophic gastritis and to a vicious circle.

Among the consequences are: Secretion in the empty stomach, protracted and continued secretion after digestion of food, or overflow of the gastric juice into the esophagus, leading to soreness, pain and heartburn. Such discomfort is caused not by hydrochloric acid, but by pepsin. Drug therapy in the treatment of peptic ulcer is in reality not the fight against HCl, but against the invisible enemy, pepsin. The following test shows the action of pepsin, clearly:

Gastric juice is poured into one glass, and into another is poured gastric juice in which the pepsin has been previously destroyed by boiling. Thumb and index finger are rubbed together in both glasses. After a time a corrosive action can be felt on the skin of the fingers in the glass containing the unchanged pepsin.

As pepsin is rendered ineffective by neutralization, absorption, buffering or by evacuation of the gastric juice, the pain vanishes. In addition to the discomfort, there are characteristic severer and periodic pains. They are the result of increased inflammation at the margin and the base of the ulcer, and are caused furthermore by pyloric spasm.

Sodium Bicarbonate

is one of the oldest drugs. At the present time it is not in fashion. One objection to this drug is that it excites renewed secretion. However it only occurs when given in exorbitant doses, otherwise it reduces secretion.¹ This stimulation may be a "protective secretion" analogous to the abundant secretion of alkaline pancreatic juice which follows the intake of hydrochloric acid solutions. Pawlow, who first observed this reaction, believed hydrochloric acid to be the normal stimulant for pancreatic secretion. However, we demonstrated this pancreatic reaction to be only a "protective secretion" against hydrochloric acid.²

More important is that sodium bicarbonate, taken as a dry powder or in solutions higher concentrated than 1-2% (that is about a level teaspoon in 200 cc of water), may somewhat irritate the inflamed mucosa of the stomach with an active ulcer.

Another objection is the fear of alkalosis. The symptoms of alkalosis were first observed in France, several decades ago, and called "cachexie alcaline". At that time patients were given thirty to forty grams daily. In this country alkalosis seems to occur more frequently after the Sippy treatment.

However, the intake of sodium bicarbonate, or baking soda, with foods and otherwise, is customary, nevertheless, alkalosis has never been observed. The therapeutic dose is about 2-3 level teaspoons a day. This quantity does not cause alkalosis, even if taken regularly. The effect in the stomach is the immediate neutralization of HCl, with subsequent inactivation of pepsin. The resulting CO₂ relaxes the pylorus and

¹R. Ehrmann, *Internat. Beitrage Pathol. and Ther. Ernaehrungsstörungen* Vol. 3, 1913.

²R. Ehrmann and R. Lederer, *Berl. Klin. W.* No. 20, 1909.
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cardia. A rapid emptying of the stomach follows. CO₂ also has an analgetic effect. No larger distension results; therefore, no danger of ulcer perforation exists. If carbonated water is taken, such perforation may occur, as observed by the author. Taken on an empty stomach, sodium bicarbonate dissolves mucus and has a favorable effect on gastritis. There is, however, one drawback: It has no lining effect.

Sodium bicarbonate is unexcelled, when it is a question of emptying the stomach. It promptly relieves pain occurring several hours after meals or in the middle of the night. If milk is given instead, the stomach will remain full, and secretion continues. A patient, overcome by sudden severe pain while without soda or food at hand, can use "his own soda". By enforcing vomiting movements, he can accelerate the secretion of pancreatic juice into the stomach, and pain will cease.

Alkaline Earths

as Magnesium Oxide, Magnesium Carbonate USP, and Calcium Carbonate, have practically the same qualities as sodium bicarbonate, in regard to neutralization gastric secretion and pepsin. Besides, they have a lining and soothing action. Calcium carbonate has the stronger lining effect. It furthermore exercises an antiinflammatory action. Magnesium oxide, in turn, adsorbs large quantities of gas. One gram is able to adsorb 1000 cc of CO₂. Therefore, it gives no relief if taken on a full stomach.

Bismuth Subcarbonate

has no effect on HCl and none on pepsin. But it has a marked lining effect. Roentgenological examination proves that it settles in the ulcer cavity, protecting it against gastric juice and food, and preventing formation of the histamin-like substance. It absorbs wound secretion and dries the wound.

Aluminum Hydroxide and Aluminum Silicate

resemble bismuth in their action. However, if in a colloidal state, they are able to adsorb pepsin and hydrochloric acid. This is a purely physical procedure. No chemical conversion occurs.

The author observed these facts several decades ago, and subsequently introduced the drugs to therapy.³ Today they are widely used. Some uncertainty, however, exists as to their action. Our opinion is that such action depends on two processes after ingestion: Peptization, that is solution in HCl, and gelatinization of the colloidal Al. The colloidal Al is then able to adsorb hydrochloric acid, though only in relatively small quantities. More important, however, is its adsorption of pepsin. This occurs only in an acid or a neutral gastric content. Through the adsorption of pepsin, pain is eliminated. In a gelatinous state, the Al drugs have the same soothing effect as mucilaginous substances, i.e. colloidal solutions of cornstarch, barley gruel, gelatine and pectin. All these colloids, organic or metallic, have the same soothing effect on the mucus membranes, which fats and oils have on the skin. They furthermore, have a constipating effect in common,

³Th. Rosenheim and R. Ehrmann, *Deutsche Med. Wo.* 36, 1910.

In addition, they exert a corrosive action. Silver-nitrate, formerly so popular, but now little used, may well have had a similar corrosive action. Because of these corrosive qualities, colloidal Al is used by factories for dyeing of materials.

After-effects are caused by the combination of Al with phosphorus in the intestines, which leads to a depletion of phosphorus in the bone structure. Rickets have been produced by feeding aluminum salts experimentally. It is generally believed that Al itself is not resorbed. The urine shows no increase beyond the normal trace. Nevertheless there is a certain degree of resorption with deposition in the liver. Both Al and bismuth are alien substances in the body. Used in cases of skin lesions, toxic effects have occasionally been observed. Al as well as bismuth therefore should not be taken continuously by the patients.

Colloidal Magnesium Silicates

are mostly hard and sandy. They adsorb pepsin readily, whereas their adsorption of hydrochloric acid is below that of aluminum drugs. They are not superior in any way.⁴

Belladonna and Atropin

are effective only if taken one-half to one hour before meals. If given after secretion has started, their action is greatly decreased or entirely lacking. It has been observed that a slight increase precedes the cessation of secretion.⁵ This, however, is of no clinical importance.

Belladonna drugs have an anti-spasmodic and analgetic effect. They delay motility and evacuation. Given together with alkalines, these remain longer in the stomach, prolonging the effect on neutralization and pepsin. Unless a slight dryness of the mouth is felt, there will be no effect on the gastric glands. Moreover, these drugs have the widest safety-margin of any of the alkaloids used in therapy. Even the effect of toxic doses can be controlled quickly by pilocarpin.

Gastric Mucin, Histidin

and other drugs widely advertised today have no real advantages.

A word on the method of administration may be added: Hard tablets may be harmful to the mucosa. Tablets should be soft and easily crushable. Powders should not be sandy, and should be taken, like crushable tablets, in the form of a suspension in water. Sodium bicarbonate, dry or in a concentrated solution, irritates the mucosa. Drugs should be taken either before or after meals, in accordance with their intended effect.

The following table demonstrates that it makes a great difference whether the drugs are administered by weight or by volume. In practice, the neutralization by volume is decisive.

⁴Brenhaus and Egerly, *An. Intern. Med.* 14, 1941.
⁵Schiffirin and Komarov, *Am. J. Dig. D.* 8, 1941.
⁶R. Ehrmann, *Intern. Beitr. z. Path. U. Ther. d. Ernahrungsstoerungen.* Vol. 3, 1913.

Table

Dose	Substance	Neutralization or absorption of 1/10 N.HCl	Arrest of Pepsin
<i>Gram</i>			
1	Magnesium Oxide, Light	500 cc	+ Instantly
1	Magnesium Carbonate USP	300 cc	+ Instantly
1	Calcium Carbonate	200 cc	+ Instantly
1	Sodium Bicarbonate	125 cc	+ Instantly
1	Aluminum Hydroxide Colloidale	50 cc	+ About 15 Minutes
1	Aluminum Hydroxide	0 cc	None
1	Bismuth Subcarbonate	0 cc	None
<i>Level</i>			
<i>Teaspoon</i>			
1	Calcium Carbonate	600 cc	+ Instantly
1	Sodium Bicarbonate	550 cc	+ Instantly
1	Magnesium Carbonate USP	300 cc	+ Instantly
1	Magnesium Oxide, Light	250 cc	+ Instantly
1	Aluminum Hydroxide Colloidale	50 cc	+ About 15 Minutes
1	Aluminum Hydroxide	0 cc	None
1	Bismuth Subcarbonate	0 cc	None

Generally Magnesium oxide is considered the most effective neutralizing agent. It is correct that 1 gram of Magnesium Oxide neutralizes more HCl than any other substance. But, to neutralize 500 cc of 1/10 N. HCl, we need 2 level teaspoons. In contrast to that fact, less than 1 teaspoon of sodium bicarbonate is needed for the same quantity of acid.

SUMMARY

The different drugs have different indications.

Belladonna and Atropin check the secretion of gastric juice considerably, if given before secretion begins, and if administered in proportionate quantities. They help overcome pyloric spasm, and are analgetic. Taken

on a full stomach they delay the passage of food.

Alkalis and Alkaline Earths instantly neutralize HCl, reduce secretion and render pepsin ineffective. They have a different effect on the bowel movement. Magnesium and Calcium have a lining effect.

Sodium Bicarbonate has other specific actions. It empties the stomach quickly, by formation of CO₂. It has a beneficial effect on the accompanying gastritis. It is harmless if given in doses which are therapeutically sufficient. There can be no danger of alkalosis or subsequent secretion.

Bismuth Subcarbonate absorbs practically no hydrochloric acid, and no pepsin at all, but it is the best protective for the ulcer cavity. Because of its adhesiveness and oily consistency it is beneficial to ulcers and gastritis. It prevents the formation of histamin-like substances in the ulcer cavity.

Colloidal Aluminum Hydroxide and Aluminum Silicate render pepsin ineffective through adsorption. They are peptized and gelatinized in the gastric juice, and have a soothing effect similar to that of the colloidal starch solutions and mucilaginous substances. They have a corrosive quality which is perhaps the same as that of the formerly popular silver nitrate. They are not free from after-effects, and should not be taken by the patient on his own responsibility. The same is true for bismuth.

In contrast to aluminum and bismuth preparations, all the alkalis and alkaline earths are perfectly harmless, if taken in the required doses and concentrations. They are not alien substances in the organism. Considerably smaller doses are needed to absorb hydrochloric acid, and, what is more important, to render pepsin ineffective immediately.

Appetite and Obesity

By

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VARIOUS studies have shown that appetite tends to reflect body needs (1, 2, 3) but the excessive appetite associated with obesity would seem to be an exception to this rule. Another apparent exception is the decrease in appetite produced by undernutrition and fasting. This decrease was referred to in previous papers (3, 4, 5) and was attributed to dehydration. Similarly, the increased appetite associated with obesity appears to be explainable as a result of increased general hydration. In any case, this possibility and its bearing upon the problem of obesity seems to be worth considering.

The occurrence of water retention in cases of obesity has been pointed out by Newburgh (6) and an explanation of the tendency of adipose tissue to retain water as well as fat is suggested by the lymphatic-like

origin and structure of adipose tissue. Wassermann and his associates (7) found that adipose tissue develops from the same embryonic elements as lymph nodes and a lymphatic-like structure of adipose tissue is grossly discernible in fully developed human fat pads. I observed the lymphatic-like structure of adipose tissue in cadavers while serving as technician in gross anatomy at the College of Medicine of the University of Illinois (1916-1917). First, it was found that subcutaneous nodular cords, similar to lymphatic cords, could be palpated through the skin in the region of the brachial and femoral arteries of some of the fresh bodies that were brought to the morgue of the medical college. Incisions made to reach the arteries for embalming purposes revealed that the palpable subcutaneous lymphatic-like cords were adipose structures. Subcutaneous fat pads in regions like the gluteal region where nodular cords could not be palpated through

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