one of these factors, and a major one, is a dietary deficency of an as yet unindentified substance necessary to the local resistance of the gastric mucosa.

CONCLUSIONS

1. Experimental gastric ulcers may readily be produced in chicks on a deficient diet.
2. Gastric acidity in chickens following histamine injection is comparable to that found in man.
3. Chickens with gastric ulcers have hyperacidity.
4. The increased acidity in chicks with ulcers over those without ulcers suggests that it is a result of whatever causes the lesions and not a direct cause in itself.
5. The cause of the ulcers and the hyperacidity is apparently the lack of a dietary factory which has a specific effect on the resistance of the gastric mucosa.

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Some Recent Advances in the Physiology of Gastric Secretion*

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PHYSIOLOGICAL experiment in the field of gastroenterology during the last few years has indisputably shown that the digestive glands are organs of compound structure, composed of different sets of epithelial cells, whose activity is regulated—*i.e.* stimulated or inhibited—by different nerves or by various hormonal or chemical agents. The secretory work of a gland therefore is not regulated as a whole, but the final product of this activity, namely the glandular secretion, and in particular its composition are dependent on the participation of various mechanisms—nervous or humoral—which stimulate different parts of the gland. It may thus be concluded that the *quantitative* changes which under physiological conditions occur in some of the digestive juices, produced by glands of compound structure, in response to various stimuli are due to unequal *quantitative* activity of different groups of epithelial cells in these glands (Babkin, 1931, 1934). This theory is not inconsistent with two well established facts, *viz:*

(1) The influence—positive or negative—that one nervous or humoral stimulus, which affects predominantly one group of glandular cells, may exert on another stimulus, which controls some other group of cells, and *vice versa*. The best example of this is the so-called "augmented salivary secretion," where the preliminary stimulation of a parasympathetic nerve increases the effect produced by subsequent stimulation of the sympathetic nerve.

(2) The alternation in the volume and composition of the secretion that may be brought about by a change in the intensity of stimulation applied to a nerve which acts on only one group of secretory cells. Many examples of this could be quoted. For instance, it is well known that, when the chorda tympani is stimulated with an electrical current of a certain intensity and the intensity of the current is then raised, not only is the volume of the submaxillary secretion increased, but the saliva is enriched with organic colloidal material and inorganic salts. Again, under vagal stimulation an increase in the volume of the gastric and pancreatic secretions and in their respective enzyme contents is to be noted as a rule on any increase in the strength of the current applied to the vagus nerve. The probable cause of this phenomenon is that the glandular cells which supply the digestive juices with organic colloidal material and enzymes are subject not to the "all or none" law but to some other law (Babkin, 1931; Mansfeld, Hecht and Kovács, 1931).

With particular reference to the gastric mucosa it should be mentioned that, in addition to the fact that it is composed of different structural elements—surface epithelium cells, mucous cells of the neck, peptic cells and parietal cells—the relative numbers of these cells vary in different parts of the fundus and corpus mucosa (Aschoff, 1923). Thus what one may term the "functional topography" of the gastric mucosa must not be overlooked in considering the various ailments of the stomach.

Furthermore, in the region of the lesser curvature (which includes the so-called *"Magenstrasse"*) the mucous membrane is much thinner than in the fundus and the corpus of the stomach, and it should be noted that this region and also the pyloric region are under much more effective nervous control than the rest of the organ. Thus, according to Schabadash (1930), a section of the gastric wall with a surface of 4 sq. cm. will on the average contain:

In the region of the fundus, 80 to 200 nerve cells.

In the region of the corpus, 250 to 320 nerve cells.

In the region of the pylorus and lesser curvature, 320 to 450 nerve cells. Presumably on account of the abundant nerve supply the secretory activity of a pouch constructed in the region of the lesser curvature is distinctly more under the control of the vagal innervation and less under hormonal control than that of a pouch formed from the gastric wall at the greater curvature (Alley, 1933; Davidov, 1935).

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With these preliminary data in mind we shall discuss some of the problems relating to the function of the gastric mucosa in normal and abnormal conditions. As a result of our own experiments on the dog and cat and on man, and taking into consideration the data obtained by other investigators, we may draw the following conclusions.

(1) It is well known that, while gastric secretion is at its height, there is very little variation in the acidity of the juice and in the concentration of total and of neutral chloride. Towards the end of the secretory period the acidity usually becomes somewhat less, and the concentration of total chloride diminishes, while that of the neutral chloride increases. Several theories have been suggested in explanation of this phenomenon.

According to Pavlov (1910), the small amount of gastric juice of constant acidity which is produced during this period of secretion is neutralized by the alkaline mucus of the surface epithelium. This view has recently been upheld by Webster (1929) and by Bolton and Goodhart (1931). In addition to the neutralizing influence of the gastric mucus, Hollander (1934, 1936) emphasizes the importance of the neutralizing effect of the "alkaline component"—a fluid secreted by cellular groups of the gastric glands other than the parietal cells, which latter always produce a secretion of constant acidity. Hollander supposes that the "alkaline component" is a mixture (isotonic with blood) consisting of neutral chloride and various buffer salts, chiefly bicarbonate; as such it may contain only 350 to 380 mg. per cent (99 to 108 m.eq. per liter) of Cl, whereas the Cl values of the acid gastric juice very often attain a level of 575 to 585 mg. per cent or more (up to 170 m.eq. per liter). He believes that the concentration of total chloride in the gastric juice is not constant but increases with the increase of the acidity. The same relations between the total chloride and the acidity were found by Welin and Frisk (1936) to exist in human gastric juice. Since, as we shall see later, the volume of the "alkaline compound" is small, and its alkalinity very moderate, its effect becomes noticeable only when the secretion of acid has greatly diminished, and results in an increase in the concentration of neutral chloride in the juice. Unfortunately data concerning the actual composition of the "alkaline compound" are lacking. However, a few facts are known regarding the composition of gastric mucus, the source of which is the surface epithelium and perhaps also to some extent the mucous (chief) cells of the neck. According to Bolton and Goodhart (1931), the gastric mucus of the cat under ordinary conditions contains from 0.28 to 0.36 per cent of inorganic chloride. Mucus collected from the entire stomach of a dog by Webster (Ph.D. Thesis, McGill University, 1933—unpublished) contained 471 mg. per cent of total chloride; its alkalinity amounted to 16.8 m.eq. per liter. Gastric mucous secretion obtained on stimulation of the splanchnic nerves in the cat (Baxter, 1934) possessed an alkalinity of from 11.2 to 14.0 m.eq. per liter and a total chloride content of 462 to 510 mg. per cent. The chloride content of gastric mucus in humans averages 100 m.eq. per liter (Welin and Frisk, 1936). It would be of great assistance to the physiologists in determining the composition of the gastric secretion minus the hydrochloric acid, if some of the clinical investigators would analyze the secretion produced by the gastric glands in cases of achylia gastrica where no hydrochloric acid is being secreted but pepsin is still present in the juice.

According to the above theory, the composition of the principal components of the secretions of various cellular groups of the gastric glands is constant. On the other hand, Rosemann (1907, 1920) and his followers believe that the composition of the gastric juice may vary. In their view the concentration of total chloride in the gastric juice is practically constant, but the intensity of the stimulus determines the distribution of chloride between the hydrochloric acid and the neutral chloride. The stronger the stimulus, the more chloride will be present in the juice in the form of hydrochloric acid and the less in the form of neutral chloride.

It seemed to me (Babkin, 1929) that the variations in the acidity of the gastric juice could be accounted for by abnormally increased secretion of the "chief (or mucous) cells of the neck." These cells are present in the gastric tubules in considerable numbers; they gradually become more numerous towards the pyloric end of the stomach, the number of peptic cells correspondingly diminishing. Therefore the admixture of the secretion of the "chief cells of the neck" to the gastric juice must be substantial. It is quite possible that the glucoprotein present in the gastric juice in soluble form (so-called "dissolved mucin"—Webster and Komarov, 1932; Komarov, 1935) is secreted partly by the "chief (or mucous) cells of the neck" and partly by the peptic cells. However, very little is known as to the conditions governing their activity under various physiological and especially under pathological circumstances. Of the clinicians Maclagan (1934) considers it possible that in the human gastric glands these cells secrete a fluid containing neutral chloride.

All the above theories regarding the variations in the acidity of the gastric juice are based almost exclusively on data obtained from the investigation of healthy animals. The variations in the composition of the gastric juice in such cases are not at all great and this makes it difficult for the advocates of one theory or another to offer convincing proof of the correctness of their surmises. Thus the gastric glands of the dog, even when stimulated to activity by such different agents as vagal impulses and histamine, produce a juice with an almost maximal content of hydrochloric acid. We (Babkin, 1931; Toby, 1936) have shown that under these circumstances the parietal cells are able to secrete almost all the chloride of the juice in the form of hydrochloric acid. But does this mean that the parietal cells are under all circumstances able to concentrate the chloride from the blood and to combine almost all of it with hydrogen-ions? It seems to me that the best approach to a solution of this problem—a problem which has occupied the attention of investigators for more than half a century—would be by careful study of clinical cases and by special experiments on animals in which certain pathological conditions of the gastric secretory function have been reproduced. It might be expected that under the influence of a pathological process some phases of glandular activity would become exaggerated, others diminished or even perverted, so that the entire functional capacity of a particular group of secretory cells would be revealed.

(2) In normal canine gastric juice, secreted under

either nervous (sham-feeding) or histamine stimulation, the greatest part of the fluid and of the total chloride is produced by the parietal cells. This is evident from the data obtained by Miss Toby (1936), who showed that the concentrations of total chloride in "sham-feeding" juice and "histamine" juice are practically equal and are maximal in both secretions. Whereas the "sham-feeding" juice is extremely rich in organic material (*e.g.* pepsin, mucin), the "histamine" gastric juice is almost completely devoid of it. If the organic material produced by the peptic and mucoid cells were secreted along with a considerable amount of fluid, the total chloride of the "sham-feeding" juice would have to be much lower than that of the "histamine" juice, because in the secretion from these cells the chloride concentration is presumably much less than in the parietal secretion. However, this is not the case. Therefore it may be assumed that under normal conditions the peptic and mucoid cells of the dog's gastric mucosa discharge their colloidal organic material with a minimal amount of fluid. This is in agreement with the well known fact (*cf.* Katsch, 1926, p. 447; Bloomfield and Polland, 1933, p. 41) that in some cases of achylia gastrica in humans it is possible to obtain from the stomach a small amount of secretion, possessing peptic power but no acidity. In some dogs the neutral chloride of the "sham-feeding" juice may be slightly higher than that of the "histamine" juice (*e.g.* 52 and 32 mg. per cent respectively—Toby, 1936); at all events, in both these types of gastric juice it constitutes only a very small proportion of the total chloride secreted.

What is the composition of pure, human gastric juice? The nearest approach to normal gastric secretion is that obtained in response to histamine administration. This secretion is uncontaminated, and neither diluted nor partly neutralized by saliva and the food substances of a test-meal. But, as we shall see later on, it merely represents the result of the secretory activity of one particular group of glandular cells, namely, the parietal cells. Miss Toby (1937b), working in our laboratory and in co-operation with the Royal Victoria Hospital, Montreal, analyzed the "histamine" gastric juice of some normal persons and some patients. Only absolutely pure samples of the juice were employed. Human "histamine" gastric juice was found to differ from normal canine gastric juice in the following respects. There was no great difference in the two juices as regards acidity and total chloride concentration, although the values for both moieties—especially for the acidity—were lower in the human gastric juice. The most striking difference was in the content of neutral chloride. Whereas in dog's histamine juice it averaged only 32 to 41 mg. per cent, *i.e.* 5.6 to 7.2 per cent of the total chloride, in normal human gastric juice secreted in response to histamine it averaged from 103 to 132 mg. per cent, *i.e.* 19 to 26 per cent of the total chloride. The concentration of the organic constituents (total nitrogen, dissolved mucin and pepsin) was also much higher in the human gastric juice. The concentration of pepsin was particularly high; very often it was as much as 2,000 Mett units, equalling the highest values for pepsin found in canine juice elicited by stimulation of the vagi. We cannot yet adequately explain such an abundance of pepsin in the human gastric juice. At all events Miss Toby's observations show what a powerful and at the same time potentially dangerous digestive agent man possesses in the gastric juice.

(3) It has been conclusively established in our laboratory (Babkin, 1930; Vineberg and Babkin, 1931; Webster, 1931; Bowie and Vineberg, 1935; Toby, 1936), and independently of us by Gilman and Cowgill (1931), that the parietal cells are practically the only cells of the gastric glands that are stimulated by histamine, this substance exerting hardly any excitatory effect on the peptic and mucoid cells. It is true that under a small dose of histamine (*e.g.* 0.5 mg. to a dog of 15 to 20 Kg. body-weight) the concentration of pepsin and other organic substances in the gastric juice does not fall to an extremely low level or become practically nil, but it is incomparably less than in the juice obtained by means of sham-feeding (Webster, 1931). In a very carefully controlled investigation on man Welin and Frisk (1936), using a double gastric and duodenal tube, compared gastric secretions obtained with insulin (20 units) and histamine (1 mg.) respectively. Whereas the concentration of total chloride in the "insulin" gastric juice (15 m.eq. per liter) was only a little less than in the "histamine" gastric juice, the total acidity in the former (100 m.eq.) was markedly less than in the latter (150 m.eq.). On the other hand, there was a fair amount of mucus in the juice throughout the insulin test and only traces of it after histamine. This is proof that in man also histamine acts selectively on the cells of the gastric glands. No pepsin determinations were made by Welin and Frisk. Thus, even if it be maintained that histamine is capable of stimulating the peptic cells, it must be recognized that its effect is very weak and variable. In fact, it has been demonstrated in our laboratory (Alley, 1935) that histamine inhibits the secretory activity of the peptic cells and possibly that of the mucoid cells (chief cells of the neck).

Having regard to what has been said above (§2), and as might be expected, histamine produces a copious flow of gastric juice having a maximal content of total chloride and acid and very low peptic power. The first samples of juice obtained after histamine administration usually possess a moderate digestive power (for coagulated egg-white), which, however, quickly diminishes and may disappear altogether in the subsequent samples. This was attributed to the "washing-out" effect resulting when a flow of parietal secretion carries off the colloidal secretion of the peptic cells accumulated in the glandular tubules during a period of rest or of diminished activity of the gastric glands. The inhibitory effect of histamine on the secretory activity of the peptic cells must also be taken into consideration.

The above-mentioned peculiar action of histamine on the gastric glands is daily observed in the laboratory in experiments on dogs and cats. However, many clinicians do not agree that histamine exerts a similar effect on man, believing that the administration of histamine in the human subject results not only in a flow of acid gastric juice but also in an increased output of pepsin (Polland, 1932; Bloomfield and Polland, 1933; Rivers *et al*, 1936; Osterberg *et al*, 1936—to quote only the more recent papers). Miss Toby (1937a) in our laboratory re-investigated this problem on some patients in the Royal Victoria Hospital. First of all it must be remembered that usually a much

larger dose of histamine is injected in animals than in human subjects. Whereas the former receive from 0.5 to 0.66 and even 0.75 mg. per 10 Kg. of body-weight, the latter are given as a rule not more than 0.1 mg. per 10 Kg. Therefore Miss Toby proceeded to test in one and the same patient the effects of a small dose of histamine (0.5 mg.) and of a larger dose (1.0 mg.). With the smaller dose, the result was indefinite as regards pepsin concentration, but with the larger dose it was quite striking. As soon as the volume of the secretion increased, the concentration of pepsin fell, and it remained at the same low level or even fell still further when the flow of juice diminished. This is to be explained by the fact that, after most of the pepsin previously accumulated had been "washed out" from the glandular tubules, there was not a sufficient secretion of pepsin to restore the concentration of this enzyme in the juice to its former level.

Another special feature observed by Miss Toby in all the patients investigated was the so-called "fasting secretion" of the gastric glands. When the secretion provoked by histamine was superimposed on this continuous "fasting secretion," the very variable enzymatic content of the latter was reflected in the composition of the gastric juice. Therefore in man the output of pepsin cannot be taken as a true indication of the effect of histamine on the peptic cells, even though this substance may be credited with exerting some stimulatory effect. In their last paper Rivers and Vanzant (1937) recognize the phenomenon of the "washing out" of pre-formed pepsin during secretion provoked by histamine. However, they still maintain that histamine actually elicits a secretion of pepsin (unfortunately through some error they ascribe this function to the parietal cells). They employed a double histamine test in human subjects, administering small doses of the drug. The second injection of histamine, given ten minutes after the gastric secretion provoked by the first dose had greatly diminished, produced a less marked, though still considerable rise in the concentration of pepsin in the juice. These authors argue that, in the short interval between the two injections of histamine, pepsin could not accumulate in sufficient quantity in the tubules. Nevertheless, there is the possibility that this was so. In their experiments the maximum secretion of pepsin occurred during the twenty minutes following the first histamine injection and probably coincided with the initial copious secretion of fluid. Most of the parietal cells are located in the neck of the glandular tubules and only a few are found in their lower part, which is occupied chiefly by the peptic cells. Therefore pepsin has time to accumulate in this part of the tubules during the period when the parietal cells are less active, which lasted in Rivers and Vanzant's experiments from 30 to 40 minutes. The second injection of histamine produced at the beginning of the secretory period a maximal effect (for the dose of histamine employed) on all the parietal cells, including those situated at the bottom of the gland. It is probably the profuse secretion from these cells that washes out pepsin accumulated in the lower part of the tubules.

Another argument against Rivers and Vanzant's explanation is the fact that both the concentration and the output of pepsin continuously fell almost to the very end of the experiment. Even if it is the case that histamine is able to stimulate the activity of the peptic cells, its positive effect must be neutralized in some degree by the inhibitory effect of the drug on these cells—a fact which Rivers and Vanzant have not taken into consideration.

I realize that at the present stage of clinical research on these problems and in their application to medical practice these details of glandular activity may seem unnecessary to the physician. But of what value then is the determination of pepsin in the gastric juice if the drug employed for the production of the secretion is a specific stimulant for only one group of cells, *i.e.* those secreting hydrochloric acid solution, and has no definite relation to the activity of the peptic cells and may even inhibit their effect? I repeat here what I said in 1930, namely, that histamine is the best known test for the functioning of the parietal cells and may be used with great advantage for the purpose of determining the ability of the human gastric glands to secrete fluid and hydrochloric acid, but nothing else.

(4) Such is the state of affairs in perfectly normal animals and in healthy humans. Under pathological conditions the relations are much more complicated. It is a fact of common knowledge among clinicians that in certain pathological cases the acidity of the gastric juice may be considerably below normal, whereas the concentration of total chloride may remain approximately at a normal level (Katsch, 1926, p. 450). Might these changes in the composition of the gastric juice be due to an excessive secretion of alkaline gastric mucus? Opinions on this point differ. A well known German gastro-enterologist, Katsch (1926, pp. 446 and 450), states definitely that cases of true *"Hypochlorhydrie"* sometimes occur. By *"Hypochlorhydrie"* he means a pathological condition in which some secretion is still produced, but the HCl concentration is greatly diminished or this constituent may even be completely absent from the juice. Under these circumstances the gastric glands lose their ability to concentrate acid up to the normal level although the secretion of total chloride is little affected. Katsch proposes to discriminate between cases of achylia gastrica with cases and, without *"Hypochlorie."* In the latter not only is the acidity of the juice diminished but the total chloride concentration as well. Later on the gastric glands may also begin to lose the capacity to produce gastric juice with a normal content of chloride, and the volume of the secretion may also diminish. Of the American clinicians, Chron and Reiss (1921) have drawn attention to a special type of gastric hypersecretion which is not accompanied by hyperacidity and may even be found in cases of complete anacidity.

On the other hand Welin and Frisk (1936) hold the view that there is no alteration in the mode of hydrochloric acid secretion in cases of hypoacidity. The submaximal values for the acidity they attribute to the decreased rate of gastric secretion and the neutralizing and diluting effect of the mucus being continuously produced by the gastric mucosa.

The clinical literature on gastric secretion is enormous and very conflicting. The chief criticism that may be made against the results of so many of the earlier investigations on man is the unsatisfactory technique employed in obtaining pure gastric juice. It was not until the introduction of the histamine, and later of the insulin test that the clinician had the

opportunity of studying a more or less pure secretion, although in the case of histamine not all the different cells of the gastric glands are activated but only those responsible for the formation of hydrochloric acid. As an investigation of pathological cases seemed to be so essential to an understanding of the normal secretory processes of the stomach, Miss Toby (1937a) at my suggestion studied the composition of the histamine gastric juice of some patients with gastric or duodenal ulcers, applying the same chemical methods as she used in the investigation of canine gastric juice. In this study only samples of juice that were absolutely uncontaminated with food-residues, saliva or duodenal juices were subjected to chemical analysis. It was found that in the gastric ulcer patients the acidity of the juice and its concentration of total chloride were lower, while the neutral chloride was much higher than normal. Whereas in normal persons the chloride present as neutral chloride constitutes from 19 to 26 per cent of the total chloride of the juice, in this group of patients it averaged 50 per cent of the total chloride. The volume of juice secreted in response to the same dose of histamine was on the average less than in normal persons. In the duodenal ulcer patients the acidity of the gastric juice and its concentration of total chloride deviated very little from the normal. The percentage of chloride present as neutral chloride was from 17 to 31, *i.e.* it was practically the same as in the juice of normal subjects. There was a tendency to hypersecretion.

How are these facts concerning gastric ulcer to be interpreted? One explanation might be that the ability of the parietal cells (1) to convert neutral chloride into hydrochloric acid, and (2) to concentrate chloride up to the normal level, becomes impaired. This is indicated by the lower concentration of the total chloride, the lower acidity and the abnormally high concentration of neutral chloride in the juice.

Another interpretation that suggests itself is that the secretion of gastric juice (of constant acidity) is diminished and therefore the acid is more effectively neutralized and diluted by the gastric mucus than normally. Unfortunately this simple explanation is unacceptable owing to the following facts. In some of the gastric ulcer cases the concentration of total chloride in the juice was fairly high (up to 480-490 mg. per cent) and the total acidity rather low (219-257 mg. per cent), although the volume of mucus was less than in normal subjects. In some other cases, where the rate of secretion was almost normal, the total chloride concentration (*e.g.* 320 mg. per cent) and the total acidity (*e.g.* 141 mg. per cent) were too low to be explained by a slight increase in the total secretion of mucus.

Yet another explanation of the peculiarities of the gastric juice in gastric ulcer patients might be offered, *viz.* that under pathological conditions the secretory activity of the various cellular groups lining the gastric tubules is altered quantitatively. The parietal cells then produce a less amount of acid secretion, as shown by the diminished volume of the gastric juice. On the other hand, the secretion of other cell groups—namely, the peptic cells, chief cells of the neck and surface epithelium mucous cells—may be increased. Therefore the secretion of neutral or slightly alkaline fluid with a low concentration of chloride will be more abundant than under normal conditions. As a result, the gastric juice will be less acid, although the parietal cells will continue to secrete a fluid of constant acidity, and it will contain less total chloride and more neutral chloride. It is difficult to say which of these cellular groups is in a state of hypersecretory activity in a patient with gastric ulcer. The quantity of visible mucus produced by the surface epithelium varied greatly from patient to patient and in several cases was even lower than normal. Therefore this mucus can hardly be held responsible for the changes in the composition of the gastric juice of the gastric ulcer patients investigated by Miss Toby. Neither did the peptic cells display exaggerated activity in gastric ulcer patients, for the peptic power of the juice was not at all high. This was only to be expected, since the secretion of gastric juice was provoked by histamine. Furthermore, the peptic power varied greatly from case to case. It had no relation to the concentration of neutral chloride. Thus the "chief cells of the neck" remain the only group of secretory elements which may be held responsible for the dilution and neutralization of the acid parietal secretion. Unfortunately we have no direct proof that such is the state of affairs, but if this supposition is really correct then it is clear (1) that the chief (or mucous) cells of the neck are somehow affected by the ulceration process, and (2) that they respond to histamine stimulation to a far greater extent than under normal conditions.

I must frankly admit that none of these explanations satisfactorily answers the question under discussion. Whereas normally the activity of the different cellular groups in the gastric glands is strictly confined to one definite function or another and the activity of each group is finely adjusted to that of the others, in the diseased gastric mucosa these relations may be distorted. Under normal conditions the parietal cells produce a fluid secretion of practically constant acidity, and the peptic cells and mucous cells of the neck discharge their secretion with a minimal amount of fluid. In pathological cases several possibilities of deviation from the normal functioning may be assumed. Thus the activity of one group of cells may be increased over that of another; or a particular group of cells may lose its capacity to function with the same precision as normally; or another group of cells becomes overexcitable and now responds with exaggerated secretion to stimuli which under normal conditions hardly affect it at all. The physiologist seldom has the opportunity of observing these and other deviations from the normal. They may be studied perhaps by means of specially planned experiments in which the function of different groups of gastric cells is revealed. However this may be, before we accept any theory of gastric secretion which can be applied equally satisfactorily to the interpretation of normally and pathologically functioning gastric mucosa, a great many more experimental pathological, as well as carefully controlled clinical studies must be performed. I firmly believe that a full understanding of the secretory mechanism of the gastric glands can be finally achieved only through the closest co-operation between laboratory and clinic.

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Report of an Apparent Case of Secondary Pellagra*

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IT is rather surprising that after a considerable search no clear nor accurate description could be found dealing with the state of the rectum and colon during or after an attack of Pellagra.

Diarrhea is a common symptom in Pellagra and being common has apparently been accepted as diarrhea without further investigation. We find no detailed records of proctoscopic examination with descriptions as to what the mucosa may look like nor as to the structural state of the rectum and lower colon.

It would at least be interesting to know the results obtained from a series of post mortem studies upon the changes that take place in Pellagra. There may be such a study but the common disposition in the current literature is to speak of a diarrhea that has symptoms of variable degrees, sometimes preceding the other symptoms, and at other times present in severe form towards the end of the disease. That diarrhea occurs in Pellagra is evident, but it is not so clear just what destructive processes accompany this disease.

It has been shown that Pellagra occurs with, or secondary to, various chronic lesions of the intestinal canal, particularly those lesions that are destructive to the mucosa or those that interfere with the functions of this membrane.

Ian Murray (1), writing in the Glasgow Medical Journal, quotes Fakhry as finding that "a definite relationship between the incidence of Pellagra and intestinal schistomiasis, and also recalled the fact that among sixty-five German prisoners of war who developed Pellagra, sixty-three were suffering from amoebic dysentery or bacillary dysentery.

Turner (2), in the American Journal of Tropical Medicine, makes the observation that "most of the exhaustive monographs in Pellagra give little information concerning organic lesion of the gastro-intestinal tract in this disorder. Most of them refer to chronic gastritis and ulcers in the large and small intestines." His work in the Charity Hospital has led him to the conclusion that gross organic disease of the gastro-intestinal tract may be associated with Pellagra much more commonly than is generally detected. He reports 16 cases out of 75 seen as having definite gastro-enterological changes, most of which occurred in the lower or terminal gut.

Larimore (3) discusses a case in which for ten years there was persistent ill health marked by duodenal ulcers for which a number of operations were performed, including gastro-enterostomy, two explorations for hepatic abscess and re-operation for gastric and duodenal drainage. In this patient Pellagra developed.

Eusterman and O'Leary (4) discuss the probable secondary invasion by Pellagra and report 13 additional cases.

Numerous reports through the literature have led to the conclusion that Pellagra apparently does appear as a secondary manifestation in a proportion of individuals ill from various diseases of the gastro-intestinal tract.

The following report is that of a young colored male whose predominating symptoms were rectal and lower colon inflammation, that this inflammation was present for a long time preceding the pellagric symptoms, and that extensive changes took place in the rectum and sigmoid with marked deformity occurring.

HISTORY

A patient, J. J., Negro, male, age 23, admitted to the Atlantic City Hospital, April 23, 1935, with the chief complaint of diarrhea and pain in the rectum. The family history and past personal history were essentially negative. The history of the present illness revealed that a bloody diarrhea occurred about three years prior to the present time, at which time he had eight to nine bowel movements a day, lasting about four days; treatment not ascertained. Two years later, December 1, 1934, or five months prior to admission to the Hospital, there re-occurred the loose bowel movements having from nine to twelve a day with bleeding and griping pains in the abdomen, which condition persisted for approximately two months; during which time he had lost thirty-five to forty pounds. There was no loss of appetite at any time. For the next three months, the patient had only about five to six pass-

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