

pregnancy may apparently wake up a latent malaria or transform a chronic attack into the pernicious form. Whilst fears have been expressed lest quinine given in a pregnancy complicated by malaria may lead to abortion from the oxytocic action of the drug, Laffont agrees with most modern authorities in thinking it may be given freely and fearlessly. In so treating the mother one best treats the fœtus.

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## THERAPEUTICS.

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### THERAPEUTICS OF BILE.

FOR many years it was believed that bile exercised an action on intestinal bacteria, resulting in the prevention or limitation of putrefactive and fermentative changes of the contents of the bowel. The fact that intestinal fermentation was believed to be considerably increased in animals with biliary fistula and in the human subject with biliary obstruction seemed to support this view. On the other hand, many observations of more recent date make it necessary to keep an open mind in regard to this matter. Thus Bidder and Schmidt state that not only does bile possess no toxic action on putrefactive microbes, but that it tends to putrefy too easily to possess such properties, many bacteria thriving on it. Inouye and Sato say that animals with a biliary fistula, when given little or no fat in an otherwise sufficient diet, show no greater putrefactive changes of the bowel contents than do normal animals. Therefore if increased putrefaction does occur on a diet unrestricted in fat, it is not directly due to absence or deficiency of bile, but to the diminished absorption of fat which such biliary deficiency produces. That bile does not have any antimicrobial function also appears from the experiments of Matsushita and Strasburger. So long ago as 1902 Matsushita showed that the bacillus of typhoid fever and other intestinal bacteria grow better on media containing bile than on those containing none. Sato has recently confirmed Matsushita's work. Again, Strasburger found that in animals in which a biliary fistula had been made the fœcal bacteria were less than the normal, viz. in the proportion 3:2:8.

The problem is made more puzzling still by Schmidt and Sato, who have independently shown that fatty stools do not ferment or putrefy; they attribute the increased odour of fatty stools to the larger percentage of fatty acids contained in them. Padoa has recently shown

that ox bile and (though to a less extent) human bile possess an antitoxic action towards the toxic products of human fæces and of filtrates of *B. coli*. It is also known that bile increases peristaltic action and hastens the evacuation of the bowels. It was also supposed that bile had a diastatic action, and bile or bile salts seem to render the diastatic property of the pancreatic juice more active when they are mixed with it. There is, however, no amylase in bile. So far as our present knowledge goes, the most important function which bile performs is the promotion of fat splitting and fat absorption. Fleischer believes that bile contains a fat-splitting ferment, while others suggest that bile merely activates the pancreatic steapsin. Fat splitting is increased  $2\frac{1}{2}$  to 3 fold in the presence of bile according to Hencki. Fat splitting also results from the action of the intestinal bacteria, and as bile is now by some supposed to promote the growth of bacteria, it should therefore indirectly promote bacterial fat splitting.

*Therapeutic Action of Bile.*—Inouye and Sato recommend the administration of bile on the same principle as trypsin or thyroid therapy. Long ago in Europe a certain value was attributed to the giving of bile. By its introduction physicians sought to further the secretory function of the diseased liver or to hold in check the disturbances of digestion resulting from deficiency of bile. In Japanese and Chinese medical literature a therapeutic value was ascribed to bile, especially as a vermifuge, analgesic, and nerve stimulant. The bile of the bear was especially sought after. In diseases of the stomach, diabetes mellitus, and as an antidote for arrow poisoning bile was also tried, but with doubtful results.

In ancient times, too, disease of the liver and icterus were treated by bile administration, but in more recent times such treatment was discredited, as the bile appeared to interfere with pepsin digestion. Attempts were made to overcome this difficulty by coating the bile with some substance, unaffected by the gastric juice but digested or dissolved in the bowel. The following preparations fulfil these conditions:—(1) Sahli's glutoid capsules made of gelatine hardened in formaldehyde. These are usually quickly dissolved in the bowel, and are supposed to escape digestion in the stomach. When the obstruction involves both the common bile and pancreatic ducts, such capsules are useless, as the solution of the capsule depends chiefly on pancreatic action. (2) Rumpel's capsules. An improved form of Sahli's capsules, a more suitable concentration of formaldehyde being used to harden the gelatine. (3) Pills made with sheep fat according to Jaworski. Inouye has conducted careful experiments which confirm Jaworski's opinion that these pills do not melt or dissolve in the stomach and dissolve quickly in the bowel. (4) Ovogal. This is a chemical combination of fresh ox bile with albumen, which does not dissolve till it reaches the intestine.



As the above preparations are sometimes difficult to obtain, Inouye and Sato of Japan made a series of observations to determine whether watery solutions of bile of definite concentration caused subjectively recognisable disturbances of the gastric function. They administered a watery solution to a large number of patients and healthy men, and in no case did they observe disagreeable symptoms. Everyone was able to take 3 grms. of a preparation which was equivalent to 30 grms. of fresh ox bile. The bile was administered to the fasting stomach, as it is still an open question if bile neutralises the gastric acid and interferes with the peptic digestion.

Inouye and Sato conducted a further series of experiments in the treatment of disturbed bile secretion by administration of dissolved inspissated ox bile. Twenty-three cases of icterus were treated. Eighteen of these were of the catarrhal type, and those cases which were continuously treated with ox bile ran a shorter course than those in which the treatment was not given or was interrupted. This type of case does not, of course, furnish a conclusive therapeutic test; but the remaining cases of the series included cancer of the liver, gallstones, and gastroduodenal catarrh, and it was noted that, in every variety of case, improvement followed on this treatment, the pains in the abdomen vanishing and the appetite improving; diuresis was increased, and the bowels were regulated without purgatives. On examination of the faeces it was found that the amount of fat in the stools was greatly reduced. The fat resorption was increased 18 to 63 per cent. in 15 cases in which, owing to disease, there was a deficiency of bile entering the bowel, and it was found that all forms of fat were better absorbed during the treatment.

In this series of experiments Inouye and Sato confirmed their former observation that bile well diluted with water and administered on an empty stomach does not disturb the gastric digestion, as has hitherto been believed. Both these experimenters regard this treatment as a rational form of organic therapy and an effective means of treating the symptoms resulting from various forms of icterus. Although the taste of the watery solution of bile is very bitter, they found it fairly well borne, and they had no experience of the treatment being resisted. The solution is best administered in peppermint or other aromatic water with the addition of sugar, the daily dose being 2 to 3 grms.—0.5 to 1.0 gm. is given thrice daily one hour before meals. Husemann recommends the addition of a laxative such as aloes or jalap, but Inouye and Sato agree with Brunton that bile, given alone, leads to satisfactory evacuation of the bowel.

Eichler and Latz have recently made an experimental study of various purgatives which have an English and French reputation as cholagogues. Their latest experiments refer to iridin and euonymin. In regard to iridin, no increase of bile flow occurred, and there was no

real change in its composition. Euonymin likewise caused no increased secretion but rather a diminution of bile. The solid constituents were also slightly diminished.

Z. Inouye und T. J. Sato, *Archiv. f. Verdauungs-Kr.*, Bd. xvii. Heft 2, S. 185.  
F. Eichler und B. Latz, *Ibid.*, Bd. xvii. Heft 2, S. 133. G. Padoa, *Rivist. Critica di Clin. Med.*, Juliheft, 1910.

#### TREATMENT OF EXOPHTHALMIC GOITRE.

An interesting paper by Anastasia Tschikste has been published in the *Deutsch. med. Woch.*, No. 48, 1911, based on work carried out by him in the Bern Surgical Klinik (Th. Kocher) and in the Mediz. chemisch Institut of the university. Tschikste states that clinical and experimental investigations prove that iodothylin has not the full actions of thyroid extract, and A. Kocher has shown that colloid contains a phosphorus body which varies in amount inversely with the iodine. He refers to Cyon's work as evidence of the physiological antagonism between iodothylin and sodium phosphate in its action on the cardio-vascular nerves, and to Kocher's view that there is a substance in colloid which acts favourably in exophthalmic goitre. Such is the theoretical basis of the phosphorus treatment by thyroid nucleoproteid. Tschikste obtained nucleoproteid from goitrous thyroids in Kocher's clinic by the method of Oswald, the thyreoglobulin being separated in a half saturated solution of ammonium sulphate and the nucleoproteid in a fully saturated solution. The proteid contained 0.35 per cent. phosphorus. The total quantity obtained was so small that its action could be tested in only one case of exophthalmic goitre in regard to (1) metabolism, and (2) the general condition of the patient. The mode of administration was by deep injection in the gluteal region. After the patient had been under observation for three weeks the first injection of 10 grms. of a 2 per cent. solution in normal saline was given on 26th February. Thereafter 20 grms. of a 1 per cent. solution were administered on 2nd March, 13th March, and 18th March. The food given was measured and analysed, and the stools and urine were carefully examined quantitatively for nitrogen and phosphorus. It was found that after injections there was a retention of nitrogen, so that for the first time a positive balance was established. A similar effect was found in regard to phosphorus metabolism.

The observations appear to have been made with care, and confirm the allied work of Cyon on the action of sodium phosphate. Tschikste lays emphasis on the fact that the retention of phosphorus and nitrogen did not gradually occur, but rather suddenly, and in relation to the nucleoproteid injections. The retention synchronised with rapid increase of the patient's weight, the total increase being 10.5 kgs.



from 18th March to 26th April. The other characteristic symptoms of the disease were not influenced greatly, except the pulse frequency, which diminished gradually.

Marine and Lenhart have made a very full investigation of their cases of exophthalmic goitre (*Arch. of Internal Med.*, vol. viii. pp. 265-316). The only practical suggestion made is that in extreme cases the use of 5 minims of the syrup of the iodide of iron should be given once daily for a week, increased during the second week to two doses daily, and double this amount in the third week. It is difficult to understand how such doses can be of material service, but they believe that by such means a colloid state of the gland may be promoted.

The multiplicity of suggestions alone suffices to show that neither medical nor surgical treatment is at present satisfactory. A genuine improvement in the mode of treatment may not be recorded until the physiologist and physiological chemist add considerably to our knowledge of the functions of the gland, and of the specially related internal secreting glands.

The opinions of Marine and Lenhart, based as they are on very careful work, can scarcely be disregarded, however heterodox they appear in the following words:—"The essential physiological disturbance of the thyroid in exophthalmic goitre is insufficiency, its reaction compensatory, and its significance symptomatic."

## OPHTHALMOLOGY.

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### PHLYCTENULAR CONJUNCTIVITIS.

IN his thesis presented to the Faculty of Medicine of Liège in May 1911 Weekers (*Ophthalmology*, October 1911) seeks to establish in this clinical study, by anatomical and experimental investigation, the analogy between ocular phlyctenulæ and cutaneous tuberculides.

The work is divided into three parts:—

1. New pathogenesis of ocular phlyctenulæ.
2. Pathological anatomy of ocular phlyctenulæ.
3. Experimental researches on ocular phlyctenulæ.

*First Part.*—Tuberculosis is frequent in patients who have phlyctenular conjunctivitis. In 156 children examined—116 girls, 40 boys—and in adults—40 women and 18 men—the author has made the following observations:—