

without its counterparts to the first disorders of pregnancy, and as the derangements progress in either case we have often the same curious perversions of the appetite, like the cravings for wholly abnormal articles. The gastric troubles of pregnancy are explained by reflex irritation from the ovarian and uterine plexuses, but just such reflex irritation may occur from deranged menstruation.

Menstruation can be arrested by putting the feet in cold water, with great risk, however, of inducing the most pronounced and obstinate disorders of the functions and secretions of the entire gastro-intestinal tract. This irritation of cold, occurring under circumstances favorable for this effect, *i. e.*, while the ovaries are excited by the process of ovulation, may produce a persistent vaso-motor contraction of the arteries of the pelvic viscera first, and of other abdominal organs in succession, which effect is quite similar to that sometimes caused by a puncture or mechanical irritation of a nerve of the arm or of the leg, such as the musculo-spiral or anterior tibial, and which may radiate to all the arteries of the limb and produce tonic contraction of its muscles with coldness and wasting.

A remarkable case, published by me in the Transactions of the State Medical Society of New York for 1867, illustrates very fully how extensive and curious the effects may be of such a reflex irritation from cold during menstruation. The case was that of a girl who got a wetting during a cold thunder shower while she had her courses. They were immediately arrested, but she took no notice of any effect therefrom until she became so constipated that she passed a week without an evacuation. She was obliged then to admit that this was the case to her teacher at school, because of the excessively loud borborygmi which were heard by all in the classroom. Two physicians were called in consultation, who, finding they were unable to cause a movement, and stercoraceous vomiting having set in, summoned Dr. White, of Buffalo, late professor of obstetrics in the Bellevue Medical College of New York. He diagnosed intestinal obstruction, and advised a course of treatment which produced a number of free movements, which were remarkable for the almost total absence of any color, the fecal lumps resembling coarse plaster. On my seeing the case and recommending a free use of nitromuriatic acid, some copious "bilious" discharges followed, and hopes of recovery were entertained, when the same constipation and stercoraceous vomiting returned, along with a singular and very different train of symptoms. Her urine was suddenly suppressed one morning, but in twenty-four hours the saliva and tears welled out to the extent of from one to three pints a day. This continued for about a week with total suppression of urine-meantime, when it suddenly ceased and the urine commenced as before; and this strange alternation of secretion reoccurred again and again about every week, for two months, with alternate arrest of the bowel movements to be followed by fecal vomiting, until the death of the patient occurred from sheer exhaustion. This instructive case at least proves that a shock of cold proceeding from the feet may not only arrest the menses by reflex irritation but may also proceed to the production of virtual obstruction of the intestines by paralysis, and then continue to spread from one sympathetic ganglion to another, until the entire association of secretory nerves becomes deranged in turn, and the whole process of alimentation perverted.

It is quite conceivable, therefore, that until menstruation is thoroughly established, many young girls may have an undue susceptibility to sudden chill, particularly of the feet, whose vaso-motor nerves are in such close association with the pelvic circulation that the impression of cold made upon them checks, while heat promotes, the menstrual flow. The sudden derangement of menstruation thus induced by cold might then be propagated, as the first effects of pregnancy are propagated, until serious disorder of the gastro-intestinal secretions intervenes, with consequent impoverishment of the blood. Clinically it

is very frequently found that long antecedent to the development of the special symptoms, chlorotic girls have suffered from coldness of the feet, often with muscular pains in the lower extremities indicative of a pelvic vaso-motor irritation. It may be objected to this view that although amenorrhœa is the rule with chlorotics, yet some have a normal flow in amount or even more than normal; but, even with these cases, the function becomes in time very irregular and ultimately is suppressed.

TREATMENT.—Iron is the specific for chlorosis, and its remarkable curative effect in this complaint is doubtless the reason why iron is prescribed for every form of anæmia under the impression that it must act as a simple restorative when the blood becomes deficient in red corpuscles. The problem, however, is not so simple as it seems, for iron is actually mischievous in all febrile anæmias and of no avail in many grave forms that are not febrile. Moreover, in chlorosis the best results are secured by giving iron in large and not in small doses, in fact, in doses which are far larger than the corpuscles can possibly take up. Its presence in the intestinal canal seems to act as a stimulus to the assimilation of a normal quantity of iron to restore the deficient hemoglobin, and clinically it makes but little difference what the preparation of the drug is. Certainly the elaborate forms advertised as closer imitations of nature's own processes for taking up iron do not prove in practice to have any superiority over the common and much cheaper ferruginous salts. After repeated and careful comparative observations with different preparations, I am convinced that the sulphate of iron given in pill form in doses of from gr. iv. to vii., three times a day, is more effective than most other preparations, not excepting Bland's pills. A bi-weekly action on the bowels with aloes and rhubarb seems to hasten the assimilation of the iron, and in all cases characterized by intestinal flatulence it is a good plan to give gr. x. of sodium benzoate with gr. v. of salicin in capsules an hour after meals.

William H. Thomson.

CHLOR-SALOL.— $C_6H_4(OH)CO_2OC_6H_4Cl$ —Chlorophenol salicylate, salicylic-chlorophenol-ester. By the action of phosphorus pentachloride on a mixture of ortho- and para-chlorophenol, crystals are formed of the ortho- and para-salicylic-esters, differing from salol in containing an atom of chlorine in place of an atom of hydrogen. Both are insoluble in water and soluble in alcohol, the former melting at 55° C. (131° F.) and the latter at 72° C. (161.6° F.).

Nencki found that they split up in the intestines into a salicylic acid relative and chlorophenol, and that salicylic acid appeared in the urine. Girard speaks highly of them as intestinal antiseptics in diarrhœa and cystitis. Passerini obtained good results in bronchitis and pulmonary tuberculosis from the inhalation of fifteen drops once or twice a day for five to ten minutes. The first effect is said to be irritative, but after a day or two the cough begins to lessen and the secretion to diminish. The dose by mouth is 0.33-1 gm. (gr. v.-xv.) three to six times a day.

CHOCOLATE. See *Cacao, Butter of.*

CHOLÆMIA. See *Auto-Intoxication.*

CHOLAGOGUES.—This term is applied to medicines that increase the secretion of bile. It has been in use for more than two thousand years. The ancients observed, after the administration of certain purgatives, that the feces became markedly yellow or dark. They supposed this change of color to be due to an increased secretion of bile, and hence distinguished the purgatives producing it from others by the term cholagogues.

Until the middle of the nineteenth century clinical experience afforded the only evidence of the existence of cholagogues. The color of the feces was held to be a certain criterion of the quantity of bile excreted: dark-colored stools indicating redundancy, light-colored ones

deficiency of bile. Medicines that produce highly colored dejections, it was supposed, notably augment the secretion of bile. But the researches of physiological chemists have given little support to this theory. While it was found in experiments on animals upon which biliary fistulæ had been made, and in observations on patients with accidental biliary fistulæ, that a considerable quantity of bile is secreted in twenty-four hours, only very small quantities could be detected in the feces. Bidder and Schmidt¹ estimated the quantity of bile in the feces passed by a dog in five days, and detected only about one-eighth of the amount of the bile acids that had been secreted. Hence it was evident that the greater part of the bile acids—in the dog seven-eighths—is reabsorbed. Besides, it was shown by Frerichs² that the solid constituents of the bile, especially the pigments, suffer great changes in the intestine. These may vary much in health as well as in disease, depending upon the length of time the bile sojourns in the intestines, the kind of food eaten, the medicines taken, and other unknown conditions. Hence it followed that the color of the feces affords no certain clue to the quantity of bile secreted. It became extremely doubtful, therefore, whether the medicines that produce highly colored stools have any influence on the biliary function.

Nor have the numerous experiments made in the last half-century to determine the influence of medicines on the biliary function fully dispelled this doubt. Nearly all investigators found that the medicines to which an eminent cholagogue action had been attributed, especially calomel and other mercurials, are destitute of the power of increasing the biliary secretion. And in regard to those medicines that have gained celebrity in the treatment of diseases of the bile passages, especially the alkalies and alkaline mineral waters, the results of experimental researches have been so discrepant and mostly so negative that some of the best authorities deny that their utility is due to a stimulant action on the biliary function. Indeed, no other subject in the domain of pharmacology and therapeutics is in so unsettled a condition as that of cholagogues, and some recent competent writers aver that nearly all of the experiments on animals which seemed to demonstrate that numerous medicines increase the secretion of bile were made under such faulty or abnormal conditions as to be utterly valueless.

It seems proper, therefore, to consider in detail only those reputed cholagogues that are of recognized value in diseases of the liver and bile passages, and to adduce the experimental evidence pertaining to their cholagogue action only in so far as it may be conducive to a better understanding of their practical application.

Bile.—According to recent researches, bile itself is the mightiest cholagogue. Its power to increase the secretion of bile has been known for three decades. Schiff³ observed, when he injected bile into the duodenum of an animal upon which a biliary fistula had been established, that in twelve or fifteen minutes a very decided flow of bile took place from the fistula. In a dog with a biliary fistula, the amount of bile secreted was about 2 c.c. in twenty minutes. The injection of 180 c.c. of fresh ox bile into the duodenum was followed by a surprising increase of the amount of bile, so that after a short time 10 c.c. of bile could be collected from the fistula in twenty minutes. An analysis of the bile showed that the solids as well as the water were increased.

Prevost and Binet⁴ investigated the action of numerous drugs on the secretion of bile in dogs with biliary fistulæ. Among those that markedly augmented the flow of bile from the fistulæ, bile itself had the most pronounced effect.

Doubtless the most important experiments demonstrating the action of bile on the liver are those of Pfaff and Balch,⁵ made on a woman who had a biliary fistula after the operation of cholecystotomy. The quantity of bile this patient ordinarily secreted in one hour varied from 8 to 42 c.c. Sometimes the maximum was shortly before, sometimes shortly after meals. The secretion, though very irregular, generally increased after meals and dur-

ing the day, and lessened during the night, reaching the minimum early in the morning. The amount secreted in twenty-four hours, estimated for three days, was nearly constant, varying only from 501 to 525 c.c.

In order to administer the patient's bile, it was evaporated and formed into pills with glycerin, so that each pill corresponded to 25 c.c. of bile. After three pills, given in one day, the amount of bile secreted in twenty-four hours was 546 c.c.; after twelve pills, 600 c.c., and after twenty pills, 685 c.c. The solids of the bile increased from 1.7 per cent. to 2.04 per cent.

Ox gall dried to a powder and made up into pills with glycerin, each containing 0.5 gm. ox gall, had a more notable effect, twenty pills, given during a day, increasing the bile secreted in twenty-four hours to 770 c.c.; and increasing the solids of the bile from 1.69 to 2.62 per cent.

A mixture of pure salts of glycocholic and taurocholic acids was given in pills, each containing 0.25 gm. of bile salts. Two pills, given in a day, increased the bile to 701 c.c.; and eleven pills, given in a day, increased the bile secreted in twenty-four hours to 787 c.c., and the solids to 2.18 per cent.

Pfaff and Balch recommend, in cases indicating cholagogues, inspissated ox gall in pills each containing 0.25 gm., two to five pills to be taken three times a day. They suppose that bile may sometimes be useful in constipation and in cases of defective absorption of fat.

Stadelmann⁶ is of the opinion that for therapeutic purposes the bile acids deserve consideration, because they are thrown out unchanged with the bile and sometimes increase the water of the bile as much as eighty to ninety per cent. Besides, the salts of the bile acids are the best solvents of cholesterolin; hence they may be employed to dissolve concretions in the gall bladder and to promote the absorption of fat when it is defective in consequence of scanty secretion of bile. The presence of icterus contraindicates their use, because the toxic action of the bile acids might result in slowing of the pulse and destruction of the red blood corpuscles. Sodium glycocholate has been found to be ten times less poisonous than is sodium taurocholate; hence for therapeutic purposes inspissated ox bile, which contains chiefly the former, is an appropriate preparation. Gall stones, however, do not usually consist of pure cholesterolin, but of layers of lime salts alternating with cholesterolin; hence bile or bile salts will rarely dissolve them.

Gautier⁷ states that he has frequently used ox gall with success in cholelithiasis. He began its use in 1891 in the case of a woman who for a number of years had suffered severely from so-called gastralgia. After a very severe attack, which was followed by slight icterus and the passage of numerous gall stones, Gautier had recourse to a decolorized and sterilized extract of ox gall, each decigram of which corresponded to about 1 gm. of gall. This was given in pills containing 0.1 gm. The patient took one or two of the pills during meals for several years. The attacks of colic ceased. Gautier holds that ox gall will not dissolve gall stones nor prevent their painful passage through the bile ducts, but that it will prevent the formation of fresh concretions, and a relapse after surgical removal of the calculi.

Sodium Salicylate.—This medicine has been much employed in various febrile affections, and as a specific in acute rheumatism, since first recommended by C. E. Buss⁸ in 1875. Although large doses were administered, no effects were observed that could be attributed to an increased secretion of bile. The credit of the discovery of its cholagogue action belongs to Rutherford.⁹ Having found experimentally that the benzoates increase the secretion of bile, he supposed, from the near chemical alliance of salicylic and benzoic acids, and from the fact that both combine in the body with glycocholic, that sodium salicylate would exert some effect on the secretion of bile. A series of experiments on fasting dogs with temporary biliary fistulæ gave a positive result. Within half an hour after the sodium salicylate, dissolved in water, was injected into the duodenum, a marked in-

crease of the bile flow ensued. The dose administered was small, in one experiment gr. xxv., in all the other experiments gr. xx.

The researches of Lewaschew¹⁰ confirmed the results obtained by Rutherford. This experimenter made his observations on fasting dogs with permanent biliary fistula, but in all instances he gave the drug internally in gelatin capsules. He found that the quantity of bile secreted became greatly increased within an hour after the administration of 0.5 gm. Such small doses sometimes, though very rarely, failed to augment the bile flow, which never occurred when the dose exceeded 1 gm. Larger doses than 2 gm. did not produce a corresponding increase, the maximum effect resulting from doses of 1.5 to 2 gm., and continuing for more than twenty-four hours. Lewaschew found the solids increased, but the water much more, so that the bile was very fluid.

Prevost and Binet (*loc. cit.*) also confirmed the results obtained by Rutherford, noticing a very decided increase of the biliary secretion in dogs after the administration of sodium salicylate. And since then all experimenters have found this salt to be a very powerful cholagogue.

Körte¹¹ observed the action of sodium salicylate on two patients with complete (that is, with occluded common bile duct), and on several with simple biliary fistulae. He states that, after doses of 2 or 3 gm. of sodium salicylate, dissolved in water, he noticed a decided increase of the secretion of bile. His observations are very important, since they prove that sodium salicylate acts upon the liver of man in the same manner as it has been found to act on that of the dog.

From the experiments on dogs and Körte's observations on patients with biliary fistulae, we may infer that doses of 0.5 to 2 gm. will produce a very marked flow of watery bile in affections of the bile ducts that may be benefited by such an increase of the biliary function. Numerous reports made within the last decade have shown that such small doses proved efficient. Thus Fürbringer¹² stated that he had obtained good effects from sodium salicylate in cholelithiasis. In one case four times, in another five times, both women, gall stones were discharged on the day after administering the salt. As a rule, he gives the medicine in doses of 0.5 gm. with an equal quantity of sodium bicarbonate, four times a day.

Stiller¹³ reported, in 1890, that he had used sodium salicylate for five years, and regarded it as a powerful cholagogue. In cases of gall stones he gave 0.5 gm. four times a day, generally with 0.01 gm. of extract of belladonna.

In biliary colic Strisower¹⁴ at first gave two doses of antipyrin, each 0.6 gm., at an hour's interval, and afterward sodium salicylate, 0.6 gm., three or four times a day. The attacks became less frequent and soon ceased entirely.

In a discussion on cholagogues in the *Berliner medizinische Gesellschaft*, Senator¹⁵ stated that he had obtained good results from the use of sodium salicylate, especially when given in combination with extract of belladonna. Ewald claimed to have obtained undoubted success in cholelithiasis from sodium salicylate.

Naunyn's¹⁶ experience with sodium salicylate was also favorable. He repeatedly gave 2 or 3 gm. with success in the beginning of attacks of biliary colic. While Stadelmann¹⁷ fully agrees with other investigators as to the power of sodium salicylate to increase the biliary function, he having observed in experiments after giving 2 to 3 gm. a very marked increase of the bile flow, he dissents from all of them as to the utility of this cholagogue action in catarrhal icterus and in cholelithiasis. He holds that all cholagogues are worse than useless when the ductus choledochus is occluded, because the bile is secreted under very low pressure, and cannot in any circumstances overcome a higher pressure than 120 to 220 mm.

Sodium Bicarbonate.—It has long been observed that mineral waters containing a notable amount of this salt are of decided utility in catarrhal icterus, in hyperemia

of the liver from dietetic excesses, and in cholelithiasis. Frerichs¹⁸ entertained the opinion that alkaline mineral waters, especially Carlsbad, Vichy, and others, produce a copious secretion of alkaline bile, and that such bile exerts a solvent effect upon cholesterol, mucus, and lime salts. Ewald¹⁹ also attributed to the alkaline mineral waters the property of increasing the secretion of bile, and rendering it more watery and alkaline. Murchison²⁰ held that the undoubted utility of alkaline mineral waters and alkalies in cases of gall stones is due to improvement of the general health, reduction of hepatic congestion, and such alterations of the bile as prevent the formation of fresh concretions. Semmola and Gioffredi²¹ say that alkalies have a well-deserved reputation in the treatment of hepatic disorders, not because of a purgative or cholagogue action, but because they act upon the hepatic cell, upon the circulation of the liver, and upon the composition of the bile in such a way as to restore the normal functional powers of the hepatic gland.

The eminent writers on diseases of the liver and bile passages referred to based their opinions chiefly on clinical observations. These had indeed conclusively proved the utility of alkalies in affections of the bile passages, but not that they act by rendering the bile more watery and alkaline. Nor do the recent experimental researches on the physiological action of alkalies upon the biliary secretion sustain this view. Stadelmann,²² after investigating the action of alkalies upon the biliary secretion of dogs and finding that they do not increase the alkalinity of the bile, surmises that their favorable influence in cholelithiasis is probably due to inspissation of the bile, which, in more concentrated form, may be capable of dissolving gall stones.

Experiments to elucidate the influence of sodium bicarbonate upon the secretion of bile have been made by numerous investigators. The only one that found a decided increase of bile was Lewaschew. He made a series of experiments on fasting dogs with permanent biliary fistulae. One gram or less did not alter the bile in either quantity or consistency, but larger doses notably increased it in quantity for several hours, and rendered it more watery, the maximum effect resulting from 4 gm. The change in the composition of the bile occurred when the dry salt was administered in gelatin capsules, but was more pronounced when it was given dissolved in a large amount of water.

Glass,²³ a pupil of Stadelmann, experimented on dogs to determine whether the salts of sodium, dissolved in a large amount of water and given internally, render the bile more alkaline. Other pupils of Stadelmann had previously found in experiments that neither water in large quantities nor alkalies increase the bile flow in dogs with permanent biliary fistulae. All the conditions necessary to obtain trustworthy results were observed in the experimentation: the animals were in good health, and were well fed with a fixed diet; the bile was measured every two hours, and the observations continued for twelve hours. Glass summarizes the results of his experiments as follows:

1. Alkalies taken *per os* do not enter the bile.
2. The alkalinity of the bile is not augmented by the ingestion of alkalies.
3. The relative proportion of the sodium and potassium salts in the bile is constant.
4. A cholagogue action of the sodium salts is not perceptible.

The last conclusion, it seems to the writer, does not follow from the details of the experiments. In five experiments, in each of which the dog received 5 gm. of sodium bicarbonate in 500 c.c. of water, the average of the quantity of bile secreted in twelve hours was 11.5 per cent. greater than in previously made control experiments. In three experiments in which the dog received 10 gm. of sodium bicarbonate in 500 c.c. of water, the average increase was 4.2 per cent. In four experiments in which 15 gm. of the salt were given in the same quantity of water, the average increase in the amount of bile was 1.3 per cent. In four experiments in which 25 gm.

of the salt were given in the same amount of water, a diminution of the biliary secretion amounting to two per cent. took place. Upon this diminution of the secretion of bile by large doses of sodium bicarbonate, Stadelmann seems to base his supposition that the favorable influence of this salt in cholelithiasis is due to inspissation of the bile.

Sodium Sulphate.—This salt is the principal constituent of certain alkaline mineral waters, as those of Carlsbad and Marienbad, long celebrated in diseases of the liver and bile passages. It is the well-known purgative called Glauber's salt, which, on account of its nauseous taste, is now rarely used.

The influence of sodium sulphate upon the biliary secretion of dogs was found by Rutherford and Vignal to be a slight increase; so also by Prevost and Binet. Glass could find no change either in the amount or in the composition of the bile. But Lewaschew observed that 4 gm. markedly augmented the secretion of bile, especially increasing the water.

Lewaschew investigated also the action of the following mineral waters: Carlsbad, Vichy, and Essentuck. All rapidly increased the flow of bile, augmenting both solids and fluids, but the latter more. The effects of the different mineral waters were nearly the same, and hence Lewaschew concluded that they act upon the liver with equal energy.

The results obtained in experiments upon dogs by different investigators as to the action of sodium bicarbonate and sulphate and the alkaline mineral waters are remarkably contradictory and may create some doubt as to their utility. It should hardly be necessary to remind the reader that the utility of the sodium salts has been established beyond doubt by innumerable clinical observations, and cannot be shaken or made doubtful by negative experiments on dogs. When experiments on human beings have been made in sufficient number, the true solution of their mode of action, whether by an increase of secretion or by inspissation of the bile or otherwise, will become clear. Thus far only one surgeon has utilized the opportunity of observing the action of Carlsbad salt upon his patients. Körte (*loc. cit.*) gave this salt to two patients with complete and to several with incomplete biliary fistulae. The dose was one teaspoonful dissolved in one-fourth litre of warm water. A decided increase in the amount of bile from the fistulae was observed.

Sodium Phosphate.—This salt is held by some pharmacologists to be a useful cholagogue. Its action upon the biliary secretion was investigated by Rutherford and Vignal in one experiment. They observed a decided increase of the flow of bile, with diminution of its consistency. Lewaschew, in a series of experiments, confirmed this result. Four grams, both in the dry form and in solution, produced a very marked augmentation of the bile flow, and rendered the bile more watery. Doses of 1 gm. and less had no effect, while larger doses than 4 gm. did not cause a corresponding increase. He concluded that sodium phosphate acts as powerfully upon the biliary secretion as do sodium bicarbonate and sulphate, and that all of these salts produce the maximum effect upon the bile flow of dogs in doses of 4 gm.

Sodium Benzoate.—Rutherford and Dods (*loc. cit.*) found that this salt rapidly and decidedly increased the bile flow from biliary fistulae in dogs. Prevost and Binet, in their experiments, also observed a very pronounced cholagogue action. It greatly resembles sodium salicylate in its behavior in the body, and may be given in the same doses, from 0.5 to 2 gm. several times a day.

Olive Oil.—Olive oil has been used for many years to relieve the pain incident to the passage of gall stones. Dunglison²⁴ quotes a case in which olive oil was taken to allay severe pains in the stomach which were ascribed to the passage of gall stones. It caused the discharge of masses of fatty matter of globular form varying in size from that of a small pea to that of a moderate grape. Flint²⁵ relates that a patient who consulted him, having suffered much from the passage of gall stones, at one time took, for a number of days, a pint or more of olive

oil daily, at the suggestion of some one who assured him that in this way he had gotten rid of a large number of stones without pain. The patient stated that, under the use of this remedy, he discharged from the bowels an immense number of small, hard bodies, which were supposed to be biliary calculi. Flint held these bodies to be composed of a concrete form of fatty matter.

Rosenberg²⁶ says that, although the masses of concrete fatty matter were mistaken for gall stones, the use of olive oil was often speedily followed by a subsidence of the intense pain attending the passage of biliary calculi. He refers to twenty-one cases, three in his own practice, in nineteen of which the administration of large doses of olive oil was followed either by improvement or by complete cure. In a series of experiments on a dog with a permanent biliary fistula, Rosenberg found large doses of olive oil to cause regularly a marked increase of the biliary secretion, and he says that the influence of the oil upon the hepatic activity was greater than that of bile and of salicylate of sodium. He supposes that the calculi are forced out of the bile passages by the rapid influx of a large quantity of bile, and when they are not driven out, the pressure of the bile so changes their position that the symptoms of impaction cease and the bile finds its way into the bowel.

The committee of the therapeutic section of the Philadelphia Polyclinic Medical Society²⁷ appointed to investigate the results of the treatment of gall stones (hepatic colic) with olive oil, reported that records of fifty-four cases had been received; of these cases two had died, and three were not benefited; in all the other cases, ninety-eight per cent., positive relief was afforded. The beneficial effects appeared to be produced chiefly by the increased secretion of bile, and not by a solvent action of the oil on the biliary concretions.

Schulz,²⁸ in a case of pseudo-hepatic colic due to obstruction of the outflow of bile by carcinoma of the liver, observed that olive oil decidedly increased the secretion of bile, evidenced by aggravation of the colicky pains and great distention of the gall bladder; calomel, on the contrary, did not increase the pain and did not distend the gall bladder.

Troitzky²⁹ observed a case in which there was a fistulous communication between the gall bladder and the exterior. He found that, when he gave olive oil, the secretion of bile became more abundant. He supposes that, in cases of gall stones in which the administration of olive oil appears to be of benefit, the extra quantity of bile raises the pressure behind the calculi, and thus forces them onward, this action being aided by increased peristaltic movements of the bile ducts.

It is difficult to reconcile the above evidence supporting the view that the favorable action of olive oil in biliary colic is due to an increase of the secretion of bile with the opinion of Stadelmann,³⁰ that cholagogues cannot possibly be of service when there are obstacles in the bile passages, because increased secretion of bile is not attended by augmented bile pressure. Senator,³¹ contrary to Stadelmann, holds that in partial obstruction of the bile passages it is quite possible for an increase of the bile pressure to take place and to overcome obstacles. Doubtless he bases his opinion on the fact that he had often obtained favorable results from olive oil.

Podophyllin.—A cholagogue action was attributed to this purgative because frequently the stools that it produces have a dark color. It had been observed also that, when the motions are white or clayey, moderate doses often speedily restore the normal color to the evacuations. Murchison held podophyllin to be a good substitute for mercury when from any cause this is contraindicated.

Anstie investigated the physiological action of podophyllin on dogs and cats. He found that occasionally bile was poured out in large quantities. This he attributed not to a direct action on the liver, but to irritation of the mucous membrane of the small intestine. Experiments on dogs with biliary fistulae were made by the Edinburgh Committee³² and by Rutherford and Vignal. The committee found that podophyllin diminished the secre-

tion of bile. Large doses were administered and free purgation resulted, which doubtless, as shown by later investigations, prevented the action on the liver. In the experiments performed by Rutherford and Vignal, doses that did not purge severely always caused a very decided increase in the bile flow. The composition of the bile did not become changed. They inferred that the augmented flow was due to increased secretion, and not merely to expulsion. Since the influence of bile itself has been carefully investigated on dogs with biliary fistulae, the decided increase of the bile flow in Rutherford's experiments has been attributed to the bile used as a vehicle for the podophyllin. Rutherford says, in his comment on his ninth experiment, in which he had injected 12.2 c.c. of bile into the dog's duodenum, and about an hour later nine grains of podophyllin suspended in 12 c.c. of bile, that "the increase might possibly have been owing to the injected bile" (*op. cit.*, p. 17).

That podophyllin increases the biliary secretion in consequence of a direct action on the secreting apparatus of the liver is strongly sustained by an extended series of experiments on cats and dogs by Podwysotzki.²³ He investigated the physiological action of podophyllin, and of podophyllotoxin and picropodophyllin, two active principles he had isolated from podophyllin and from the rhizome of *Podophyllum peltatum*. Frequently the dejections had a bilious color. In the autopsies he found the liver soft, very dark, and hyperæmic, and the gall bladder much distended. Neuberger,²⁴ in experiments in which he investigated the action of crystallized podophyllotoxin, also found the liver hyperæmic and the gall bladder enormously distended with bile. Loewenton,²⁵ one of Stadelmann's pupils, found in experiments on dogs with permanent biliary fistulae that small doses of podophyllotoxin promoted the secretion of bile.

Calomel.—This medicine was formerly supposed to be a very powerful cholagogue, because it frequently produces green stools, and was found useful in congestion of the liver. At the present time, however, it is held that, in purgative doses, calomel lessens the secretion of bile.

Numerous experiments to elucidate the influence of calomel on the biliary function have been made, both on human beings and on animals. In all the experiments, when the methods were not faulty, small doses had no effect, and large purgative doses diminished the bile flow. But how explain the green stools and the undoubted benefit resulting from the use of calomel in certain hepatic affections? Do the stools contain large quantities of bile? Of this there can be no doubt, since Michea, Simon, Buchheim, and Radziejewsky found large quantities of bile in calomel stools. Radziejewsky found in calomel stools also notable quantities of the products of pancreatic digestion, peptone, tyrosin, and leucin. The presence of these substances in the dejections has been variously explained. It was supposed that calomel, acting strongly upon the upper part of the small intestine, causes them to be carried forward so rapidly that their absorption is prevented. To the same irritant action on the duodenum was ascribed also the presence of large quantities of bile in the stools, a reflex contraction of the gall bladder and bile ducts resulting which expels the bile previously secreted.

It was surmised by Buchheim²⁶ that possibly the large quantities of green bile in the evacuations might be owing to arrest of decomposition in the intestines. Wassilief's²⁷ researches show that this is probably the correct explanation. Under normal circumstances the bile pigments, bilirubin and biliverdin, are greatly altered by the putrefactive processes taking place in the intestines. Calomel restrains or arrests these decompositions; hence the biliary pigment retains its green color, and, in consequence of the accelerated peristalsis, is discharged before reabsorption can take place.

If it be true that calomel prevents those chemical changes of the bile and of the products of pancreatic digestion that naturally take place in the intestines, and

in this way, and in part by accelerating peristalsis, prevents their absorption, it is readily understood why calomel should have been found of special utility in certain hepatic diseases. By diminishing the amount of material absorbed into the portal circulation, it effectually depletes the liver, reduces its functional activity, and lessens the secretion of bile.

In a number of experiments on dogs Rutherford and Dods (*op. cit.*, p. 147) had observed a very decided increase of the bile flow after injecting mercuric chloride into the duodenum. All other observers who have since experimented on dogs or have given this salt of mercury to patients having biliary fistulae have been unable to verify their observations. It is supposed, therefore, that the increase of bile observed by Rutherford and Dods was caused reflexly by the intense irritation produced by the mercuric chloride in the duodenum of the fasting dogs.

The physiological action of numerous other medicines on the biliary function has been investigated. The following were found, by one or another experimenter, to increase the secretion of bile: aloes, baptisin, colchicum, colocynth, cathartic acid, euonymin, hydrastin, iridin, ipecacuanha, jalap, juglandin, oil of turpentine, potassium chlorate and sulphate, phytolaccin, leptandrin, propylamine, muscarin, salol, rhubarb, and antipyrine.

But with the exception of oil of turpentine, which in combination with ether has been used longer than a century, none is of any practical importance.

Therapeutic Uses of Cholagogues.—Cholagogues are indicated when the secretion of bile is defective, and active hyperemia, inflammation, and organic diseases of the liver are absent. But there are no certain criteria of this condition. The symptoms pertaining to the alimentary canal, which generally supervene when the flow of bile into the duodenum is impeded or arrested, such as perverted digestion, flatulency, constipation, and impaired absorption of fat, may be caused also by other pathological conditions. If the absorption of fat be found very defective and there be present no evidence of retention of bile, the secretion of bile is probably defective. Cholagogues may then be carefully tried. If the diagnosis be correct, ox gall will doubtless give much relief.

Cholagogues are sometimes useful in the complex disorder known as biliousness, which is characterized by symptoms denoting disturbance of the alimentary canal, liver, and nervous system. The most salient phenomena are a disagreeable or bitter taste, a coated tongue, defective appetite, sometimes nausea and vomiting; a sallow complexion, light-colored stools, and dark or lateritious urine; headache, giddiness, dimness of vision, languor, and mental depression. The primary cause of the disorder is usually a notable derangement of the digestive process, produced by dietetic excesses or the ingestion of indigestible or decomposing substances. In consequence of the perverted digestion, bodies having toxic properties are developed, which, being absorbed into the portal circulation, act deleteriously upon the liver and nervous system.

In the lighter forms of biliousness, which usually last only a few days, cholagogues are not required. Abstinence from food and the use of a mild cathartic generally quickly restore the stomach and bowels to a normal state. When the complexion has become sallow, and a deposit occurs in the urine, the treatment that experience has shown to be useful—namely, a purgative dose of calomel or other purgative mercurial, followed by a saline cathartic—is certainly appropriate. If the disorder have existed for some time, alkalies and the cholagogues that produce a free secretion of watery bile, sodium salicylate and benzoate, together with laxative doses of podophyllin, should be resorted to.

Cholagogues are generally used in cholelithiasis. After the severe pain due to the passage and often to the impaction of gall stones in the cystic duct or in the common bile duct has been relieved, sodium salicylate may be given in two or three one-gram doses at intervals of an hour. Each dose should be dissolved in a tumblerful of

hot water. Afterward the sodium salicylate may be given in 0.5-gram doses four or five times a day. At the same time it will be useful to move the bowels every morning by means of the artificial Carlsbad salt. The dose of this is generally a heaping teaspoonful, which should be dissolved in about a pint of warm water, one-fourth of which should be taken every quarter of an hour. If the patient have no icterus, and have repeatedly suffered from attacks of hepatic colic, ox gall will be preferable to other cholagogues. This remedy is more suitable than sodium salicylate and benzoate, because it increases the bile acids as well as the water of the bile, and thus tends to prevent the formation of fresh concretions, and possibly to disintegrate calculi, especially if they consist almost entirely of cholesterolin. But to accomplish these purposes its use must be continued for a long time.

If in severe hepatic colic sodium salicylate and Carlsbad salt do not give relief in a reasonable period of time, recourse may be had to olive oil. This should be given in large doses, from six to eight ounces. The following mixture recommended by Rosenberg is less disagreeable to take than the pure oil: oleum olive, 200.0; cognac, 20.0; vitell. ovor. ij.; menthol, 0.2-0.5. To be taken in two portions within one hour.

Cholagogues are often used in icterus. When this disease results from thickness and tenacity of the bile, a condition that impedes its free flow through the intrahepatic bile-ducts and causes its absorption by the lymphatics, those cholagogues should be used that increase only the water of the bile, especially sodium salicylate and benzoate.

In catarrhal jaundice not cholagogues, but means to lessen and subdue the catarrh of the duodenum and common bile duct, are of the first importance. Some of the means, however, used to meet this indication do probably increase the secretion of bile; this is true especially of the sodium salts. But whether or not this be the case, sodium phosphate in slightly laxative doses and Carlsbad salt are of undoubted value in catarrhal jaundice. The former may be given in doses of 2 to 6 gm., in much warm water, three times a day. Carlsbad salt is usually given early in the morning on an empty stomach in the dose of one or two teaspoonfuls. This should be dissolved in a pint of water having a temperature of about 100° to 105° F., and drunk in several portions at intervals of ten or fifteen minutes. The patient should defer taking food for one or two hours after the last portion. Often it is found that the symptoms rapidly abate under the influence of sodium salicylate, which may be given to the extent of 3 or 4 gm. daily for some time.

There are cases of catarrhal icterus of great obstinacy, and all the cholagogues mentioned may fail to cause the bile to flow into the intestine. One might then be tempted to use cholagogues that increase the bile *in toto*; but these will probably do no good and may greatly damage the patient. Samuel Nickles.

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CHOLECYSTECTOMY, CHOLECYSTOTOMY. See Gall Bladder.

CHOLERA, ASIATIC. See THE APPENDIX.

CHOLERA INFANTUM.—(Synonym: Gastro-Enteritis Cholericiformis, Choleraic Diarrhœa, Summer Cholera, Acute Milk Infection.) Cholera infantum is an acute gastro-intestinal catarrh affecting young children, and characterized by large watery stools, profuse vomiting, high temperature, great prostration, and rapid wasting.

It is the most sudden and dangerous form of gastro-intestinal inflammation to which children are liable, and is largely instrumental in causing the excessive infant mortality of the summer months. Cholera infantum is especially a disease of the crowded cities, but is far from uncommon in the sparsely settled country districts.

The custom, so general with physicians everywhere, of grouping all severe infantile diarrhœas under the generic name of cholera infantum, leads to much confusion, and seriously vitiates the deductions drawn from compiled mortality tables. The term cholera infantum should be strictly reserved for cases of genuine cholericiform diarrhœa.

The line of demarcation between cholera infantum and the ordinary summer diarrhœa, enterocolitis, cannot always be sharply drawn. Every epidemic exhibits cases which, beginning with distinct choleraic symptoms, soon subside into more or less protracted intestinal catarrh, and others in which the course of the latter disease is disturbed, perhaps abruptly ended, by an attack of infantile cholera.

But, although this is true, typical cholera infantum contrasts so strongly in symptomatology and fatality with all other forms of summer diarrhœa as to entitle it to a separate chapter and a distinctive name. Little or no difficulty would be experienced if the term were rigidly restricted to the form of gastro-intestinal inflammation outlined in the above definition.

ETIOLOGY.—Cholera infantum finds its analogue in Asiatic cholera. The clinical features of both point unmistakably to a bacterial origin, although no specific organism for the infantile disease has been yet discovered. The evidences of a profound infection are too strong to be ignored.

Infancy, excessive atmospheric heat, improper feeding, bad food, and bad sanitary surroundings are all important factors in the causation. Except in occasional instances they are singly inoperative, but together they develop conditions under which the specific germs or toxins