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 fistulæ, 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 Podwyssotzki.[33] 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,[34] 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,[35] one of Stadelmann's pupils, found in experiments on dogs with permanent biliary fistulæ 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 Buchheim[36] that possibly the large quantities of green bile in the evacuations might be owing to arrest of decomposition in the intestines. Wassilieff's[37] 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 fistulæ 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 hyperæmia, 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. Abstention 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 cholesterin. 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 olivæ, 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 Nicklès.*

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CHOLECYSTECTOMY, CHOLECYSTOTOMY. See *Gall Bladder*.

CHOLERA, ASIATIC. See THE APPENDIX.

CHOLERA INFANTUM.—(Synonym: Gastro-Enteritis Choleriformis, 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 mortuary tables. The term cholera infantum should be strictly reserved for cases of genuine choleriform diarrhœa.

The line of demarcation between cholera infantum and the ordinary summer diarrhœa, entero-colitis, 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

multiply, and exert their deleterious influence on the heart, nerve centres, and intestinal vaso-motor system.

Cholera infantum, as the name implies, is a disease of early childhood, and in the presence of favorable conditions, the liability to its development is in direct proportion to the age of the infant.

It occurs more often during the first six months than at any other period of infancy, and is rarely met with after the completion of the first dentition. There is, however, no ground for the belief that dentition is a factor in the causation, save that the great developmental and functional activity of the intestinal follicles during this period is a powerful predisposing cause to all kinds of intestinal derangement.

Cholera infantum is a disease of the summer months, and attains its greatest prevalence when the thermometer ranges the highest.

In this latitude cases begin to appear in the latter part of May, and occur with varying frequency until October. The disease, however, rarely assumes an epidemic form except in the months of July and August, when it reaches its maximum prevalence and fatality. High atmospheric heat exerts its deleterious influence by enervating the child's physical powers, by impregnating the air with the poisonous exhalations of decaying animal and vegetable matters, and by promoting the growth and distribution of all toxicogenic germs.

Improper food is the cause of multiplied digestive disorders in the infant, but, except in the presence of summer heat, rarely, if ever, lights up a choleraic attack. Its close dependence upon an impure milk supply is well established. A few writers maintain that "the cause is invariably in the food, and the poisons which induce the symptoms are not known to originate in any other food than milk or some milk preparation" (Vaughn). Not infrequently a single improper meal will transform a mild diarrhœa into the graver form of disease, and will sometimes develop an attack when the previous health is undisturbed.

Premature weaning, the use of commercial baby foods, and the American habit of admitting infants to the family table invite the disease. Hand-fed babies, however intelligently cared for, are prone to choleraic seizures, especially when exposed to the anti-hygienic surroundings, personal or domiciliary, of tenement life in the larger cities. For obvious reasons the disease attains its greatest frequency and mortality among the children of the city poor and in foundling hospitals.

Morbid Anatomy.—The pathological lesions vary with the period at which death occurs, and are rarely as pronounced as the alarming character of the symptoms would indicate. In many cases which proceed rapidly to a fatal issue, the post-mortem revelations are negative, or at most only disclose a few patches of arborescent injection scattered over the intestinal mucous membrane. In the more protracted cases, the lesions are better marked, and are very similar to those found in ordinary entero-colitis.

The mucous membrane is reddened, thickened and softened, uniformly or in patches. The intestinal glands exhibit the most constant change. Both the patches of Peyer and the solitary glands are enlarged, and form translucent projections above the surface. Many of these enlarged glands soften, break down, and leave the mucous membrane more or less thickly studded with follicular ulcers. The mesenteric glands are congested. The brain is anæmic and wasted, and serum is freely effused into the ventricles and on its surface. More or less hypostatic congestion of the posterior lobes of the lungs is nearly always observed.

Symptoms.—Cholera infantum usually begins abruptly with violent vomiting and purging, but it may be preceded by a short and ill-defined prodromal stage.

In this latter event, anorexia, fever, fugitive abdominal pains and a few liquid stools precede, for a few hours, or a day or two at most, the peculiar serous evacuations which give character to the attack.

It is a matter of common observation that the disease very frequently occurs in the course of a diarrhœa, more or less protracted, attended with emaciation and associated with intestinal inflammation; but, even in these cases, the distinctive choleraic symptoms almost invariably begin suddenly and are sharply outlined.

The antecedent diarrhœa unquestionably exerts a powerful influence in precipitating the attack, but it is not an essential feature of, nor can it be properly considered a preliminary stage of cholera infantum.

The stools first voided contain the contents of the intestines, milk curds, and particles of undigested food, mingled with intestinal mucus and liquid fæces. As long as fæcal matters are present, the discharges have a peculiarly fetid and penetrating odor, which clings to the clothing and person after repeated washings. These discharges are soon replaced by large odorless stools, devoid of fæcal matter, and so thin as to soak through the diapers like water, leaving only a greenish stain. The number of the stools varies. Ten, twenty or more may be passed in the twenty-four hours; occasionally they recur at long intervals—four or six hours apart—but are so copious as to deluge the clothing and bedding. The discharges are quite irritating, and give rise to an erythema about the anus, which adds greatly to the child's discomfort.

Abdominal pains and tenderness on pressure are usually not marked. Vomiting soon succeeds, or occurs simultaneously with, the intestinal discharges. It may precede them. It is nearly always persistent, and causes the immediate rejection of everything—food or drink—taken into the stomach. The stomach is speedily emptied of its contents, and afterward the ejected matters consist of the food taken, a greater or less quantity of serous fluid, the contents of the duodenum and bile. Even should it subside the taking of drink or food provokes an immediate renewal.

The reaction of the vomited matter is at first acid, but subsequently becomes neutral or alkaline when the intestinal fluids and bile enter largely into its composition. The evacuations, both gastric and intestinal, take place suddenly, with little or no warning, and are ejected with considerable force.

The two symptoms just enumerated—free watery purging and vomiting—recurring again and again, either simultaneously or in close succession, constitute the prominent and distinctive features of cholera infantum.

The quantity of fluid discharged in a few hours through these channels is sometimes enormous. This excessive depletion necessarily causes rapid wasting and speedy exhaustion. Loss of weight takes place more rapidly than in any other disease of childhood. The child soon loses its plumpness, the muscles become soft and flabby, and the skin hangs in folds about the joints. The features become more and more pinched and drawn, and so changed in appearance as to seem unnatural. The child is extremely restless and moans continuously, not so much from pain as from thirst and the general ill-feeling which comes from rapid exhaustion.

Fever is present from the first. The surface may seem to the touch but little warmer or even cooler than natural, but measured by the thermometer in the rectum the temperature, in a case of ordinary severity, will range from 102° to 105° F. "There is no disease of infancy in which the temperature of the blood is higher" (Smith). The mouth soon becomes dry and glazed, and the lips deeply fissured. The tongue is dry and shining or coated with a brown fur. The loss of fluids causes intense thirst, and the little patient eagerly accepts the proffered breast or cup. Water and ice, if allowed, are taken almost incessantly, though rejected by the stomach as soon as they are swallowed.

The secretion of urine is always greatly diminished, and in some of the graver cases totally suppressed.

Cerebral complications develop in a large proportion of the severe cases. These are sometimes due, especially when the urinary secretion is scanty or suppressed, to uræmic poisoning; but are more often attributable to that form of cerebral anæmia which was first described by

Marshall Hall under the name of spurious hydrocephalus. When this condition is imminent, the evacuations suddenly cease or recur at lengthened intervals. The fever disappears and the temperature sometimes drops below normal. The fontanelle, if unclosed, is deeply depressed, and, owing to the wasting of the brain tissue, the bones of the skull frequently overlap and render the surface of the cranium uneven. If the case does badly, the child becomes dull and heavy, the occiput is bored into the pillow, the eyelids remain half-open, the cornea is bleared and the pupils are irresponsive to light. Drowsiness, which has been marked from the first, gradually deepens into fatal coma. Convulsions occur in many of the fatal cases.

The duration of cholera infantum is short. Death may occur in eight or ten hours from the first disturbance of the intestinal canal. The mildest cases rarely last longer than a week, by which time death ensues or convalescence is assured. It must be remembered that an entero-colitis may indefinitely prolong convalescence or even cause a fatal termination long after the disappearance of the choleraic symptoms.

In those cases which pursue a favorable course, the first indication of improvement is the cessation of the vomiting. The child takes food and retains it; next, the diarrhœa becomes less violent, and the fever soon abates. On the other hand, if the profuse flux from the gastro-intestinal tract is not arrested, fatal exhaustion necessarily results. In this event, the face grows more and more haggard and old-looking; the eyes are shrunken, bleared, and surrounded by dark rings; the surface is cold and cyanosed; the respiration sighing, and the pulse uncountable.

Prognosis.—The prognosis is grave. The frequency with which collapse and brain complications arise in cases apparently pursuing a favorable course, always justifies a guarded prognosis. Marked remissions in the symptoms occasionally occur, even in the later stages, and these lead to the building of false hopes by parents and friends. The duration of the disease is largely influenced by the severity of the attack and the vigor of the child. It usually proceeds promptly to death or recovery. A constitution impaired by bad inheritance or previous illness, exposure to unhealthy surroundings, early age, and recent weaning, affect the prognosis unfavorably.

The mortality is greatest in children, under a year old, deprived of the breast.

The choleraic attacks which occur in the course of ordinary summer diarrhœas are less amenable to treatment than those which have developed in rugged health.

The occurrence of collapse, or the hydrencephaloid condition, unless promptly relieved, renders the outlook hopeless.

Death occurs from exhaustion or cerebral effusion. Œdema of the lungs, due to failure of the heart, often hastens the fatal termination.

Diagnosis.—The diagnosis is easily made. In fact, there is no disease, excepting Asiatic cholera, for which it can be mistaken.

The severe serous vomiting and purging, the high fever, the rapid wasting and exhaustion, stamp it with an individuality which almost precludes the possibility of error.

Treatment.—Every case of true cholera infantum should be looked upon by the medical attendant as an emergency case. It is essentially an acute poisoning, in which exhaustion often comes so quickly that intelligent interference is always demanded and demanded promptly.

In the way of prophylaxis the importance of suitable food, good nursing, and proper hygienic surroundings can scarcely be overstated.

During the hot months the most scrupulous cleanliness of person, clothing, nursing bottle, and everything about the infant must be observed.

No case of summer diarrhœa in a hand-fed infant should ever be ignored. Special emphasis should be put upon this axiom, as the writer is thoroughly in accord with Holt that the choleraic symptoms are almost always preceded by some gastro-intestinal derangement.

When the attack develops the coolest and best-ventilated room in the house should be chosen for the patient. It should be darkened and all noises and sources of irritation suppressed.

The first, and an imperative indication, is to assist nature in her efforts to remove the poison from the alimentary tract. There is no time to await the action of the traditional purge, if the stomach did not promptly resent its administration, and emetics are inadmissible. This indication is best fulfilled by lavage of the stomach and enteroclysis. The former rarely fails to lessen or stop the vomiting, and should be employed whenever this symptom is violent and distressing and does not promptly yield to milder means. The stomach should be thoroughly washed with warm, sterilized salt or soda water until the fluid returns clear. Ordinarily a quart will be needed. Oftentimes one thorough cleansing will suffice, but in obstinate cases it may be repeated several times.

The flushing of the stomach should be followed by small doses of calomel (gr. $\frac{1}{10}$) dropped on the tongue every half-hour until from one to two grains are taken.

Thorough irrigation of the colon is of the utmost importance. It should be begun early in the attack and repeated two or more times daily until convalescence is well established.

A flexible tube should be introduced high into the colon and from one to three quarts of water used at a sitting, allowing it to flow in and out freely. The escape of the water may be facilitated by passing a second catheter through the sphincter. To be effective the water must find access to the whole of the large intestine. This douching should be immediately followed, after the method of Professor Cantani, by an equally large quantity of a warm tannin solution (gr. xx. to a pint). "The object of the tannic-acid irrigation is to render inert any soluble poisonous proteids which may remain after the first washing" (Vaughn).

All irrigations should be given slowly, and to prevent undue pressure the water supply should not be raised over two or three feet above the body of the patient.

The child must not be overfed. The intense thirst leads to the eager taking of everything which the mistaken kindness of mother or nurse may proffer. Healthy breast milk should be supplied when practicable. Cow's milk in every form or preparation should be positively prohibited until the brunt of the attack is over. The same may be said of proprietary baby foods. Usually it will be advisable to cut off all foods (not drinks) for the first ten to twenty hours. If this is not deemed judicious, or when feeding is resumed, small quantities of a thin rice or barley water alone, or into which has been strained the white of an egg and seasoned with salt may be given. Later on, animal broths, beef juice, or whey may be added to the dietary, and, still later, peptonized milk and the malted foods.

To relieve the thirst, water may be given freely but in small quantities at a time, or the child may be permitted to suck pieces of ice wrapped in a napkin. A very weak tea, or water acidulated with phosphoric or hydrochloric acid, is both grateful and beneficial. But in severe cases it is not possible to replace the excessive intestinal drain with mouth-given fluids. The indication is, however, fully met with hypodermoclysis.

A saline solution (sodium chloride, gr. xlv. to the pint) warmed (110° F.) and sterilized should be slowly injected into the cellular tissue of the thigh or buttocks. From one to two pints may be given every twenty-four hours.

There is no one remedy in our experience so generally useful as opium, although its use is condemned by excellent practitioners. It should always be given alone: in this way the dose and frequency of administration can be readily changed without interfering with other remedies. It should be, of course, carefully watched and withdrawn at the first appearance of cerebral symptoms.

The hypodermatic injection of morphine (gr. $\frac{1}{10}$) and atropine (gr. $\frac{1}{100}$)* give the best results: other eligible preparations are the deodorized tincture of opium (gtt. i.) and paregoric (gtt. x. to xxx.).

When the violence of the vomiting has abated recourse may be had to the so-called intestinal antiseptics. Sodium salicylate (gr. i.); salol (gr. ss.); creosote (gtt. $\frac{1}{2}$–$\frac{1}{2}$); resorcin (gr. $\frac{1}{2}$), and many other drugs are commended by authors. The writer has been accustomed to rely with the most confidence on the bismuth preparations, of which the subnitrate (gr. x.) and the subgallate (gr. ij.–iij.) are the best.

I have seen good results from the aromatic sulphuric acid (gtt. iij.) given in a teaspoonful of bitter almond water.

French authors speak highly of the nitrate of silver. It may be given by the mouth (gr. $\frac{1}{12}$–$\frac{1}{8}$) or the rectum. When used by rectal injection the anus should be first washed with a solution of common salt, as otherwise even weak solutions may cause severe tenesmus. The hyperpyrexia, which is in itself an element of danger, and the attendant nervous phenomena are best treated by repeated cold sponging or the graduated bath. The use of antipyretic drugs, especially the coal-tar derivatives, cannot be too strongly condemned.

For the bath the child is gently immersed in water at 100° F. when the temperature is gradually reduced by the addition of cold water or ice to 85° F. An ice cap should be worn on the head. The immersion is continued for from ten to twenty minutes and should be repeated whenever the temperature approaches the danger line. It is inadmissable should symptoms of exhaustion or collapse be present.

Stimulants are needed in nearly all cases. It is a common mistake to delay their use too long. If not retained by the stomach they should be given hypodermically and per rectum.

Good old whiskey in gtt. x. to xxx. doses, repeated as required, fulfils every indication. It is surprising how much whiskey can be profitably taken by a child threatened with collapse.

Strychnine nitrate (gr. $\frac{1}{300}$) and atropine sulphate (gr. $\frac{1}{500}$) given hypodermically will often carry a flagging heart over a critical period.

During convalescence the child should be carefully watched, as one attack increases the liability of a recurrence. *W. J. Conklin.*

CHOLESTEATOMA is a term applied to a tumor-like mass composed of flat, cornified cells which are usually packed more or less closely together into a spherical, pearl-like, glistening body.

The first to call attention to this tumor was Cruveilhier in 1829; he applied to it the descriptive term *tumeur perlée*. The name cholesteatoma was given it in 1838 by Johannes Müller, who was the first to describe accurately its gross and histological characteristics. Virchow considered the subject very fully in 1855. Recently (1897) it has been reviewed in a masterly way by Bostroem.

Typical cholesteatomata are found chiefly, perhaps exclusively, in connection with the central nervous system and the bones of the skull. Similar pearl-like formations are found in other parts of the body, such as the middle ear, the ovary, and the testicle, but their exact origin has not yet been determined.

In the central nervous system the tumors are found chiefly at the base of the brain, on the posterior surface of the cord, and in the ventricles.

The tumor may form one compact pearl-like body, or consist of one or more pearls and irregular, soft, friable masses. The form is usually round or oval; the surface may be smooth or nodular. The tumor generally occurs singly, but Trachtenberg has reported a case in which multiple tumors were present on the surface of the brain and cord, and in the ventricles.

The size may vary from a pin-head to 5 or 6 cm. in greatest diameter.

The surface of a cholesteatoma usually presents, at least in places, a white, glistening, pearl-like appearance, the pearly lustre being limited to the surface; on section the mass is of a yellowish-white color. The consistence of these growths at the surface is fairly firm, but within it is usually soft and friable.

Microscopically the growth consists of large, flattened, folded, dried up, and cornified cells usually disposed in layers. In at least some of the cells a shrunken nucleus can be demonstrated. Between the lamellæ of cells occur cholesterine crystals to the presence of which the tumor owes its name. In sections the laminæ of cells seen from the side resemble fibrillæ.

The effect of a cholesteatoma on the adjoining brain tissue is purely mechanical. It causes pressure atrophy with increase of the neuroglia tissue.

The origin of these tumors has led to much discussion. Virchow believed that the dried-up cells came from transformed connective-tissue cells. Of late years, however, it generally has been held that the cells are of endothelial or epithelial origin. Bostroem in his monograph comes out very strongly in favor of their epithelial origin, and presents an array of facts which would seem to settle the question for all time.

According to him it is always possible to find at some point in the periphery of the tumor a relatively small, sharply limited area covered with typical epidermis. This represents the growing part of the tumor mass; the rest of it is made up almost entirely of dead, desquamated cells. The growing cells undergo cornification and in a certain layer, as in the skin, produce granules of keratohyalin. They also give rise to drops of eleidin and crystals of cholesterine.

The epidermis with an underlying connective-tissue layer derived from the pia or a choroid plexus forms a membrane which may cover a varying proportion of the cholesteatoma, but never the whole of it. The rest of the tumor is uncovered or adjoins brain tissue or pia.

Bostroem believes that these tumors arise from aberrant epidermic cells which become included in the central nervous system at the time of its formation. The aberrant cells develop in case they find proper conditions for nourishment; this happens only when they come in contact with the vascular pia or a choroid plexus. The growing part of the tumor, therefore, is always attached to one or the other.

The epidermic origin of these cells is based on their arrangement in the form of a pavement epithelium, on their producing keratohyalin and undergoing cornification, and on the formation of eleidin and of cholesterine crystals. Bostroem proposes that these tumors, in view of their origin, shall be called epidermoids.

Another point in favor of the epidermic origin of the cholesteatomata is the fact that a few of them are found containing hair. This is to be explained on the supposition that the aberrant cells in these cases consisted of cells not only from the epidermis but also from the cutis. The growing surface in these cases contains hair follicles and sebaceous glands. This class of cholesteatomata should be classed with the dermoids.

The cholesteatomata which occur in certain bones of the skull probably owe their origin also to aberrant epidermic cells which grow in the vascular marrow and derive their nourishment therefrom.

We have had at the Boston City Hospital, during the past two years, three cases of cholesteatoma of the brain.

The first consisted of a pearl the size of a pea and of several small, irregular, white, friable masses more or less embedded in the cerebellar tissue on the left side just where it joins the pons.

The second tumor was larger, measuring 3.5 cm. in diameter and 2 cm. in thickness, and was attached to the velum interpositum at the posterior end of the third ventricle.

The third tumor was still larger. It lay at the base of the brain on the right side and extended from the optic commissure out beneath the right frontal lobe. It was irregularly oval in shape, measuring 7 cm. in length and 3.5 cm. in diameter. It lay beneath the pia and had so shoved itself into, displaced, and compressed the adjoining brain tissue that it might almost have been thought to have originated within it (Fig. 1290).

The histological appearances of these three tumors agree in all respects with the description given above.

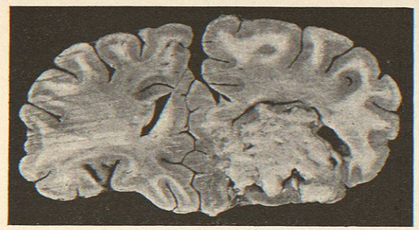

Fig. 1290.—Section of the Brain in the Third Case Mentioned Above, showing how the cholesteatoma in its anterior portion has pressed into the substance of the brain. (Original.)

For a complete bibliography up to time of publication see Bostroem: *Centralblatt Für Pathologie*, 1897, viii., 1. For multiple cholesteatomata see Trachtenberg, Virchow's *Archiv*, 1898, cliv., 274. *F. B. Mallory.*

CHOLESTERIN ($C_{26}H_{44}O$).—As its name indicates this substance was first recognized as a constituent of the bile and was regarded as a bile fat (cholestearin); but its proper designation is cholesterin (bile solid). When pure it crystallizes in white mother-of-pearl leaflets which have a fatty feel but possess no taste or odor. It has a neutral reaction, melts at 145° C., and sublimes without change in a vacuum at 360° C. According to its reactions it is probably a monovalent alcohol.

Cholesterin is insoluble in water, dilute acids, dilute and concentrated caustic alkalies, and in cold alcohol. It is soluble in hot alcohol, ether, chloroform, benzole, and in the volatile fatty oils; but dissolves with difficulty in solutions of the bile-acid salts, and is only slightly soluble in water solutions of soaps. The solution in ether is neutral, and turns the polarized ray of light to the left.

From ether solutions cholesterin crystallizes on evaporation in large, thin, transparent, rhombic plates, ($C_{26}H_{44}O + H_2O$), whose edges and corners are frequently irregularly notched, so that the plates as they lie heaped up have the appearance of being cut out in step-like forms. The formation of the plates is frequently preceded by a stage of fine needles which gradually change into blunt cones and then pass into the plate form. Cholesterin is unchanged by the action of boiling caustic alkalies. With concentrated nitric acid it yields cholesteric acid ($C_{12}H_{16}O_7$) in addition to acetic and butyric acids. Concentrated sulphuric acid gives cholesterin a red color, and breaks it up into a variety of isomeric hydrocarbons (cholesterilin). When heated with organic acids for long periods of time at 200° C. cholesterin passes into ether combinations: as for example with acetic acid it forms acetic-acid-cholesterin-ether, ($C_{26}H_{43}$-C_2H_3O,O).

When treated with a mixture of five parts concentrated sulphuric acid and one part water, cholesterin crystals take on a deep carmine red which gradually passes into violet. A weaker solution causes a violet coloration of the edges of the crystals which on the addition of water becomes lilac. Sulphuric acid containing a trace of iodine colors the crystals violet, blue, green, and red.

If cholesterin is dissolved in chloroform in a dry test tube, and acetic acid anhydride added, the addition of concentrated sulphuric acid, drop by drop, produces a rose color which quickly becomes blue and after a few minutes changes to vivid green. When only very small amounts of cholesterin are present the green color alone appears. This is one of the most reliable tests for this substance, and the presence of .05 mgm. can be shown by it. When substances containing a small amount of cholesterin are evaporated with a drop of concentrated nitric acid upon the water bath, a yellow coating is left which on the addition of ammonia becomes bright red.

Cholesterin is a constant constituent of the bile of all animals, in which it is held in solution by the bile-acid salts and the soaps. The proportion in normal human bile has not yet been ascertained. It is also found in the intestinal contents as a result of the presence of the bile. In the blood it occurs only in a very small amount, which is held in solution by the fats and soaps of the blood. The various nerve structures contain it in large proportion; more than half of the dry substance of nerve fibres consists of fat and cholesterin; the gray matter of the brain contains about one-fifth. Burchard has found traces of cholesterin in every organ and tissue of the body. It is found also in roots and seeds, especially in peas, beans, and the cereals. From its wide distribution cholesterin may be said to be a constant and essential constituent of both animal and vegetable protoplasm.

Under certain pathological conditions the cholesterin of the bile may be separated, giving rise to the formation of calculi, which consist largely or entirely of cholesterin or of cholesterin in connection with bile pigment, phosphates, carbonates, etc. An ethereal extract of the crushed calculi will yield cholesterin crystals on evaporation. The tests mentioned above may be applied to the extract.

Cholesterin is also found in old exudates and in the contents of cysts, especially in ovarian and hydrocele fluids. In these it may occur in so great an amount that the crystals may be seen with the naked eye as small shining particles. It may be found also in the fatty changes occurring in atheromatous conditions of the blood-vessels, wens, cholesteatomata, caseating tubercles, and degenerating tumors. It is a constant constituent of pus, probably arising from the fatty degeneration of the leucocytes. Cholesterin crystals are also found in echinococcus cysts, and rarely in cataractous lenses.

The origin and fate of cholesterin in both the plant and the animal organisms are unknown. It is most probably an intermediate product in the metabolism of proteids, but the physiological significance of this substance remains to be discovered. It is not excreted in normal urine. Its pathological significance is likewise obscure. Austin Flint's view that the severe nervous symptoms in icterus gravis are due to the retention of cholesterin is not supported by animal experiments. Injections of cholesterin into the blood stream of dogs produce no pathological effects. It is more probable that these symptoms are due not to cholesteræmia but to the presence of some poison not yet discovered. *Aldred Scott Warthin.*

CHOLINE.—Choline is a basic body derived from ammonium hydroxide; it is, in fact, trimethyl-oxyethel-ammopium hydroxide, and is represented by the following formula:

$$N\begin{cases}(CH_3)_3\\C_2H_4OH\\OH\end{cases}$$

It was discovered by von Babo and Hirschbrunn in the seeds of white mustard and named by them sinkaline.

The same body was isolated from the animal body in 1862 by Strecker[1] and named by him choline, since he obtained it from bile. The closely related but far more poisonous base, neurine (trimethyl-vinyl-ammonium hydroxide), was discovered about the same time; the name neurine has been frequently applied to choline, and much confusion has thus arisen. Choline may be made synthetically by the union of ethylene chlorhydrin and trimethylamine; it can also be obtained from a large number of animal and vegetable tissues. It is obtained

* The doses given in this article are for a child one year old.