(two drops of Fowler's solution *ter in die*), the compound sirup of the hypophosphites or sirup of the lacto-phosphate of lime, and cod-liver oil, are to be strongly commended. The phosphates and cod-liver oil should be taken for many months at a time. The chloride of gold and sodium and the corrosive chloride of mercury, the author believes, have the power to retard the changes in the connective tissue taking place in chronic alcoholismus. To effect any obvious results, they must be given before the changes are too far advanced, and must be continued in small quantity for a long period. With these measures must be conjoined a suitable hygiene, proper occupation, and abstinence from alcoholic beverages of all kinds.

AMYLOID DISEASE.

Definition.—*Amyloid disease* is a general condition in which a peculiar albuminous material is deposited from the vessels into the adjacent tissues. The deposition of this morbid material is usually preceded by chronic suppuration in some form. Various names have been applied to this disease, as colloid degeneration, lardaceous disease, waxy degeneration, bacon-like (*speckig*, of the Germans) degeneration, etc.

Causes.—Suppuration, in connection with caries of the bones, long continued, is the most frequent cause. By no means so often does suppuration of the soft parts produce the same result. Among the conditions of this kind are ulcers of the leg of long standing in elderly subjects, old fistulæ, rectal, urethral, and vesical, but especially empyema with or without fistulous communication externally, or by a bronchus. Bronchiectasis, phthisical cavities long suppurating, chronic abscesses, pyelitis and pyelonephritis, chronic dysentery, etc., have been followed, after a more or less protracted course, with amyloid disease. The vast extent of suppurating surface in phthisis, when the tubercular ulcerations occur in the larynx, bronchi, lungs, gastro-intestinal and genito-urinary mucous membrane, furnishes the occasion for amyloid disease in a considerable proportion of all the cases—in a majority of the cases, according to some observers (Schueppel). It is certain that amyloid degeneration is caused by the syphilitic cachexia, especially when there are ulcerations and prolonged suppuration in parts of the body, more certainly when the bones are affected. Hereditary syphilis is also sometimes a cause. There is much reason to believe that a protracted cachexia, produced by chronic malarial poisoning, has given rise to amyloid deposits. Although it appears necessary that suppuration be protracted, Cohnheim* has shown that, as regards gunshot wounds of bones, three months of suppuration, only, is sufficient. He records three cases in which death ensued after wounds of bone, in

* Virchow's "Archiv," Band liv, p. 271; "Zur Kentniss der Amyloidentartung."

six, five, and three months respectively, the amyloid deposits being widely distributed.

As regards sex, men are much more liable to the disease than women—the proportion being from two thirds to three fourths. It occurs at all periods in life, but is more frequent at the most active and exposed age.

Pathological Anatomy.—The term *amyloid*, or starch-like, is rather misleading, since the material is albuminoid in its characteristics. The *corpora amylacea*, as found in pathological products of the nervous system, present a strong resemblance to starch-granules, but the amyloid matter, as deposited in the cachexia, with which we are now concerned, is very different in appearance, and "probably has nothing in common" with those bodies (Wagner).*

It has not been possible, hitherto, to separate the amyloid deposit from the tissues in which it is deposited; hence the published analyses are misleading. It is closely related to glycogen. It has the distinctive property that it resists the action of digestive ferments, and but slowly yields to putrefactive fermentation. Its presence in tissues is readily determined by the reagents originally proposed by Virchow—iodine and sulphuric acid. The suspected material is washed over with a solution of iodine in iodide of potassium, when the amyloid parts are stained of a mahogany brown, the healthy tissue appearing a faint yellowish tint. If dilute sulphuric acid (two *per cent.*, Kyber) is afterward brushed over, the amyloid matter assumes slowly a dark-blue color. The iodide of methylanilin has been brought forward lately as a test. Parts of the suspected organ (the liver, for example), hardened in alcohol, are placed in a solution of the iodide of methylanilin, and in a few minutes the amyloid deposits are stained a ruby-red, while the rest of the tissue presents a cloudy, bluish tint. This is less certain than iodine and sulphuric acid, is the judgment of Kyber.

In some way, not now understood, the albuminous body, which must exist in the blood prepared for tissue-formation, is precipitated in an insoluble form in the walls of the nutrient vessels or in the tissues adjacent. There are two theories now held in regard to the deposits: according to one, the deposits occur in the tissues adjacent to the vessels; according to the other, into the walls of the vessels. Just about the vessels, and in their walls, is deposited a thick, colorless, waxy material which, as it solidifies, has the transparency, almost, of glass. The German name given to it signifies that this material resembles lard in appearance. The deposits do not follow any regular plan, and are variously distributed in the affected organs. The initial deposit takes place in the liver, and in that zone of the hepatic structure which is concerned, as is supposed, in the formation of glycogen. The branches of the hepatic artery are first attacked, then the capilla-

* "A Manual of General Pathology," by Prof. Dr. E. Wagner, *op. cit.*, p. 325.

ries of the lobules are invaded. According to Virchow and his followers, the deposits occur in the liver-cells, while Wagner maintains that the capillaries only are invaded, the liver-cells perishing by atrophy and fatty degeneration. Schueppel is inclined to agree with Wagner, but Kyber * affirms that the liver-cells are invaded by deposits, as he has isolated them and recognized the changes. As a result of the deposits the organ enlarges, sometimes enormously, reaching the weight in some instances of twelve pounds, and averaging twice the weight of the normal organ. The shape is not materially altered, except that the anterior edge is smooth, rounded, and thickened. In color, the organ assumes a light-grayish brown, or yellowish gray, and in consistence is very firm, resilient, or elastic, giving the impression of soft rubber, but not offering much resistance to the knife in section, although much tougher than the normal liver-tissue. The cut surface seems dry, is nearly bloodless, and has a grayish-yellow or brown color, like smoked bacon. The surface is not homogeneous, for the outlines of the acini are distinct, and the loblules are separated by a yellowish line. When the deposits are slight in extent, the whole organ will not appear changed, but in the middle zone of each lobule the amyloid infiltration first takes place, and here will be exhibited the peculiar grayish color and glassy translucency characteristic of the deposit. According, then, to the extent of the infiltration will the organ deviate from the normal. Instead of occupying a considerable portion of the liver, deposits may occur in spots forming nodular masses, the rest of the organ being healthy. Amyloid deposits in the liver may be associated with fatty degeneration of parts of the organ, with syphilitic nodules, and with metastatic abscesses.

In the spleen amyloid deposits are seen in two forms: in isolated, small nodules, formed about the Malpighian vessels—the *sago spleen*—and a general degeneration; the latter being merely a continuation and final development of the former. In the true amyloid spleen the whole organ is enlarged, firm in its structure, and having a light-brown or even grayish-yellow color. The cut surface is smooth and firm, and is not broken up into a pulp by pressure, as in the healthy organ. The trabeculæ are thickened and infiltrated by the amyloid material, giving to them the characteristic grayish appearance and vitreous luster. The deposits form thick and rather lustrous rings around the venous sinuses, and the walls of the larger and smaller arteries are infiltrated.

The amyloid kidney, like the amyloid liver and spleen, is larger and heavier than normal. Externally, the cortex is pale, even white, from anæmia, and has the peculiar glistening appearance characteristic of this degeneration. On section the same appearances are manifest,

* "Weitere Untersuchungen über die amyloide Degeneration," Virchow's "Archiv," vol. lxxxi, p. 1, *et seq.*

and the broad, whitish, translucent-looking cortex contrasts strongly with the dark cones. The vessels of the glomeruli are first changed; then the afferent arteries, and afterward the efferent, become the seat of considerable deposits which, however, are most extensive in the vasa recta. Subsequently the tubules and their epithelium are infiltrated. The supra-renal bodies, in a large proportion of cases—fifteen out of eighteen cases, according to Kyber—are affected in the course of the general disease. In extreme cases they are very large, pale, and waxy in consistence. The genito-urinary organs, the vessels of the mucous membrane of the ureters and bladder, of the uterus and prostate, and the muscular fibers of these organs, are also affected by amyloid change. The vessels of the mucous membrane of the tongue, œsophagus, stomach, and intestines, and sometimes the mucous membrane itself, are attacked. The arteries of the sub-mucous tissue of the intestines and the muscular layer of the stomach and intestines are also affected.

In a considerable proportion of cases the endocardium and the great vessels are affected, as well as the vessels of the body generally. The inner coat of the large arteries and the middle coat of the smaller arteries and veins are the parts invaded by the deposits (Kyber). We possess no information in regard to amyloid degeneration of the nervous system.

Symptoms.—When the various organs are affected by the lardaceous disease, a peculiar constitutional state—a cachexia—is induced. Previous to the deposition of amyloid matter, the vital forces are depressed by chronic suppuration, by the syphilitic cachexia, by chronic malarial poisoning, etc. Persons attacked with this disease are already pale, sallow, thin, weak, and depressed, in varying degrees, according as exhausting suppuration or syphilitic lesions or malarial toxæmia precedes its development. When the intestinal canal becomes affected, the appetite declines, there is considerable nausea, sometimes vomiting. As changes in the liver occur, hyperæmia and a catarrhal state of the mucous membrane are constantly maintained. Under these circumstances thrombosis of a stomach-vein may occur, resulting in ulceration, usually about the pylorus, and then vomiting of blood takes place. An intractable diarrhœa, colliquative in character, also comes on. The discharges are thin, offensive, very light or very dark in color; the latter, when blood is present. Particles of food, undigested and decomposing, are present in the evacuations, and ultimately such food as beef-tea, even milk, pass largely unchanged. Sometimes the stools appear like rice-water, are mucilaginous, and have little odor.

The clinical feature of amyloid liver is a persistent enlargement of the organ. As the weight of the liver, in extreme cases, may reach twelve pounds, it is usual to ascertain that the organ extends beyond

its ordinary boundaries, to the breadth of the fingers, or more, below the inferior margin of the ribs. When thus enlarged, it can be readily felt through the abdominal parietes as of almost stony hardness. Sometimes the inferior edge of the liver may be grasped, and its condition noted, through the relaxed walls. Besides its hardness, the liver feels smooth, and is free from tenderness. It is but rare that jaundice occurs. Ascites is usual, and there may be general œdema or dropsy from the accompanying renal lesions. When ascites is alone present, there may be œdema of the feet and legs. Often the dropsy assumes a high grade; the abdomen becomes enormously distended, the scrotum attains vast dimensions, and the whole body is flooded with its own fluids.

Another large and hard body—the spleen—can also be made out in the abdomen. As the spleen is damaged, the anæmia increases. When the deposits are most pronounced in this organ, and when the disease begins its course by the changes in the spleen, an increasing leucocythemia is the most prominent symptom. When, however, the splenic disease is only a part of the general changes, and comes on after the lesions are well advanced elsewhere, there will be little alteration in the course of the malady except the more pronounced anæmia; but in the absence of ascites the splenic tumor may be made out.

The amyloid degeneration of the kidneys is manifest in the changes of the urinary secretion. As a rule, the amount of urine passed is great, except when a profuse, watery diarrhœa carries off the surplus fluid. The urine is, also, pale and of low specific gravity, when abundant, appearing to be little more than water. When scanty, the urine becomes dark and the specific gravity high. It may thus fluctuate between the extremes 1002 and 1035. The urea, chlorides, and phosphates are in very small quantity when the amount of urine voided is large, and relatively considerable when the urine passed is small in quantity. As the disease progresses, the relative quantity of solid matter in the urine diminishes. Albumen early appears in the urine, at first occasionally, as a mere trace, but, as the deposits increase, in constantly enlarging quantity, although never rising to the percentage of certain acute affections. Besides serum-albumen, the urine of amyloid kidneys contains a considerable quantity of globulin. Casts are only occasionally found, and are narrow and of the pale, hyaline variety. When the urine is condensed, dark in color, and loaded with albumen, which is an exceptional condition, the casts will be more abundant, chiefly of the narrow, hyaline kind, but also of highly refracting, yellowish, waxy material. General dropsy is comparatively infrequent, while ascites and œdema of the inferior extremities are common. Symptoms of uræmic intoxication are only rarely present, and for the obvious reason that the elimination of the urinary constituents, including urea, is not materially lessened by the amyloid degeneration. Even at the end when the quantity of urine passed is extremely scanty, there are but rarely slight symptoms of cerebral derangement, including headache, drowsiness, failure of memory, muscular weakness and tremors, and twitching of the facial and other muscular groups.

Diagnosis.—Amyloid disease, coming on in the course of some chronic malady with suppuration, can usually be readily diagnosticated. The coincident enlargement of the liver and spleen, the occurrence of polyuria with traces of albumen, and the troublesome diarrhœa, make up a morbid complexus of a very significant character. The enlarged liver may be confounded with the first stage of sclerosis or with echinococcus cysts. As regards the first, it is to be noted that the history is different, but the chief distinction lies in the fact that in sclerosis the enlargement is slight and is transient, whereas in amyloid disease it is considerable and persistent. In sclerosis the liver is irregular in outline and somewhat tender; in amyloid disease it is hard and without tenderness. The renal affection of amyloid disease may be confounded with interstitial nephritis. The history of the case becomes very important as a means of differentiation. In sclerosis of the kidney the albumen is more abundant; a marked reduction in the amount of urine, after a considerable increase, is observed; and cerebral symptoms are much more constant. The character of the casts, and especially the appearance of the yellow, highly refracting casts, responding to the iodine reaction, are of great value in the differentiation.

Treatment.—There are obvious indications for treatment in the debility and wasting with which the disease begins and is attended throughout its course. A full diet, rich in all the materials of nutrition, and especially of fats, should be prescribed. As the intestinal canal may be much damaged, foods converted into peptones in the stomach, and the aids to stomach digestion, acids and pepsin, are necessary. For the diarrhœa, two or three drops of Fowler's solution and twice the quantity of tincture of opium, persistently used, are probably the most efficient remedy. Hope's mixture, or an extemporaneous combination of nitro-muriatic acid and tincture of opium in camphor-water, may be substituted. Bismuth in full doses, with aromatic powder, is a useful astringent. Without a careful regulation of the diet, no remedies will succeed. Cod-liver oil, as a food and restorative, will sometimes improve the diarrhœa. As remedies for the local deposits—to convert the insoluble albuminous material into a soluble—phosphorus, the phosphites, and phosphates, are, in the author's experience, entitled to the first place as remedies. Phosphorus in minute quantity ($\frac{1}{120}$ grain), dissolved in cod-liver oil, is probably first. Phosphites, in the form of the compound sirup, is a valuable combination. The phosphates rank next. The author has had excellent results from

the phosphate of soda in cases without diarrhœa, which is a contra-indication to its use. These remedies should be used persistently and for lengthened periods. The iodide of potassium, with a generous diet and iron, is a method of treatment strongly urged by Bartels, and with which he has, he says, succeeded in effecting a cure. A careful mercurial course, with or without conjoint or alternate administration of the iodide of potassium, may be useful in cases originating in the syphilitic cachexia. Dickinson, influenced by his theory of amyloid deposits, administers alkalies, which restore their solubility. Alkalies may be serviceable, but the depression caused by them should be prevented by the timely administration of iron and a generous diet.

ANIMAL POISONS.

HYDROPHOBIA.

Definition.—*Hydrophobia* is a specific disease due to the inoculation of a poison contained in the saliva of rabid animals, notably the dog, and characterized by pain and stiffness of the inoculated part; by exaltation of the reflex faculty; by spasms of the throat on the attempt to swallow, and subsequently at the sight of liquids; by delirium, exhaustion, and death. It is also known as *rabies canina*.

Causes.—The sole condition necessary for the causation of hydrophobia is the inoculation of man with a contagious principle contained in the saliva of the dog, cat, wolf, and some other rabid animals. This principle is not absorbed through the unbroken skin, but from a wound or abrasion. A certain predisposition is also necessary, it is probable, for, of all bitten by animals unquestionably rabid, but a small proportion are attacked by hydrophobia. The proportion is variously stated from five to fifty per cent., but, while the former is much too small, the latter is excessive. Accident more than predisposition is, however, the real cause of the exemption of so many who are bitten. The teeth, in inflicting the wound, pass through clothing, which removes the saliva, and hence the most of those bitten through the clothing escape infection. On the other hand, wounds of exposed parts, or an abrasion receiving the saliva, is very certain to be followed by the disease, unless there be a decided insusceptibility to the action of the poison. All ages and both sexes are liable, but more men than women are attacked,

because the former are more exposed. Various moral impressions favor the occurrence of the disease. These are apprehension, fear, excesses of all kind, fatigue, etc.

Pathological Anatomy.—There are but few changes found *post mortem* really typical, if any such exist, but are common to all the diseases of the same group. The cadaveric rigidity is well marked; there are extensive suggillations, and putrefaction soon begins; the coloring matter of the blood stains the vessel-walls, and the blood itself is fluid and has a violaceous color. These facts only indicate a changed state of the blood common to many maladies. The fauces are red and swollen, the salivary glands enlarged; the trachea and bronchi are hyperæmic and contain a quantity of frothy mucus; the lungs are also hyperæmic and sometimes œdematous. More or less congestion of the brain, effusion into the ventricles, and hyperæmia, with enlargement of the vessels of the medulla oblongata, have been observed. In some cases changes of texture, softening, etc., have been seen at the apparent origins of the seventh, eighth, and ninth nerves. The pneumogastric, phrenic, and sympathetic nerves have also been found in a more or less hyperæmic state.

Symptoms.—The period of incubation is by no means confined to fixed limits. In 214 cases collected by Jaccoud, the period of incubation was less than one month in one fourth of the number, from one to three months in 143, from three to six months in 30, and from six months to a year in 11. According to Gamgee, in the large majority of cases, the period of incubation is four to eight weeks. Age apparently affects the duration of this period. Thus in nine new-born infants, the incubation period was thirteen to fifteen days. A very remarkable case has been reported of a man two years in prison, who had hydrophobia, and who had been bitten seven years before. During the period of incubation there is nothing in the wound, nothing in the state of the organism, to indicate the existence of any mischief. The wound or abrasion may be very slight, may have healed long since and been forgotten. At the termination of the incubation, the attention of the patient is attracted to the wound by some uneasiness felt in it. If it has not healed, the wound takes on a livid appearance, and becomes exceedingly painful, the pain shooting toward the trunk from the extremities if the wound is so situated. If the wound has cicatrized, the scar becomes painful, red, irritable, swollen, and sometimes exudes a bloody serosity. Sometimes a sensation of coldness and of numbness is felt in the bitten member, and occasionally the lymphatics of the limb are swollen, and marked by hard, red lines. The local symptoms are soon accompanied by systemic disturbances. The patient is depressed, apprehensive, peevish. So marked is the condition of melancholy that the first stage of hydrophobia has been called the *stadium melancholicum*. The skin becomes hot, the pulse rapid and bounding.