left in the area are the endothelial cells, which may persist for a long time. The intermediate zone of the lobule is almost always affected to a greater extent than either the central or the peripheral one. The walls of the larger blood-vessels may also show the deposit. In more advanced cases the entire lobule may be replaced by amyloid. This marked change is usually confined to single scattered lobules, so that these appear to the naked eye as grains of boiled sago (sago liver). More rarely the greater part of the liver may be replaced by confluent masses of amyloid, whereby the organ acquires a wooden hardness and in section resembles the translucent portions of bacon (*Speck-Leber*).

Spleen.—In the spleen the amyloid deposit takes place in the fine reticulum of the pulp beneath the endothelium of the blood spaces. The follicles may alone be affected, appearing enlarged and translucent like boiled sago (sago spleen); or the chief deposit may be throughout the pulp, or may involve both pulp and follicles (*Speck-Milz*, lardaceous spleen). The arterioles of the follicles are often the only portions of the organ which show the deposit, and it is in these that the earliest appearance of amyloid in the body as a rule occurs.

Kidney.—The afferent arterioles of the glomeruli are usually first affected, then the glomerular capillaries and efferent vessels, and finally the smaller vessels throughout the entire organ. The change is never so marked in the medullary pyramids as in the cortex, but it may appear early in the straight vessels of the former. As the disease advances the deposit extends from the intertubular capillaries to the basement membrane of the tubules, which may appear as if surrounded by a hyaline ring. The intima of the larger branches of the renal artery may show small and irregularly scattered deposits. Since the glomeruli are the chief seat of the deposit, they appear on the freshly cut surface of the organ as small, firm, translucent dots usually about the size of pinheads.

Lymph Glands.—Extensive amyloid deposit is not common in the lymph glands, but scattered masses are very frequently found in them; and the walls of their small arterioles usually show a moderate degree of change in all cases in which the liver, spleen, and kidneys are extensively affected. Local inflammatory changes, both of the lymph glands and the tonsils, are very frequently accompanied by the formation of small masses of amyloid in connection with hyaline deposit, and the close relation of these substances is nowhere else so well shown as in these organs. In advanced cases the deposit may extend from the neighborhood of the capillaries into the reticulum, causing atrophy of the lymphadenoid cells.

Heart, Fat Tissue, &c.—In striated muscle amyloid deposit is rarely found. It has been found in the tongue and in the muscles of the larynx in the shape of nodular masses. The deposit takes place first in the walls of the capillaries of the endomysium, and as it increases in size the sarcolemma comes to be surrounded by a clear, hyaline mass. As the muscle fibre is thus separated from its blood supply it undergoes atrophy and degeneration, finally disappearing so that the deposits of amyloid become confluent into nodular masses. A similar process may take place in heart muscle and in unstriated muscle, but is of rare occurrence. The amyloid deposits in striped muscle occur very frequently in the shape of gummata, but occasionally no evidences of preceding pathological changes can be made out. Adipose tissue is often extensively affected by amyloid disease, the deposit taking place in the walls of the larger blood-vessels and of the intercellular capillaries, so that the fat cells come to be surrounded by a thin hyaline layer.

Mucous Membranes.—The mucous membranes of the respiratory tract are very rarely affected. Scattered deposits may occur in the mucosa of the stomach and intestine, producing more or less extensive thickenings of the mucosa, which show the characteristic homogeneous, glassy appearance of amyloid. Large elevations may undergo ulceration, and at the bottom of the ulcer remains of the amyloid may be preserved. The large intestine is more frequently affected than the small. The deposit is in the walls of the capillaries of the mucosa and submucosa. Only in very rare cases is amyloid found in the mucosa of the genito-urinary tract.

General Nature of Amyloid Disease.—As stated above, the formation of amyloid is almost always secondary to other processes which are ulcerative or inflammatory in character, and of infective nature. While not in itself a true degeneration of cell protoplasm, the process is essentially degenerative in character, in that it leads to marked disturbances of nutrition. The deposit in the walls of the blood-vessels leads to partial or complete obliteration of their lumina, thus producing permanent interference with the circulation. As a result of this disturbance of nutrition, atrophy, fatty degeneration, or necrosis of the tissue cells takes place. The pressure of the amyloid deposits between the cells leads to similar results. Fatty degeneration and infiltration are almost always present to a greater or less degree in amyloid disease, and to a certain extent must be regarded as coincident processes produced, perhaps, by the same general disturbances of metabolism which give rise to amyloid. Severe anæmia is usually associated with the condition, and death takes place as a rule from a gradually increasing marasmus.

Symptoms.—The marked alterations in the structure of the affected organs and tissues lead to functional disturbances, which, however, may be very slight when compared to the extent of the deposit. The general clinical picture of the condition will vary, of course, with the organ affected and with the extent of the disease, so that a comprehensive description is not possible. Moreover, from the nature of the case, it is manifestly difficult or impossible to separate the symptoms of amyloid deposit from those of the disease leading to or associated with it. The nature of the primary process will modify very much the clinical appearances dependent upon the amyloid change. Frequently the beginning of the condition is shown by a rapid increase in the marasmus already existing, and by the enlargement of liver and spleen. These phenomena are always more marked in syphilis and in chronic ulcerative processes than in pulmonary tuberculosis. In such conditions as chronic varicose ulcers of several years' standing a rapid increase of the cachexia is usually pathognomonic of amyloid disease.

Associated with enlargement of the liver certain disturbances of digestion go hand-in-hand: absence of bile pigment in the fæces, fecal decomposition, meteorism, etc. Icterus is rarely present, and ascites only as associated with a general hydræmic or cachectic anæmia. Marked amyloid deposit in the kidneys is not always shown by disturbances of its function. The urine may show no changes; but as a rule albumin is present, the amount is increased, and the sediment contains hyaline casts, though usually not in great numbers. The latter may give the amyloid reaction, in spite of the repeated statements that they do. As amyloid deposit in the kidneys is, in the majority of cases, associated with chronic inflammatory changes, the character of the urine may vary greatly. Marked amyloid disease of the intestine is usually accompanied by foul diarrhœa.

Course.—The nature of the primary affection must first be considered. If in patients affected with any one of the chronic diseases known to be associated with amyloid disease, tuberculosis, syphilis, chronic suppurative processes, or long suppurating wounds of the liver and spleen arise, in connection with albuminuria and extreme paleness of the skin and mucous membranes, the diagnosis of amyloid is made very probable.

Duration.—The earliest stages of amyloid change cannot be ascertained clinically. It is probable that in many cases the process develops through several or even many years with alternate periods of improvement and exacerbation. It may, however, develop within shorter periods, as is exemplified by Cohnheim, in which suppuration of bone after a fracture led to well-developed amyloid disease within a few months. The duration of well-marked cases depends upon the organ chiefly af-

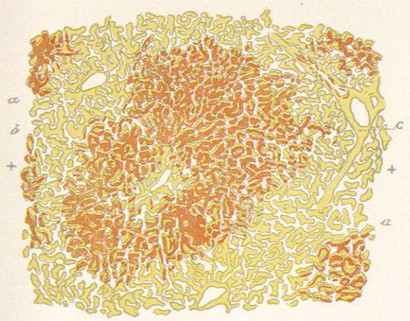

Fig. 1.

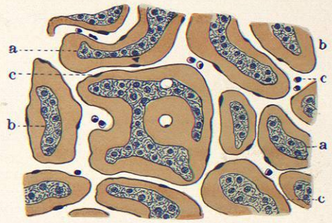

Fig. 3.

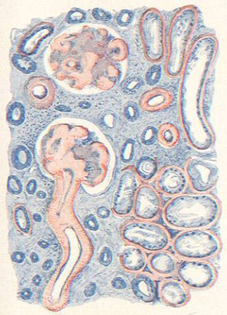

Fig. 2.

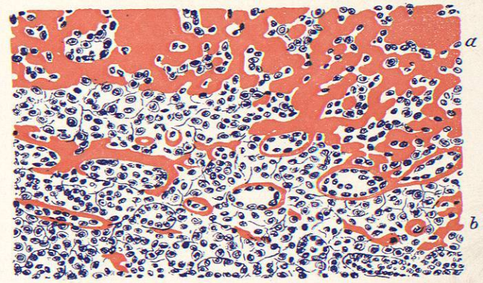

Fig. 4.

AMYLOID DEGENERATION IN DIFFERENT ORGANS

Fig. 1. Section of an Amyloid Liver, Showing the Effects of Staining it with a Solution of Iodine. *a*. Normal liver tissue; *b*, tissue that has undergone amyloid degeneration; *c*, Glisson's capsule magnified 35 diameters. (Ziegler.)

Fig. 2.—Amyloid Kidney, Stained with Aniline Violet. The amyloid is stained red. The deposit is most marked in the capillaries of the glomeruli and in the small arteries, and is seen also as a fine hyaline ring surrounding the membrana propria of the tubules. Magnified 400 diameters. (Ribbert.)

Fig. 3.—Section of an Amyloid Liver After being Treated with Methyl Violet and Acetic Acid. *a*, Elongated masses of liver cells; *b*, amyloid substance; *c*, endothelium of the capillaries; *e*, colorless blood corpuscles. Magnified 150 diameters. (Ziegler.)

Fig. 4.—Amyloid Degeneration of the Follicles and Pulp of the Spleen. (Alcohol; methyl violet; hydrochloric acid.) *a*, Follicular tissue in a marked state of amyloid degeneration; *b*, pulp tissue in which the degeneration has begun. Magnified 300 diameters. (Ziegler.)

fected. Extensive changes in the kidney are much more serious than those of the liver or spleen, as they lead to death within a few weeks or months.

PROGNOSIS.—This is in general unfavorable. It is probable that amyloid, when once formed, is not removed from the site of deposit. In all cases in which the condition is so marked that the diagnosis is certain, death usually occurs within short periods. Temporary improvement may take place; and in some cases, especially after operation for chronic purulent conditions of bone, the disease apparently comes to a standstill, marked general improvement takes place, the liver swelling decreases, and the albuminuria disappears. It is, of course, impossible to say to what extent these symptoms were due to the amyloid disease. A similar improvement has been noticed as the result of a prolonged inunction cure in a case of amyloid associated with syphilis. Corneal tumors may slowly disappear under the influence of local irritation and inflammation.

TREATMENT.—For the well-established condition it is hardly probable that treatment will avail, though iodine, ammonium chloride, potassium iodide, dilute nitric acid, etc., have been recommended. The improvement of the local or general primary condition is, of course, the most important therapeutic line to be followed; and in connection with this the general improvement of nutrition. Of far greater importance are prophylactic measures, even to the extent of such radical procedures as amputation in cases of chronic varicose ulcerations, chronic suppuration of bones, etc., in which persistent operative and therapeutic measures have been without result. *Aldred Scott Warthin.*

ANABOLISM. See *Metabolism.*

ANACARDIACEÆ, or **TEREBINTHINACEÆ.**—(The Cashew family.) A remarkable and important family of some fifty-nine genera, chiefly tropical or subtropical, exceedingly varied in the nature of its products. The mango, the cashew, and the spondias or hog-plum, are important fruits; those of Pistacia furnish a well-known flavoring agent, while its bark yields the commercial resin mastic; the milk juice of several Japanese species of Rhus furnishes Japanese lacquer, and the leaves and fruits of other species of this genus yield tanning agents. The oil which abounds in several species of Rhus (more properly called *Toxicodendron*), and in some other genera, acts as a powerful cutaneous poison. (See *Poisonous Plants.*) *H. H. Rusby.*

ANÆMIA, PERNICIOUS.—(Synonyms: *Progressive perniziöse Anämie,* Biermer; *Idiopathic anæmia,* Addison; *Essentielle Anämie,* Lebert; *Essentielle maligne* or *Essentielle fébrile Anämie,* Immermann; *Perniziöse Anämie,* Quincke; *Anémie progressive,* Lepine.)

DEFINITION.—Pernicious anæmia is a grave form of anæmia which is characterized by a reduction in the total amount of the blood and by a change in its physical, anatomical, and chemical characters. The blood is thin and pale and not coagulable. The red corpuscles are lessened in number and changed in size and shape. It is a peculiar circumstance that the adipose tissue is generally maintained, while at the same time secondary fatty degeneration of the heart is almost always found to be present. The disease is distinguished, clinically, by the symptoms of grave anæmia, often by an irregular fever, retinal hemorrhages, and hemorrhages underneath the skin and from mucous membranes. Its course is usually progressive, its termination fatal, its duration from seven weeks to from two to three years. Complications are rare; death is due to exhaustion, to syncope, to œdema of the lungs, or to cerebral complications.

This symptom complex may be dependent on some evident anatomical change or it may have no demonstrable organic basis. Thus we distinguish secondary or symptomatic progressive pernicious anæmia and a primary, essential, or cryptogenic form. Some authors limit the term pernicious anæmia to the latter group, but it seems better, in view of the identity of the two conditions anatomically and clinically, to apply the term to that peculiar form of anæmia which possesses the characteristics enumerated above, whatever its cause may be. In the secondary form of pernicious anæmia the symptoms of the blood changes dominate the clinical picture so that the symptoms referable to the causal lesion are comparatively insignificant, and the anæmia becomes practically a disease *per se.* This characteristic marks the distinction between pernicious anæmia and simple chronic anæmia in which the symptoms of the primary disease hold the first place, although the anæmia may be severe.

HISTORY PREVIOUS TO 1872.—The publication by Biermer, in 1872, of a series of cases of this disease, and his assertion that he was the first to recognize it, aroused the latent energies of the English, so that since then they have justly and successfully shown that to one of their countrymen is due the credit of having identified it long before that time. Addison certainly had observed and taught the clinical course of the disease, and had made inquiries into its pathology. He clearly established that what he called idiopathic anæmia was an independent affection, and so impressed it upon his colaborers and students that ever since then it "has not been lost sight of at Guy's." The wards of that hospital have furnished most of the cases for English memoirs, and its reports contain many observations and discussions on this disease. Prior to Addison, Coombe, Marshall Hall, and Barclay reported isolated cases of fatal anæmia. Since then, and before Biermer's publication, Wilks, Bristowe, Leared, and Habershon made contributions to our knowledge of the disease. The labors of Taylor, of Pye-Smith, of Mackenzie, and of others have clearly proven the fact of English priority. Professor Eichhorst, in his elaborate monograph, admits these claims, while Pepper, in the United States, was one of the earliest to point out the credit due Addison. In the mean time, the French, through Lepine, presented their claims of priority in the early recognition of the disease. Lepine justly admits the valuable work of Addison and his followers, but says that Andral was the earliest observer, and that Piorry, Cazenave, and Perroud had recognized the affection, the latter detailing four cases, with autopsies. A dissenting voice arose among the Germans. Lebert claimed that he had, in separate papers, described this disease, but the evidence from them shows that he had confused chlorosis with pernicious anæmia. Lately, it has been found that American physicians can enter claims of priority for one of their countrymen. Channing described cases of fatal anæmia in connection with, and independent of pregnancy as early as 1832. Not only was he himself perfectly familiar with it, but so also were many of his associates.

HISTORY SINCE 1872.—The time of the publication of Biermer's essay on "Progressive Pernicious Anæmia" makes an epoch in the history of this strange disease. He not only embodied in his essay as faithful a portrayal of the disease, as Addison and others had done, but he added to it more accurate accounts of the blood changes and the occurrence of retinal hemorrhages. Moreover, he so impressed the medical world with the important results of his observations that since then the knowledge of the disease, instead of being confined mostly to England, has become universal, and multitudes of observations have been in a short time added to the previous comparatively scanty data. In 1874 Immermann, in 1875 Zenker, and in 1876 Quincke, made valuable contributions to the study of the disease, while in 1877 important and elaborate monographs, by Müller and Eichhorst respectively, appeared. Since then German literature has been rich in observations of isolated cases. Among Englishmen, Pye-Smith, in 1875, published two cases in the *Deutsches Archiv,* and since then, among others of his countrymen, Bramwell, Mackenzie, Finney, Coupland, and William Hunter have written interesting and important articles. In America, Pepper, Howard,