general œdema ; but usually the œdema is about the ankles. The skin may contain petechiæ of a purplish or brownish tint, scattered over the trunk and limbs. There may be ecchymoses, having the various colors characteristic of extravasated blood at different periods, and vibices, due to the same cause, and produced by pressure. There is more or less serum in the various cavities, and the organs generally are pale and bloodless. The changes in the heart and arterial system are the same as already described (see ANÆMIA), and consist in fatty degeneration of the cardiac muscles (papillary) and of the intima of the aorta and principal arteries. The alterations in the composition of the blood are also similar to those of anæmia, but they are more extensive and profound. The volume of the blood is lessened, the red corpuscles are fewer, the albuminates of the blood diminished, and the fibrin is deficient. There is no constant disturbance in the normal ratio of the white and red corpuscles, although cases have been reported in which the leucocytes were increased.

Symptoms.—The exact beginning of pernicious anæmia usually passes unnoticed ; an unwonted paleness, a sense of fatigue on the least exertion, hurried breathing, and palpitation of the heart, at length attract attention. This may be entitled the chronic form. In a few cases, happening during pregnancy, the onset is rather sudden, and extreme pallor, palpitation, and breathlessness on making any effort appear within a short period. The progress is comparatively rapid in both forms after the symptoms are fully developed, and in a short time the weakness is such that the patient is confined to bed, is unable to rise, and faints on attempting to assume the erect posture. Various local hæmorrhages take place, as epistaxis, bleeding from the gums, menorrhagia, extravasations under the skin and into the retina. The hæmorrhages into the retina are very common, and consist, on ophthalmoscopic examination, of small, blackish, brownish, or yellowish-brown spots, or larger patches covering more or less of the fundus. They may, when very minute, not affect the vision, although present in great numbers ; but an extravasation in the retina of considerable size obscures the field of vision correspondingly (Immermann). Small extravasations or larger hæmorrhages may take place in the brain, with the usual results. A constant symptom is fever, but it does not appear until near the end of the case, and does not pursue a definite plan or type. When death is imminent, the fever not only ceases, but the temperature declines below normal, falling to 95° Fahr., or even lower.

Course, Duration, and Termination.—Although pernicious anæmia has been separated from allied states, yet in its course and behavior it strongly resembles anæmia and chlorosis, especially the latter, or more closely a combination of the two. It seems, as it were, anæmia added to chlorosis, and the worst features of each fully developed. The duration is not self-limited, and hence varies greatly. The acute cases usually terminate within two months, but the more chronic ones

continue for three or four months. The mode of dying is by exhaustion usually, but life may be unexpectedly terminated by sudden paralysis of the heart, or by cerebral hæmorrhage. In some instances the end has been reached by the condition known as "Kussmaul's Coma." Sudden unconsciousness occurs in consequence of cerebral capillary embolism (white-cell embolism ?), or from the development of acetone (acetonæmia).

Diagnosis.—Pernicious anæmia is distinguished from anæmia and chlorosis by the severity of the symptoms ; from albuminuria by the absence of albumen from the urine ; from leucocythemia by the normal condition of the spleen, liver, and lymphatics ; from Addison's disease by the absence of the bronzing. The prognosis is highly unfavorable, no cases of cure having been reported.

Treatment.—There is no specific plan of treatment. The anæmic symptoms require iron ; but, if hæmorrhages are occurring, iron must be discontinued, when arsenic, ergot, and quinia may be substituted. A generous diet and stimulants must be administered from the beginning. The best results have been obtained from the administration of phosphorus, and from arsenic given subcutaneously and in full doses.

THROMBOSIS AND EMBOLISM.

Definition.—By the term *thrombus* is meant the formation of a clot in a blood-vessel—an *ante-mortem* coagulation. The mechanism of its formation and the pathological changes associated with it are called *thrombosis*. A detached clot, or parts of a clot, or any new formation circulating in the blood-current, is designated an *embolus*, in the plural *emboli*, as fibrin embolus, fat embolus, pigment embolus, etc. The secondary obstruction and the changes consequent thereon, produced by an embolus, are known as *embolism*—as cerebral embolism, pulmonary embolism, etc.

Causes.—The process of coagulation of the blood consists in the precipitation and consolidation of certain of its constituents, which, under normal conditions, remain fluid. When a blood-clot forms, the fibrino-plastic substance acts on the fibrinogenous, the former contained in the blood corpuscles, the latter in the liquor sanguinis. This formation of fibrin, by the reaction between two other principles, is like the production of prussic acid by the reaction between amygdalin and emulsin, or of the volatile oil of mustard, by myrosin and myronic acid. The formation of fibrin, or the coagulation of the blood, only takes place in the vessels when there occurs a slowing of the current, or when there is a change in the parietes of the vessels. In diseases characterized by abnormal increase of the fibrin (*hyperinosis*), should the blood-current be much reduced in rapidity and force, coagulation will take place. Thus in *post-partum* hæmorrhage, a thrombus not infrequently forms in the pulmonary artery. When the *vis-a-tergo* is

weak, and an obstacle is placed in the capillary region in front, thrombi may form in the veins next the capillary system—as, for example, in the pulmonary veins, in chronic interstitial pneumonia; in the renal veins, in parenchymatous nephritis, etc. Again, when vessels are divided, hæmorrhage is arrested by thrombi which close the divided extremity. Thrombosis, the result of changes in the tunics of the vessels, is more frequent in relation to disease of the arteries than of the veins. Formerly the notion was entertained that phlebitis played an important part in the process of thrombosis and embolism; that the intima was the seat of exudations and other products of inflammation to which the formation of a clot was immediately due, but it is now known that inflammation of veins is interstitial; that the tunica intima, deprived of its nutritive materials, undergoes necrosis, and becomes a foreign body, about which coagulation of blood takes place. This, however, is a comparatively rare cause of thrombus formation, as this process occurs in the veins. It is in the arterial system that those changes take place which enter so largely into the phenomena of thrombosis and embolism—the results of endocarditis and endarteritis. The formation of vegetations in endocarditis, especially on the valves, is a fruitful source of embolisms. In endarteritis slow degenerative changes occur in the walls of the vessels, the internal layer (intima) becomes involved—thickened, roughened, necrotic—and then thrombi form. Any foreign body, as a needle introduced into a vessel, will induce coagulation and the gradual formation of an obliterating thrombus. An embolus is formed when a portion of a thrombus, detached from the parent clot, enters the blood-current. The density of the clot and its position are important elements in the detachment of emboli. The softer the clot the more easily it is broken up, and, if situated near to the entrance of a communicating vein, the more certain a portion of it will be broken off from the main mass. The conical shape which the thrombus assumes, projecting beyond the point of attachment to the intima, and floating freely at its end, are physical conditions favoring its separation. Besides the action of these forces, emboli are detached by coughing, vomiting, sudden jars, straining muscular movements, etc. After fractures an immense number of fat emboli may enter the systemic circulation, and now and then a phlebolithe is a cause of obstruction; cancer products may penetrate the blood and be distributed widely; multiple embolisms may be caused by the entrance, from a depot of putrefactive matters, of putrid ferments; and pigment emboli may be a product of malarial fevers.

Pathological Anatomy.—Recent thrombi consist of soft, brownish-red coagula, either in the form of a plug which fills the vessel and entirely shuts off the circulation, or in a *plaque* or tablet attached to one side of the vessel-wall, permitting still a part of the blood to pass through. In the case of the latter, successive deposits of fibrin produce a stratified clot, which may ultimately obstruct the vessel. When

a vessel is ligated, the clot formed does not extend beyond the first communicating vessel, but, when the thrombus is spontaneous, the coagulum may increase by successive deposition of material until it extends into a neighboring vessel. If a thrombus is suddenly formed, there will be a uniform distribution of the red and white globules throughout the coagulum; if slowly formed, the mass will have a stratified arrangement, due to the adhesion of the white corpuscles to each other, and their accumulation along the walls of the vessel, and on the surface of the clot, so that, when a section is made of a thrombus formed by successive deposition, it will be found to be made up by alternating layers of ordinary blood-clot and of white corpuscles. Thrombi are, therefore, of two kinds, stratified and unstratified. The first steps in the organization of a thrombus consist in a process of condensation: the liquid disappears, the red globules lose their color, and the mass contracts an intimate adhesion to the intima of the vessel. Vessels are formed by the union and canalization of migrated white corpuscles (Rindfleisch), and the remainder of the thrombus consists of a fine reticulation of fibers and corpuscles, but the corpuscles have usually disappeared at the expiration of two months. Softening of the clot begins in the oldest part. There is no attempt at organization, and the delicate reticulation of fibrin breaks up into a uniform granular mass. The red globules lose their coloring matter, and, mixed with the other contents of the thrombus, form a white or yellowish-white fluid having the consistence of cream, and an appearance like "laudable pus," but differing from pus in structure, for on microscopic examination it is seen to be composed of albuminous particles, fat-molecules, and altered blood-globules. While the interior of the thrombus presents this puriform appearance, the exterior may have the brownish-red of the clot, and there may be various shades of color representing various stages in the process of softening. When the process is complete there remains a puriform-like collection, in which no red globules remain undestroyed, and together with the white are transformed finally into fat-granules. An embolus derived from a thrombus will have the appearance belonging to the age and condition of the latter. The vessel in which it is lodged will be damaged at the point of lodgment, but in front and behind the embolus, will be healthy. The vessel may be completely or only partially obstructed. If completely, coagulation will ensue behind the point of obstruction forming a thrombus; if partially, successive depositions of coagulum will occur, and a thrombus will form about the embolus. The bifurcation of arteries is the usual point at which an embolus lodges. Its effects are not limited to the point of lodgment, but include the whole area nourished by the vessel, and the wider zone supplied by the branches remaining permeable. The part receiving blood through the obstructed vessel at once becomes anæmic; but the neighboring district is the

seat of an active hyperæmia, which is designated *collateral hyperæmia.* One result of the increased pressure in this hyperæmic area is the rupture of small or large vessels and extravasation of blood. If the vessel obstructed is small and not a terminal artery, the anastomoses may be sufficient to supply the anæmic district. If, however, the compensatory circulation is insufficient or absent, the ischæmic part dies—undergoes *necrobiosis*, *gangrene*, or *necrosis.* The consequences following arrest of the circulation by an embolus depend largely on the position, still more on the size, of the obstructed vessel. Dry gangrene is produced by embolic blocking of a vessel of an extremity. In internal organs, especially the brain, centers of softening and fatty transformation of the tissue elements, and hæmorrhagic extravasations in the area of collateral hyperæmia, are results of embolism. Besides the hæmorrhagic extravasations, infarctions occur in the parenchyma of those organs supplied with Cohnheim's terminal arteries.*

Symptoms.—The position of a thrombus or an embolus exercises a most important influence on the symptoms caused by them. When a thrombus occupies a vein of an extremity, œdema of all the parts below is a result, and, if the obstructed vein is adjacent to important nerves, excessive pain, or troubles of motility, will also be present by reason of the pressure of the distended vessel. Gangrene is not a result, since the nutrition of the parts is accomplished, although feebly and imperfectly, but moist gangrene may be produced if other injuries are superadded—as erysipelas, traumatism, compression, etc. A cure in such a case is in part effected by the collateral circulation, but in a truer sense by the canalization of the thrombus. Notwithstanding the similarity in the symptoms, caused by thrombosis and embolism respectively, there is a great difference in the time at which the phenomena manifest themselves: the symptoms of autochthonous thrombosis come on gradually; of embolism suddenly, with shock (Wagner). Two classes of symptoms arise—affections of nutrition, from the simplest disorder up to gangrene, and functional disturbances, proper to the organ affected. These symptoms are not ascertained with the same facility in all situations. In the extremities, every step in the local process is easily followed and interpreted, but in internal embolisms only those symptoms due to perversion or suspension of function are recognizable. Embolic obstruction of a member is announced by a sudden and often intense pain and a chill, with numbness, loss or diminution of tactile sense, coldness, pallor of the skin, and a feeling of deadness and weight, and paralysis of the muscles; the pulsations wanting below, while above the obstruction they are full and strong. If embolic blocking of a vein in the brain, there occur defects of speech, hemiplegia, etc.; if of a pulmonary artery, sudden difficulty of breathing and sense of oppression, with, it may be, intense oppression and anxiety and death. Sudden attacks of amaurosis in puerperal fever, acute rheumatism, and pyæmia, are usually due to embolism of the central artery of the retina. Those organs not well supplied with nerves, as the liver, kidneys, and mucous membranes, do not offer distinct reactions on embolic blocking of their vessels, and hence the symptoms are obscure.* If the immediate danger of an embolic obstruction is past, even if the symptoms are very formidable, provided terminal arteries are not obstructed, they may disappear in some hours or days by establishing a collateral circulation.

* Wagner, *op. cit.* "Untersuchungen über die embolischen Processe," von Dr. Julius Cohnheim, Hirschwald, pp. 112. Berlin, 1872.

Treatment.—As all the symptoms are due to the obstruction of vessels by a blood-clot, the point in the treatment of special importance is to effect a solution of this obstructing material. Theoretically, ammonia possesses a solvent power, and in its use the author has had most striking results in the case of thromboses and embolisms of the brain. To accomplish the purpose in view, ten grains of the carbonate of ammonia may be administered in a tablespoonful of solution of the acetate, three or four times each day. As, however, the action must be slow, the point of contact being small, the remedy must be very persistently employed. The iodide of ammonium may be administered in a solution with the carbonate also, and usually with good results. Other alkalies possess the same power, but to a less extent. The most generally useful is the phosphate of soda, in drachm-doses, three times a day, used for many weeks. As, however, prompt and speedy action is needed to avoid the serious structural alterations which occur so quickly, the ammonia preparations are preferable to any other having the same effects.

DISEASES OF THE HEART.

TOPOGRAPHY OF THE CARDIAC REGION.—METHODS OF PHYSICAL DIAGNOSIS.

The heart lies somewhat obliquely in the chest, behind the sternum, and extends downward to the left, so that the apex-beat is below and a little internal to the left nipple, and between the fifth and sixth ribs. The position of the heart varies somewhat with the position of the subject: it gravitates downward and forward when the posture is erect; backward and upward when the posture is recum-