from the work of Peters, who showed that the chorionic epithelium in the first week formed a distinct, many-layered capsule which he designated as trophoblast, the greater part of which consisted of distinct cells, though here and there small areas of syncytium could be observed. He therefore concluded that the fœtal ectoderm originally consisted of distinct cells, which assumed a distinctly syncytial appearance where they came in contact with the maternal blood. Peters' conclusions appear to be borne out by the facts, and at present most writers upon the subject subscribe to them.

For years this question has been a prolific source of discussion, and a voluminous literature has resulted from it. In 1890 Waldeyer carefully analyzed the literature, and was able to classify the theories concerning the origin of the chorionic epithelium into ten groups, to which several others have recently been added, all of which are carefully considered in Peters' monograph.

When the tips of the villi come in contact with the decidua serotina, the chorionic epithelium proliferates and invades the decidua to a greater or less extent. This was first recognized by Nitabuch, who pointed out that one could distinguish three layers in the decidua: a deep layer composed exclusively of decidual tissue, above which was a layer of fibrin, and above this another layer of cells which resembled the decidual cells very closely, but which were really fœtal in origin. She pointed out that the fibrinous line, which separated these two varieties of cells, was probably the result of degenerative changes in the chorionic epithelium, and accordingly represented the boundary line between the two tissues. Her views have been indorsed by most investigators, and at present it is generally believed that the decidua serotina is not made up entirely of maternal (decidual) tissue, but that its upper portion contains large numbers of fœtal cells.

On examining sections through the chorion outside the placental site, one finds at the end of pregnancy that it differs markedly from the chorion frondosum. Fig. 1297 shows a section through the fœtal membranes and the underlying decidua, and in it one can clearly distinguish the following layers: 1. The cuboidal epithelium of the amnion. 2. The amniotic connective tissue. 3. The chorionic connective tissue. 4. The chorionic epithelium. 5. Degenerated villi. 6. More or less canalized fibrin. 7. Typical decidua.

The chorionic epithelium is arranged in a number of layers, and consists of definite cells whose protoplasm stains lightly; the nuclei are vesicular in shape and stain quite darkly. Here and there in the chorionic epithelium one sees numerous large, pale, oval, or round, more or less structureless areas, which represent all that is left of the villi of the chorion læve. Occasionally they contain a few connective-tissue cells, but usually consist of a mass of transparent hyaline material. Beneath the epithelium and degenerated villi one finds a thicker or thinner layer of fibrinous material, which is evidently the result of the degeneration of chorionic epithelium. This tissue was first described by Langhans as canalized fibrin, and is characterized by the presence of numerous slits or canals of varying size. External to the canalized fibrin and chorionic epithelium one sees typical decidual tissue with its characteristic large, pale epithelioid cells.

Where the canalized fibrin is absent, the chorionic epithelium and the decidual cells come in intimate contact, the former extending down a slight distance into the latter. Where the two varieties of cells are commingled, it is almost impossible to differentiate between them; but when one compares distinct masses of chorionic epithelium with typical decidual tissue, it is readily seen that the former is composed of somewhat smaller cells with fairly darkly staining nuclei, while the latter is made up of larger, more irregularly shaped, paler cells, whose nuclei stain less intensely.

After the first few months degenerative changes are almost universally observed throughout the chorion, and usually appear as canalized fibrin. This tissue stains deeply with eosin and the usual dyes, and on close examination is seen to contain large numbers of spaces of varying shape, whence its name. It apparently results from coagulation necrosis of the chorionic epithelium, especially of the Zellschicht. And in many villi one sees a thicker or thinner layer of canalized fibrin, lying between the syncytial layer and the stroma. As the change becomes more marked, the syncytial layer is likewise converted into canalized fibrin, which eventually may even invade the stroma. Large quantities of this tissue are always present on the fœtal surface of the chorionic membrane, especially where it takes part in the formation of the placenta, and plays an important part in the formation of placental infarcts.

I have lately shown, in an article upon infarcts of the placenta, that the formation of canalized fibrin and infarcts is usually associated with more or less endarteritis of the villous vessels, and is to be regarded as a sign of senility of the placenta. It occurs so frequently that I believe it should be described as one of the normal constituents of the chorion. Similar changes are observed in the chorion læve, and it is probable that the degeneration of its villi is brought about in an identical manner.

In the early weeks of pregnancy, only a small portion of the cavity of the chorionic membrane is occupied by the embryo and the amnion (see Fig. 1292). This rapidly changes, however, and in a short time the amnion increases so rapidly in size as to line the entire interior of the chorion, so that the connective-tissue layers of both membranes lie in close contact. They do not appear to become organically united, as they can be readily separated in the full-term placenta after birth.

J. Whitridge Williams.

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CHORION. (PATHOLOGICAL.)—The pathology of the chorion remains at the present day largely an unknown field. Owing to the change of view regarding many of the conditions of the membrane formerly considered as pathological, but which are now looked upon as being only an expression of the senile decay of the organ, the

known pathological conditions of the placenta have been brought within very narrow limits. It must be emphasized in this connection that the placenta is a temporary structure, and at time of delivery represents a senile, worn-out organ whose tissues are in an advanced stage of senile or physiological degeneration. These degenerative changes have in the past been looked upon as pathological and their true significance misunderstood. Having been interpreted as evidences of disease, serious misconceptions have crept into pathology regarding these purely physiological changes, and as a result the study of placental pathology has been greatly retarded. The majority of the conditions of the chorion described in the textbooks as pathological, such as calcification, fatty change, sclerosis of the chorionic vessels, infarction, etc., are no more pathological than are the atrophy and sclerosis of old age, and should be regarded as possessing a similar significance. On the other hand, the peculiar pathology of the placenta—the causes of abortion, death of the fœtus, the part which the placenta plays in the transmission of disease, etc.—remains at the present time an unexplored field.

Circulatory Changes.—It is impossible with our present knowledge to say to what extent the disturbances of the chorionic circulation are pathological. General hyperæmia and anæmia of the chorionic vessels are essentially dependent upon similar conditions in the fœtal circulation, but the conditions of pressure to which the placenta is subjected during delivery make it impossible for us to judge accurately of the former blood content of the organ. Though the placental end of the umbilical cord is usually ligatured, and the blood in this way retained in the chorionic vessels, the pressure of the uterine contractions during delivery will have materially altered the amount of blood in these vessels, even to such an extent that a previously existing hyperæmia may have been made to disappear entirely. On the other hand, if the placental end of the cord is not ligatured the chorionic vessels may be rendered anæmic through hemorrhage from the severed umbilical vessels. A general hyperæmia of the chorion may be caused by disturbances of circulation in the body of the fœtus, stenosis of the umbilical vein through thickening of its wall, twisting of the cord, etc. General anæmia of the chorion may be due to general anæmia of the fœtus, stenosis of the umbilical artery, twisting, knotting of the cord, etc. Local hyperæmia of the chorionic villi may be caused by some obstruction to the onward flow in the veins of the chorionic stems, or may be collateral dependent upon some neighboring anæmic area. Local anæmia of the vessels of the villi may be caused by pressure, obstruction of the larger arteries in the chorionic stems through thrombosis, sclerosis of the vessel walls, etc. As a result of thrombosis of the maternal sinuses a portion of the intervillous spaces may be deprived of maternal blood. The empty spaces collapse, the villi are pressed closely together, and as a result of the intraplacental pressure the vessels of the tightly packed villi become emptied of blood, giving rise to pale pinkish areas which have been regarded as infarcts. Necrosis of the villi (infarction) results from any severe degree of anæmia. In the case of twins arising from one ovum marked disturbances in the chorionic circulation may arise from the abnormal relations of the umbilical vessels. If one-sided hydramnion is also present the disturbance of the umbilical circulation may be very severe.

In general hyperæmia of the placenta the organ is deep red, swollen, bleeds freely when cut, and is of softer consistence than normal. Local areas of hyperæmia are deep red to black in color, and are frequently mistaken for hemorrhage. In general anæmia the placenta is pale, smaller than normal, and of firmer consistence. Localized anæmias appear as pale, pinkish, or white areas.

Hemorrhage.—Though hemorrhage from the maternal portion of the placenta is one of the most important pathological conditions of the organ, the escape of blood from the chorionic vessels is of very rare occurrence. Hemorrhage of the fœtal placenta has been very frequently described in the literature, but as the majority of these descriptions have been based upon the gross appearances alone, they cannot be accepted as conclusive. The term "placental apoplexy" has been applied to the circumscribed collections of fibrin and red blood cells so frequently found in the chorion, which from their occurrence in almost every ripe placenta can hardly possess a pathological significance. To the naked eye these appear as larger or smaller areas, deep red or black in color, of a firm consistence, and on section usually slightly elevated above the cut surface of the organ. They are found in greatest number near the maternal surface, but are also of frequent occurrence in the central portion of the organ, and at times extend entirely through it. On microscopical examination they consist of blood clots lying in the intervillous spaces. The blood may be freshly coagulated, or large masses of laminated or hyaline fibrin enclosing degenerating red blood cells may be found in the spaces between the villi. The clot may be so large as to compress the neighboring villi or to separate the chorion either partly or entirely from the maternal portion of the placenta. The blood in these cases of so-called "placental apoplexy" is of maternal origin, and since the blood is in the intervillous spaces which are themselves blood-vessels, it is not proper to consider this condition under the head of apoplexy or hemorrhage.

Numerous theories have been advanced to explain this condition, but none have proved satisfactory. Bustamente held that it is probably due to the occurrence of hemorrhage into a beginning infarct formation, the extravasation occurring into spaces bounded by necrosing villi instead of into the normal intervillous spaces. It is, however, more probable that the process is essentially a thrombosis beginning in the maternal vessels, and spreading thence into the intervillous spaces, involving a smaller or larger portion of the placenta. The majority of the cases described in the literature as hæmatoma of the placenta are, from their descriptions, evidently cases of infarction. Organization and encapsulation, calcification, liquefaction with cyst formation have been reported to occur as sequelæ of placental hæmatomata; but these were probably cases of infarction. The causes ascribed are varied: trauma, congestion, albuminuria, slow thrombosis of the maternal sinuses, excessive heart's action, etc. As a result of large hæmatomata the number of villi destroyed may be so great as to cause asphyxiation of the fœtus. True hemorrhage from the maternal sinuses does occur, and large extravasations may burrow downward through the decidua and escape from the uterus. Since in these cases the hemorrhage is of maternal blood, serious symptoms may be produced in the mother. Decidual hemorrhage plays also an important rôle in the production of abortion.

Rupture of the umbilical vessels or of the larger branches of the chorionic stems may lead to the production of true chorionic hæmatomata between the amnion and chorion. Death of the fœtus and abortion result if the hemorrhage is at all large. In some instances the hæmatoma may contain all of the blood of the fœtal body, the fœtus having bled to death into its own structures. Small hemorrhages from the capillaries of the villi into the chorionic stroma are occasionally seen. They are most probably dependent upon the changes in the walls of the chorionic vessels, or in many cases may be due to uterine contractions.

Œdema.—Œdema of the entire placenta occurs in retention of the dead fœtus and in connection with general anasarca of the fœtus caused by cardiac or renal disease, obstructions to fœtal circulation, fœtal leukæmia, etc. The placenta is swollen, boggy, and lighter in color, and tears very easily. The infiltration may be so great that fluid exudes when the organ is cut. The connective tissue of the villi is separated by the fluid, and the syncytial cells may contain large vacuoles. Hydramnion is usually associated with placental œdema.

Thrombosis.—While thrombosis is of very frequent occurrence in the intervillous spaces, it occurs much less frequently in the chorionic vessels. In both places it is

in the majority of cases to be considered as a physiological process, a part of the means by which the placenta is freed from the uterus. Thrombosis of the chorionic vessels is one of the causes of placental infarction. It is directly dependent upon the senile changes in the walls of the chorionic vessels, which are of the nature of an obliterating endarteritis. If the thrombus is formed some time before the completion of term, it may become organized or undergo calcification. Early or excessive thrombosis must be regarded as pathological, but the conditions leading to this are not yet clear. Syphilis, maternal cachexias due to nephritis and other conditions, appear to be associated with more extensive thrombosis than is found in the chorion of normal placentas. It is probable that any thrombosis of the chorionic circulation before the beginning of the seventh month of gestation must be regarded as pathological. In the case of the physiological thrombosis occurring after this time the obliteration of the affected vessels is, in the first place, due almost entirely to the proliferating endarteritis, the obstruction being completed by the thrombosis. Following the obliteration of the main chorionic branch, there is a progressive thrombosis of the smaller arterioles, capillaries, and veins belonging to it. As a result of the shutting-off of the blood supply to the villi there follow marked degenerative changes in the structures of the villi which will be described under the head of infarction.

Infarction.—The so-called anæmic or white infarct of the placenta is one of the oldest described conditions of this organ. In the beginning mistaken for inflammation of the chorion, the history of the placental infarct and that of placentitis are for the greater part identical. Guillemeau in 1648, Mauriceau, Portal, and Morgagni a little later, were the first to note the occurrence of placental infarcts, but interpreted them as being inflammatory in nature. Later the same appearances of the placenta were accorded a great variety of interpretations, such as: atrophy, hepatization, phthisis, apoplexy, hæmatoma, fatty degeneration, hyaline, amyloid, gumma, etc. In recent years the minute changes underlying the gross appearances have been more clearly understood, and the present tendency is to consider them in the light of an anæmic necrosis dependent upon senile changes and having a physiological significance.

To the naked eye the infarcts of the placenta appear as yellowish-white or red areas, more or less sharply outlined, firm in consistence, and lacking the usual spongy appearance of placental tissue. They vary greatly in their location and size. They may be very large, involving several cotyledons or even half or two-thirds of the placenta. Usually they are of small size, varying from areas just visible to the naked eye to wedge-shaped or irregular areas several centimetres in diameter. They occur most frequently just beneath the fœtal and maternal surfaces of the organ, but may extend entirely through it. Not infrequently they form broad or narrow bands lying upon the surface of the chorion just beneath

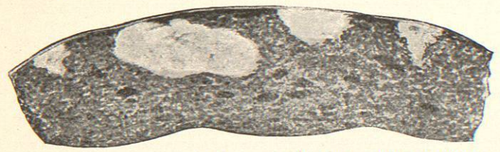

Fig. 1298.—Placental Infarction. Natural size. (After Kaufmann.)

the amnion. These bands are usually but a few millimetres in thickness. They may occasionally run around the margin of the placenta (placenta marginata), or they may form a zone around the centre of the organ some distance from its periphery (margo placentæ), being separated from its edge by apparently normal tissue. In other cases red or yellowish areas are scattered through the substance of the organ and are discovered only when the placenta is cut. The red infarcts may vary in color from a pale pink to black. They occur most often upon

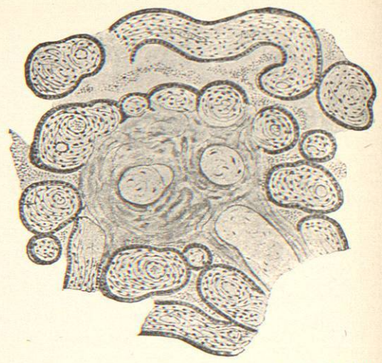

Fig. 1299.—Small Infarct of Chorion. Several necrosed villi surrounded by fibrin. The necrosed villi have lost their syncytial covering. (After Kaufmann.)

the maternal side, but may extend completely through the organ. To these red areas the term "placental apoplexy" has been usually applied.

The red infarct may be elevated above the surface of the placenta, and in some cases the organ may be studded with small dark-red nodules (placenta truffé). The yellow or white infarct is more often depressed, and when of large extent may cause furrow-like depressions over the placental surface. On section the light-colored infarcts have a more or less fibrillated or laminated structure, but frequently appear cheesy. The red ones have a more granular surface. Calcification occurs with great frequency in the infarcts of all colors.

Microscopically the infarct consists of chorionic villi more or less necrosed and compressed together, surrounded by fibrin, red blood cells, and necrosing decidual septa. The nuclei of the connective-tissue cells of the villi have either entirely lost their chromatin or are disintegrating, the villous elements becoming fused into a hyaline mass, taking a uniform pink stain with eosin. The syncytial cells are partially desquamated and fused into black-staining masses of chromatin, while the cells of the decidual septa between the villi are swollen, vacuolated, and exhibit various stages of necrosis. Fibrin is deposited upon and around the villi, and is made up of closely packed fibrillæ so that it appears almost hyaline. It stains with Weigert's fibrin stain in the same manner as does fibrin found elsewhere.

In other cases the infarct consists only of large masses of laminated fibrin in which no traces of villi can be found. Others contain shadows of necrosed villi, and between the infarcts containing no villi and those exhibiting necrosing ones every stage of transition may be found. Those consisting only of fibrin are probably to be regarded as older infarcts. In the fibrin masses degenerating red cells are found in large numbers, and not infrequently there is a well-marked infiltration of leucocytes into the fibrin. Lime salts may be deposited in the dead villi, the syncytial cells, or the necrosing decidual cells, or in the fibrin. Fatty degeneration of the necrosing villi is rare. In large infarcts a liquefaction or simple softening of the central portion may take place, resulting in the formation of a pus-like fluid, which may lead to an incorrect diagnosis of abscess of the placenta. As a rule, the villi immediately bordering upon the infarct show no change, but occasionally there may be a sequestration of the infarct, or formation of a connective-tissue capsule about it. Rarely a leucocyte infiltration is seen about the infarct.

In small infarcts the changes are not so marked, and the villi (one or several in number) may be but slightly changed, and surrounded by a narrow ring of hyaline fibrin. The syncytium usually shows some evidence of necrosis or desquamation, but the stroma of the villus may remain unchanged. The structure of the surface and central infarcts is essentially the same. The large pink infarcts are similar to the white ones except in the fact that the red blood cells are preserved. The red infarcts may present a microscopical appearance exactly similar to that of the white ones. In other cases the fibrin composing them contains many red cells. Non-fibrinous infarcts may also occur, to the naked eye resembling the white fibrinous ones, but microscopically consisting of necrosed villi crowded closely together without intervening fibrin. Eden believes that these are caused by the shutting off of the blood in the decidual sinuses whereby the supply to the intervillous spaces is obstructed. These, being no longer filled with blood, collapse, and the villi being thus closely crowded together, become anæmic and undergo necrosis.

The larger blood-vessels of the chorionic stem to which the infarcted villi belong, show, as a rule, a well-marked obliterating endarteritis and periarteritis associated with thrombosis, and it is probable that the infarction is due to these conditions.

While there is among recent writers a universal agreement as to the minute structure of placental infarcts, there is still some diversity of opinion as to their etiology and pathological significance. Two schools exist. One holds that infarcts are the result of degenerative changes occurring in the decidua and extending thence to the neighboring villi, the intervillous fibrin masses representing degenerated decidua. Proliferation of the decidua may even first take place. The changes in the chorionic vessels are regarded as purely secondary. The other school holds that the vascular changes in the chorion are primary, and that as a result of these, necrosis of the villi occurs followed by the deposition of fibrin upon and about the dead villi. This school also regards the infarction process as physiological and not the result of disease changes. This latter view must be accepted in view of the recent observations concerning the occurrence of infarcts in the ripe placenta.

Delore, in 1899, found in the examination of several thousand cases that infarcts occurred in one hundred per cent. Williams, in 1900, states that he has found infarction in greater or less extent in every full-term placenta examined. The writer in an examination of one hundred successive placentas found them in every case. Many of the older writers at widely separated periods of time expressed the belief that infarcts (described under various heads) were found in the majority of all placentas. Eden was one of the first of the more recent writers to emphasize the constant occurrence of placental infarcts as being of a physiological nature and not as evidence of disease. His views have recently been confirmed by Williams and others.

According to Ackermann, Eden, and Williams, the chief factor in the production of placental infarction is to be found in the changes occurring in the chorionic vessels. These are of the nature of an obliterative endarteritis and periarteritis, and are usually most marked in the vessels of the chorionic stems and in the larger arterioles of the villi. The degree to which this change occurs varies greatly; in many cases the lumen of the vessel may be almost or entirely obliterated, while in others there is but a slight thickening of the intima. The endarteritis is similar to that found in other regions of the body; there is a proliferation of the subendothelial connective tissue with resulting narrowing of the lumen, the newly formed tissue becomes hyaline and gradually loses its nuclei. There may or may not be an increased number of wandering cells in the vessel wall. Calcification occurs much less frequently than in sclerotic vessels in other parts of the body.

These sclerotic changes occur in all healthy placentas; their etiology is unknown, but inasmuch as they form a part of the life history of the organ, the causes leading to their production must be sought for in the operation of the general laws of histogenetic development and decay. Under ordinary conditions, to be regarded as an expression of senile degeneration, these vascular changes can come to have a pathological significance when they appear at an earlier period than normal. In such case they are to be taken as an indication of premature senility.

As a result of these vascular changes disturbed nutrition of the tissues of the villi occurs. This is shown in the first place by a necrosis of the cells lying just beneath the syncytium. This leads gradually to a desquamation of the syncytial layer. Changes in the chromatin of the syncytial cells take place but slowly, leading to the inference that these cells may derive some nourishment from the maternal blood. They do not begin to degenerate until the tissue beneath has reached a certain degree of necrosis. As the process advances the connective tissue of the villus undergoes necrosis, becoming changed into a hyaline mass which stains deep red with eosin. The necrosis of the surface of the villi is of the nature of a coagulation necrosis, fibrin is deposited upon the dead cells. As the process advances larger pieces of syncytium degenerate, and upon these dead cells there is deposited a thick layer of hyaline fibrin which binds the dead villi together in a firm fibrinous mass. In the oldest portions of the infarct the villi gradually lose their contour, the central portion of the infarct becoming after a time an indistinguishable mass which may either liquefy or undergo calcification. The syncytial cells may be preserved for a long time in the meshes of the fibrin, appearing as deeply staining clumps of chromatin.

According to Williams, the death of the stroma of the villus is also of the nature of a coagulation necrosis by which the tissue of the villi becomes changed into canalized fibrin. The writer, in the study of a large number of infarcts, has never seen anything warranting the belief that fibrin may be formed from necrosing villous stroma. While the dead villi stain similarly to fibrin with many stains, the proper management of Weigert's fibrin stain will always differentiate between the dead villi and the true fibrin derived from the blood elements.

While the great majority of all placental infarcts are undoubtedly due to the vascular changes in the chorion, it seems possible that in certain cases the infarction is the result of changes beginning in the so-called decidual septa which extend into the chorion. Eberhardt, Williams, and others believe that these septa are of ectodermal origin and not maternal. If this is the case the primary factors in the production of infarction are to be sought always in fœtal structures. On the other hand, Steffeck and others hold that infarction is always of maternal origin, the primary change taking place in the cells of the septa, the latter being extensions of the maternal decidua into the chorion. The necrosis of these cells leads to the formation of fibrin in the intervillous spaces which contracting compresses the villi and so leads to their necrosis.

The pink infarcts do not differ in their etiology from the white ones, but are most probably to be regarded as more recent infarcts, the blood between the necrosing villi having undergone but imperfect coagulation. The large dark-red infarcts commonly regarded as "placental apoplexy" are due to dilatation and thrombosis of the intervillous spaces, and are not hemorrhages. Their etiology and significance are not yet known, but it is probable that they are connected with the thrombosis of the maternal sinuses which gradually extends into the intervillous spaces involving a larger or a smaller portion of the placenta. The origin of the non-fibrinous infarcts is probably that suggested by Eden, as mentioned above.

As sequelæ to infarction there may result a gradual atrophy or absorption of the dead villi and fibrin, simple softening with formation of a pus-like material, calcification, or in rare cases organization may lead to the formation of a fibroma-like mass of connective tissue. Chorionic cysts may also be formed by the liquefaction of the central portion of an infarct.

The sclerotic changes in the chorionic vessels and the resulting infarctions must be considered as purely physiological processes in the great majority of all full-term placentas. Unfortunately, the significance of these conditions is at the present time but little understood, and consequently normal phenomena have been accorded the most varied pathological interpretations. Such mistakes are due entirely to a lack of familiarity with the changes found in normal placental tissue. In all healthy placentas infarcts are constantly found, and are present at all stages of gestation from the earliest period of chorionic development. A progressive atrophy and disappearance of the villi in the chorion læve occur from the very beginning of placental formation, and this is the normal way in which the extraplacental villi are disposed of in the earlier weeks of gestation. In the fœtal placenta itself from the very beginning there is on one hand a progressive formation of new villi and a progressive destruction on the other. This process is but the extension of that from the extraplacental chorion, and a definite progression can be traced between the infarctions of the extraplacental villi and those of the placental chorion. As Eden has pointed out, infarction is therefore "not the result of pathological factors but forms a part of the normal life history of the placenta, and its etiology is to be looked for in the operation of the natural forces of evolution and decay."

Yet many authors seek to give a pathological meaning to the infarcts found in the full-term placenta. Von Franqué holds that the vascular changes in the chorionic vessels are pathological and lead to placental œdema, excess of the amniotic fluid, etc. Cohn, Wiedow, Martin. Pinard, and others believe that there is some definite relation between maternal albuminuria and placental infarction, and that the latter process leads to marked changes in the condition of the fœtus even to the extent of death and abortion. A relation has also been claimed to exist between infarction and eclampsia. Zilles, Prinzing, Orth, and others believe that there is a causal relation between syphilis and infarction. Favre, Martin, and Delore hold that infarcts are caused by the presence of bacteria in the blood of the intervillous spaces, that these cause degeneration and necrosis of the syncytial cells which in turn lead to infarction. Williams examined twenty placentas bacteriologically and found the infarcts to be sterile. The latter writer holds that moderate infarction is not pathological and exerts no harmful influence upon either mother or fœtus. Marked infarction he believes to be associated usually with maternal albuminuria, and often results in the death or imperfect development of the fœtus. He is unable to account for the relationship between the two conditions.

According to the results of the writer's study of a hundred full-term placentas, large infarctions may be found in cases in which there was no albuminuria and in which both mother and child were apparently normal. Such infarctions are, however, of greater frequency in the placentas from mothers suffering from cachectic conditions of all kinds, tuberculosis, syphilis, nephritis, anæmia, severe endometritis, etc.; and it is probable that in such conditions the infarct acquires a pathological rôle and may affect the development of the fœtus. Especially is this likely to be the case when large infarctions occur in the early months of gestation. The occurrence of large infarcts before the seventh month seems to be especially associated with syphilis. The significance of chorionic infarction may then be summed up as follows:

1. Moderate infarction of the placenta after the seventh month is physiological.

2. Marked infarction of the ripe placenta may have apparently no pathological significance, but is usually associated with maternal cachexias and may affect fœtal development.

3. Marked infarction of the placenta in the earlier stages of gestation is especially associated with syphilis, tuberculosis, and nephritis of the mother, and may result in abortion.

Atrophy.—There is in the fœtal placenta from the very beginning of its development a progressive atrophy of the chorionic villi on the one hand, and a new formation on the other. The superfluous villi of the chorion læve undergo a simple atrophy, and the process extends from them to the placental chorion. At term the villi are, as a rule, of much smaller size than in the early months, and this decrease in size is to be looked upon as being of the nature of a histogenetic or senile atrophy. The myxomatous tissue of the young villi takes on with age somewhat of the character of mature connective tissue, and while many of the villi never lose entirely their embryonic character, their interstitial tissue becomes firmer and more compact, and contracting causes a marked decrease in size. The small vessels of the villi are, however, not affected by this contraction; on the contrary, they become relatively much larger. If these atrophic changes occur to any great extent before the seventh month they must be regarded as pathological. Premature atrophy may be due to syphilis, or to marked cachexias due to other causes. The direct cause of both physiological and pathological atrophy lies in the sclerotic changes in the larger chorionic vessels. Slow obliteration of these vessels leads to simple atrophy of the villi, while a more rapid shutting-off of the circulation leads to infarction. The first structure of the villus to show signs of atrophy is the deep layer of the chorionic epithelium. In the young placenta the epithelial covering of the villi consists of two layers: a superficial layer of nucleated plasmodium, and a deep one of well-defined nucleated cells. After the third month this deeper layer undergoes atrophy so that in the ripe placenta it has almost entirely disappeared, being represented only by scattered nuclei beneath the plasmodial layer. The plasmodial layer undergoes a similar atrophy in the last months of gestation. In the ripe placenta many of the villi show in places complete atrophy of the plasmodium, so that underlying capillaries may be directly exposed to the maternal blood. The loss of vital energy in the syncytium is further shown in the last two months by the gradual cessation of bud and process formation whereby the development of new villi comes to a standstill. The changes in the stroma occur at the same time with those in the syncytium. Fibrin is never deposited upon villi showing simple atrophy alone, but only upon those showing necrosis or degeneration.

Necrosis.—Necrosis of the villi occurs in infarction as described above. It is usually of the nature of a simple necrosis, but many writers regard it as being a form of coagulation-necrosis. The stroma just beneath the syncytium is the first part affected; its nuclei become swollen, irregular in shape, and there is a gradual loss of chromatin. The syncytium then necroses and fibrin is deposited upon the dead surface of the villus. The formation of fibrin from the degenerating structures of the villus, as claimed by Williams and others, is not yet an established fact. Necrosis of the villi occurs also in retained placenta after the birth of the fœtus, after abortion, or in connection with a retained dead fœtus. Infection with putrefactive organisms may occur, and moist gangrene result. In a number of cases gaseous emphysema of the necrosing placenta has been observed, and the Bacillus aërogenes capsulatus was found to be present both in the fœtus and in the placenta. The sequelæ of necrosis of the villi are the same as those given under infarction.

Cloudy Swelling.—Preceding the necrosis in infarction there is a stage of degeneration in the syncytial and subsyncytial cells which is analogous to the cloudy swelling of parenchymatous organs. The cells become swollen, their nuclei larger, the cell outline irregular, and there is a gradual disintegration of the chromatin. Such changes are very commonly found throughout the entire placenta

in retention of the organ after abortion, delivery, or in connection with death of the fœtus.

Hydropic Degeneration.—This occurs in œdematous placentas, in necrotic placentas retained after abortion or delivery, in gangrene, placental inflammation, hydatid moles, and in the chorionic villi of ectopic gestation. The villi showing this degeneration contain large vacuoles throughout their stroma. Vacuoles may be found also in the syncytium and in the cells of Langhans' layer.

Fatty Degeneration.—A very slight degree of fatty degeneration of the villous stroma must be looked upon as a normal condition in the last months of pregnancy. Extensive fatty degeneration of the placenta was first described by Barnes, but there can be no doubt that the changes which he saw were those of infarction. As the result of his error the literature from 1851 to 1890, both in England and in this country, contains numerous reports of fatty changes of the placenta based upon the gross appearances, and the descriptions in all of these cases correspond to the gross changes seen in infarction. Marked fatty degeneration of the villi is very rare, and is confined almost entirely to the villi in ectopic gestation after the death of the fœtus, but the degeneration occurs to a lesser degree in placentitis, infarction, retained placenta, etc.

Myxomatous Degeneration.—The stroma of the chorionic villi and also of the chorionic stems is during the early months of pregnancy of the nature of myxomatous tissue. In the later months it takes on more of the nature of mature connective tissue, especially in the stems, where it comes to resemble fully developed fibrous connective tissue. Many of the villi, however, never entirely lose their embryonic type. In some cases the entire chorion may retain the character of myxomatous tissue, in other cases there is a myxomatous degeneration of the mature connective tissue of the stems and larger villi. This degeneration occurs in the placentas of cachectic individuals and in retained placentas after delivery at full term. Associated with a persistence of embryonic type or with a myxomatous degeneration there may be a hyperplasia of the chorion which gives rise to the condition known as vesicular mole, hydatid mole, etc. (see below).

Hyaline.—Within certain limits a hyaline change in the walls of the blood-vessels of the chorionic stems is physiological in the ripe placenta. Early or excessive change of this nature must be regarded as pathological. This occurs in the pre-senile condition caused by syphilis and other cachexias.

Amyloid.—The presence of amyloid in the chorion has been reported a number of times, but it is highly probable that the changes seen were those of infarction, and that hyaline fibrin was mistaken for amyloid.

Calcification.—The deposit of lime salts in the chorion is also within certain limits to be regarded as a senile process. Small areas of calcification are very common in the ripe placenta, occurring practically in every one, and are entirely without pathological significance. The deposits may be scattered throughout the chorion, as many as five hundred concretions having been found in one placenta, or the entire surface of the chorion beneath the amnion may be covered with a calcareous deposit. In the latter case the deposit is found in the layer of fibrin lying between the amnion and the chorion. In the scattered deposits the calcification occurs chiefly in the intervillous fibrin masses, but may be found in any portion of the chorion, in the syncytial layer, the connective tissue of the villi, or in the walls of the blood-vessels of the chorionic stems. The deposits occur most frequently in or about areas of infarction. They are usually of small size. To the naked eye the presence of calcareous masses in the placenta is shown by whitish areas having a firm consistence, a gritty feel, and giving a grating sound when struck with a knife. Microscopically the deposit consists of irregular masses of calcium carbonate, phosphate, or magnesium phosphate, giving the characteristic staining reaction with hæmatoxylin.

Just when calcification takes on a pathological significance it is at present impossible to say. Extensive deposits may occur when both mother and child are apparently in perfect health. On the other hand, it has been claimed that calcification to an extensive degree is associated with syphilis and death of the fœtus, but no constant association can be shown to exist. In placentas before the seventh month calcification has the same significance that infarction or sclerosis has at this period; it is to be taken as an evidence of premature senility, and dependent upon nutritional changes resulting from syphilis, tuberculosis, or other cachectic conditions. In both syphilis and nephritis a fatty degeneration of the terminal villi usually precedes the calcification. Early infarction dependent upon early obliteration of the chorionic vessels is almost always followed by calcification if the nutritional disturbances are not so great as to produce abortion. Syphilis is the most commonly associated condition, and may therefore be regarded as an etiological factor. Since calcification most frequently follows infarction, the greater the number of infarcts the more extensive the calcification. It may therefore be taken to a certain extent as an expression of the degree of senile change, but it must be remembered that in many cases infarction is not followed by any deposit of lime salts. In the retained placenta, either after delivery or after abortion, calcification is of very frequent occurrence. It is also very frequently found in the chorion in ectopic gestation. Both membranes and fœtus may be entirely calcified (lithopædion). On the other hand, sclerosis of the chorionic vessels is but rarely followed by calcification of the vessel wall.

Pigmentation.—Pigmentation of the chorion is very rare. Hæmatoidin and hæmosiderin may be found in old infarcts, but, as a rule, these pigments are not formed in the placenta from the disintegration of the red cells. They are of more frequent occurrence in retained placentas. In malaria of the mother the blood in the intervillous spaces contains both the malarial organism and its pigment. The latter may be deposited upon the surface of the syncytium, but does not pass through this layer. Retained placentas in cases of severe icterus of the mother become stained with bile pigment, the pigmentation being confined to the syncytial layer except in those portions of the villi denuded of syncytium where the stroma of the villus is also bile stained.

Fibrinoid Degeneration.—Much has been written upon the origin of placental fibrin, and the subject cannot be said to be definitely settled. Ackermann holds that it arises from the decidual cells and from the plasmodial and cellular layer of the villi, and not from the maternal blood. Minot also affirms that it arises from a degeneration of the chorionic epithelium. Williams believes likewise that the syncytium undergoes coagulation necrosis and is converted into canalized fibrin. Eden considers it to be largely a product of the maternal blood. The process has been styled hyaline, fibrous, fibrinous, hyaline-fibrinous, and fibrinoid degeneration of the placenta by the various authors who regard it as being of the nature of a degeneration, but who have given but little proof of their assertions. The writer, after a careful study of many placental infarcts, has been unable to convince himself that the placental fibrin has any other origin than that of the maternal blood. While with ordinary stains the intervillous fibrin has a hyaline, homogeneous appearance, indistinguishable from the necrosed syncytium and decidua, a differentiation can always be made with Weigert's fibrin stain. When stained by this method, the fibrin always shows a reticulated structure, in the meshes of which lie necrotic cells of the syncytium and decidua.

Progressive Changes.—During the first seven months of gestation there is a constant new formation of chorionic villi. Proliferation of the nuclei of the syncytium takes place, leading to the formation of a plasmodial bud or offshoot, which becomes vascularized from the villous capillaries, and a stroma is formed for the young villus from the proliferation of the stroma cells of the parent villus. During the last two months of pregnancy the formation of the plasmodial buds continues, but very few become vascularized. The number of buds is, more-