not for the fact that many were observed at dispensaries, where the attendance is so irregular and floating—I found that in 40 per cent. of the cases there were 2 relapses.

The residual paralysis is sometimes, though rarely, quite lasting. If a hemichorea exist for a year, it is quite likely to be associated with some loss of muscular substance. In one of West's cases—a girl—it was found, three months after the movements had ceased, that the left arm was half an inch smaller than the right. In another patient—who had kept her hands clenched for a long time—there was wasting and contraction.

The DIAGNOSIS of chorea should be simple enough, if we throw out of consideration those cases of organic origin, the so-called "post-hemiplegic chorea." The movements themselves can hardly be confounded with any others. They are coarse, jerky, and irregular, and in no sense rhythmical. The same cannot be said of the movements observed in post-hemiplegic chorea, in which, besides eccentric jactitations, there is usually more or less tremor. The movements of chorea may in simple cases (I may say always in chorea minor) be controlled, in part or wholly, by the exercise of the will. Embarrassment and diversion of attention seem to aggravate the intensity.

The age of the subject is also a determining factor. Those forms of degeneration of the brain or spinal cord in which hyperkinesis is a symptom are very rare in children, the exception, perhaps, being cerebral hypertrophy and hemiatrophy; and here we find errors in development and other concomitant symptoms which render diagnosis quite simple.

In paralysis agitans we have an affection which resembles to some extent certain varieties of adult chorea. We find festination, associated movements, no aggravation by attempt at control, and a "fineness" of the spasms which can hardly be called choreic.

In the diagnosis of the particular cases much depends upon our ability to determine the probable nature of the chorea itself; whether it be due to eccentric irritation, to anæmia; whether it be a sequence of one of the zymotic diseases; or whether it be a symptomatic affection, the result of some form of tissue change. These things are important when we come to predict the course of the malady. It will readily be seen how much credit may be gained by recognizing the true nature of a chorea dependent upon intestinal worms or other irritative causes, and promptly curing the same by expulsion of the irritating agents. The connection of the disease with some affection of the heart is also most important to recognize.

The TREATMENT of chorea has probably received more attention than that of any other nervous disorder, and the list of remedies, good, bad, and indifferent, is very long. As I have said, there is very little difference between the duration of the malady in those patients for whom the expectant treatment is ordered, and the duration in the case of those who are subjected to a rigorous course of medication of the orthodox kind. In the practice of medicine, masterly inactivity is not always the most prudent method of procedure, but in chorea minor I would counsel the simplest treatment possible. Of the vast horde of remedies, I think we can discard all but three or four, and I will name them in their order of usefulness: (1) Arsenic; (2) strychnine; (3) iron; (4) the fats.

There is a second list of remedies which are employed for the purpose of reaching special conditions, and among these I may mention heat and cold, anthelmintics, sedatives, the coal-tar products, etc.

If we do use any of the remedies of the first order, it must be freely and with the idea of getting their full physiological effects; especially is this true of arsenic and strychnine. In children the dose of the former should be rapidly increased until slight œdema becomes visible below the eyes, while the good effects of strychnine are obtained only when there is complaint of tension of the back-leg muscles. For reasons of safety as well as on account of greater efficacy, a bulky solution of strychnine is recommended in preference to drops or granules. In combination with the syrup of the iodide of iron, the latter drug is of especial service in the anæmia of chorea.

To this mixture may be added digitalis, especially in many cases in which cardiac asthenia is a feature. The French writers favor the division of chorea into many forms with relation to the etiological factors. When such forms are clearly made out, of course it becomes our aim to direct special treatment to the individual cases. In those forms with *rheumatismal* history, the salicylate of soda, the tincture of cimicifuga racemosa, sulphur and vapor baths and alkalies, are of great service; hysterical cases are most helped by the valerianate of zinc, cypripedin, or cannabis indica. In many cases the removal of an ulcerated wisdom tooth is sufficient to effect the disappearance of a violent chorea, and when intestinal worms exist, we are to turn to turpentine, kousso, or santonin.

Should the movements be sufficiently violent, as they often are, to necessitate the use of restraint, I know of no better remedies than hyoscyamine or chloral hydrate. Of the benefit of calabar bean in such cases, I have little to say. It has never been of the slightest service in several cases in which I have tried it, and I may say the same thing of belladonna. Axenfeld recommends opium in large doses, but he wisely cautions those who administer it to children. Gery and Fuster recommend the repeated use of chloroform—in inhalation—several times a day.

In some cases the remedies cited above may be used hypodermically, but, as a rule, this is an unnecessarily painful mode of treatment. Arsenic has been used in this way.

Four or five drops of Fowler's solution may be injected daily in the affected member; and by Radcliffe, Eulenburg, and others, it is said to act more quickly than when administered by the stomach.

The use of cold is occasionally of great benefit to the choreic patient. The application of the ether spray to the entire spine every day, for ten or fifteen minutes, or the application of cold by means of the ice-bag, is excellent, especially in violent cases. I have of late applied the needle douche, using several gallons of water.

It is of the utmost importance that the patient should be kept quiet, and that muscular exercise should be forbidden. A few hours' seclusion daily, in a dark room, works wonders, and at other times the patient should be made to assume a recumbent position, if possible.

There is no other nervous disease which is helped so much by proper diet as this. Fats are essential, and a liberal administration of milk and cream as well as fresh butter is highly recommended. Good substantial soups, raw meat, and condensed nitrogenous nourishment should be provided to the exclusion of everything else which simply satisfies hunger or gratifies the capricious appetite of the patient. Sea air is of immense service, and sea baths, if not too wearisome, are to be advised. Still-water bathing, of course, is to be preferred to surf bathing.

Moral treatment is of great value in many cases. West, whose sensible ideas of treatment I have always adopted, when possible, calls attention to the emotional perversion in choreic children, and speaks as well of the hebetude and weariness of mind, which seem to disappear with the movements. He considers moral therapeutics inapplicable to those cases of partial chorea which sometimes, though not often, last through life. The treatment should consist in removing mental strain, abridging study, and instituting a regular life and proper habits, and in building up the child's will power. The consciousness of the child, in regard to his infirmities, should not always be awakened, except when it is clearly a bad habit and not the result of disease.

Allan McLane Hamilton.

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[3] Boston Med. and Surg. Journal, vol. cxii., No. 14.
[4] Annales Medico-Psych., 1865.
[5] On Idiocy and Imbecility, p. 242.
[6] British Medical Journal, vol. ii., 1873, p. 9.
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[8] Ein Fall von angeborner Chorea. Wiener med. Wochenschrift, 1876, xxvi., 456.
[9] On Functional Nervous Disorders, p. 350.
[10] *Op. cit.*, p. 388.

[11] Archives Générales de Méd., March, 1865.
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[14] Wien. med. Wochenschrift, 1868, xviii., 227, 244; Wien. med. Presse, 1868, ix., 194–196.
[15] Deutsches Archiv für klinischer Med., 1877, xx., 383, 396.
[16] Cincinnati Journal of Medicine, 1867, ii., 398.
[17] British and Foreign Medico-Chir. Rev., 1868, xii., 208, 465.
[18] Text-Book of Nervous Diseases, 4th edition, 1898.

CHORION.—The chorion is the outermost of the membranes which surround the embryo, and plays a most important part in its development, as it soon comes in contact with the decidua and takes an active part in the formation of the fœtal portion of the placenta.

According to Minot, "the chorion is the whole of that portion of the extra-embryonic somatopleure which is not concerned in the formation of the amnion." This definition is undoubtedly correct for a large number of animals, but recent investigations render it doubtful whether it applies to man; as all of the earliest human ova which have yet been described (from the latter part of the first and the beginning of the second week) possess a distinctly formed chorion before there is any apparent differentiation into somato- and splancho-pleure.

According to Kollmann, it is more than probable that a distinct chorion is formed by the time the ovum reaches the uterine cavity, but unfortunately so young a specimen has not as yet been observed.

Theoretically, the chorion represents the outer layer of the blastodermic vesicle, and accordingly its epithelial layer must be derived from the primary ectoderm of the ovum. The earliest human ova which have yet been described are those of Peters and Graf Spee, in both of which the chorion is perfectly developed, while the embryo is in a very rudimentary condition.

Peters obtained his ovum at an autopsy upon a woman who committed suicide three days after missing a menstrual period, and he believed that it was not more than three or four days old. From his description, however, it appears to be somewhat older, but certainly not older than ten days. The ovum measured 1.6 x 0.8 x 0.9 mm. in its various diameters, and is therefore the smallest which has thus far been reported. It was embedded in the decidua and lay beneath its surface, having apparently burrowed its way through the epithelium; and it gives most important information concerning the mode of implantation of the ovum and the development of the decidua reflexa. The ovum presented a well-developed chorion which consisted of two layers: an inner layer of mesoderm and an outer layer composed of many layers of epithelial cells, which Peters designated as trophoblast.

Protruding from the surface of the chorion were a few elevations, whose interior was filled with connective tissue, representing the earliest stage of villous formation. The trophoblast was arranged in many layers and surrounded the connective tissue of the chorion as a distinct capsule. It was made up in great part of round or polyhedral cells, which stained deeply and presented distinct vesicular nuclei, between which were a few masses of protoplasm which showed no tendency to

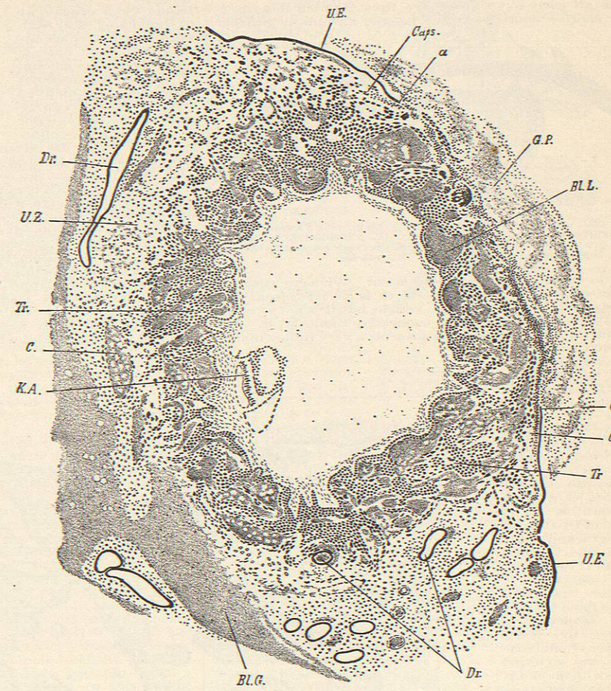

FIG. 1291.—Peters' Early Ovum. *U.E.*, Uterine epithelium; *Bl.L.*, lakes of blood; *Caps.*, decidua reflexa; *G.P.*, "Gewebspilz"; *Dr.*, uterine glands; *U.Z.*, decidua vera; *Tr.*, trophoblasts; *C.*, capillaries; *K.A.*, beginning embryo; *Bl.G.*, large blood-vessels; *a–b*, point of entrance of ovum.

divide into individual cells, through which were scattered irregularly shaped, darkly staining nuclei. The trophoblastic cells were apparently growing very rapidly, and had opened up dilated capillaries in the surrounding decidua, so that numerous small cavities were formed, which were lined by trophoblastic cells and filled with blood, and which probably represent the earliest stages in the formation of the intervillous circulation (Fig. 1291).

Spee's embryo was cast off from the uterus as an oval body, 9 x 6.5 mm., and consisted of a vesicle which en-

closed the beginning embryo. In this specimen the chorion was definitely formed, and consisted of an epithelial and a connective-tissue layer, and distinct villi arose from one portion of its exterior (Fig. 1292).

Very early ova have likewise been described by Reichert, Mall, and Leopold, the first two having been discharged from the uterus, while Leopold's ovum was still in contact with the uterine wall and surrounded by the decidua reflexa. The specimens of Leopold and Mall presented well-developed chorions, with villi over their entire periphery; while in Reichert's specimens they were limited to the equator of the ovum (Fig. 1293).

In all early ova which have thus far been described, the chorion consists of two layers: an outer epithelial

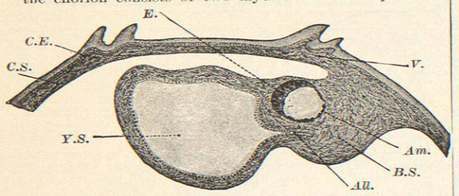

Fig. 1292.—Section through Spee's Early Ovum. No. 9 Zeiss. 6 mm. Magnified 24 times. *Am.*, Amnion; *All.*, allantois; *B.S.*, Bauchstiel; *C.E.*, chorionic epithelium; *C.S.*, chorionic connective tissue; *E.*, beginning embryo; *V.*, villi; *Y.S.*, yolk sac.

and an inner connective-tissue layer. We have already indicated that the epithelial layer is derived from the ectoderm of the blastodermic vesicle, but it is not so easy to explain the origin of the connective-tissue layer. In all the early ova, the amnion presents a very rudimentary appearance; and it is therefore improbable that the connective tissue of the chorion is derived from the somatopleure, in the same way as in many of the lower animals.

In its earliest stages the chorion consists of a membranous sac composed of two layers, ectoderm and mesoderm, and includes within it the beginning embryo. In all the specimens which have thus far been observed, a greater or lesser number of villi arise from the external surface of the chorion. At first they are purely epithelial in character, and in Peters' ovum are represented by mere projections of trophoblastic cells. At a little later period, however, the centre of the villus becomes filled with connective tissue, which is continuous with the inner layer of the chorionic membrane. The youngest chorion which I have examined was obtained from a two weeks ovum in the possession of Dr. Mall. Fig. 1293 gives a very good idea of its structure and shows that it is made up of two parts: (1) a chorionic membrane, and (2) the villi which spring from it.

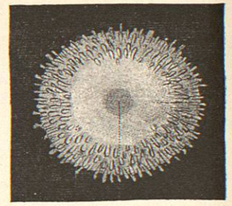

Fig. 1294.—Reichert's Ovum. Magnified six times.

The chorionic membrane is composed of an inner layer (toward the embryo) of connective tissue, which is made up of branching and star-shaped cells, which are separated from one another by a large amount of mucoid intercellular substance, in which no trace of vessels can be observed. Its exterior is composed of epithelial cells, which are arranged in two layers: an inner layer consisting of distinct cuboidal cells with round vesicular nuclei, and an outer layer made up of a band of protoplasm which is not divided into individual cells, and scattered through which are numbers of irregular-shaped, darkly staining nuclei.

The villi are arborescent structures which project from the outer surface of the chorionic membrane, and consist of a single trunk or stem, from which numerous branches are given off at something less than right angles. The tips of some of the larger branches extend down to the decidua, and serve to fasten the chorion to it; but the great majority of the smaller branches, after branching repeatedly, end freely and project into cavities which are filled with blood, and which constitute the intervillous

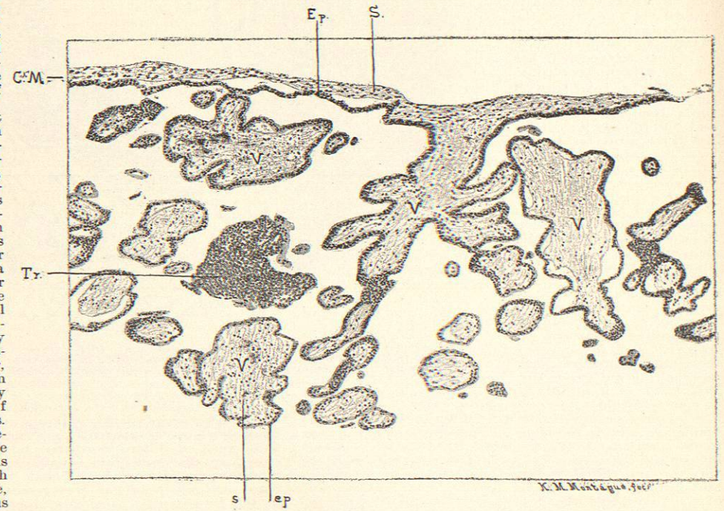

Fig. 1293.—Section through Chorionic Membrane and Villi of a Two-Weeks Ovum. Magnified 33 times. *C.M.*, Chorionic membrane; *Ep*, epithelium of chorionic membrane; *S*, connective-tissue layer of chorionic membrane; *V*, villi; *s*, stroma of villus; *ep*, epithelium of villus; *Tr*, decidual island (remnant of trophoblast).

spaces of the placenta. I do not believe that there is any evidence of anastomosis between the branches of the different villi, any more than between the branches of individual trees in a park.

The villi consist of a connective-tissue core which is continuous with the connective tissue of the chorionic membrane, and is covered by two layers of epithelium, just as is the chorionic membrane. None of the villi contain blood-vessels at this period. In several places the epithelium covering them appears to be arranged in many layers, and this is due either to tangential sections through the periphery of a villus or to the formation of epithelial buds, which represent the earliest stage in the formation of new branches. At one point in the section (Fig. 1293, *Tr.*) there is a mass of cells which present a distinctly epithelial appearance. Such structures are usually designated as decidual islands, and are supposed to be due to sections through decidual septa, which extend from the decidua toward the chorionic membrane. But in view of the marked similarity of the cells composing the mass to those which cover the villi, I am inclined to believe that they represent a remnant of trophoblast rather than a section through a decidual septum.

At a little later period the chorionic membrane becomes vascularized, and large numbers of vessels, both arterial and venous, are found just beneath its epithelial covering, branches from which extend into the villi, where they break up into a capillary network. These vessels are derived from the umbilical arteries and veins of the fœtus, and do not communicate with maternal vessels. Their arrangement is clearly shown in Fig. 1295.

It is not definitely known how the vessels first make their way to the inner surface of the human chorion. In many of the lower animals it has been definitely demonstrated that they are derived from a vesicular allantois, which grows out from the embryo between the amnion and chorion, and eventually applies itself to the inner surface of the latter. In man, however, this does not occur, as the extra-embryonic portion of the allantois is very rudimentary and does not assume a vesicular form, being merely a small epithelial duct which extends from the intestinal tract for a short distance into the umbilical stalk (Bauchstiel) (Fig. 1292).

The Bauchstiel is a prolongation of the caudal end of the embryo, and serves to connect it with the inner surface of the chorionic membrane. It contains the umbilical arteries and veins, and at a later period becomes converted into the umbilical cord.

At a still later period of development the chorionic membrane takes on a more complicated structure, and we are indebted to the classical article of Langhans for our first definite information concerning it. He stated that it was made up of four layers: gelatinous (Gallertschicht), fibrillar, vascular, and epithelial. The gelatinous is the innermost layer and lies in apposition with the connective tissue of the amnion. It is composed of mucoid connective tissue, analogous to the Whartonian jelly of the umbilical cord. External to this is the fibrillar layer, in which the connective-tissue cells are more abundant and have become more fusiform in shape, and are arranged in such a way as to give the tissue a distinct fibrillar appearance. External to this is the vascular layer which is composed of loose connective tissue, which surrounds large numbers of blood-vessels, both arteries and veins; while the outermost layer is composed of epithelial cells. The epithelium outside of the placental site consists of several layers of round or cuboidal cells, which stain palely with the ordinary reagents, and present distinct vesicular nuclei with a faint chromatin network, which readily stains with the ordinary dyes. At the placental site these cells are covered by a layer of syncytium, which is lacking in other parts of the chorionic membrane.

The above-mentioned cells were designated as the "Zellschicht" by Langhans, who considered that they were of connective-tissue origin. Further study, however, convinced him that they were epithelial cells and derived from the ectoderm of the ovum. This layer of cells has given rise to a great deal of misconception, and many observers believe that they are decidual in origin, having been designated by Kölliker as the decidua subchorialis, and by Winckler as the "Schlussplatte" of the decidua.

For the first few months, the entire periphery of the chorion is covered to a greater or less extent by arborescent and branching villi, except in Reichert's ovum, in which they were limited to its equator. Almost immediately after its formation the chorion becomes completely enclosed by a capsule composed of the decidua serotina and reflexa, from which it is separated by the growing villi, and the spaces thus formed become filled with maternal blood and constitute the intervillous spaces. This condition is very clearly demonstrated by the two ova which Leopold has lately described in his Atlas.

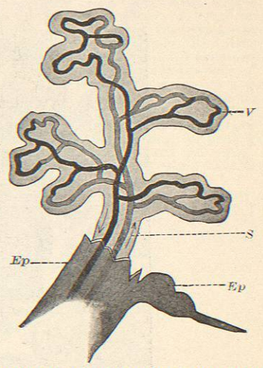

Fig. 1295.—Chorionic Villus from Full-Term Placenta. Highly magnified. (After Kollmann.) *Ep*, Epithelial covering; *S*, stroma of villus; *V*, vascular loop.

After a few months, however, the villi which are in contact with the decidua reflexa begin to atrophy, so that within a short time the chorionic membrane and the decidua reflexa come to lie in intimate contact, with only the degenerated remains of the villi separating them; while the villi which are in contact with the decidua serotina continue to grow and become larger and larger and give rise to the fœtal portion of the placenta. At this period we distinguish between the chorion læve and the chorion frondosum, the latter being the portion which takes part in the formation of the placenta. For further particulars concerning the structure of the placenta, the reader is referred to the article upon that subject.

The villi of the chorion frondosum, as we have just indicated, increase rapidly in size and complexity, and give off numerous branches which form the bulk of the placenta. But it is not probable that the primary villi increase in number after the first few months, the increased thickness of the placenta being due to the branching of the pre-existing villi; just as a row of trees, when first planted, is represented by a number of isolated stems, which at a later period are converted into large trees with myriads of branches and twigs. This fact has been strikingly demonstrated by de Loos, who has shown that one can roughly estimate the age of a placenta by the shape and size of its villi. Sections through a young placenta show a few large villi with comparatively few branches; while in a more mature placenta one sees large numbers of small branches, which become smaller and smaller as the placenta becomes older.

The stroma of the villi likewise undergoes marked changes as the placenta becomes older. In its early stages it is distinctly mucoid in appearance, and is made up of a small number of stellate cells which are separated by a large amount of mucoid intercellular substance. As the villi become older their stroma becomes denser, and the cells are more abundant and more fusiform in shape, so that at the latter part of pregnancy it presents a distinctly fibrous appearance.

Coincident with the changes in the stroma the villi become more vascular, and in the second half of pregnancy contain distinct vessels, many of which attain considerable size, the large arteries being surrounded by thick walls.

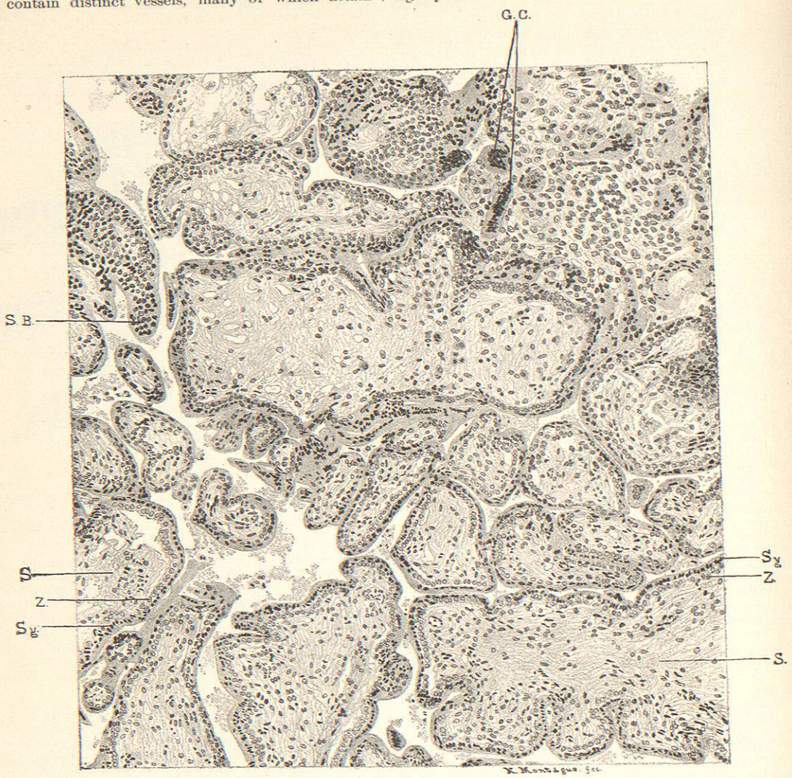

FIG. 1296.—Section through a Three-Months Placenta, Showing Structure of Chorionic Villi. Magnified 110 times. *S*, Stroma of villus; *Sy*, syncytium; *Z*, Zellschicht; *S.B.*, syncytial bud; *G.C.*, so-called placental giant cells.

The epithelium covering the chorionic villi was first described by Dalrymple in 1842, and we now know that it is arranged in two layers: an outer, which consists of a band of protoplasm, which is not divided into individual cells, and to which the term "syncytium" has been applied; and an inner layer of definite cuboidal cells, which were designated by Langhans as the "Zellschicht." The protoplasm of the syncytium presents a coarsely granular appearance, which on careful examination is seen to be due to the presence of vacuoles of varying size. The nuclei which are scattered through it are irregular in shape and contain a thick chromatin network which stains deeply with the ordinary dyes. The Zellschicht is composed of a single layer of distinctly cuboidal cells with vesicular nuclei. Their protoplasm stains very lightly and thus contrasts markedly with that of the syncytium; while the nuclei have a very delicate chromatin network, and therefore stain far less darkly than those of the syncytium.

These two layers are readily recognized during the first half of pregnancy, and are clearly shown in Fig. 1296, which represents a section from a three-months placenta. As the placenta grows older, however, the inner layer gradually disappears, so that in the last months almost all trace of it is lost, when the villi are covered only by syncytium. The failure to recognize this fact was the cause of a great part of the discussion concerning the arrangement of the chorionic epithelium, and only recently has it been generally recognized; but it is now universally admitted that two layers of epithelium can always be distinguished in the earlier months, and only one in the latter months of pregnancy.

The syncytium is not always arranged in a single layer, and several layers of nuclei may be observed in many places, while distinct buds of syncytial tissue frequently project from the surface of the villi and represent an attempt at branching. In microscopic sections, variously shaped masses of syncytium, containing many nuclei, are frequently found lying free in the intervillous spaces, and are frequently described as placental giant cells. The examination of serial sections will, however, always show that they are cross sections through such buds, or are due to tangential sections through the tips of the villi.

The term syncytium was introduced by Kossmann, though its characteristic features were described by Kastchencko in 1885, who designated it as plasmodium.

The chorionic epithelium has been the subject of marked controversy ever since it was first described, and various attempts have been made to explain its origin. The earlier writers supposed that the villi grew down into the uterine glands and obtained an epithelial covering from them. But Langhans, in 1877, was the first observer definitely to describe two layers, and, as we have already indicated, designated the inner layer as Zellschicht. At that time he believed that it was derived from the stroma, while the outer or syncytial layer represented the fœtal ectoderm. A few years later, however, he modified his opinion and stated that both layers were epithelial in origin. Langhans' views were soon adopted, and Minot, Kastchencko, and many other investigators recognized the existence of two layers, and considered that they were ectodermal in origin, and that the inner layer was derived from the outer.

In 1892–93, Kossmann and Merttens revolutionized for a time the teachings upon the subject, by stating that the Zellschicht represented the fœtal ectoderm, while the syncytium was derived from uterine epithelium, which then grew up over the villi. Their articles were very well illustrated and plausibly written, and distinctly demonstrated that the uterine epithelium could take on a syncytial character in places; but they were in error in supposing that it formed the outer layer of the chorionic covering. I have been able to confirm their observations to a certain extent, and have many specimens which positively demonstrate the transformation of tubal or uterine epithelium into syncytium. But the change is limited to isolated areas, and does not affect the entire epithelium, the greater part of which gradually becomes cuboidal and even flat, and eventually disappears. I therefore consider the formation of syncytium from the uterine epithelium as an accident, and perhaps a degenerative change which has nothing to do with the epithelial covering of the villi. Indeed, Gebhard and others have shown that the uterine epithelium may present a syncytial appearance without the existence of pregnancy, and have reported cases in which it was found in carcinoma of the uterus.

The theory of Kossmann and Merttens was presented so plausibly, and apparently so well confirmed, that it was rapidly accepted by most writers, among whom we may mention Marchand and Kollmann. It gradually lost ground, however, and at present the majority of the most recent writers upon the subject, among whom His may be mentioned, no longer believe in it, but state that both layers of the chorionic epithelium are ectodermal. The latter view has recently received marked confirmation

FIG. 1297.—Section through Fœtal Membranes and Decidua at Term, Outside of the Placental Site. Magnified 77 times. *Am.ep.*, Amniotic epithelium; *A.C.*, amniotic connective tissue; *C.C.*, chorionic connective tissue; *C.ep.*, chorionic epithelium; *V.* degenerated villi; *F.*, fibrin; *Dec.*, decidua.