

FIGURE 47. Simplified representation of the peripheral part of a mature placental villous tree, together with typical cross sections of the various villous types. For

further details see text and Figures 48 to 54. (From Kaufmann & Scheffen, 1990, with permission).

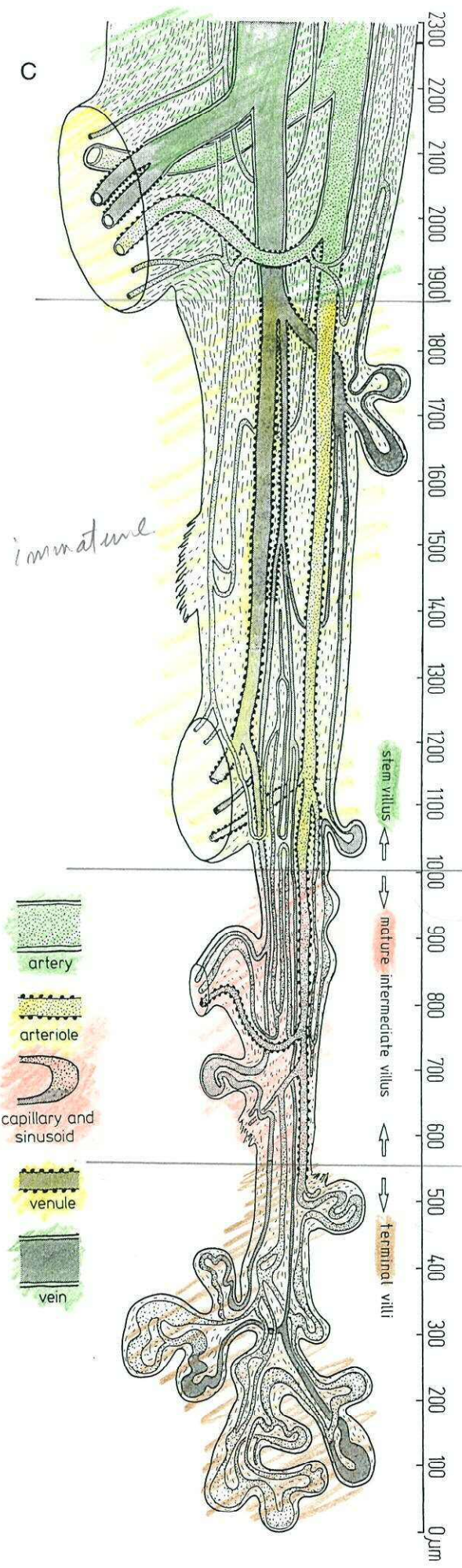
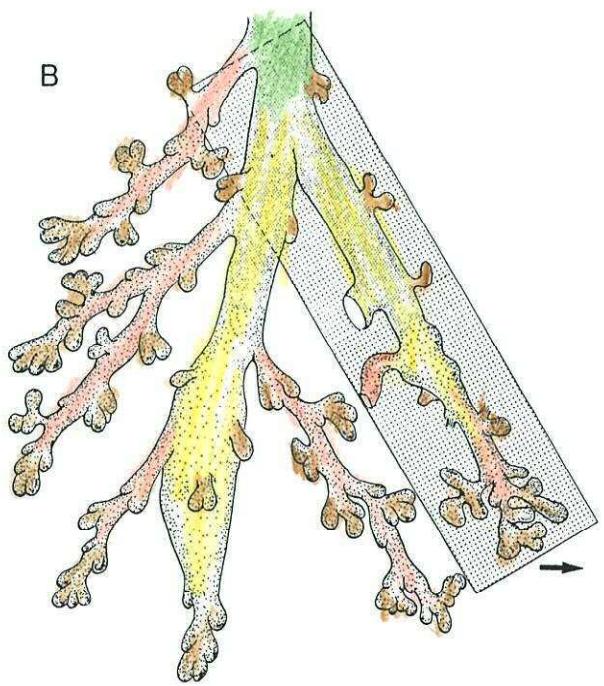
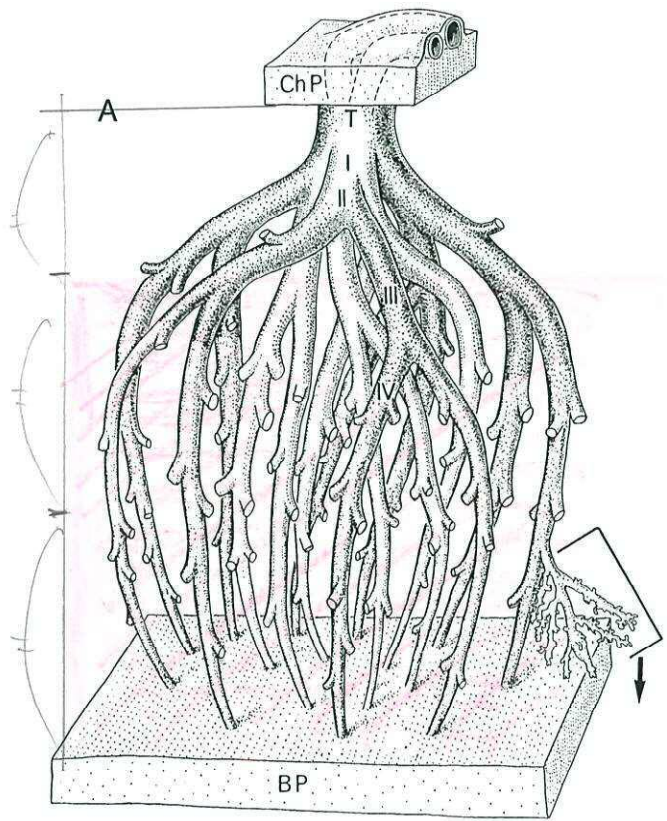


TABLE 1 Types of Villi and Their Structure

Type	Structure	Term placenta
Stem villi <i>幹性血管</i> <i>vessel: muscle ⊕</i>	Condensed <u>fibrous</u> stroma, arteries, veins, and branches with <u>media</u> or <u>adventitia</u> (stem villi connect the chorionic plate with the villous tree)	20–25% of villous volume formed by these villi
Mesenchymal villi	Most primitive villi present in the first stages of pregnancy; there is loosely arranged stroma with mesenchymal cells, Hofbauer cells, and poorly developed capillaries	<1% of villous volume formed by these villi
Immature intermediate villi <i>球</i> <i>Hofbauer ⊕</i>	<u>Bulbous</u> villi, which are a continuation of stem villi; these prevail in immature placentas; they have <u>reticular</u> stroma with numerous channels containing Hofbauer cells, capillaries, and vessels; these villi appear around the 8th week	0–5% of villous volume formed by these villi
Mature intermediate villi <i>vessel: muscle ⊕</i> <i>MΦ ⊖</i>	Long, <u>slender</u> villi with blood vessels not having a <u>media</u> or <u>adventitia</u> ; occasional stromal channels without macrophages are present	~ 25% of volume at term formed by these villi
Terminal villi	Final <u>grape-like</u> ramifications of mature intermediate villi; these villi have a high degree of capillarization and are the main site of gas and nutrient exchange	50% of villous volume normally formed by these villi

chorionic plate) should be taken for histologic examination. Assessment of the membrane for chorioamnionitis is incomplete unless chorion is present in the sections. A cross section of the umbilical cord a few centimeters from the insertion should be included in this cassette (Figure 22).

- Two sections of the central part of the placenta, including the maternal surface, are placed in the second cassette.
- One section from the central part of the placenta, including the fetal surface, and one cross section from the middle segment of the cord are placed in the third cassette.



PLACENTAL VILLI:

Kaufmann, P., Sen, D. K., Schwikhart, G.: Classification of human placental villi. Cell Tiss. Res., 200: 409-23, 1979.

Villous tree:

1. stem villi: D(um), vessel wall, stroma
a. trunci chorii: 3000-900, media(++), fibrous
b. rami chorii: 1000-300, *
c. ramuli chorii: 500- 50, *
2. intermediate villi:
a. immature : 200- 60, media(-), Hofbauer(++), loose
b. mature : 80- 40, * , Hofbauer(+), *
3. neck region : 40- 20, non-dilated sinusoid
4. terminal villi: 80- 30, dilated sinusoid

Synctial knot: 10 a 30%

Sinusoid 1/2 b/villi =

(10 \leq chorionvoss)

AGEING

blastocyst-out cell layer-primitive trophoblast
implantation

trophoblast-inner; cytotrophoblast, outer; syncytiotrophoblast
basal plate-anchoring villi

8 w.: cytotrophoblastic cell column, cytotrophoblastic shell

10 w.: syncytial buds in cytotrophoblastic shell, syncytial
invagination into decidua, 2nd. syncytial villi

11 w.: decrement of shell, syncytial buds, and cell islands

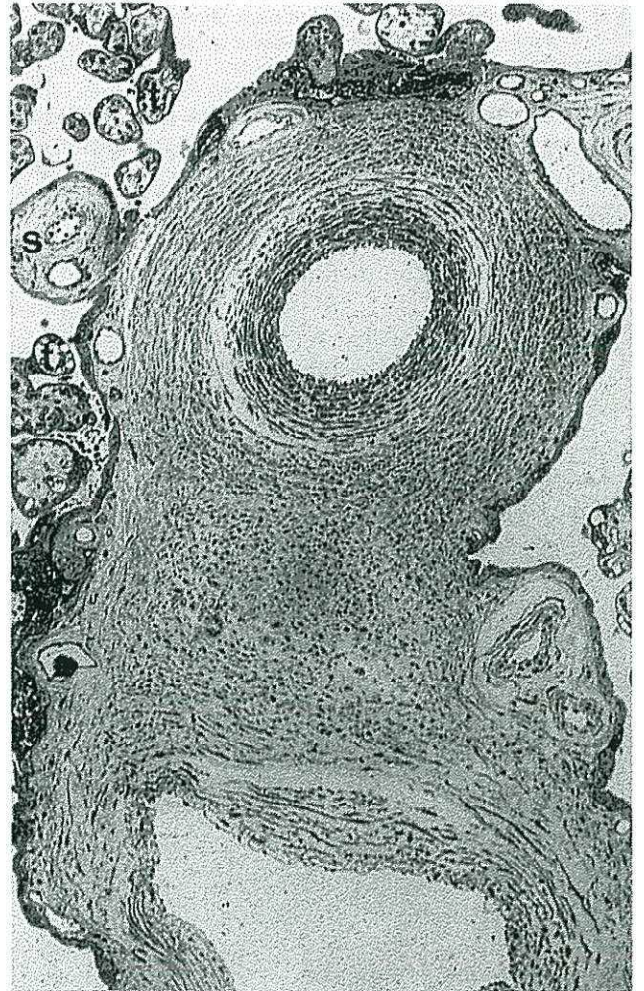
14 w.: cease of column and shell resulted in direct contact
of villi to decidua

1st. trimester: few in number, 170 μ m in diameter, two
easily distinguishable layers of trophoblastic epithelium,
delicate brush border on syncytiotrophoblast, loose
primitive mesenchymal tissue, numerous Hofbauer cells 25 μ m
eccentrically placed nucleus considered as tissue
macrophages possessing a surface Ig G receptor, stromal
mesenchymal cells are stellate, and stainable collagen is
absent, rather mucoid appearance, vessels first appear in 8
week and small centrally situated vessels lined by large
immature endothelial cells are present

2nd. trimester: numerous and smaller 70 μ m, cytotrophoblastic
cells are less prominent, syncytial layer becomes thinner
and aggregation into small focal clusters, trophoblastic
basement membrane is present, fibroblasts and delicate
collagen fibers, Hofbauer cells to be less numerous,
vessels prominent and a little dilated, endothelial cells
are fully mature and flattened, but situated towards the
centre of the villi

3rd. trimester: 40 μ m, trophoblast thinner and irregular to
attenuated, syncytial knots (10 - 30 % in term), vasculo-
syncytial membrane, thickening of BM after 34 w. reached to
1 - 3 μ m, dilated vessels (sinusoidally) 1 - 6 / villus,
mast cells

stem



b



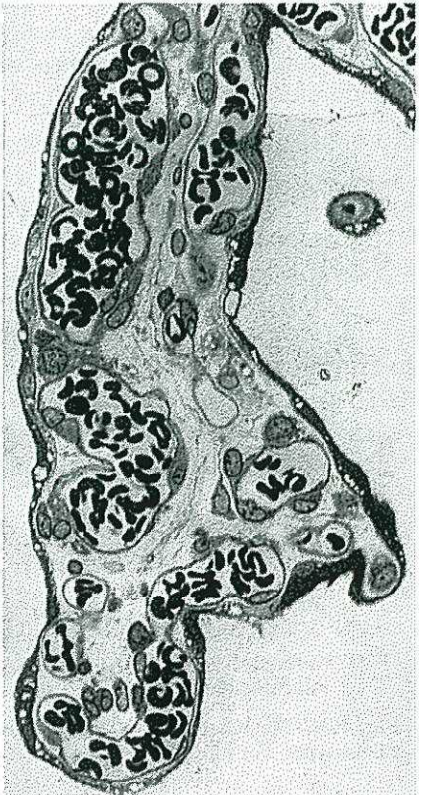
c

immature



d

mature



e

terminal

Fig. 46.6 Semithin plastic sections of human placental villi.

a This survey picture demonstrates the structural and staining variability of villous cross sections. s = stem villus; m = mature intermediate villus; t = terminal villus; * = tangential sections of villous trophoblastic surfaces; p = perivillous fibrin (fibrin-type fibrinoid); v = villous fibrinoid necrosis (mostly fibrin-type fibrinoid). × 165. (Reproduced with permission from Benirschke & Kaufmann, 1995.)

b Cross section of a large stem villus, surrounded by smaller stem villi (s) and terminal villi (t). Note that the adventitia of the artery (above) and of the vein (below) continue directly into the surrounding villous stroma. Superficially, numerous smaller cross sections of the paravascular capillary net of the stem villi are seen. × 115. (Reproduced with permission from Leiser et al, 1985.)

c Section of an immature intermediate villus from the 22nd week of pregnancy with its typical reticular stroma. The rounded, vacuolated macrophages (Hofbauer cells) are located in stromal channels which are devoid of collagen fibres and appear as empty holes (cf. Fig. 46.7). In faintly stained paraffin sections, such features can be misinterpreted as villous oedema. × 520. (Reproduced with permission from Kaufmann, 1981a.)

d Cross section of the typical poorly vascularized mature intermediate villus. Note the peripheral position of the narrow capillaries and the loose connective tissue. × 730. (Reproduced with permission from Benirschke & Kaufmann, 1995.)

e Longitudinal section of a richly vascularized terminal villus. The capillaries are locally dilated making the so-called sinusoids. The latter protrude the trophoblastic surface forming epithelial plates. × 430. (Reproduced with permission from Kaufmann et al, 1979.)

media and/or adventitia. Fetal capillaries are poorly developed and make up the so-called paravascular net (Arts, 1961; Leiser et al, 1985) which is underlying the trophoblast. The stem villi comprise the following structures:

- a. the main stem (truncus chorii) (Fig. 46.11) of a villous tree which connects the latter with the chorionic plate (diameter 1000–3000 µm)
- b. about four generations of short, thick branches (rami chorii) which are usually derived from the truncus already in the vicinity of the chorionic plate
- c. up to 20 further generations of asymmetric dichotomous branchings (ramuli chorii) which are more slender branches (diameter ranging from 80–300 µm), extending into the periphery of the villous trees
- d. a special group of stem villi is represented by the anchoring villi. These are ramuli chorii which connect to the basal plate by a cell column. The latter acts as the growth zone for this ramulus as well as for the basal plate.

The probable functional rôle of the stem villi is to support the mechanical stability of the villous tree and to provide the peripheral villi with fetal blood. About one-third of the total villous volume of the mature placenta is made up of this villous type.

2. Mature intermediate villi (Figs 46.5, 46.6d and 46.9b) are peripheral ramifications of villous stems, arranged in bundles of long, slender, multiply branching villi, their calibre at term ranging from 80 to about 120 µm. Most of their vessels are fetal capillaries, in between which are some small arterioles and venules. The vessels are embedded in a very loose connective tissue, with scanty fibres and cells, and occupy more than half

of the villous volume. To their surfaces at least 95% of all terminal villi are connected (Fig. 46.9b and d). This demonstrates that these are the main sites of growth and differentiation of the terminal villi. As concluded from the increased degree of fetal vascularization, their share in maternofetal exchange cannot be ignored. Highly active enzyme patterns indicate their metabolic and endocrine activities. About 25% of the villous branches are of this type. The first typical mature intermediate villi are formed in the 25th week post menstruation.

3. Terminal villi (Figs 46.3a, 46.5, 46.6e and 46.9b) are the final, grape-like ramifications of the intermediate villi, characterized by their high degree of capillarization (> 50% of the stromal volume) and the presence of highly dilated sinusoids, showing mean capillary diameters of about 14 µm and maximum values of more than 40 µm (Kaufmann et al 1985). Moreover, they are characterized by the presence of epithelial plates (Amstutz, 1960) or vasculo-syncytial membranes. These are thinned anuclear syncytiotrophoblastic lamellae which are directly apposed to the sinusoidally dilated segments of the fetal capillaries (Fig. 46.3a).

One or a small group of terminal villi are connected to the intermediate villi by a narrow neck region (diameter about 40 µm), characterized by thin trophoblast surrounding a scant stromal core, most of which is occupied by two to four narrow capillaries. The extremely high degree of fetal vascularization in the terminal villi and neck region, and the minimal maternofetal diffusion distance of less than 4 µm, make this villous type the most appropriate for diffusional exchange. The terminal villous volume amounts to 30–40% of the villous tree. Terminal villi develop shortly after the first mature intermediate villi, roughly around the 27th week post menstruation (Table 46.2).

4. Immature intermediate villi (Figs 46.5, 46.6c and 46.7) are peripheral continuations of stem villi. They prevail in immature placentas and normally persist, in small groups, in the centres of the villous trees (placentones). They represent the immature forerunners of stem villi. By lightmicroscopy their typical structural feature is the presence of a voluminous reticularly structured connective tissue that is rich in Hofbauer cells and poor in fibres. As can be seen by electronmicroscopy, sail-like processes of the fixed stromal cells form a system of collagen-free intercommunicating channels parallel oriented to the major axis of the villi (Castellucci & Kaufmann, 1982). The Hofbauer cells lie mostly inside the channels. Functionally, the rôle of immature intermediate villi in the maternofetal exchange at maturity should be negligible. Their main functions probably are, firstly, to act as precursors of the stem villi, into which they are continuously transformed, and secondly to produce villous sprouts.

Immature intermediate villi may cause diagnostic problems, since their reticular stromal core has only a weak

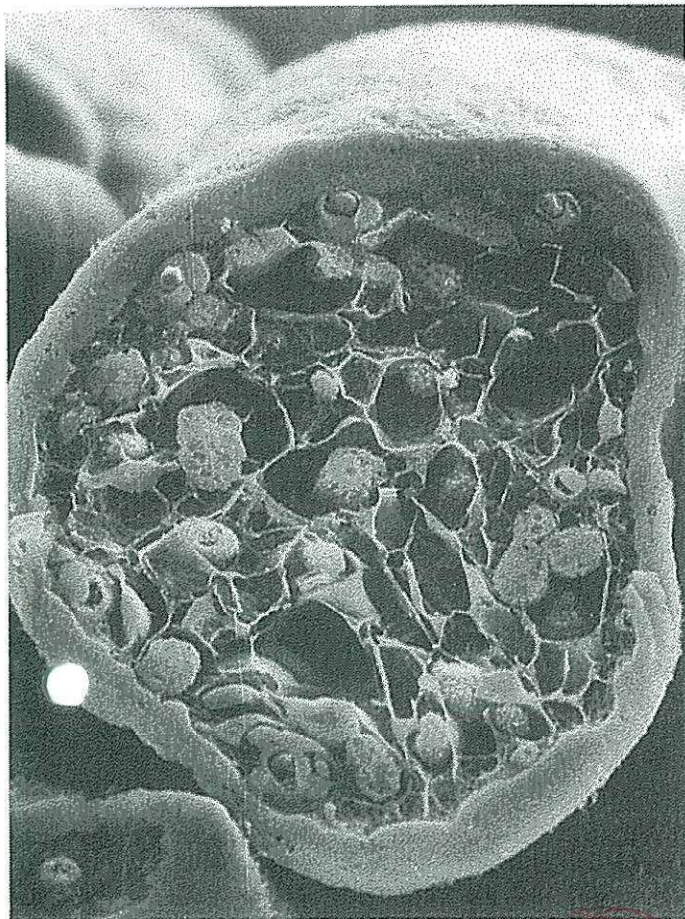


Fig. 46.7 Scanning electronmicrograph of a freeze-cracked immature intermediate villus demonstrating the three-dimensional view of reticular stroma with fixed connective tissue cells surrounding the stromal channels in which the macrophages can be found. $\times 550$. (Reproduced with permission from Castellucci & Kaufmann, 1982.)

affinity for conventional stains due to the lack of collagen. The resulting histological picture is that of a seemingly oedematous villus which has accumulated much interstitial fluid (cf. Fig. 46.14c). We believe that many villi referred to as 'oedematous villi' in the literature are in fact normal, immature intermediate villi. They can be very numerous in several pathological conditions in which villous development and differentiation is impaired, as in, for example, most cases of maternofetal rhesus incompatibility (Pilz et al, 1980; Kaufmann et al, 1987).

5. Mesenchymal villi (Figs 46.5 and 46.14a and b). These are the first tertiary villi. They prevail in the early stages of pregnancy, where they are the forerunners of immature intermediate villi. In the mature placenta, the mesenchymal villi are inconspicuous. They are transient stages of villous development, derived from villous sprouts. They differentiate either via immature intermediate villi into stem villi (first to second trimester), or directly into mature intermediate villi (third trimester). Structurally, the mesenchymal villi can be identified by

their slender shape, by numerous Langhans cells, poorly developed fetal capillaries, and a connective tissue that consists mostly of large, poorly branched cells, surrounded by scanty bundles of connective tissue fibres. Immunohistochemically, they can be identified by the presence of tenascin which is diffusely present in the villous stroma whereas this morphogenetically important matrix molecule is only poorly expressed in other villous types (Castellucci et al, 1991a).

Development of the villous trees

The five villous types described above represent different stages of development and differentiation of the villous trees (Fig. 46.8) (Castellucci et al, 1990b). The process starts with trophoblastic sprouts which are produced by trophoblastic proliferation along the surfaces of mesenchymal and immature intermediate villi. Mesenchymal invasion into the trophoblastic sprouts leads to the formation of villous sprouts. As soon as capillaries are formed they are named mesenchymal villi. Until the 7th week post menstruation, mesenchymal villi may fibrose directly to primitive stem villi. However, from the 8th week post menstruation onwards, mesenchymal villi differentiate into immature intermediate villi, which produce ample new sprouts before they are transformed into stem villi (Fig. 46.8). From this date onwards, this is the only route for the formation of stem villi. As long as these processes are active, the placenta is rapidly growing though not differentiating.

This situation changes considerably during the third trimester, in which placental growth slows and villous differentiation starts. The mesenchymal villi no longer transform into immature intermediate villi but rather into mature intermediate ones which later produce terminal villi along their surfaces (Fig. 46.8). The remaining immature intermediate villi differentiate into stem villi. As a consequence, the number of immature intermediate villi steeply decreases towards term. Because of this fact, the base for the formation of new sprouts is also reduced, and the growth capacity of the villous trees gradually slows. Only in the centres of the villous trees (placentone centres) do some mesenchymal villi persist and continue to produce immature intermediate villi. It follows that at term these two villous types can only be found around the central cavity where they are responsible for the typical loose and apparently immature structure of the placentone centres (Fig. 46.2a) (cf. section on intervillous space and placentone architecture). There they serve as persistent growth zones of the villous trees (Schuhmann, 1981).

The above described events at the beginning of the last trimester are the most important steps for understanding villous development. At this time, the transformation of newly formed mesenchymal villi into immature intermediate villi switches to a transformation of the former into

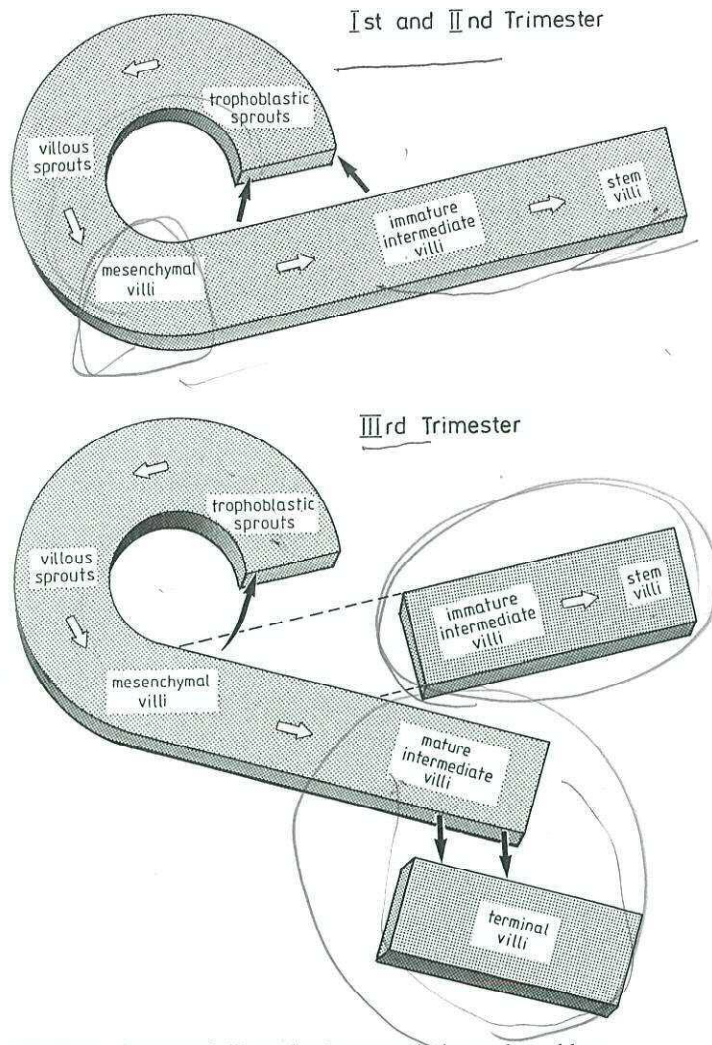


Fig. 46.8 Routes of villous development during early and late pregnancy. White arrows indicate the transformation of one villous type into another, whereas black arrows symbolize the formation of new villi along the surfaces of others. Throughout the first and second trimesters, trophoblastic sprouts are produced along the surfaces of mesenchymal and immature intermediate villi. They are transformed into mesenchymal villi and then differentiate into immature intermediate villi before they are transformed into stem villi. Throughout the third trimester, the mesenchymal villi become transformed into mature intermediate villi, which later produce terminal villi along their surfaces. The remaining immature intermediate villi continue to differentiate into stem villi. Thus their number steeply decreases towards term. Only in the centres of the villous trees may the villous developmental mode of the first and the second trimester persist until term. Because of this, the base for the formation of new sprouts is reduced and the growth capacity of the villous trees gradually slows. (Reproduced with permission from Castellucci et al, 1990b.)

mature intermediate villi (Fig. 46.8, Table 46.2). If this switch takes place early in gestation, the placenta differentiates prematurely but stops growing too soon, due to the deficit of immature intermediate and mesenchymal villi. By contrast, if the switch is delayed, the placenta is characterized by persisting immaturity and striking growth since immature, quickly growing villi prevail.

Angioarchitecture of the villous trees

Fetal arteries and veins are restricted to the stem villi (Fig. 46.6b), whereas arterioles and venules are mainly located in the smaller stem villi, as well as in mature and immature intermediate villi (Kaufmann et al, 1985; Leiser et al, 1985). All of the above larger fetal vessels are accompanied by a system of long, slender capillaries, the so-called paravascular net (Arts, 1961). In the mature, intermediate villi, the arterioles and venules turn into long coiled terminal capillary loops. In areas of maximum coiling, the capillaries stretch the surface of the mature intermediate villi, producing bulges, the terminal villi. This mechanism takes place in the course of the last trimester. As soon as the longitudinal growth of the capillaries exceeds that of the mature intermediate villi, the capillaries coil and cause the protrusion of the terminal villi. This process is accentuated under hypoxic conditions where capillary growth is stimulated (Bacon et al, 1984), resulting in a higher number of multiply branched terminal villi (cf. Fig. 46.9c and d) (Jackson et al, 1987; Kaufmann et al, 1987, 1988).

Particularly within the terminal villi, the capillaries may dilate considerably, thus forming sinusoids (Figs 46.3a and 46.6e). One capillary loop may supply several terminal villi 'in series', dilating and narrowing several times for each single terminal villus. The main function of the sinusoids is probably to reduce blood flow resistance and, thus, to guarantee an even blood supply to the long terminal capillary loops (mean 4000 μm) and the shorter paravascular capillaries (1000 μm) (Kaufmann et al, 1985). There is no convincing proof for the earlier view that the sinusoids are dilated, specialized venous parts of the capillary loops, which were thought to increase the materno-fetal exchange rate by reducing the blood flow velocity.

Intervillous space and placentone architecture

The human placenta is of the haemochorial, villous type. After leaving the spiral arteries, the maternal blood circulates through the diffuse intervillous space and flows directly around the villi (Fig. 46.2a). Most anatomical investigations of the intervillous space have been made on delivered placentas which are no longer exposed to the *in vivo* effect of maternal blood pressure distending the intervillous space. Therefore, the usual appearance of the intervillous space of the delivered placenta is that of a system of extremely narrow clefts. Calculations based on intervillous blood volume and villous surface make it likely that the mean width ranges between 16 and 32 μm (Benirschke & Kaufmann, 1995).

Wigglesworth (1967) studied corrosion casts of fetal vessels and suggested that most villous trees are arranged as hollow-centred bud-like structures. When he injected the spiral arteries, he found that the injection mass collected in the loose centres of the villous trees. This is in

Table 46.2 Summary of the structural and developmental characteristics of the five villous types from the 4th to the 40th week post menstruation

	Stem villi	Immature intermediate villi	Mesenchymal villi	Mature intermediate villi	Terminal villi
4			Only mesenchymal villi (120-250 μm) and trophoblastic sprouts (30-60 μm) are present. Large mesenchymal villi (>200 μm) may show diffuse and moderate stromal fibrosis.		
5					
6					
7					
8		Within the mesenchymal villi, the first stromal channels appear.			
9		Numerous immature intermediate villi (100-200 μm) with reticular stroma; calibre of the largest vessels is 20-30 μm.	Numerous short mesenchymal villi (60-100 μm), partly continuous with slim trophoblastic sprouts, branching from the surfaces of immature intermediate villi.		
10					
11		Increasing amount and size of immature intermediate villi (100-400 μm); calibre of stem vessels increased up to 100 μm; vessel walls with 2 to 3 concentric layers of cells.			
12					
13					
14					
15		Lightmicroscopically apparent bundles of collagen fibres arranged around vessel walls.			
16					
17	About 50% of all villi with calibres >150 μm show fusion of the fibrosed adventitial sheaths around the primitive arteries with those of the veins. This is the first step towards formation of the fibrosed stromal core of stem villi.		The amount of mesenchymal villi and of trophoblastic sprouts is slowly decreasing.		
18					
19					
20	First true stem villi appear. Smaller ones (150-300 μm) show centrally fibrosed core with arterial and venous adventitia being fused. Those >300 μm show a largely fibrosed core.	Immature intermediate villi are still the dominating villous type. Those with calibres from 100-150 μm show no stromal fibrosis. The larger ones show fibrosis of the walls of larger vessels.			
21					
22	Calibre >300 μm; completely fibrosed stroma; calibre <300 μm; superficial layer of reticular stroma below the trophoblast.	Number and size of immature intermediate villi is decreasing.	The number of mesenchymal villi with poorly fibrosed and poorly vascularized stroma, rich in cells, considerably increases. They grow in length and in width (calibres 80-150 μm) and show a continuous transition into mature intermediate villi.		
23					
24					
25					
26					
27					
28					
29					
30	Calibre >200 μm; completely fibrosed stroma; calibre <200 μm; incomplete superficial film of reticular stroma.	Still few evenly distributed immature intermediate villi can be found; the stroma is only partly reticular in nature.	Typical mesenchymal villi are rare and mostly located near to immature intermediate villi.	Mature intermediate villi with dense stroma, rich in stromal cells and poor in fibres, with calibres ranging from 100-150 μm are the dominating villous type.	Local spot-like groups of first typical terminal villi appear; they show calibres of about 60 μm, about half of their stromal volume being occupied by capillary lumina.
31					
32					
33					
34					
35	Usually, all stem villi are devoid of reticular stroma; however, below the trophoblast there still is a less densely fibrosed rim, rich in fibroblasts.	The few remaining immature intermediate villi are no longer evenly dispersed but rather concentrated as small groups in the centres of the villous trees lining the central cavities. The extremely loose reticular stroma shows only a few typical stromal channels.	Mesenchymal villi are histologically inconspicuous; the few identifiable ones are usually located around the central cavities.	The relative amount of mature intermediate villi is decreasing to about 25% of total villous volume. The calibre is reduced to 80-120 μm.	Terminal villi are the dominating villous type; they amount to about 40% of total villous volume.
36					
37					
38	All stem villi (except a few around the central cavity) are completely fibrosed. The trophoblast of the larger ones often is replaced by fibrinoid.				
39					
40					

II

辛嵐

20-25%

<1%

<25%

<1% <40 μm

60% 90%

III

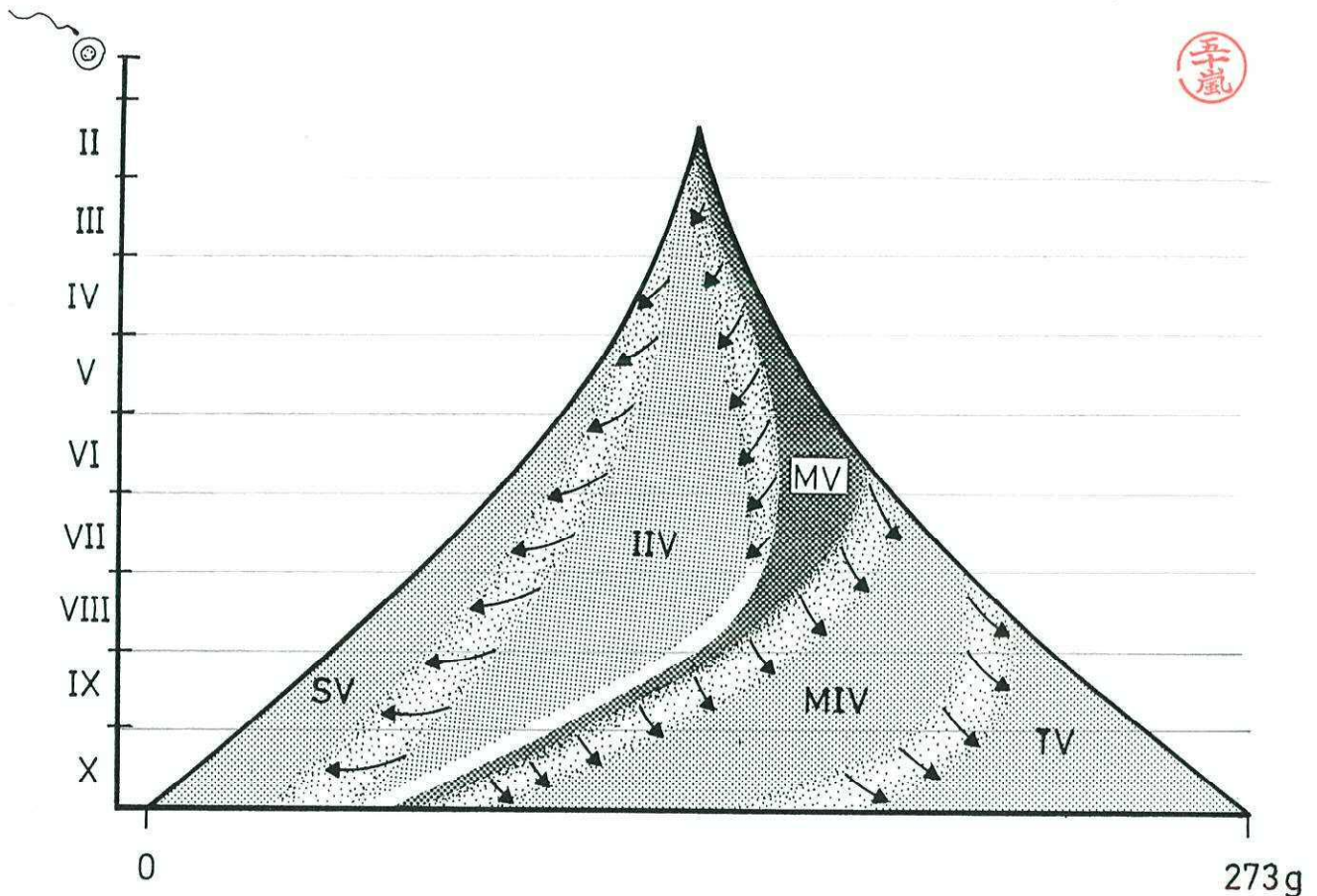


FIGURE 57. Development of the total villous volume and the volume of the various villous types (in grams), from the 2nd month p.m. until term. Abscissa: villous volume in grams per placenta. Ordinate: gestational age p.m. in months. The arrows demonstrate the routes of transformation or formation of villi. The lightly stippled areas around the arrows symbolize transitional stages between closely related villous types. At term the mean villous volume per placenta amounts to 273 g. After morphometric evaluation of representative histological sections, this volume can be assigned to the various villous types at term as follows: stem villi (SV): 31 g = 11%; transitional stages to immature intermediate villi: 24 g = 9%; immature intermediate villi (IIV): 9 g = 3%; mesen-

chymal villi (MV): less than 3 g = less than 1%; transitional stages to mature intermediate villi: 3 g = 1%; mature intermediate villi (MIV): 77 g = 28%; transitional stages to term villi: 31 g = 11%; terminal villi (TV): 95 g = 35%. Rough data for earlier stages of pregnancy can be deduced from the diagram. It must be pointed out that these data are preliminary, obtained from only a few placentas. There is a considerable local and inter-individual variation. It becomes evident that the sum of stem villi (SV) plus immature intermediate villi (IIV) decreases throughout the last 3 months of pregnancy; the decrease can be explained by a massive transformation of stem villi into fibrinoid. (Modified from Castellucci et al., 1990, with permission.)

opinion, it is more likely a result of reduced intravillous blood flow. We found a generally increased degree of stromal fibrosis within the mature intermediate villi of the condition "terminal villi deficiency" (Schweikhart & Kaufmann, 1983; Schweikhart, 1985; Kaufmann et al., 1987). This entity not only is often combined with prolonged pregnancy but seems to be the result of reduced fetal vascularization as well.

Development of the Mature Intermediate Villi

One of the most important steps for understanding villous development occurs at the beginning of the last trimester. At this time, the transformation of newly formed mesenchymal villi into immature intermediate villi switches to a transformation into mature intermediate villi (Figures 56, 57, 227,

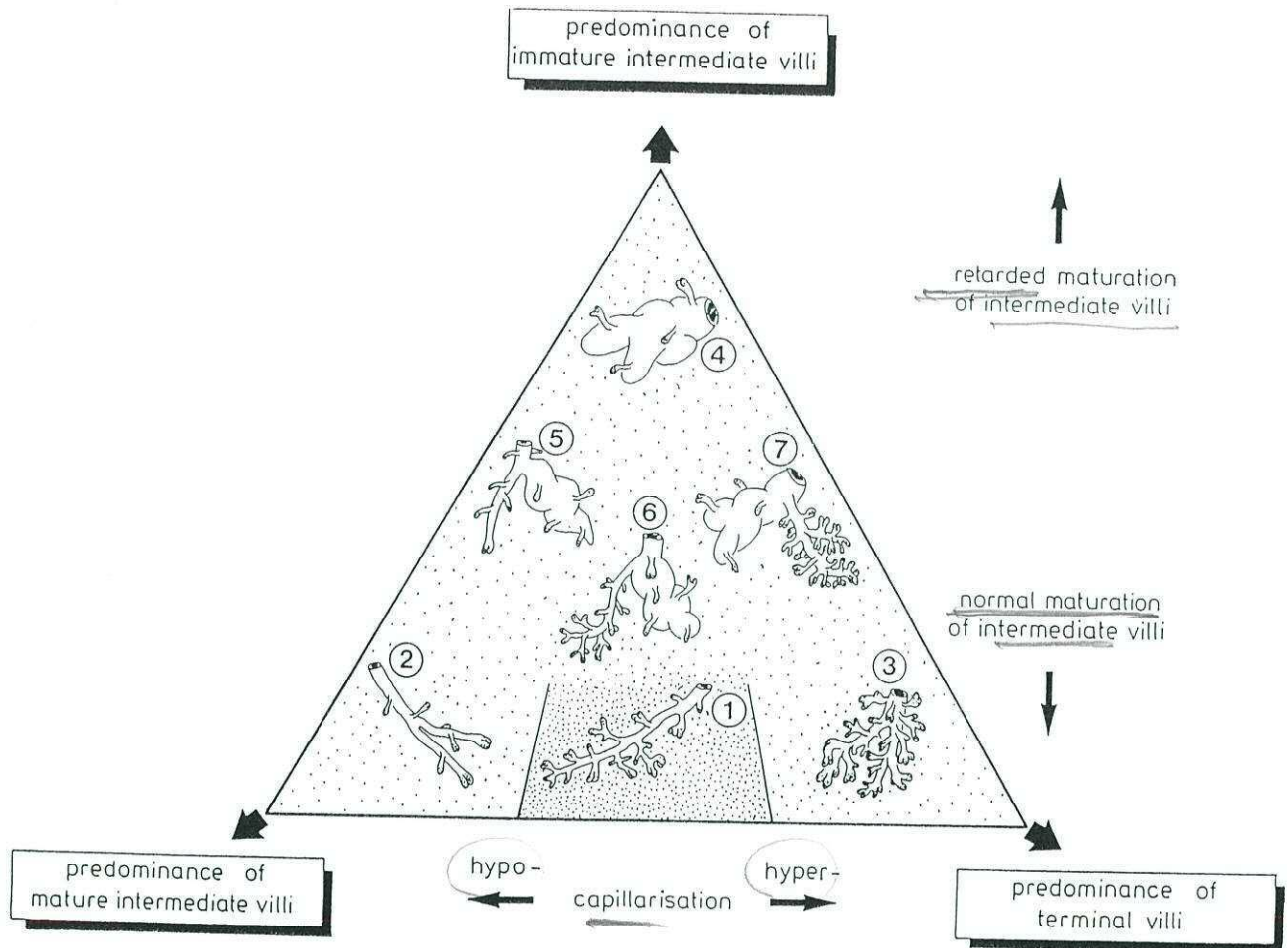


FIGURE 77. Normal and abnormal villous ramification patterns at term. Because villous maldevelopment affects mainly immature and mature intermediate and terminal villi, the stem villi are neglected in this diagram. The different kinds of development and maldevelopment are arranged in such a way that each corner of the triangle represents the predominance of one of the three villous types. Thus the upper corner of the triangle, with immature intermediate villi as the prevailing type, includes cases with synchronous immaturity and retarded villous development. The base of the triangle represents three types of fully mature placenta that differ from each other with respect to fetal capillarization and production of

terminal villi. 1 = Normal mature placenta with a balanced mixture of mature intermediate and terminal villi; 2 = terminal villi deficiency with prevailing mature intermediate villi but largely lacking terminal villi owing to hypocapillarization; 3 = predominance of terminal villi as a result of "hypermaturity" at term or hypoxic hypercapillarization; 4 = immaturity at term (e.g., rhesus incompatibility); 5, 6, 7 = intermediate stages between maturity and terminal villi deficiency (5), immaturity and normal mature placenta (6), immaturity and hypoxic hypercapillarization (7). (From Kaufmann et al., 1987, with permission.)

capillaries. This situation is compatible with a decrease in capillary diameter, which is highly characteristic for hypoxic villi. The expanded capillary bed, together with the decreased capillary diameter, increases the diffusion capacity for oxygen (Bacon et al., 1984).

The richly branched capillaries (Figures 62 and 68) are responsible for a characteristic deformation of the outer shape of the terminal villi (Figures 68 and 75A). The trophoblast directly covers the capillary surface, as the connective

tissue is usually reduced. It results in short, knob-like, multiply indented villi that resemble fists. Preparation of histological sections of such villi unavoidably results in increased flat sectioning. Groups of villi are connected to each other by syncytial bridges (Figure 75B). Often a net-like appearance is achieved, the extent of which depends on the thickness of the section. That depicted in Figure 75B is at 1 μm . One can easily imagine the amount of bridging in the thicker paraffin section.

図2 妊娠前期胎盤

絨毛の直径は 100μ 程度である。表層の合胞体栄養膜細胞(↑)は、立方状で、個々の細胞境界は不明瞭である。合胞体栄養膜細胞の下に細胞性栄養膜細胞(↑)が存在し二層構造をなしている。間質は薄い星形の原始間葉組織で形成され、多くのHofbauer細胞(↑)が認められる。写真：中山

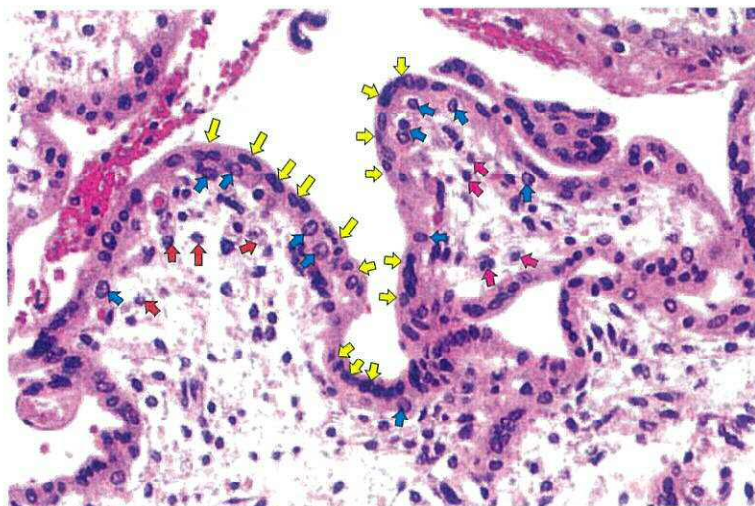


図3 妊娠中期胎盤

絨毛の大きさは 70μ 程度である。細胞性栄養膜細胞(↑)は少量認める。合胞体栄養膜細胞(↑)は立方-扁平状で、高さも不均一である。間質は密で、線維芽細胞やコラーゲンが認められる。Hofbauer細胞(↑)の出現はやや少ない。絨毛毛細管(↑)はかなり目立つ。写真：中山

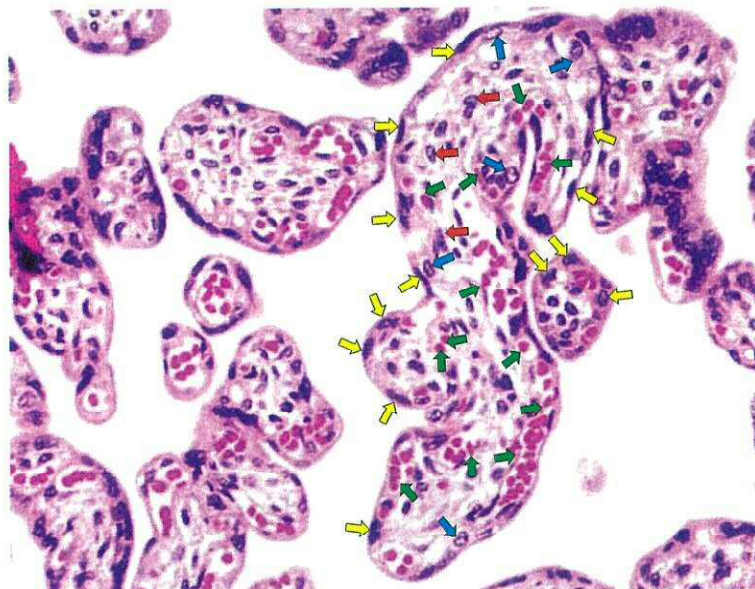
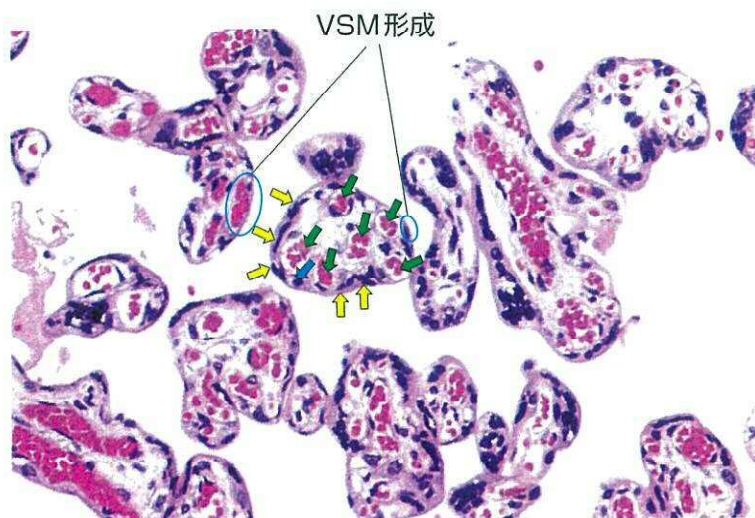


図4 妊娠後期(成熟)胎盤

絨毛の直径は約 40μ になり、満期の胎盤は $10\sim 20\mu$ 程度のものも多い。合胞体栄養膜細胞(↑)は薄く、不規則である。細胞性栄養膜細胞(↑)はごくわずかである。毛細管(↑)は表層の合胞体栄養膜細胞に限りなく近づき、合胞体栄養膜細胞の基底膜や絨毛間質や血管の基底膜はあたかも一層の膜であるかのごとく見え、血管合胞体膜 vasculo-syncytial membrane; VSM (○)とよぶ。Hofbauer細胞は認めがたい。写真：中山



11

Characterization of the Developmental Stages

This chapter is a synopsis and presents brief descriptions of the average data of placenta and membranes throughout the single stages of placental development. Embryological data concerning embryo and fetus are given only insofar as they are of importance for the definition of the stage. It is not the intention of this chapter to compare data of various sources on a scientific level but, rather, to present data that are directly applicable for the pathological and histological examination of human material. For this purpose, all data have been extrapolated and were standardized where necessary. The data are based on the following publications: embryonic staging according to O'Rahilly (1973) and Boyd and Hamilton (1970); crown-rump-length, embryonic and fetal weight, mean diameter of the chorionic sac, placental diameter and thickness, placental weight: Boyd and Hamilton (1970), O'Rahilly (1973), and Kaufmann (1981); placental and uterine thickness in vivo: Johannigmann et al. (1972); length of umbilical cord: Winckel (1893); villous surfaces, villous volumes, villous diameters: Hörmann (1951), Knopp (1960), Clavero-Nunez and Botella-Llusia (1961, 1963), Aherne and Dunnill (1966), Kaufmann (1981), Schiemer (1981), and Gloede (1984); mean trophoblastic thickness, distribution of villous cytotrophoblast, mean maternofetal diffusion distance: Kaufmann (1972), Kaufmann and Stegner (1972), Gloede (1984), and Kaufmann (1981). For further details see the summarizing tables at the end of the chapter.

Day 1 p.c. (p.c. = post coitum). Carnegie stage 1: one fertilized cell; diameter 0.1 mm.

Day 2 p.c. Carnegie stage 2a: from 2 to 4 cells; diameter 0.1 to 0.2 mm.

Day 3 p.c. Carnegie stage 2b: from 4 to ± 16 cells; diameter 0.1 to 0.2 mm.

Day 4 p.c. Carnegie stage 3: free blastocyst, from 16 to ± 64 cells; diameter about 0.2 mm.

Day 5 to early day 6 p.c. Carnegie stage 4: blastocyst attached to the endometrium, from about 128 to ± 256 cells; diameter 0.2 to 0.3 mm.

Late day 6 to early day 8 p.c. Carnegie stage 5a: implantation, prelacunar stage of the trophoblast; the flattened blastocyst measures about $0.3 \times 0.3 \times 0.15$ mm. The blastocyst is partially implanted. The implanted part of the blastocyst wall is considerably thickened, largely consisting of solid syncytiotrophoblast. The still not implanted, thin part of the blastocyst wall consists of a single layer of cytotrophoblast. The embryonic disk measures about 0.1 mm in diameter.

Late day 8 to day 12 p.c. Lacunar or trabecular stage.

Late day 8 to day 9 p.c. Carnegie stage 5b: diameter of chorionic sac $0.5 \times 0.5 \times 0.3$ mm; embryonic disk about 0.1 mm. The syncytiotrophoblast at the implantation pole exhibits vacuoles as forerunners of the lacunar system.

Day 10 to day 12 p.c. Carnegie stage 5c: diameter of chorionic sac $0.9 \times 0.9 \times 0.6$ mm. The vacuoles in the syncytiotrophoblast fuse to form the lacunar system; first lacunae at the antiimplan-

tation pole. First contact of lacunar system with eroded endometrial capillaries. Some maternal erythrocytes may be observed in the lacunae. Around day 11, implantation is complete; the defect in the endometrial epithelium becomes closed by a blood coagulum and is covered by epithelium on day 12. At the implantation site, the endometrium measures 5 mm in thickness; first signs of decidualization.

Day 13 to day 14 p.c. Carnegie stage 6, villous stage (first free primary villi).

Day 13 p.c. The nearly round chorionic sac has a diameter of 1.2 to 1.5 mm; length of embryonic disk is 0.2 mm.

Day 14 p.c. Diameter of chorionic sac 1.6 to 2.1 mm; length of embryonic disk 0.2 to 0.4 mm. First appearance of primitive streak and yolk sac.

With expansion of the lacunar system, the syncytiotrophoblast becomes reduced to radially oriented trophoblastic trabeculae, the forerunners of the stem villi. After invasion of cytotrophoblast into the trabeculae, free trophoblastic outgrowths into the lacunae, "free primary villi," are formed. The trabeculae are now called "villous stems." By definition, from this date onward the lacunae are transformed into the intervillous space. Cytotrophoblast from the former trabeculae penetrates the trophoblastic shell and invades the endometrium. During the second half of day 14, at the implantation pole some mesenchyme may invade the trabeculae (first formation of secondary villi).

Days 15 to 18 p.c. Villous stage (secondary villi).

Days 15 to 16 p.c. Carnegie stage 7: diameter of chorionic sac about 5 mm; length of embryonic disk less than 0.9 mm; appearance of notochordal process and primitive node (Hensen).

Days 17 to 18 p.c. Carnegie stage 8: diameter of embryonic sac less than 8 mm; length of chorionic disk less than 1.3 mm. On the germinal disk, the notochordal and neurenteric canals, and primitive pit can be discerned.

Starting at the implantation pole and continuing all around the circumference to the antiimplantation pole, mesenchyme (derived from the extraembryonic mesoderm in the chorionic cavity) invades the villi, transforming them into secondary villi.

The basal feet of the villous stems, connecting the latter with the trophoblastic shell, remain free of mesenchyme and thus persist as a primary villous stage (forerunners of the cell columns).

Days 19 to 42 p.c. About 2nd month post menstruation (p.m.), villous stage (early tertiary villi):

Days 19 to 21 p.c. Carnegie stage 9: diameter of chorionic sac less than 12 mm; length of embryonic disk = crown-rump length of the embryo 1.5 to 2.5 mm; 1 to 3 somites. Neural folds appear; first heart contractions.

Days 22 to 23 p.c. Carnegie stage 10: diameter of chorionic sac less than 15 mm; crown-rump length 2.0 to 3.5 mm; 4 to 12 somites. Neural folds start to fuse; two visceral arches.

The villous mesenchyme is characterized by fetal capillaries (tertiary villi). The villous diameters are largely homogeneous, presenting two differently sized groups of villi. The larger villous stems and their branches exhibit diameters of 120 to 250 μm . Histologically, the stroma of both is mesenchymal in nature. Along their surfaces, one finds numerous small (30 to 60 μm) trophoblastic and villous sprouts.

Days 23 to 26 p.c. Carnegie stage 11: diameter of the chorionic sac less than 18 mm; crown-rump length 2.5 to 4.5 mm; 13 to 20 somites; closure of the rostral neuropore; optic vesicles identifiable.

Days 26 to 29 p.c. Carnegie stage 12: diameter of chorionic sac less than 21 mm; crown-rump length 3 to 5 mm; 21 to 29 somites; closure of the caudal neuropore; three visceral arches; upper limb buds appear.

The length of villous stems between chorionic plate and trophoblastic shell varies from 1 mm (antiimplantation pole) to 2 mm (implantation pole). The central two-thirds is supplied with mesenchyme and capillaries (Figure 221), the peripheral one-third remains in the primary villous stage (cell columns). The villous calibers are similar to those described for the previous stage. Because of advanced branching of the stems, the relative amount of trophoblastic and villous sprouts is reduced. Most villi contain loose mesenchyme together with centrally positioned fetal capillaries (mesenchymal villi). Peripherally, they

6w/8w

11. Characterization of the Developmental Stages

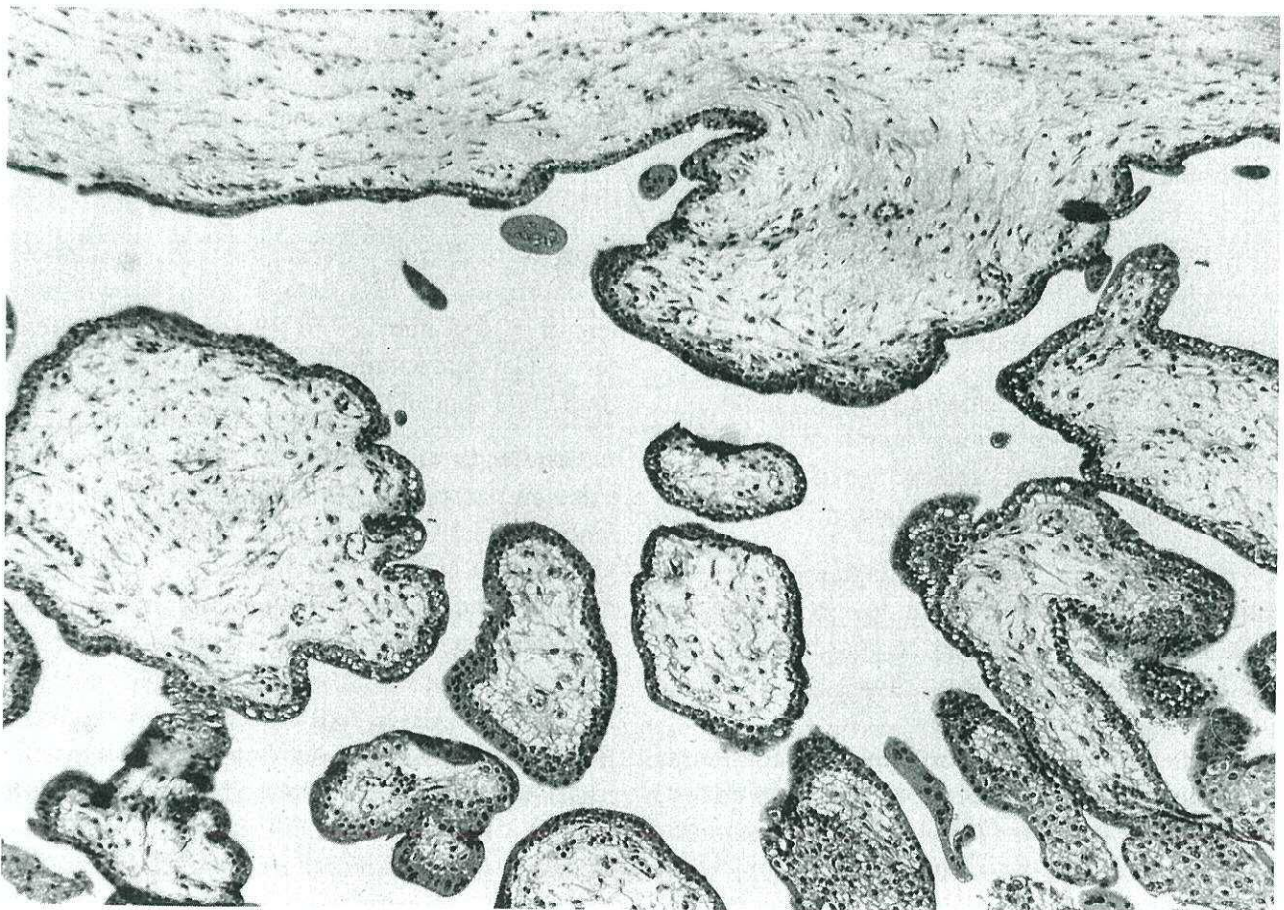


FIGURE 221. Paraffin section of placental villi of the 6th week p.m. Note the thick trophoblastic covering consisting of complete layers of cytotrophoblast and syncytiotrophoblast. Fetal capillaries are poorly developed or, in

some places, still lacking. In the lower right corner, an early step of the formation of a cell island can be seen attached to the villous surface. $\times 125$.

continue into massive trophoblastic sprouts. In the villous stems, vessels of larger caliber achieve first signs of a surrounding adventitia (start of formation of typical stem villi characterized by fibrous stroma). The villous trophoblastic surface is composed of an outer syncytiotrophoblast and complete inner layer of cytotrophoblast. Together they measure 20 to 30 μm in thickness. The chorionic plate, consisting of fetal mesenchyme, cytotrophoblast, and syncytiotrophoblast and bordering the intervillous space, still lacks fibrinoid. The trophoblastic shell is transformed into the basal plate by intense mixing of decidual and trophoblastic cells. Tissue necrosis of both cell types causes the appearance of the first spots of Nitabuch fibrinoid. The superficial syncytiotrophoblastic layer of the basal plate, bordering the intervillous space, becomes locally replaced by Rohr fibrinoid.

Days 29 to 32 p.c. Carnegie stage 13: diameter of chorionic sac less than 25 mm; crown-rump-length 4 to 6 mm; 30+ somites; four limb buds and otic vesicle.

Days 32 to 35 p.c. Carnegie stage 14: diameter of chorionic sac less than 28 mm; crown-rump-length 5 to 8 mm; first appearance of lens pit and optic cup.

Days 35 to 37 p.c. Carnegie stage 15: diameter of chorionic sac less than 31 mm; crown-rump-length 7 to 10 mm; closure of lens vesicle; clear evidence of cerebral vesicles; hand plates.

Days 37 to 42 p.c. Carnegie stage 16: diameter of chorionic sac less than 34 mm; crown-rump-length 8 to 12 mm; embryonic weight about 1.1 g; retinal pigment visible; foot plates.

The net weight of the chorionic sac in stage 16 is about 6 to 10 gm; thickness of the chorion at the implantation pole is about 6 mm, at the antiimplantation pole about 3 mm. The uterine lumen is still open, and parietal and capsular decidua are not yet in contact. The range of villous calibers changes slightly from the previous stage (Figure 222). The largest stem reaches a diameter of less than 400 μm . The obvious gap between the 200 μm villi and the small sprouts meanwhile is closed by a variety of medium-size mesenchymal villi. The mean villous caliber is 204 μm . The total placental villous surface is 0.083 m^2 . The connective tissue layer of the chorionic plate is completely fibrosed, the fibrous tissue partly extending in the initial parts of the villous stems. The overwhelming share of the villous stroma is still mesenchymal in nature. The villous cytotrophoblastic layer is incomplete; 85% of the villous surface is double-layered (cytotrophoblast plus syncytium). The thickness of the villous trophoblast varies between 10 and 30 μm (mean 15.4 μm). Near the end of this period, most of the mesenchymal villi show increased numbers of macrophages, as well as the first signs of reticular transformation of their stroma toward immature intermediate villi. Only 2.7% of the villous volume is occupied by fetal vascular lumens. The mean maternofetal diffusion distance is 55.9 μm . The villous stems are nearly completely occupied by connective tissue. Basal segments, persisting in the primary villous stage, are the exception. Those segments now show the typical appearance of cell columns. Short portions of villous side branches, persisting on the primary villus stage and positioned somewhere between chorionic and basal plate, may increase in size by con-

FIGURE 222. Paraffin section of placental villi of the 8th week p.m. All villi are vascularized. As can be seen from the diffuse stromal structure, the villi still belong to the

mesenchymal type. $\times 125$. (From Kaufmann, 1981, with permission.)

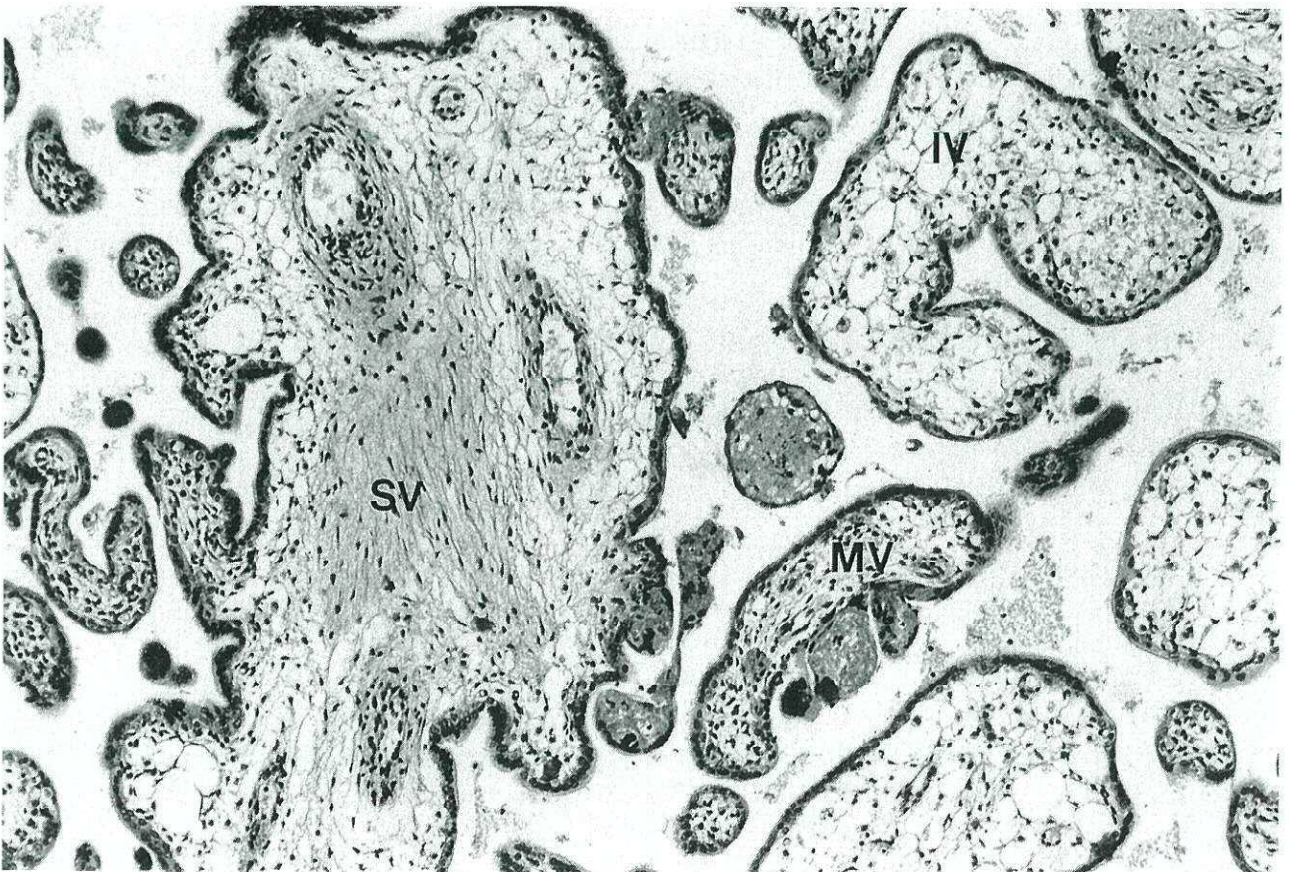


FIGURE 223. Paraffin section of placental villi of the 12th week p.m. The larger villi have achieved the reticular stroma of typical immature, intermediate villi. The

smaller villi are mesenchymal in structure. The first small fetal arteries and veins can be seen. $\times 125$.

tinuous cell proliferation with subsequent fibrinoid degeneration; they thus establish the first cell islands.

3rd month p.m. 9th to 12th weeks p.m. Days 43 to 70 p.c.

Days 43 to 44 p.c. Carnegie stage 17: maximum diameter of chorionic sac 38 mm; crown-rump-length 10 to 14 mm; finger rays.

Days 44 to 48 p.c. Carnegie stage 18: maximum diameter of chorionic sac 42 mm; crown-rump-length 12 to 16 mm. Elbow region, toe rays, nipples, and eyelids appear.

Days 48 to 51 p.c. Carnegie stage 19: maximum diameter of chorionic sac 44 mm; crown-rump-length 14 to 18 mm.

Days 51 to 53 p.c. Carnegie stage 20: maximum diameter of chorionic sac 47 mm; crown-rump-length 17 to 22 mm. Upper limbs bent at the elbow region; first signs of finger separation.

Days 53 to 54 p.c. Carnegie stage 21: maximum diameter of the oval chorionic sac 51 mm; crown-rump-length 20 to 24 mm.

Days 54 to 56 p.c. Carnegie stage 22: maximum diameter of the oval chorionic sac 58 mm; crown-rump-length 23 to 28 mm.

Days 56 to 60 p.c. Carnegie stage 23: maximum diameter of the oval chorionic sac 63 mm; crown-rump-length 26 to 31 mm.

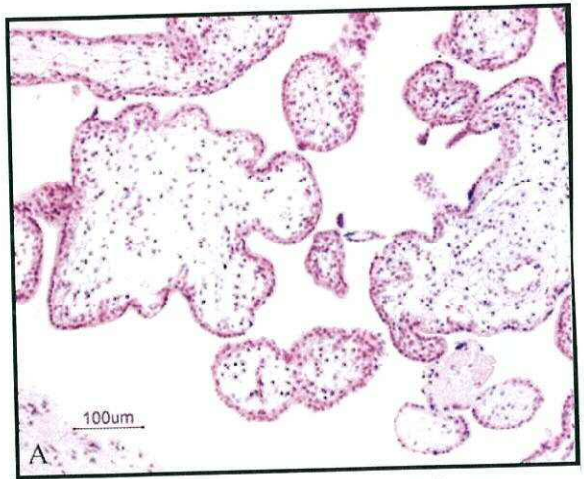
Days 61 to 70 p.c. Maximum diameter of the oval

to irregular chorionic sac 68 mm; crown-rump-length 30 to 40 mm.

The embryonic weight increases throughout the 3rd month from 2 g to 17 g and the net weight of the chorionic sac from 10 g to 30 g. The chorionic sac is covered by villi over its entire surface; it is not yet subdivided into smooth chorion and placenta. All villi are vascularized. Around the antiimplantation pole, the increased degenerative changes of villi and fibrinoid deposition in the intervillous space indicate that the formation of the smooth chorion will commence soon. Parietal and capsular decidua may come into contact locally, but they remain unfused. Heterogeneity of villous diameters and villous structure increases. Fibrosis of the villous stems slowly extends into the more peripheral parts of the largest villi (diameters less than 500 μm). During the course of the 3rd month, most of the villi measuring between 100 and 400 μm establish the typical reticular appearance of immature intermediate villi (Figure 223), characterized by numerous macrophages (Hofbauer cells). Small villi with diameters less than 100 μm show mesenchymal stroma. Trophoblastic and villous sprouts are numerous. Total villous surface is about 0.302 m^2 . The trophoblastic thickness varies from 10 to 20 μm . Eighty percent of the villous surfaces are covered by cytotrophoblast. Fetal vessel lumens occupy about 4% of the villous volume. Some of the larger fetal vessels achieve a thick adventitia, consisting of fibrous stroma, which occupies large parts of the villous stroma. The reticular stroma, a sign of immaturity of the stem villi, is restricted to the superficial parts of the

FIGURE 224. Paraffin section of placental villi of the 15th week p.m. The larger immature intermediate villi exhibit the first signs of central stromal fibrosis, originating from the larger fetal vessels, thus establishing the first stem villi (SV). Several typical immature intermediate villi

(IV) and mesenchymal villi (MV) can be seen. As is typical for mesenchymal villi of the second and third trimester, they are associated with degenerating villi being more or less transformed into fibrinoid. $\times 125$.



13w

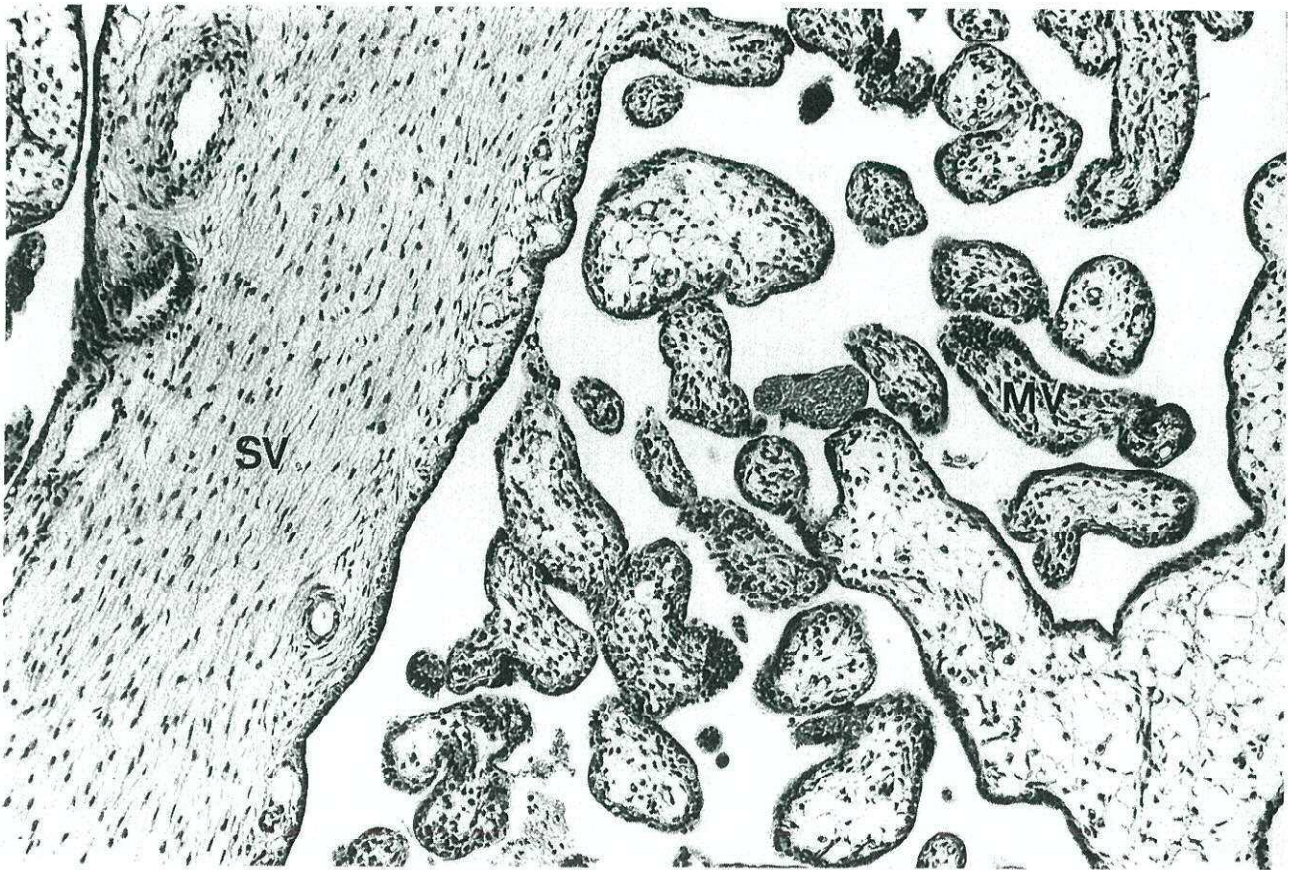
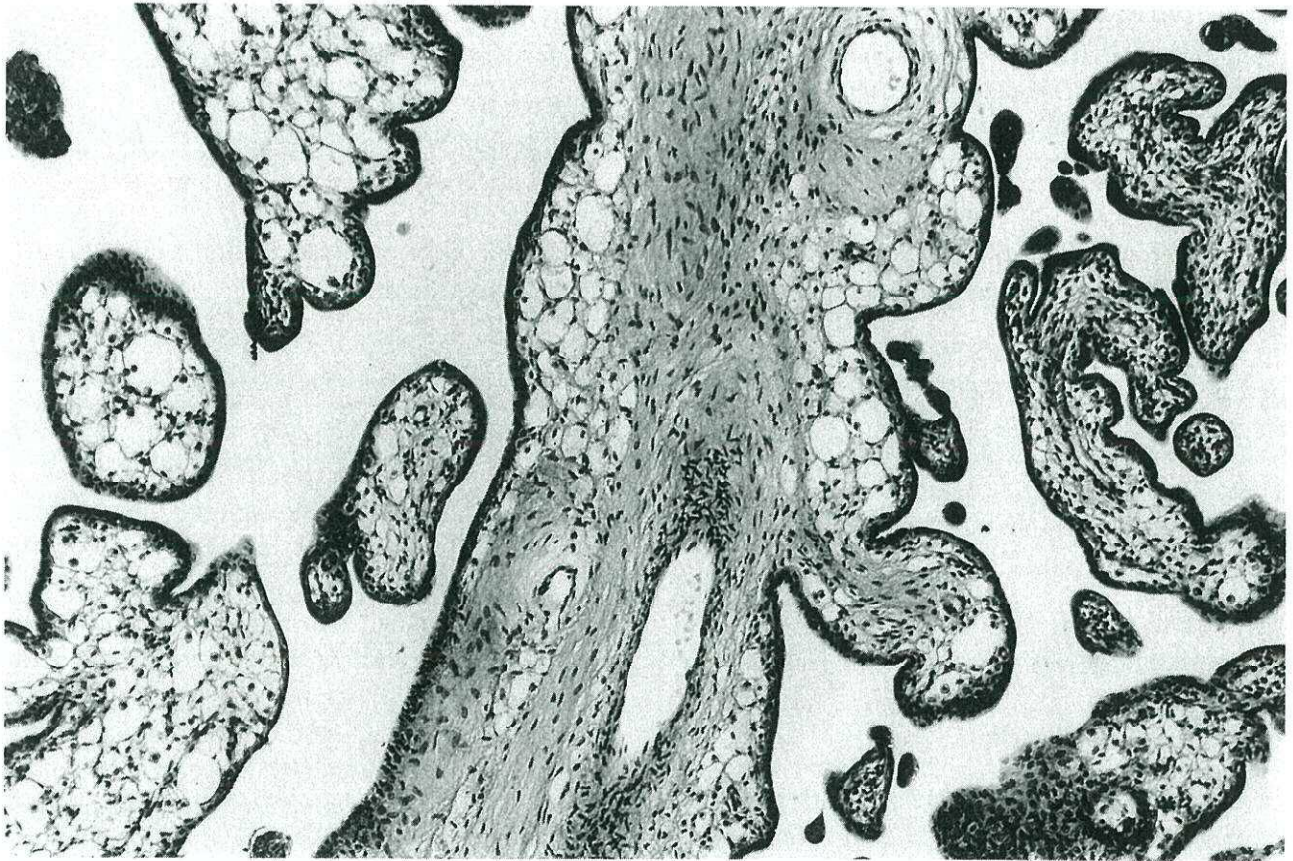


FIGURE 225. Paraffin section of placental villi of the 18th week p.m. The picture is comparable to that of the preceding stage. Formation of stem villi with stromal fibrosis is somewhat more expressed. $\times 125$.

stroma positioned under the trophoblast. Whereas in the previous stages fibrinoid was restricted to the cell islands and the basal plate, spot-like fibrinoid deposition at some of the villous surfaces can be observed now. Fibrinoid deposition at the intervillous surface of the chorionic plate is still an exception. The amnionic cavity has extended to such an degree that the amnionic mesoderm in many places comes into contact with the connective tissue layer of the chorionic plate.

4th month p.m. 13th to 16th week p.m. 11th to 14th weeks p.c. The shape of the chorionic sac becomes more and more irregular because of compression between uterine wall and fetus. Its maximum diameter increases throughout this period from 68 mm to 80 to 90 mm. The crown-rump length grows from 45 mm to 80 mm and the fetal weight from 20 g to 70 g. The length of the umbilical cord is between 160 and 200 mm.

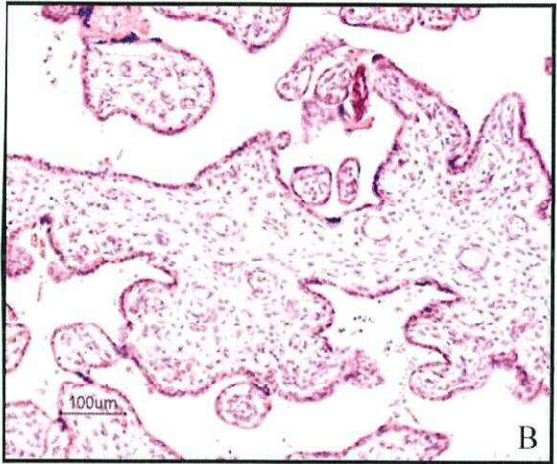
The continuous degeneration of placental villi at the antiimplantation pole, which is free of villi from the middle of the 4th month onward, as well as the villous proliferation at the implantation pole, initiate the differentiation of the chorionic sac into smooth chorion and placenta. The placental diameter increases from 50 mm to 75 mm at the end of this month and the placental weight from 30 g to 70 g. The maximal placental thickness in the delivered specimens is 10 to 12 mm. Numerous placental septa become visible. The cell columns become more deeply incorporated into the basal plate by fibrinoid deposition in their surrounding. The chorionic plate is in close contact with the amnion over its entire surface, giving it the definite shape and layering. It consists of amnionic epithelium, amnionic mesoderm, chorionic mesoderm, cytotrophoblast layer, and superficial syncytiotro-

phoblast. The distribution of the villous caliber (Figure 224) is similar to that described for the preceding month. The inhomogeneous mixture of villi is composed of stem villi with diameters of 300 to 500 μm , the vascular adventitia of which occupies at least 75% of the villous stroma, and of immature intermediate villi with diameters of 100 to about 300 μm . Mesenchymal villi and sprouts, 40 to 80 μm in diameter, are numerous; but because of their size they occupy only a small proportion of the total villous volume. Because the immature intermediate villi have the most characteristic reticular stroma in this stage and comprise the highest proportion of villi, one observes more villous macrophages (Hofbauer cells) than at all other stages of placental development. The total villous surface was measured to be 0.544 m^2 . The share of fetal vessel lumens is increased to about 6%. Some of the capillaries establish contact with the villous trophoblast. In such places the syncytial nuclei are moved aside, resulting in the first epithelial plates. Therefore the trophoblastic thickness varies between 2 and 12 μm (mean of 9.6 μm). As during the previous month, one observes cytotrophoblast over about 80% of the villous surface. Fibrinoid deposition becomes a usual finding on the villous surfaces.

5th month p.m. 17th to 20th week p.m. 15th to 18th week p.c. Because of the geometrically irregular outer shape of the fetus, the diameter of the chorionic sac cannot be estimated from this period onward. Over the course of the 5th month the crown-rump length increases from 80 mm to 130 mm, and the fetal weight from 70 g to 290 g. The placenta is clearly separated from the smooth chorion. The placental diameter is between 75 mm and 100 mm, and placental weight increases from

FIGURE 226. Paraffin section of placental villi of the 21st week p.m. The stroma of the stem villi (SV) is largely fibrous. Only a thin superficial rim of reticular connec-

tive tissue is reminiscent of their derivation from immature intermediate villi. $\times 125$.



230

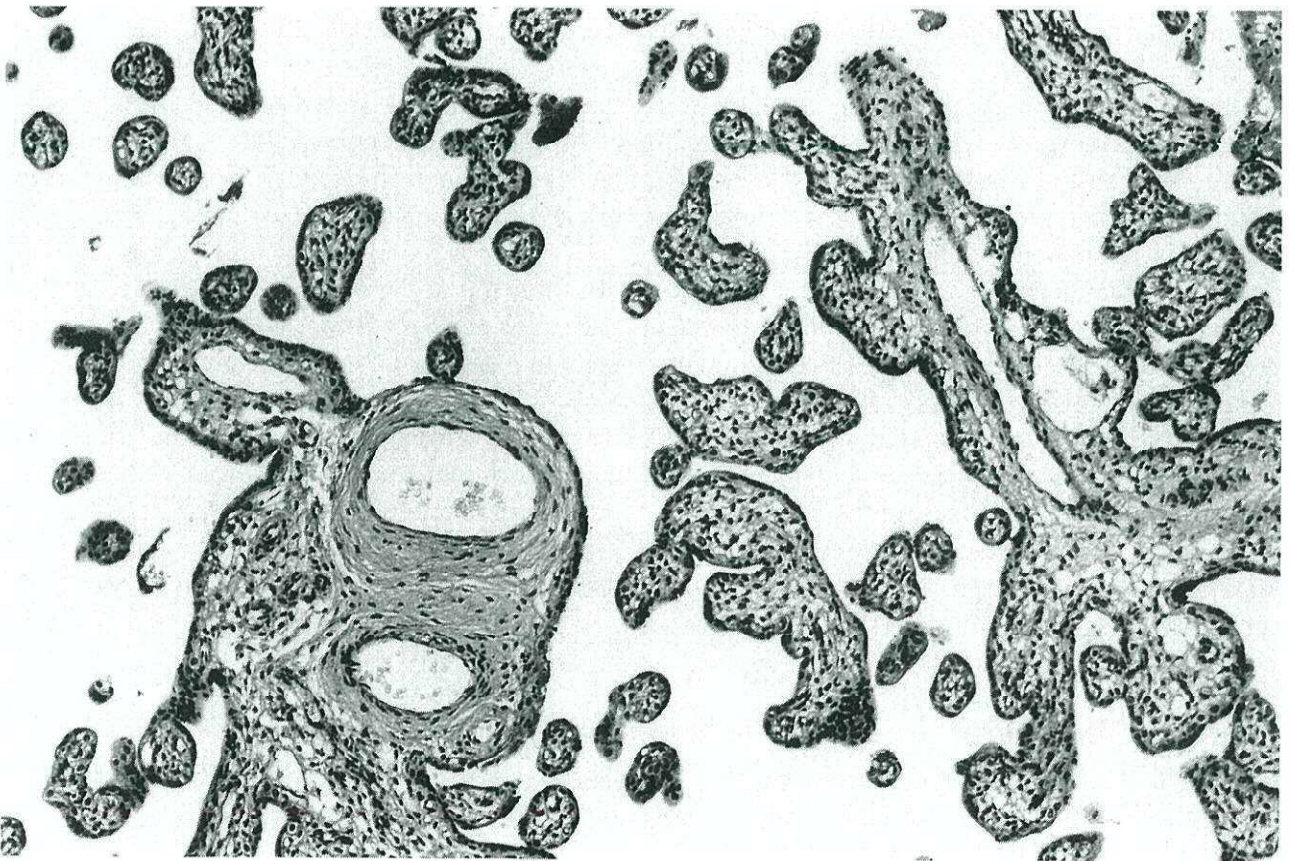
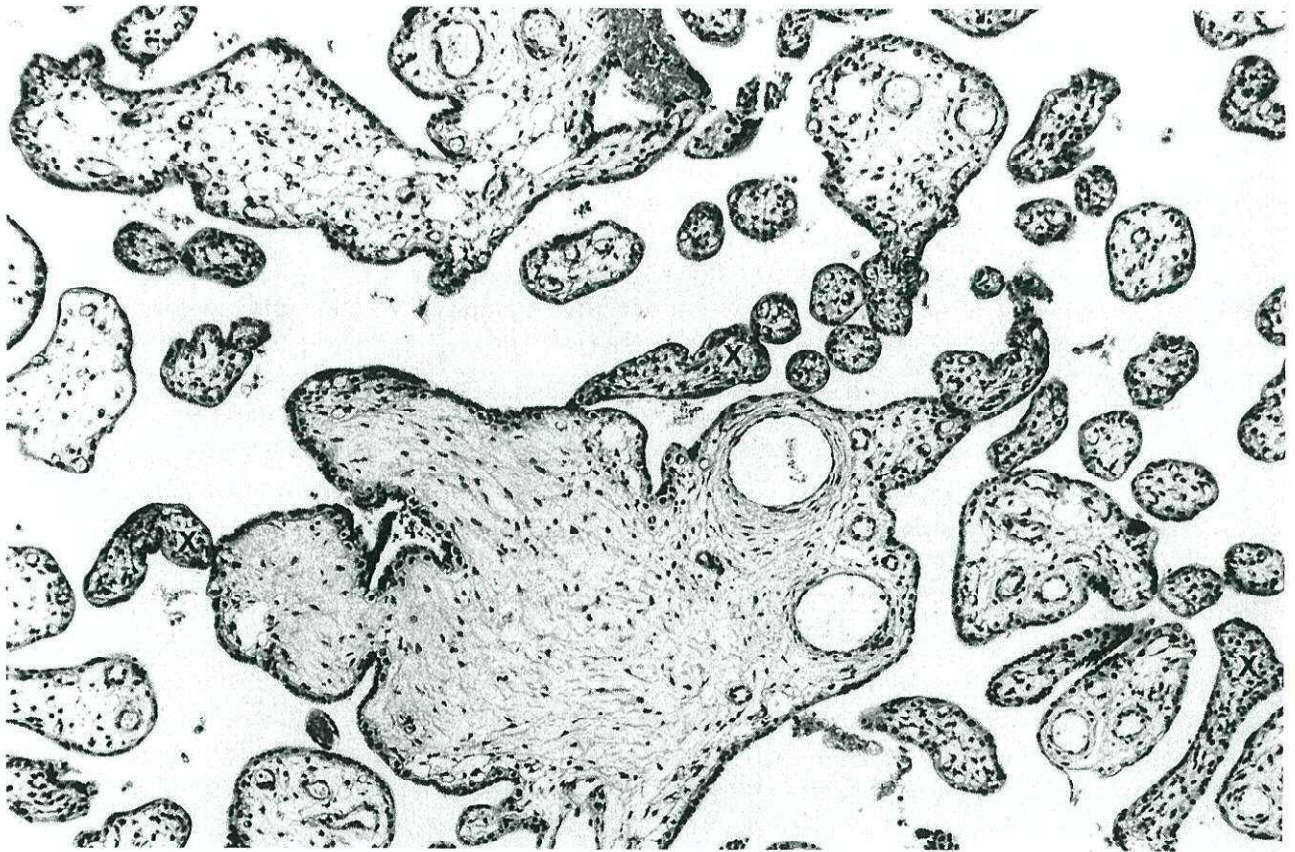


FIGURE 227. Paraffin section of placental villi of the 24th week p.m. Compared to the preceding stages, the variability in villous shapes and diameters is sharply increased.

ing. The population of small slender villi, originally referred to as mesenchymal villi, has achieved structural characteristics of mature intermediate villi. $\times 125$.

70 g to 120 g. The maximum placental thickness after delivery is about 12 to 15 mm; measured by ultrasonography in situ, including the uterine wall, it is approximately 28 mm. The length of the umbilical cord varies between 200 and 315 mm. The structure of the stem villi is nearly the same as in the previous month; however, their number is considerably increased throughout this month (Figure 225). During the 24th week p.m., most of the large caliber villi (those exceeding 300 μm) have achieved the fibrous stroma of stem villi. The number of slender, long mesenchymal villi with diameters around 80 to 100 μm increases. The mean diameter of the remaining immature intermediate villi is slightly reduced to values around 150 μm . The mean villous diameter is 108 μm . The total villous surface is 1.48 m^2 . Because the amount of villous cytotrophoblast is reduced to about 60% of the villous surface, the extent of thin trophoblastic areas from 1 to 2 μm thickness is increasing. Continuous development of fetal capillaries causes a reduction of the mean maternofetal diffusion distance to 22.4 μm . Septa and cell islands, which originally consisted mainly of accumulations of cells, now grow considerably in apposition of fibrinoid. In their centers, cysts sometimes form.

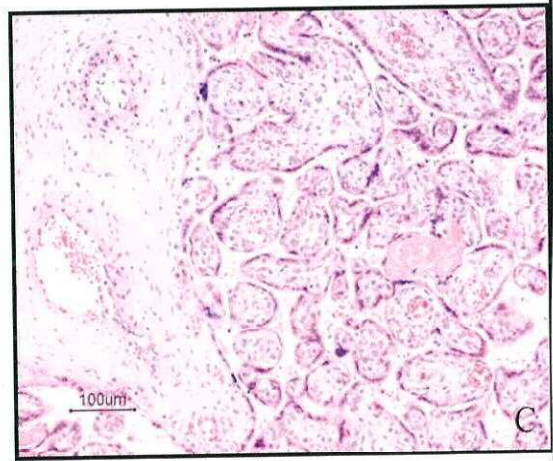
6th month p.m. 21st to 24th week p.m. 19th to 22nd week p.c. The fetus grows from 130 mm to 180 mm crown-rump length. Its weight increases from 290 g to 600 g. The placental diameter is between 100 and 125 mm, and the placental weight increases from 120 g to 190 g. Placental thickness after delivery is 15 to 18 mm, and

ultrasonographic measurements in situ, including the uterine wall, indicate a thickness of about 34 mm. The mean length of the cord is between 315 and 360 mm.

The histological features change considerably: Most of the immature intermediate villi become transformed into stem villi of large caliber. Most of the stem villi measure around 200 μm in thickness, some achieving diameters of more than 1,000 μm . Their fibrous stroma still exhibits a small superficial rim of reticular connective tissue, indicating their immaturity (Figure 226). Different from all earlier stages, increasing numbers of newly formed intermediate villi exhibit small calibers (of only 100 to 150 μm). Some of these villi are reticular in structure, as their parent villi, whereas others are slender, mature intermediate villi with poorly vascularized and poorly fibrosed, nonreticular stroma (80 to 120 μm) (Figure 227). At their surfaces, the first richly capillarized terminal villi are formed. They are difficult to identify in the large group of smallest villi, measuring 50 to 80 μm , as the other members of this group, the small mesenchymal villi and villous sprouts, exhibit structural features similar to those of the terminal villi in paraffin sections. The total villous surface amounts to 2.81 m^2 . The mean trophoblastic thickness is reduced to 7.4 μm , and the mean maternofetal diffusion distance is 21.6 μm .

7th month p.m. 25th to 28th week p.m. 23rd to 26th week p.c. Compared to the 6th month, there are only quantitative changes. The crown-rump length increases from 180 mm to 230 mm and the fetal weight from 600 g to 1050 g. The placental diameter is 125 to 150 mm, and the placental

FIGURE 228. Paraffin section of placental villi of the 29th week p.m. During this period the mature intermediate villi and the stem villi are the prevailing villous types. $\times 125$.



275

33w / 35w

11. Characterization of the Developmental Stages

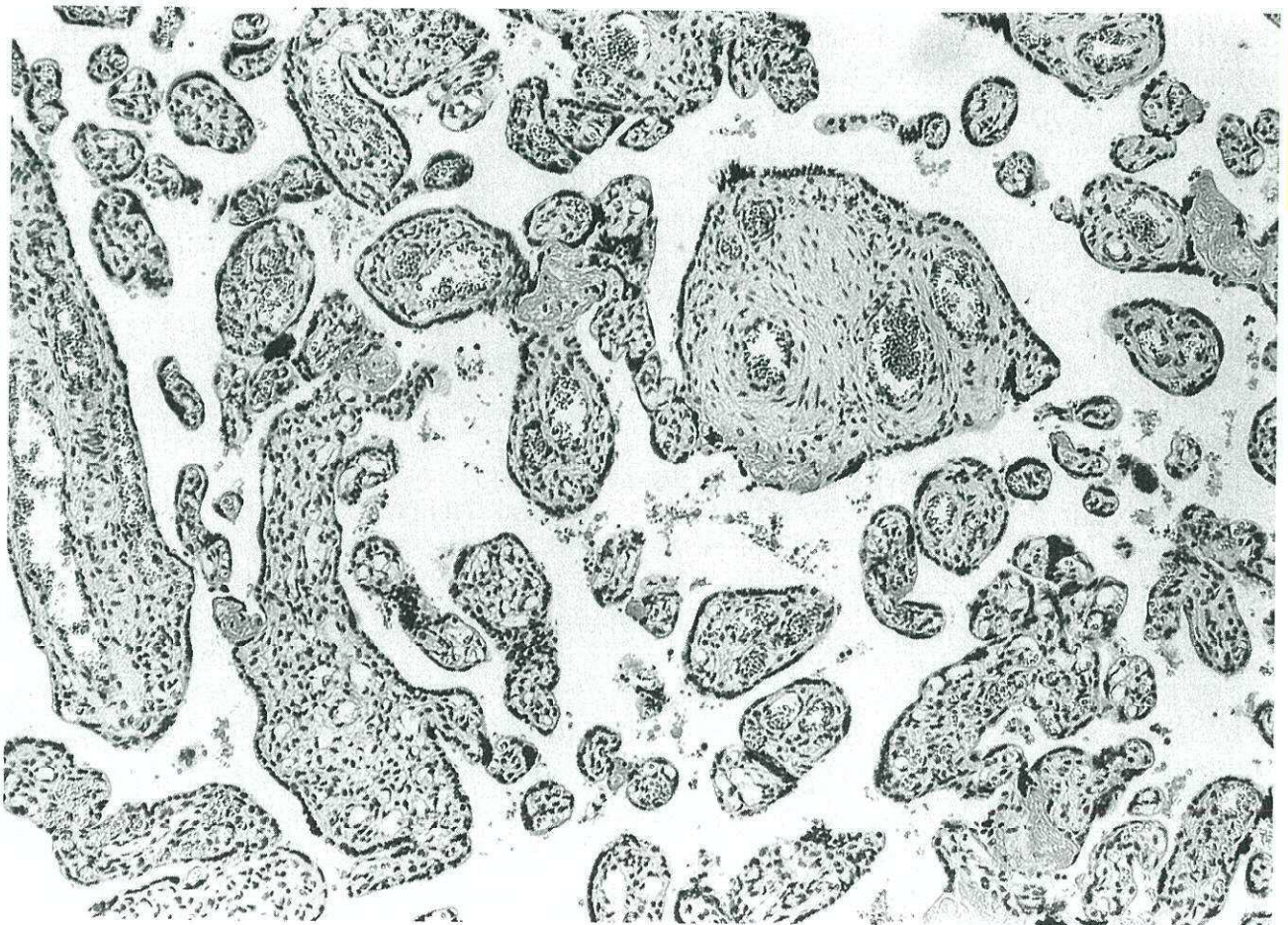


FIGURE 229. Paraffin section of placental villi of the 33rd week p.m. The number of immature intermediate villi is decreasing. Most villi are stem villi and mature intermediate villi; the latter are intermingled with the first few terminal villi which in paraffin sections (because of

their similar diameters) are difficult to differentiate from mature intermediate villi. The stem villi are still not fully fibrosed; rather, they show a thin superficial stromal layer that has few fibers and is rich in connective tissue cells. $\times 125$.

weight is increased to 190 to 260 g. The thickness of the delivered placenta is 18 to 20 mm; by ultrasonography, including the uterine wall, it is 38 mm. The mean length of the umbilical cord increases from 360 to 410 mm.

The total villous surface per placenta is about 4.22 m². The distribution of structure and caliber of the villi are similar to what was seen during the 6th month. Only 45% of the villous surface is covered by cytotrophoblast. The trophoblastic thickness varies between 0.5 and 8 μm , (mean 6.9 μm). The number of immature intermediate villi decreases in favor of stem villi and mature intermediate and terminal villi. The fetal vessel lumens amount to 9.1% of the villous volume. Cell columns are surrounded by increasing amounts of fibrinoid and become deeply invaginated in the basal plate. The syncytiotrophoblastic covering of the chorionic plate begins to degenerate. It becomes replaced by an initially thin layer of fibrinoid that throughout the following weeks grows in thickness and forms the Langhans' stria.

8th month p.m. 29th to 32nd week p.m. 27th to 30th week p.c. Crown-rump length 230 to 280 mm, fetal weight 1,050 to 1,600 g. The placental diameter normally varies between 150 and 170 mm; the placental weight increases from 260 g to 320 g. Placental thickness after delivery is about 20 to 22 mm; measured by ultrasonography in situ, and including the uterine wall it is 43 mm. The umbilical cord has a mean length of between 410 and 455 mm.

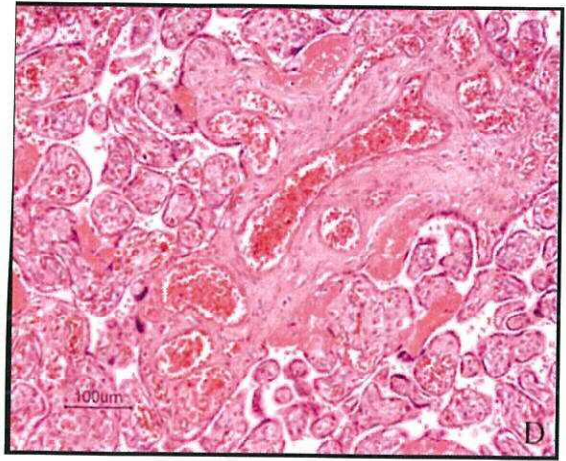
Steeply increasing numbers of mature intermediate villi and terminal villi, both of which exhibit calibers of 40 to 100 μm , are the reason for considerably increased numbers of villous cross sec-

tions per square millimeter of histological sections (Figure 228). The total villous surface is increased to a mean of 7.22 m². In addition to the villi of small caliber, which comprise most of the villi, there are mainly stem villi of large caliber. Intermediate calibers of 100 to 200 μm are rare, causing a typical gap in the range of calibers. At times this gap is evident as early as the second half of the 7th month. The few existing villi of this particular caliber, mostly immature intermediate villi, are grouped together in the centers of the villous trees. Villous cytotrophoblast is reduced to about 35% of the villous surface. As a result of beginning sinusoidal dilatation of the fetal capillaries in the newly formed terminal villi, the amount of vasculosyncytial membranes (epithelial plates) is increased, and the mean trophoblastic thickness reduced to about 6 μm .

9th month p.m. 33rd to 36th week p.m. 31st to 34th week p.c. Crown-rump length 280 to 330 mm, fetal weight 1,600 to 2,400 g, placental diameter 170 to 200 mm, placental weight 320 to 400 g. Placental thickness postpartum is 22 to 24 mm, by ultrasonography in situ, including the uterine wall, it is 45 mm. The mean cord length increases from 455 mm to 495 mm.

Histologically, the developmental processes described for the preceding month become even more prominent: The total villous surface per placenta is increased to 10.1 m². Capillary growth and continuous sinusoidal dilatation cause the mean maternofetal diffusion distance to decrease to 11.7 μm , and the mean trophoblastic thickness to 5.2 μm . Cytotrophoblast is found on only 25% of the villous surfaces. The largest stem villi reach 500 to 1,500 μm in diameter. The small stromal

FIGURE 230. Paraffin section of placental villi of the 35th week p.m. The distribution of villous types is largely comparable to that demonstrated for the preceding stage. $\times 125$.



35W

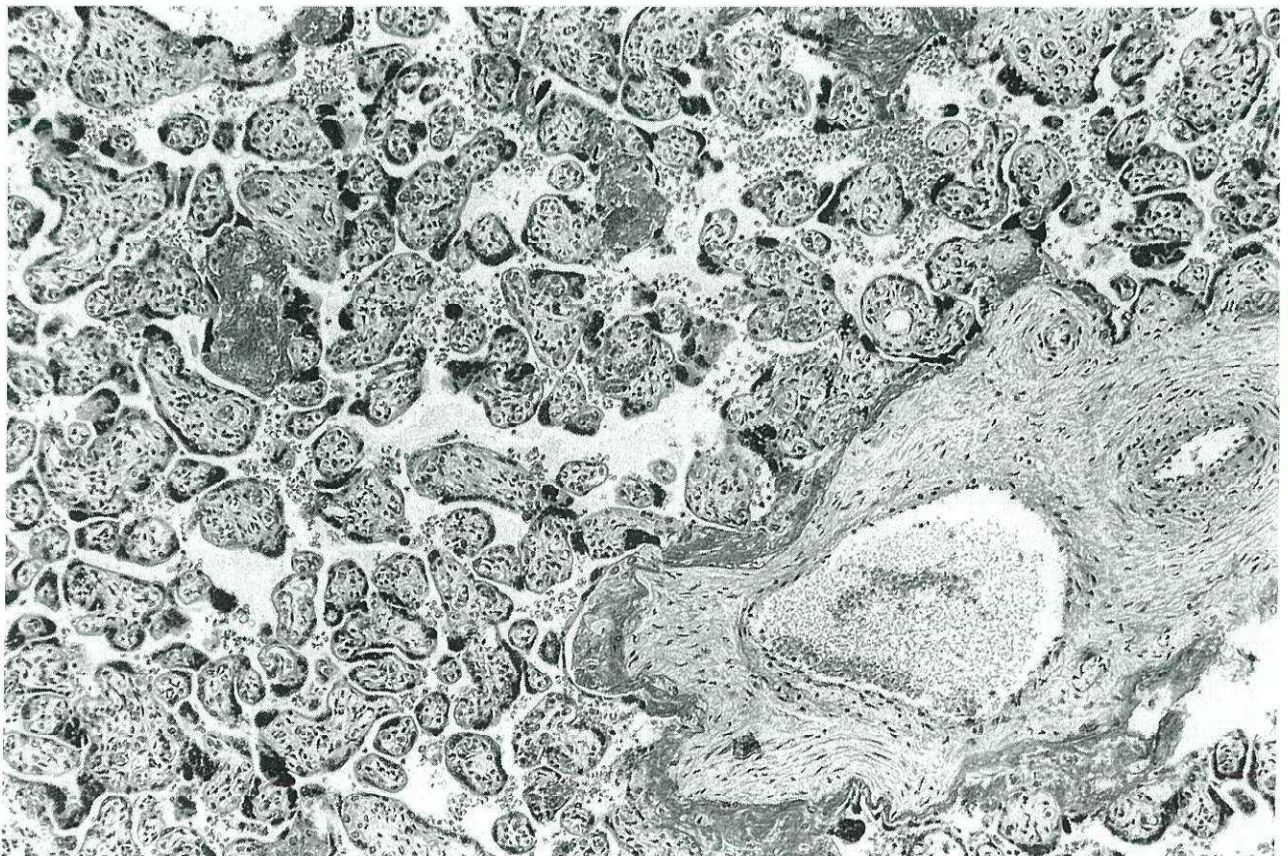
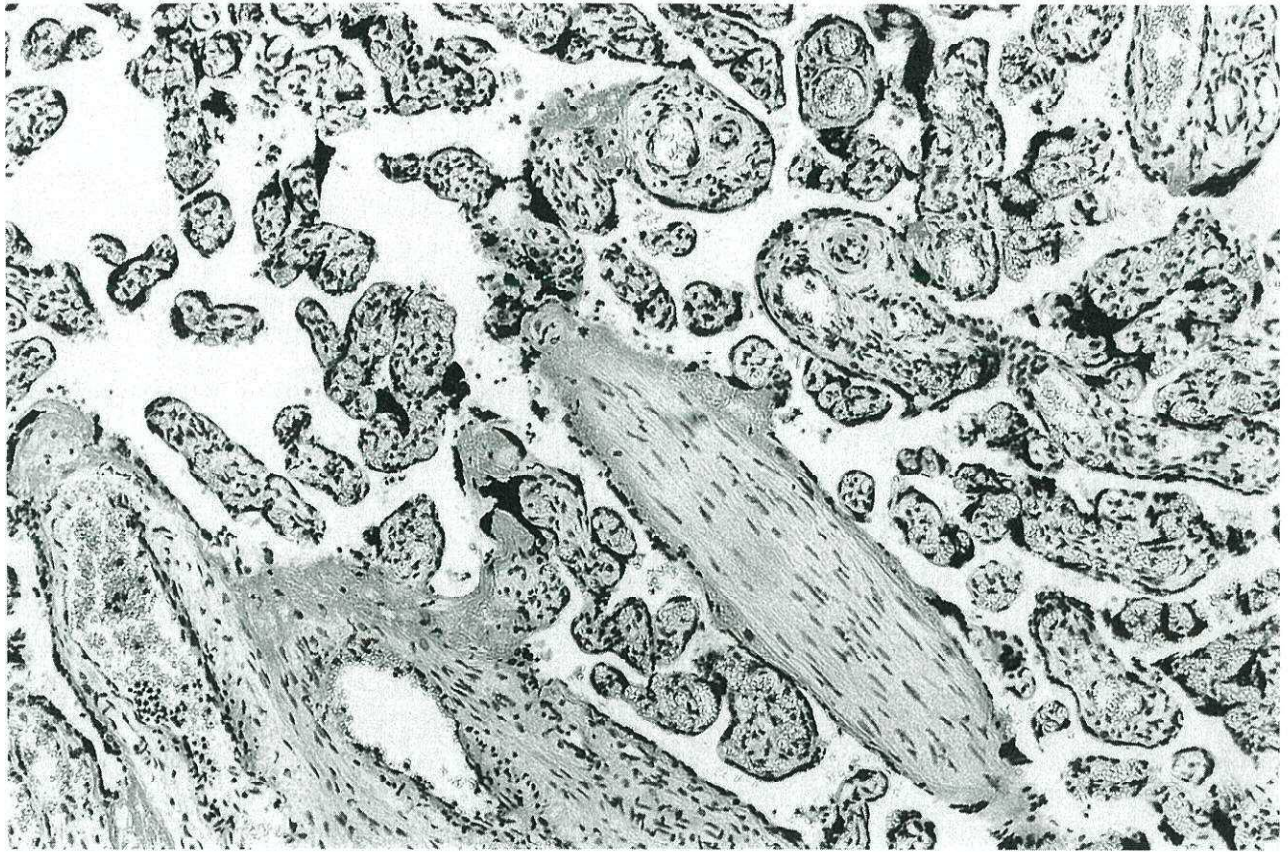


FIGURE 231. Paraffin section of placental villi of the 38th week p.m. Dominating villous types are mature intermediate villi and terminal villi, both of small caliber. Several stem villi of varying caliber can be seen in between. As is typical for near term placentas, the trophoblastic cover

of the stem villi is partly replaced by fibrinoid. The stromal core is completely fibrosed. Reticular stroma or cellular connective tissue (which as a typical sign of immaturity was visible below the trophoblast in earlier stages, throughout the last few weeks) is absent. $\times 125$.

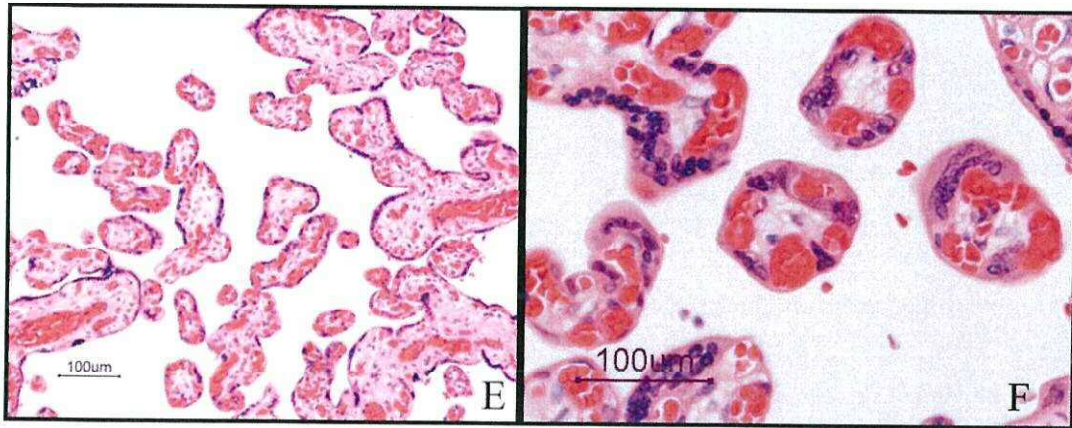
rim, consisting of reticular connective tissue and indicating their immaturity, has normally disappeared to the credit of fibrous stroma and completely occupies the villous core (Figure 229). The originally reticular superficial zone of the stroma shows an increased number of fibroblasts for a few weeks, compared to the more central parts of the stem villi. This difference usually is no longer observed at term. Large parts of the syncytiotrophoblast of the stem villi are replaced by fibrinoid. The vast majority of villi are mature intermediate and terminal villi (Figure 230). Small groups of immature intermediate villi, with calibers of 100 to 200 μm , can regularly be found in the centers of the villous trees, indicating still active placental growth.

10th month p.m. 37th to 40th week p.m. 35th to 38th week p.c. The mean crown-rump length is increased from 330 mm to its final value of 380 mm and the mean fetal weight from 2,400 to 3,400 g. The placental diameter during the last month of pregnancy varies between 200 and 220 mm, and the mean placental weight increases from 400 g to 470 g. There are considerable individual variations. Early clamping of the cord after delivery of the baby may even increase placental weight by as much as 100 g. The final maximal placental thickness postpartum is about 25 mm; measured by ultrasonography in situ, the uterine wall and placenta amount to 45 mm. The mean cord length at term is 495 to 520 mm.

The kind and amount of villous types differ from the foregoing stage in several aspects. There are considerably increased numbers of terminal villi (about 40% of the total villous volume of the placenta) (Figure 231) and a higher degree of capillarization of the latter, mainly due to the fact that many of the capillary cross sections are dilated sinusoidally to maximally 40 μm . In well preserved, early fixed placentas that are not suffering from fetal vessel collapse, the terminal villous capillary lumens amount to 40% or more of the villous volume. About 20% of the villi are stem villi. In the fully matured placenta, the fibrous stroma reaches the trophoblastic or fibrinoid surface of the stem villi everywhere; a superficial reticular rim, or a superficial accumulation of fibroblasts, as during the 9th month, is usually absent at term. If not, it has to be interpreted as a sign of immaturity. The syncytiotrophoblastic cover of the stem villi is degenerated in most places and often is replaced by fibrinoid (Figure 232). About 30 to 40% of the villous volume is made up of mature intermediate villi which histologically can be differentiated from the terminal villi by their reduced degree of fetal capillarization, the absence of large fetal vessels with light microscopically identifiable media and adventitia, and the high proportion of connective tissue cells. Maximally, only 10% of the villi are of the immature, intermediate variety, which normally appear as small, loosely arranged groups in the centers of the villous trees, sometimes surrounding a central cavity.

FIGURE 232. Paraffin section of placental villi of the 40th week p.m. The caliber distribution is little different from that of the 38th week. Despite this fact, some remarkable changes exist: The fibrinoid deposits around the larger stem villi and the number of terminal villi are con-

siderably increased; also, because of the irregular shapes of terminal villi at term, numerous flat sections of villous surfaces can be seen. Here these structures appear as dark spots of seemingly accumulated nuclei. $\times 125$.



and fig. E and F normal placenta at 40 weeks of gestational age. Terminal villi are formed in the third trimester. At 40 weeks of gestational age 40% of the villous volume are terminal villi. Terminal villi can be recognised by the syncytio-capillary membranes. Anchoring villi are covered with fibrin.

40w

terminal villi

