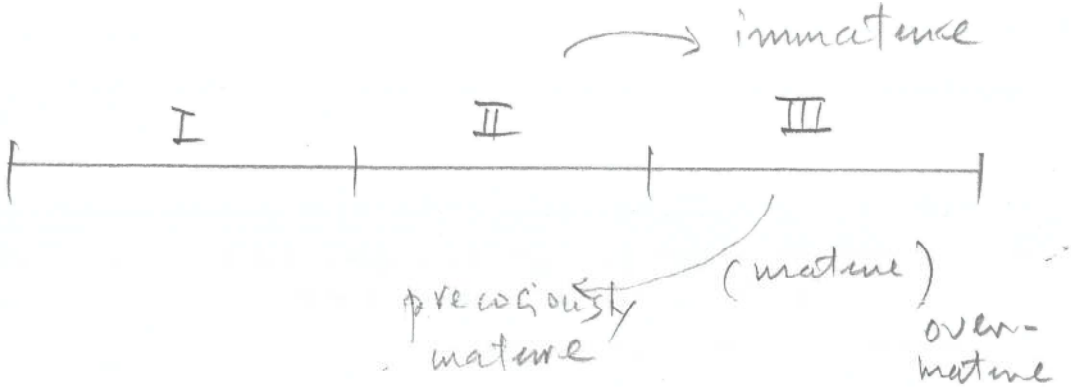
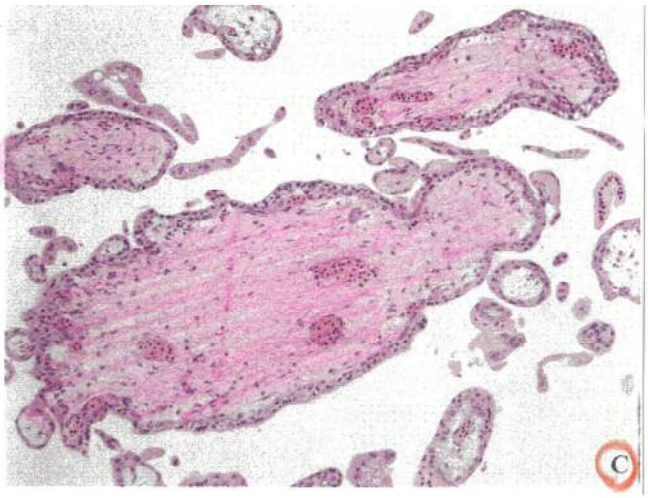
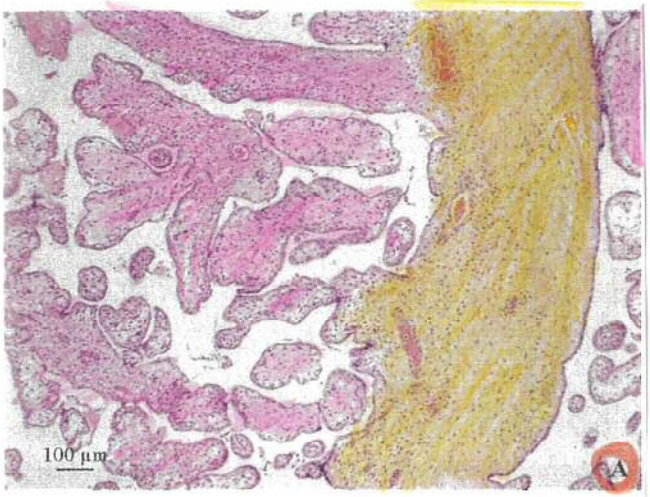
表2 絨毛の発育

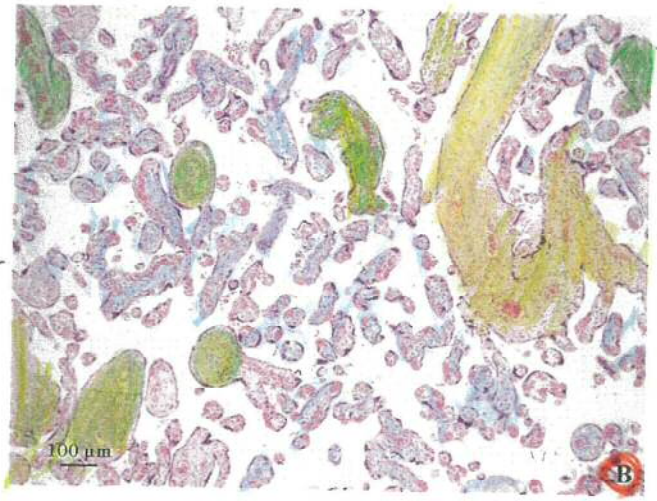
	絨毛の種類	出現時期	最も多い時期	満期胎盤で占める割合(%)	大きさ	特　徴
I	mesenchymal villi 間葉絨毛	5週から満期	0~8週	<1%	0~8週：120~250 μm 8週~満期：60~100 μm	未分化な間質，厚い栄養膜細胞 血管は乏しい
II	immature intermediate villi 未熟中間絨毛	8週から満期	14~20週	5~10%	100~200 μm (最大400 μm)	網状間質
III	stem villi 幹絨毛	12週から満期	満期	20~25%	150~300 μm	緻密な線維性間質，大型の血管と周囲の平滑筋
	mature intermediate villi 成熟中間絨毛	妊娠第3期	妊娠第3期	25%	80~150 μm	緻密な細胞性間質，血管は横断面の50%未満
	terminal villi 末端(終末)絨毛	妊娠第3期	満期	40~50%	60 μm	血管が横断面の50%以上を占める

(Baergen RN：Manual of pathology of the human placenta, 2nd ed, Springer, 2011 より)









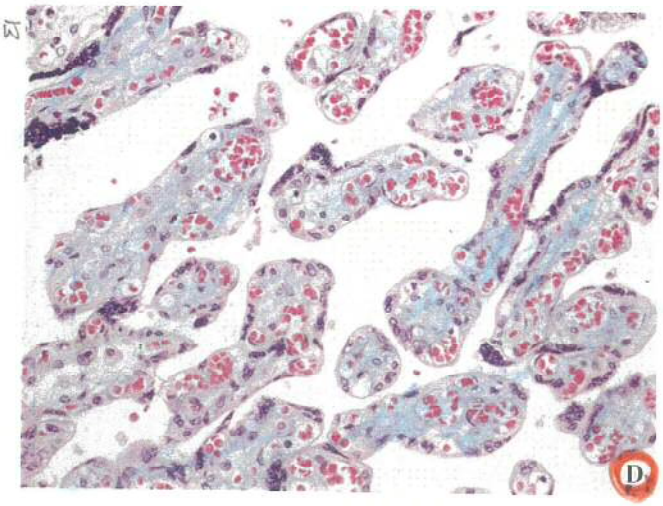


図 24 様々な週数の絨毛

A：20 週の未熟絨毛．幹絨毛および未熟中間絨毛が主体で，分岐は乏しい．B：38 週の成熟した絨毛．幹絨毛がみられるが，成熟中間絨毛と末端（終末）絨毛が大部分を占める．C：9 週の未熟中間絨毛．網状の絨毛間質内には血管が侵入し，有核赤血球を認める．D：40 週の末端（終末）絨毛．表面を覆う栄養膜細胞は伸展し直下に血管が接して，vasculosyncytial membrane を形成している．

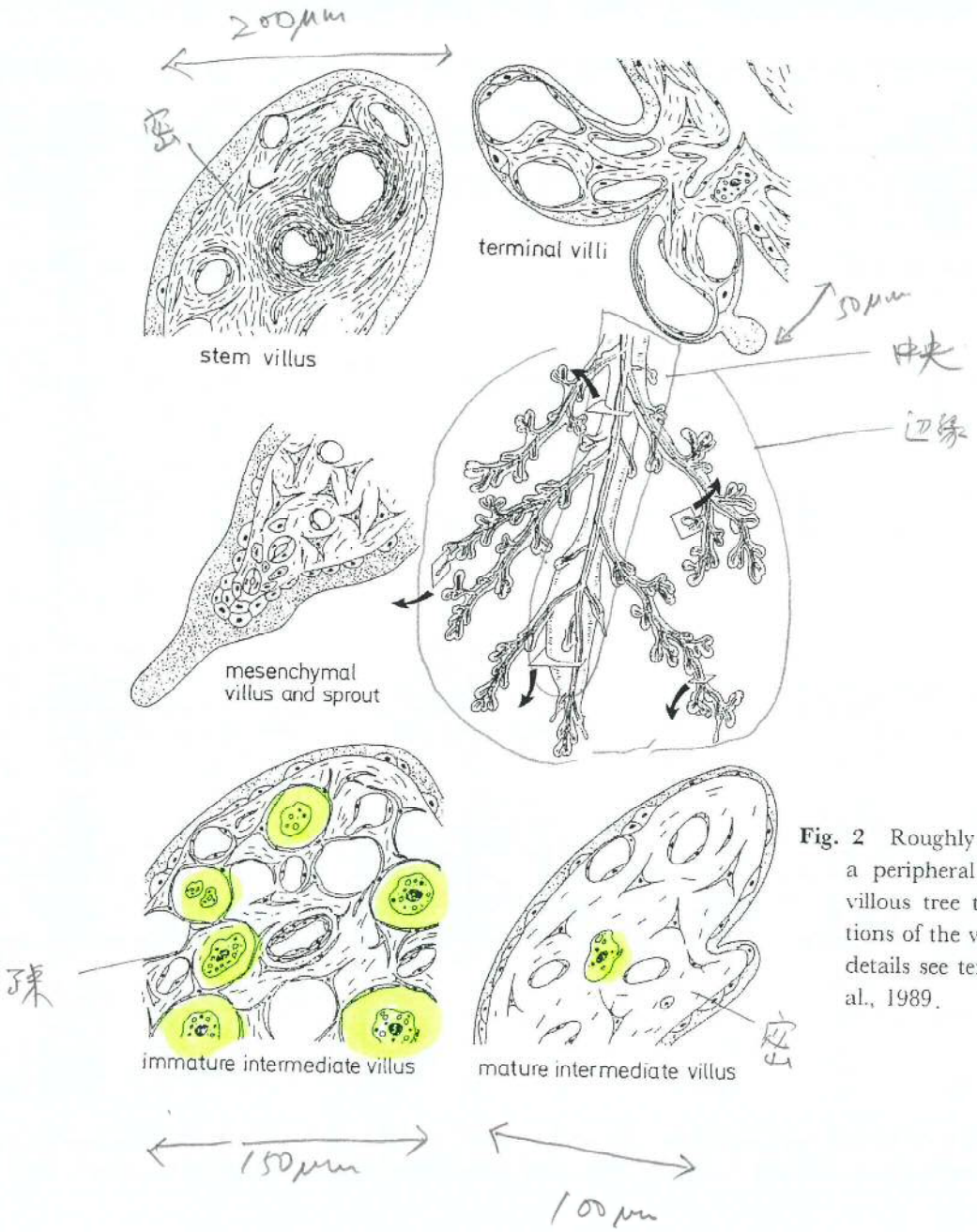


Fig. 2 Roughly simplified schematic drawing of a peripheral part of the mature placental villous tree together with typical cross sections of the various villous types. For further details see text. Modified after Castellucci et al., 1989.

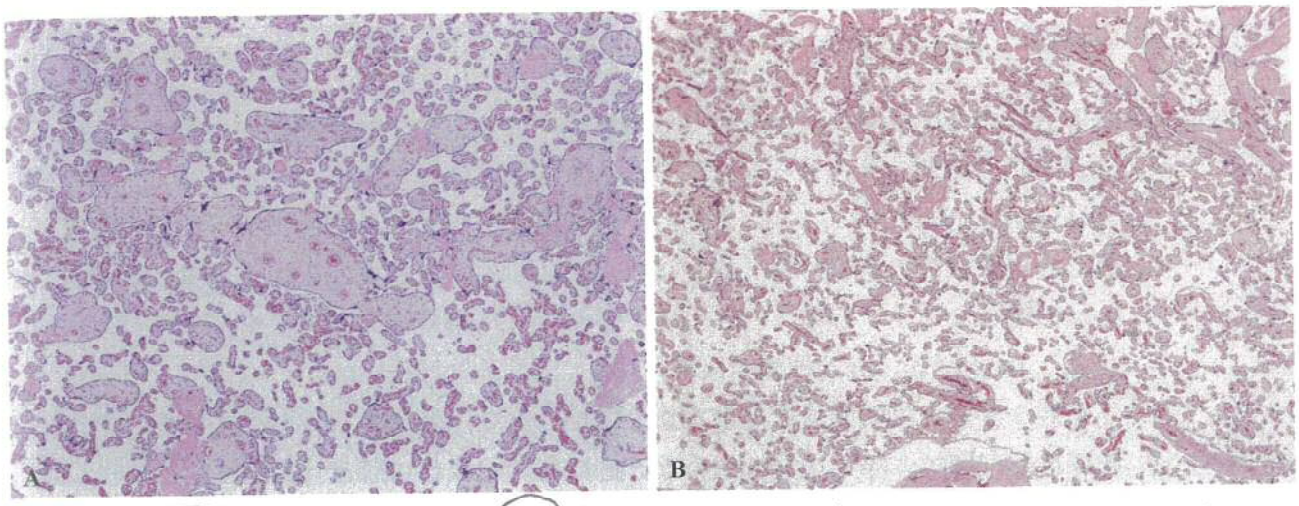


図 25 絨毛成熟異常(dysmaturity)と絨毛過成熟(accelerated maturation)

A：糖尿病にみられた dysmature villi．大型の絨毛で，絨毛間質は豊富で syncytiotrophoblast は目立たたない．

B：accelerated maturation．分岐の乏しい萎縮性の小型の絨毛が認められる．

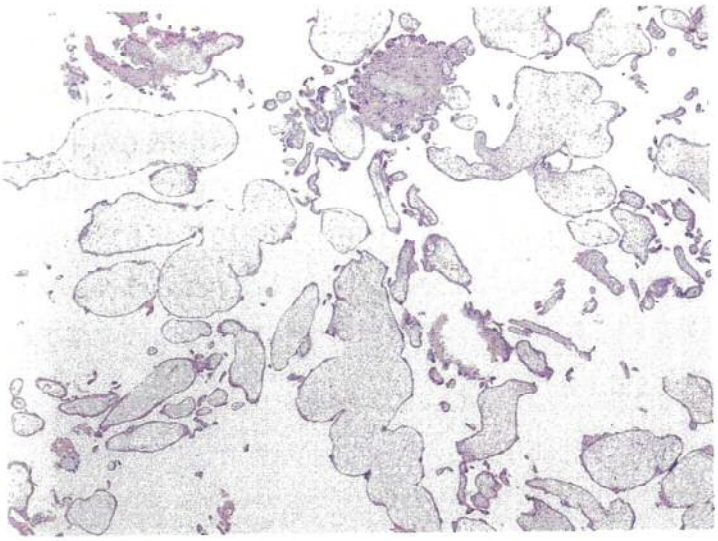


図 26 染色体異常(16 トリソミー)でみられた異常形態絨毛

辺縁は不整で，間質は浮腫状で，血管は不明である．

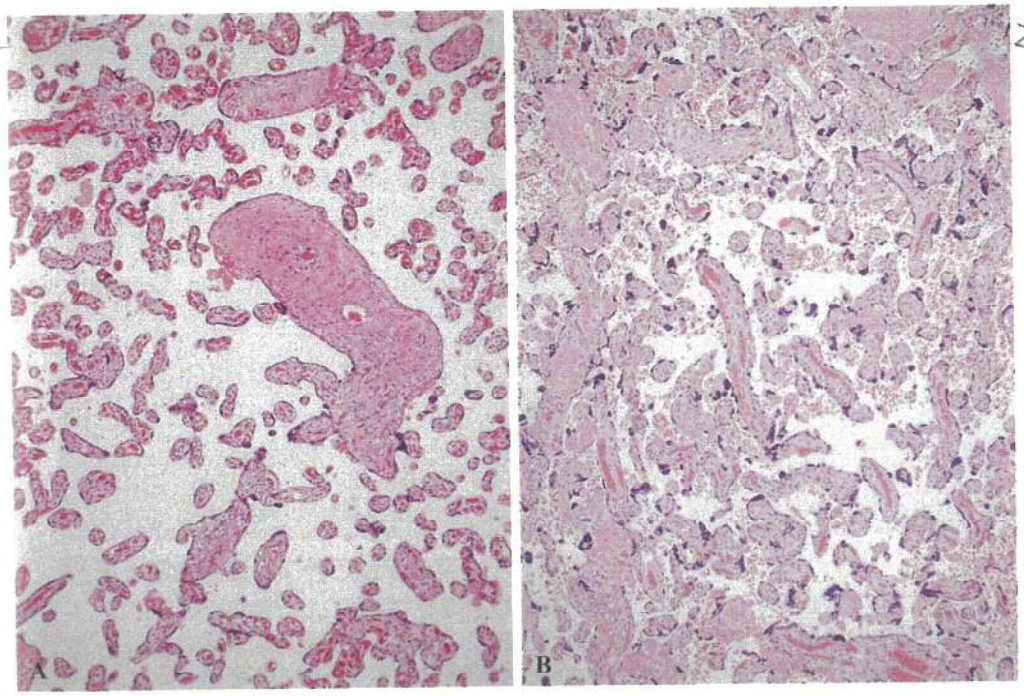


図 27 syncytial knots の増加

A：40 週，正常胎盤．末端絨毛は成熟して小型で，合胞体型栄養膜細胞は目立たない．

B：29 週，FGR 症例の胎盤．妊娠週数に比して絨毛は小型で，細い．絨毛表面を覆う合胞体型栄養膜細胞が密集して，増えているようにみえる．

HDP で認めることの多い胎盤所見として，絨毛間腔の灌流不全すなわち母体血管灌流不全(MVM)による低酸素に伴う末梢絨毛低形成(distal villous hypoplasia)(図 2)，絨毛過成熟(accelerated maturation)，syncytial knots(合胞体結節)の増加，胎盤梗塞，脱落膜内母体血管病変(血管壁のフィブリノイド変性，アテローシス)，常位胎盤早期剝離などがある(図 3)．HDP ではこれらの病変が同時に複数認められることが多く，胎盤発達障害による小さな胎盤，胎盤機能不全による FGR を生じる．

臨床的に HDP と診断されている場合，これらの所見の有無を検索し，いずれかの所見があれば病理学的に矛盾がないと診断する．ただし，病的所見の多さ，程度の重さが臨床病態，重篤度を常に反映するものではないことに留意する．

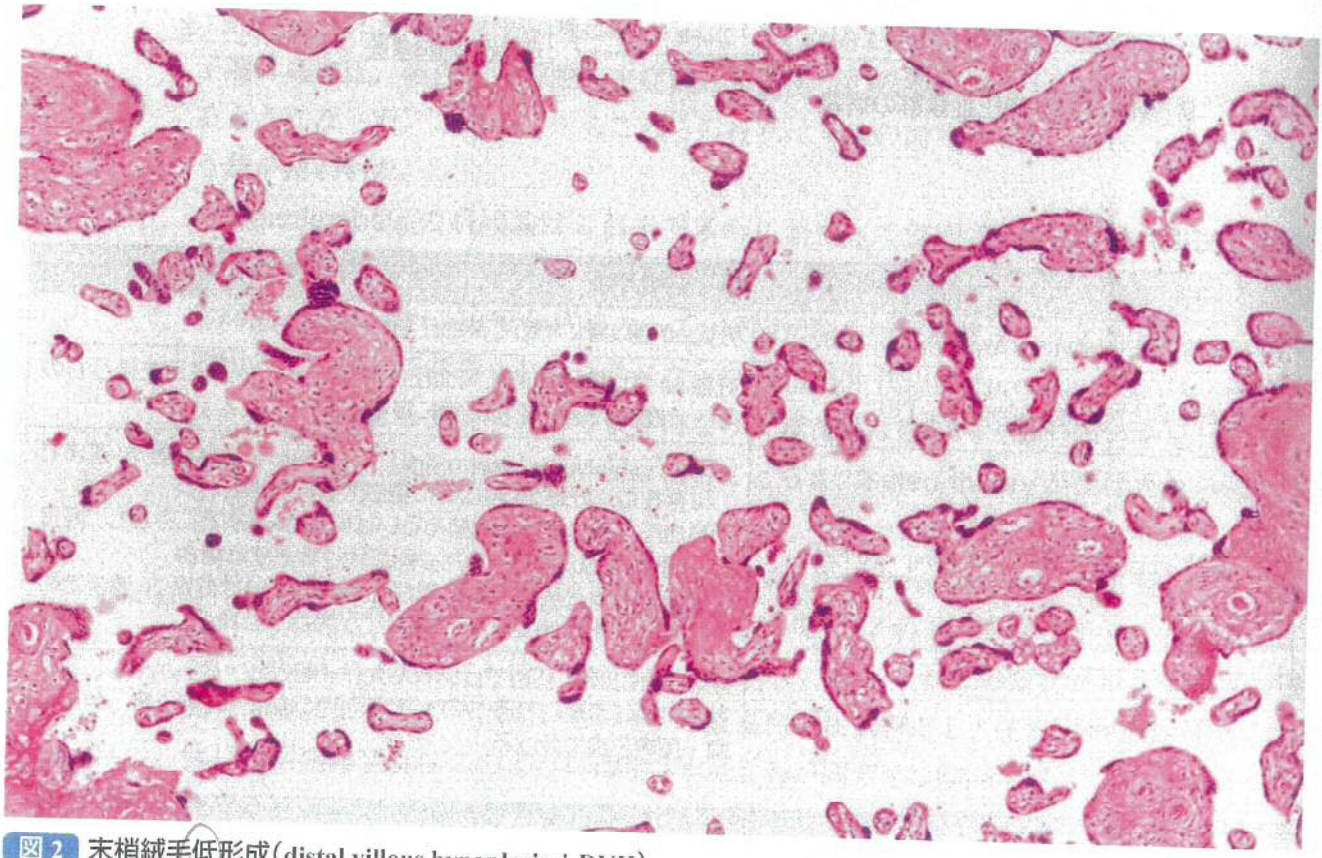


図 2　末梢絨毛低形成(distal villous hypoplasia：DVH)
絨毛数の減少がみられ，それらの多くは細く延長している．syncytial knots は増加する．

APMIS JOURNAL OF PATHOLOGY, MICROBIOLOGY AND IMMUNOLOGY

APMIS 126: 602–612

DOI 10.1111/apm.12858

REVIEW ARTICLE

Re-view and view on maturation disorders in the placenta

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Turowski G, Vogel M. Re-view and view on maturation disorders in the placenta. APMIS 2018; 126: 602–612.

Until delivery, the placenta plays an important mediator role between mother and fetus. This unit is affected by peristatic conditions, such as acute or chronic maternal diseases, malnutrition, drugs, and others. But also genetic factors and fetal malformations due to embryonic developmental disorders may contribute to macroscopically visible changes and functional disorders of the placenta. In a constantly ongoing progress of maturation, the placenta records and saves changes due to fetal distress partly as maturation disorders. Understanding of maturation disorders might, therefore, be an important contribution to a better understanding of influences on villous differentiation and might improve follow up and fetal outcome to reduce recurrence risk. However, an internationally unified classification system of maturation disorders does not exist. In this review, terminology, trials, and classifications of villous maturation disorders are summed up and compared, to pinpoint the need of agreement on an international unified and reproducible classification of maturation disorders.

Key words: Fetal outcome; histopathology; maturation and maturation disorders; pathology; placenta.

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NORMAL VILLOUS MATURATION ACCORDING TO GESTATIONAL AGE

Normal villous maturation is essential for optimized placental function adjusted to fetal demands of oxygen and nutrition. Ramification and maturation from predominating immature intermediate villi in the first and second trimester to the mature intermediate and terminal villi in the third trimester reflect dynamical adaptation processes.

Formation of tertiary villi finishes embryonic placental development. In the following weeks of pregnancy until delivery, villous maturation advances in linear villous growth and branching and transformation and differentiation of the stroma, fetal capillaries, and the villous trophoblast (chorionic epithelium). In detail, this process until term is characterized by (a) numeric villous growth and (b) villous ramification and differentiation of villi into four groups with different function: (1) Stem villi, with blood conducting, media containing vessels, surrounded by a contractile cell and fiber system. Main functions of stem villi are the regulation of blood flow and maintenance of tissue tonus to warrant mechanical stability of the villous tree. (2) Intermediate villi of central (immature) type are characterized by embryonic stroma with Hofbauer cells, few diffusely localized capillaries, and a nuclear rich two-layered villous trophoblast layer. These villi are assumed to represent the villous growth zone, with centripetal transformation into stem villi and centrifugal growth in length with increased branching (ramification). (3) Intermediate villi of peripheral (mature) type present a reticular and less collagen containing stroma with several centrally or peripherally localized capillaries, single-layered epithelium, and vasculosyncytial membranes. This villous type contributes to microcirculation, hormone production, and metabolic activity. (4) Terminal villi are characterized by blood supplying capillaries and venous sinusoides, each vessel tightly connected to the surface, several developed as vasculosyncytial membranes. Function of terminal villi is to exchange fetomaternal gas and

Received 1 March 2018. Accepted 21 May 2018

nutritions and to take part in hormone production and metabolic activity (Figs 1A–C; 2A–D) (1).

Placental oxygen diffusion capacity increases from 1st to 3rd trimester until term up to 30-fold, due to reduced diffusion distance (2). The number of terminal villi increases from early pregnancy to term to about 60% (3).

VILLOUS MATURATION DISORDERS

Villous maturation disorders are described as focal or diffuse, qualitative and quantitative mismatch of villous ramification and tissue development, chronologically deviating from normal maturation for gestational age (1, 3–7).

Villous maturation disorders get manifest in mainly two sections of the villous tree: (a) Close to the immature intermediate villi which transform into stem villi, and (b) close to the transformation zone from the mature intermediate villi to terminal villi. Maturation disorders are more profound if they manifest in early development (3).

Maturation disorders are reported to be seen in small foci occupying less than 10% Medium Power Field (MPF) in 25% of placentas from normal sized and well-developed (eutrophic) fetuses without any known risk. In late pregnancy (gestational age 42 and later), maturation disorders are seen in 70% of placentas, occupying up to 50% of a MPF MPF. In placentas from preterm born children, maturation disorders are found in 90% of placentas, when associated with fetal growth restriction (FGR), histologically seen as diffuse change occupying more than 50% of a MPF (3).

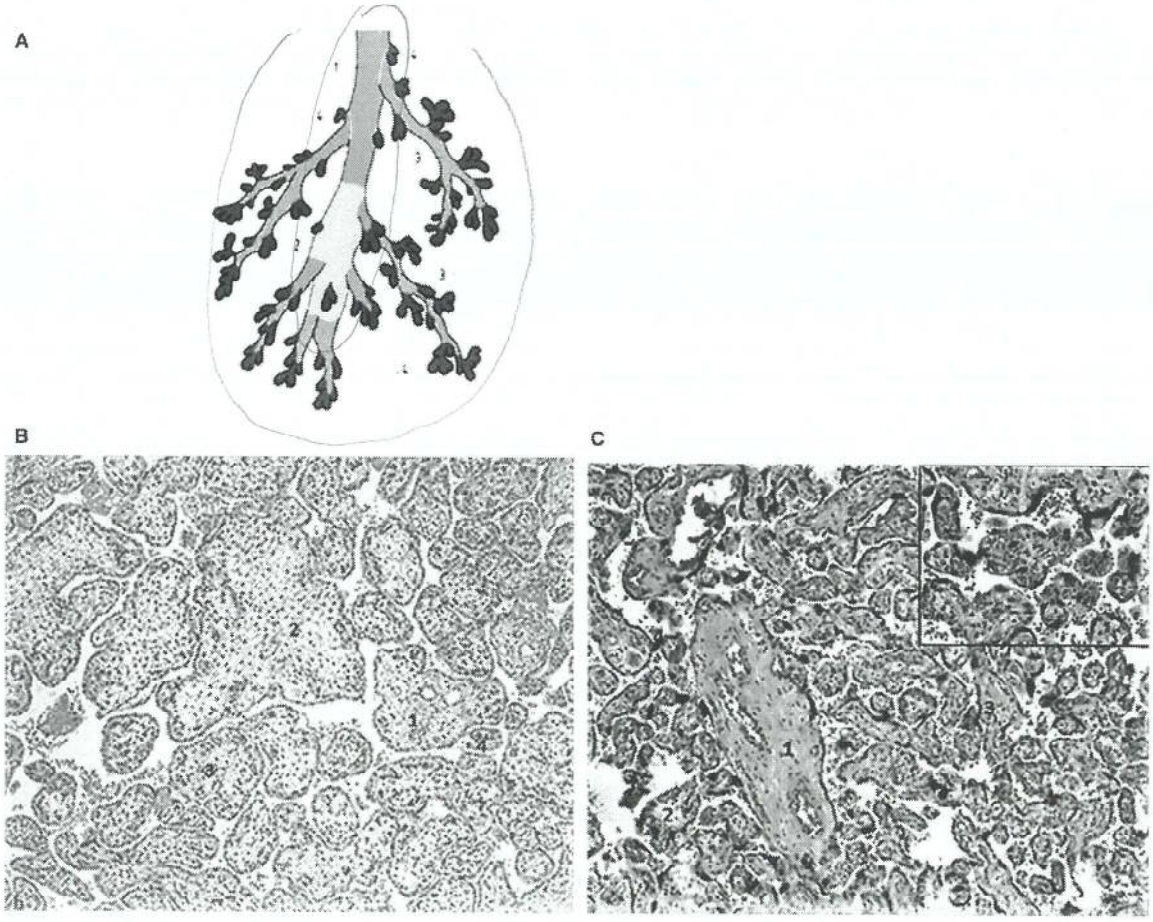

Fig. 1. (A) Illustration of the peripheral villous tree: Ramification into 1 stem villi, 2 intermediate villi of the central, immature type, 3 intermediate villi of the peripheral mature type, 4 terminal villi. (B) Histology of a placenta in gestational age 19. Villi of different size with loose stroma and few capillaries centrally localized. (C) Histology of a placenta in gestational age 38. Increased number of terminal villi with increased number of fetal capillaries (inlay shows higher magnification).

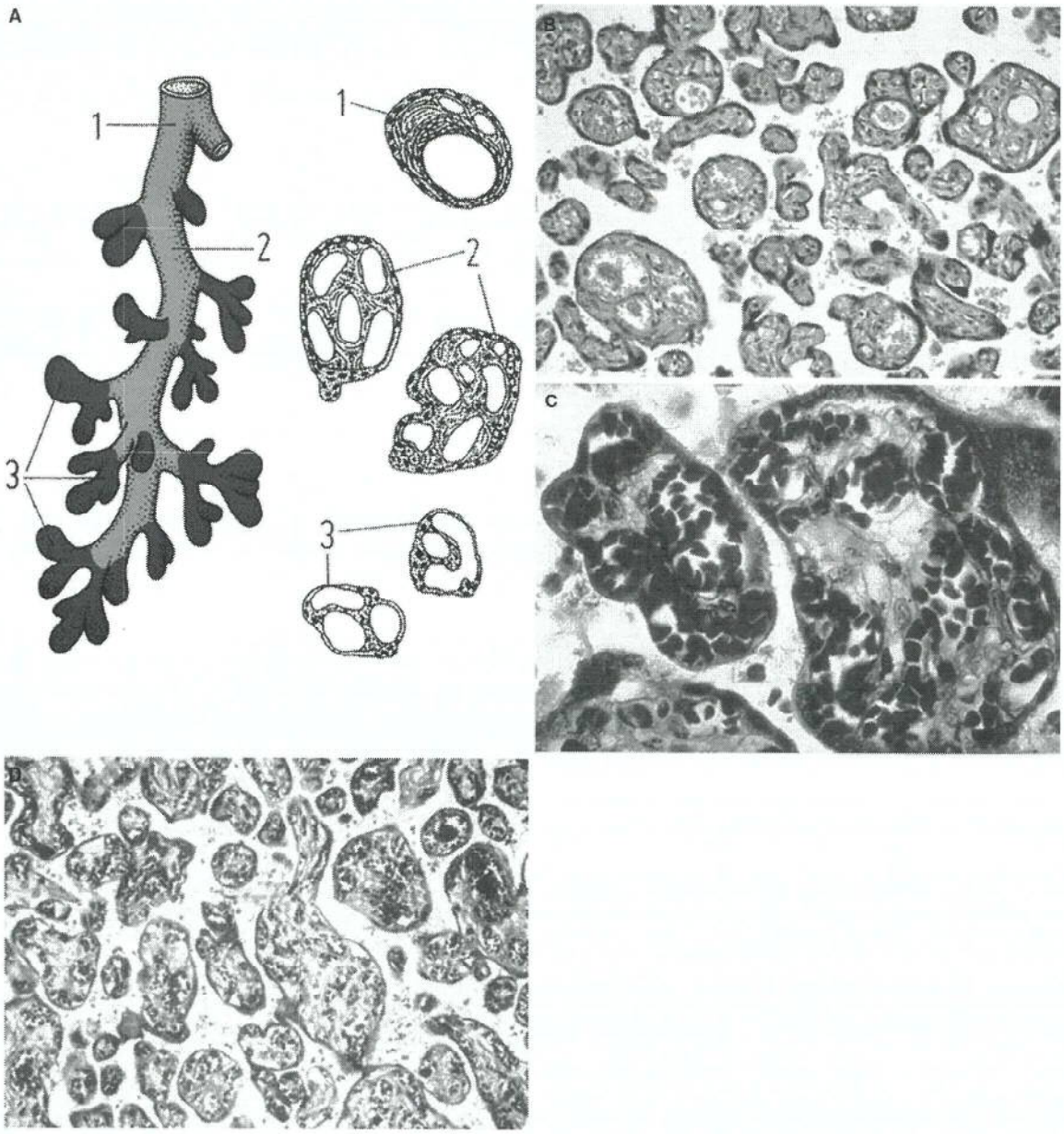

Fig. 2. (A–C) Villous maturation. (A) Villous tree; 1 stem villus, 2 intermediate villus peripheral type, 3 terminal villus. (B) Histology of a placenta in gestational week 40 (HE). (C) Mature intermediate villus (right) and terminal villus (left) in gestational week 40 (MG). (D) Dissociated villous maturation disorder, prevalence of maturity (MG) gestational week 40.

HISTORICAL OVERVIEW OF MATURATION DISORDERS

The villous maturation process causes morphological characteristic changes in the chorionic villi (4, 8). In the German literature, Hörmann in 1953 interpreted villous development and maturation as a result of centrifugal continuous proliferation of allantoic vessels, to peripheral capillaries of the terminal villi (9, 10). He described the expediency and effectiveness with regard to the fetal-placental exchange (10, 11).

He defined the differentiation of vasculosyncytial membranes of the chorionic epithelium as an optimized approximation of the fetal and maternal circulation and emphasized the law between the

Table 1. German terminology of maturation disorders in comparison and Anglo-American terminology/descriptions

Becker (1981)	Kaufmann (1990)	Vogel (1984)	Schweikhart (1986)	Anglo-American
Maturitas iusta	Synchronous maturity	Mature according to gestational age	Synchronous maturity	Normal villous maturity
Maturitas tarda		Dissociated villous maturation disorder, prevalent mature	Asynchronous maturity	
Maturitas retardata	Deficiency of terminal villi	Retardation of villous maturation; dissociated villous maturation disorder, prevalent immature	Deficiency of terminal villi, peripheral villous immaturity	Delayed villous maturation (DVM), Distal villous immaturity (DVI)
Maturation arrest	Persisting immaturity	Villous maturation arrest	Persisting immaturity	Unspecific stroma edema
Maturitas praecox	Asynchronous maturity	Preterm accelerated maturation	Hypervascularity	Accelerated maturation
	Hypermaturity	Deficiency of intermediate villi		Distal villous hypoplasia (DVH)
Chorangiosis		Chorangiosis type I		
Pseudochorangiosis		Chorangiosis type II		
Chorangiomatosis				

reduction of the villous diameter and the level of maturation. Becker defined three groups with characteristic morphology of normal maturation and emphasized the chronological concordance between placental and fetal maturation (12–14). Based on this, he pinpointed typical mismatch of placental maturation, fetal maturation, and gestational age and classified maturation disorders chronopathologically as follows: arrest of villous maturation (maturitas arrest), dissociated maturation disorder (juvenile villi in mature placenta), asynchronic maturation including premature villous maturation and retarded villous maturation (maturitas praecox and maturitas retardata) (14). This was later revised and modified into maturitas iusta, maturitas tarda, maturitas retardata, maturitas arrest, maturitas praecox. Chorangiosis, pseudochorangiosis, and chorangiomatosis were added (15) (Table 1). Placental maturation and placental growth deviant from normal maturation for gestational age and fetal development were also reported by others (4, 16, 17). Villous maturation disorders were documented at any gestational age associated with clinically diagnosed maternal diabetes mellitus or preeclampsia (8, 18–22).

From these observations, Kloos and Vogel suggested a classification of maturation disorders, derived from morphology (23). They systemized maturation disorders as placental villi which deviate in quantity and quality and/or chronology from normal morphology according to gestational age. In consequence, they stated that the earlier the onset of the villous structural disorders, the more profound is the manifestation.

This detailed classification system was later simplified due to the results of histometric examinations (3, 24).

In 1984, Schweikhart suggested the term 'terminal villous deficiency', analogous to 'retardata and peripheral villous immaturity'. Furthermore, he suggested 'persisting immaturity', analogous to the term arrest, which was later subclassified into low, moderate, and severe grade. Asynchronous postterm maturity described a varying picture of immature and mature villi. He described hypermaturity as hypervascularity, which was later modified (25) (Table 1).

Chorangiosis is characterized by an increased vascularization of terminal villi. It is still unclear if this is a primary developmental disorder or a maturation disorder (26). Chorangiomatosis is interpreted as maldevelopment (27).

In the Anglo-American literature, Kaufmann and Benirschke suggested to differentiate maturation disorders of the villous vessels into branching and nonbranching angiogenesis in correlation to pre-, intra-, and postplacental hypoxia (28, 29).

Fox and Redline differentiated between 'preterm and delayed maturation disorders' and used the term 'irregular villous maturation', if both disorders were found in the same placenta (30–32).

Langston introduced the term 'distal villous immaturity' (DVI) (26), which was followed by the 'disorders of villous development' represented by DVI with placental overgrowth (DVIPO), and 'distal villous hypoplasia' (DVH) with placental undergrowth (DVHPU (33).

In recent years, villous developmental disorders associated with defined clinical maternal and fetal

diseases were emphasized, such as distal villous hypoplasia and accelerated villous maturation associated with maternal vascular malperfusion and clinical FGR and preeclampsia (33–36).

INTERNATIONAL EXISTING TERMINOLOGY OF MATURATION DISORDERS

International terminology of maturation disorders is confusing. In Anglo-American literature (category I), terminology mainly focuses on delayed villous maturation (DVM), which is also called defective villous maturation and distal villous immaturity. In addition, villous deviation from normal, such as 'distal villous hypoplasia' and 'accelerated maturation', is interpreted as a morphological change due to maternal vascular malperfusion. The term 'ramification disorder' is not included in the terminology of villous maturation disorders (37, 38). In German literature (category II), maturation disorders have been discussed over years, and various classifications have been suggested and revised. Morphological aspects of 'accelerated maturation' and types of 'Chorangiosis' are included (3, 15).

In the following, the present terminology is summed up in detail with respect to morphological and clinical aspects.

CATEGORY I

Delayed villous maturation and distal villous immaturity

Characteristic morphology of synonymously used DVM and DVI shows villi of increased villous diameter, with cellular stroma and increased extracellular matrix. Capillaries are centrally placed and vasculosyncytial membranes are reduced. Diagnostic for DVM and DVI are more than 30% immature villi within the basal 2/3 of the placental parenchyma. Villous trophoblast is hyper cellular with persistent cytotrophoblast (35). Immature intermediate/terminal villous ratio is increased (34, 35, 39–42). All or few criteria are of diagnostic value.

Delayed villous maturation can be found few weeks before or close to term, rarely before 34 weeks of gestation, clinically associated with maternal metabolic disorder and obesity, intrauterine hypoxia, FGR, and fetal death (30, 34, 36, 43). Furthermore, it can be associated with fetal chronic diseases, and disorders of the central nervous system in children and adults, and other congenital anomalies.

Recurrence risk in following pregnancies is increased, even if a definite metabolic disorder is not diagnosed (34).

Distal villous hypoplasia

The phenotype of DVH is characterized by a poorly developed distal villous tree, with deficient distal villi in the lobulus center. Stem villi are surrounded by slender and elongated villi with non-branching capillaries. Deficiency of distal villi is accompanied by an extended intervillous space. The stroma of stem villi is fibrotic with peripheral thick walled fetal vessels. The syncytiotrophoblast shows increased regressive knots, which are often wave formed (35).

Extensive DVH is clinically associated with early-onset FGR and loss of end-diastolic flow in the umbilical cord arteries (44, 45). The placenta is from the start too small. Focal lesions are often associated with decidual vasculopathy and chronic infarct, associated with maternal vascular malperfusion (MVM) (3, 35, 36). DVH is often seen associated with clinical pre-eclampsia (Fig. 3).

CATEGORY II

Deficiency of intermediate villi

Intermediate villous deficiency is characterized by absence of intermediate villi, with only stem villi and slender terminal villi represented. The stroma is partly of fibrous type partly with vasculosyncytial membranes. Chorionic epithelium shows regressive syncytial knots in both villous types, so-called nuclear sprouts (3, 46) (Fig. 4).

Deficiency of intermediate villi causes a decrease in the total vessel volume and a decrease in perfusion capacity (3). Intermediate villous deficiency in 2nd and 3rd trimester placentas is clinically

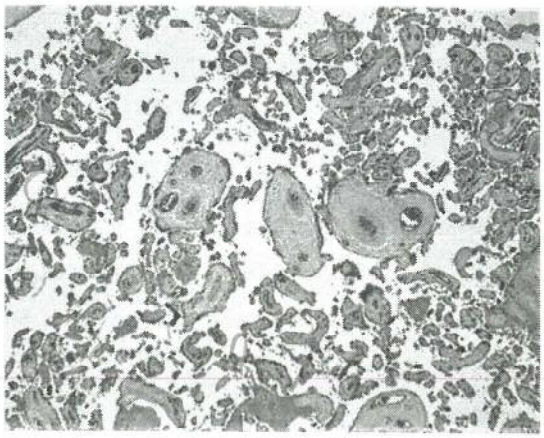

Fig. 3. Distal villous hypoplasia: Villous paucity, many of which are thin and elongated (kindly provided by College of American Pathologists).

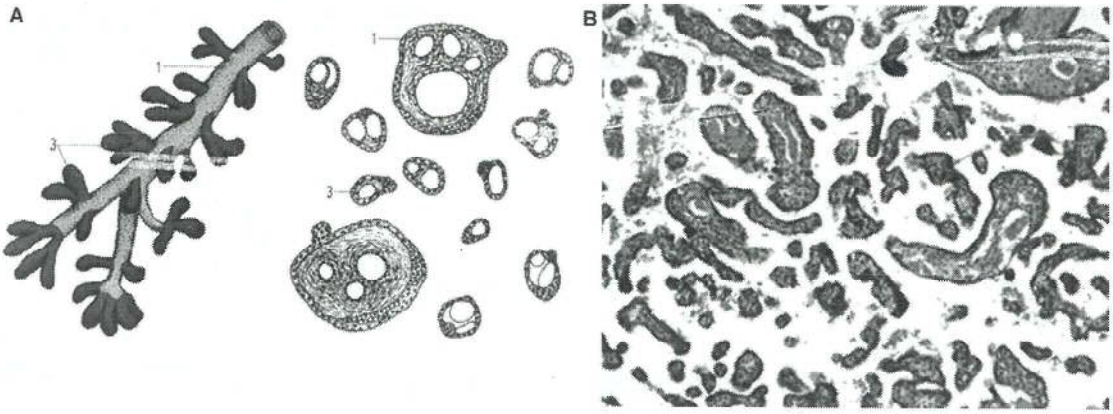

Fig. 4. Deficiency of intermediate villi. (A) Illustration: 1 Stem villus, 2 intermediate villus peripheral type, 3 terminal villus. (B) Numerous slender villi close to stem villi, deficient number of medium-sized villi (HE), stem and terminal villi side by side, partly regressive chorionic epithelium.

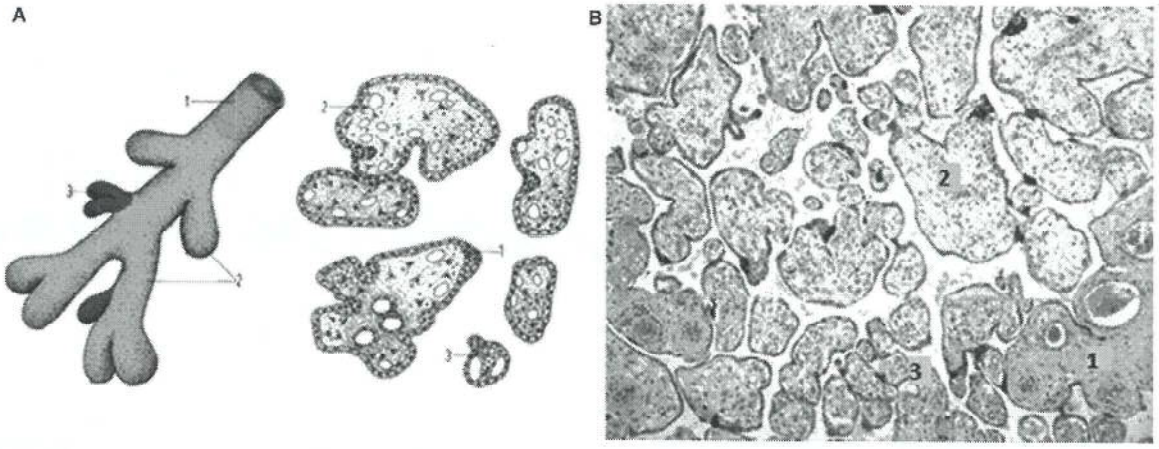

Fig. 5. Retardation of villous maturation. (A) Illustration: 1 Stem villus, 2 lumpish intermediate villus of peripheral type, 3 terminal villus. (B) Medium-sized villi, reticular stroma, few capillaries, deficient vasculosyncytial membranes in nuclear containing chorionic epithelium.

associated with pre-eclampsia, HELLP syndrome, chronic hypertension, collagenous syndromes and in the 2nd trimester associated with prematurity, placental hypoplasia, and FGR.

Retardation of villous maturation

Retardation of villous maturation is characterized by villi with medium-sized diameter, deficiently ramificated into intermediate villi of central and peripheral type. The stroma is cellular and reticular, with dense collagenous fibers, reduced capillaries, and deficient vasculosyncytial membranes. Chorionic epithelium is single layered and densely nuclear (Fig. 5).

It is mainly seen in late (≥37th gestational week) and in prolonged pregnancy (≥42nd gestational week), with increased risk of intrauterine hypoxia, 'sudden infant death syndrome' (SIDS), DM (diabetes mellitus) and associated with endangiopathia obliterans, assumed to be due to virus infection in early pregnancy (rubella, EBV, and Coxsackie B). Recurrence risk is increased to about 5% in following pregnancies (3).

Arrest of villous maturation

Deficient ramification of immature intermediate villi with large diameter and lumpy shape characterizes the arrest of villous maturation. The

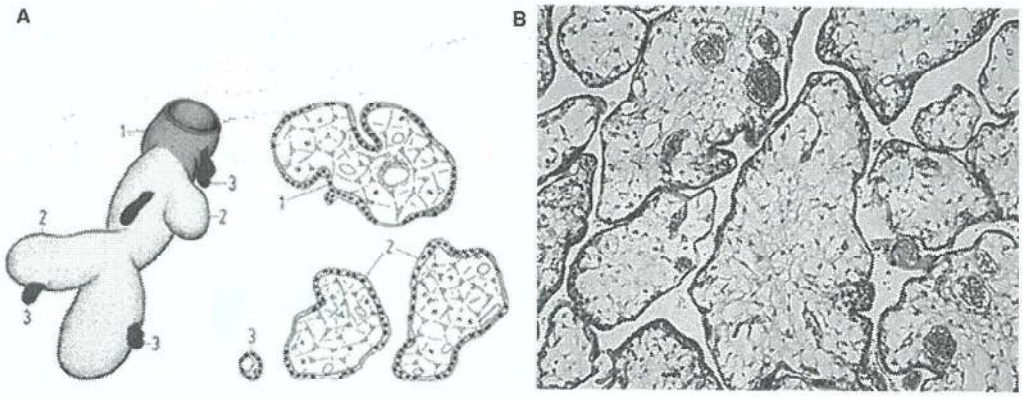

Fig. 6. Arrest of villous maturation. (A) Illustration: 1 stem villus, 2 intermediate villus of central immature type, 3 terminal villus. (B) Deficient villous ramification, loose mesenchymal stroma, deficient paravasal fibers, flat chorionic epithelium (HE).

stroma is primitive mesenchymal, embryonic, and loose reticular with Hofbauer cells and few capillaries, with only rare contact to the surface epithelium. Chorionic epithelium is smooth with only few trophoblast sprouts, infrequently flat and single layered with few cytotrophoblast cells (23) (Fig. 6).

Maturation arrest is seen in early miscarriage and late pregnancy, maternal obesity with and without diabetes, syndromes and chromosome aberration (trisomy), especially in 1st and 2nd trimester. Combination with implantation disorders may give a hint to implantation bed disorders (47). Recurrence risk is assumed to depend on the severity of the disease.

Chorangiosis type I

Chorangiosis type I is characterized by villous groups of medium diameter with loose cellular stroma and numerous capillaries with varying lumen (10 capillaries per villus), irregularly placed without connection to the chorionic epithelium (48). The villous trophoblast is broad and nuclear rich, single and double layered with few vasculosyncytial membranes (Fig. 7A).

This maturation disorder can be seen at any gestational age, but only infrequently in the 1st trimester. In growth-restricted placentas, diffusion capacity may be decreased. Clinically, it may be associated with hemolytic anemia and hydrops, α-

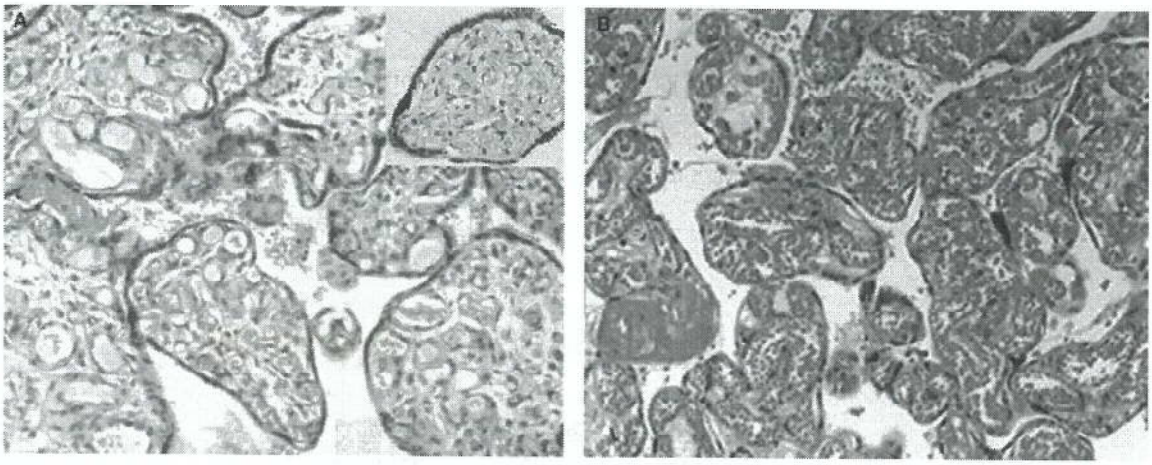

Fig. 7. (A) Chorangiosis type 1. Villi of medium size, tight luminal capillaries (more than 10 capillaries/villous cross section in MPF), deficient vasculosyncytial membranes (HE). (B) Chorangiosis type 2. Villi of varying size with more than 10 capillaries side by side, many vasculosyncytial membranes, flat chorionic epithelium with few sprouts (HE).

thalassemia if overlapping with arrest of villous maturation. Furthermore, clinical moderate fetal erythroblastosis, if overlapping with retardation of villous maturation, insulin regulated DM with vasculopathy. It may be part of mesenchymal dysplasia.

Chorangiosis type II

In chorangiosis type II, the villi are slender with numerous vasculosyncytial membranes (>10 per villus), flat and single-layered epithelium (Fig. 7B).

It is seen in the 3rd trimester close to lesions of chronic maternal vascular malperfusion (MVM), villous fibrosis, and villitis, interpreted as a compensatory villous reaction. Often, it is seen associated with retardation of villous maturation in prolonged pregnancy, maternal vitium cordis (cardiac defect), and long continuous stay at a great altitude.

Dissociated villous maturation disorder

The term 'dissociated villous maturation disorder' describes a maturation disorder with normally branched branched villi according to gestational age (normal ramification) but disturbed maturation of the stroma and the fetal vessels. Dissociated villous maturation disorders are subdivided into 'prevalent immature' and 'prevalent mature'.

Dissociated villous maturation disorder with prevalent immaturity is characterized by immature terminal villi, with deficiently developed fetal vessels. The stroma is of reticular type and the villous trophoblast is partly double layered (Fig. 8).

Dissociated villous maturation disorder of prevalent immature type may overlap with retarded villous maturation.

Placentas of prevalent immature type may cause a decreased placental diffusion capacity, when associated with villous retarded or villous-arrested maturation.

Dissociated villous maturation disorder of prevalent mature type is characterized by intermediate villi with cellular and reticular stroma, associated with slender and normal sized terminal villi with vasculosyncytial membranes.

Prevalence of maturity is often seen in premature placentas, with clinically chronic circulatory disturbances.

There is no known association with maternal diseases.

Preterm (accelerated) villous maturation

Accelerated villous maturation is interpreted as a compensatory change due to maternal vascular malperfusion. Morphologically, small or short hypermature villi for gestational age are accompanied by increased syncytial knots (>33%). Intervillous fibrin is increased alternating with areas of villous paucity.

Accelerated villous maturation is diagnosed in placentas prior to term and may be found in mild, moderate, or severe forms of placental insufficiency, which includes FGR, preeclampsia, and preterm labor (39) (Fig. 9).

In German terminology, 'preterm accelerated villous maturation' is synonymously used with 'Maturitas praecox', 'preterm villous maturation', and 'accelerated villous maturity', defined as premature villous maturation according to gestational age.

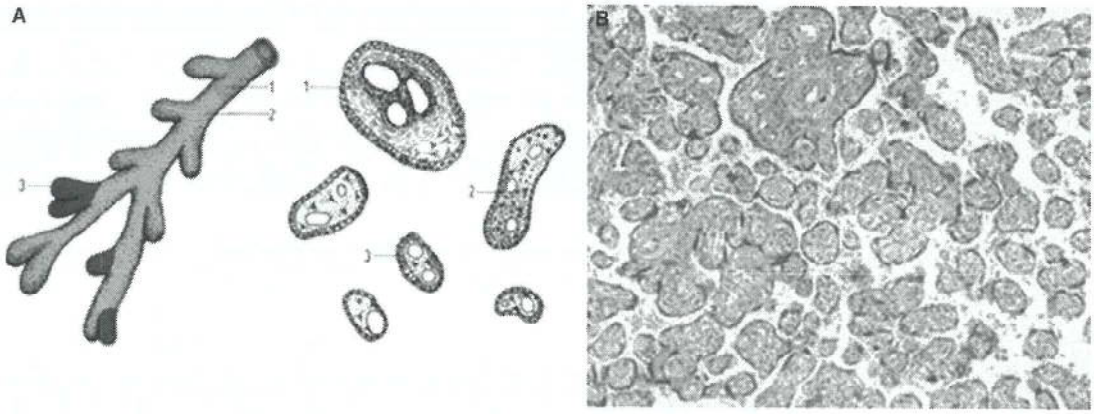

Fig. 8. Dissociated villous maturation disorder, prevalence immature. (A) Illustration: 1 Stem villus, 2 intermediate villus peripheral type, 3 terminal villus. (B) Regular villous ramification, deficient terminal villi with capillaries and vasculosyncytial membranes (MG).

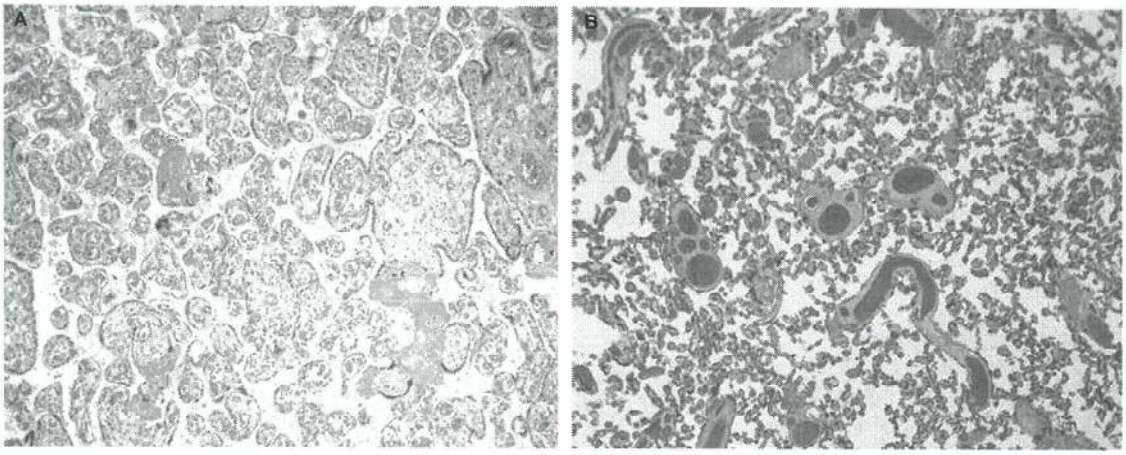

Fig. 9. (A) Following German terminology: Regularly branched villi with premature terminal villi with capillaries and vasculosyncytial membranes. Stem villi and intermediate villi with loose immature stroma. Placenta in gestational age 29.(B) Following Anglo-American terminology: combination of areas with increased syncytial knots and intervillous fibrin deposition (kindly provided by the College of American Pathologists).

Morphologically villi are regularly branched with increased terminal villi with vasculosyncytial membranes. Few stem and intermediate villi of central type contain loose immature stroma.

The pathogenesis is assumed to be a compensatory process in primarily or secondary small placentas due to early onset of chronic maternal vascular malperfusion (MVM). It is seen in first time pregnancy, hypertension, nicotine abuse, eclampsia, multiple pregnancies, and few collagenosis.

Fetal risks include preterm delivery, preterm placental abrupture, and FGR (46).

DISCUSSION

Normal villous maturation for gestational age, with transition from immature intermediate villi into mature intermediate villi and terminal villi in the third trimester, is essential to fulfill fetal demands. Oxygen diffusion is optimized by vasculosyncytial membranes, reduced stroma cellularity, and a thin chorionic epithelium (49).

In addition, if the villi are of small diameter, such as in terminal villi, the exchange surface is maximized (3).

There is international agreement on placental development and pathological disorders in the placenta, such as vascular malperfusion or inflammation. Recently, an international group of perinatal pathologists agreed up on terminology and reporting of pathologic placental entities, maturation disorders included (36). Furthermore, in our opinion all findings should include a comment with clinical correlation and estimation of recurrence risk, which also includes an interpretation of maturation disorders correlated with clinical outcome (50).

However, a unified international classification of maturation disorders does not exist (Table 1).

In the Anglo-American tradition, maturation disorders are described, but terminology is limited to the umbrella term 'delayed villous maturation' (DVM) (39). This includes the term 'defective villous maturation' and 'distal villous immaturity' (DVI), which often is used synonymously (37). Ramification disorders of the villous tree with respect to normal differentiation into villous subgroups (stem villi, intermediate villi of mature and immature type, differentiation of intermediate villi mature type, and terminal villi) are not defined (30). Fitzgerald emphasized distal villous hypoplasia (DVH) as a maldevelopmental disorder, in contrast to Anglo-American terminology. DVH is characterized by a hypoplastic villous tree with reduced numbers of abnormally shaped, long, slender villi with a nonbranching villous capillary network (35). This definition might correspond to the German definition of 'deficiency of intermediate villi' and implies that the villi are not of terminal villous type in this ramification defect. The terms DVM and DVI include morphology with increased numbers of immature villi with huge diameter. In the German literature, this morphologic type is divided into 'retardation' and 'arrest of villous maturation', which correlates clinically with different diseases and different recurrence risks.

Retarded villous maturation is interpreted as a ramification disorder, characterized by retarded

branching of intermediate villi and regular immaturity of the villous stroma and chorionic epithelium (3, 23). Retarded villous maturation is first seen from gestational week 35, associated with intrauterine virus infection (rubella and enterovirus) and latent or manifest diabetes mellitus. Recurrence risk is increased (51). In contrast, arrested villous maturation is interpreted as a ramification disorder with deficiently branched intermediate villi and following deficient transformation into stem villi. Stroma maturation and differentiation of the villous trophoblast is hampered. The mesenchymal and loose reticular, collagen poor, and edematous stroma are considered to build up a tonus which stabilizes the primitive stroma. Villi with arrested maturation are of this reason different from villi with diffuse edema. While the stroma of hydropic degeneration loses its original texture to mole like degeneration, it is preserved in villous maturation arrest. In arrested villous maturation, few irregularly placed capillaries are found and the villous trophoblast is flat with rare syncytial knots. This is in contrast to normally developed intermediate villi of immature type. Stem villi show a similar immature stroma and hypoplastic vessels, which may pinpoint pathogenesis as a disorder of transformation of immature intermediate villi into stem villi, and a centripetal growth disorder with absence of distal villous generations. Arrested villous maturation is seen in early pregnancy in spontaneous abortions and in late pregnancy in women with poorly regulated diabetes (3, 23, 52). Furthermore, it is seen associated with nonimmunological hydrops fetalis, α-thalassemia, chronic fetal anemia, Twin-to Twin-Transfusion Syndrome (TTTS), chronic intrauterine virus infection, maternal metabolic disorders, and maternal obesity.

Chorangioses type I and II and preterm (accelerated) villous maturation are differentiated and classified as maturation disorders in the German terminology (3, 5). Whether Chorangiosis is a maturation disorder or an early developmental disorder with preterm accelerated vascular proliferation is discussed previously and needs further discussion on an international platform.

In conclusion, terminology of maturation disorders is confusing and only sparsely reproducible (37, 53).

The interpretation of the morphology of villous maturation is subjective. Recent studies suggest that the interpretation of maturation disorders might be improved and objectified by immunohistochemistry and molecular analysis (54–56).

In this review, the German and Anglo-American terminology has been reviewed and compared. The most recent recommendations on the terminology of maturation disorders from the Amsterdam Placental Workshop Group Consensus Statement are included.

However, criteria on maturation disorders need to be discussed, revised, and specified and correlated with clinical diseases. The agreed criteria should then be applied and tested for reproducibility and comprehensibility.

An international agreement on the terminology of placental maturation disorders is required as a contributing parameter to optimize fetal outcome.

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