PLACENTATION IN MAMMALS

Introduction

The placenta is a mateno-fetal organ which begins developing at implantation of the blastocyst and is delivered with the fetus at birth. During that 9 month period it provides nutrition, gas exchange, waste removal, a source of hematopoietic stem cells, endocrine and immune support for the developing fetus. There are essentially 3 separate aortic/venous circulatory systems: umbilical, systemic and vitelline. The umbilical system is lost at birth, the vitelline contributes to the portal system and the systemic (embryonic) is extensively remodelled to form the mature cardiovascular system.

Placental Classification

1. **Haemochorial** - placenta where the chorion comes in direct contact with maternal blood (human).
2. **Endotheliochorial** - maternal endometrial blood vessels are bare to their endothelium and these comes in contact with the chorion (dogs, cats).
3. **Epitheliochorial** - maternal epithelium of the uterus comes in contact with the chorion, considered as primitive (pigs, bovine).

The presence of these three differing types of placenta have also been used to describe the pattern mammalian evolution.

Species Placental Comparison

Animal Model Comparison			
Postnatal Animal Models	**Mouse**	**Rat**	**Pig**
Pregnancy period (days)	18 – 21	21 – 23	110 – 118
Placenta type	Discoidal, decidual hemoendothelial choroidea	Discoidal, decidual hemoendothelial choroidea	Epitheliochorial
Litter size	6 – 12	6 – 15	11 – 16
Birth weight (g)	0.5 – 1.5	3 – 5	900 – 1600
Weaning weight male/female (g)	18 – 25/16 – 25	55 – 90/45 – 80	6000 – 8000
Suckling period (days)	21–28	21	28–49
Solid diet beginning (days)	10	12	12 – 15
Puberty male/female (week)	4 – 6/5	6/6 – 8	20 – 28
Life expectancy (years)	1 - 2	2 - 3	14 – 18

Human Villi Timeline

The placental vill development data below is based upon a recent immunochemistry confocal laser scanning microscope (CLSM) study. Note that the paper uses clinical gestational age (GA) from last menstrual period (LMP) and has been corrected for post-conception (fertilization) age, approximately 14 days later.

Placenta Villi Timeline			
Fertilization Age (weeks)	**Gestational Age** (weeks)	**Vessel Lumen Diameter** (range in microns)	**Features**
3 to 4	5 and 6	10 - 15	• complex network of cords and vessels with redundant connections • network comprises mainly cords already connected together • vessels and cords are connected to each other without any interruptions • chorionic villus dominated by this network of vascular elements • vessels and cords (centrally and peripherally) contact overlying trophoblastic layer
5 to 6	7 and 8	10 - 26	• villi dominated by capillary network of vessels and cords • capillary network contains more vessels than cords • chorionic villus tip - regular small branched off (mesenchymal) chorionic villi are present containing CD31 positive cells
7 to 8	9 and 10	60 - 75 two central vessels 26 - 34 capillary network	• villi have two large centrally located vessels • surrounded and connected to a peripheral capillary network • capillary network contains vessels with a lumen in tight contact with overlying trophoblastic layer • villous projections also contain blind ending capillary sprouts
9 to 10	11 and 12	70 - 90 two central vessels 26 - 34 capillary network	• immature intermediate villi characterized by two large vessels surrounded by a capillary network • capillary network has few cords • blind ending capillary sprouts off the capillary network
Term			Terminal villi • have an extensive surface area >10 m^2 • small calibre (40 – 100 μm)
Table data. Paper uses clinical gestational age (**GA**) table corrected also for post-conception (fertilization) age.			

Trophoblast Cells

Following implantation the initial trophoblast cells can differentiate into 2 pathways:

1. **Extravillous** - cytotrophoblastic cells proliferate and differentiate into an invasive phenotype that invade (interstitial trophoblast) the maternal decidual stroma and the spiral arteries (endovascular trophoblast) of the myometrium.
2. **Villous** - cytotrophoblastic cells proliferate and fuse to form the multi-nucleated syncytiotrophoblast cells that form the outer surface of the fetal placental villi.

Maternal Blood Flow

Maternal blood pressure normally decreases or remains unchanged during pregnancy while both cardiac output and vascular volume are increased. Uterine blood flow changes are principally due to a decrease in uterine vascular resistance. There is also an associated structural enlargement of both the uterine arterial and venous trees, reduced vascular tone (vasodilation) and placenta development.
Uteroplacental blood flow (UPBF) was historically measured by a number of different mathematical calculations and probe methods, currently the method involves trans-vaginal doppler ultra-sonography.
In human singleton pregnancies, uteroplacental blood flow (UPBF) begins at 20–50 ml/min and increases (linearly) to 450–800 ml/min, with twin pregnancy values in excess of 1 l/min.

Uterine Artery Diameter

The following data is from a study of 18 pregnant women using ultrasound and doppler analysis of the uterine artery.

- Gestational Age: week 21 doubled (from 1.4 to 2.8 mm).
- Gestational Age: week 21 to 30 remained constant (2.9mm).
- Gestational Age:week 30 to 36 increased (to 3.4 mm).

Uterine artery mean flow velocity also increased nearly eight times from non-pregnant (8.4 cm/second) to GA week 36 (61.4 cm/second).

Blood Oxygen Levels

Maternal and Fetal Placental Circulations
Showing the major compartments and published attributed in vivo oxygen values.

Term Placenta Measurements

There are a variety of diagnostic and morphological measurements that can be made of the placenta during pregnancy and at term.
Simple measurements of overall placental diameter, thickness and volume:

- **Placental diameter** - is measured in the transverse section by calculating the maximum dimensions of the chorionic surface.
- **Placental thickness** - is measured at its mid-portion from the chorionic plate to the basilar plate, on a longitudinal plane (less than 4 cm at term). Excludes any abnormalities

(fibroids, myometrial contractions, or venous lakes). The placental thickness approximates in millimeters to the weeks of gestation.

- **Placental volume** - is measured by a range of different methods and calculations, more recently with three-dimensional ultrasound.

Placental Factors

As the placenta develops it becomes the source of many different factors (hormones, growth factors) and also has the ability to metabolise both maternal and fetal factors.

Placental Growth Factor

(PGF, PLGF) A growth factor of the vascular endothelial growth factor (VEGF) family, released from the placental trophoblast cells and other sources that stimulates blood vessel growth.

Placental Abnormalities

- **Placenta Accreta** - abnormal adherence, with absence of decidua basalis. The incidence of placenta accreta also significantly increases in women with previous cesarean section compared to those without a prior surgical delivery.
- **Placenta Increta** - occurs when the placenta attaches deep into the uterine wall and penetrates into the uterine muscle, but does not penetrate the uterine serosa. Placenta increta accounts for approximately 15-17% of all cases.
- **Placenta Percreta** - placental villi penetrate myometrium and through to uterine serosa.
- **Placenta Previa** - In this placenatal abnormality, the placenta overlies internal os of uterus, essentially covering the birth canal. This condition occurs in approximately 1 in 200 to 250 pregnancies. In the third trimester and at term, abnormal bleeding can require cesarian delivery and can also lead to Abruptio Placenta. Ultrasound screening programs during 1st and early 2nd trimester pregnancies now include placental localization. Diagnosis can also be made by transvaginal ultrasound.
- **Vasa Previa** - (vasa praevia) placental abnormality where the fetal vessels lie within the membranes close too or crossing the inner cervical os (opening). This occurs normally in 1:2500-5000 pregnancies and leads to complications similar too those for Placenta Previa.Type II is defined as the condition where the fetal vessels are found crossing over the internal os connecting either a bilobed placenta or a succenturiate lobe with the main placental mass. Some recent evidence of successful in utero laser ablation of type II vasa previa at 22.5 weeks of gestation.
- **Abruptio Placenta** - a retroplacental blood clot formation, abnormal hemorrhage prior to delivery.
- **Chronic Intervillositis** - (massive chronic intervillositis, chronic histiocytic intervillositis) Rare placental abnormality and pathology defined by inflammatory placental lesions, mainly in the intervillous space (IVS), with a maternal infiltrate of mononuclear cells (monocytes, lymphocytes, histiocytes) and intervillous fibrinoid deposition.

- **Hydatidiform mole** - placental tumor with no embryo development. Several forms of hydatidiform mole: partial mole, complete mole and persistent gestational trophoblastic tumor. Many of these tumours arise from a haploid sperm fertilizing an egg without a female pronucleus (the alternative form, an embryo without sperm contribution, is called parthenogenesis). The tumour has a "grape-like" placental appearance without enclosed embryo formation. Following a first molar pregnancy, there is approximately a 1% risk of a second molar pregnancy.

Placental Cord Abnormalities

There are few abnormalities associated with umbilical cord development, other that abnormally short or long cords, which in most cases do not cause difficulties. In some cases though, long cords can wrap around limbs or the fetus neck, which can then restrict blood flow or lead to tissue or nerve damage, and therefore effect development.

- **Cord knotting** - can also occur (1%) in most cases these knots have no effect, in some cases of severe knotting this can prevents the passage of placental blood.
- **Cord torsion** - Rare event where even without knot formation can also affect placental blood flow, even leading to fetal demise.

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