65.
PLACENTAL FINDINGS AS CAUSE OF NEONATAL DEATHS

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Object: The most well-known causes of death in neonate are prematurity, immaturity, low birth weight, infection and abnormalities. In this paper I studied the causes of death, until 28 days of birth, in a neonatal department. In each case, I checked the clinical record and carried out placental pathology. The cases studied in this paper were in the neonatal department, meaning that I had access to full records and materials.
Materials: I checked 37 neonatal death cases in a neonatal unit clinically and with placental pathology examination.
Results: The deaths occurred between 0-days and 28-days. Deliveries were between 22 gestational weeks and 40 gestational weeks, with the average being 28 weeks.
The causes of death according to the clinical records were
abnormalities - 9 cases
placental dysfunction and immaturity - 22 cases
severe infection—6 cases
The causes of death according to placental pathology were
Dysmature villi - 11 cases
Maternal floor vessels abnormality - 12 cases
Chorioamnionitis or deciduitis —10cases
Conclusions: In this study I confirmed the clinical findings that the deaths of neonatal had three main causes; the first was immaturity and fatal shock at delivery, the second was abnormality, and the third was infection. Immaturity and fatal shock means that the baby could not develop. Abnormality meant that there were problems with the heart, lungs, liver, and other organs. Infection complicate with, before and after birth.
What this study found through placental pathology was dysmature villi, immature villi and vessels abnormalities. These pathological pictures prove the clinical findings, because abnormal villi is mainly associated with fatal abnormality, and maternal floor vessels abnormality associated with hypoxia of baby which leads to fatal and neonatal distress.

66.
HOW EXAMINATION OF THE PLACENTA IN PREGNANCY LOSS CAN HELP WITH FUTURE OUTCOMES

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Object: Pregnancy loss is a big issue for everyone involved. If pregnancy loss occurs repeatedly, we call it recurrent pregnancy loss and in Japan, it is treated at a special clinic. At that time records from previous placental pathology is a necessity for identifying the possible causes and, if the pathology is the same, possible treatments.
Using placental pathology is the initial key to understanding the situation and the next steps to take. After placental pathology examination we can check previous data and add results from the new examination. The role of the pathologist is sometimes underestimated, but the findings of the pathologist can be very important, and the ability to explain the causes of pregnancy loss to the clinician and family is vital.
In this paper we show the causes of pregnancy loss classified by placental pathology.
Material

1 We examined 56 placentas from cases of pregnancy loss in 12 to 21 gestational weeks in a general hospital. We later re-checked and classified these initial examinations, adding more details.
2 We examined 20 placentas from cases of pregnancy loss in 12 to 21 gestational weeks in a specialist clinic. As well as the usual placental pathology, this included a number of other specialist examinations.

Results: Out of 56 cases, we found
maternal floor vessels abnormality - 12 cases
CAM and deciduitis - 14 cases
Dysmature villi - 15 cases
Cord problems - 7 cases
Hemorrhage of decidua - 6 cases
Breus' mole - 1 case
From these 56 cases, several were recurrent.
In the special clinic all cases were recurrent and had special examinations, such as ureaplasma culture, microarray for bacterial detection, and coagulation examination.
Conclusions: Finding the cause of recurrent pregnancy loss is very important, and contributing to successful pregnancy and safe, healthy birth is our ultimate aim. For this reason, considering the vital part that placental pathology can play, we suggest that all hospitals examine the placenta from cases of pregnancy loss in more detail.

67.
MATERNAL VASCULAR MALPERFUSION(MVM) AS A CAUSE OF CHRONIC LUNG DISEASE (CLD)

Masayoshi Arizawa. *Tokyo Metropolitan Ohtsuka Hospital*

Object: The most well known cause of chronic lung disease (CLD) is Subacute necrotizing Chorioamnionitis(SNC). There are a great number of reports and papers that show how SNC leads to Cytokine release syndrome (CRS) and damage to the lungs in newborns. However, clinically, we see many cases of CLD without Chorioamnionitis (CAM) in very low birth weight babies (VLBW). In this paper, I will confirm the causes of CLD in VLBW. I will also confirm the rate of CAM and maternal vascular malperfusion (MVM).
Material: From an examination of the clinical records I chose 190 CLD cases, and examined the placentas in each one by microscope. My diagnosis of CAM or MVM was by the Amsterdam classification, 2014. SNC was diagnosed by necrosis of amnion with white blood cells invasion. CLD was defined by the newborn still needing oxygen after 36 weeks.
Results: From the 190 cases I found
53 cases of SNC
73 cases acute CAM
33 cases of MVM
Conclusions: There were a large number of severe CAM and SNC in CLD cases. This result confirms previous studies.
However, this study also shows that MVM is another significant factor in the development of CLD. MVM starts from maternal floor vascular disease (atherosclerosis, fibrinoid necrosis, decidual degeneration) and develops into fetal hypoxia and hypo nutrition and results in developmental problems, VLBW, organ damage, and complications with CLD.

68.
CLINICAL AND PATHOLOGICAL PLACENTAL ABNORMALITY IN VELAMENTOUS CORD INSERTION

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Object: There are many reports about how velamentous cord Insertion (VCI) can lead to small for gestational age (SFG) and complications with twins and triplets, Hypertension disorder of pregnancy (HDP), and gestational diabetes (GDM). VCI means membranous insertion of umbilical cord which can lead to complications.
In this paper I examine clinical and pathological pictures in VCI cases.
My hypothesis, based on my results, shows how VCI may develop from the lack of circulation on the mother's side of the placenta. This maternal floor physiological problem can lead to the shape of the placenta changing and abnormal cord insertion.
Materials: I examined both gross and microscopic pictures in 109 VCI cases and also examined the clinical records in each case.
Results:
From the 109cases, there were:
By gross examination:

- 35 cases of twins and triplets, 32.1%

By histological examination,

- Stem villous edema, intermediate villous vessels occlusions, terminal villous avascular, and decidual vascular and other lesions were observed.

By clinical record:

- 21 cases of GDM, 19.2%
- 20 cases of FGR, 18.3%
- 11 cases of HDP, 10.6%

Conclusions: Twins sharing the same ammonium cavity with just one placenta have many complications with VCI.
VCI is a problem on the fatal side, and it can be easily identified by gross examination, as can the problems in the circulation on the mother's side.
VCI shares with HDP the lack of circulation from the mother's side, and clinically, the high rate of complications is due to maternal floor vessels problems.
In regards to GDM, previously the VCI rate was not so high, but recently it has been higher than before. The reason for this is that GDM diagnosis has now become more accurate and can be seen to be more common.
Placental pathology is very effective at explaining clinical states about VCI and my hypotheses regarding the origin of VCI is backed up by both clinical and pathological pictures. These clearly show the link between HDP, GDM, and FGR and lack of circulation on the mother's side and fetal side of the placenta.

69.
AVASCULAR VILLI

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Object: Lack or diminishment of capillaries in the villi of the placenta, known as avascular villi, has several causes. Firstly, there is chromosomal abnormality (Hydatidiform mole, Turner syndrome, etc.). Secondly, Villitis of Unknown Etiology (VUE). Thirdly, villus injury from mother's abnormal circulation. And fourthly, occlusive terminal villus capillary from cord occlusion or from occlusion of the vessels on the surface of the placenta.
In this paper I examine the pathological findings and clinical findings from cases of avascular villi over the period of one year, and classified those cases according to these four causes.
Material: I examined 122 singleton avascular villi cases. I classified each pathologically and studied the clinical findings.
Results: Pathologically, there were cases of dysmature villi, avascular villi of VUE, avascular villi from problems with the circulation from mother to placenta, and avascular villi due to bad fetal to placental circulation. I saw all four categories in the 122 cases.
Pathologically, out of 122 cases, I found:
19 cases of dysmature villi
15 cases of VUE
49 cases of avascular villi from bad circulation from mother to placenta
51 cases of coiling or abnormal insertion of cord
Clinically, from the 122 cases, I found:
15 cases of IUFD
16 cases of HDP
18 cases of GDM
24 cases of FGR
18 cases of NRFS (non-reassuring fetal status)
Conclusions: In avascular villi it is usual to expect IUFD, but I also found high rates of complications with HDP, GDM, FGR and NRFS. In this paper I study how widespread avascular villi is commonly associated with more sever perinatal problems.

S-01.
AMINO ACID TRANSPORTATION IN THE PLACENTA AND ITS IMPORTANCE IN FETAL GROWTH

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Objective: Insufficient oxygen supply is closely associated with the pathophysiology of fetal growth restriction (FGR). By using transgenic mice with its oxygen delivering capacity deteoriorated, we examined the phenotype of the mice and aimed to elucidate the underling mechanism by which the phenotype is induced.
Methods: Conditional knockout mice with erythrocyte-specific gene deletion of ENT1 (eEKO), a key adenosine transporter, were utilized in this study. The oxygen delivering capacity was measured by measuring p50 and 2,3-BPG in the erythrocytes. The dams were sacrificed on 17.5 dpc (days post coitus), and blood pressure, proteinuria, and the weight of the pups were measured. Metabolic profiling was used to determine the change of nutrient transports from the dam to the fetus by using maternal plasma and the placenta. We conducted real-time PCR, western blot, and in vivo experiment using human trophoblast cell line (HTR-8/SVneo cells) to access the molecular mechanism underlining the phenotype.
Results: eEKO showed reduction in oxygen delivering capacity in both p50 and 2,3-BPG in the maternal erythrocytes. The dams did not show hypertension or proteinuria, but they showed reduction in fetal weight, suggesting they have FGR phenotype. The immuno-staining in the placenta showed overexpression of HIF-1a in the placenta of eEKO, suggesting hypoxia in the placenta. Metabolomic profiling showed reduction of broad spectrum of amino acids in the placentas from eEKO, although the amino acids were rather increased in the maternal plasma, which implies the impaired amino acid transport function. Both real-time PCR and the western blot analysis showed reduction of LAT1, amino acid transporter, in the placentas from eEKO. Culturing HTR cells in HIF-1a stabilized state showed reduction of LAT1 in the placenta.
Conclusion: Our findings suggest that maternal erythrocytes'oxygen delivering capacity mediated by ENT1 is essential for maintaining adequate placental oxygenation to support fetal growth predominantly through LAT1. Strategies to improve erythrocytes' function to deliver oxygen may provide new therapeutic possibilities for FGR.

S-02.
RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN AS AN ANTICOAGULATION THERAPY IMPROVES RECURRENT MISCARRIAGE AND FETAL GROWTH RESTRICTION DUE TO PLACENTAL INSUFFICIENCY

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Objective: Placental insufficiency is one of the major risk factors for growth restriction and preeclampsia. The purpose of this study is to investigate whether recombinant human thrombomodulin(r-TM) as anticoagulant therapy improves fetal conditions and physiological outcomes.
Methods: We used CBA/J×BALB/C mice as a control and CBA/J×DBA/2 mice — a well-studied model of recurrent spontaneous miscarriage. Pregnant mice received daily subcutaneous injections of r-TM or saline from day 0-15. The fetal resorption rate, fetal weight, and fetal size were calculated at day 15. Additionally, we analyzed the mRNA expression of angiogenic factors and the concentration of soluble Flt-1 (sFlt-1) using the ELISA kit.
Results: The rate of fetal resorption in CBA/J×DBA/2 mice treated with r-TM was significantly lower compared with mice without r-TM treatment. Additionally, fetal weight and fetal size were also significantly higher in the r-TM treated mice. Fibrinogen deposition in the labyrinth area of the CBA/J×DBA/2 mice treated with r-TM was significantly lower compared with deposits in the mice untreated with r-TM. As well, r-TM significantly increased the gene expression level of VEGF and Flt-1 mRNA in the placentas of the CBA/J×DBA/2 mice. r-TM treatment also significantly