



Pregnancy Loss

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Terminology

- ▶ Traditionally, a pregnancy loss prior to 20 weeks was called a *spontaneous abortion*, and a loss past 20 weeks' gestation was termed a *stillbirth* or an *intrauterine fetal death (IUFD)*.
- ▶ **Early pregnancy loss is defined as a loss prior to 10 weeks' gestation.**
- ▶ **Peri-implantation loss** prior to 5 weeks in which no gestational sac was visible,
- ▶ **pregnancy of unknown location** including ectopic pregnancy,
- ▶ **pre-embryonic loss** at 5 0/7–5 6/7 weeks in which a gestational sac or yolk sac is visible prior to loss but no embryo is seen
- ▶ **embryonic loss** at 6 0/7–9 6/7 weeks in which an embryo is seen on ultrasound prior to loss.
- ▶ **Fetal death** requires ultrasound documentation of a crown–rump length of at least 30 mm or passage of a fetus measuring 30 mm CRL.
- ▶ Fetal death is subdivided into early fetal death (10 0/7–15 6/7 weeks) and late fetal death (16 0/7–19 6/7 weeks). This terminology permits more useful categories for diagnosis, prognosis, and research.

Recurrent pregnancy loss or Recurrent miscarriage

- ▶ 1% to 2% of women experience recurrent pregnancy loss
- ▶ Definition:
- ▶ ESHRE: 2 or more consecutive pregnancies
- ▶ ASRM: 2 or more consecutive pregnancies
- ▶ RCOG: 3 or more consecutive pregnancies

Pregnancy Loss

- ▶ Human reproduction is an extremely inefficient process. Each menstrual cycle yields conception at most 30% of the time, and of those conceptions, approximately 50% miscarry.
- ▶ Because the majority of pregnancies are lost prior to implantation, and before the next menses, they are not clinically recognized.
- ▶ After implantation, the rate of pregnancy loss decreases to 15%–20% after 4–6 weeks' gestational age.
- ▶ By 10–13 weeks, the fetal loss rate is only 2.8%.
- ▶ Early pregnancy loss is quite common; 25% of couples attempting pregnancy experience at least one sporadic miscarriage.

Causes of pregnancy loss

1. Genetic causes, including molar pregnancies
 - ***Numerical chromosomal abnormalities***
 - ***Structural chromosomal abnormalities***
2. Infectious causes
3. Immunological causes
4. Implantation abnormalities
5. Anatomic abnormalities of the uterus
6. Endocrine abnormalities

Infectious causes

- ▶ **Viral infections**, such as cytomegalovirus, herpes simplex virus 1 and 2, human parvovirus B19, enterovirus, adenovirus, and varicella zoster virus, Influenza have been implicated as causative agents of spontaneous abortion
- ▶ *Treponema pallidum* (syphilis), *Toxoplasma gondii* (toxoplasmosis), *Listeria monocytogenes*, *Brucella* and *Plasmodium falciparum* (malaria) all have the capacity to cause transplacental infection.
- ▶ **Bacterial infections** usually cause acute deciduitis, which is associated with early pregnancy loss.

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- ▶ *A significant portion of the pregnancy losses, however, remain unexplained*

Causes of recurrent miscarriage

- ▶ Genetic abnormalities
- ▶ Structural abnormalities
- ▶ **Infection**
- ▶ Endocrine abnormalities
- ▶ Immune dysfunction
- ▶ Antiphospholipid syndrome
- ▶ Thrombophilic disorders

Genetic abnormalities

- ▶ Numerical and structural
- ▶ Most common cause of sporadic cases
- ▶ 50-60% of sporadic abortions
- ▶ 40% of recurrent cases
- ▶ trisomies (mostly involving chromosomes 16, 21, and 22), following by monosomy x
- ▶ Balanced translocations are the most common parental abnormality found in 3-5% of RPL cases followed by reciprocal translocation

Anatomical factors

- ▶ Acquired and congenital
- ▶ 20%
- ▶ Intrauterine adhesions
- ▶ Adenomyosis (endometriosis does not cause recurrent pregnancy loss)
- ▶ Endometrial polyps
- ▶ Leiomyomas
- ▶ Uterine septum or other anatomic factors
- ▶ Women with incompetent cervixes are not at increased risk of 1st trimester

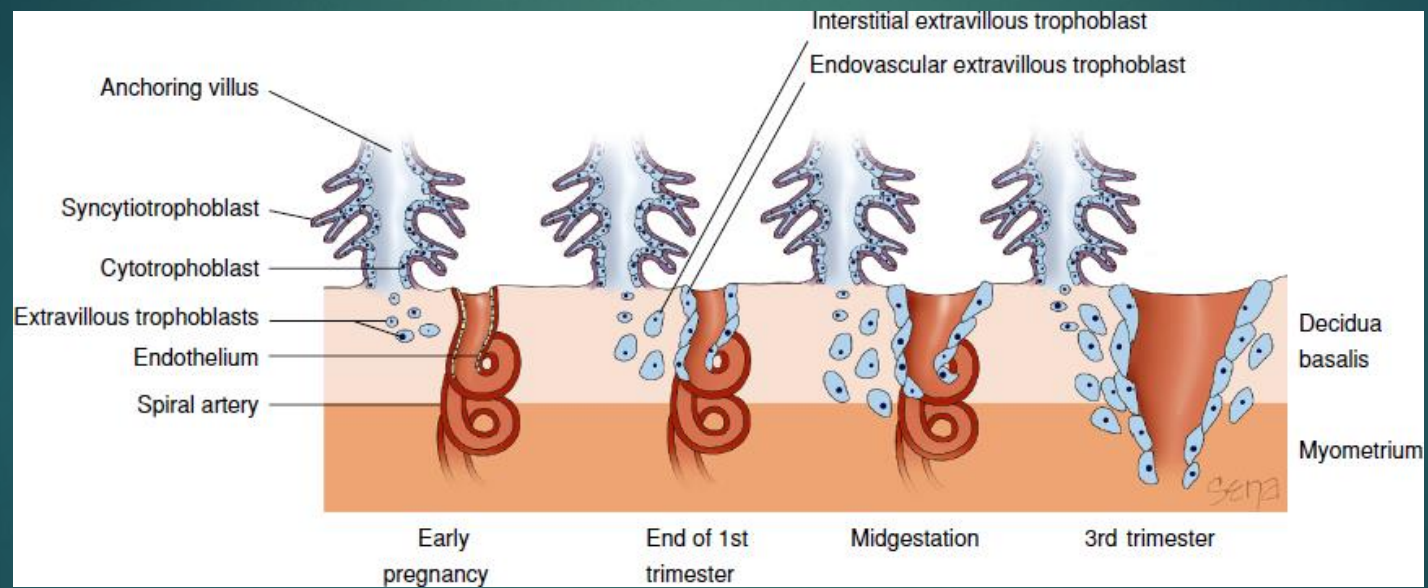
Thrombophilia

- ▶ Hereditary thrombophilia:

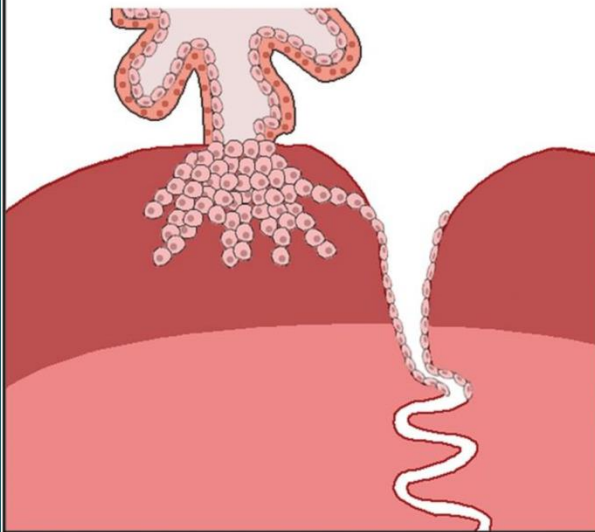
Factor V Leiden mutation, Prothrombin mutation, Protein C, Protein S and Antithrombin deficiency and MTHFR mutation.

- ▶ Acquired thrombophilia:

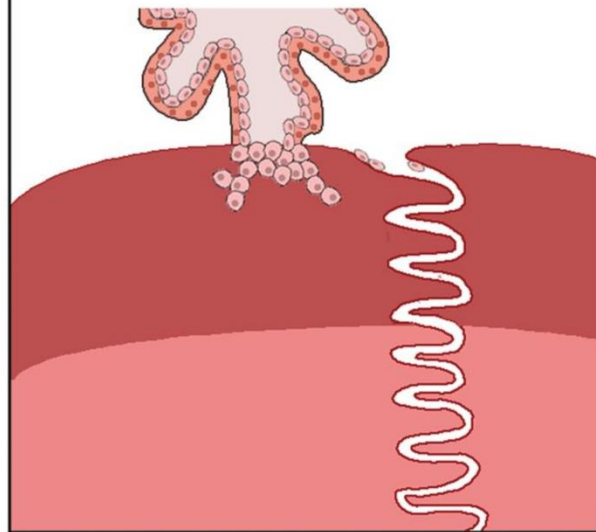
Antiphospholipid Syndrome (APS): 5-20%

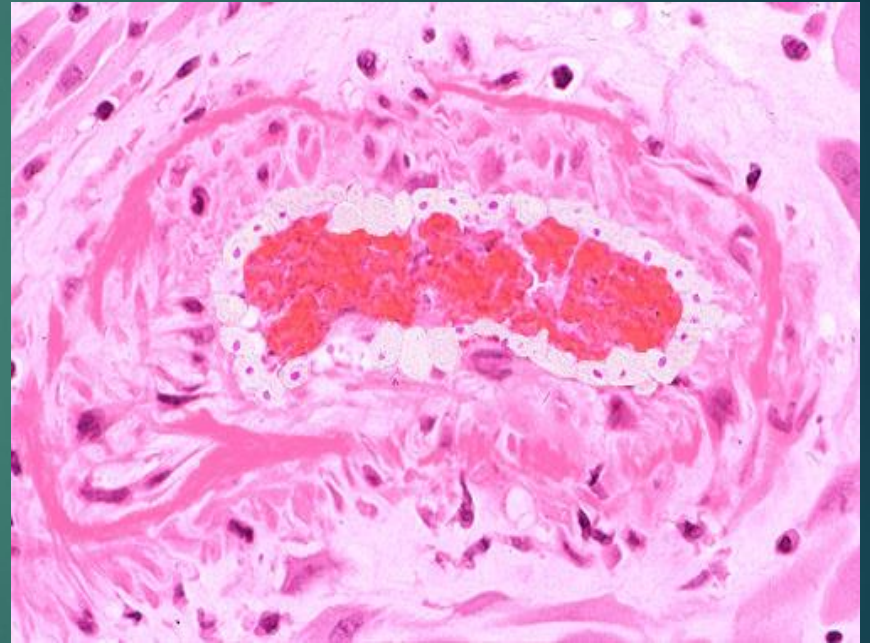
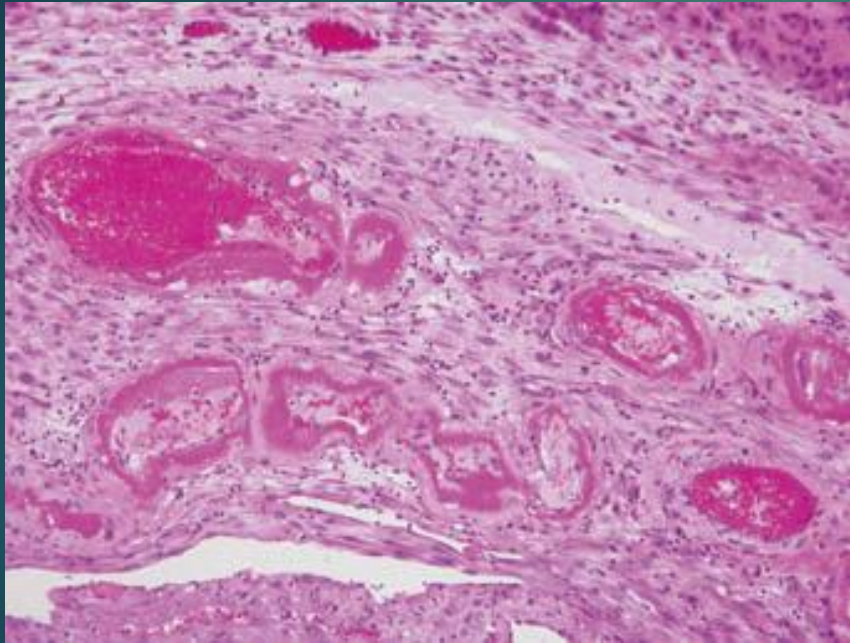


Normal:



Pathological:





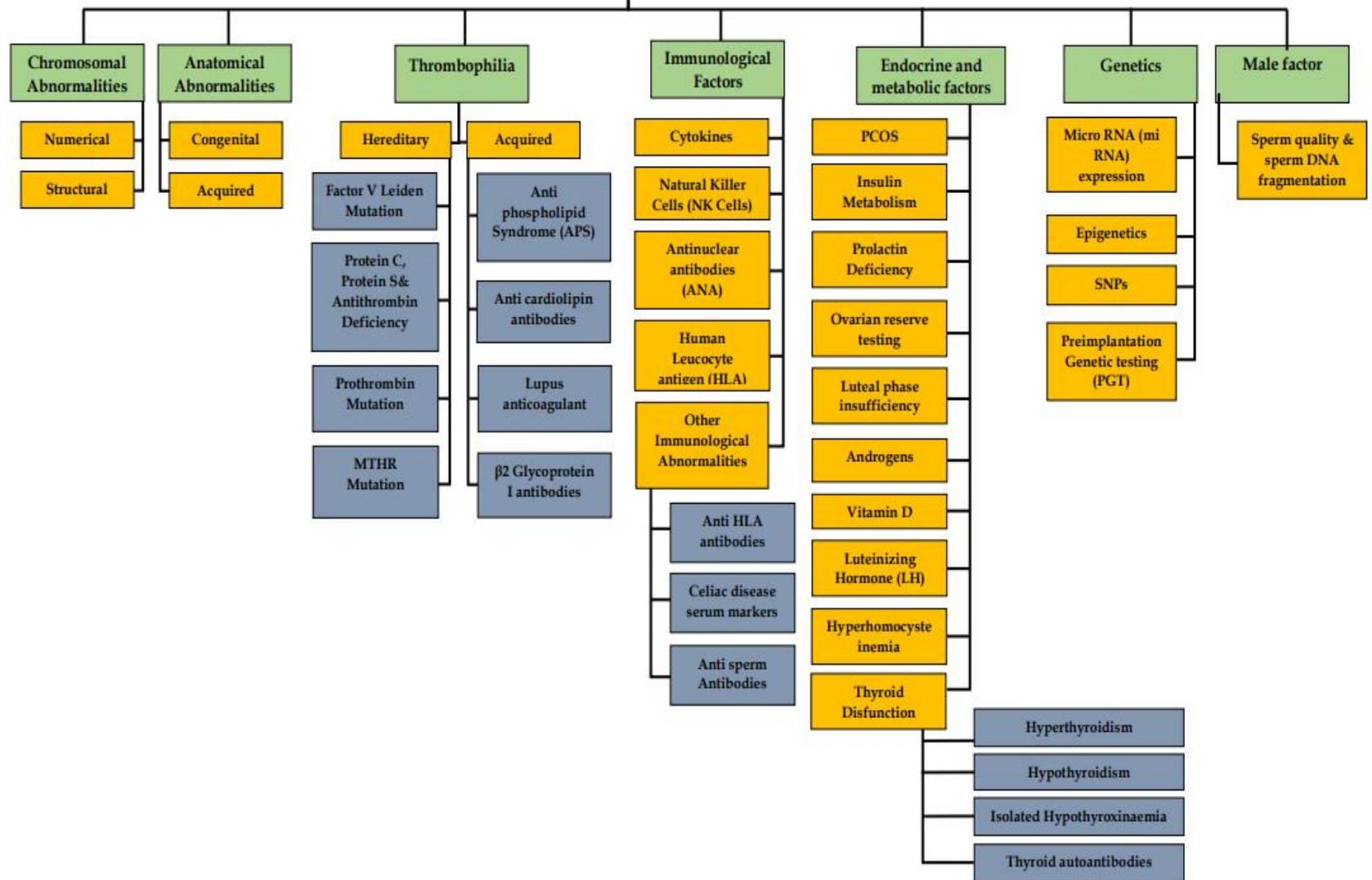
Immunological factors

- ▶ Human leukocyte antigen (HLA)
- ▶ Cytokines
- ▶ Antinuclear antibodies (ANA)
- ▶ Natural killer cells (NK cells)

Endocrine and metabolic factors

- ▶ Thyroid dysfunction
- ▶ Polycystic ovary syndrome (PCOS) and Insulin metabolism

Aetiologies of Recurrent Pregnancy Loss





Histological evaluation of products of conception

- ▶ Tissue without fixative or in normal saline
- ▶ In a fridge or cold box

Histopathologic evaluation of early pregnancy loss

- ▶ Hydatiform moles
- ▶ Villous dysmorphic features suggesting fetal aneuploidy
- ▶ Chronic intervillitis of unknown etiology (CIUE)
- ▶ Massive perivillous fibrin deposition (MPFD)
- ▶ Impaired trophoblastic vascular invasion
- ▶ Documentation of a pregnancy



Abnormalities with probable immunological basis

- ▶ *Massive intervillous fibrin deposition*
- ▶ *Nonspecific chronic villitis and/or intervillitis*
- ▶ *Abnormalities in implantation*

Recurrent causes detected in histology

- ▶ Chronic intervillitis of unknown etiology (CIUE)
- ▶ Massive perivillous fibrin deposition (MPFD)
- ▶ Recurrence rate 18-100%
- ▶ Other complications: IUFD, IUGR

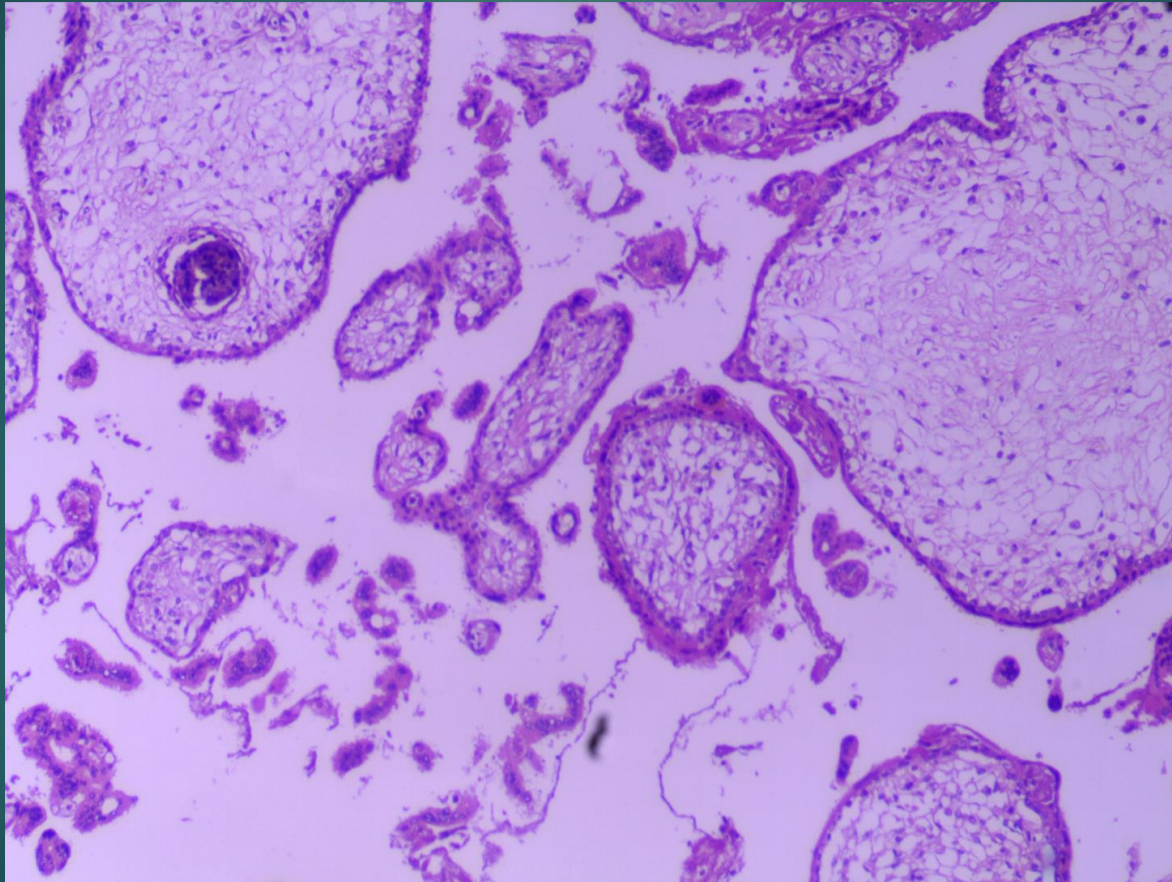
Material and Methods

- ▶ Products of conception received to Avicenna lab from March 2014 to March 2018
- ▶ below 12 gestational weeks
- ▶ 2-3 samples kept in -20 for future evaluation
- ▶ Slides prepared then stained H&E
- ▶ In cases suspicious for CIUE, IHC staining for CD 68 performed

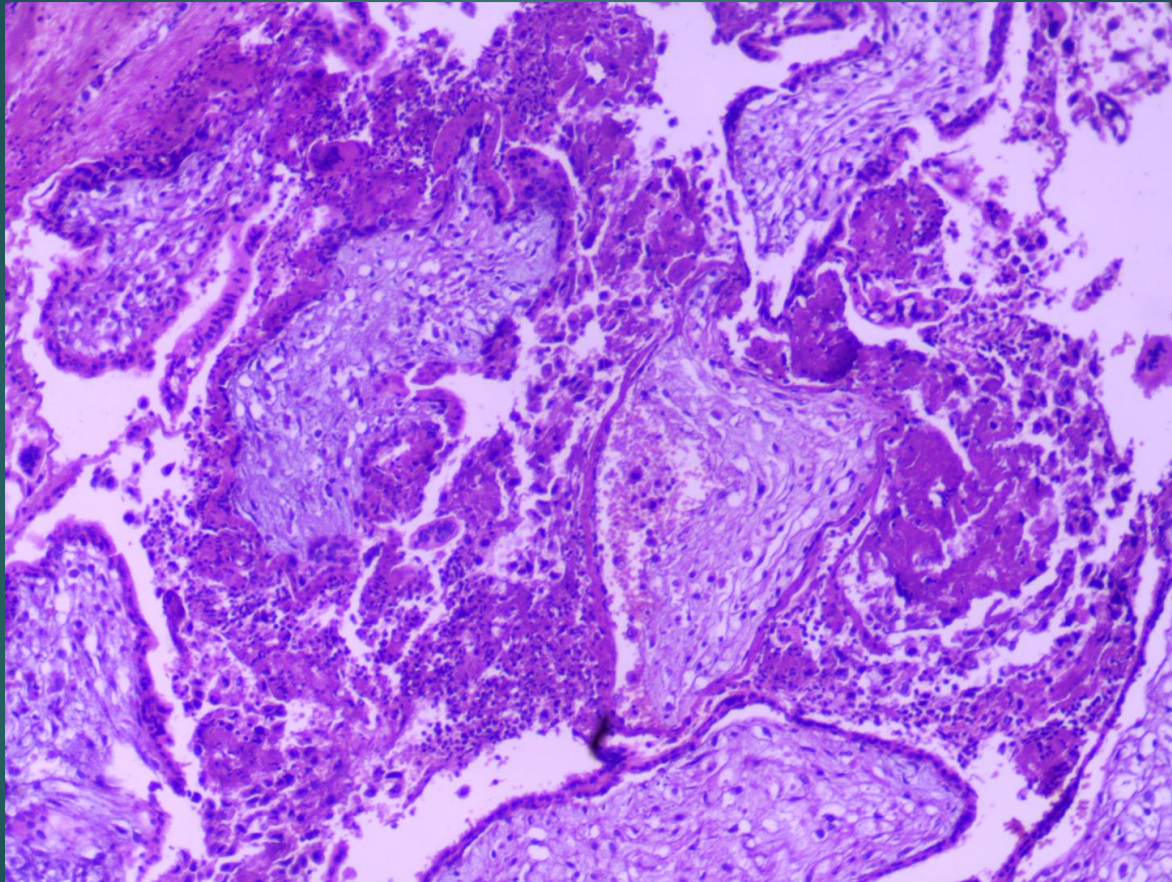
Histology findings

- ▶ Unremarkable pathologic finding
- ▶ changes suggestive of hydatiform moles,
- ▶ villous dysmorphic features suggesting fetal aneuploidy
- ▶ chronic intervillitis of unknown etiology (CIUE)
- ▶ intervillous fibrin deposit (IFD)
- ▶ vasculopathy /infarction
- ▶ miscellaneous
- ▶ decidua only samples.

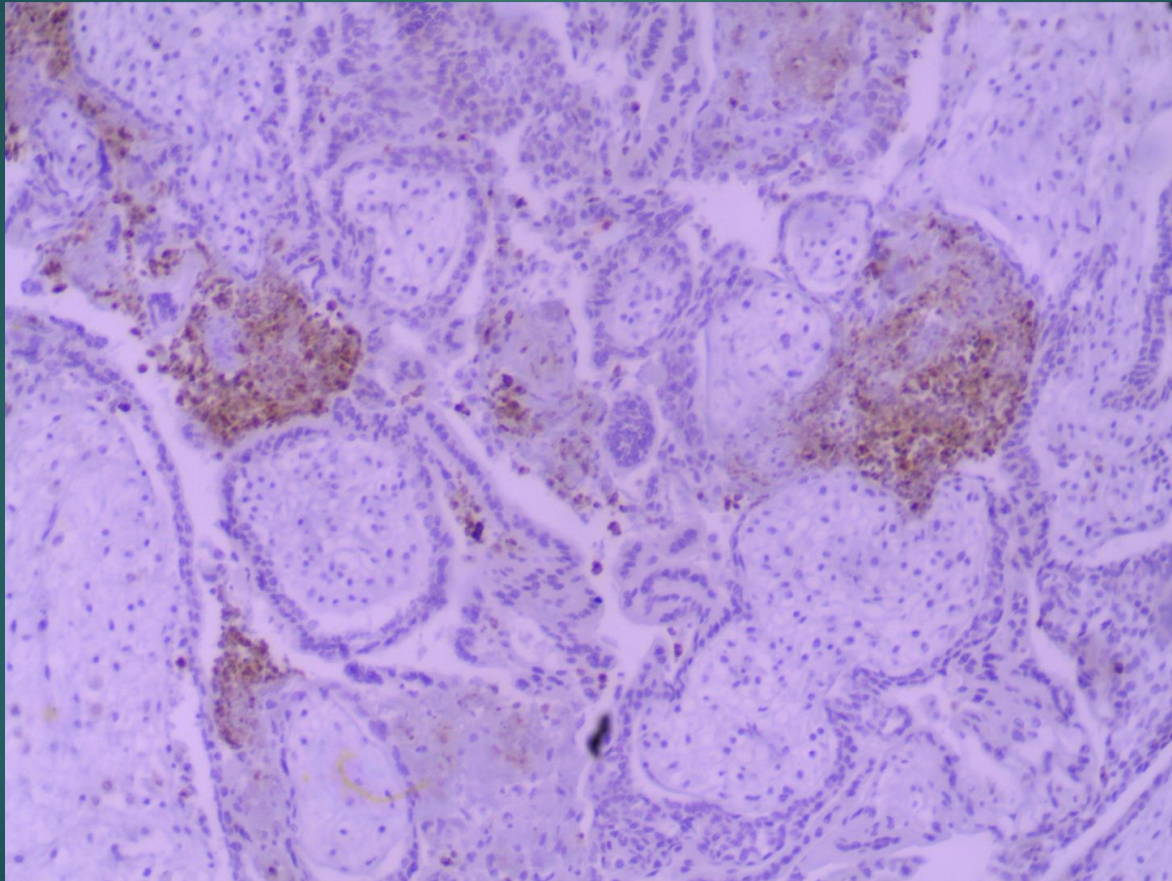
Aneuploidy



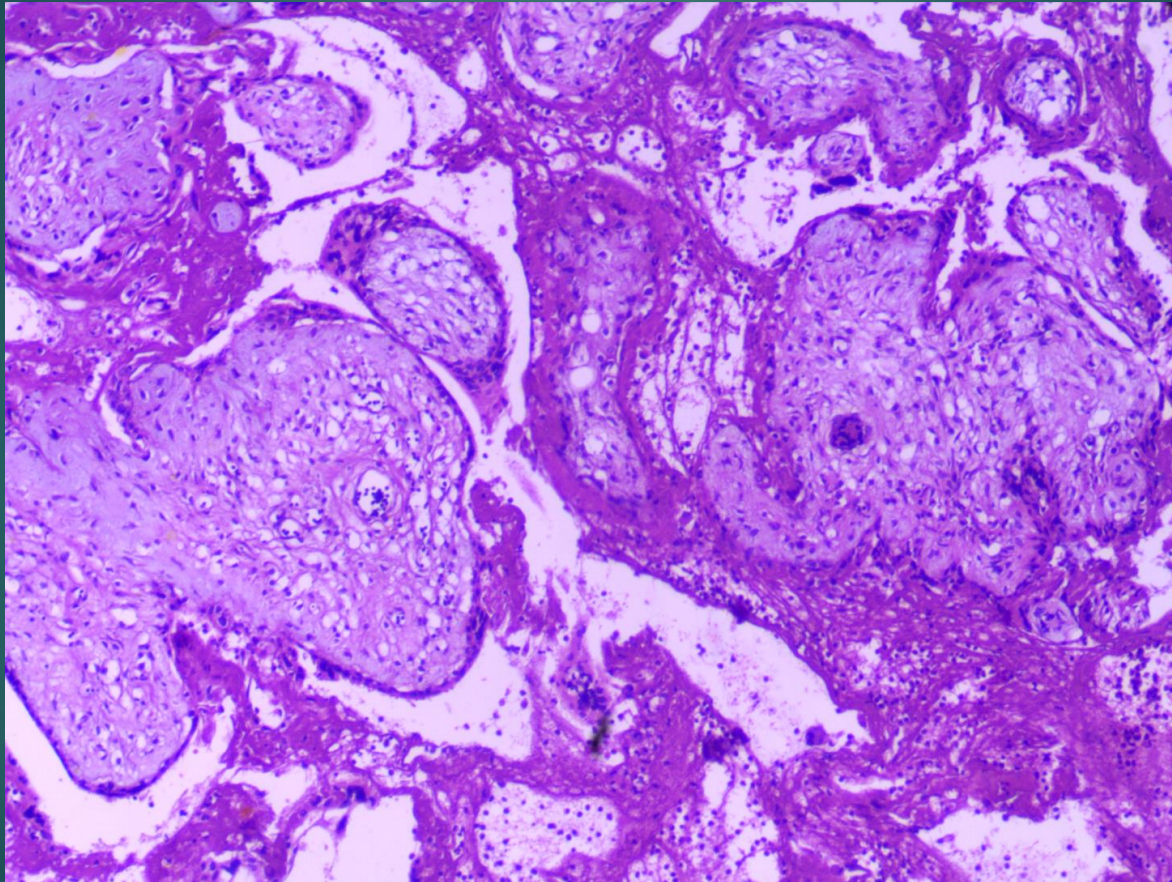
Chronic lymphohistiocytic intervillositis



CD 68



Intervillous fibrin deposition



Results

- ▶ 687 samples
- ▶ Maternal age range was 19-46
- ▶ 116(16.9%) mothers had reported previous alive child
- ▶ The number of previous abortion was between 0-15
- ▶ 117 samples revealed only decidua
- ▶ 570 samples had chorionic villi
- ▶ 352 (63.4%) cases had history of three or more abortions
- ▶ 18.8% of this group showed CIUE and 8.5% revealed IFD

Conclusion

- ▶ 27.3% had a recurrent pathology
- ▶ History of a live child was significantly higher in CIUE group than others.
- ▶ Histological evaluation was not sufficient for definite diagnosis of chromosomal abnormalities.
- ▶ 29% out of 295 cases who had a chromosomal evaluation revealed a chromosomal abnormality.

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- ▶ Significant percent of CIUE group (33.3%) had a history of a live child whereas this percentage was 14.8% in non-CIUE groups

Conclusion

- ▶ In referral centers
- ▶ In patients with higher previous abortions
- ▶ In patients with a live child

Histological evaluation of products of conception is
more important

