Reproductive Pathology What is new?

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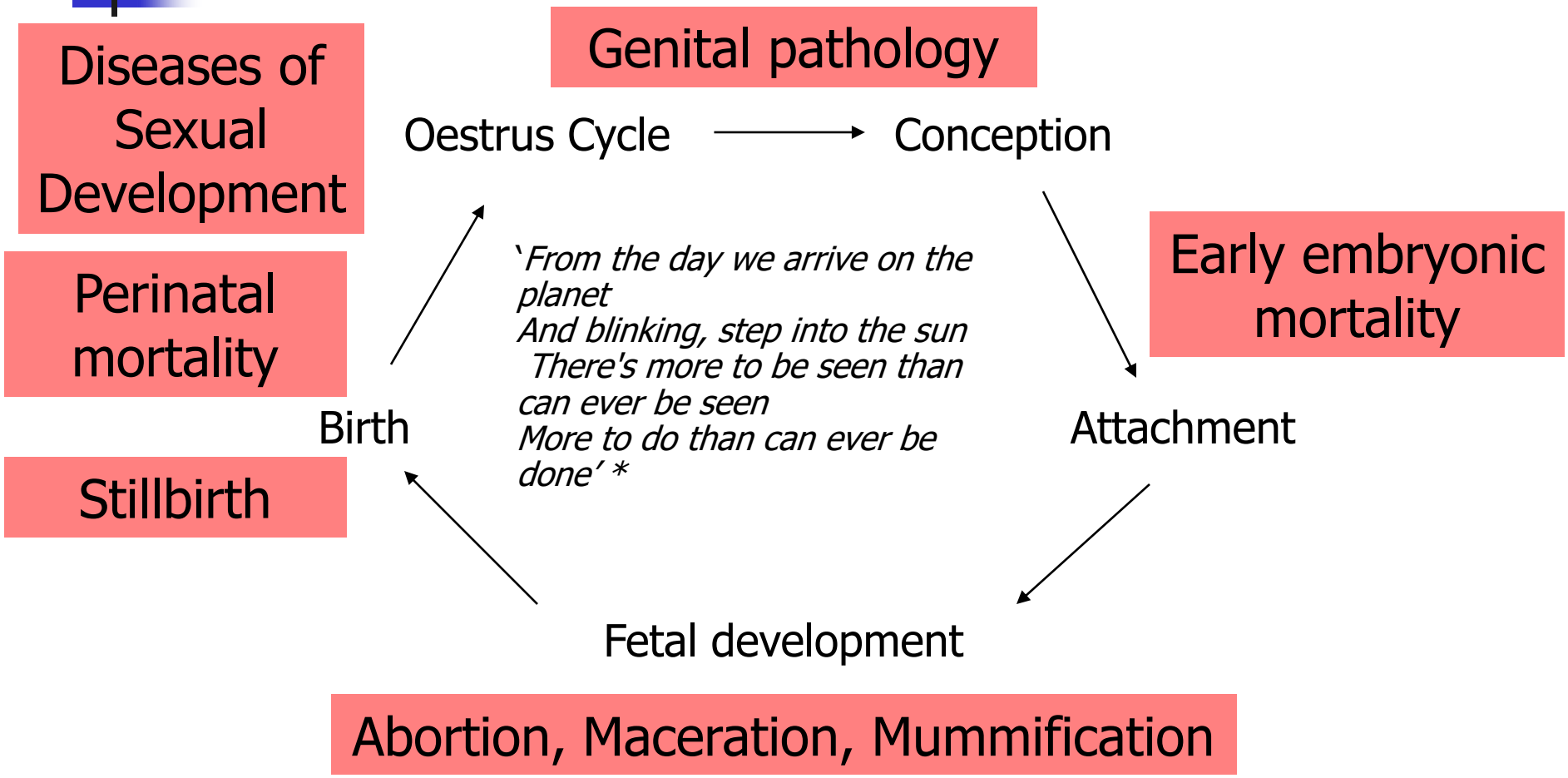
Sponsors

- Australian Animal Pathology Standards Program
  - Australian Society for Veterinary Pathology
  - Subcommittee on Animal Health Laboratory Standards
  - Animal Health Australia
- CL Davis Foundation

The Circle of Life*



* "Circle of Life" Music by Elton John, lyrics by Tim Rice, Performed by Elton John

Day 1 – Production animals

Bovine

Ovine

Caprine

Porcine

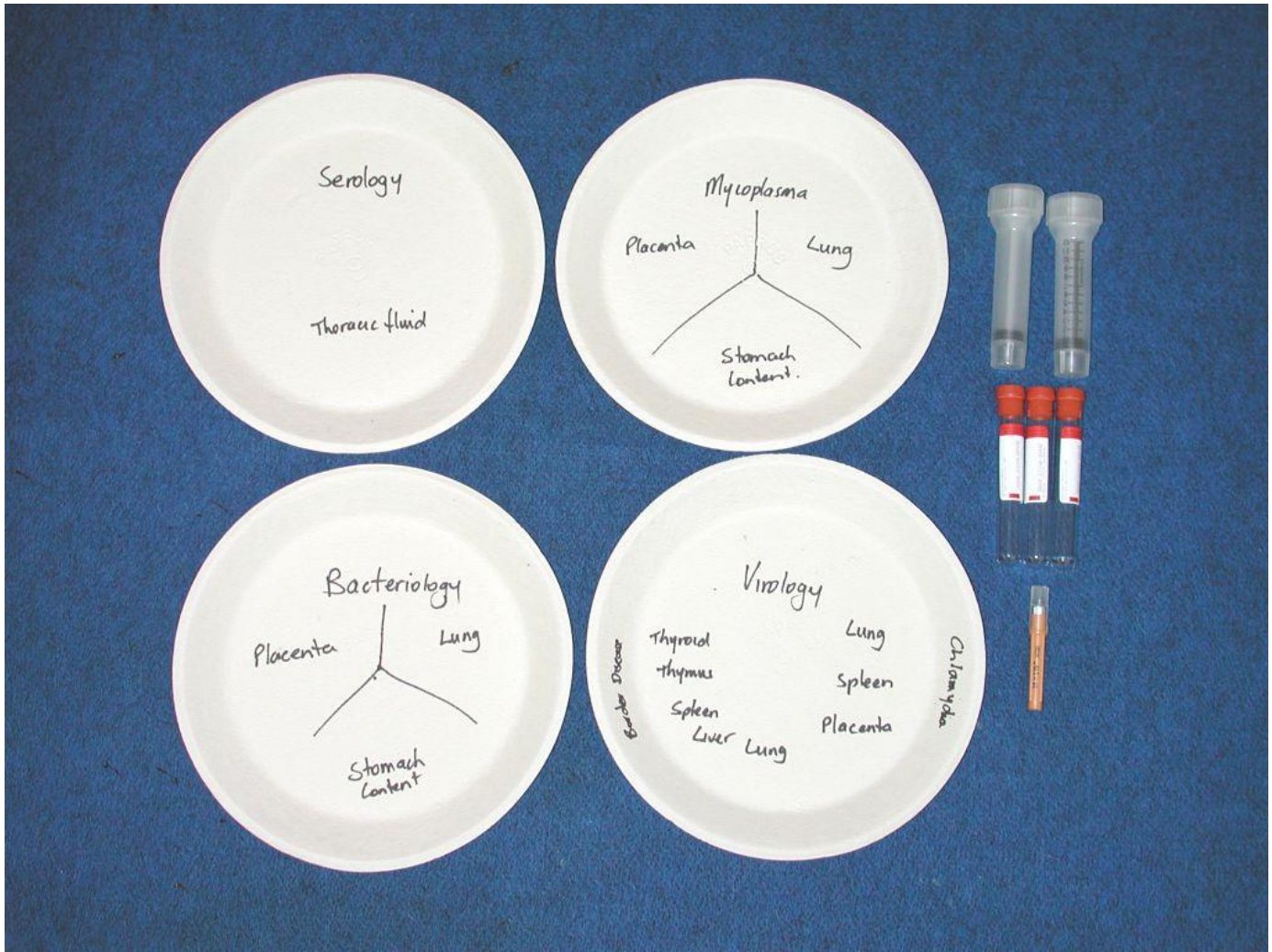
Failure of Pregnancy

The trilogy

Infectious
Non infectious
Unknown

Mother
Foetus
Placenta

Pragmatic approach



Practical approach

Results of investigation of fetus and placenta (sporadic)

Species	No Dx (%)	Infection
Cattle	58	42
Sheep	55	40
Goats	52	40
Pigs	72	28

Why the low rate

- Selection of cases to submit
  - Sporadic
  - Outbreaks
- Samples (or lack thereof)
- Laboratory challenges

- Physiology

Do pathologists have a role?

- 'Why are you involved, this is a herd health/epidemiology/microbiology problem'
- Herd approach
  - Males are expendable
- Define the disease

The awakening

- Failure is not a bad thing
- Put on a positive spin.
- Expectation, expectation, expectation (prognosis)

Conception

Estrus activity

Mating

Fertilization

Postpartum subclinical endometritis of dairy cattle

- Cytology
  - Steven Leblanc
  - Ram Kasimanickam et al
  - Cyril Stephen
- Uterine biopsy

General microbial environment

- Sterile environment
  - Ovaries
  - Uterine tubes
  - Uterus
  - Cervix
- Contamination
  - Cranial vagina
  - Caudal vagina
  - Vulva

Specific pathogens acquired

- *Campylobacter fetus*
- *Tritrichomonas foetus*
  - mummification
- *Ureaplasma*
  - Amnionitis
  - Plante, Ruhnke, Miller
- *Chlamydophila*
  - Papp, Halbert, Shewen
- Viruses

- Low pathogenicity/toxicity

Defences

- Innate
  - Conformation
  - Barrier
    - Cervical barrier
    - Epithelium
  - Uterine tone, contraction and secretions
  - Microbial Pattern Recognition Receptors (PRR) and Pathogen associated Molecular Patterns (PAMP)
    - TLR, β-defensins
  - Neutrophils and macrophages
  - Compliment
  - Cytokines
- Adaptive
  - Humoral
  - Cell mediated

Telma da Mata Martinsa, Tatiane Alves da Paixãob, Érica Azevedo Costaa, Alexandre de Carvalho Pires a, Renato Lima Santosa, Alan Maia Borgesa (2011) Postpartum toll-like receptors and B-defensin 5 mRNA levels in the endometrium of Holstein cows. Veterinary Immunology and Immunopathology 139 (2011) 277–281

Conceptus enters uterus

- Cow day 3
- Sow day 2

- Defences have time to deal with uterine environment

Maternal recognition of pregnancy

- Bovine
  - IFN-t is anti-PGF.
  - Luteostasis inhibits oxytocin production by CL
- Pig
  - Progesterone is continuously produced
  - Fetal estrogens, ↑PGE2/PGF2 ratio
  - Oxytocin secreted by endometrium

AJ Ziecik, A Waclawik, MM Kaczmarek, A Blitek, B Moza Jalali and A Andronowska (2011) Mechanisms for the Establishment of Pregnancy in the Pig. Reprod Dom Anim 2011 46 (S3); 31-44

Placental attachment

Cow day 16

Pig day 13

Pregnancy is a paradox

Foetus is an allograft
Placenta attaches, it doesn't implant

Kristen Lackey

Placenta

- Great immunological importance
  - transfer of antibodies
  - tolerance
  - regulation of foetal development
  - release of cytokines
  - many lymphocytes and immune cells
- Inflammatory cells and cytokines used to maintain pregnancy

T.M. Chucri, J.M. Monteiro, A.R. Lima, M.L.B. Salvadori, J.R. Kfoury Junior, M.A. Miglino. 2010. A review of immune transfer by the placenta. J Reprod Immunol 2010 87: 14-20

Placenta

- Protection
- Nutrition
- Respiration
- Endocrine control.

G. Schuler, H. Greven, M. P. Kowalewski, B. Döring, GR Özalp , B Hoffmann (2008). Placental steroids in cattle: hormones, placental growth factors or by-products of trophoblast giant cell differentiation? Exp Clin Endocrinol Diabetes 2008 116 429-437

Antibody transfer

- All – 0
- Transfer if placentitis
- Requires colostrum
- Failure of passive transfer.

Immune tolerance

- Fetus is genetically different
  - Inert
  - Immune modification
- Transfer of cells, nutrients and wastes between mother and fetus
- Uterus is temporarily immune privileged
- No agreement as to how.

Hansen PJ (2011) The Immunology of Early Pregnancy in Farm Animals. Reprod Dom Anim 2011 46 (S3): 18-30

Trophoblast is key

- Effective foreign object

- MHC 1 expression
- Fas/Fas ligand system
  - Apoptosis of activated immune cells expressing Fas (trophoblasts have FasL)
- Indoleamine 2,3-dioxygenase
  - Degrades tryptophan, inactivates T cells
- What about the NK cells?

Placenta - human/primate speak

- 'A flat cake' = disc
- 'Membranes' are a different structure

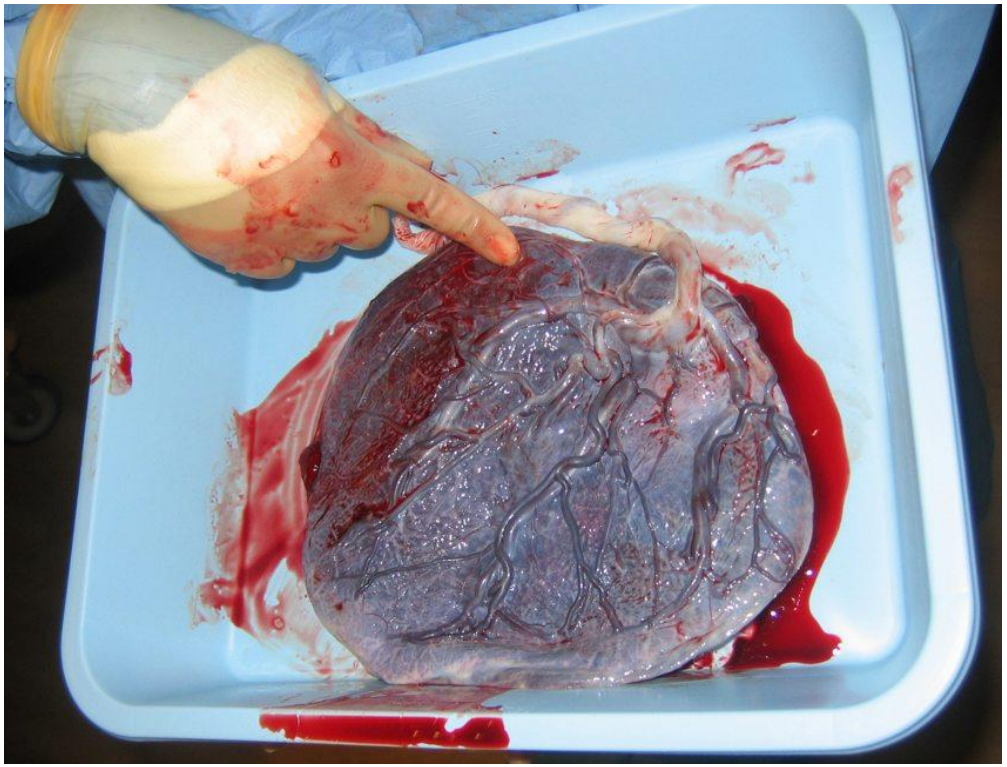
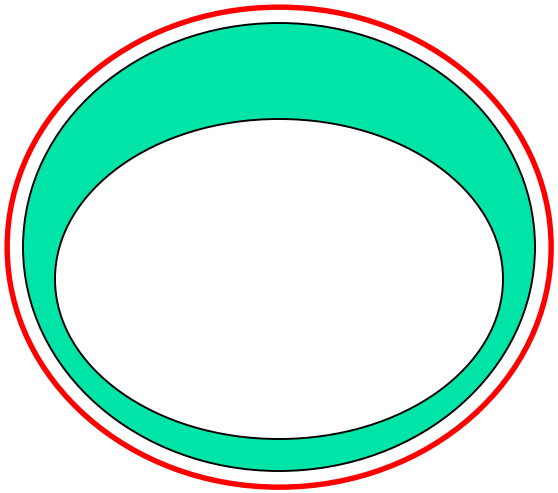


Photo complements of common.wikimedia.org

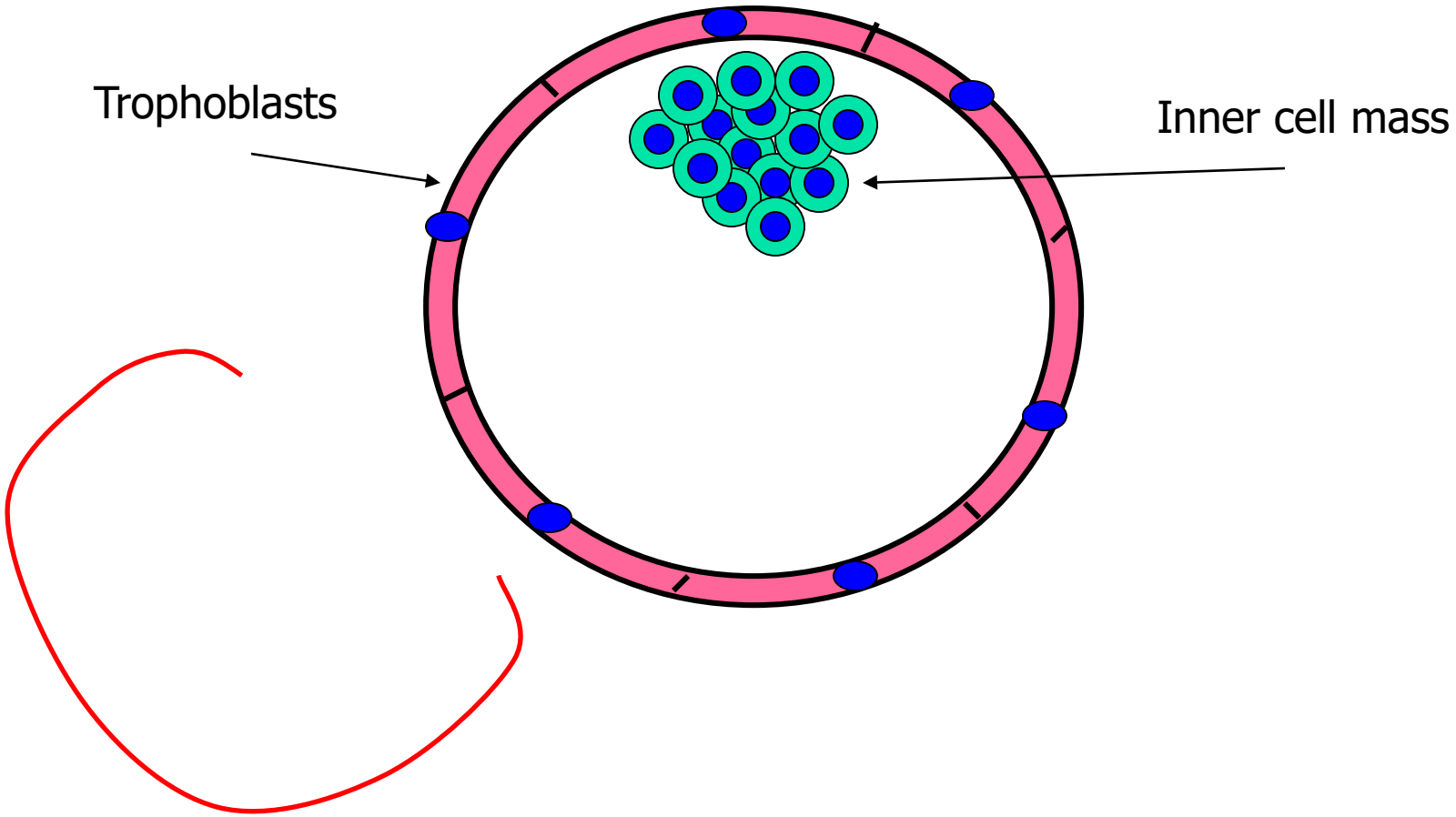
Basic embryology



blastocyst

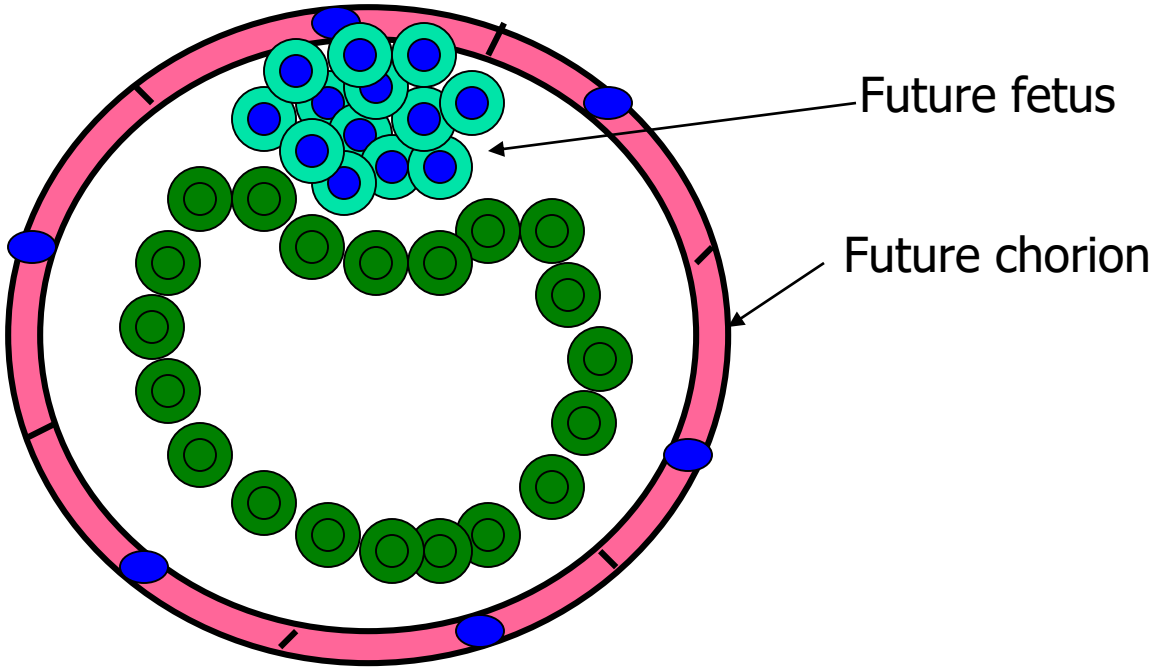
Formation of Chorion

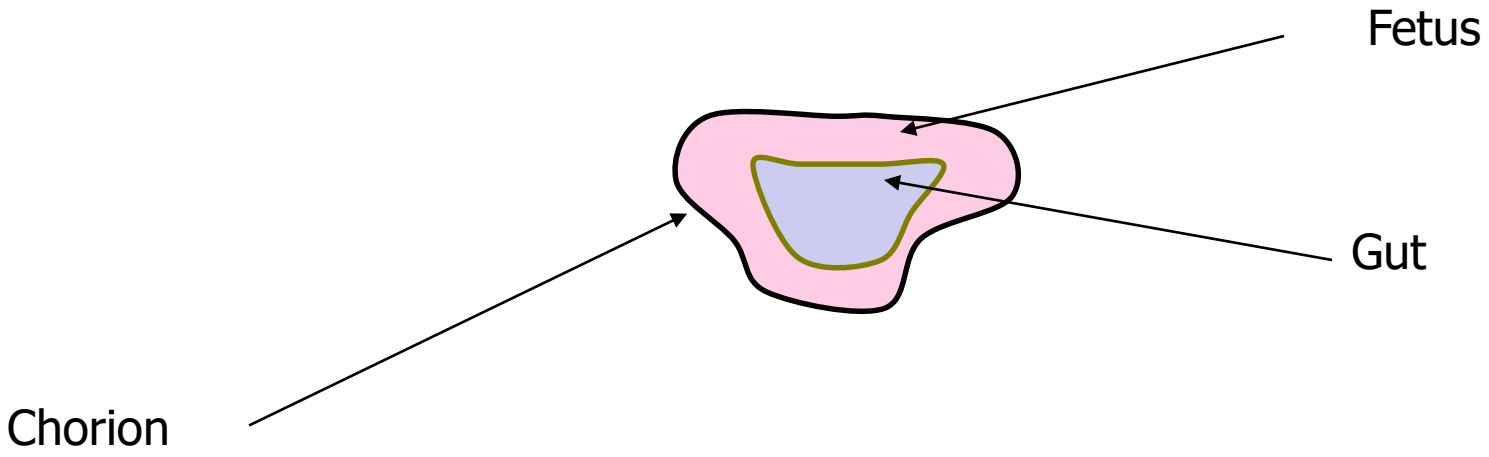
Trophoblasts (and mesoderm) form Chorion



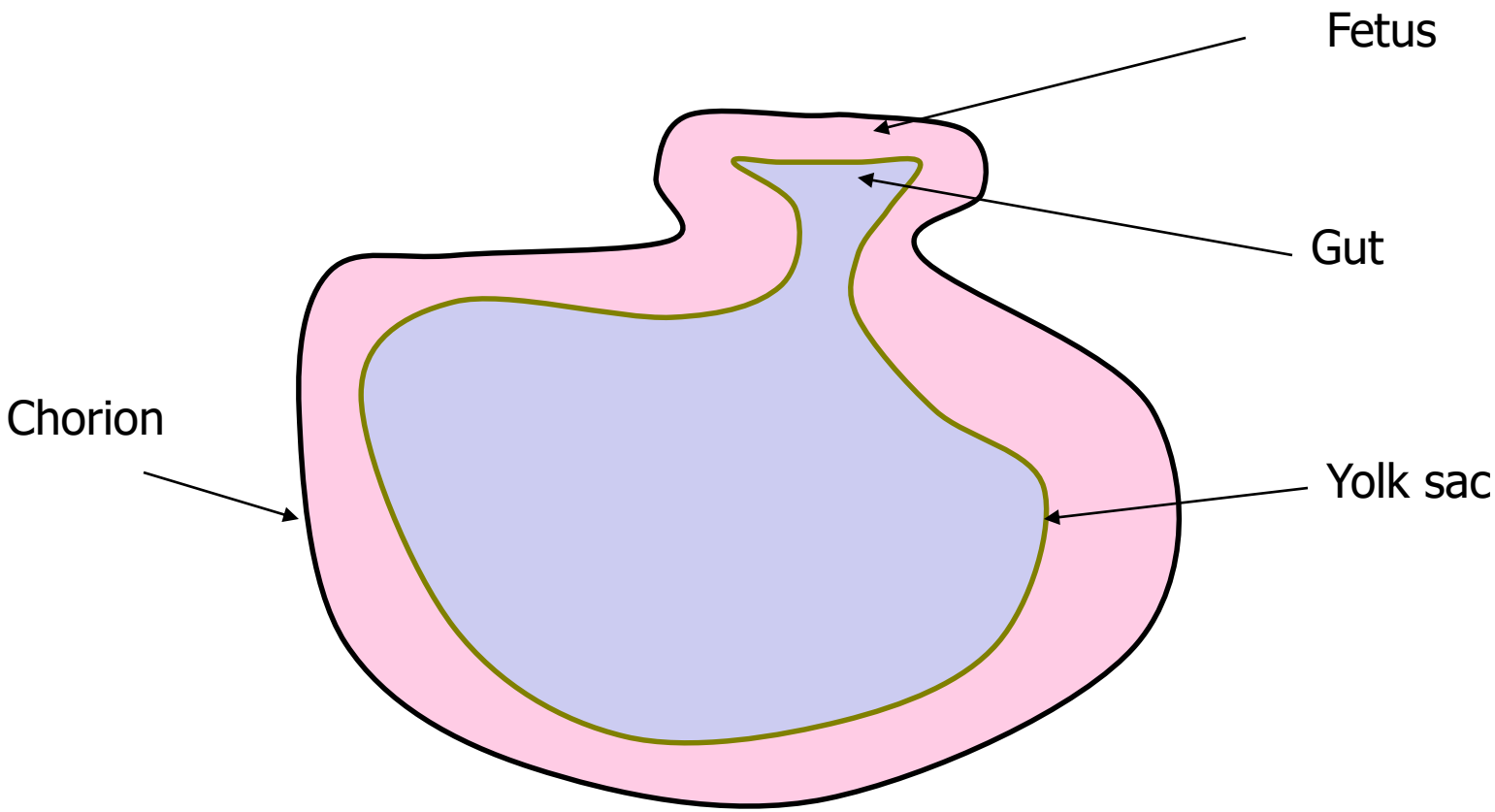
Formation of endoderm

- Endoderm = gut + yolk sac

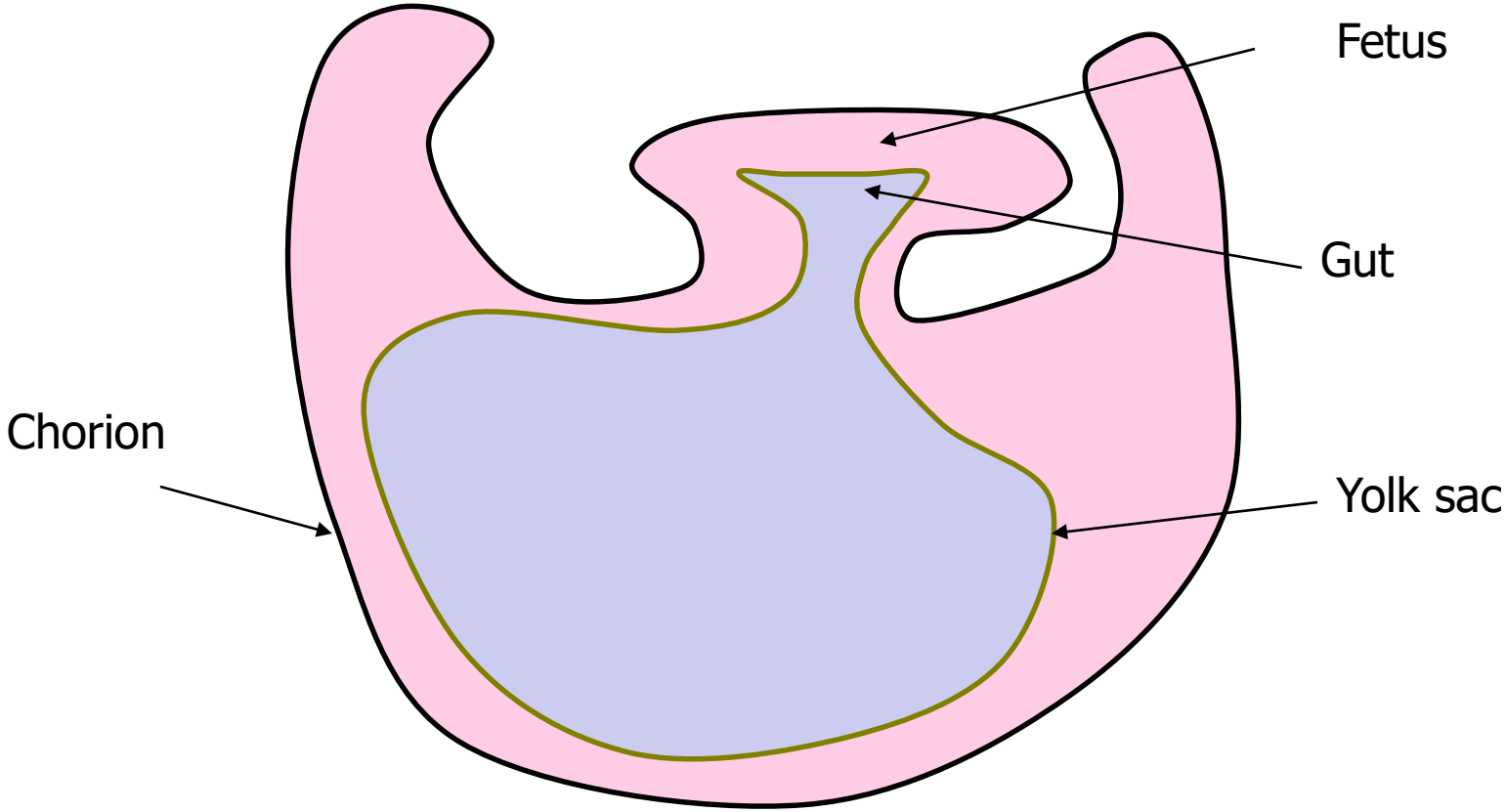



Fetus
Gut
Chorion

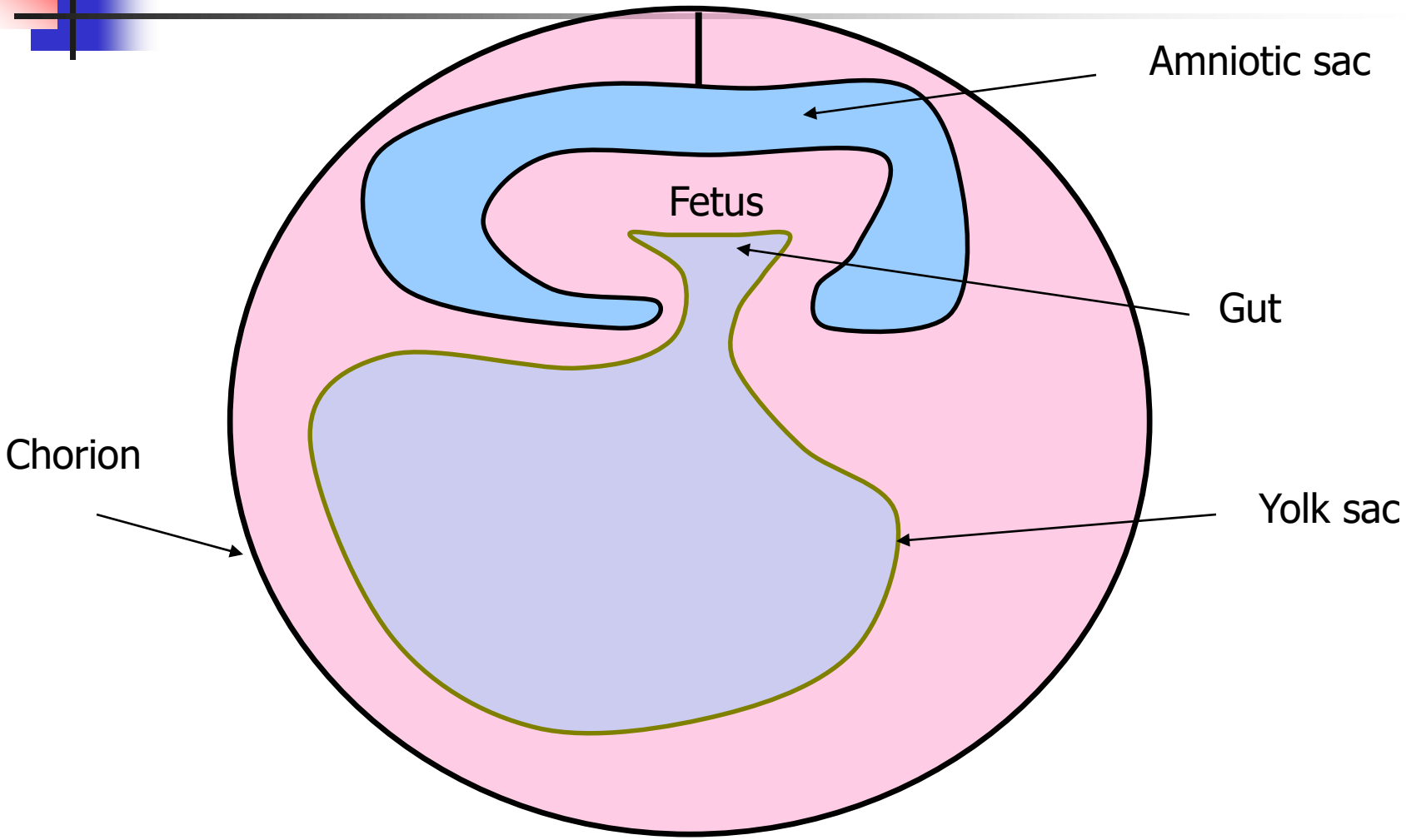
Formation of Yolk sac



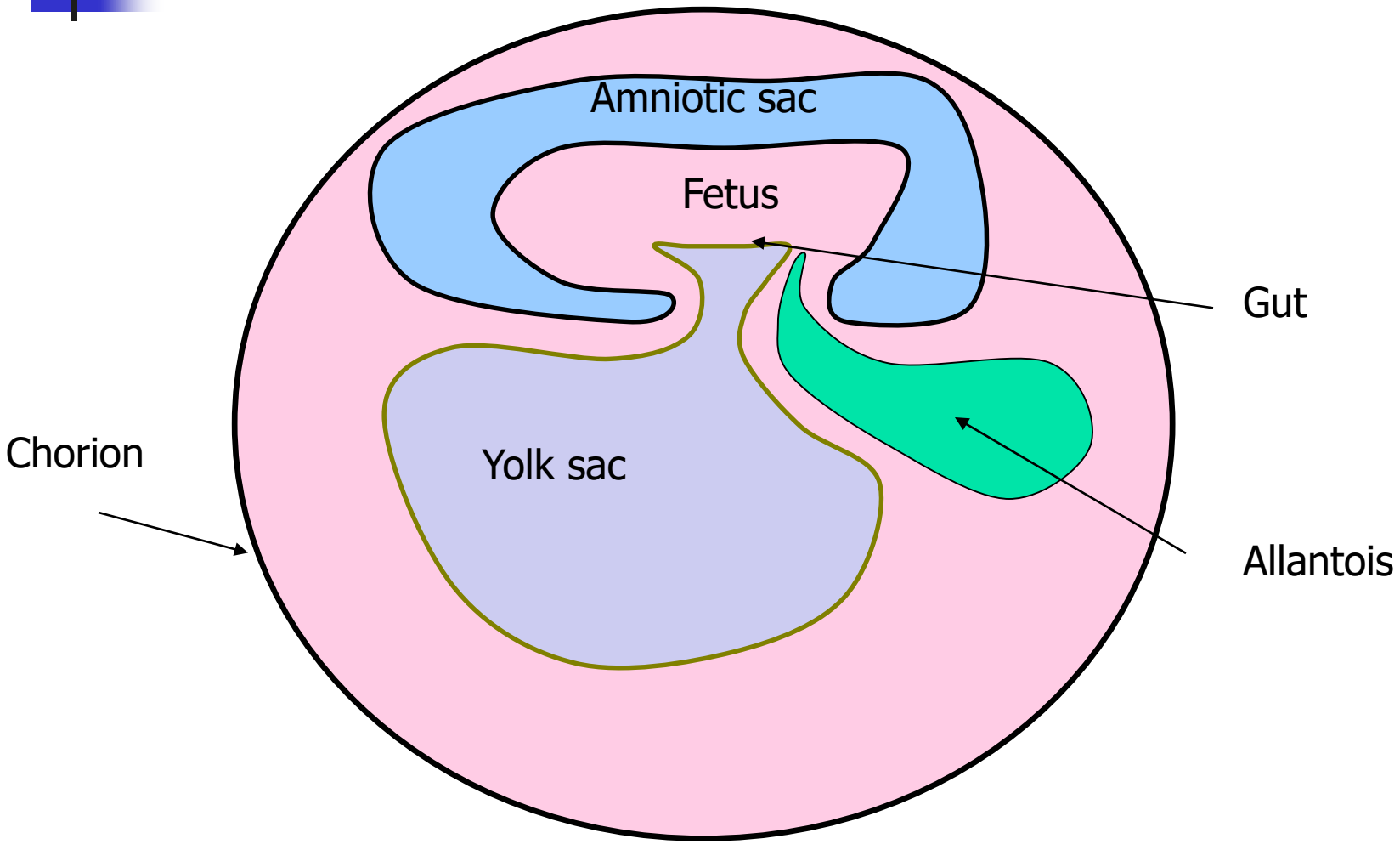
Formation of Amnion



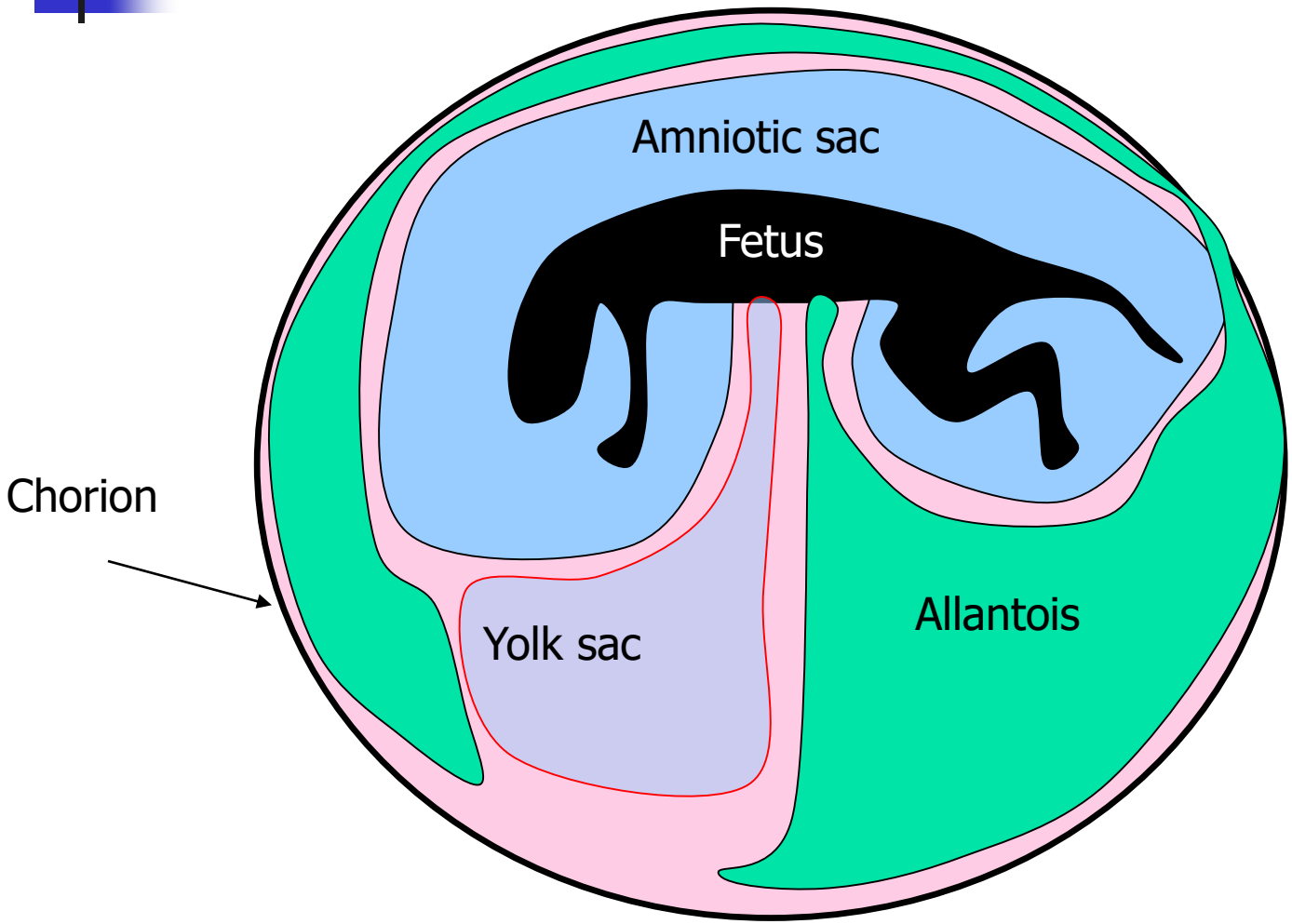
Formation of amnion



Formation of allantois

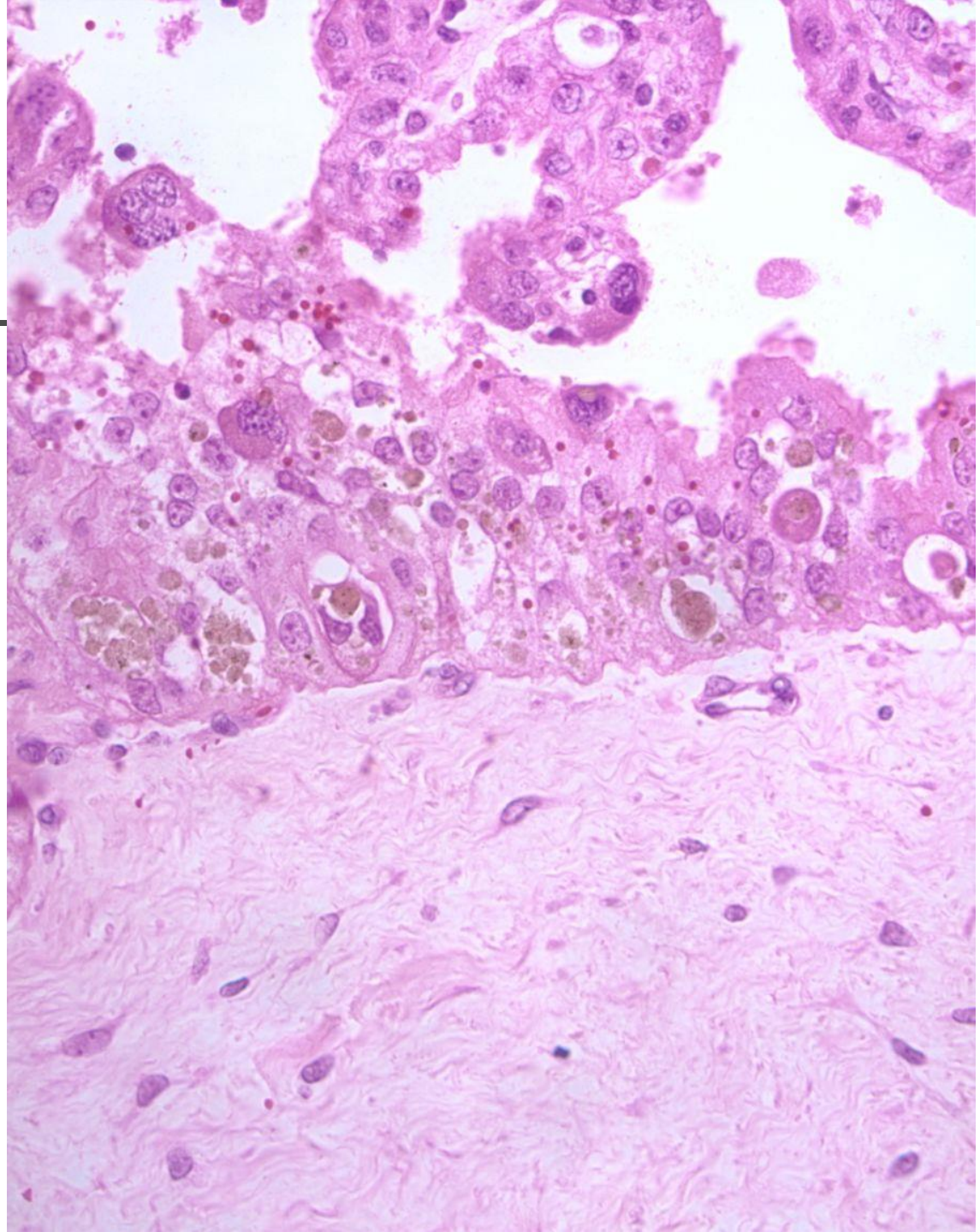


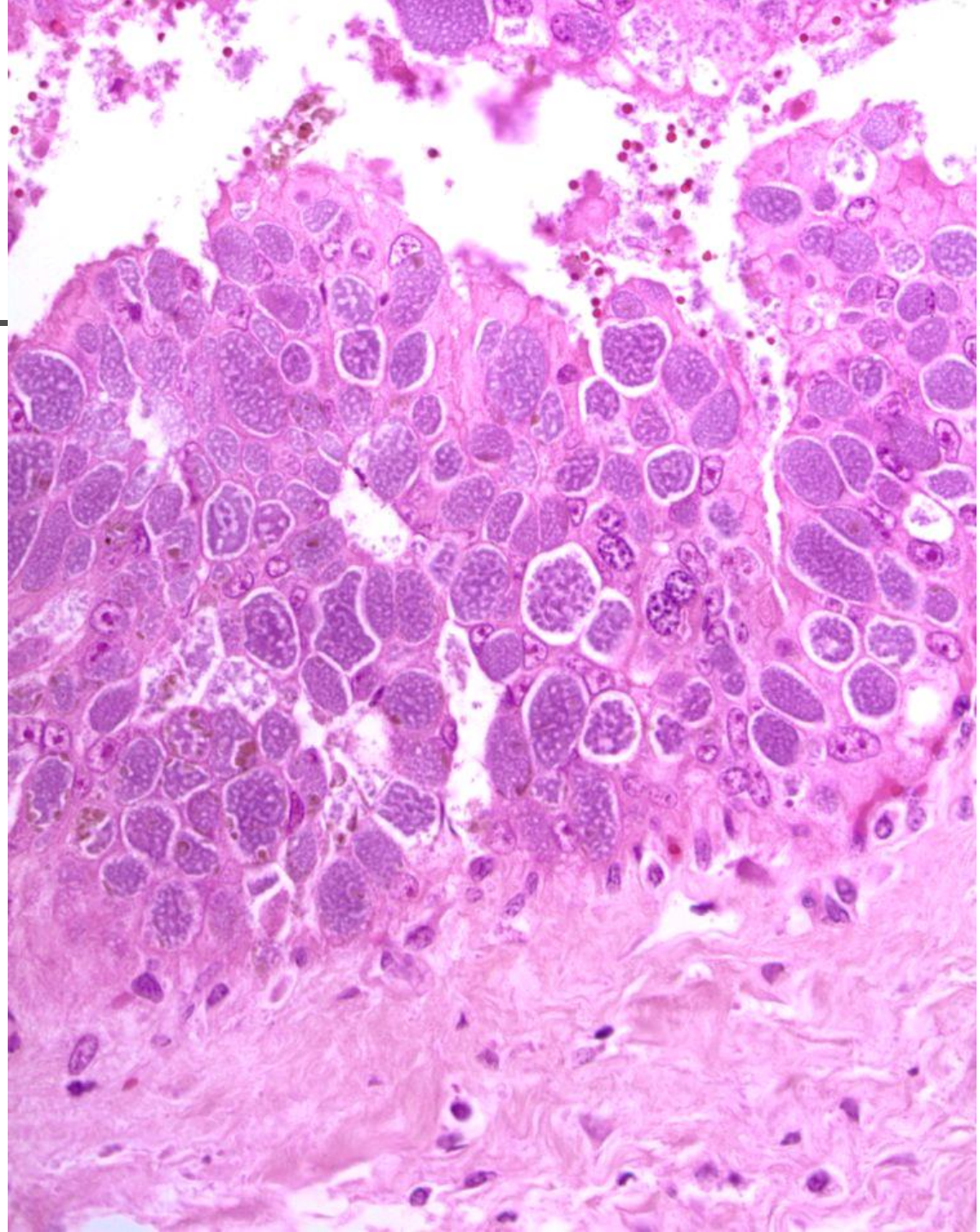
Formation of allantois



Trophobasts

- Recognition of pregnancy
  - Bovine trophoblasts release IFN-t that inhibit COX-2 expression and therefore $PGF_{2\alpha}$ release – luteotrophic.
- Immune barrier
- Phagocytic
  - Histotrophic nutrition
    - Hemophagic 'organ'
  - Brucella abortus
  - Placentitis.





Uteroplacental unit

- Cytokine balance
- Prostaglandins $F_{2\alpha}$, E
- Macrophages
- NK cells
- T cells

Establishment of pregnancy

- Maternal recognition of pregnancy
- Attachment
- Immune modulation
- Endocrine cross talk

- Embryonic period (cow: 1 - 45 days)
- Foetal period

F Lopez-Gatius, I Garcı´a-Ispierto (2010) Ultrasound and Endocrine Findings that Help to Assess the Risk of Late Embryo/Early Foetal Loss by Non-Infectious Cause in Dairy Cattle. Reprod Dom Anim 2010 45: (Suppl 3)15–24

Failure of pregnancy

Embryonic mortality

Embryonic mortality

- Early embryonic mortality
  - Most are Day 8 – 17 in cattle
- Late embryonic - early foetal
  - 10-12% are prior to day 90, but >20% in high production herds - suboptimal progesterone

- Chromosomal abnormalities
- Living cattle have traits that are heterozygous only!
- Twinning (25% of bovine twins die)
- Summer heat
- Alteration of immune profile.

F Lopez-Gatius, I Garcı´a-Ispierto (2010) Ultrasound and Endocrine Findings that Help to Assess the Risk of Late Embryo/Early Foetal Loss by Non-Infectious Cause in Dairy Cattle. Reprod Dom Anim 2010 45: (Suppl 3)15–24

Failure of Pregnancy

Abortion

Maternal disease

- Systemic disease
  - Cytokine/inflammation
- Stress and luteolysis
- Ischemia/hypoxia
- Hyperthermia

Infectious Failure of Pregnancy

Infection

Not all agents are as 'pathogenic' as we might expect.

Inflammation

This is more important than we think!

Alcina V. Carvalho Neta , Juliana P.S. Mol, Mariana N. Xavier, Tatiane A. Paixão, Andrey P. Lage, Renato L. Santos. (2010) Pathogenesis of bovine brucellosis. The Vet J 2010; 184:146–155

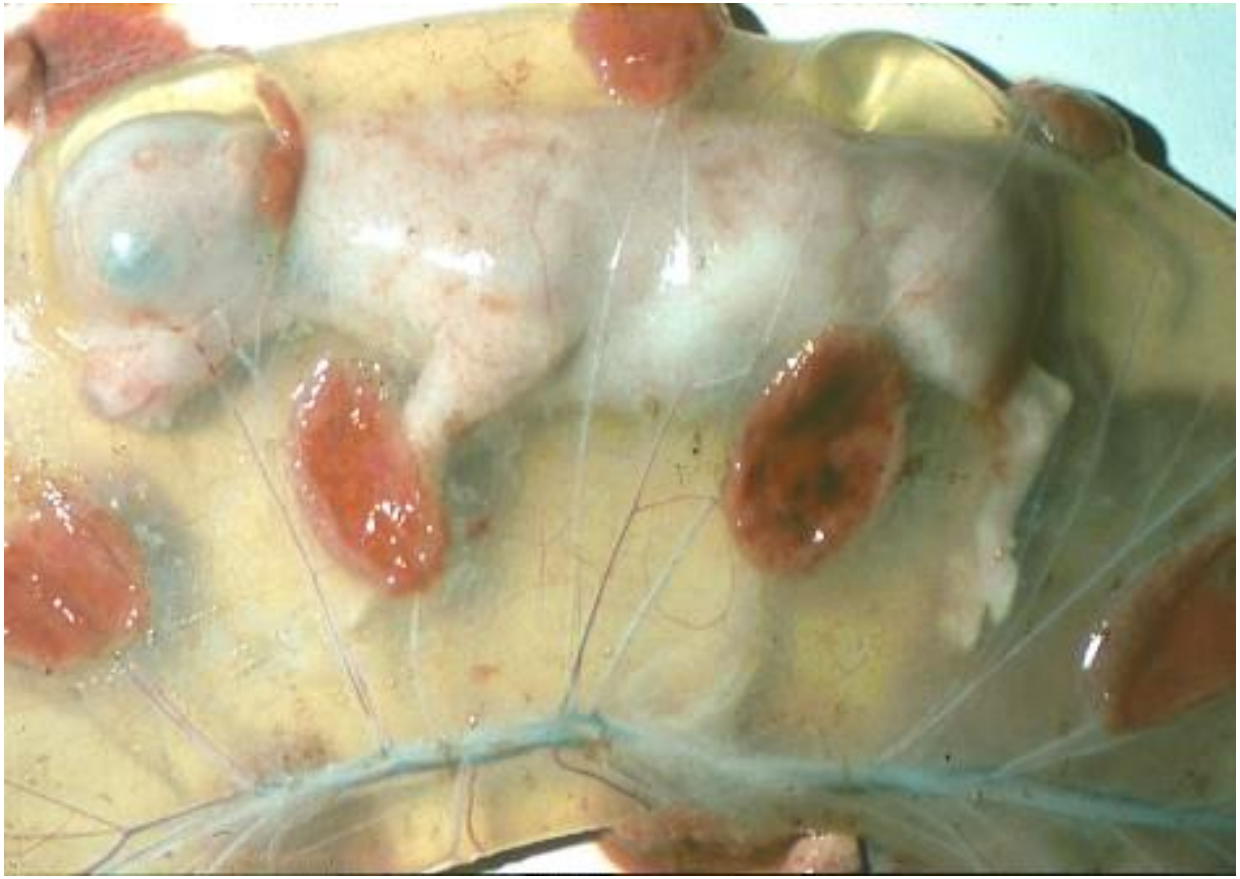
Infectious FOP: routes of infection

- Ascending at mating
  - STI's
    - Tritrichomonas
    - Ureaplasma diversum
- Ascend from vagina (not in ruminants and pigs)
- Descending from ovary
  - BVDV
- Hematogenous
  - Herpesvirus
  - Campylobacter
  - Toxoplasma

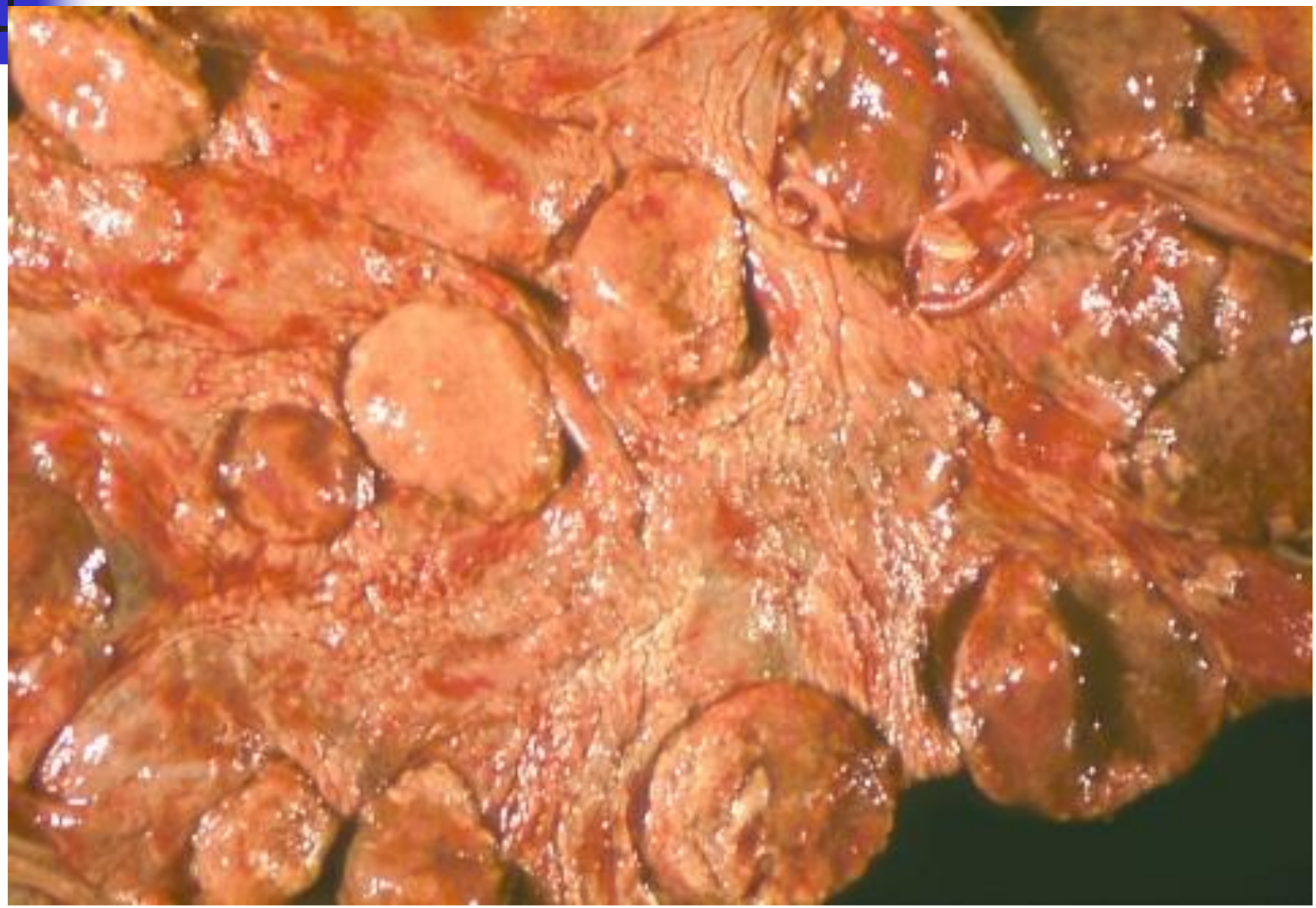
Normal uterus

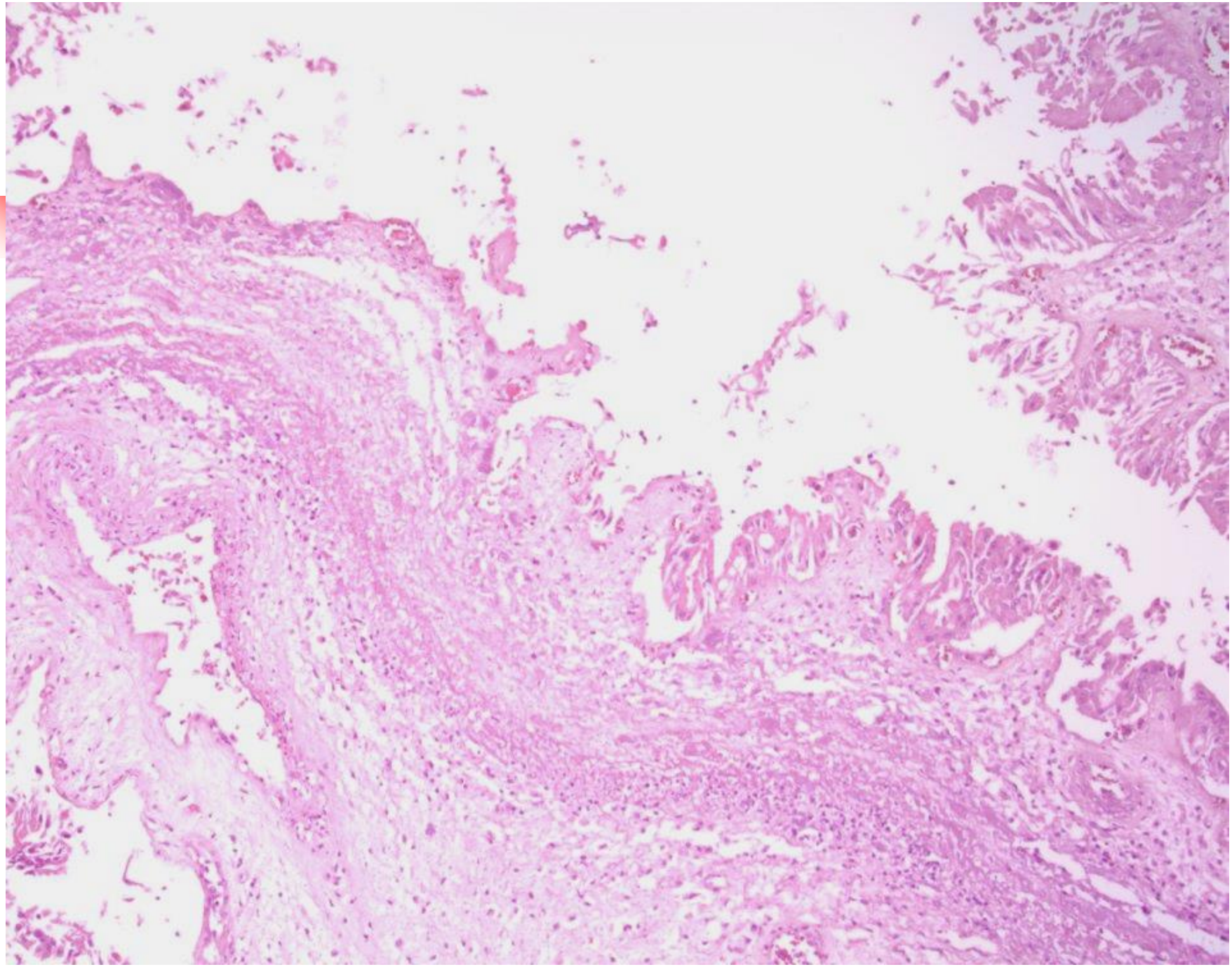
Normal uterus

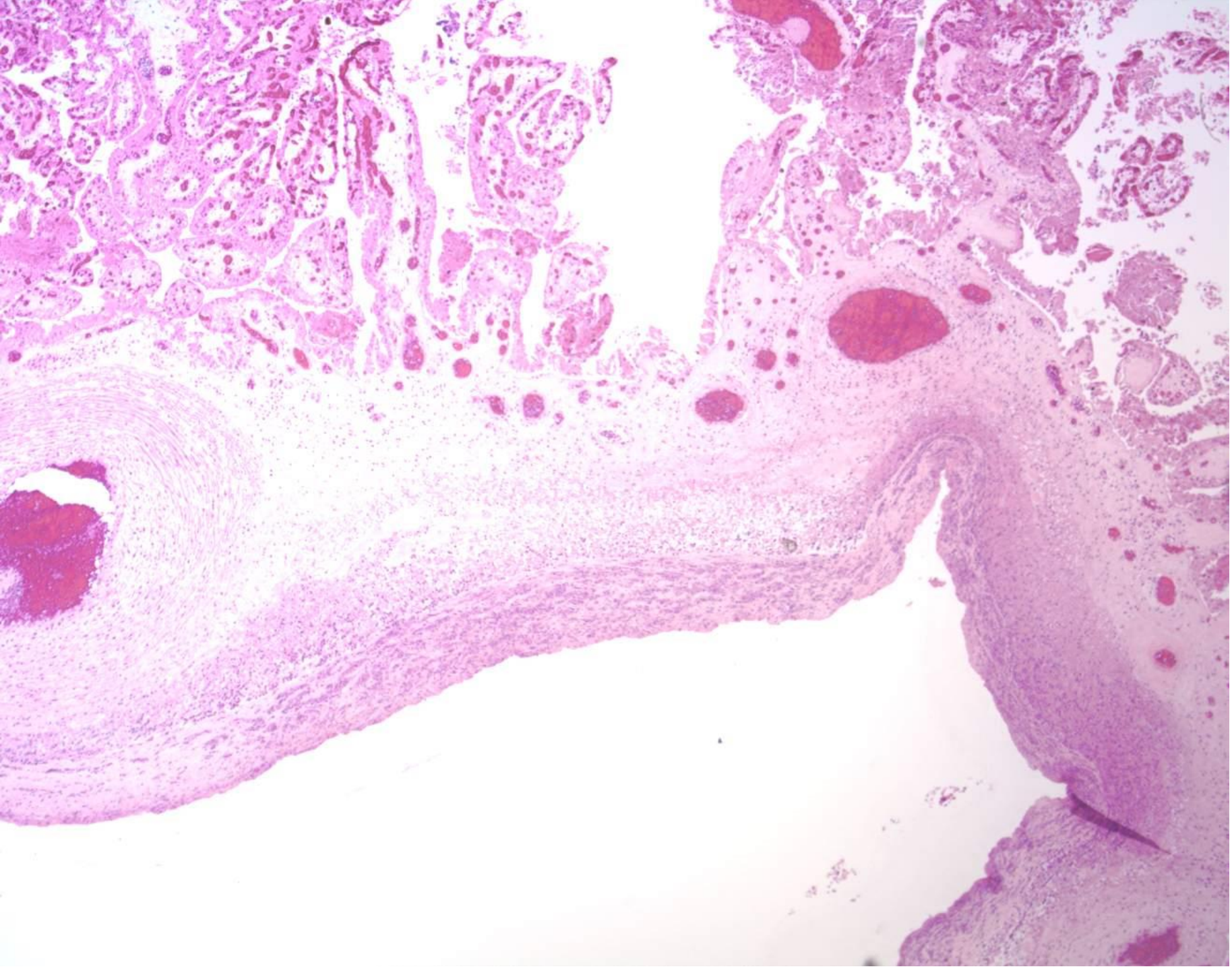
Normal Chorionic surface

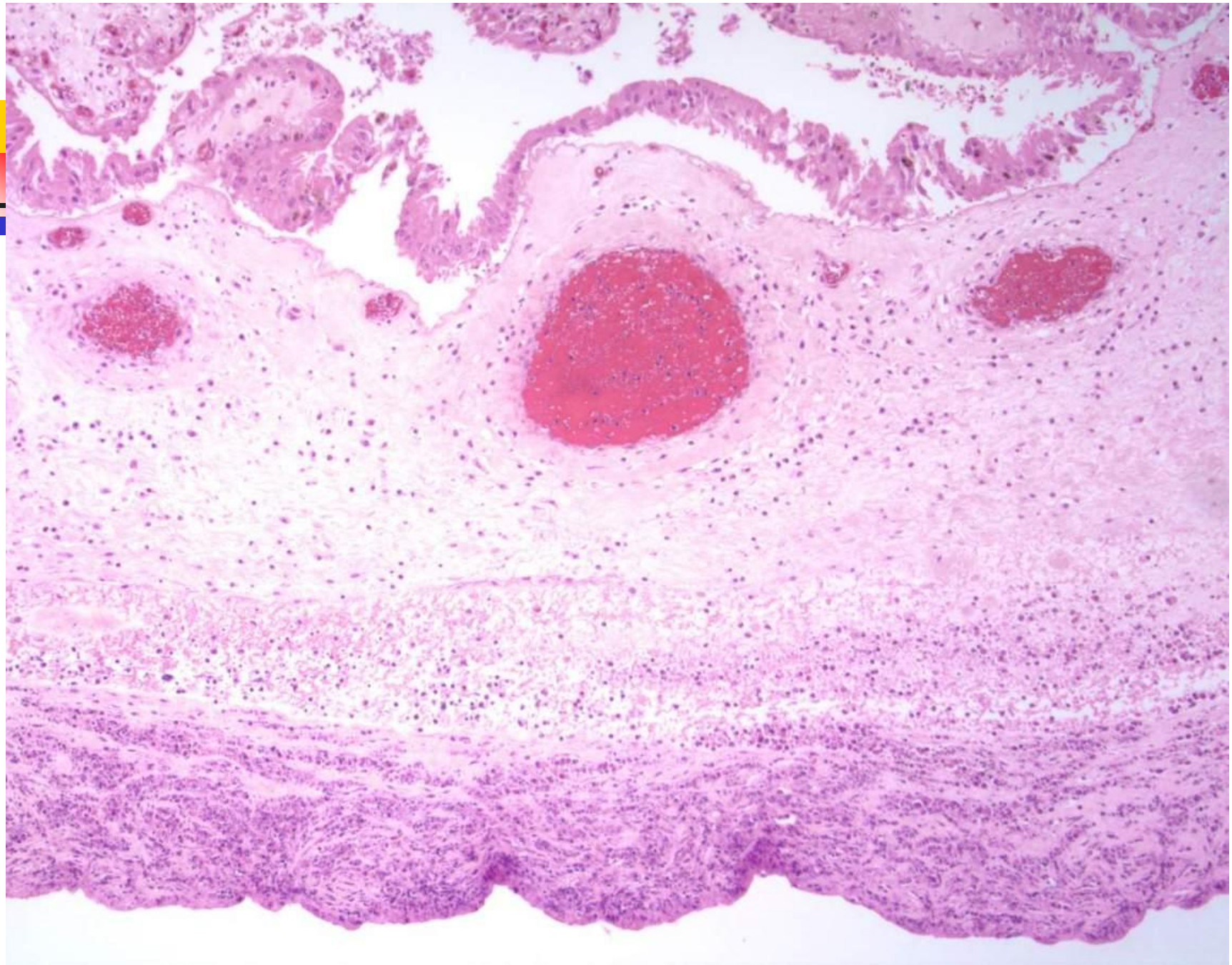


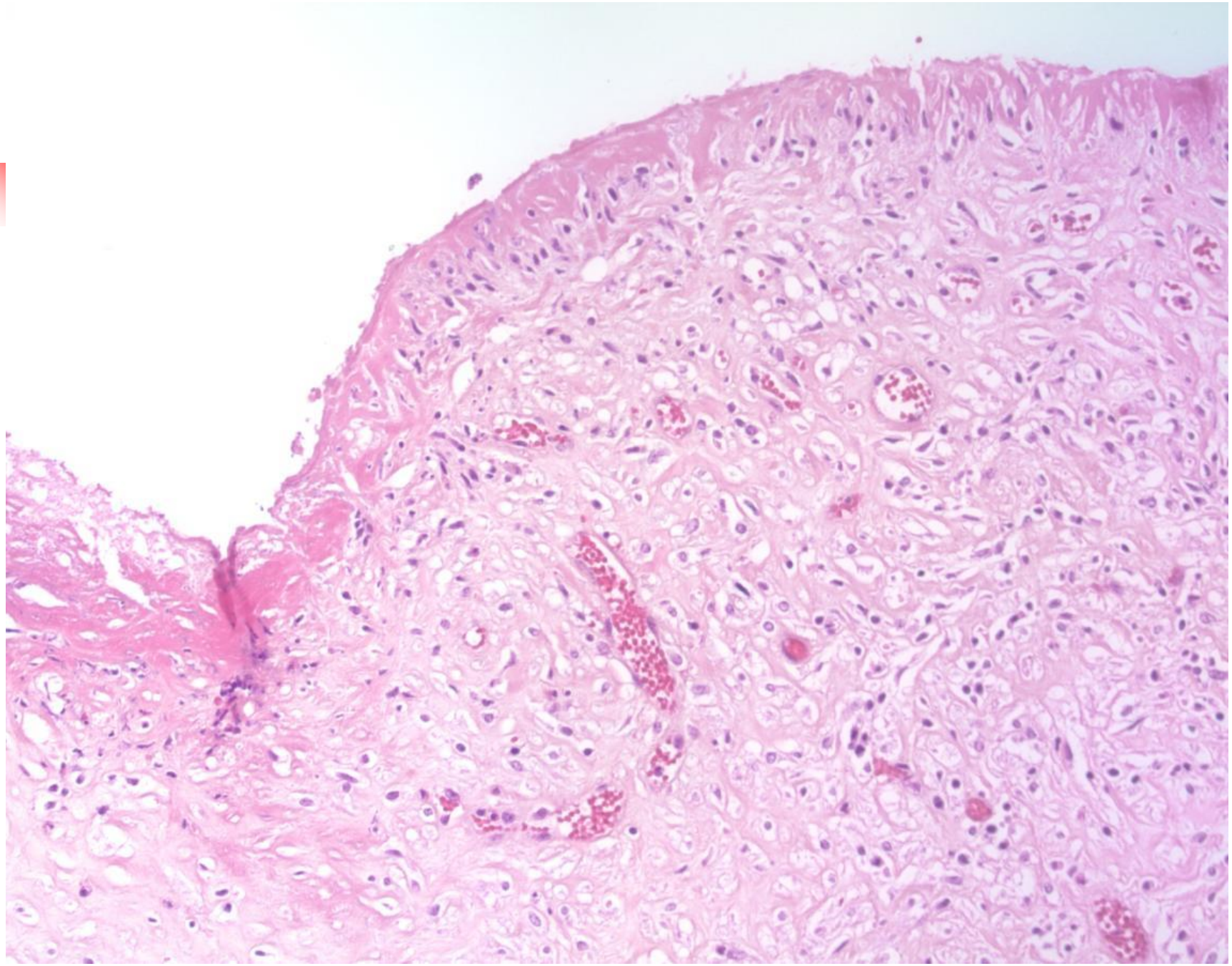
Placentitis







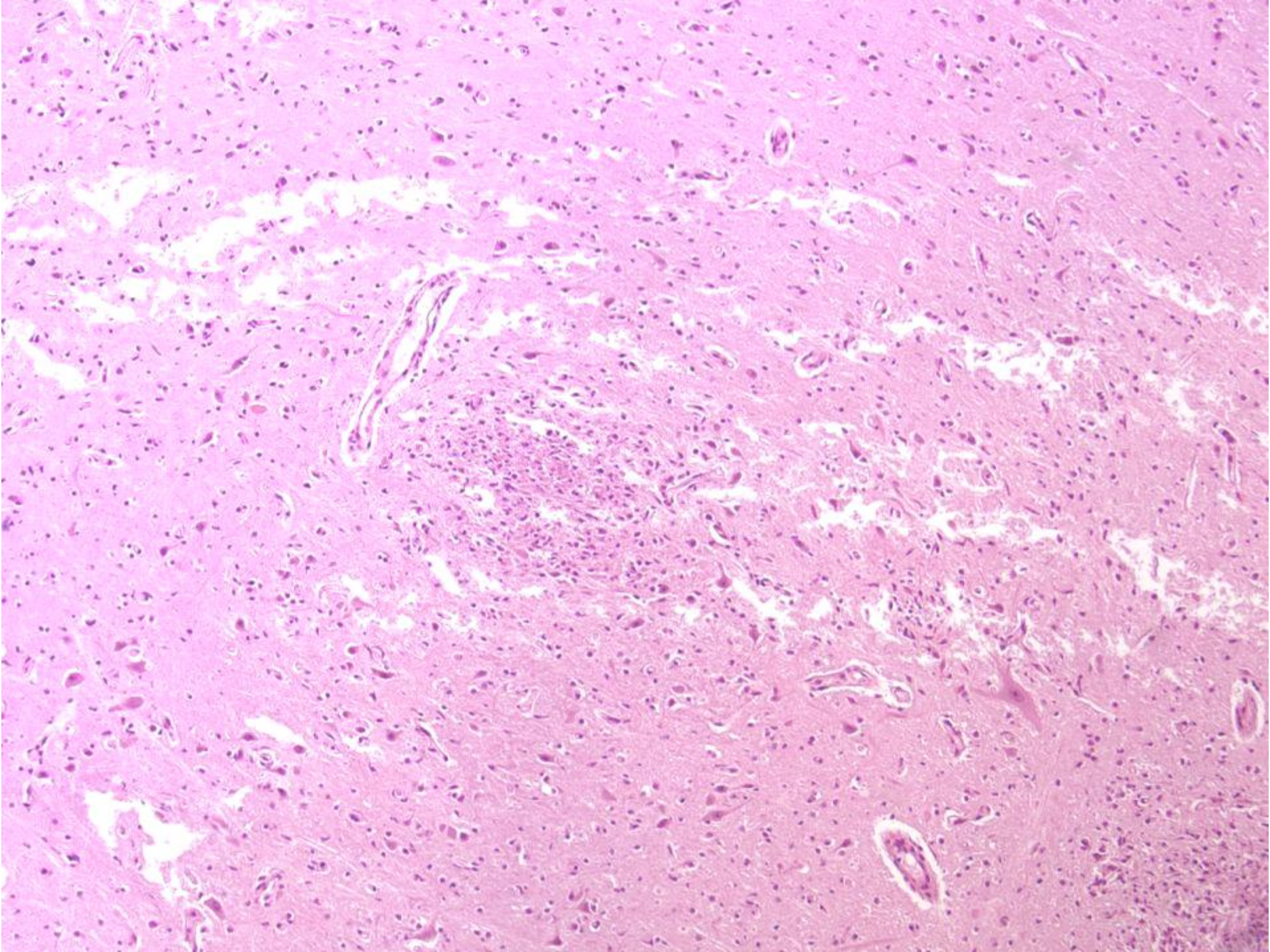


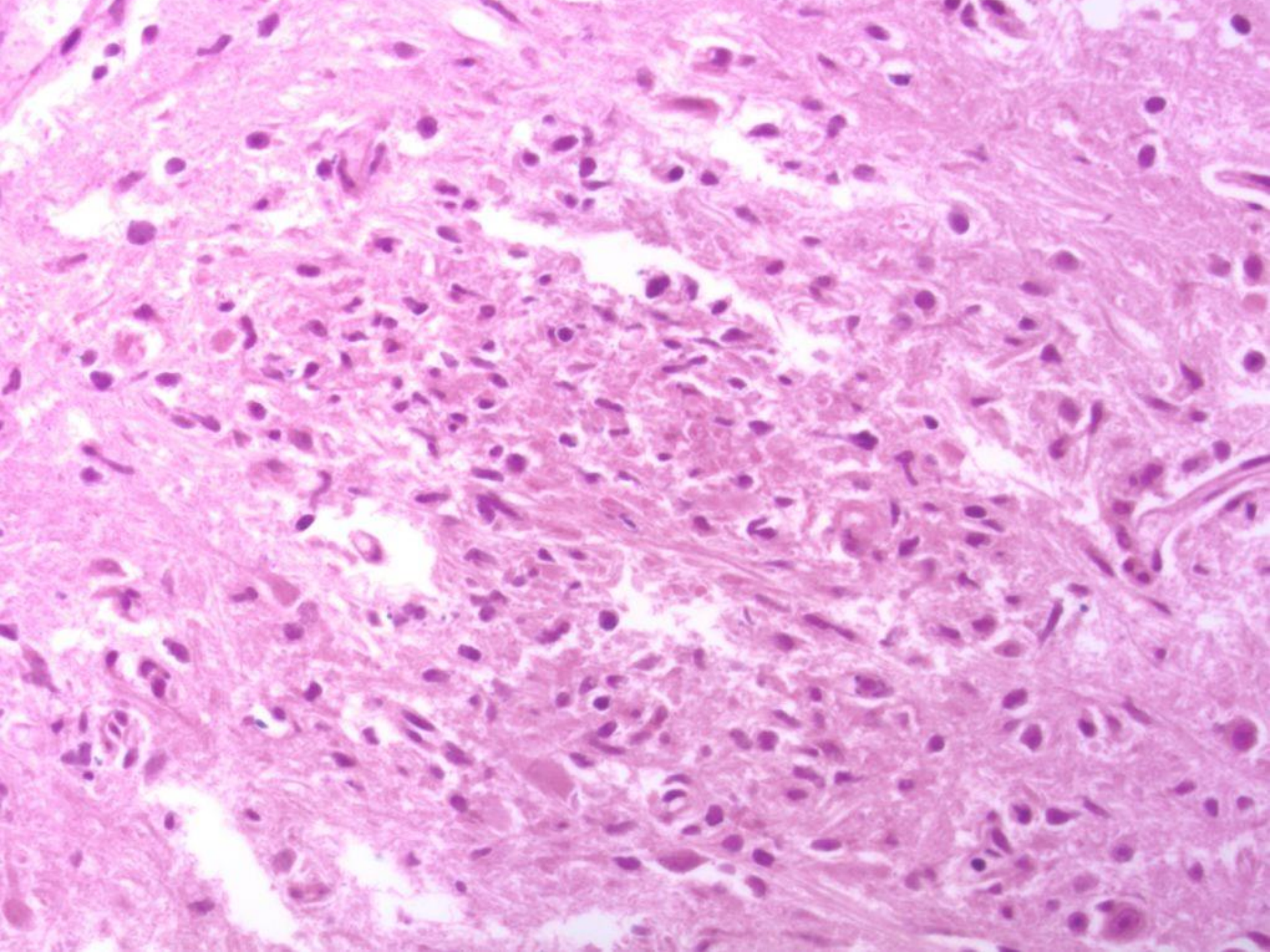


Bovine FOP

- **No diagnosis** **58**
- **Noninfectious** **1**
- **Infectious** **42**
  - Bacteria 17
  - Protozoal 16
  - Viral 4
  - Fungal 4
  - Ureaplasma 2

Jessica S. King, David J. Jenkins, John T. Ellis, Peter Fleming, Peter A. Windsor, Jan Šlapeta. (2011) Implications of wild dog ecology on the sylvatic and domestic life cycle of Neospora caninum in Australia. The Veterinary Journal 188 (2011) 24–33



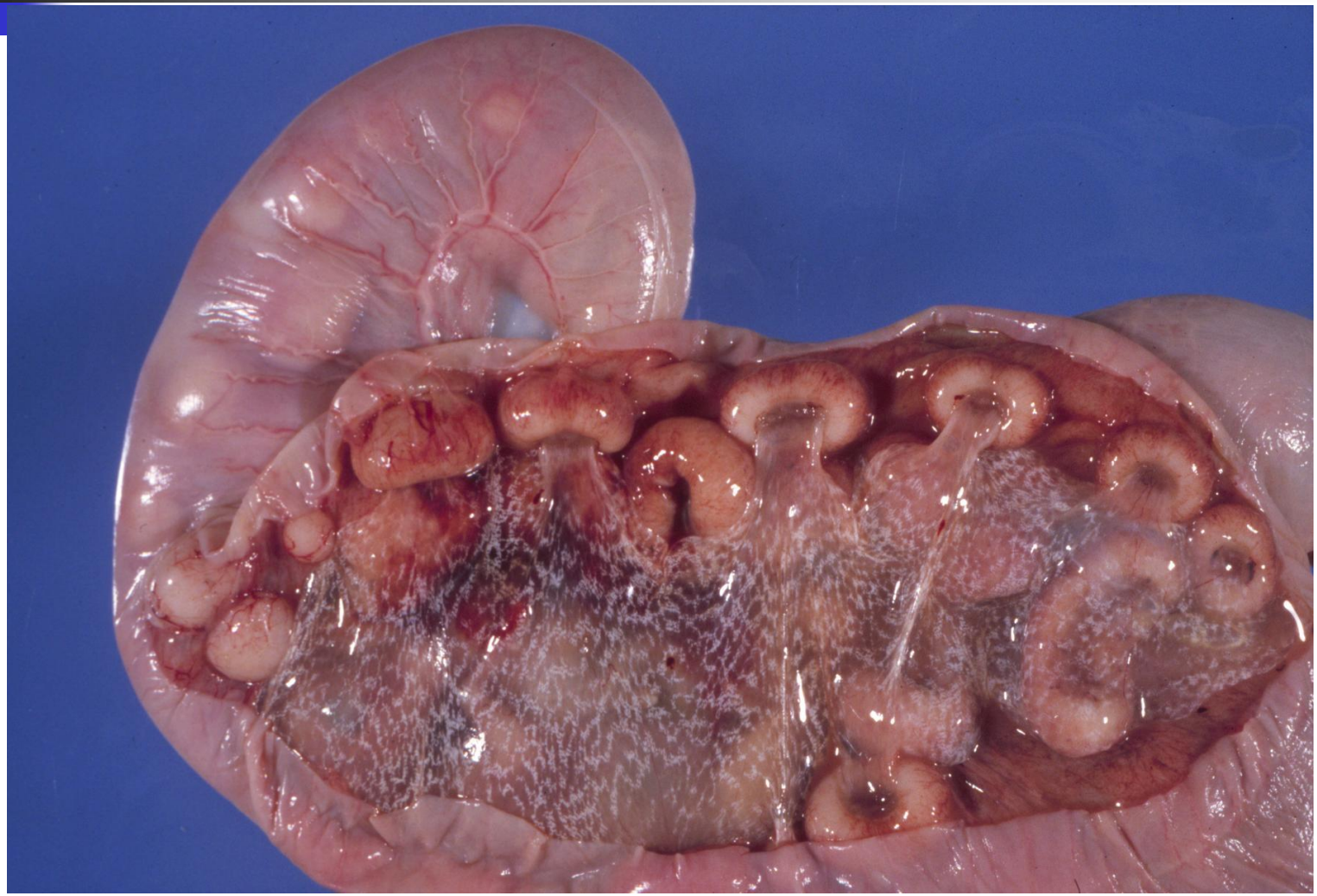


Ovine Abortion*

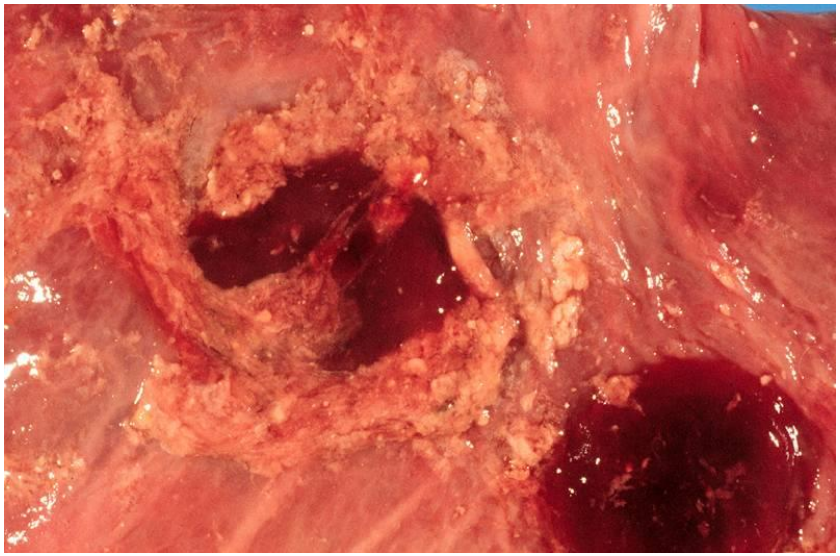
No Diagnosis	48
Noninfectious	2
Infectious	50
Chlamydophila abortus	17
Campylobacter	4
Toxoplasma gondii	19
Coxiella burnetti	5
Virus (Border disease)	0

* Animal Health Laboratory, University of Guelph

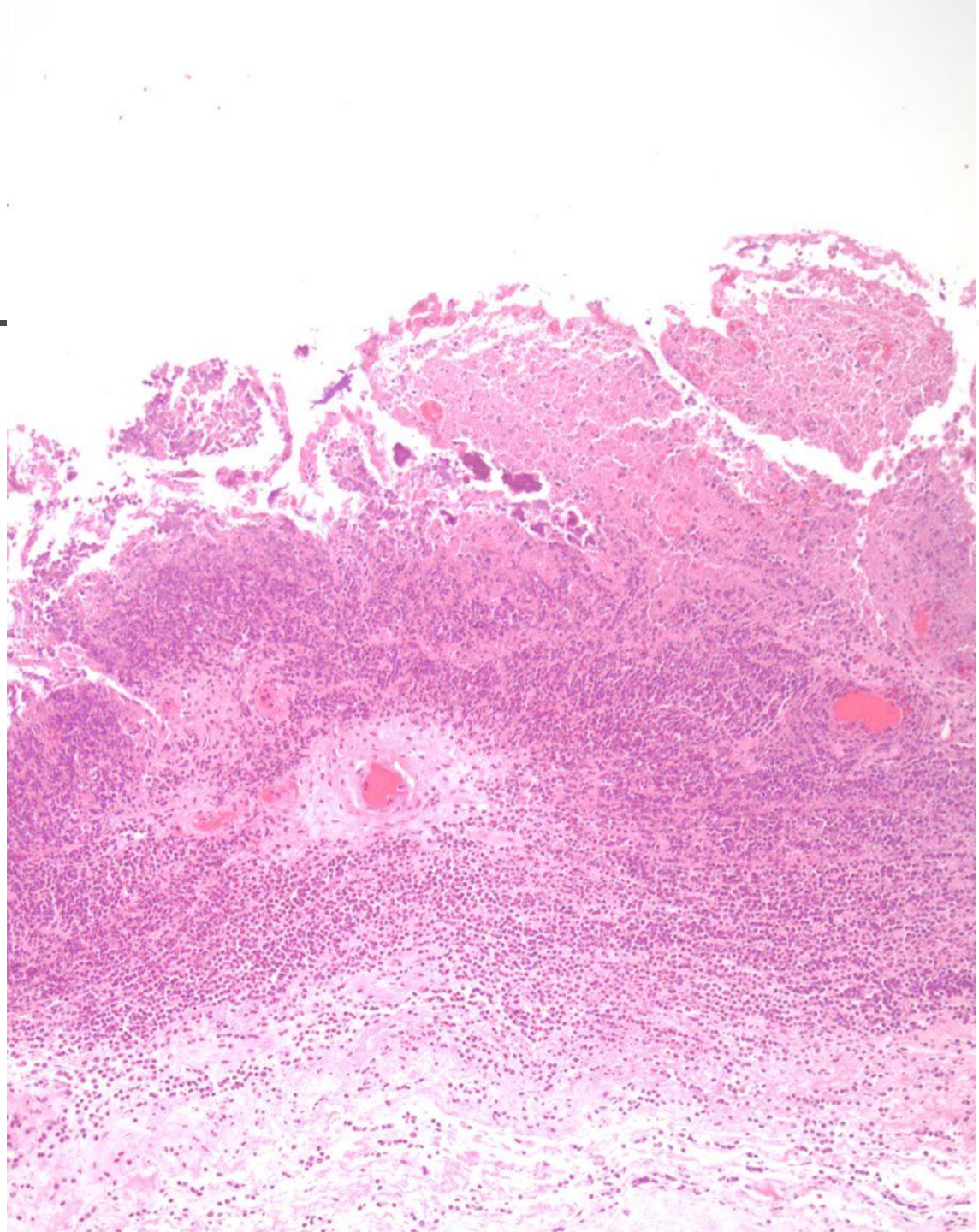
Ruminant

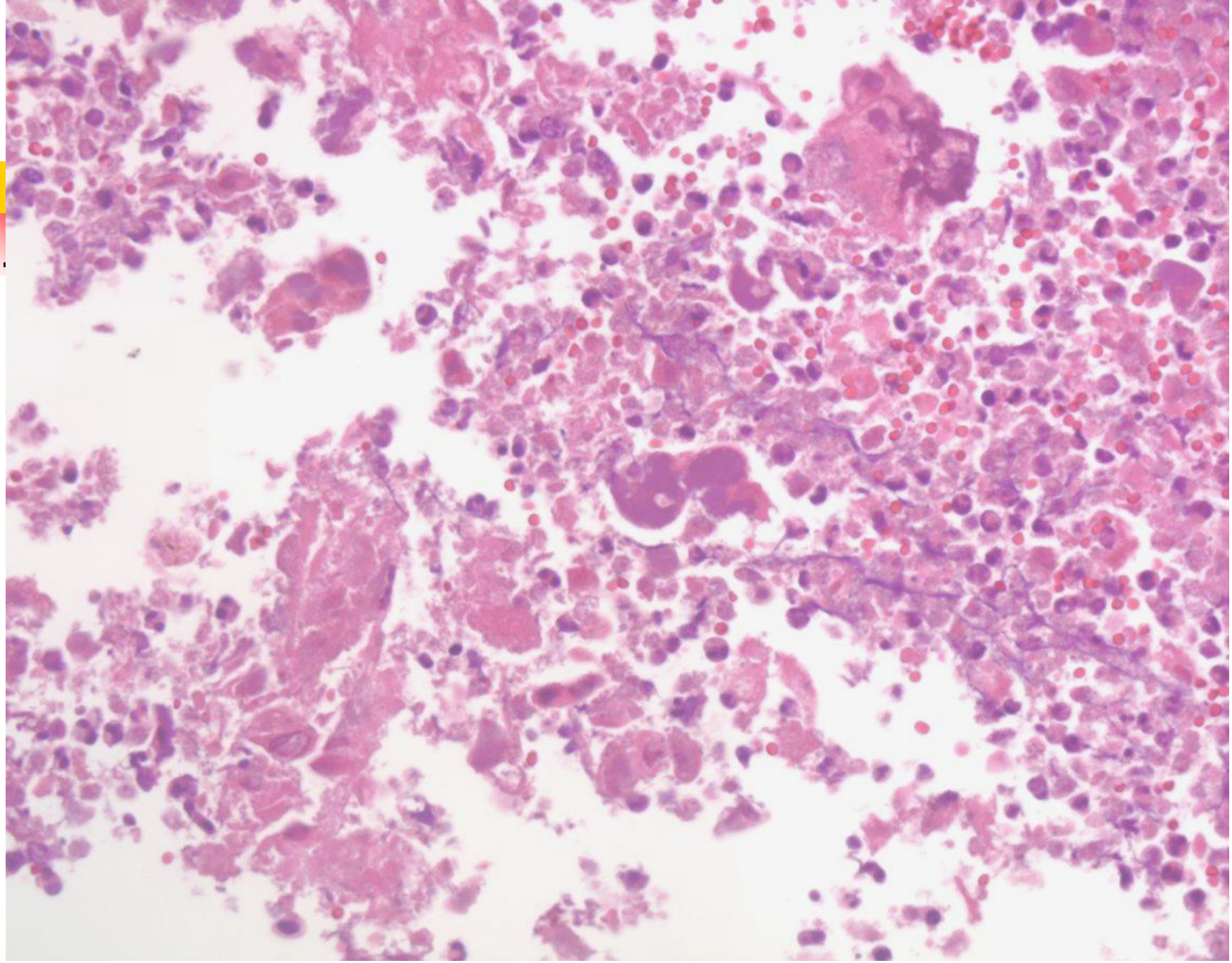


Placentitis



Chlamydophila abortus





Pathogenesis

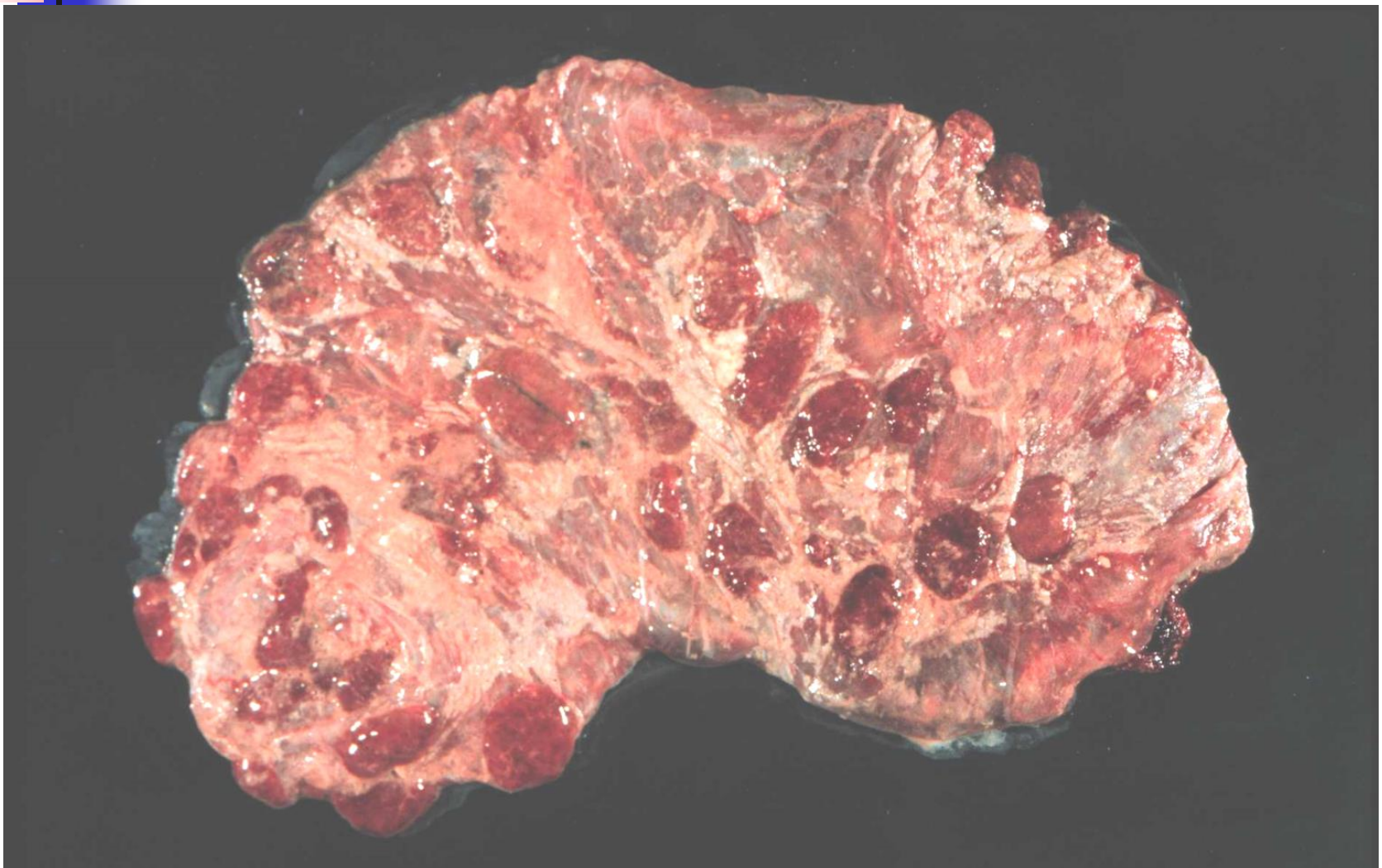
- Exposure of mucous membranes
  - Uterine discharge and fluids, aerosols.
  - Carrier ewes – secretions at estrus
  - Rams temporarily – semen, prepuce
- Ewe develops Ab in 15 d, mild lesions for month, then latency.

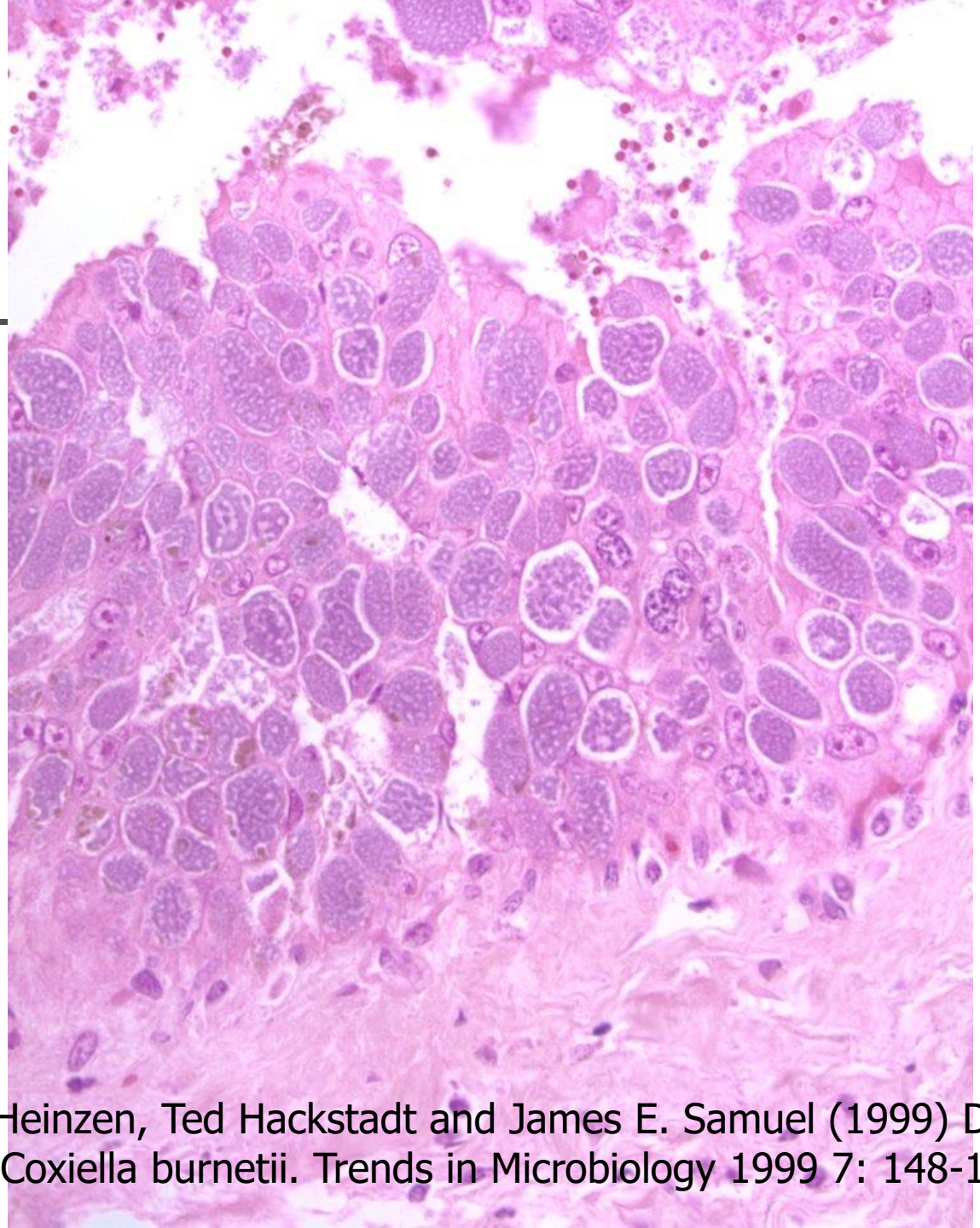
- Mononuclear cells in endometrium
- Endometrial cells of placentome, neutrophils control infection here
- Trophoblasts around placentome
- Logarithmic growth of organism
- Necrosis, neutrophilic inflammation,

Individual history

- Incubation (FOP) 50-90 days during gestation
- Gestation 150 d. (138-159)
- Infection early to middle gestation – abort.
- Infection late in gestation – abort next gestation.
- Ewe lambs abort at first pregnancy
- Carrier state despite immunity.

Coxiella burnetii





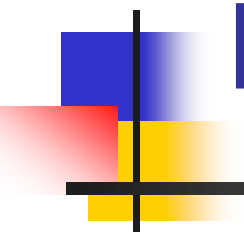
Robert A. Heinzen, Ted Hackstadt and James E. Samuel (1999) Developmental biology of Coxiella burnetii. Trends in Microbiology 1999 7: 148-154

Focal necrosis

Toxoplasma gondii

- Cat – rodent lifecycle
- Cat sheds oocyts for 7 days post infection
- Herbivores infected from contaminated feed – stored and pasture
- Adults develop immunity
- Infection during pregnancy
  - Placental and fetal infection
  - Abortion with characteristic lesions, mummification, stillbirth, weak lambs

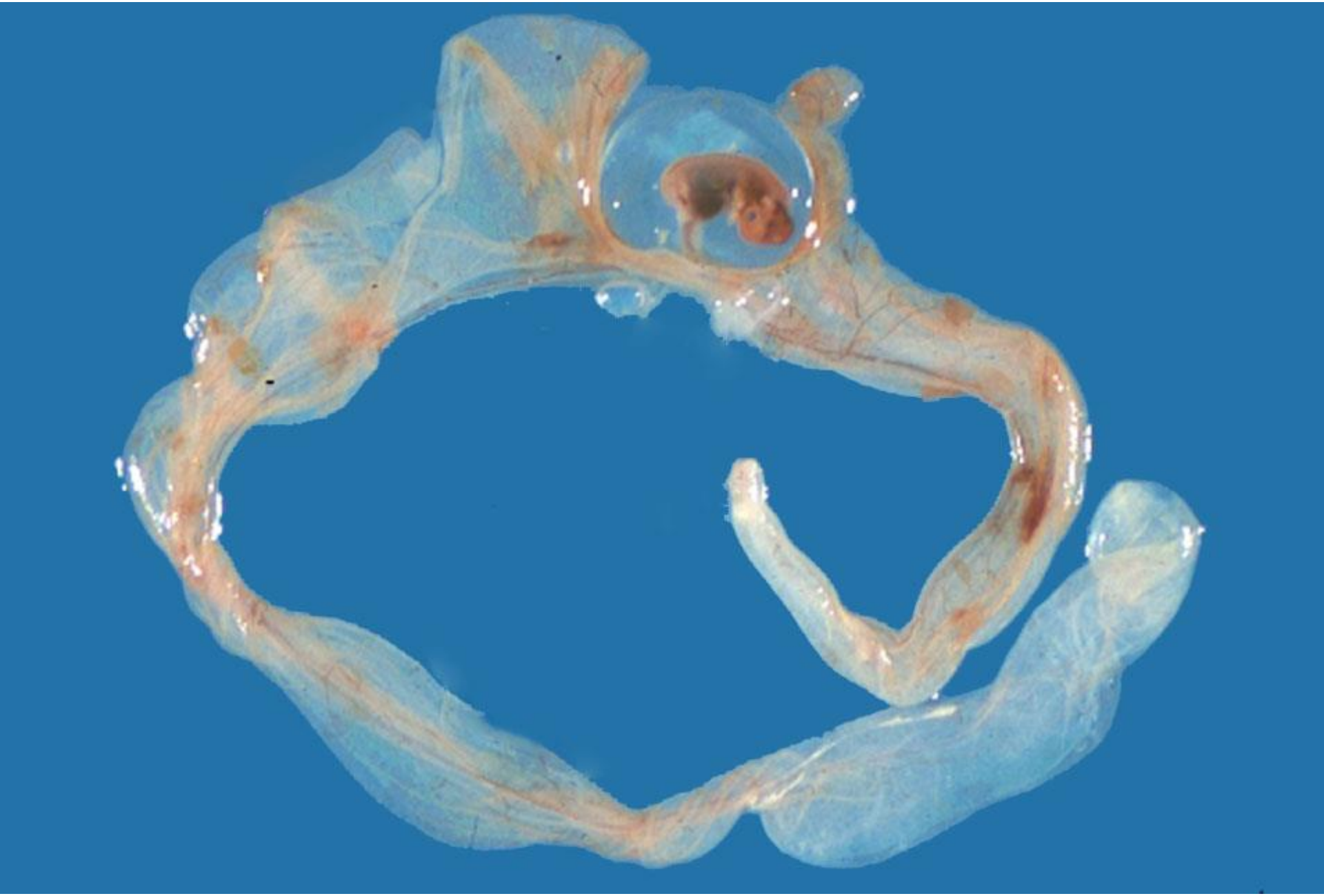
Necrotic tips

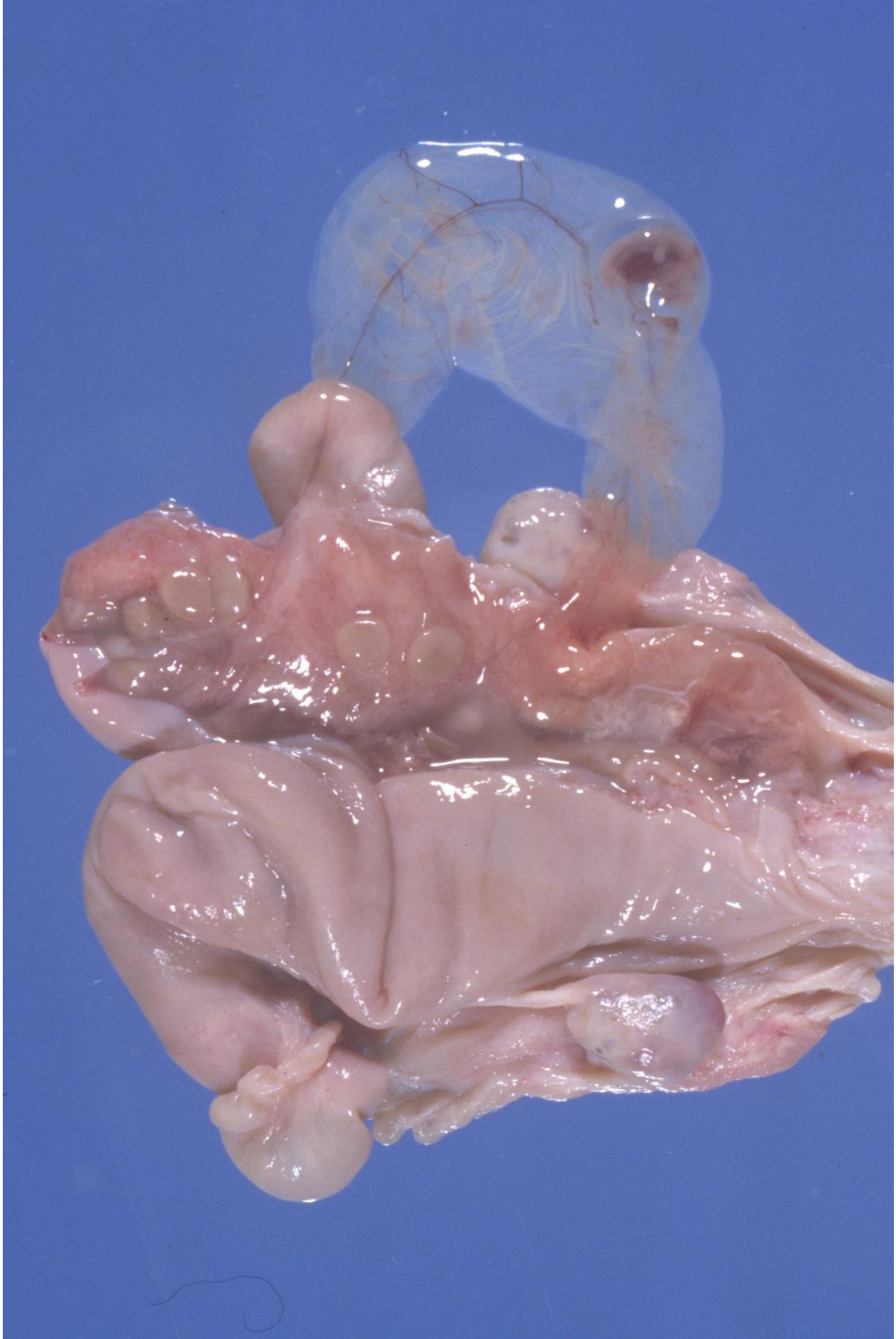


Foetus in FOP

Time of Death

- 12 hr — cornea cloudy
- 24 -36 hr — fluid in cavities
- 72 hr — dehydration begins
- 144 — mummy





Fetus *en utero*

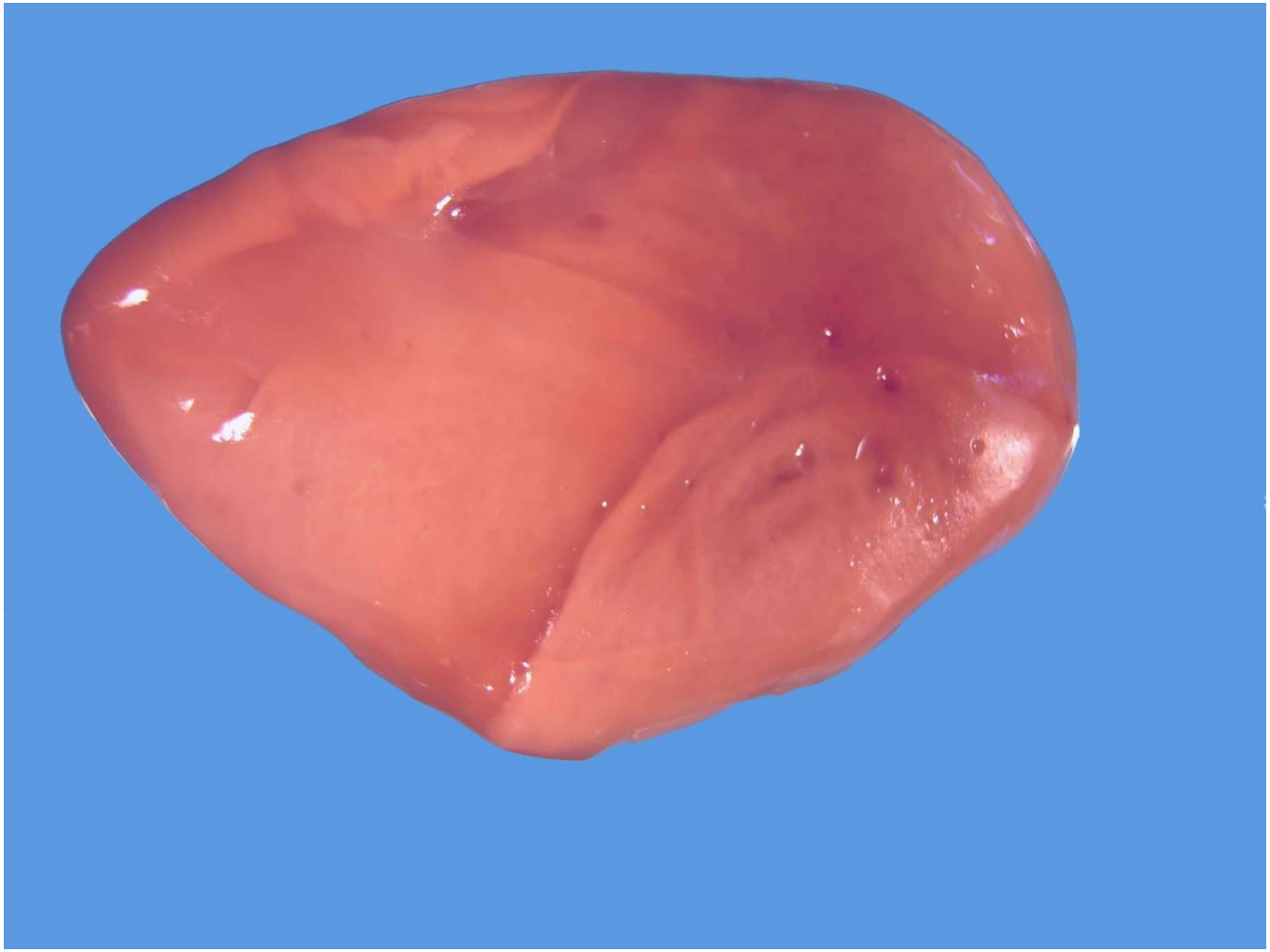
- Receives nutrients, oxygen, protection
- Wastes are removed

- Moves
- Swallows
- Doesn't 'breath'

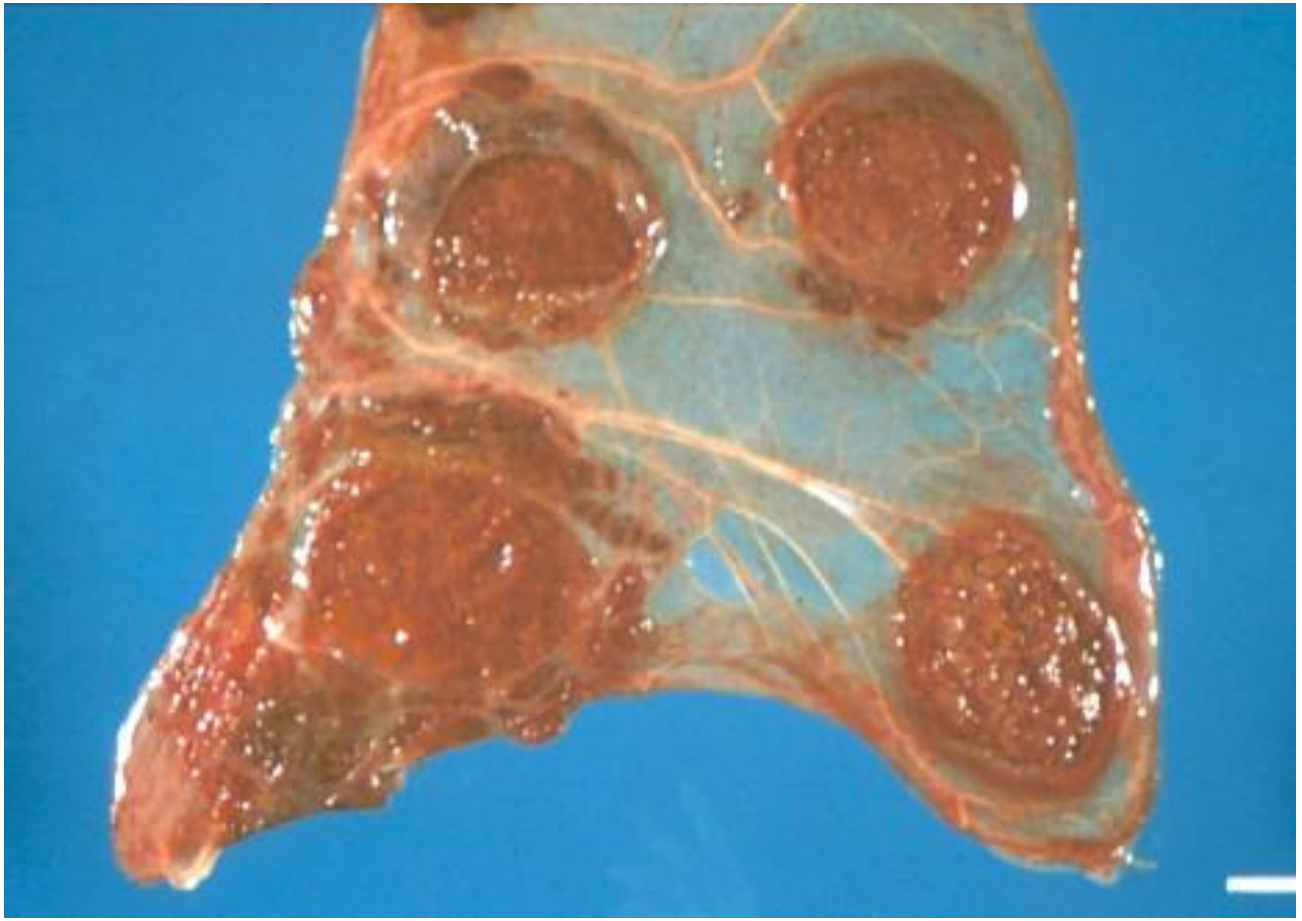
- Initiates parturition

Amorphous globosis

Hippomane

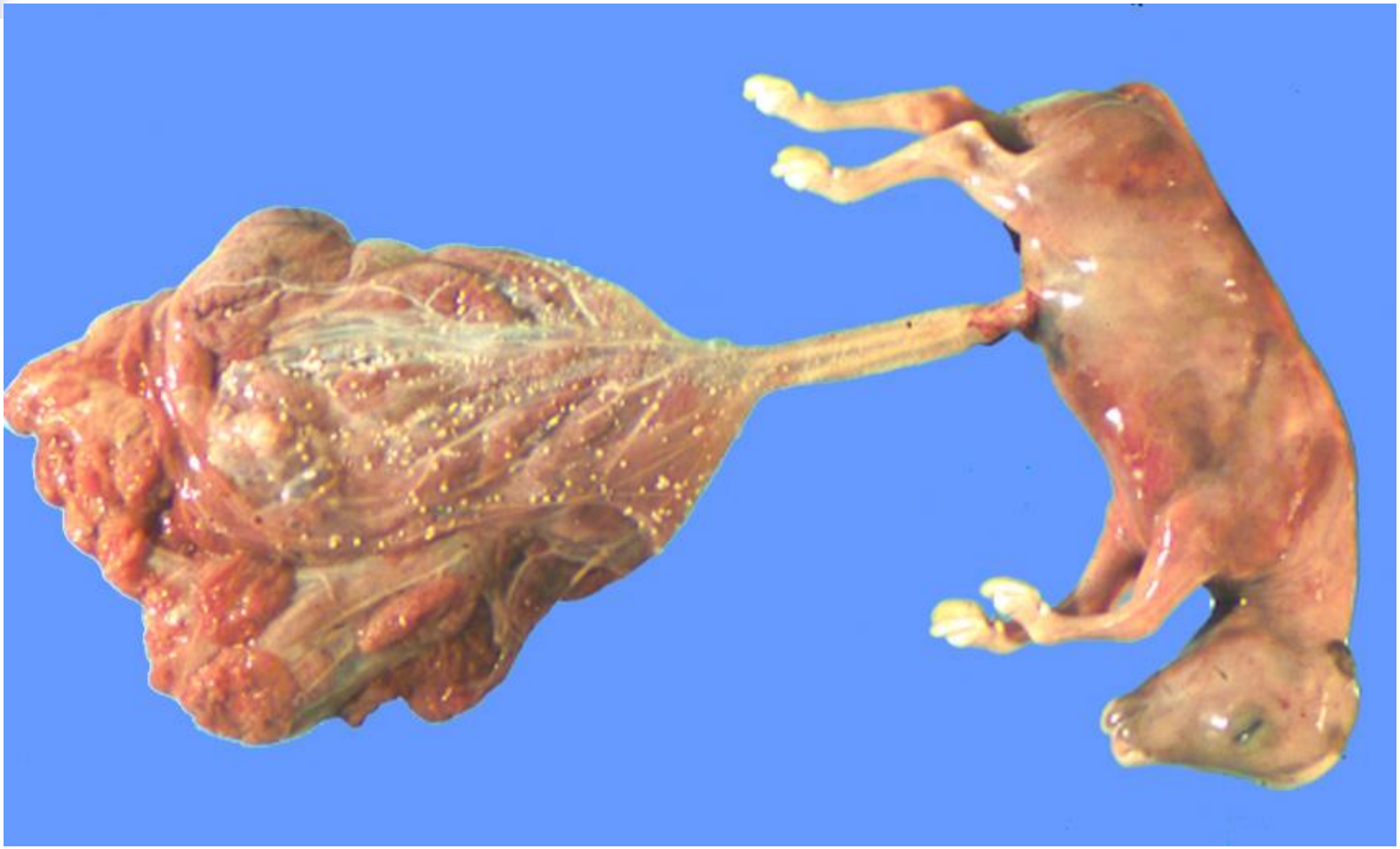


Adventitial placentation



Adventitial placentation

Amniotic plaques



Non-lesion lesions

- Amorphous globosis (bovine)
- Hippomane
- Amniotic plaques

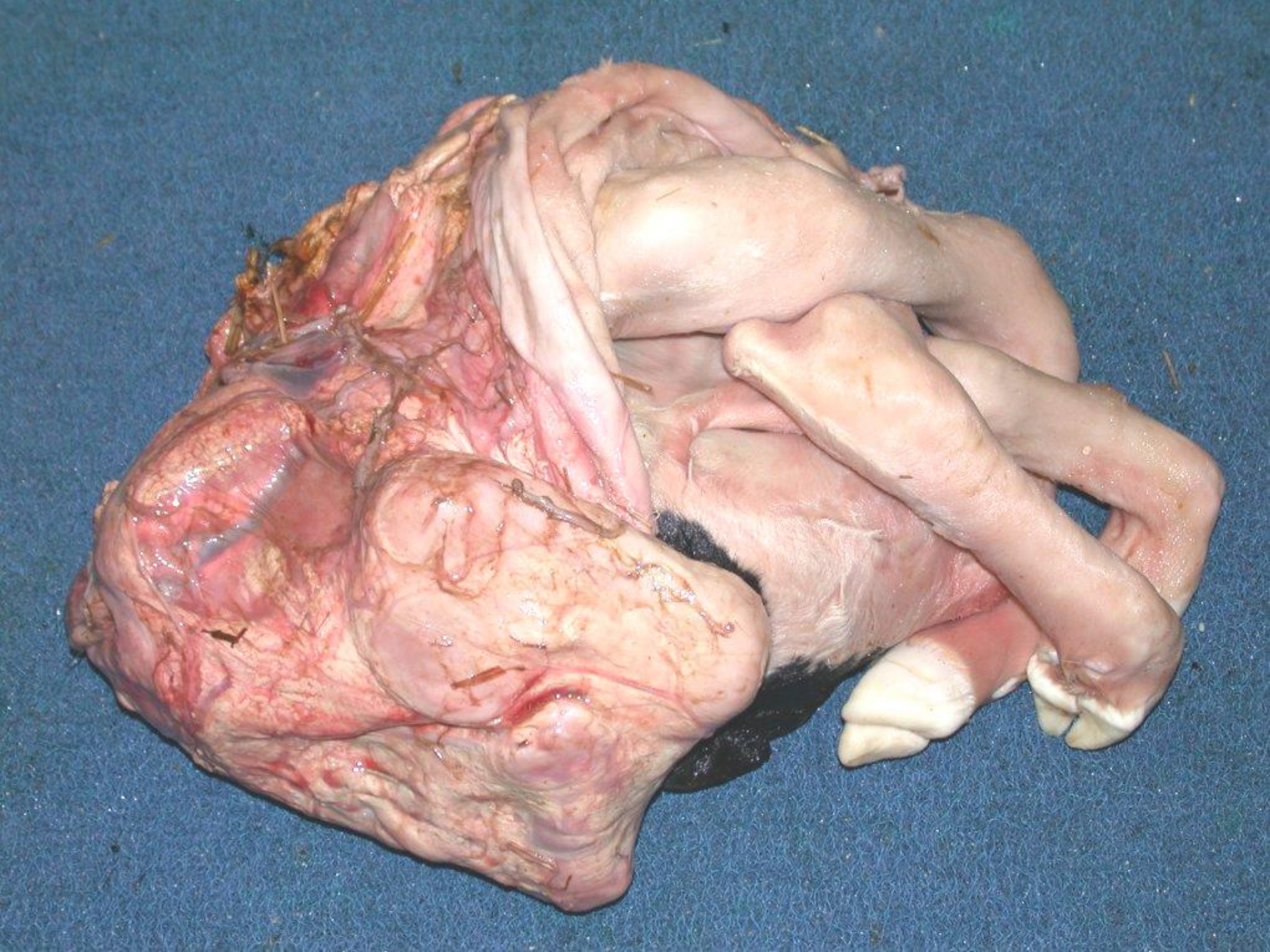
Theriogenology Question of the Month. JAVMA, Vol 238: 1261

Dystocia

Arthrogryposis

- Definition
- Pathogenesis
  - Causes?
    - Cattle
    - Sheep
    - Goats
    - Pigs
  - Movement disorder
  - Lesions

Dermatitis



Congenital anomalies

- Obvious anomalies
- Less obvious anomalies
  - No look, no find
    - Cleft palate
    - Osteopetrosis
- Lethal defects with no lesions.

Iodine deficiency

Thyroid disease

- Goitre
  - Iodine deficiency
  - Goitrogenic substances
  - Dyshormonogenic

Heart failure

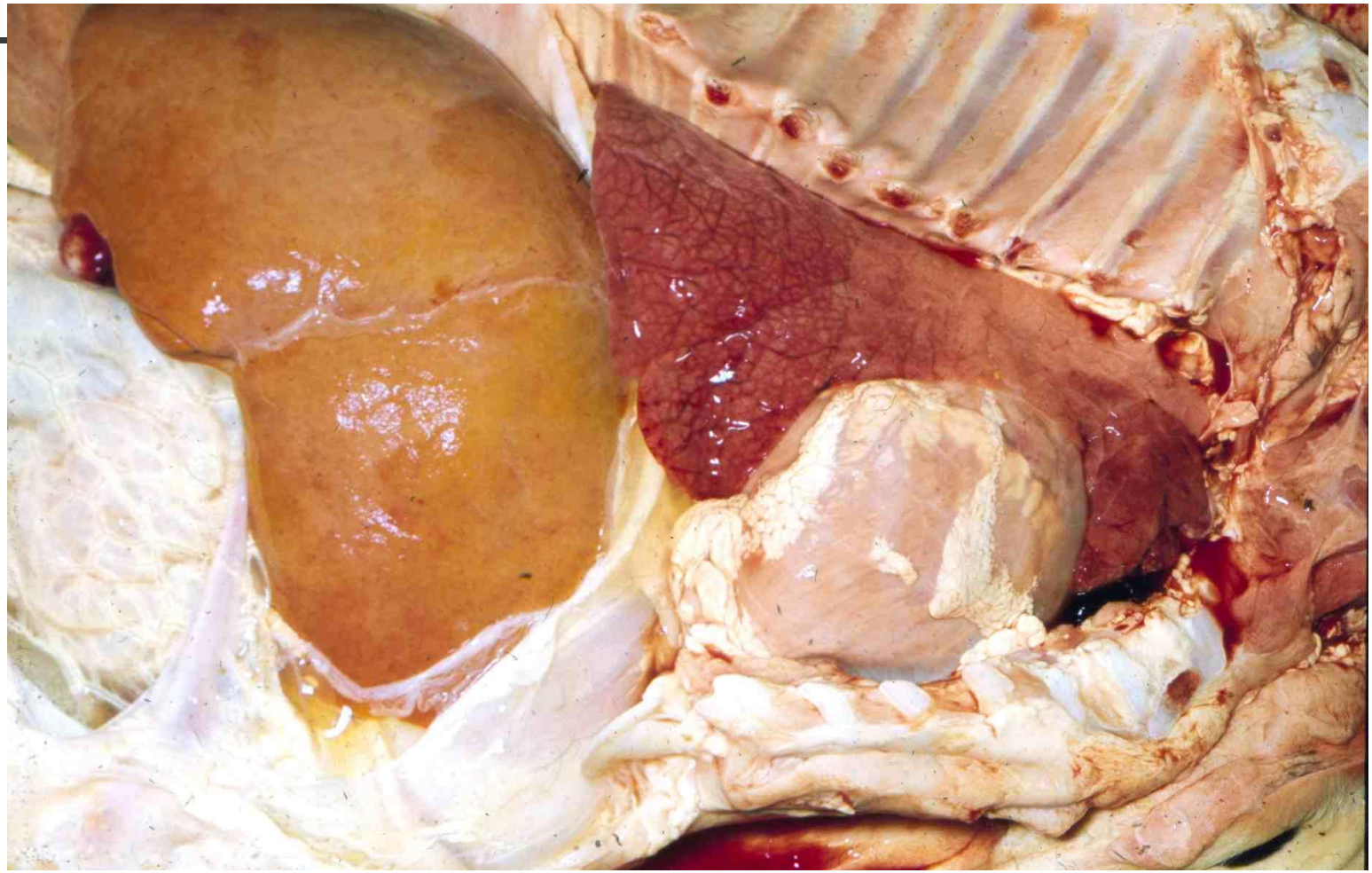


Photo complements of Dr RB Miller

Campylobacter

Photo complements of Dr D Wilson

Summary

- Expectation, expectation, expectation.
- Sporadic vs outbreak
- Maternal, fetal, placental

Birth

- Adjustments
  - Breathing
  - Circulation

Breathing

- Inhibited before birth
- Lungs atelectatic
- Begins immediately

- Hypoxia
  - Compression of umbilical cord
  - Premature separation of placenta
  - Excessive contraction of uterus (maternal supply)
  - Intracranial hemorrhage

Expansion of lungs

- Surface tension of pulmonary fluid keeps it collapsed
- First breath requires large amount of negative pressure, second is easier

Circulatory readjustments

- Fetal circulation
  - Aorta is low resistance (and BP)
  - Pulmonary artery is high resistance.
  - Blood from umbilical vein bypasses the liver and enters vena cava to be shunted to the left through the foramen ovale (atria).
  - Blood from head of fetus goes to ventricle and across ductus arteriosis

Circulation at birth

- Umbilical flow ceases, increases pressure in aorta
- Foramen ovale closes – back pressure closes flap valve
- Blood flow ceases through ductus arteriosis. High O_2 tension causes it to close (prostaglandin keeps it open).
- Ductus venosis closes

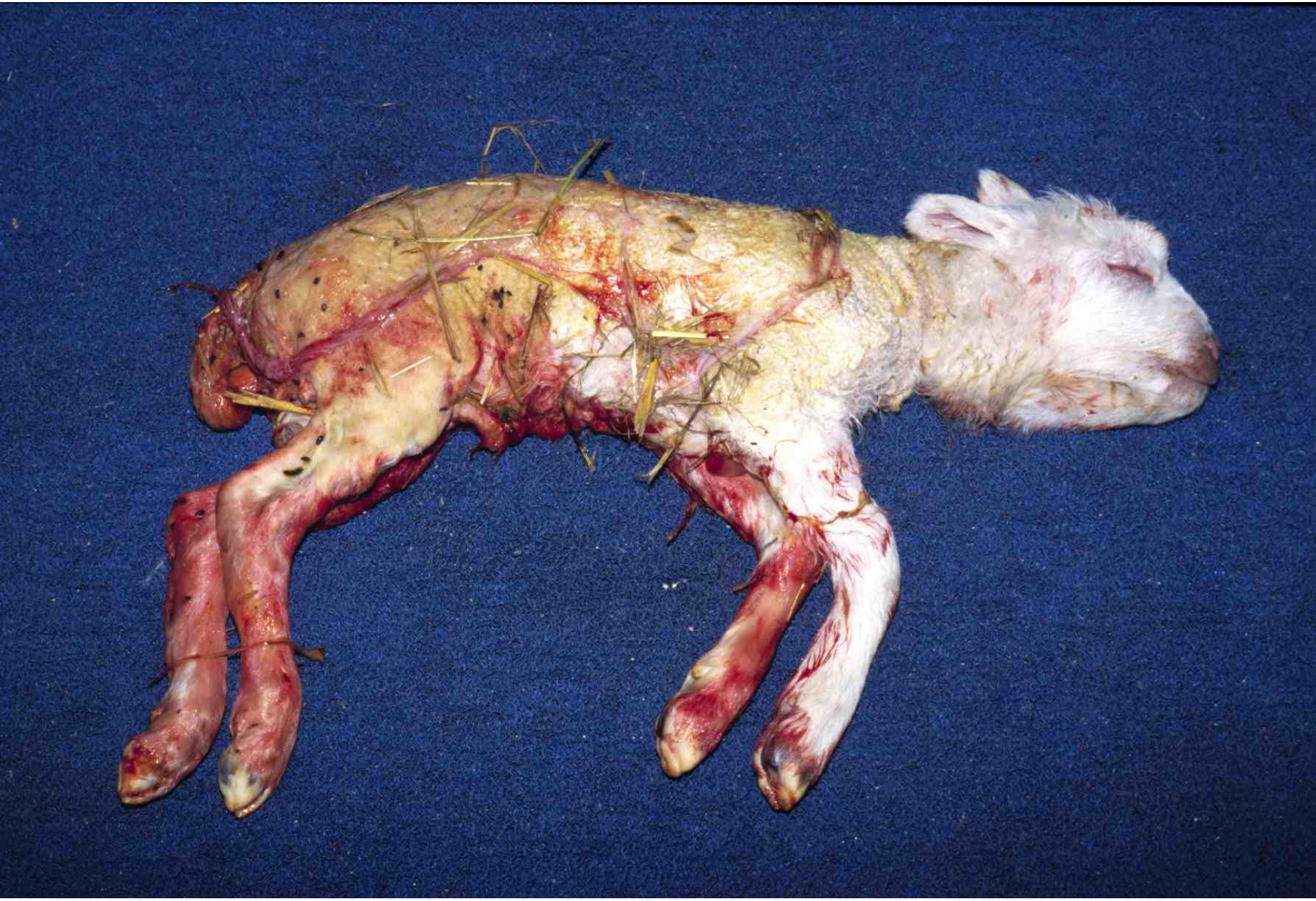
Stillbirth and perinatal mortality

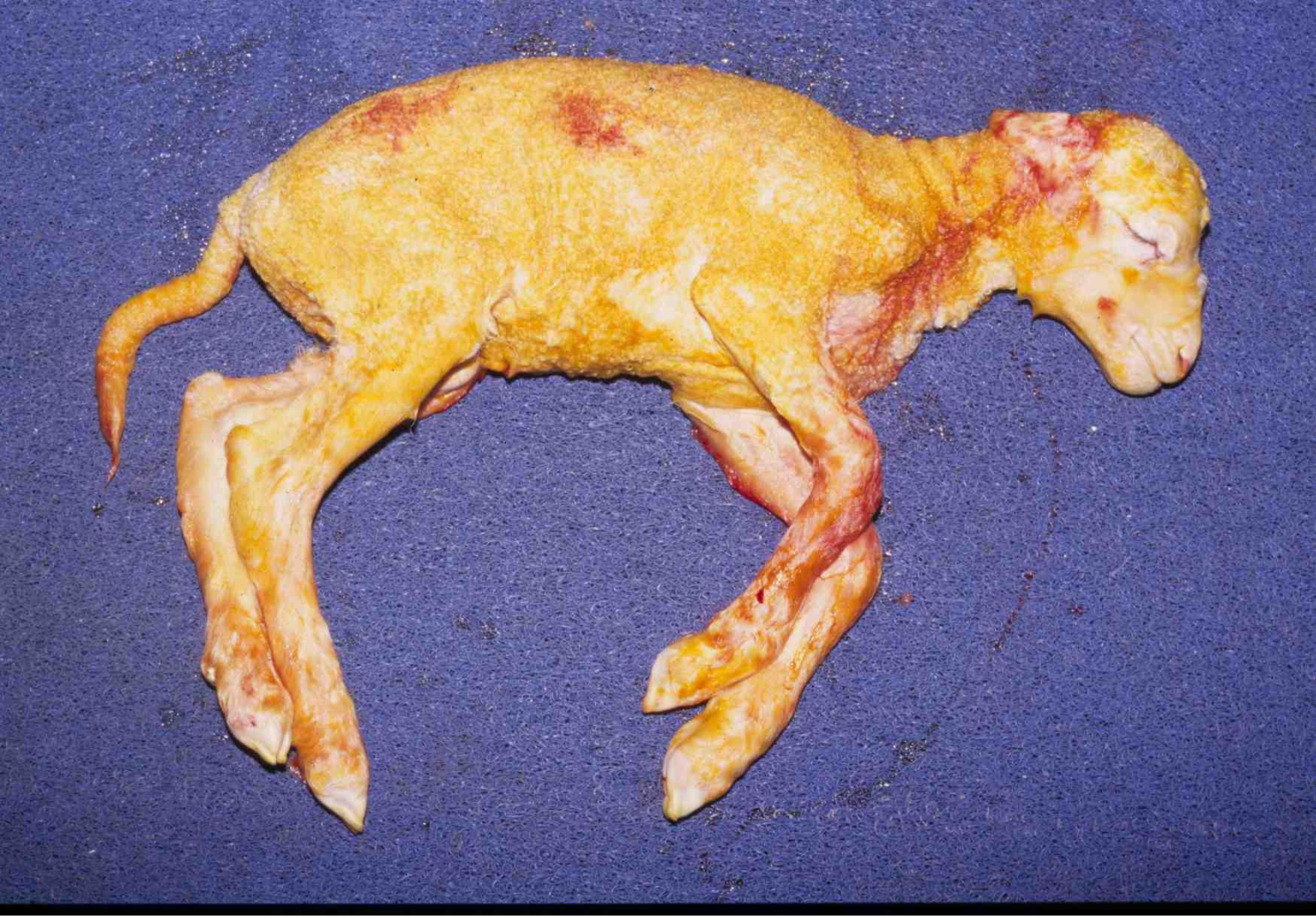
Basic algorithm

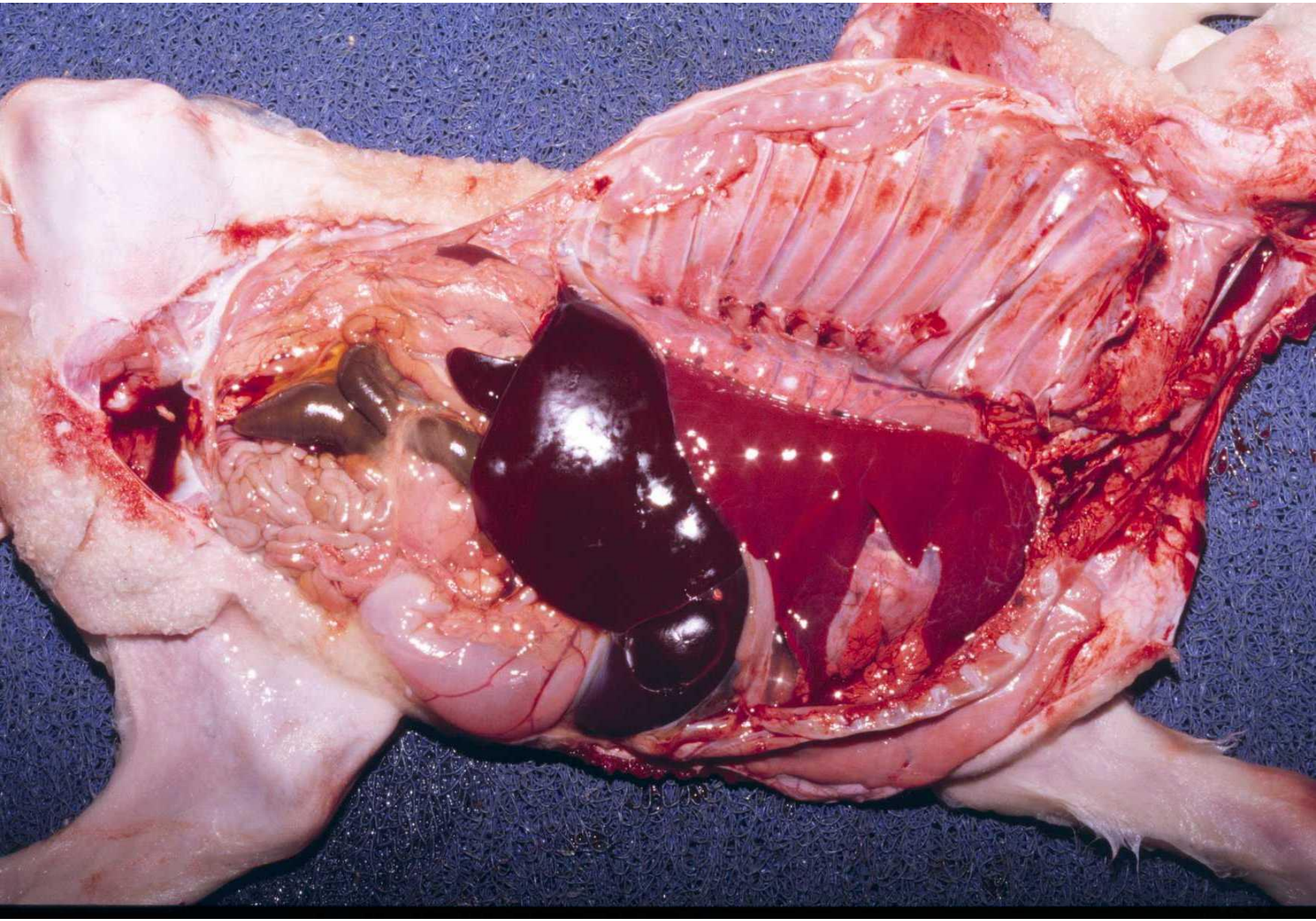
- Abortion or
- Stillbirth or
- Dystocia or
- Neonatal mortality (breathed)

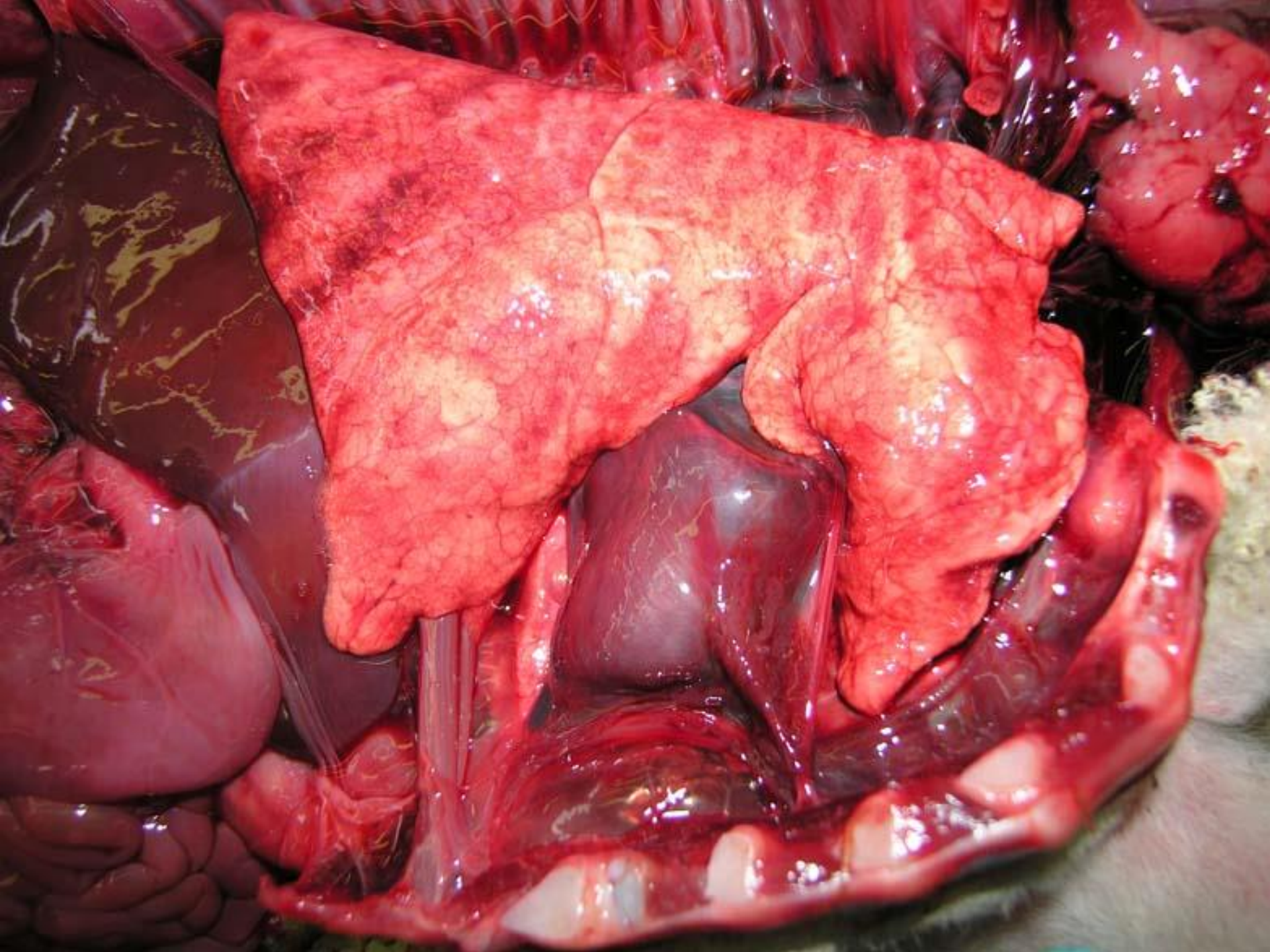
Size and maturity

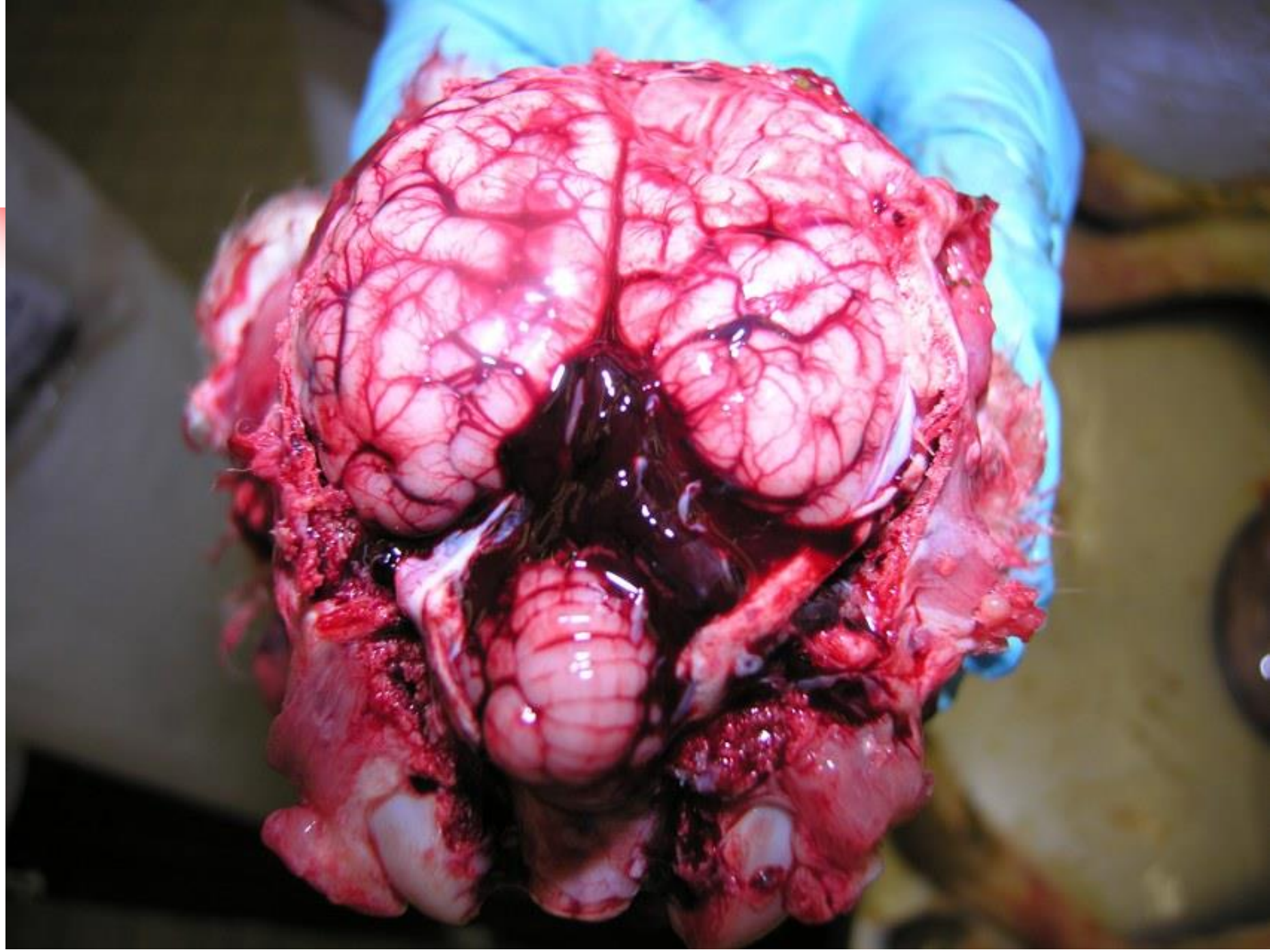
- Too small
  - Perinatal mortality
  - Placentitis
  - Lambs <3 kg
- Too large
  - Lambs >5kg
  - Dystocia

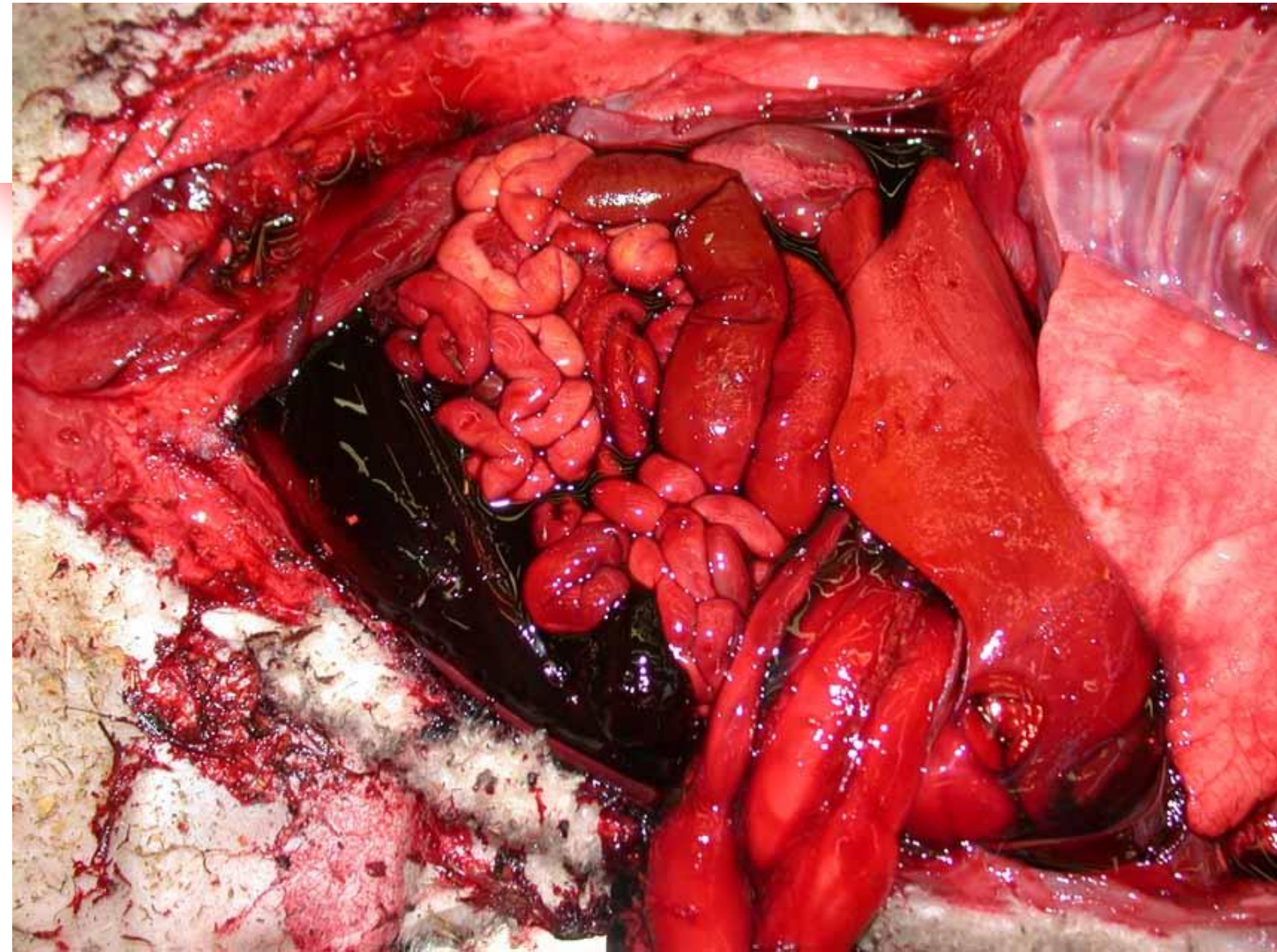


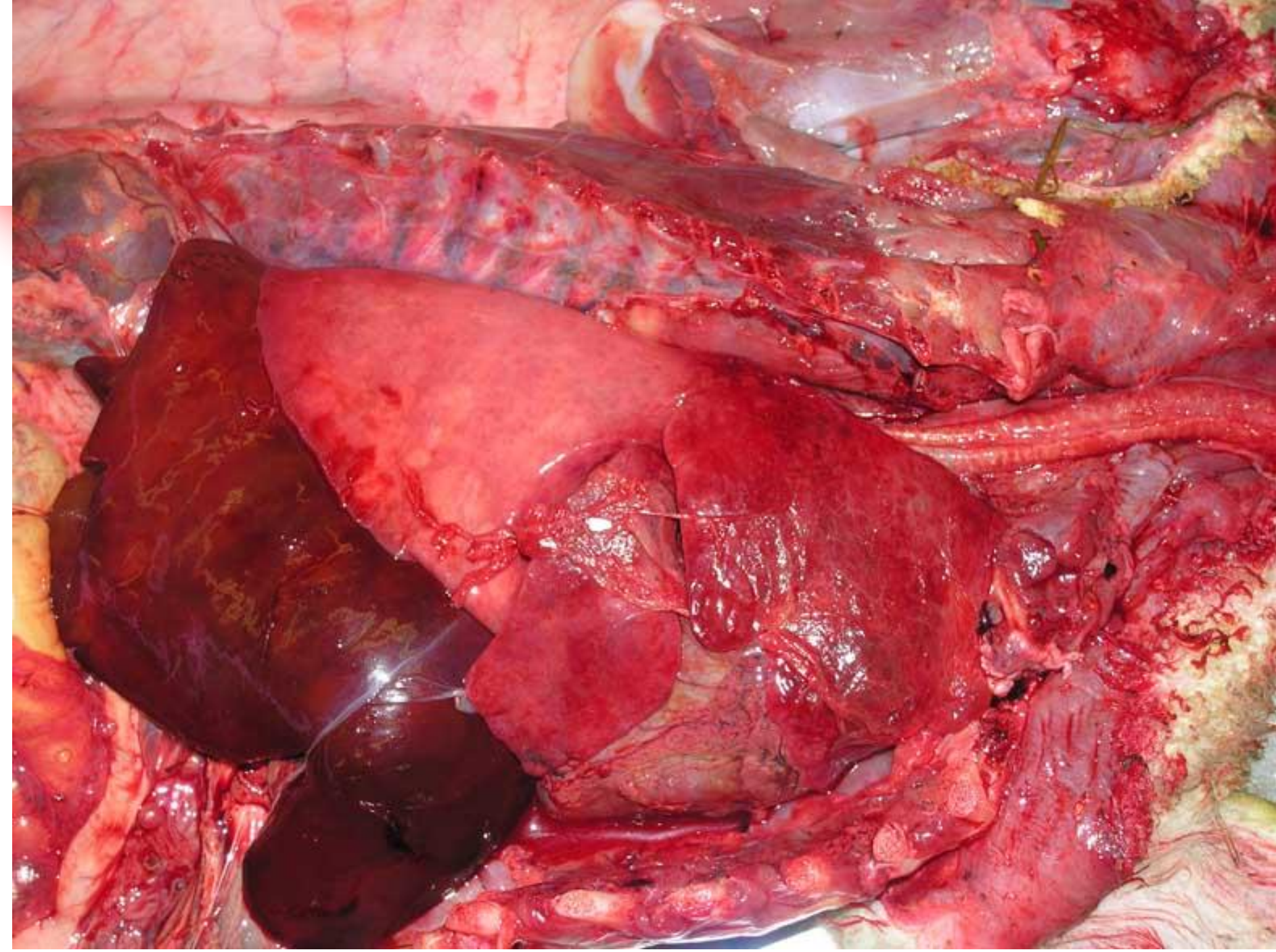




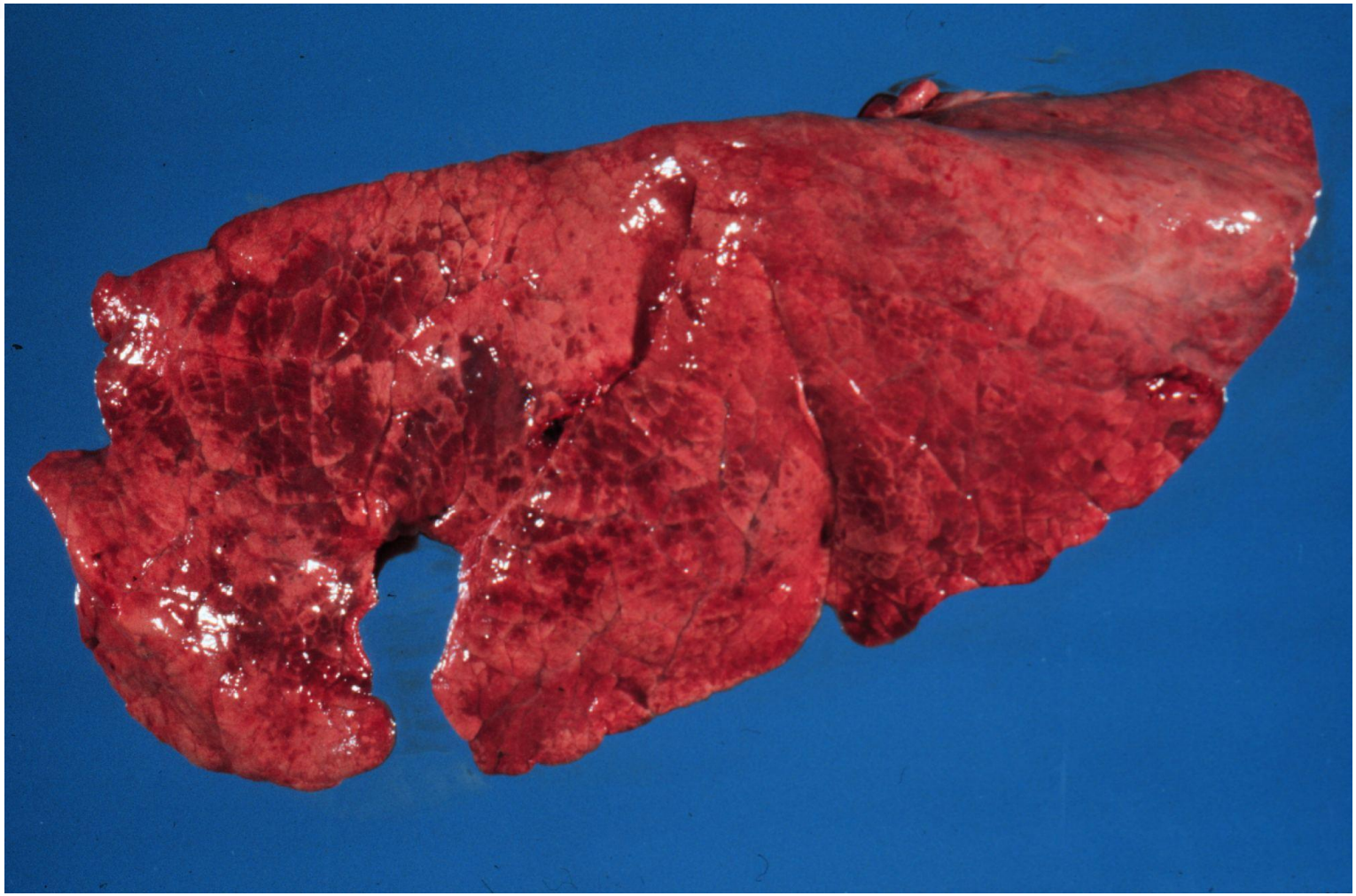








Aspiration of amniotic contents



Bovine neonatal pancytopaenia

- Bleeding calf syndrome
- Pancytopaenia with leukopaenia and thrombocytopaenia
- Association with a BVD vaccine
- Immune mediated, colostrum related disease

Philip Simon Bridger, Rolf Bauerfeind, Lisa Wenzel, Natali Bauer, Christian Menge, Heinz-Jürgen Thiel, Manfred Reinacher, Klaus Doll. (2011) Detection of colostrum-derived alloantibodies in calves with bovine neonatal pancytopenia. Veterinary Immunology and Immunopathology 141 (2011) 1–10

Female Genital Pathology

Retained foetal membranes

1. Reduced collagenase activity of fetal cotyledon-maternal caruncle interface.
   - Foetal cortisol induction of placental enzymes
   - Steroid synthesis from progesterone to estrogen
   - upregulation of oxytocin receptors on the myometrium
   - secretion of prostaglandin F2 alpha (PGF2a).
   - Prostaglandin initiates myometrial contractions and lysis of the corpus luteum (CL).
   - Lysis of the CL leads to secretion of relaxin and a further decline in progesterone.

J.C. Beagley, K.J. Whitman, K.E. Baptiste, and J. Scherzer (2010) Physiology and Treatment of Retained Fetal Membranes in Cattle. J Vet Intern Med 2010;24:261–268

Retained foetal membranes

2. Increased serotonin inhibits separation
   - High fetal and placental serotonin maintains placental attachment
   - promotes placental cell proliferation and inhibits matrix metalloproteinase (MMP) activity.
3. Reduced leucocyte chemotaxis and activity
4. Reduced maternal immunological recognition of foetal MHC 1 molecules
5. Reduced cytokine production necessary for maturation and shedding of placenta

Retained Foetal Membranes – risk factors

- Induced parturition
- Shortened gestation
- Abortion
- Twinning
- Dystocia
- Fetotomy
- Cesarean section
- Nutritional deficiencies - vitamin E, selenium, and carotene
- Infectious agents – BVDV
- Immunosuppression including dexamethasone for induction
- Serum calcium and uterine tone

Disorders of Sexual Development

Intersex
Sex reversal
Hermaphrodite
Pseudohermaphrodite
Ambiguous development

Normal female development

- Female specific genes are activated
- *WNT1*, *DAX1*, *FOXL2*, are important genes
- Upregulate *FST* (follistatin gene)
- Paramesonephric ducts develop (*WNT4*)
- Urogenital sinus – vulva, part of vagina.
- Urogenital tubercle - clitorus

Normal male development

- *SRY* gene, *TDF*,
- *WT1+KTS*, *GATA4* and *FOG2* - Sertoli cell differentiation
- *SOX9* – testis determining pathway
- *SF1* activates *AMH* gene and inhibits the paramesonephric duct
- *WNT* responsible for mesonephric duct development
- Interstitial cells produce testosterone
- External genitalia develop from urogenital sinus and tubercle.

Basis of new nomenclature - pathogenesis

- Genetic
  - Chromosomes (XX, XY, X_ mosaics, chimeras)
  - Genes (*SRY*)
- Gonadal
  - Testis
  - Ovary
  - Ovotestis
  - dysgenesis
- Phenotype

Hughes IA (2008) Disorders of sex development: a new definition and classification. Best Practice & Research Clinical Endocrinology & Metabolism 22 (1): 119-134.

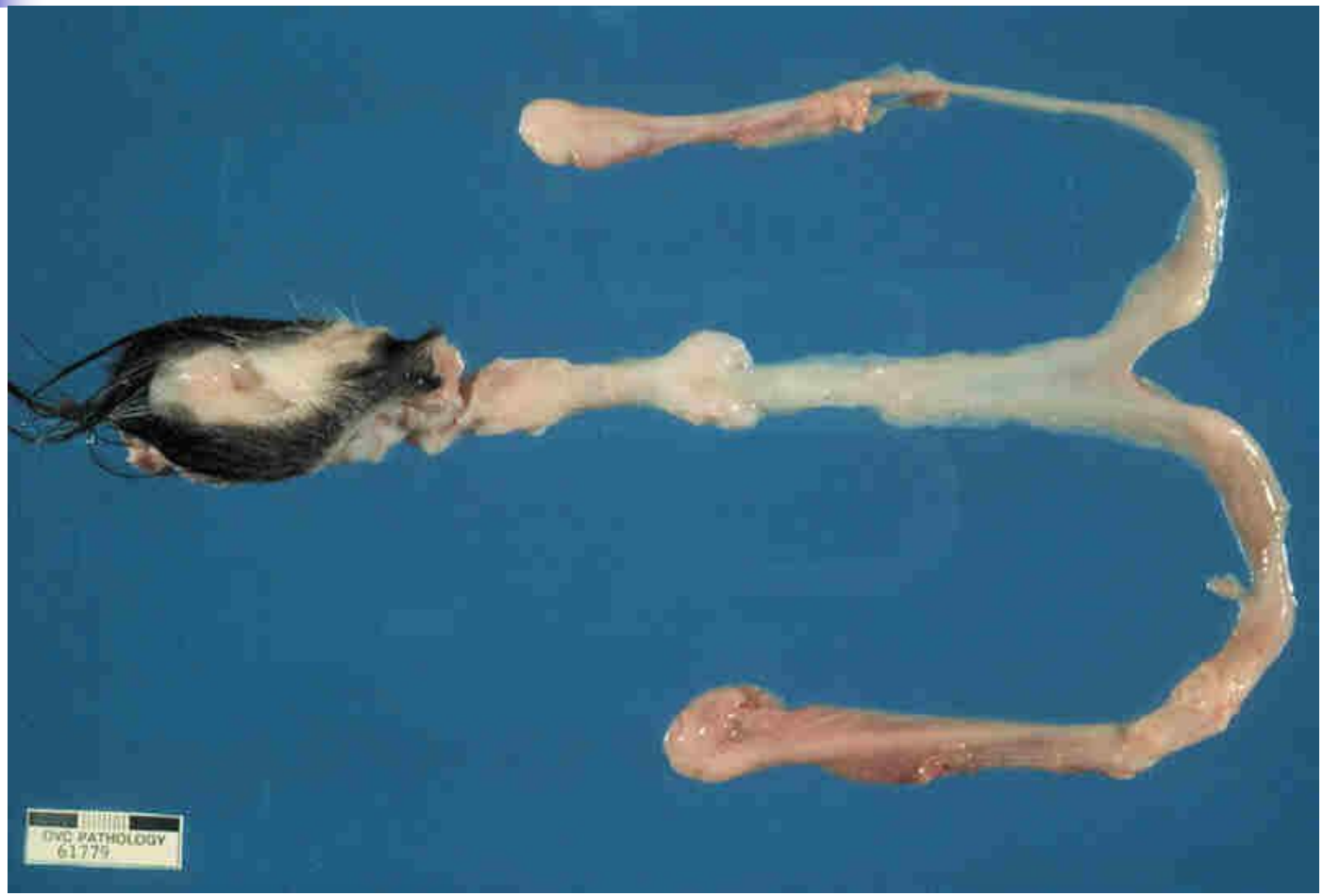
Chromosomal DSD

- Aneuploidy
  - X_ - Turner
  - XXX – Trisomy X
  - XXY - Kleinfelter
- Mosaics and Chimeras
  - Chimera (XX/XY) cells of different zygotes fuse – Freemartin
  - Mosaic – non disjunction in a single zygote

Freemartinism

- Twin and single born freemartins
- XX/XY chimera
- Ovary but paramesophric ducts don't develop.
- Masculinized external genitalia

A.M. Padula (2005) The freemartin syndrome: an update. Anim Reprod Sci (2005) 87: 93–109


OVC PATHOLOGY
61779

Goat – Polled intersex syndrome XX testicular DSD

Polled intersex syndrome

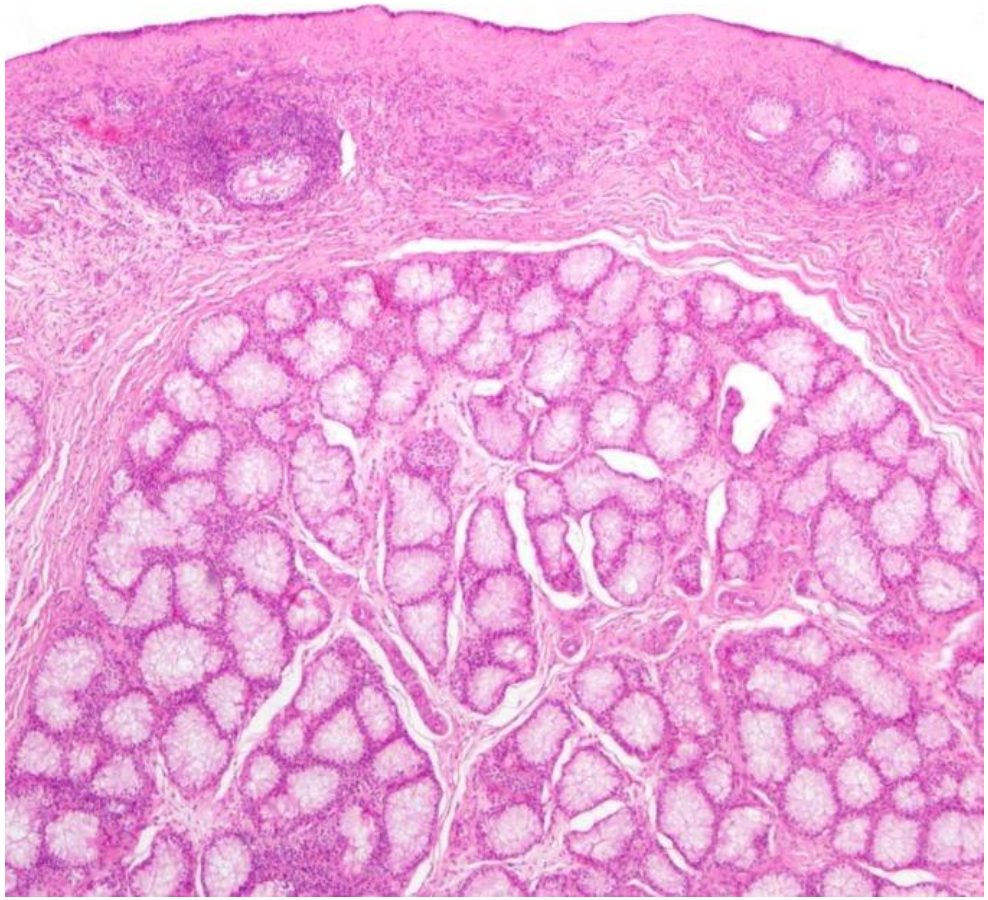
- XX testicular DSD
  - female tubular genitalia
  - Mammary glands
  - Phenotype male or female
- PIS gene causes loss of *FOXL2* locus and failure of aromatase (*CYP19*) expression

Pannetier M, Fabre S, Batista F, Kocer A, Renault L, Jolivet G. (2006) FOXL2 activates *P450 aromatase gene transcription:* towards a better characterization of the early steps of mammalian ovarian development J Mol Endocrinol 2006 36: 399-413

XX DSD

- Abnormal gonads
  - XX Gonadal dysgenesis DSD
  - XX Ovotesticular DSD
  - XX Testicular DSD
- Normal gonads
  - XX ovarian DSD

Ovotestis – XX ovotestis



XY DSD

- Abnormal gonads
  - XY gonadal dysgenesis DSD
  - XY ovotesticular DSD
  - XY testicular regression DSD
- Normal gonads
  - XY testicular DSD (PMDS, cryptorchidism)

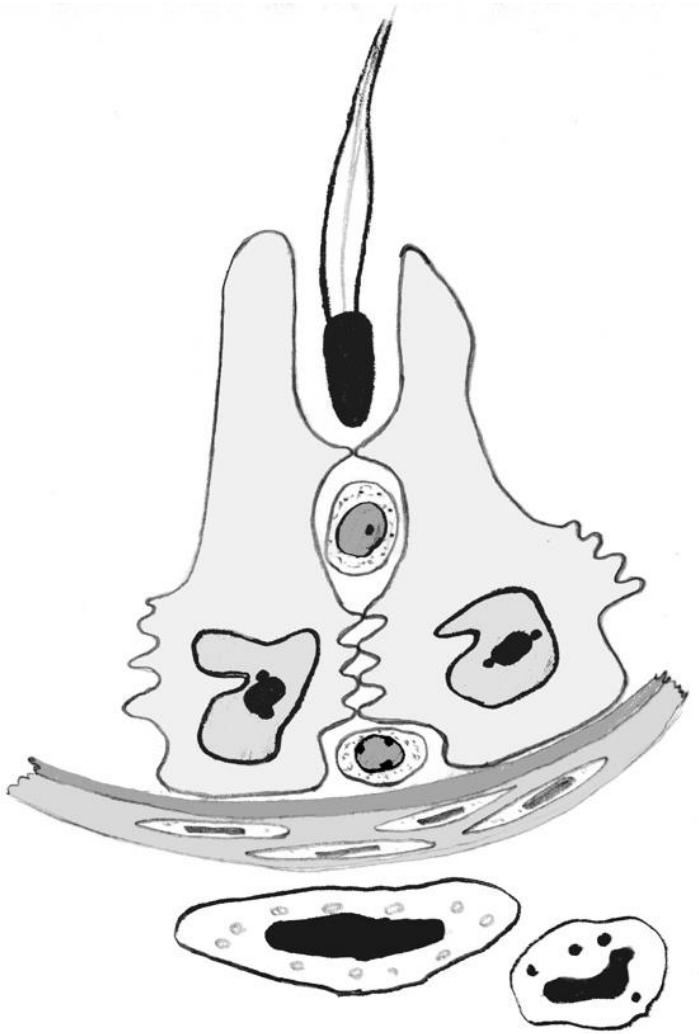
Male Reproductive Pathology

Overview

- Scrotum and contents
  - Testis
  - Epididymis
  - Spermatic cord
- Accessory genital glands
  - Vesicular glands
  - Prostate
- Penis and prepuce

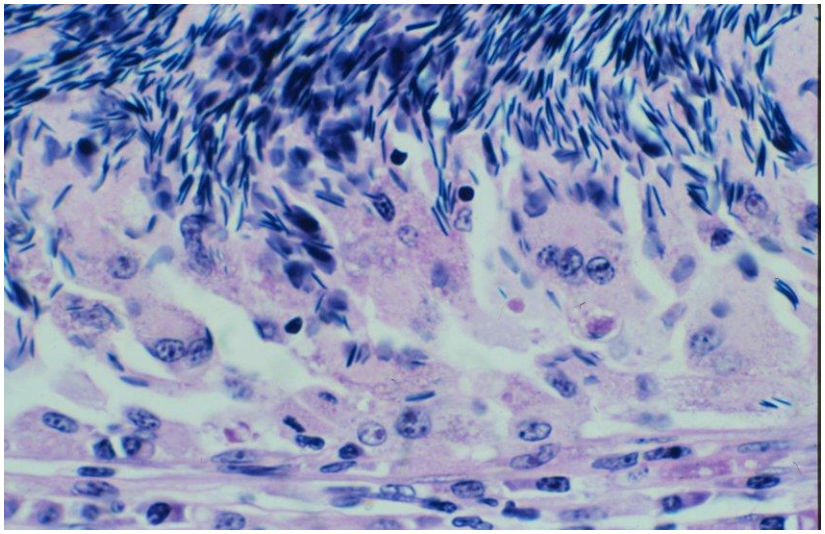
Spermatic granuloma

- Blood testis barrier
  - Sertoli cells
  - Basement membrane
  - Myoid cells
- Immune suppression
  - 'Immune privilege'
  - Antiinflammatory environment,



Immune suppression - why

- Gametes develop after self-tolerance
- Structure of spermatozoa
  - Foreign body reaction
  - Antigenic – adaptive immunity



Immune suppression - how

- Macrophages – diminished capacity
- Antiinflammatory cytokine environment
  - Immune cells
  - Somatic cells
- Androgens
  - Suppress proinflammatory cytokines
  - Shift cytokine balance
- Testicular dendritic cells suppress.

Physical barriers

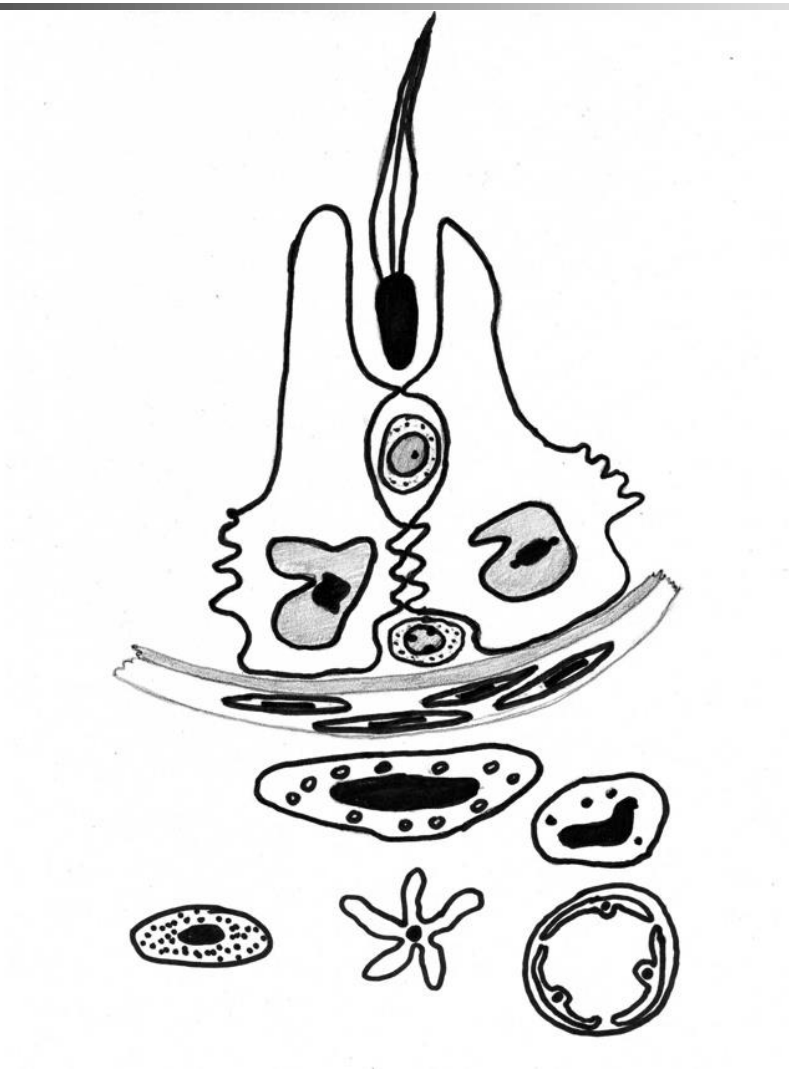
- Sertoli cells
  - Highly complex alteration of cell junctions to allow spermatogenesis
- Peritubular cells
  - Pressure
  - Minimal barrier
  - Cytokines, growth and differentiation factors

Oxidative stress

- Reactive oxygen species vs antioxidant systems
- High metabolism and cell generation
- Increasing oxidative stress
  - Toxicant exposure
  - Chemotherapy
  - Ionizing radiation
  - Inflammation
  - Varicocele
  - Cryptorchidism
  - Aging
  - Torsion

R. John Aitken* and Shaun D. Roman. Antioxidant Systems and Oxidative Stress in the Testes. Adv Exp Med Biol 2008 636 154-71
Terry t. Turner*{ and jeffrey j. Lysiak. (2009) Oxidative Stress: A Common Review Factor in Testicular Dysfunction. J Androl 2008 29 488-499

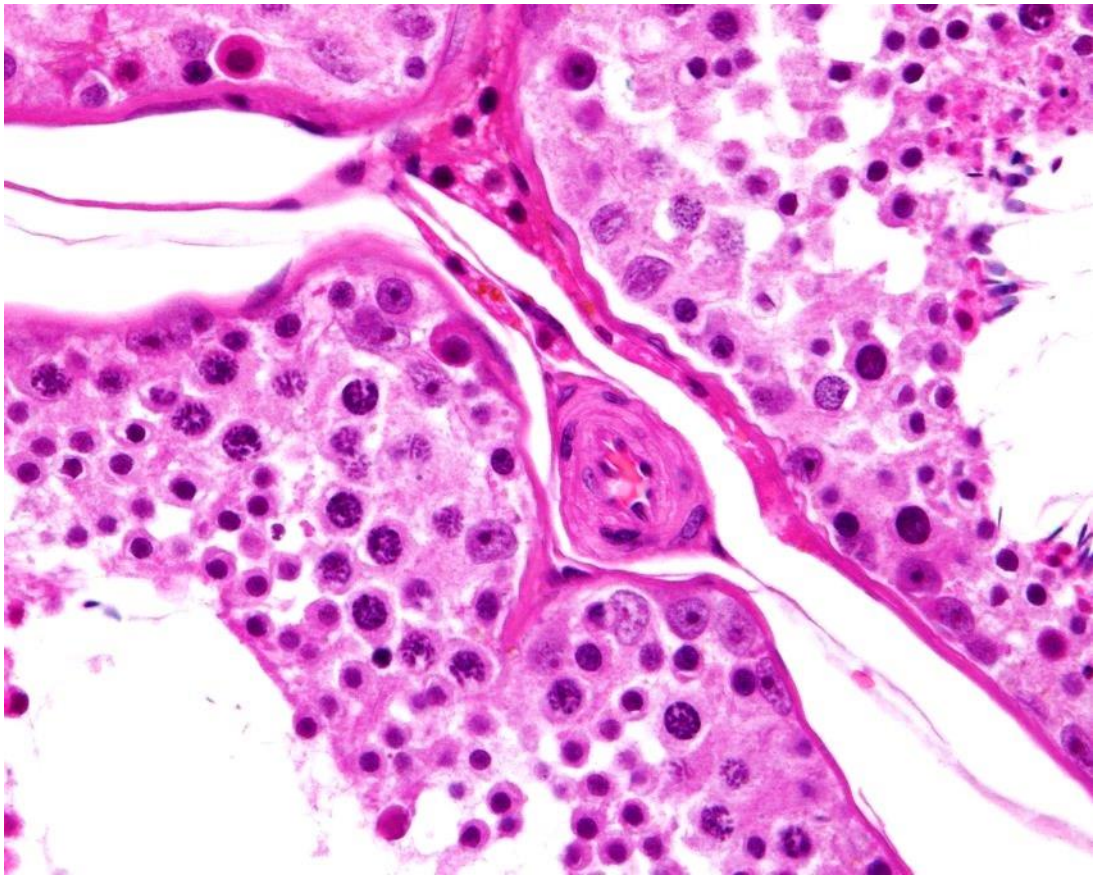
New view of testis



Spermatogenesis

Interstitial endocrine cell

Sertoli cell



Peritubular myoid cell

Germ cell

Hormonal and biomolecular soup

Biomolecular soup

- Androgens and estrogens
- Inhibin and activins (TGF family)
- Transferrin
- IGF-1
- Relaxin like factor
- POLMC and β endorphin
- Oxytocin
- Toll-like receptors

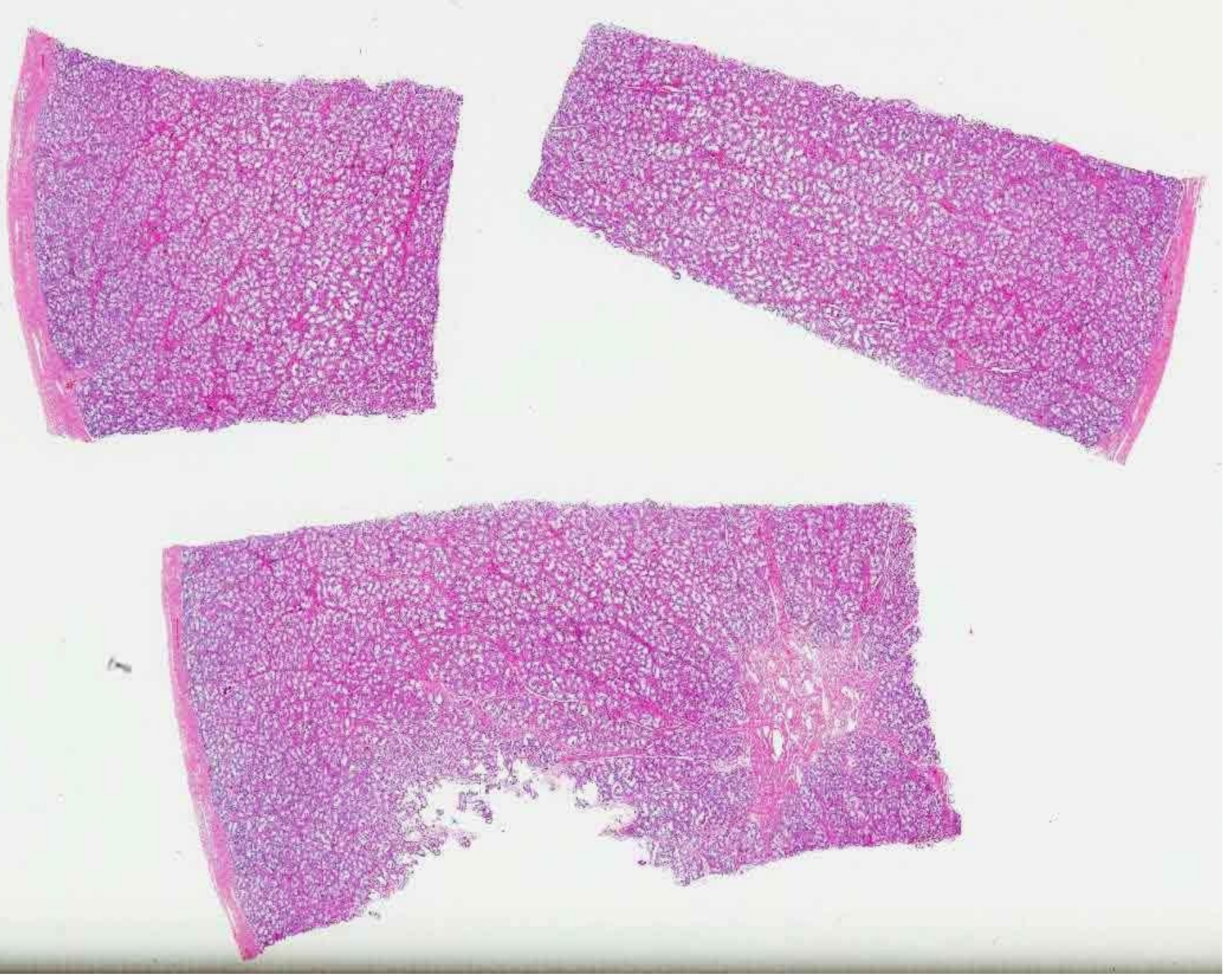
Take home message

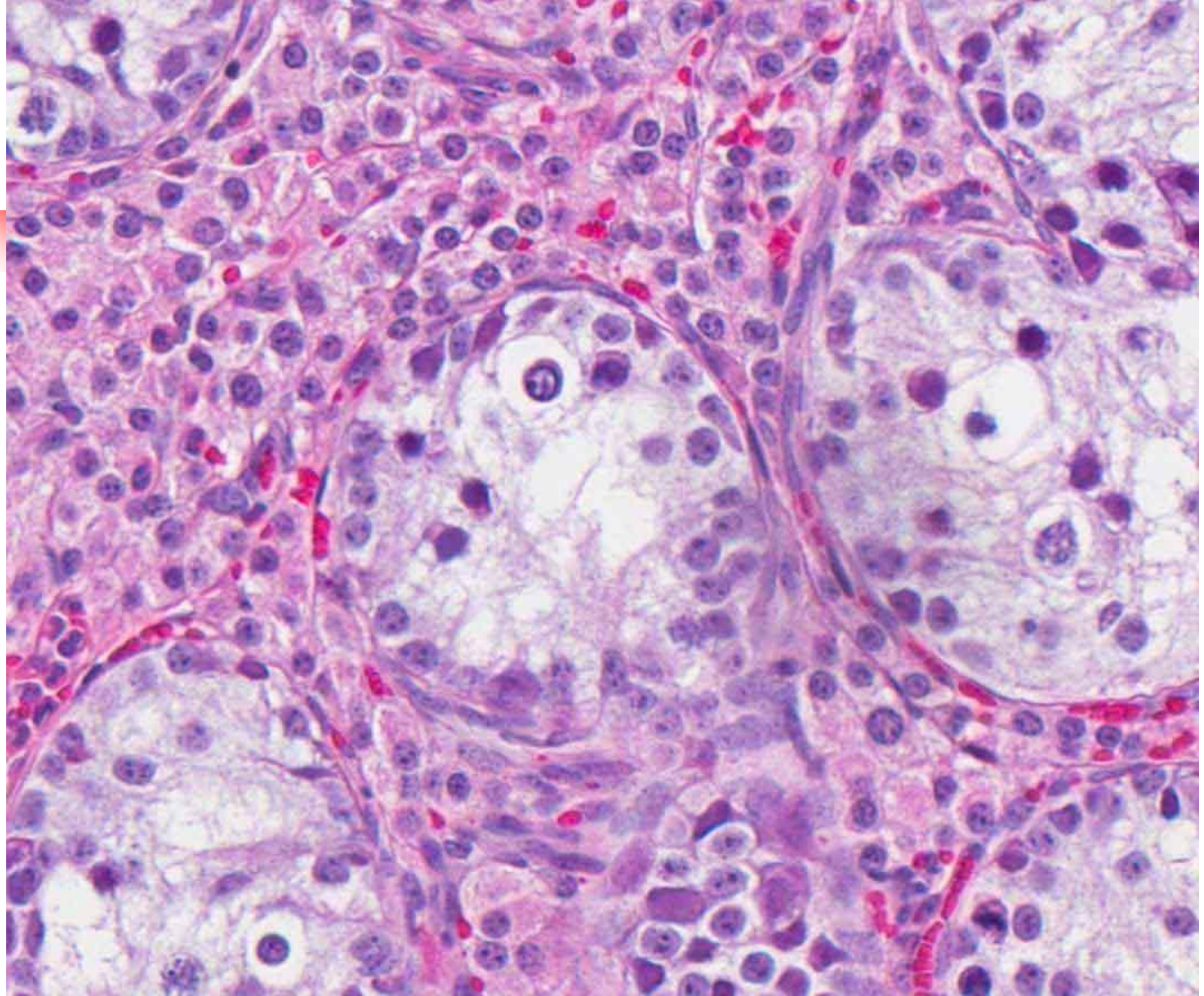
- Hormonal, paracrine and autocrine interactions are complex
- Interfer with soup = hypoplasia or degeneration

- Oxidative stress is very important in disturbing soup.

Diagnostic case

- Very large boar stud supplying major pork producer
- Problem: Poor semen quality of young boars.
- Approach: euthanasia and collection of reproductive tracts. Histology by several pathologists.





Small testes

- Hypoplasia
  - Testes and epididymides are small at puberty
- Degeneration/atrophy
  - Testes are smaller than they were
  - Occurs in hypoplastic testes
  - Epididymides larger than in hypoplasia alone

Hypoplasia - Degeneration

- Mechanisms similar
  - Alteration of ‘biomolecular soup’
- Timing of insult is different

Hypoplasia

- Disorders of Sexual development
  - Chromosomal DSD
    - XXY cat
  - XX DSD
    - American Cocker, polled goat
  - XY DSD
    - Persistent Müllerian duct syndrome
    - Cryptorchidism
    - 'Uncomplicated hypoplasia'

‘Uncomplicated’ hypoplasia

- XY *SRY*+ testicular DSD

- Common in bulls
- Scrotal circumference at puberty
- Cull rate is up to 50% in some species

Testicular hypoplasia

- Chromosomal anomalies
- Genetic
- Testicular artery branching and blood flow
- BVDV
- Nutrition

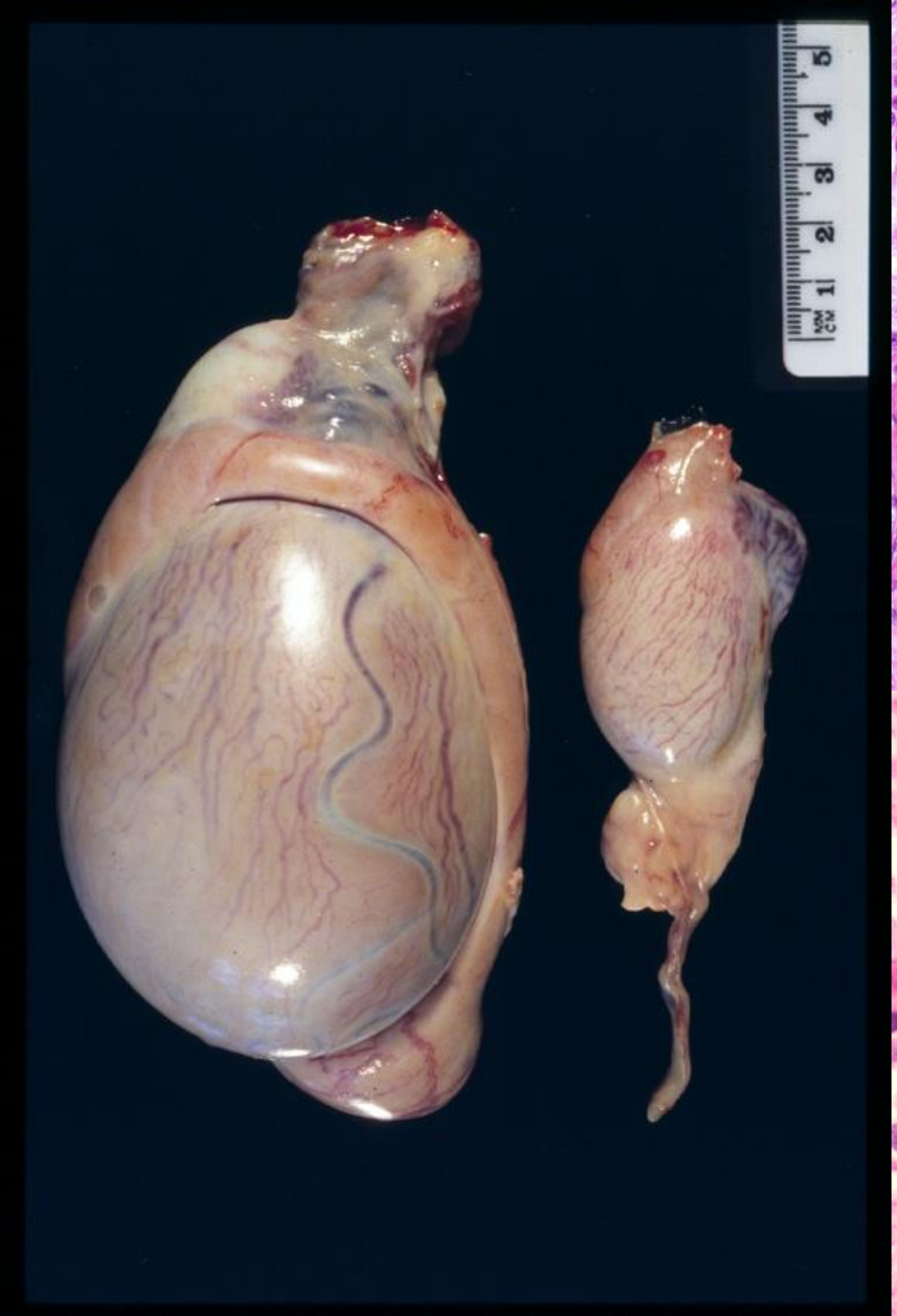
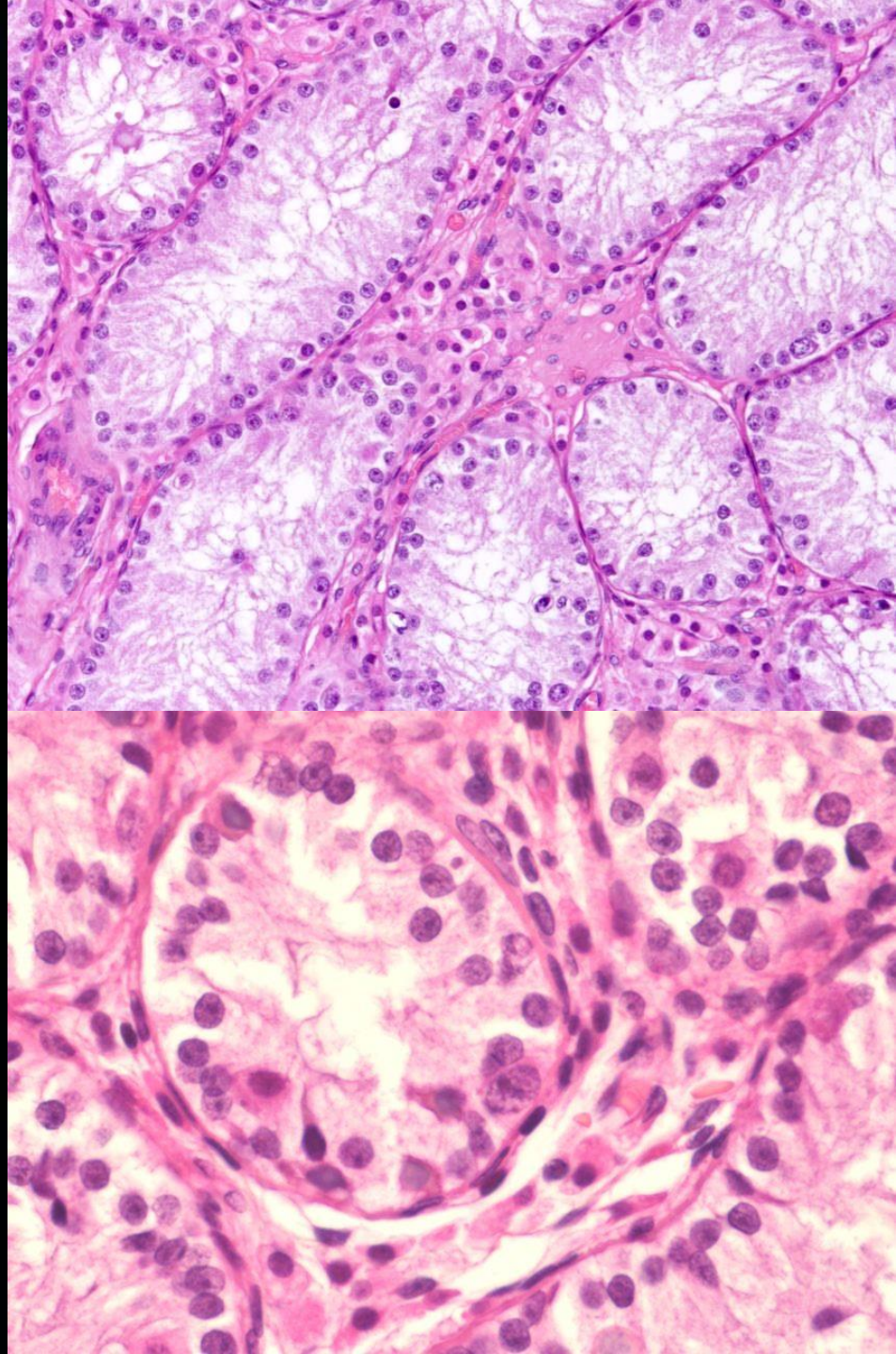
Cryptorchidism

- XY *SRY*+ testicular DSD
- Genetic
  - Heredity basis
- Hormonal
  - Androgen?
- Structural
  - Fusion
  - Gonadal ligaments
- Other

Cryptorchidism

- Abdominal translocation
  - Insulin like peptide 3
  - Anti-Müllerian hormone
- Transinguinal migration
  - Gubernacular enlargement
  - Intraabdominal pressure
- Inguinoscrotal migration
  - Androgen
  - Genitofemoral nerve
  - Calcitonin gene related protein

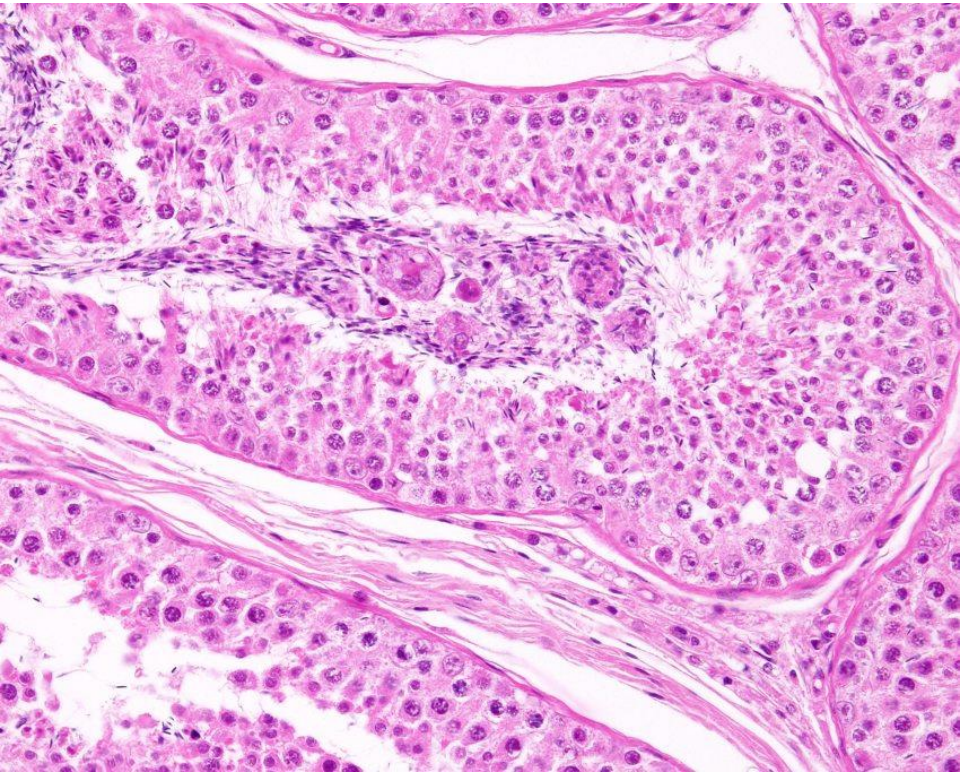
Ieuan A Hughes and Carlo L Acerini (2009) Factors controlling testis descent. European Journal of Endocrinology (2008) 159 S75–S82

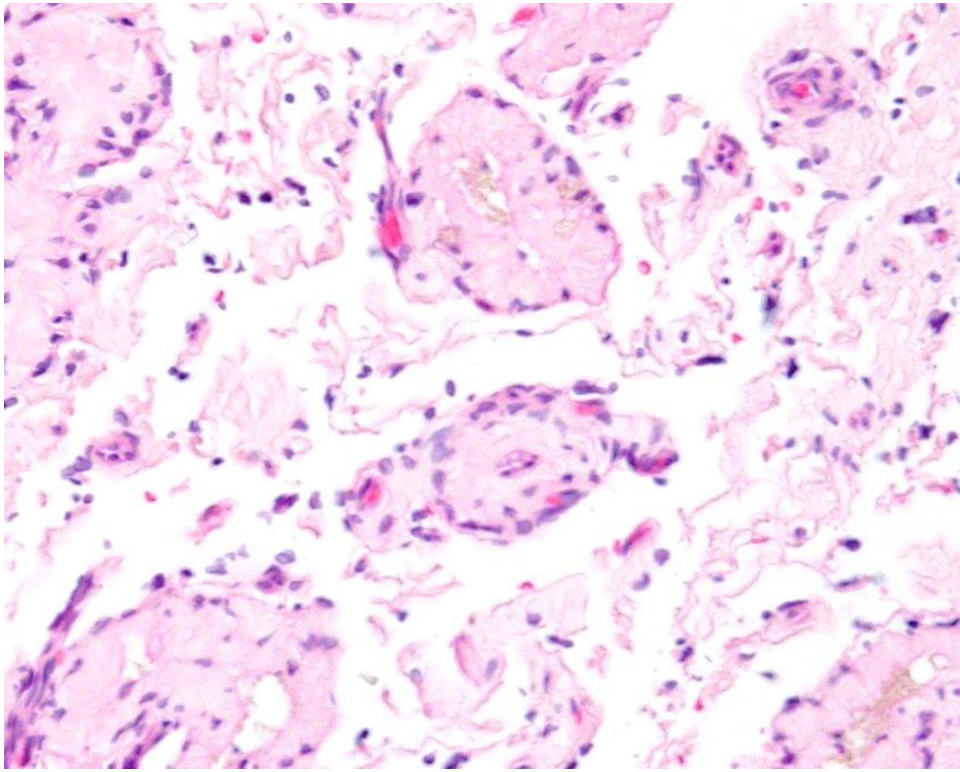



Testicular atrophy/degeneration

- Age
- Oxidative injury
- Blood flow
- Temperature
- Chemicals
- Hormones
- Neoplasia
- Nutrition

Degeneration



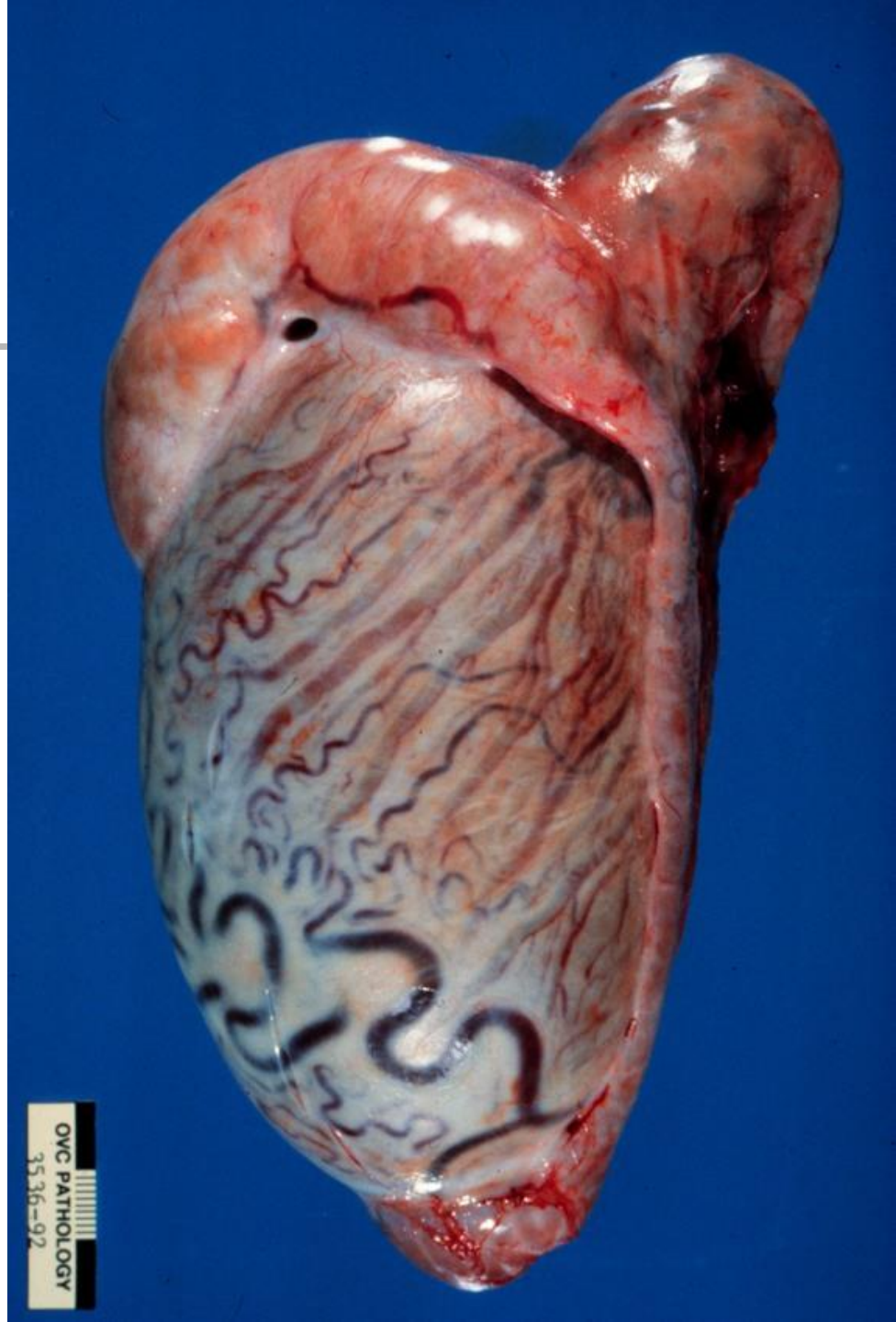


Orchitis!

Photo by Tracey Chenier

Bull

Spermatic granuloma of epididymal head



Ram

Ram

Spermatic cord

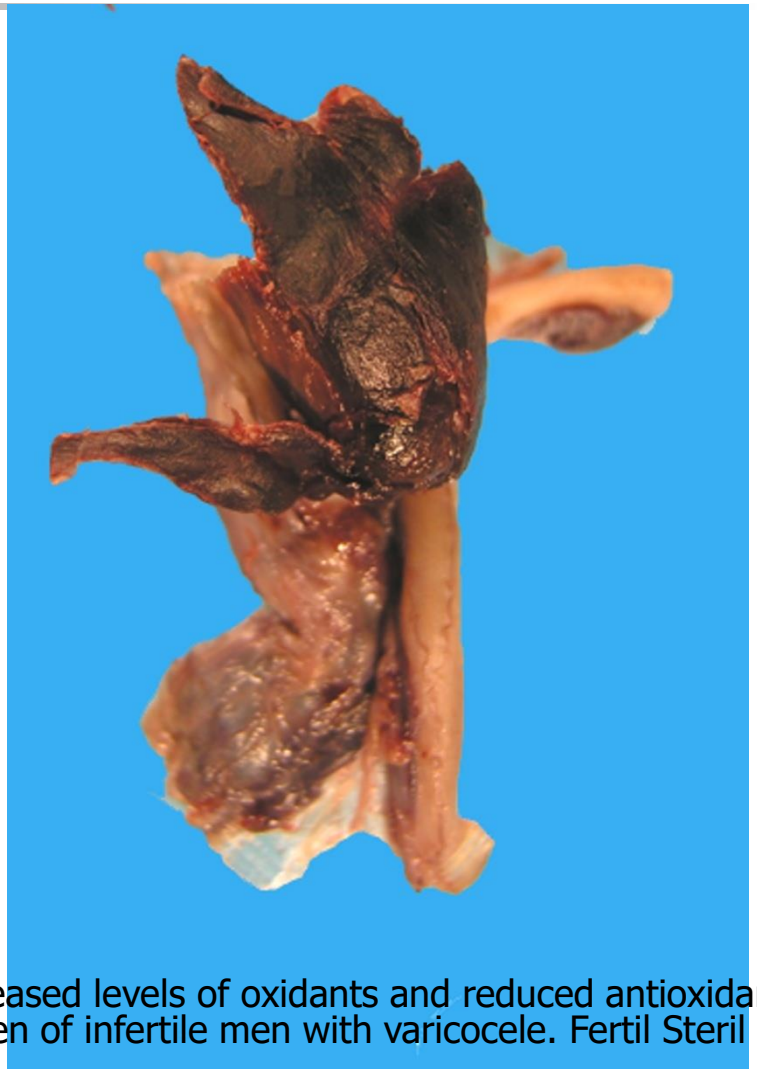
Deferent duct

Cremaster muscle

Pampiniform plexus

Nerves

Varicocele



Increased levels of oxidants and reduced antioxidants in semen of infertile men with varicocele. Fertil Steril 2010

Accessory genital glands

Ampullae

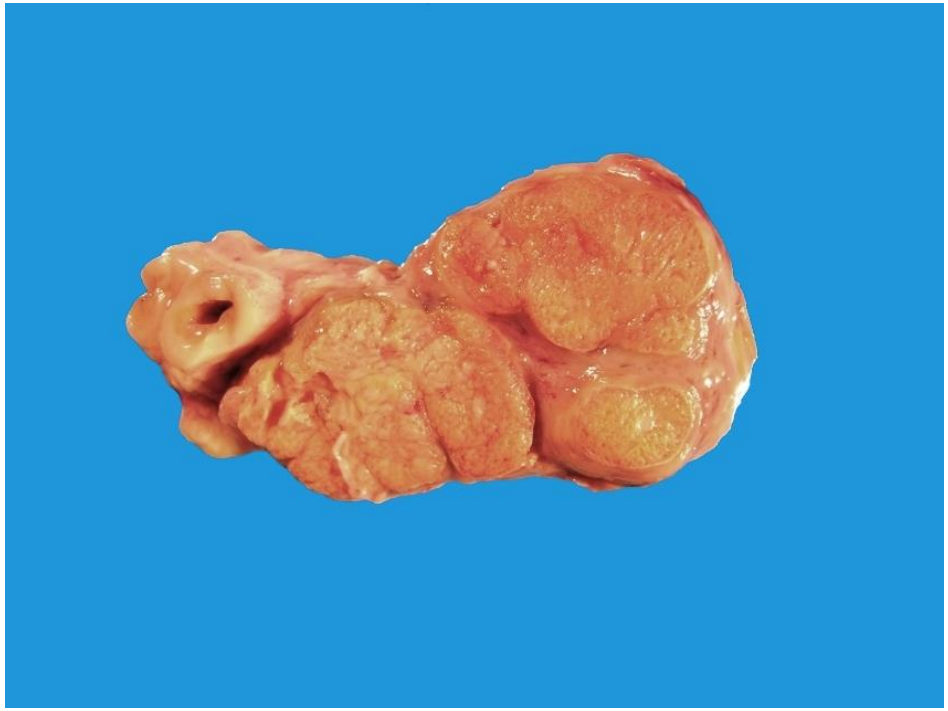
Prostate

Vesicular glands

Bulbourethral glands

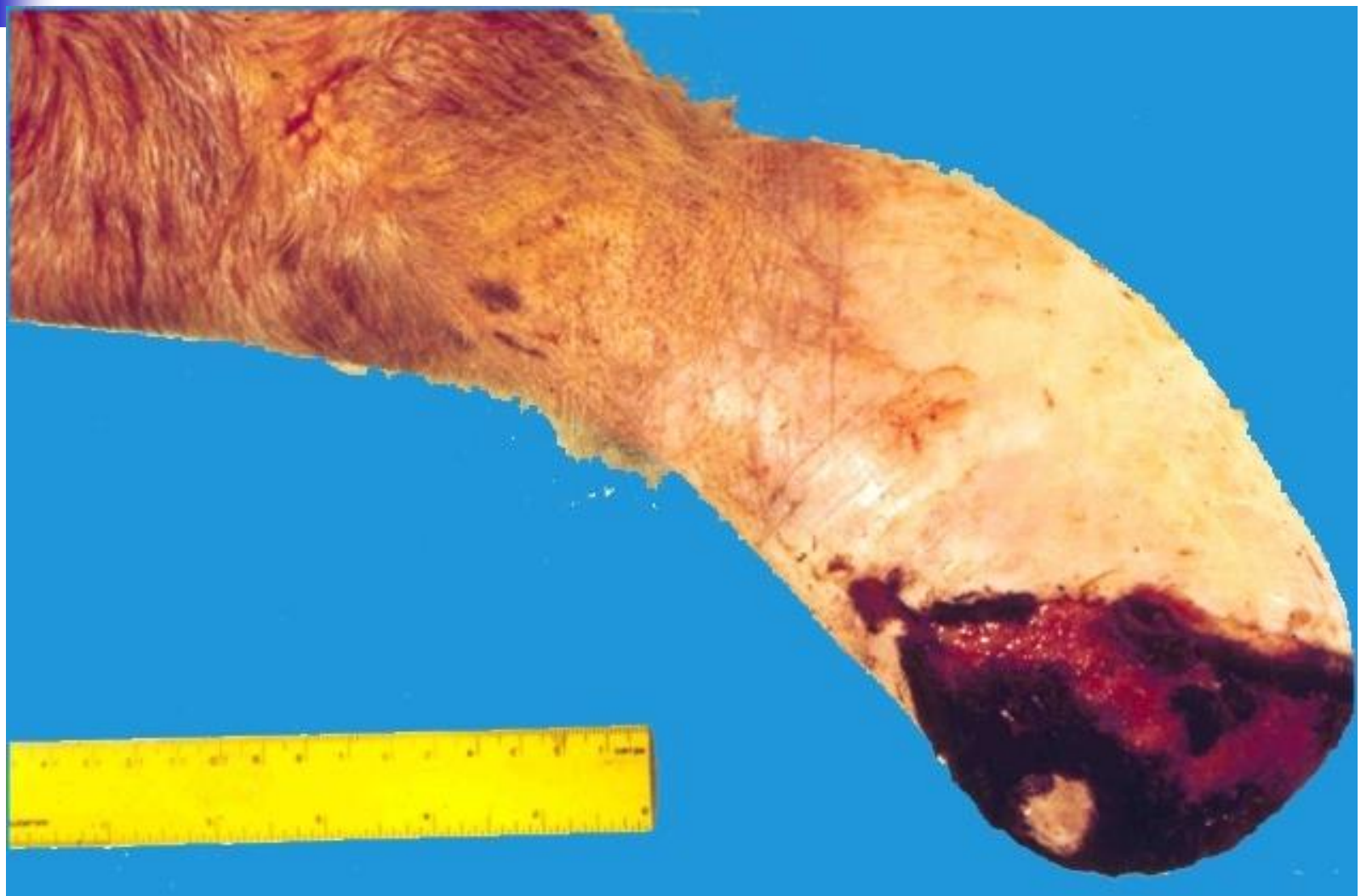
Vesicular adenitis

- Acute fibrinopurulent form
- Chronic interstitial form

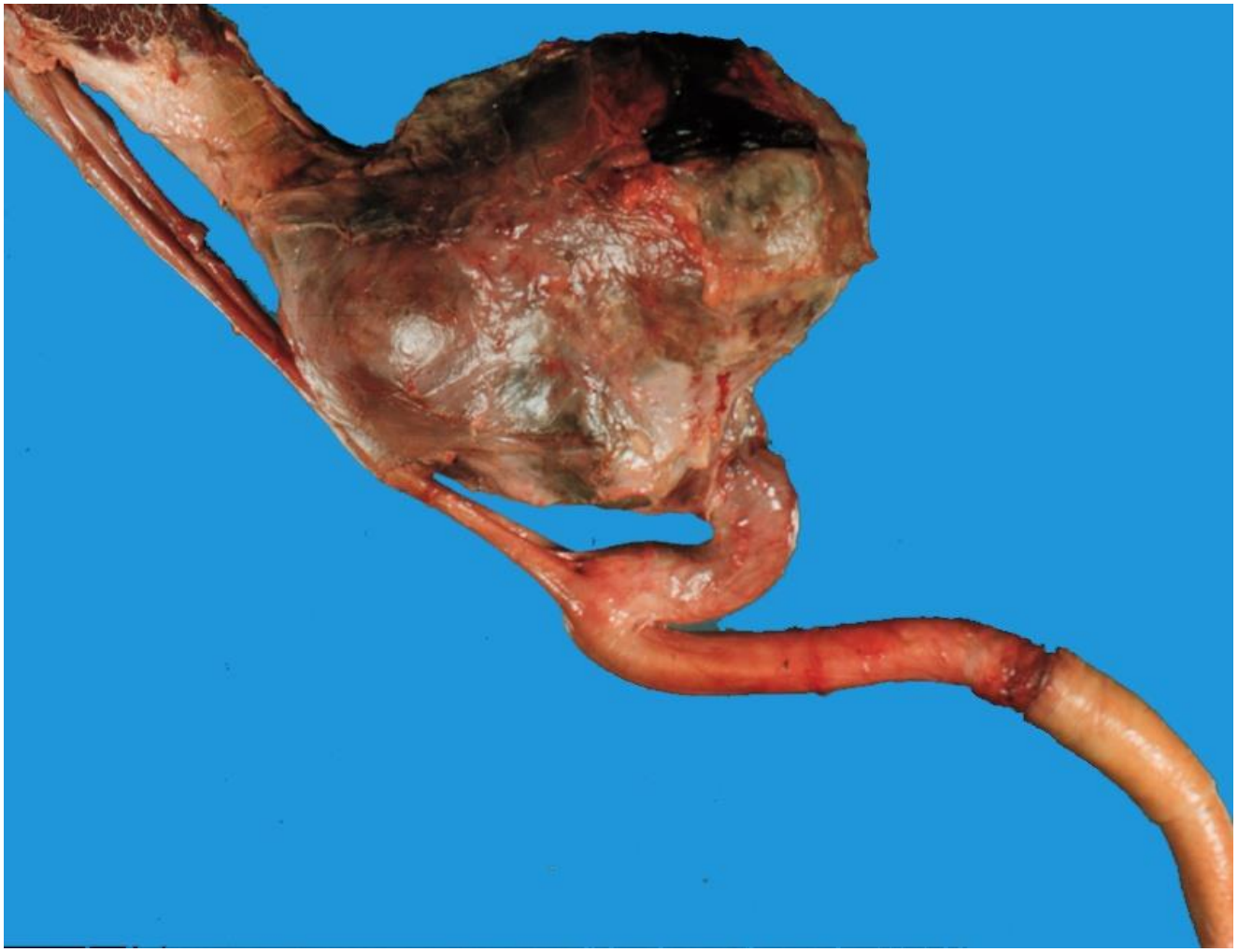


Penis and prepuce

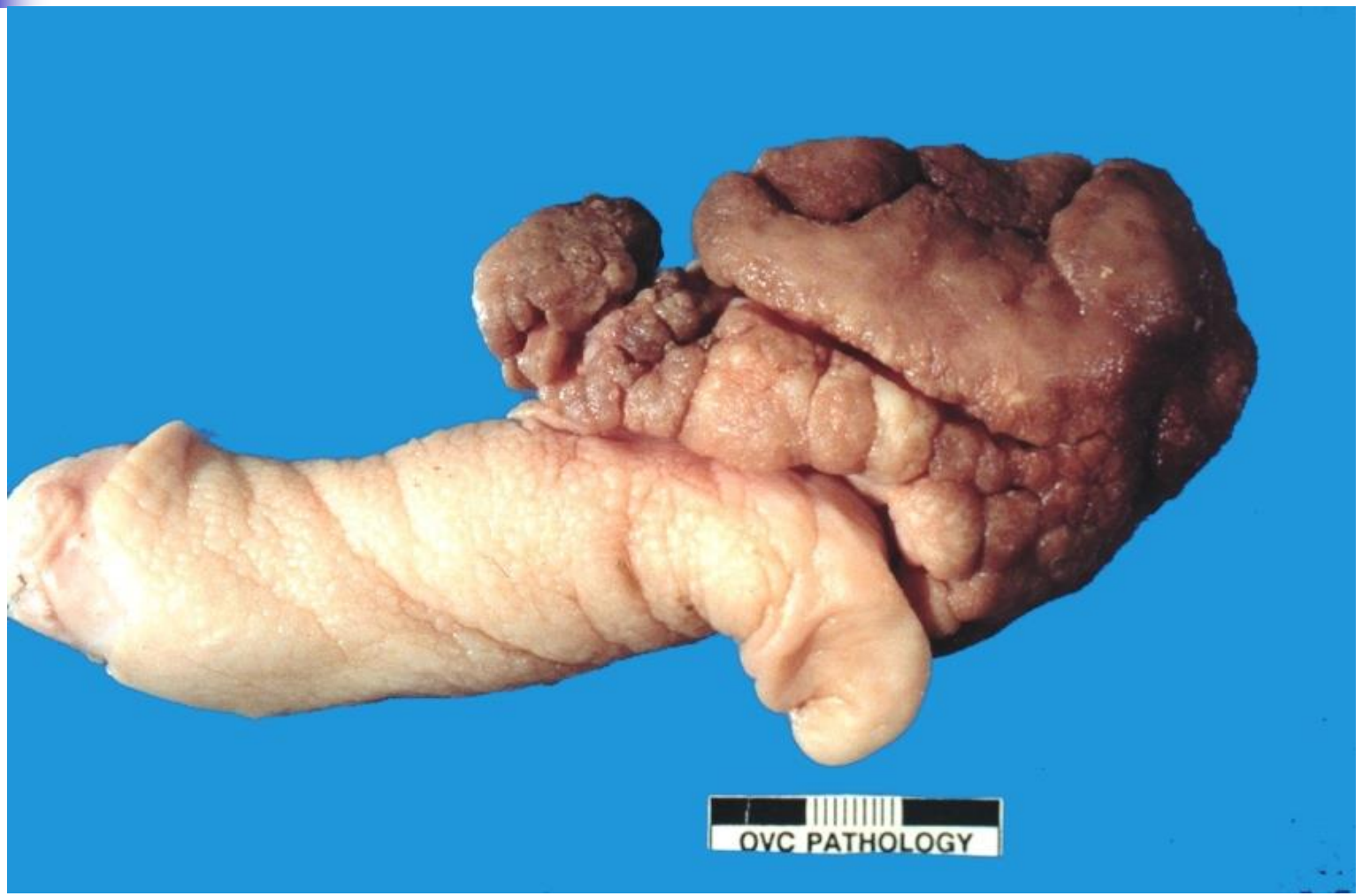
Preputial eversion and prolapse



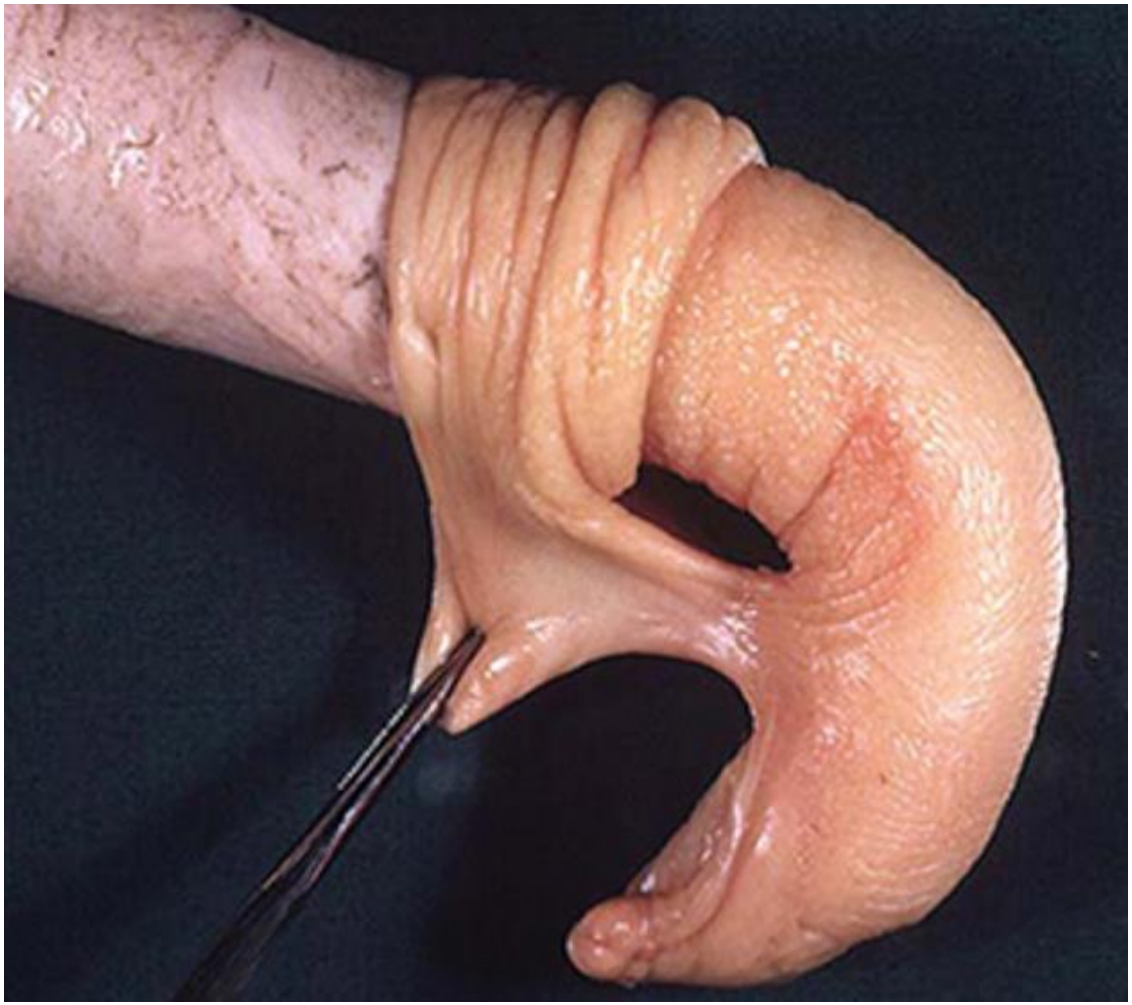
Forced deviation and hematoma



Neoplasia - fibropapilloma



Balanopreputial bands



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- Histovet Surgical Pathology
  - Dr Wilcock

- Submitters and website visitors

Sponsors

- Australian Animal Pathology Standards Program
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  - Animal Health Australia
- Charles Louis Davis Foundation