Perinatal acute respiratory failure, autopsy remains the best quality control

Eumenia Castro, Ninad Patil, Edwina Popek

Pavilion for Women, Texas Children's Hospital

Baylor College of Medicine

BACKGROUND

- Autopsy
  - Autopsy rates have been declining significantly in recent decades
    - Adult autopsies:
      - 1959: 50%
      - 1992: 1.5%
    - Pediatric autopsies
      - Less significantly decrease:
        - 25-53% EXCLUDING MEDICAL LEGAL CASES

BACKGROUND:

- Why we did this study?
  - Acute Respiratory Failure is one of the most common problems seen in premature and term babies
    - Etiology: Surfactant deficiency, MAS, sepsis, persistent pulmonary hypertension, pulmonary hypoplasia, others
  - Autopsy examination is an important quality control
  - Often establishes the etiology for the perinatal respiratory depression and cause of death

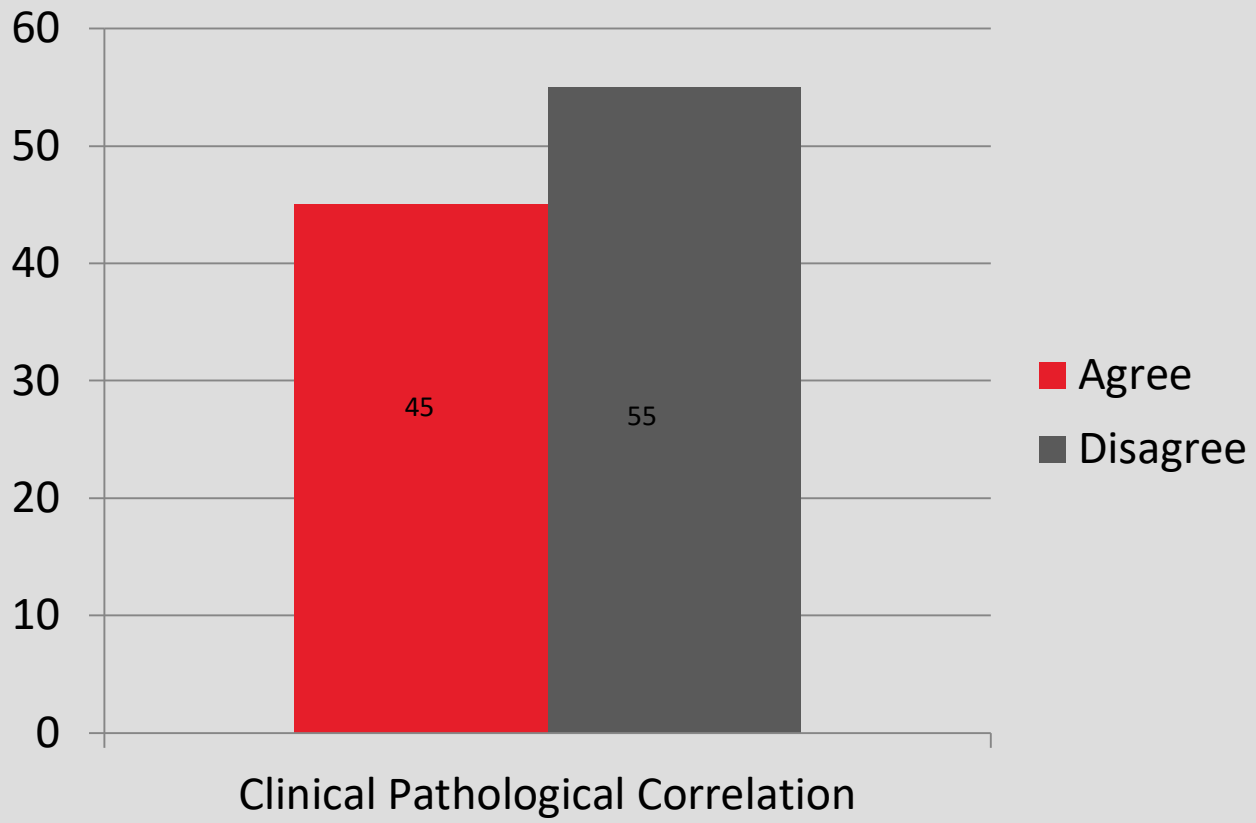
AIM:

- Correlate autopsy findings with initial clinical impression in cases of failure to resuscitate in early perinatal period

MATERIAL AND METHODS:

- 200 autopsy reports were reviewed from 2000-2019
- Inclusion criteria:
  - Age>0-10 days
  - Clinical history of respiratory failure unresponsive to treatment
- Exclusion Criteria
  - Cases with imaging only autopsies

RESULTS

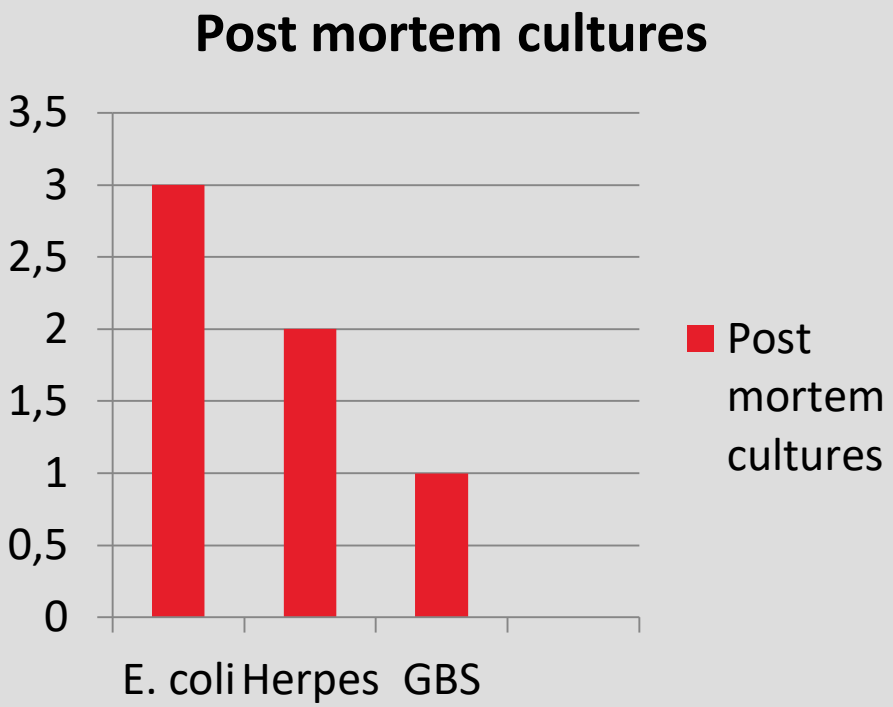

60
50
40
30
20
10
0
45
55
Agree
Disagree
Clinical Pathological Correlation

MAJOR DISCREPANCIES

- Infection: 4%
- Congenital Heart Disease: 2%
- Congenital lung abnormalities: 1%

RESULTS

- Infection
  - Routine in autopsies: lung and blood cultures
- Most frequent post mortem cultures:
  - E. coli: most frequent 3%
  - Herpes
  - GBS
  - Candida
  - MRSA
  - Pseudomonas



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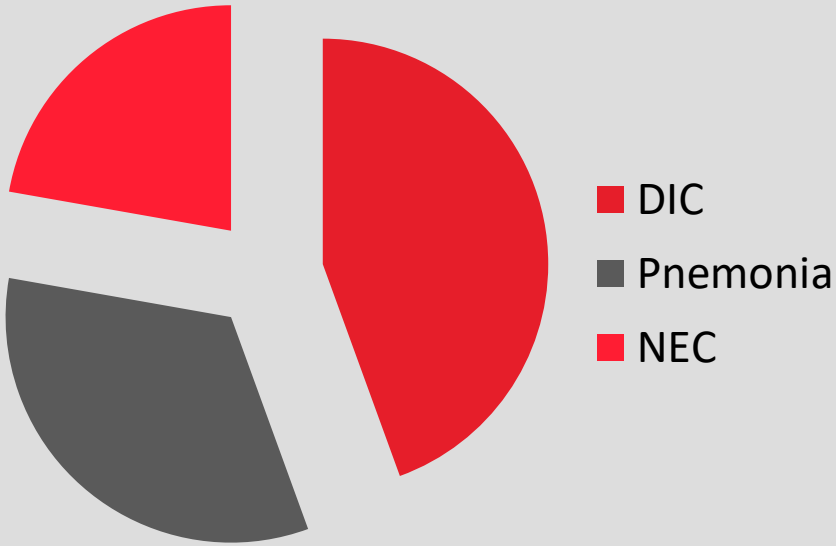
RESULTS

- Placenta
  - 50% of the cases had acute placental inflammation
- Clinical cause of Death
  - 4% DIC
  - 3% pneumonia
  - 2% necrotizing enterocolitis



RESULTS

- Lethal Complex Malformations

Pre mortem Diagnosis	Postmortem Diagnosis
Preeclampsia	IUGR and craniocerebellarcardiac syndrome Ritsher-Schinzel
Congenital Heart Disease	Necrotizing enterocolitis totalis
Twin B, perinatal hypoxia	Copy number loss with Chromosomal band 8p22 of unclear significance; cause of death: bronchopneumonia and DIC, negative cultures
Respiratory Insufficiency	Trisomy 13, Double outlet right ventricle, pulmonary valve atresia Hypoxic-ischemic encephalopathy
Fetal bradycardia	Dextrocardia, L-transposition of great arteries, Ebstein's anomaly and dysplastic valves, pulmonary hypoplasia

RESULTS

- Lethal Complex Malformations

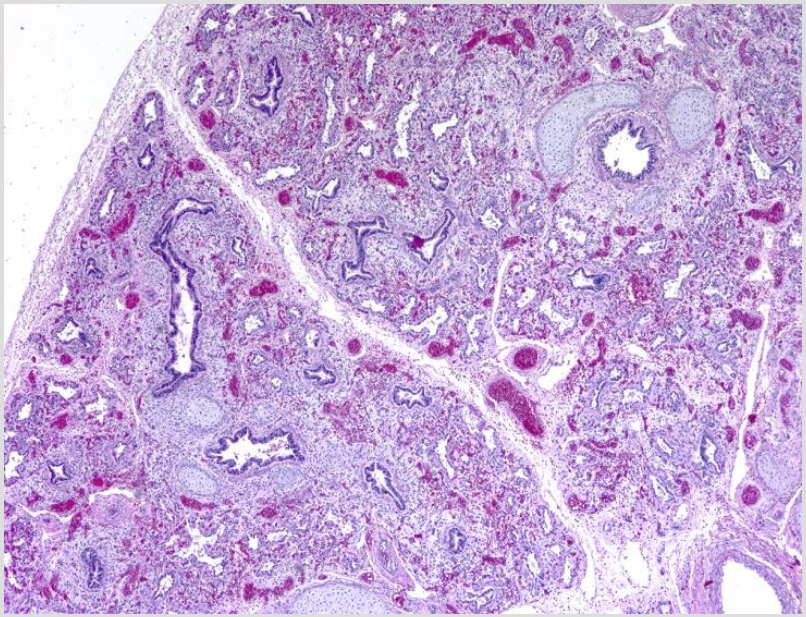
Pre mortem Diagnosis	Postmortem Diagnosis
Respiratory insufficiency, fetus of diabetic mother	Di George Syndrome, absent kidneys, severe pulmonary hypoplasia
Non-reassuring fetal heart rates	Neonatal sudanophilic orthochromatic leukodystrophy bacterial sepses and pneumonia
Fetal bradycardia	Complex cardiac congenital disease, pulmonary hypoplasia, marked cardiomegaly

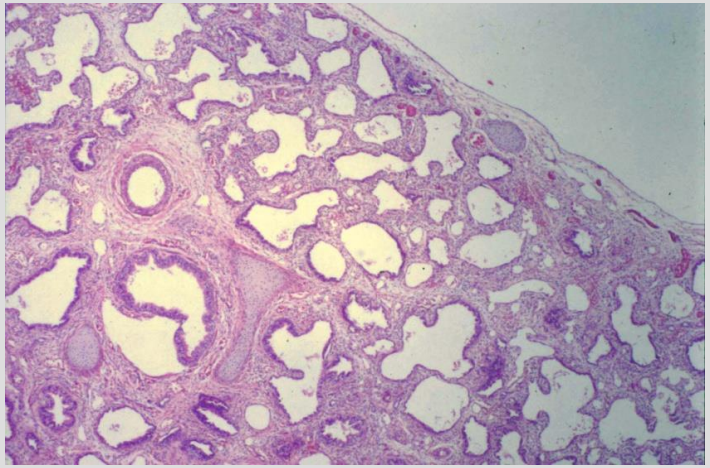
RESULTS

- Lethal lung abnormalities
- All of them the clinical picture was ”respiratory insufficiency at birth even with intensive support”
  - Acinar Dysplasia
  - Alveolar Capillary Dysplasia
  - Alveolar Capillary Dysplasia with misalignment of pulmonary veins

ACINAR DYSPLASIA

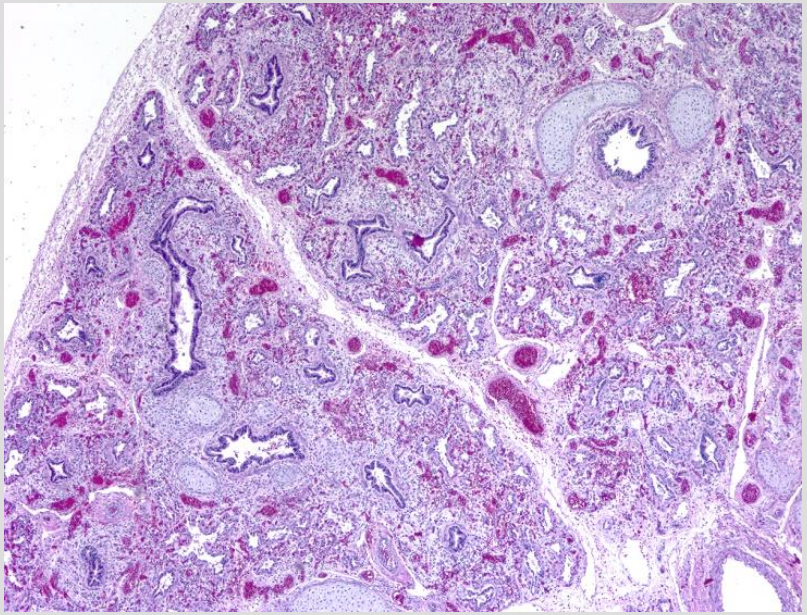
- Diffuse bilateral impairment of the development of respiratory bronchioles, alveolar ducts and alveoli
- Females
- Neonatal lethal due to respiratory insufficiency at birth, generally survive only hours, even with support

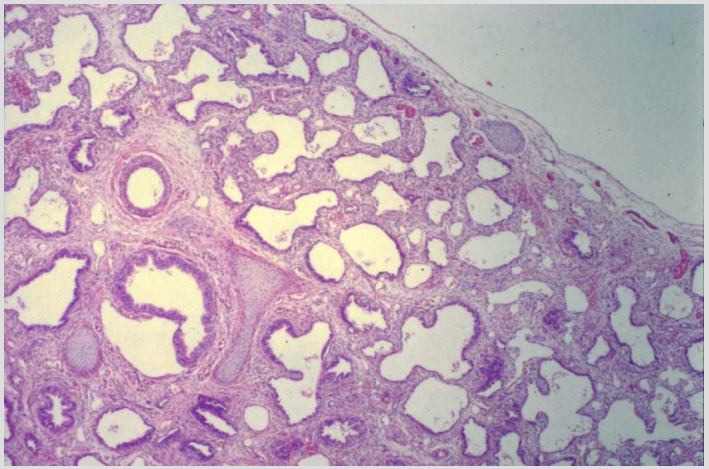




ACINAR DYSPLASIA

- The *TBX4* gene (MIM 601719) spans about 50 kb on chromosome 17q23.2 and consists of eight (or possibly nine) exons
- During organogenesis, *TBX4* is expressed in the hind limbs, mandibular mesenchyme, lung mesenchyme, atrium of the heart and body wall

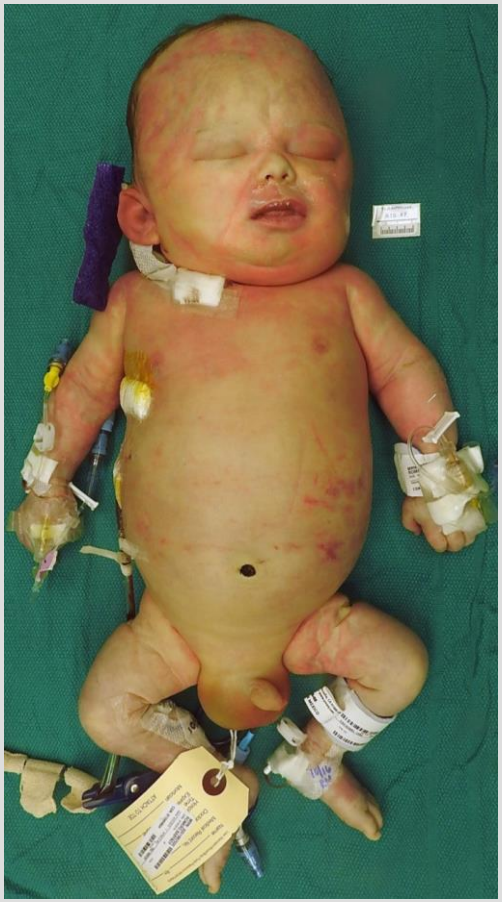




ALVEOLAR CAPILLARY DYSPLASIA WITH MISALIGNMENT OF PULMONARY VEINS

Full term, AGA, respiratory distress within a few hours of birth and death within days to weeks

- 80% have malformations outside the lung
  - Heart defects (19% with HLH, PFO, PDA), tracheoesophageal fistula (3%), gut malrotation (22%), absent gall bladder, renal agenesis, hydronephrosis (24%), imperforate anus (8%), and single umbilical artery (19%), cerebellar heterotopia (3%)
  - Lungs may also have abnormal lobation and lymphangiectasis (33%), rarely small



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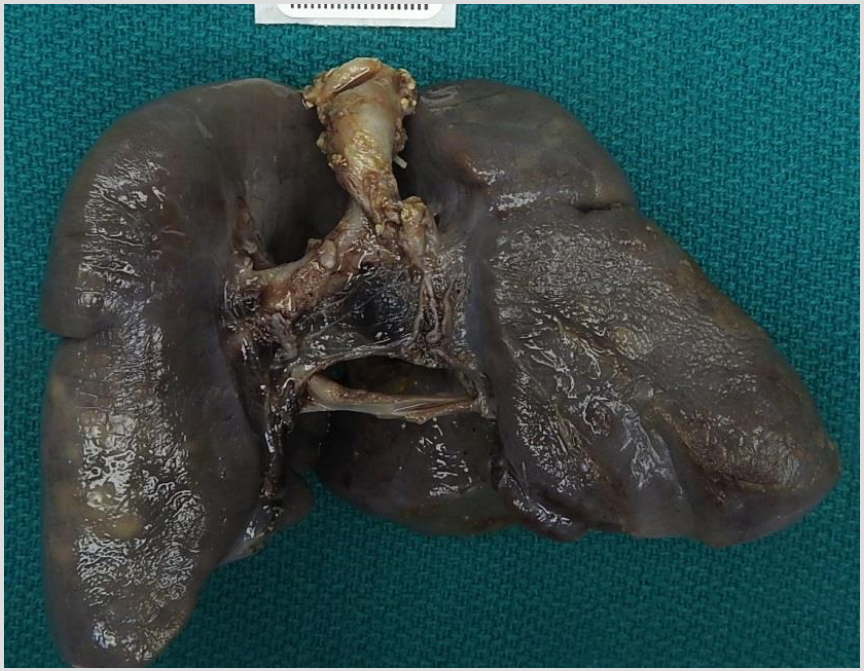

Bilobed lungs

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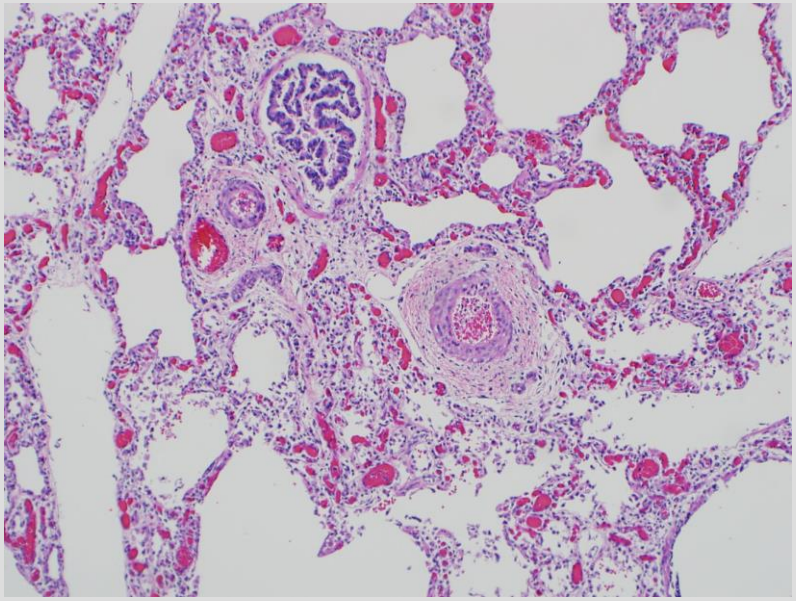
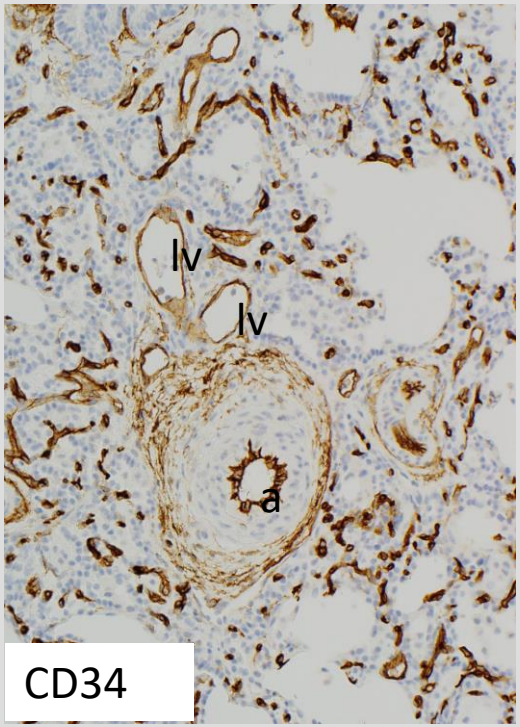
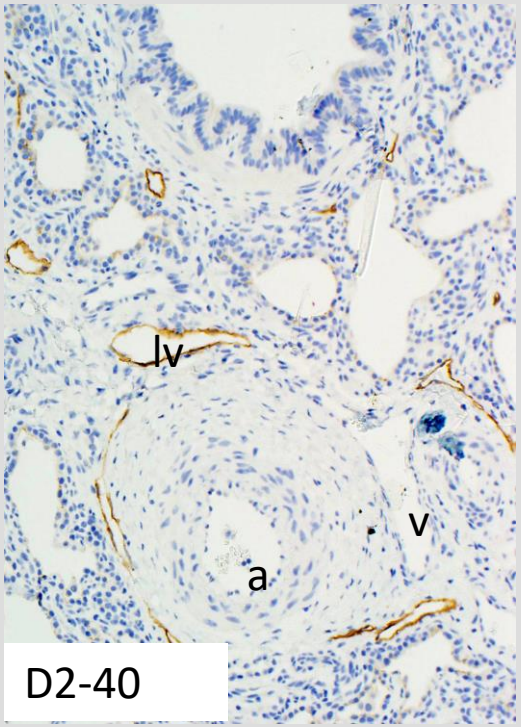




CD34



D2-40

ACD/MPV- CLINICAL

Full term, AGA, respiratory distress within a few hours of birth and death within days to weeks

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ACD/MPV- CLINICAL

- Heterozygous point de novo mutations or genomic deletion copy number variants involving *FOXF1* or its 60-kb tissue-specific enhancer region mapping 270 kb upstream of *FOXF1* and involving fetal lung-expressed long non-coding RNA genes and CpG-enriched sites on chromosome 16q24.1
- 141 families studies, have 86 pathogenic variants in the *FOXF1 locus*: 38 deletion CNVs, one complex rearrangement and 47 point mutations

CONCLUSIONS

- Postmortem examination:
  - Determine the cause of death is just one of the goals of perinatal autopsy
    - Quality of Medical Care
    - Unexpected findings with possible implication for the family
    - Unidentified infection
    - Clarification of the clinical differential diagnosis

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COMMENTS/QUESTIONS?