ISOM 2012
The role of the autopsy after maternal death

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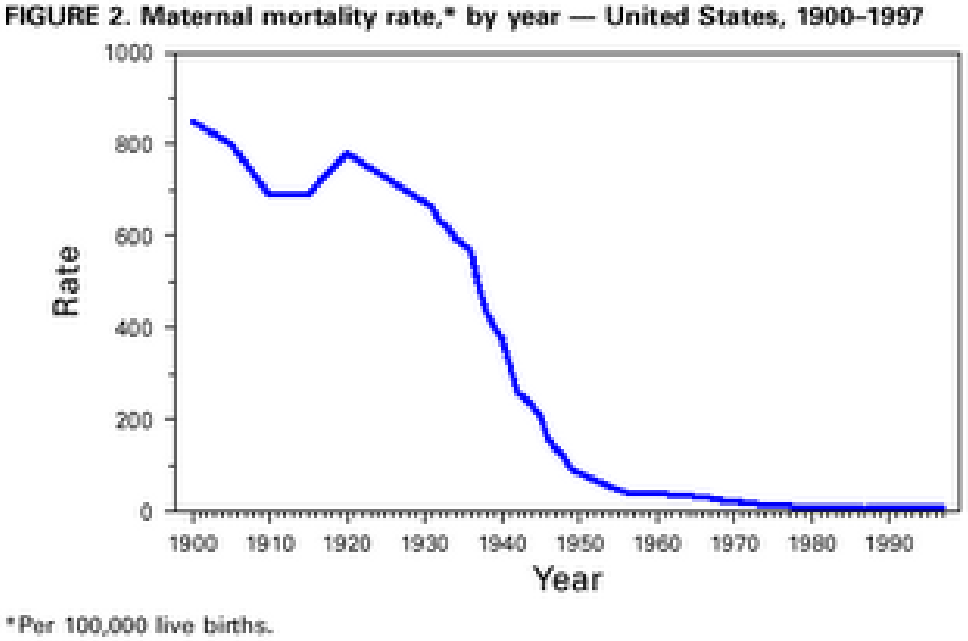
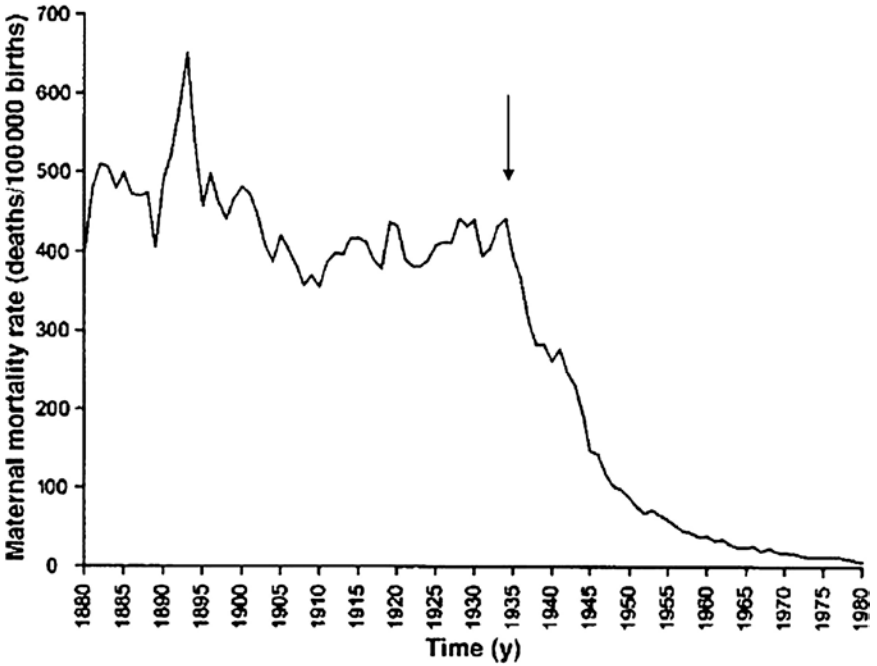
Maternal mortality rates:
did autopsy data cause the decline?

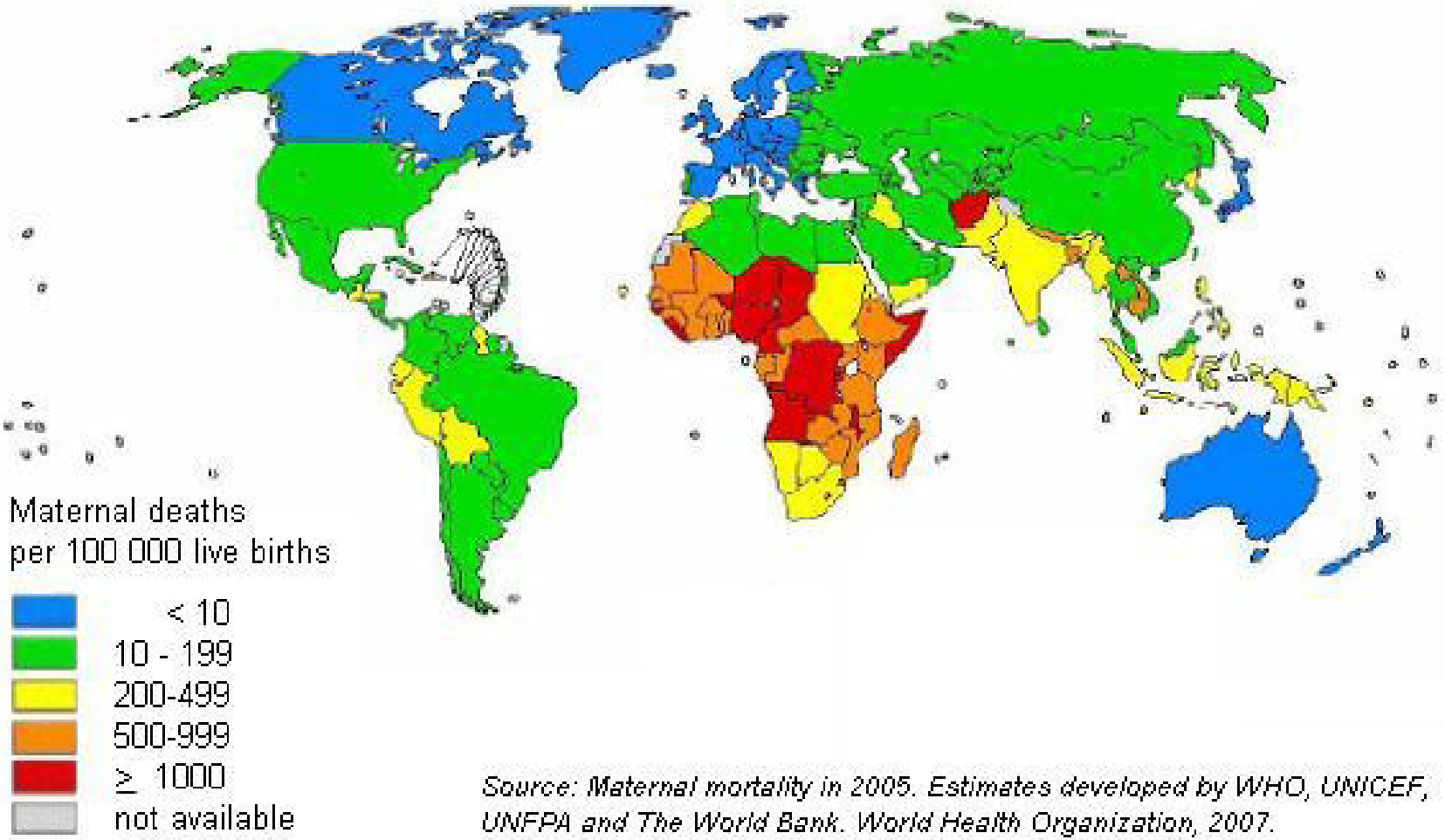


USA



UK

Maternal mortality ratio, by country, 2005



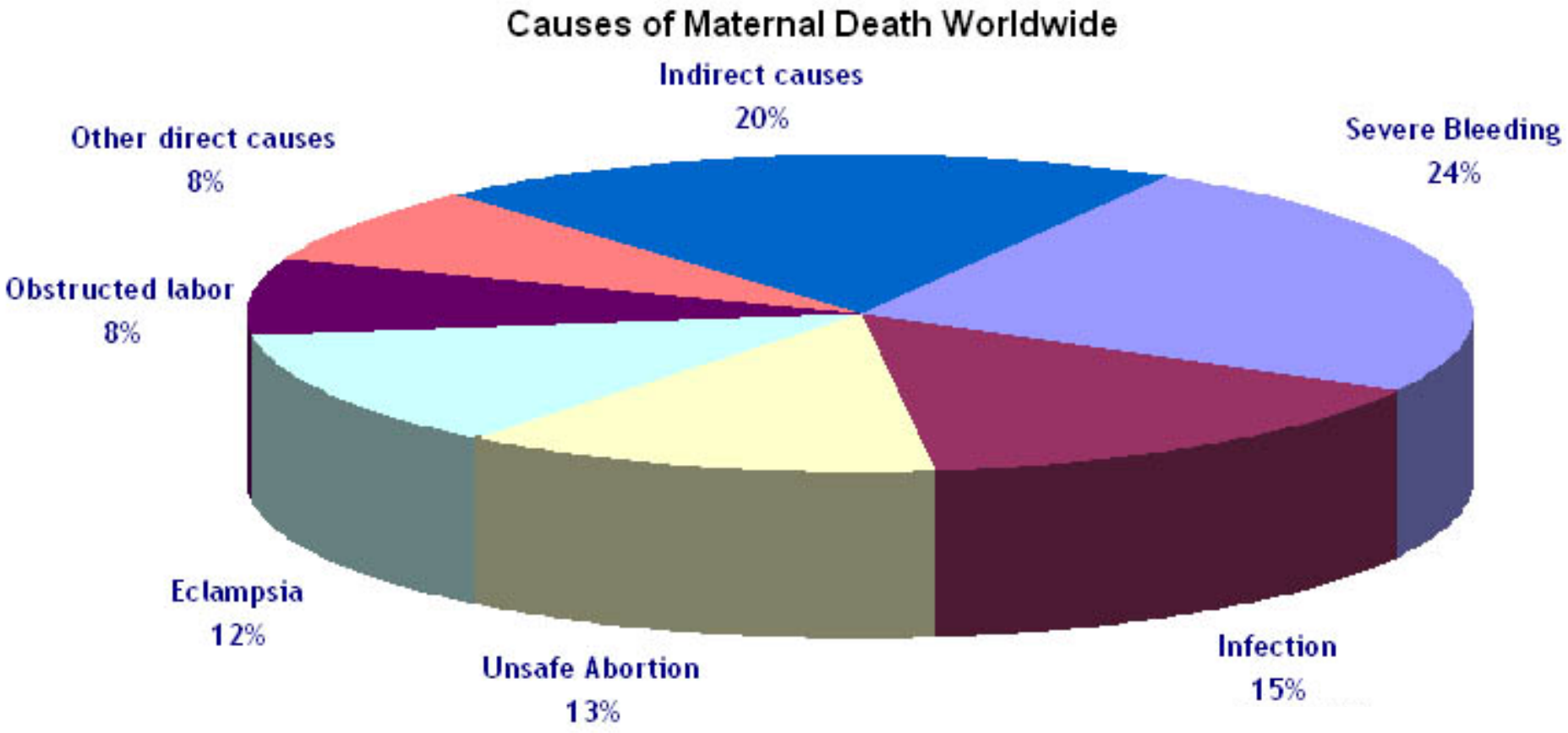
Source: Maternal mortality in 2005. Estimates developed by WHO, UNICEF, UNFPA and The World Bank. World Health Organization, 2007.

Current UK
MMR = 12/100,000

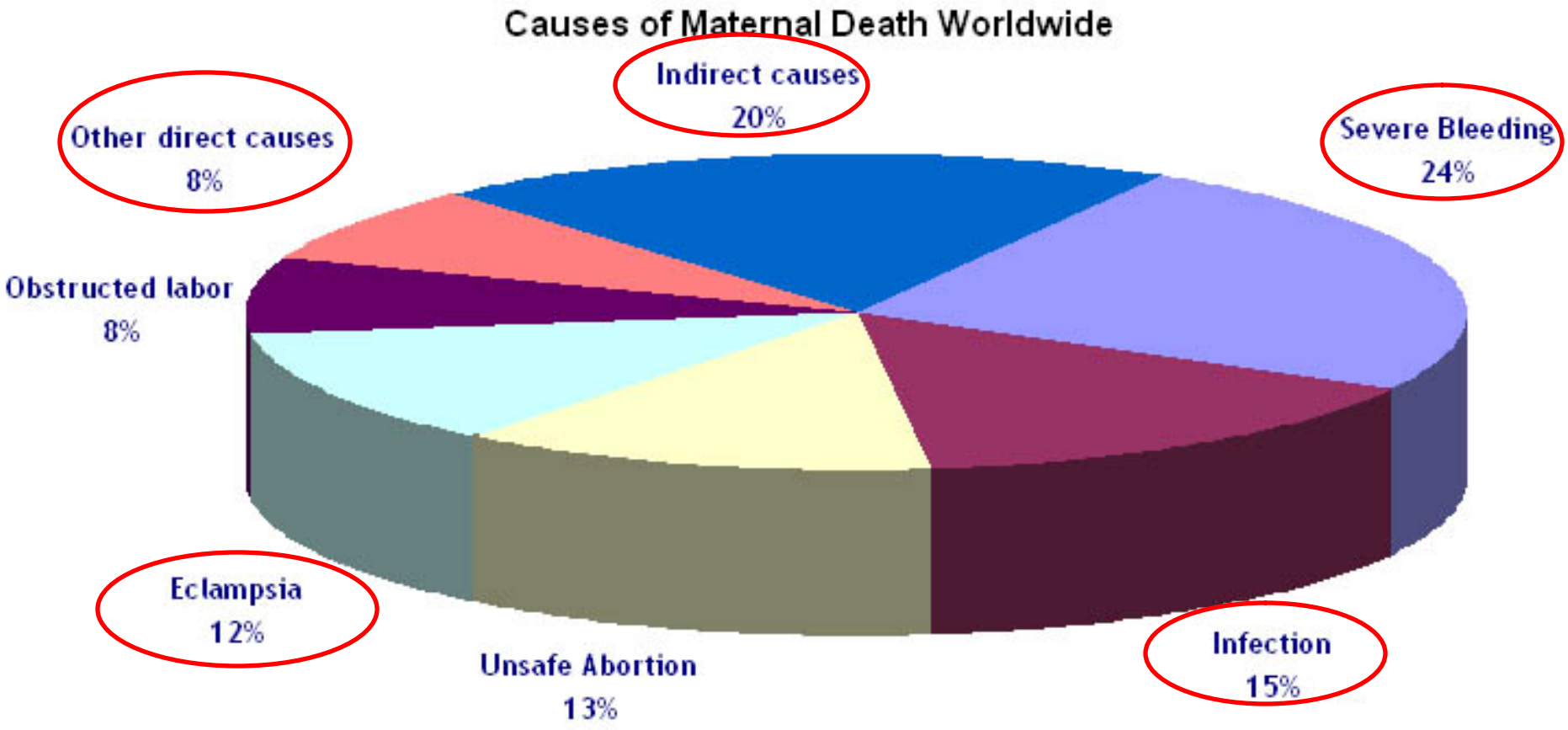
In BJOG, supplement, on website

The Gordon Museum collection

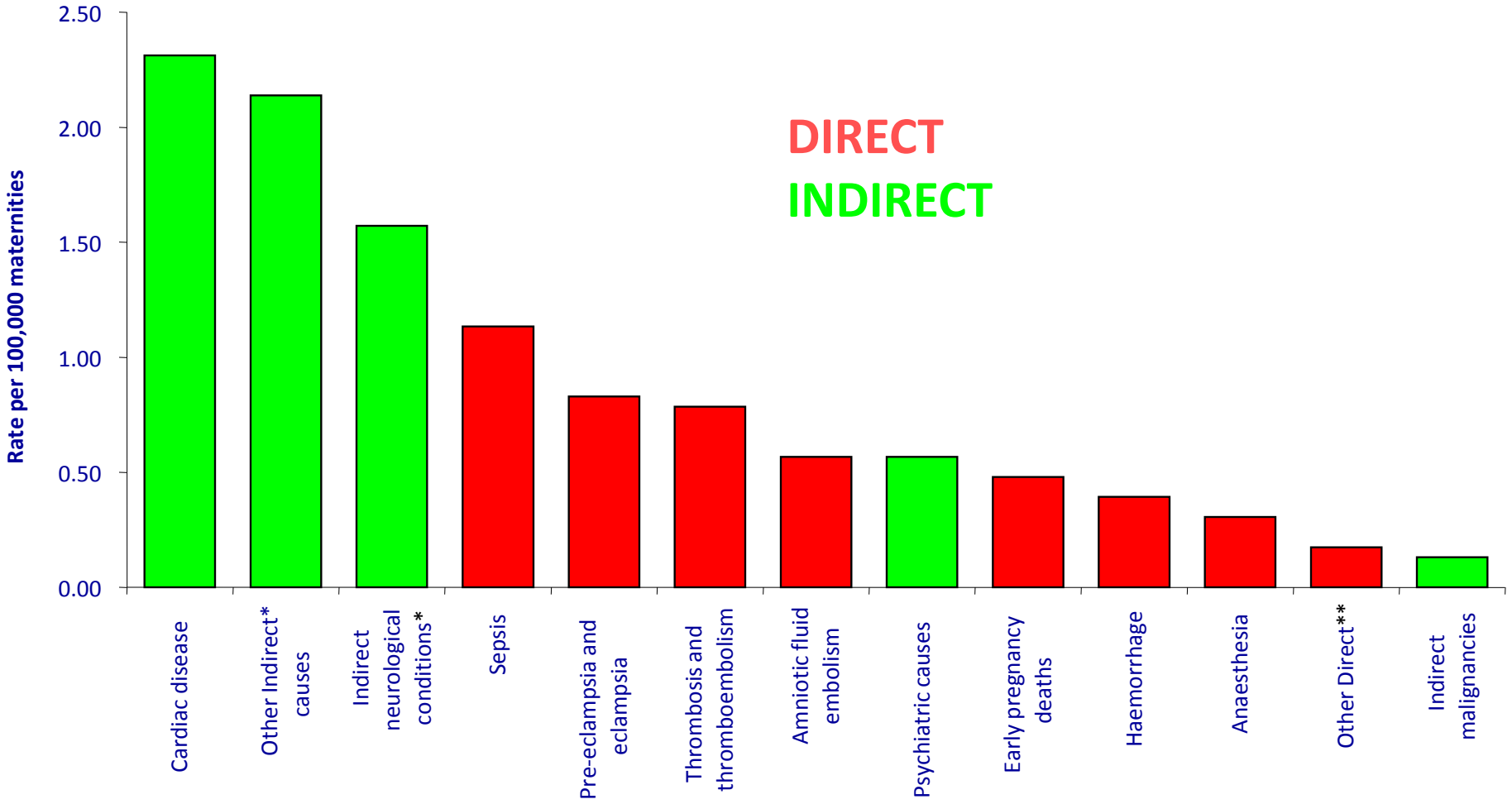
Global causes



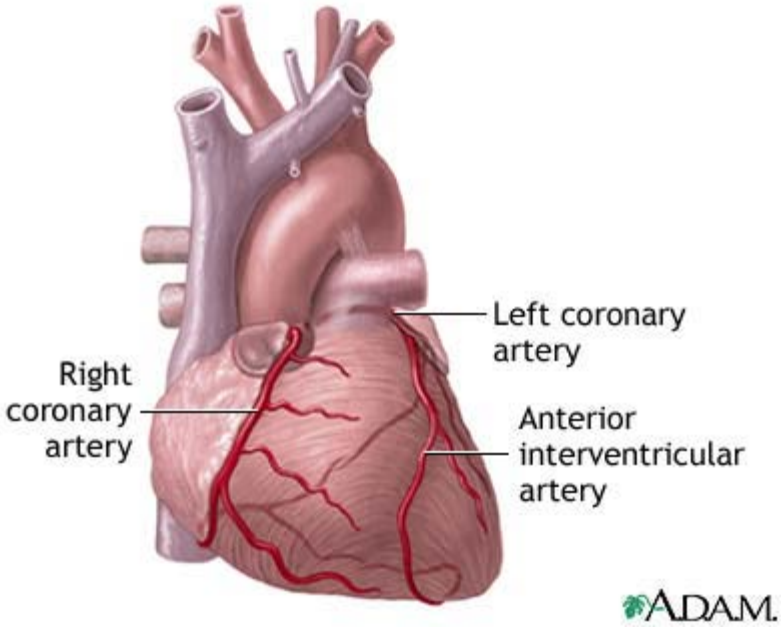
Global causes

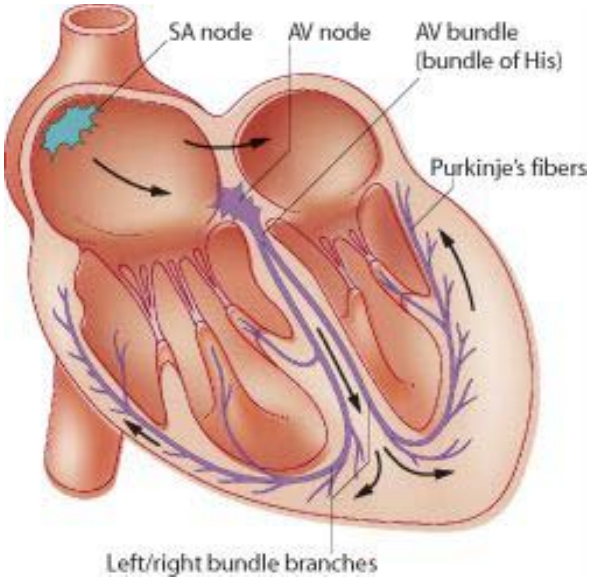


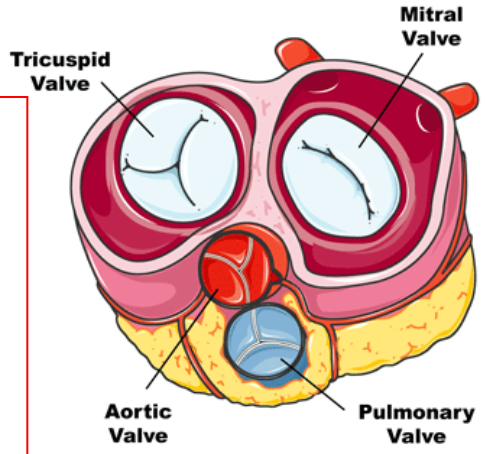
Leading causes of maternal deaths 2006-08, UK



What can go wrong?







- **Muscle disease**
- **Coronary artery perfusion**
- **Valve function**
- Conducting system
- **Depolarisation/repolarisation in myocardium**

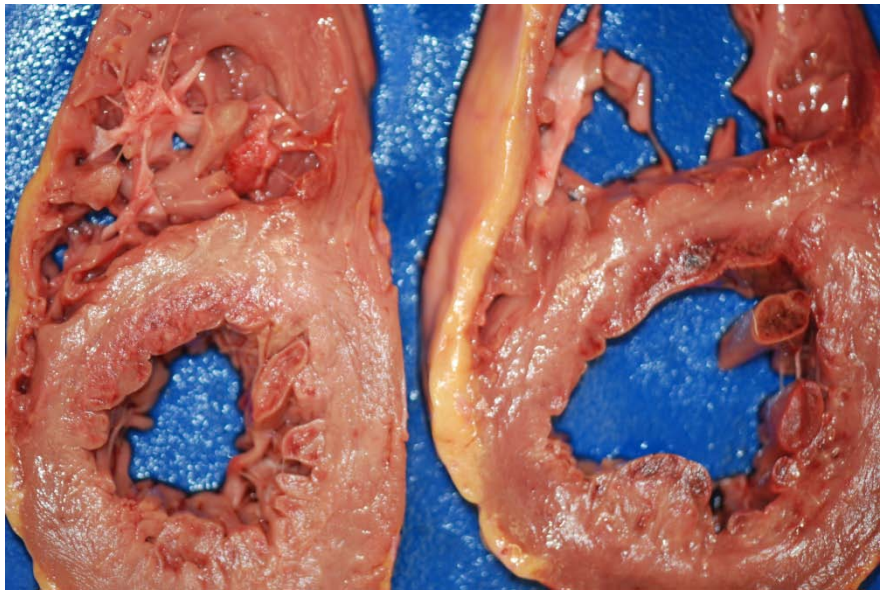
Cardiac deaths; UK 2000-2008

Type and cause of death	2000-02	2003-05	2006-08
Acquired			
Aortic dissection	7	9	7
Myocardial infarction (MI)	8	12	6
Ischaemic heart disease (No MI)	0	4	5
Sudden Adult Death Syndrome (SADS)	4	3	10
Peripartum cardiomyopathy	4	0*	9**
Other Cardiomyopathy	4	1	4
Myocarditis or myocardial fibrosis	3	5	4
Mitral stenosis or valve disease	3	3	0
Thrombosed aortic or tricuspid valve	0	0	2
Infective endocarditis	1	2	2
Right or Left ventricular hypertrophy or hypertensive heart disease	2	2	1
Congenital			
Pulmonary hypertension (PHT)	4	3	2
Congenital heart disease (not PHT or thrombosed aortic valve)	2	3	1
Other	2	0	0
Total	44	48***	53

*12 Late cases reported in 2003-05
**2 late cases reported in 2006-08
***includes one women for whom little information on cause was available

Cardiac

1. **Coronary artery diseases**
   - Atheroma
   - Dissection
   - Vasculitis
   - [anatomical anomalies]

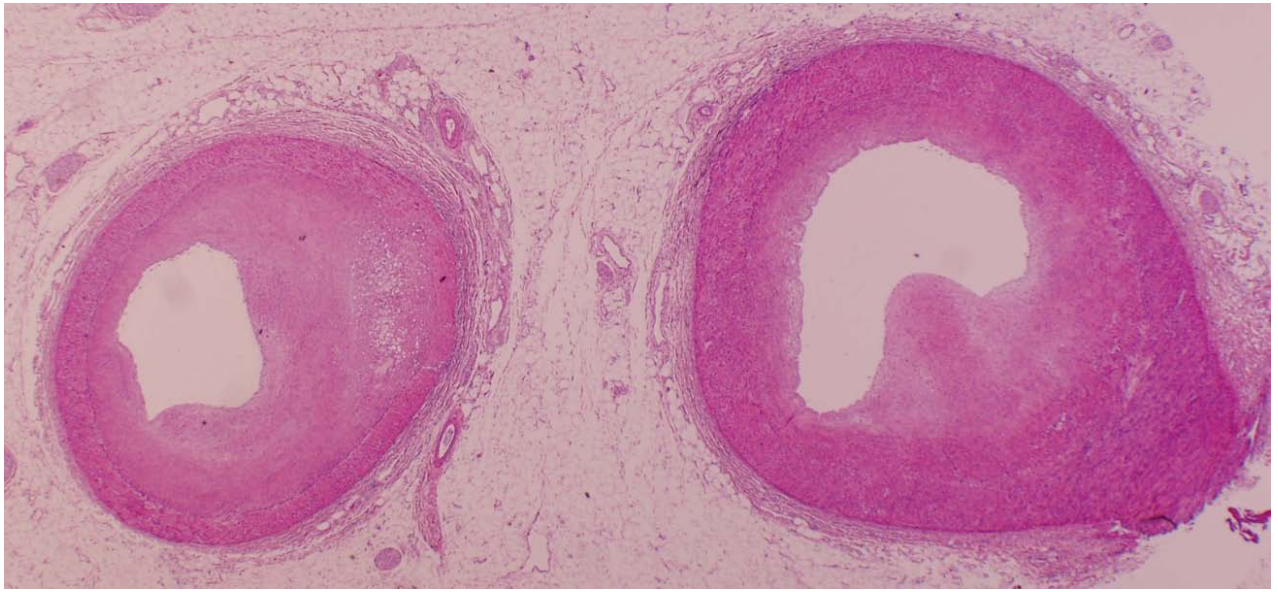


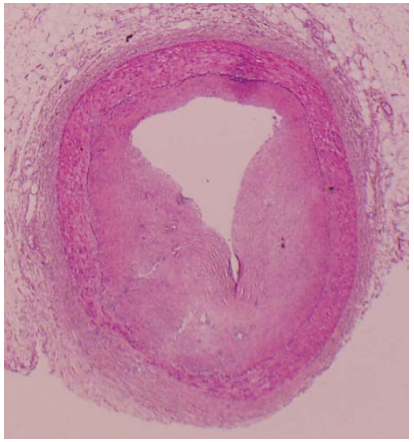
Case

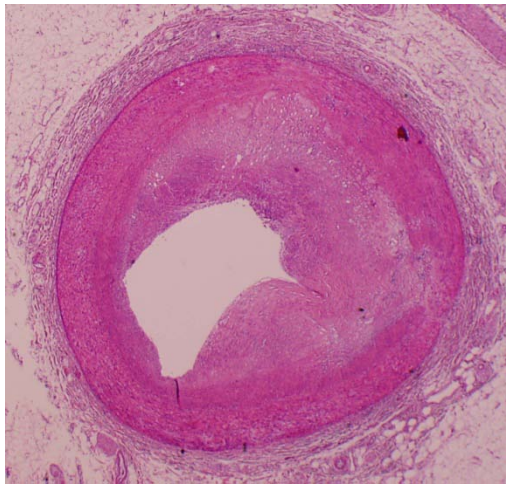
- 40yr
- Unplanned pregnancy
- Labile hypertension
  - But 137/85 on TOP day
- Surgical termination @ 21 weeks
- Syntocinon + ergometrine
- Collapsed and died in Recovery

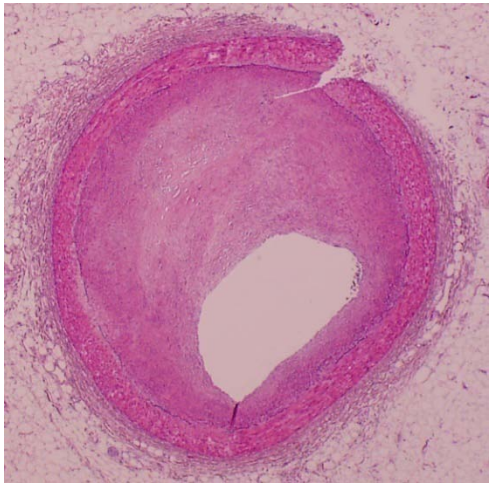
- Autopsy
- BMI about 30 = obese
- Heart enlarged - 390gm
- Coronary artery stenoses – all 3 vessels

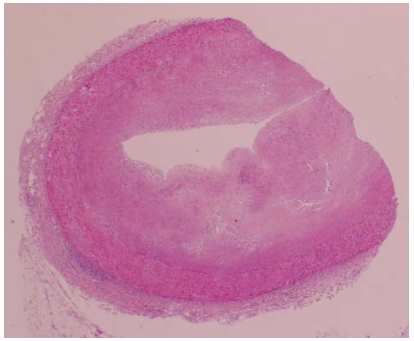
Soft coronary artery atheroma











Q: did ergometrine contribute to coronary spasm?

F35yr. Myocardial infarction, 3 days pp. Coronary artery dissection

Cardiac

2. Heart muscle

- Cardiomyopathies
  - HOCM
  - ARVCM
  - LV hypertrophy - idiopathic
  - Idiopathic fibrosis
  - EFE
- Peripartum cardiomyopathy (DCM - PPCM)
- Myocarditis
- Hypertension
- SADS/MNH
  - Channelopathies
  - Diabetic dead-in-bed syndrome
  - Obesity

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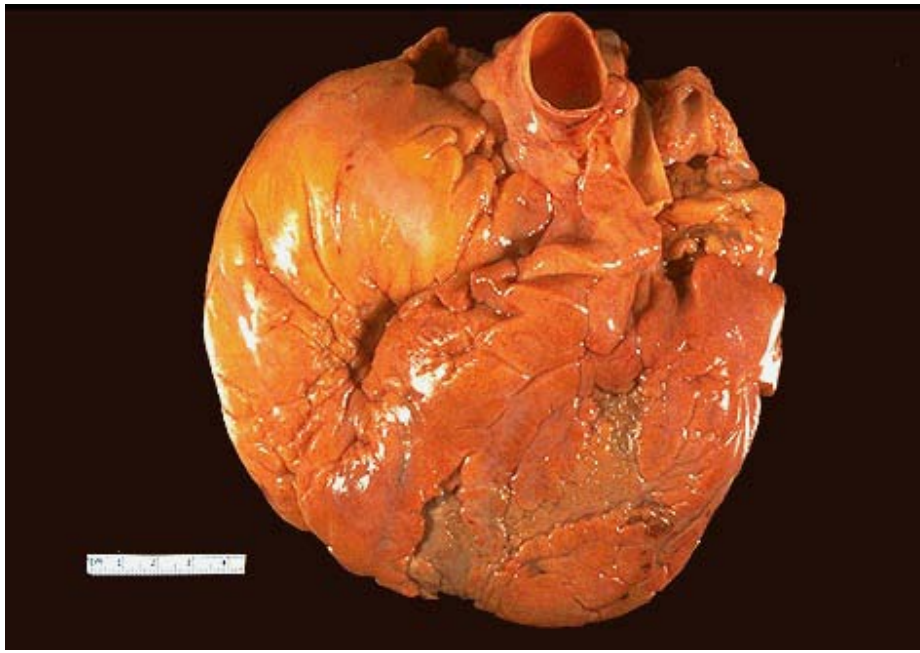
Puerperal cardiomyopathy (PPCM)

- Cardiac failure
  - between one month pre-delivery & 5 months post-delivery
  - other causes excluded
- A dilated cardiomyopathy
  - Occasionally biopsied
- *Very complex endocrine pathogenesis (progesterone receptors), with an inherited component*



Case

- 31 yr old Asian
- 1st pregnancy, no problems
- Final week (40)
- At home, not in labour
- Collapse in bathroom
- To A&E
- Peri-mortem Caesarean section – baby dies

- Autopsy
- Not obese
- Nothing to see
- Heart normal – 240gm
  - Grossly
  - Histopathologically

- Mast cell tryptase = 17µg/L
- Toxicology screen not done
  - cocaine

Case

- Diagnosis by exclusion

- SADS/MNH
- *Sudden arrhythmic death syndrome with a morphologically normal heart*

UK Cardiac Pathology Network current database list

Sudden cardiac death - explained

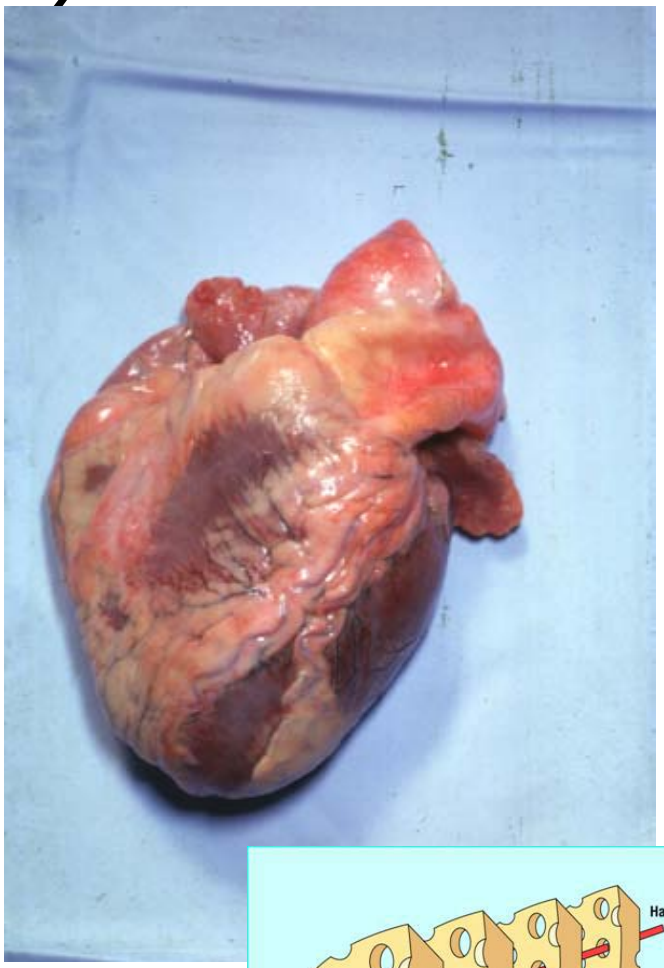
- 1. **Dilated cardiomyopathy**
  2. Histiocytoid cardiomyopathy
  3. Hypertrophic cardiomyopathy
  4. Mitochondrial cardiomyopathy
  5. Arrhythmogenic cardiomyopathy
  6. Cardiomyopathy NOS
  7. LV non compaction
  8. **Idiopathic left ventricular hypertrophy**
  9. Idiopathic left ventricular fibrosis
  10. **Hypertensive heart disease**
  11. Amyloidosis
  12. Fabrys disease
  13. Glycogen storage disease
  14. Haemochromatosis
  15. Myocarditis NOS
  16. Sarcoidosis
  17. Giant cell myocarditis
  18. Coronary artery anomaly
  19. **Coronary artery dissection**
  20. Fibromuscular dysplasia of coronary arteries
  21. Kawasaki disease
  22. Marfans syndrome
  23. **Sudden death in congenital heart disease**
  24. Mucoid degeneration of the mitral valve
  25. Sickle cell disease
  26. Sudden cardiac death with illicit drug usage
  27. Sudden cardiac death with prescription drug usage
  28. Sudden death with other cardiac pathology

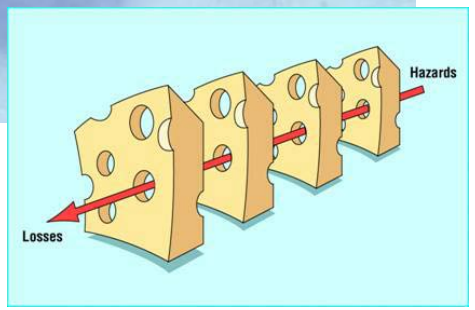
Sudden cardiac death - unexplained

- 1. Sudden unexplained death in epilepsy (SUDEP)
  2. Sudden unexplained cardiac death in alcohol abuse
  3. Sudden unexplained cardiac death in obesity
  4. Sudden unexplained cardiac death in anorexia
  5. Sudden unexplained cardiac death in diabetes
  98. Sudden unexplained cardiac death with another association
  99. Sudden arrhythmic death syndrome (SADS)

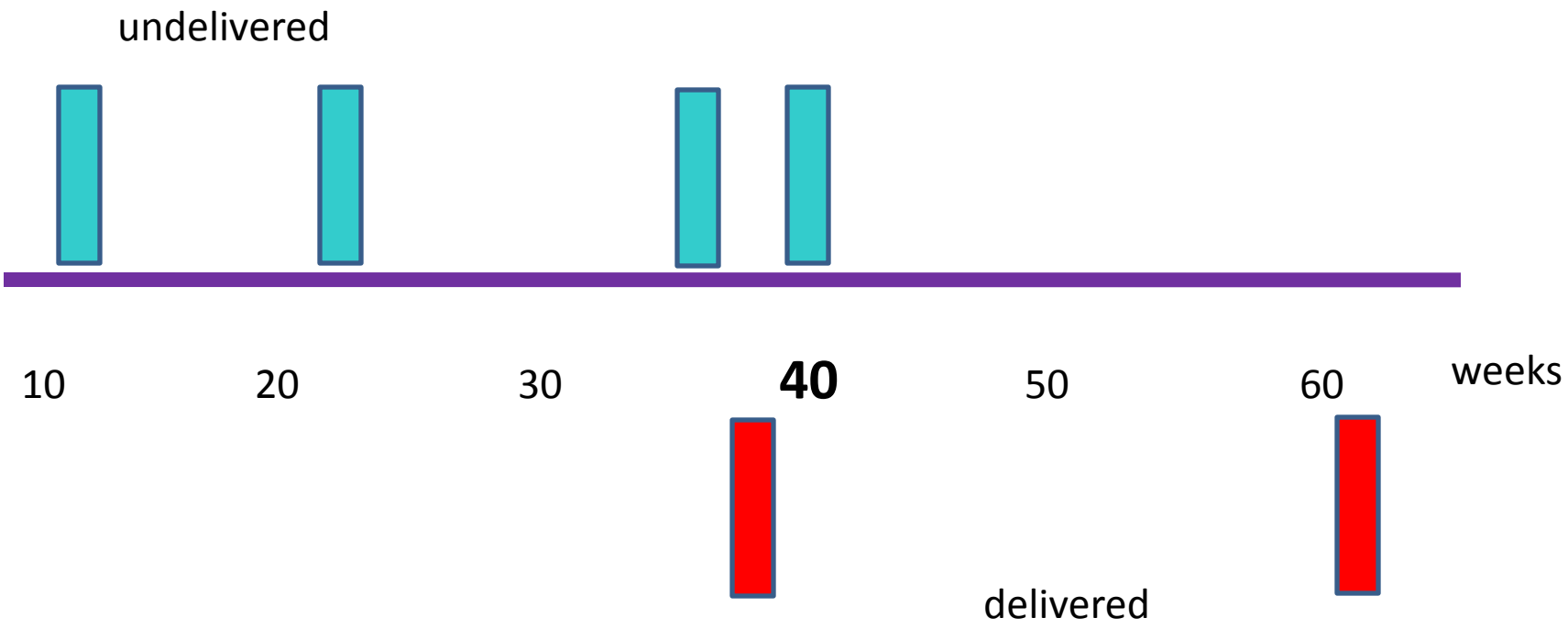
SADS – an emerging problem
many are inheritable syndromes

- Sudden unexpected arrhythmic death syndrome
- Pre, peri- and post-partum
- ALL other causes of death excluded
- Morphologically normal heart
  - Gross
  - Histopathology
  - Negative drug screen
- Stress of pregnancy & delivery
- Underlying electrical instability
  - long QT etc





SADS – MNH deaths in 2011: gestation & timing



Are pregnant women more susceptible to SADS than non-pregnant?

- "SADS: a national survey of sudden unexplained cardiac death"
- Behr, Sheppard et al
- Heart 2009, 93:601-605

- Coroner records 1997-99
- Women, *caucasian* 4-64 yrs
- 202 deaths = **$0.74/10^5$pa**

- "Saving Mothers Lives 2006-8"
- Cardiac deaths n =53
- 10/53 = SADS
- = **$0.43/10^5$ maternities**

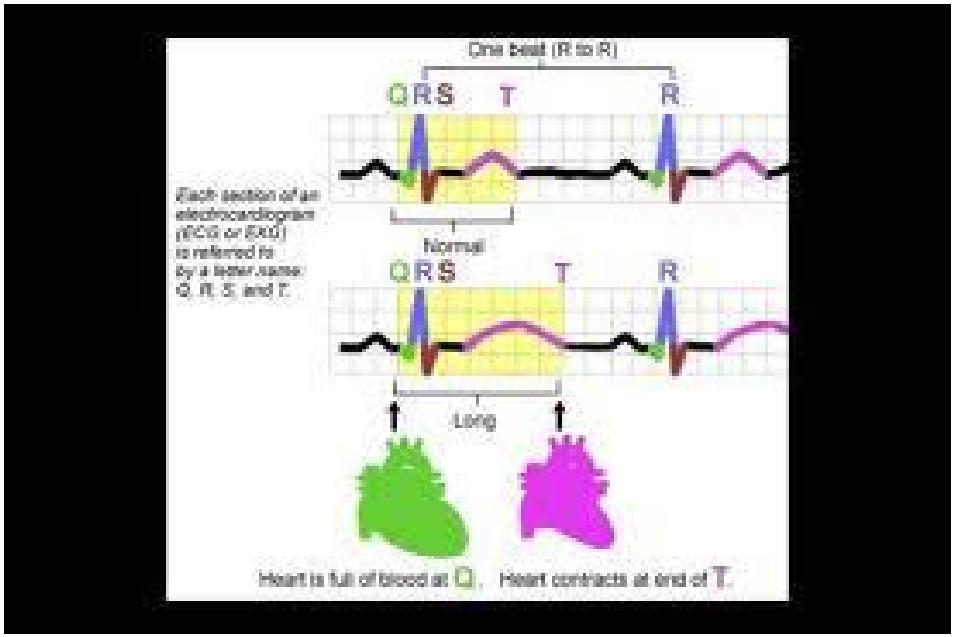
SADS with morphologically normal heart

- Channelopathies
- Ion channel disorders
  - **Long QT syndrome**
  - Short QT syndrome
  - **Brugada syndrome**
  - Catecholaminergic polymorphous ventricular tachycardia
  - Lev-Lenegre disease
  - etc

- Familial bradycardia
  - **Lamin A/C disease**
  - Dsytrophinopathies
  - Mutation of gamma subunit of the adenosine monophosphate activated protein kinase (PRKAG2)
  - Holt-Oram syndrome
  - etc

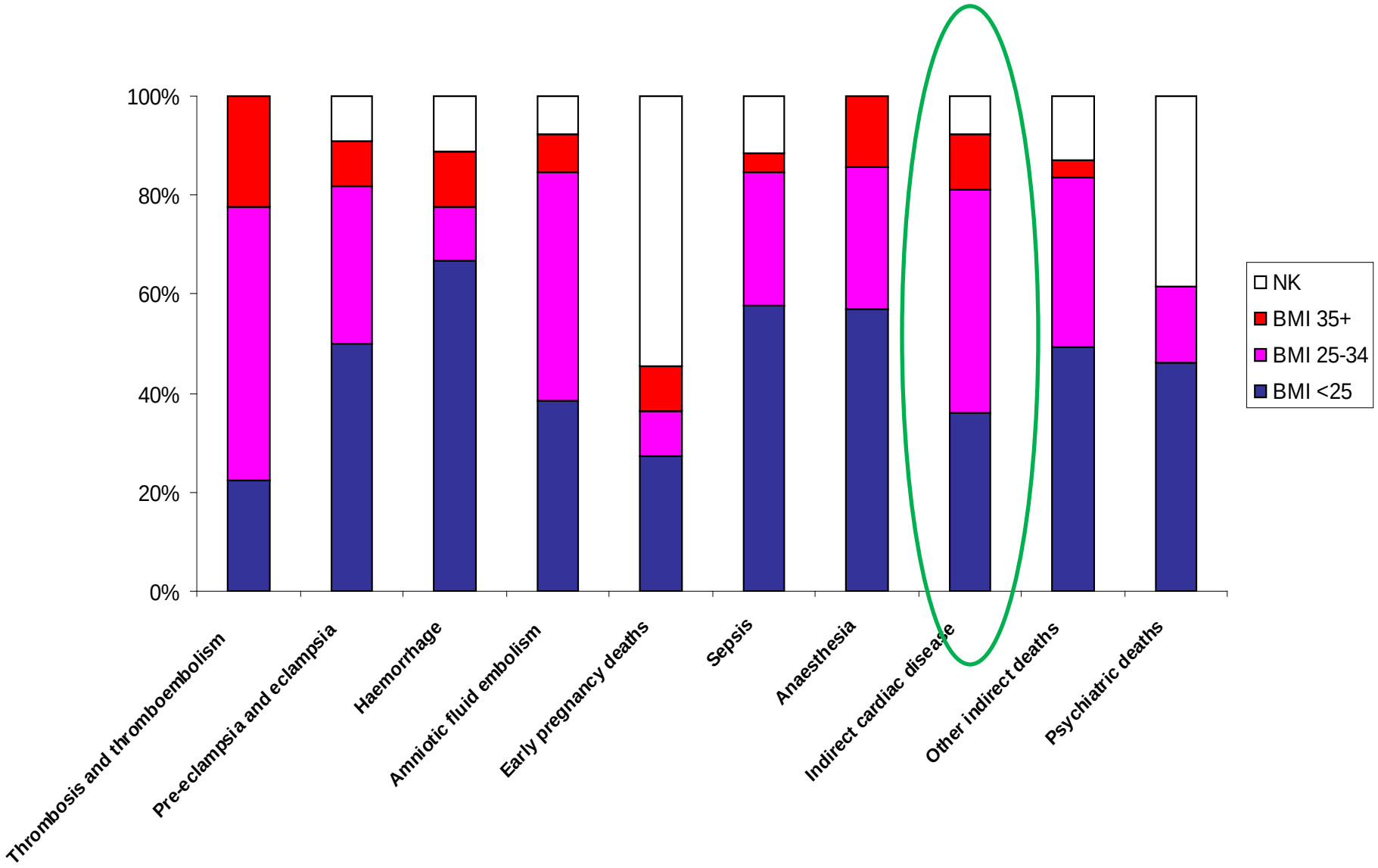
Long QT and pregnancy

- Pre-pregnancy risk of cardiac event = 1
- During pregnancy = 0.28 (0.1-0.76)
- First 9 months post-partum = **2.7** (1.8-4.3)
- Post-post-partum = 0.91



Seth et al,
J Am Coll Cardiol 2007, 49:1092-8

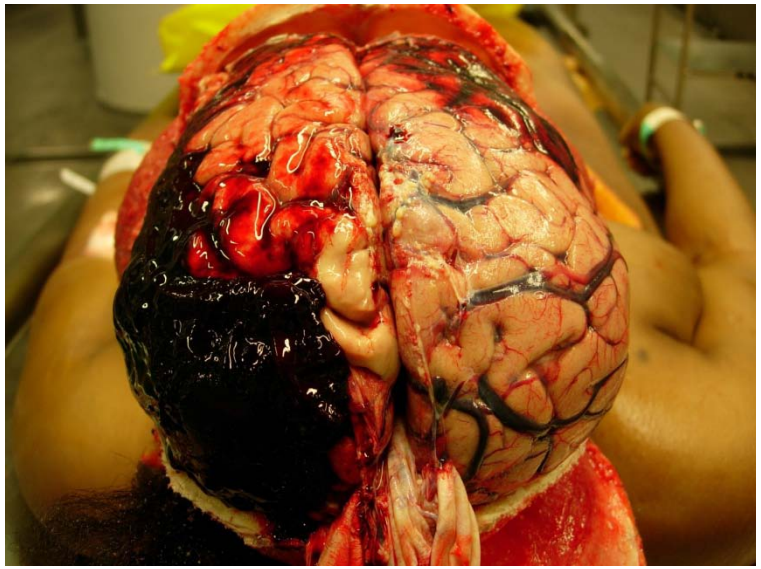
Maternal deaths obesity by cause UK 2006-08

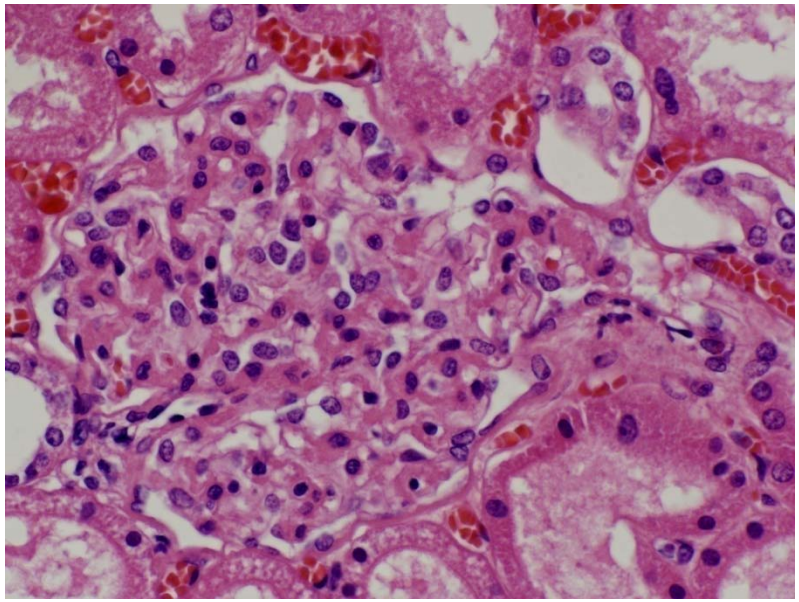


Final conundrum on SADS in pregnancy

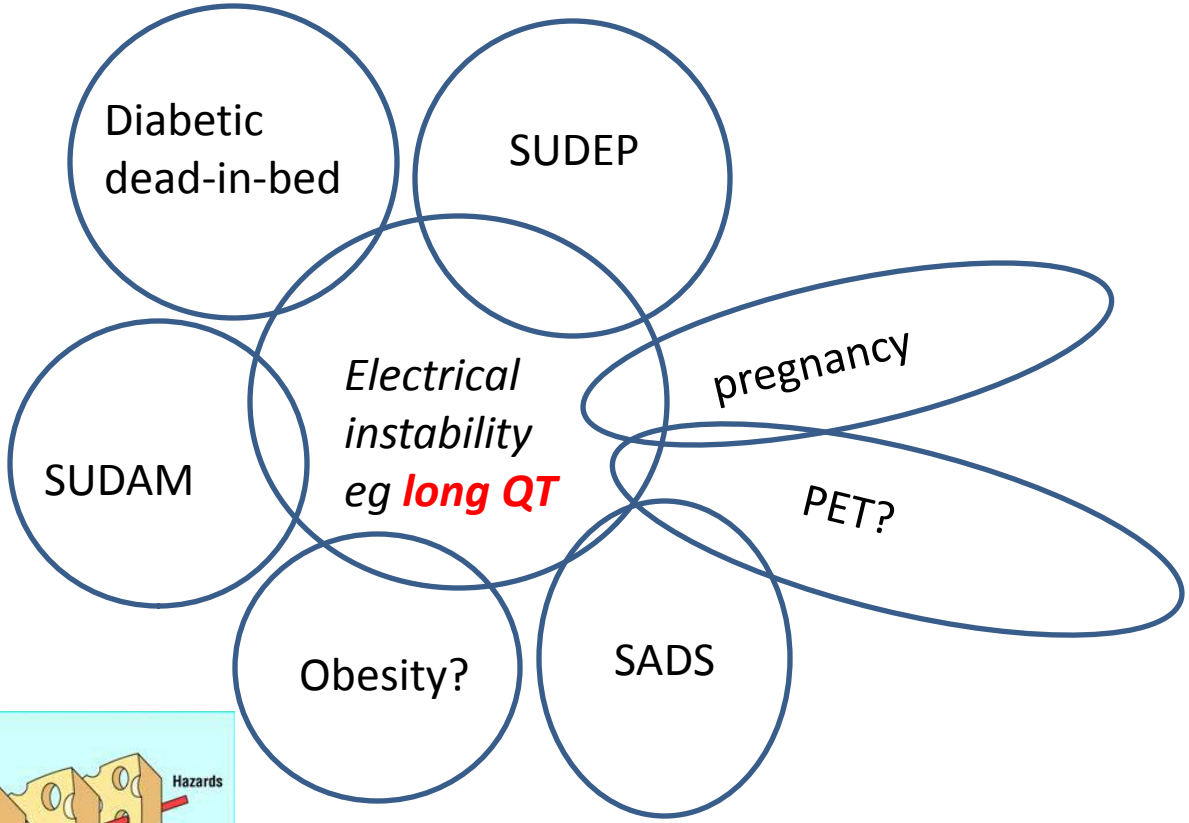
- Two patients
- Third trimester
- **Known or suspected PET**
- *Both died at home, unwitnessed*

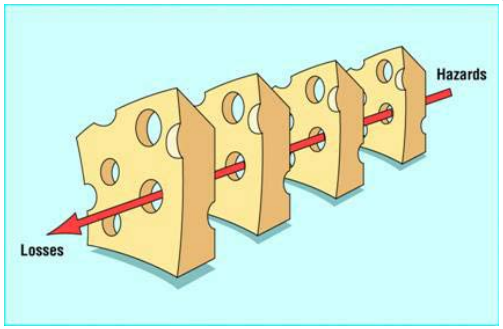
- Autopsies:
- Grossly normal
- No CNS haemorrhage
- But kidney histology...
  - *Glomerular endotheliosis*





A new understanding for sudden cardiac death syndromes?



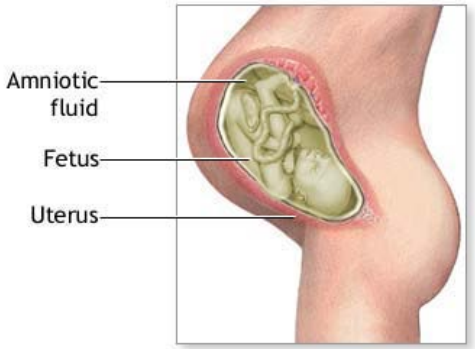


1st conclusion

Case definitions and epidemiology can only come from systematic protocol-driven autopsy practice to confirm/exclude known conditions

Amniotic fluid embolism (AFE)
typical scenario

- F 39yr
- Three children A&W
- Fourth pregnancy, delivery @41 weeks
- Vaginal delivery
- As baby head crowns, becomes unresponsive
- Develops uterine bleeding, necessitating hysterectomy
- Dies hours later, never recovering cons



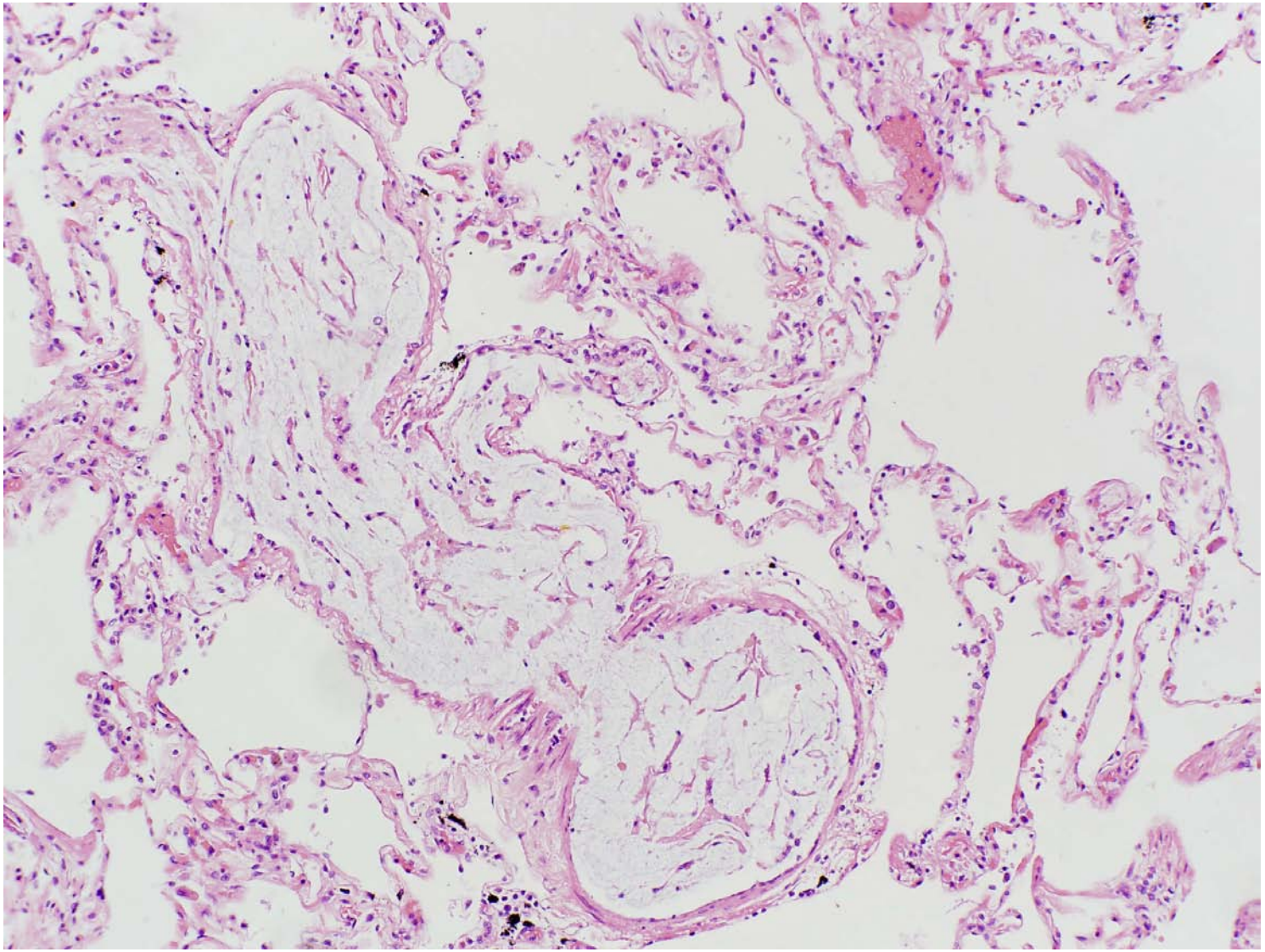
AFE

- Autopsy:
- Major organs grossly normal

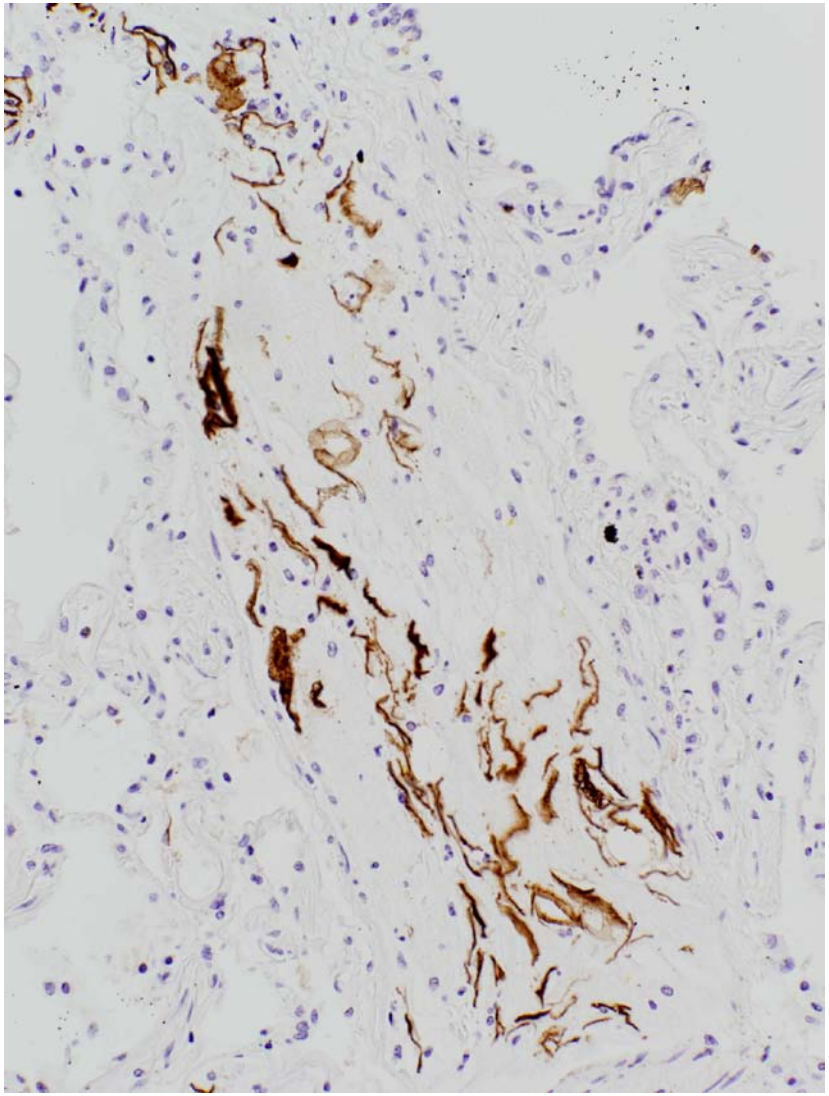
- No pulmonary thrombo-embolism

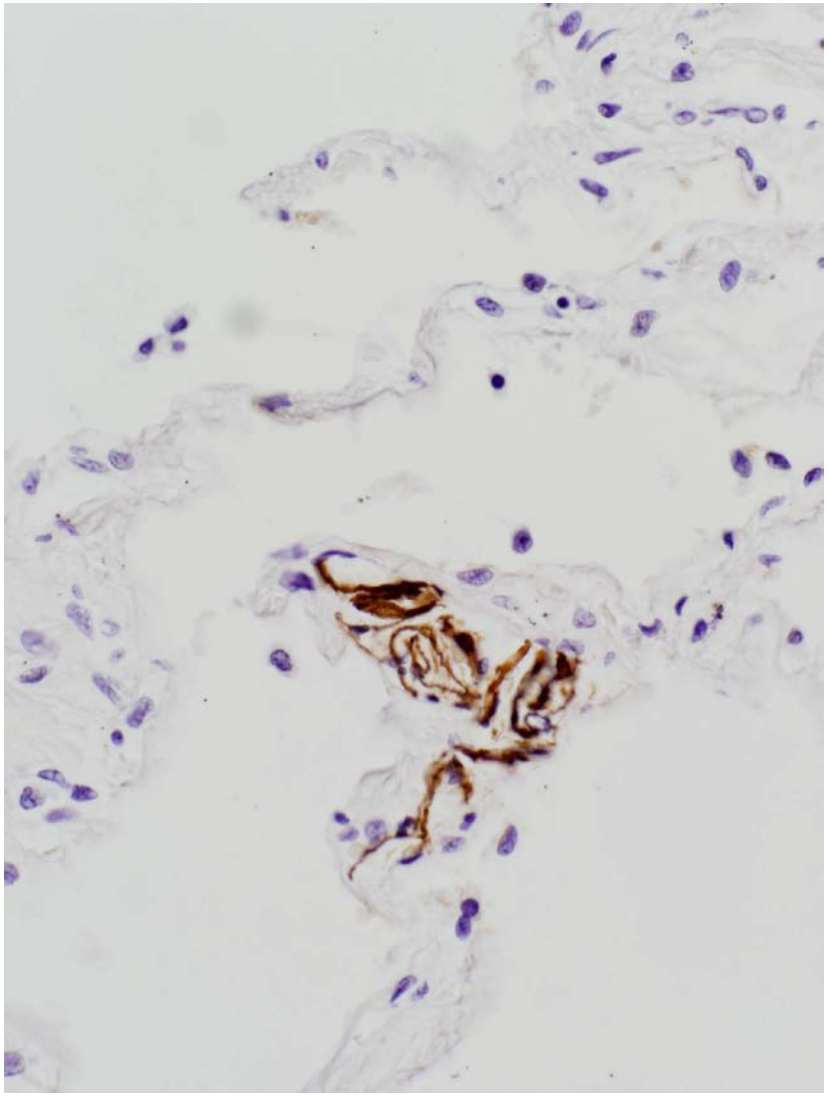
- Hysterectomy specimen unremarkable for gestation and recent delivery

Lung arteriole



LP34 – fetal squames in amniotic fluid





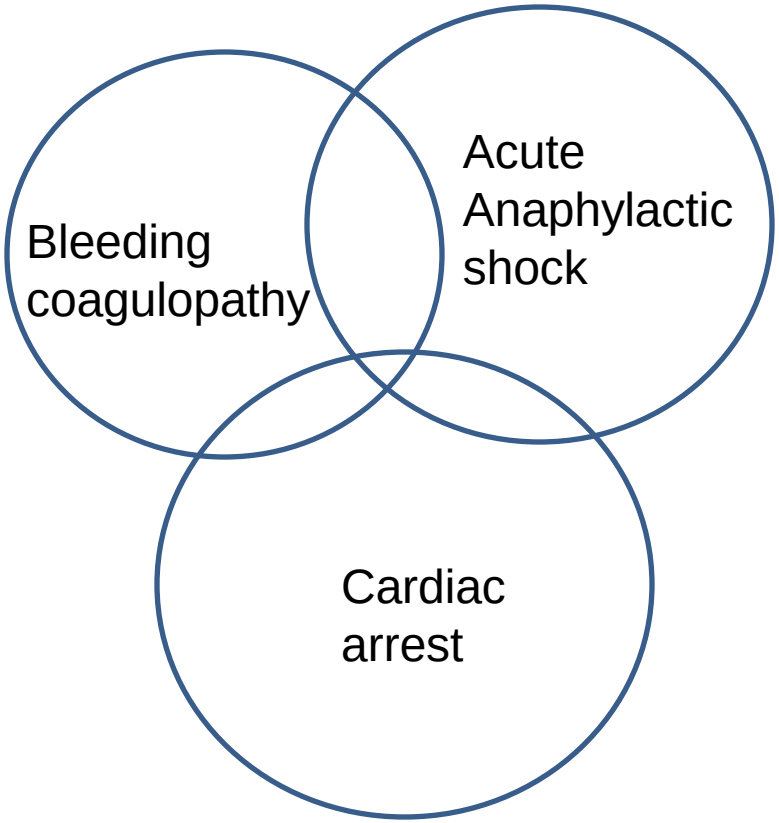
AFE

- Risk factors
- Medical induction of labour
- Caesarian section
- Forceps and vacuum delivery

- Higher maternal age
- Diabetes
- Polyhydramnios
- Eclampsia
- Cervical laceration
- Placenta previa and abruption

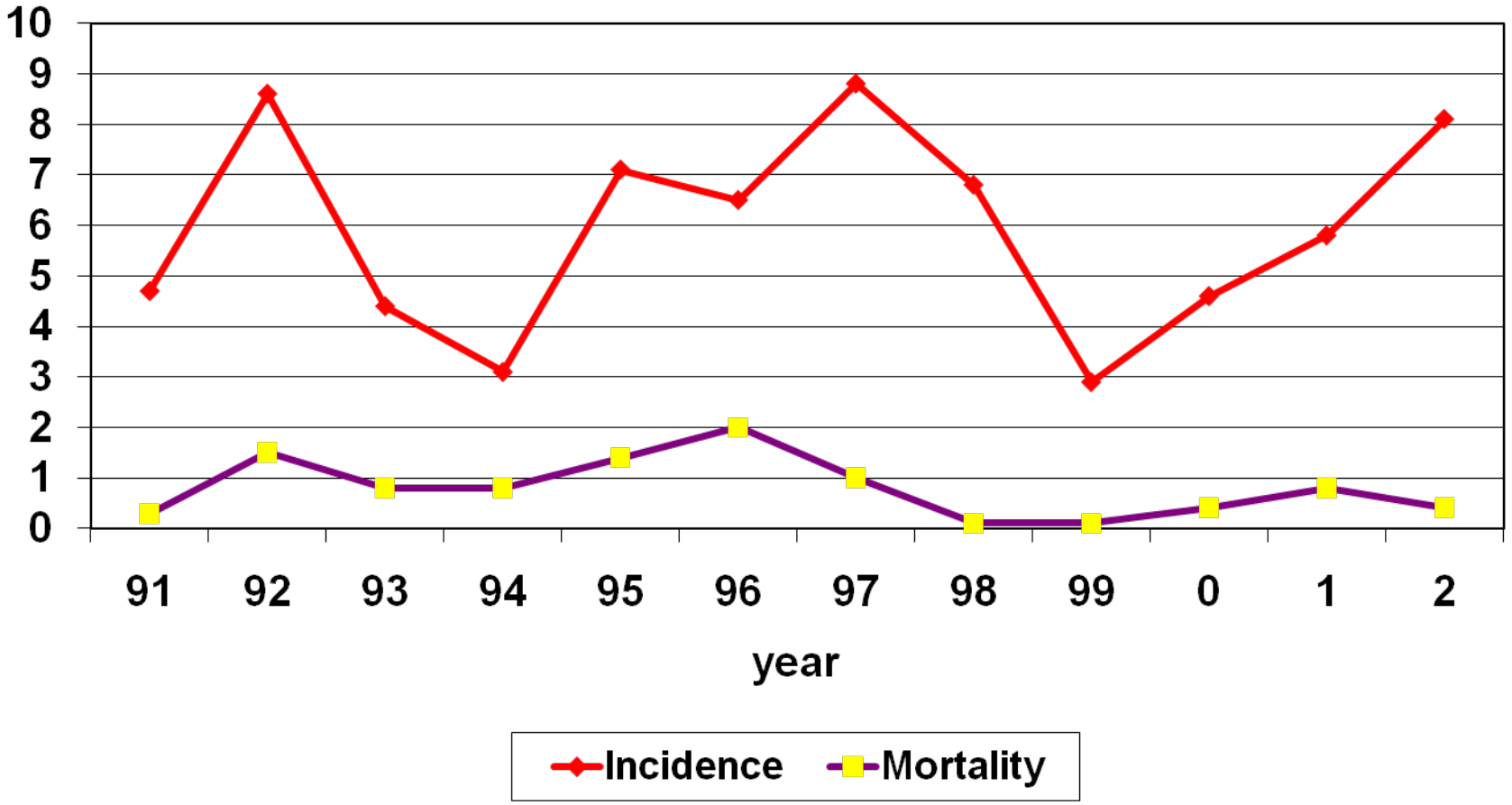
- *But most just happen out the blue*

- Pathogenesis

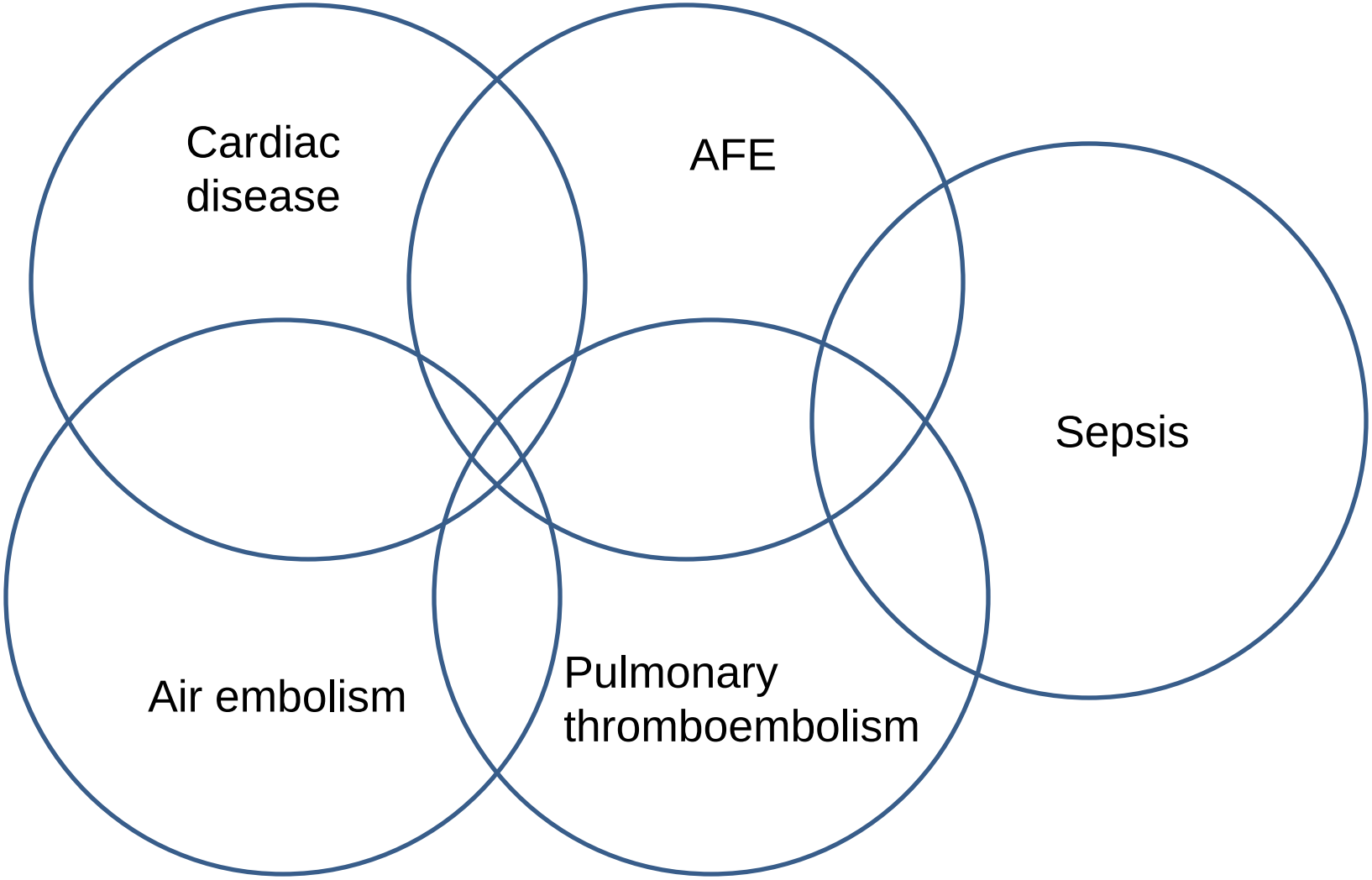


AFE in Canada 1991-2002

Incidence = 6/100,000
Mortality = 0.8/100,000

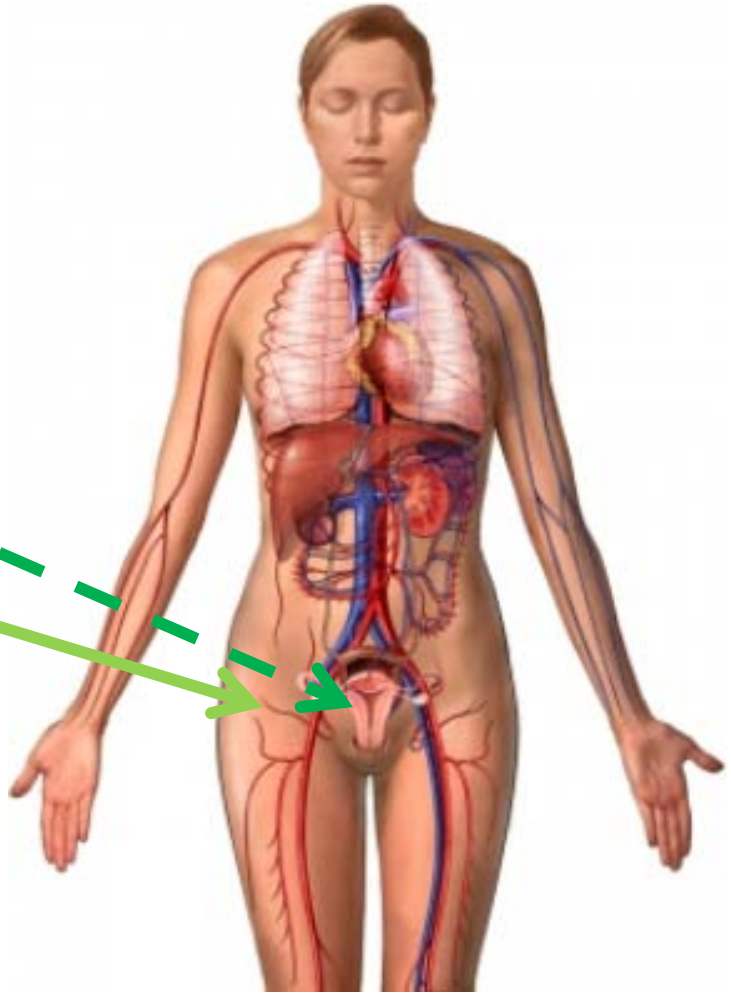


A diagnostic problem for autopsy:
collapse before-during-after delivery

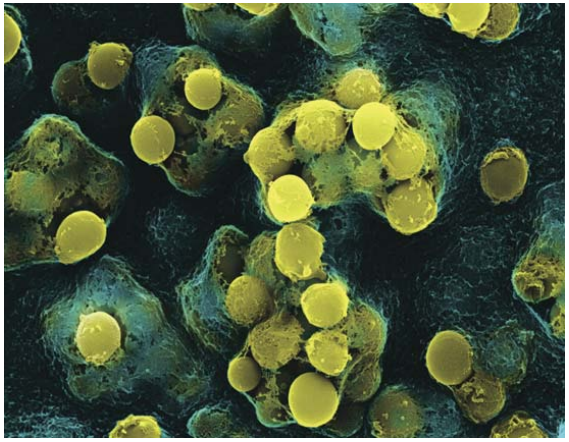


How does maternal sepsis happen?

Is it all just genital tract (puerperal) sepsis?

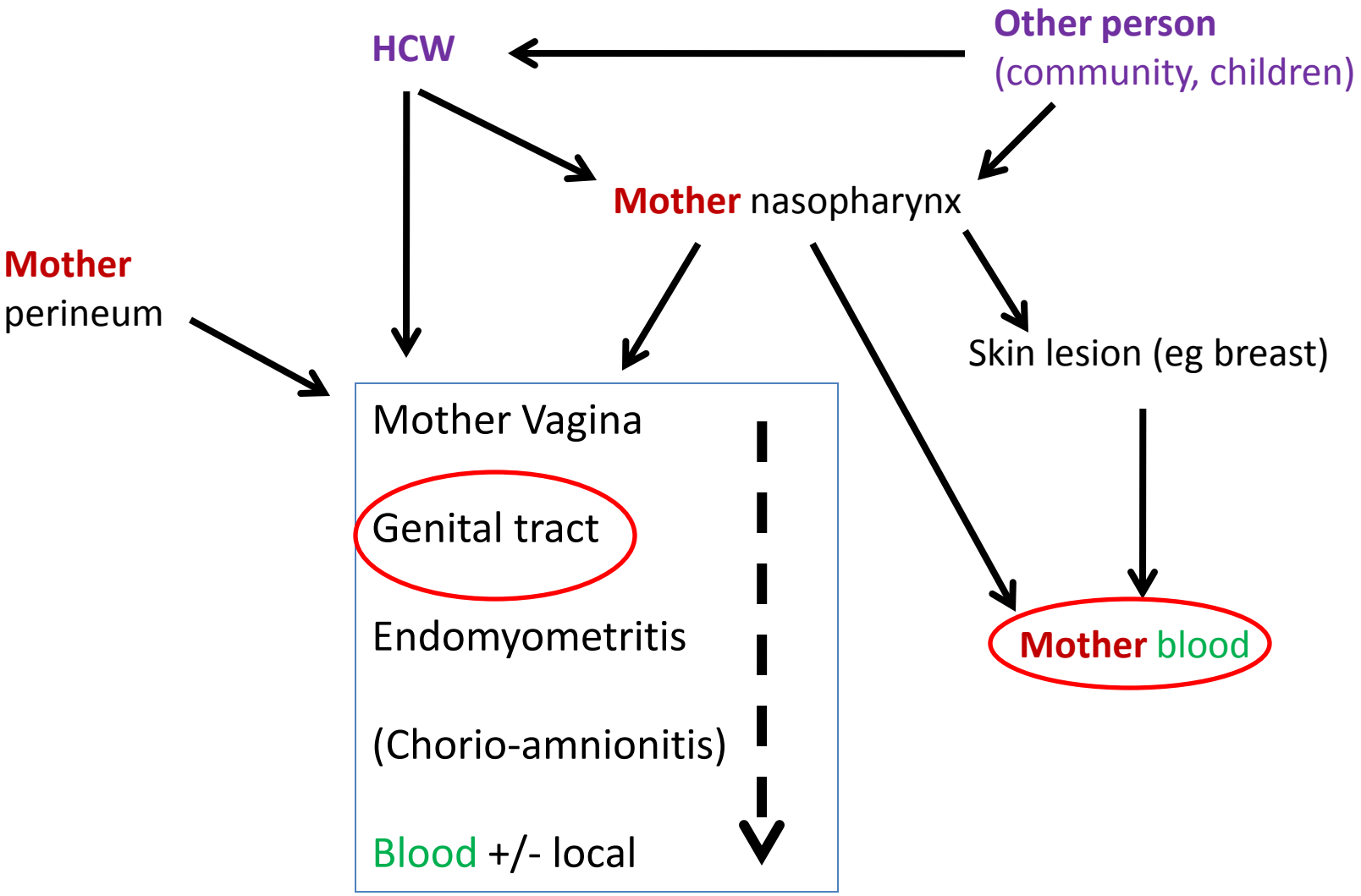


Ignaz Semmelweis
(Vienna)

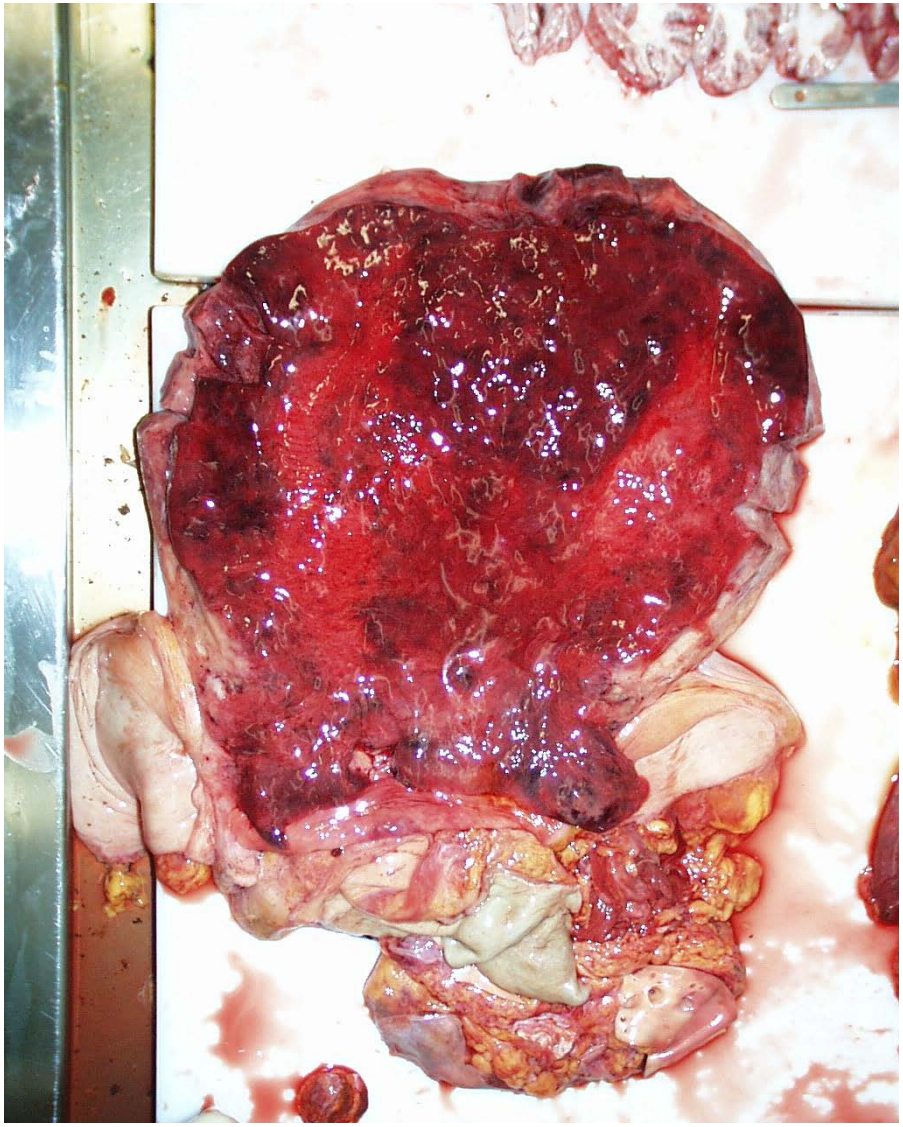


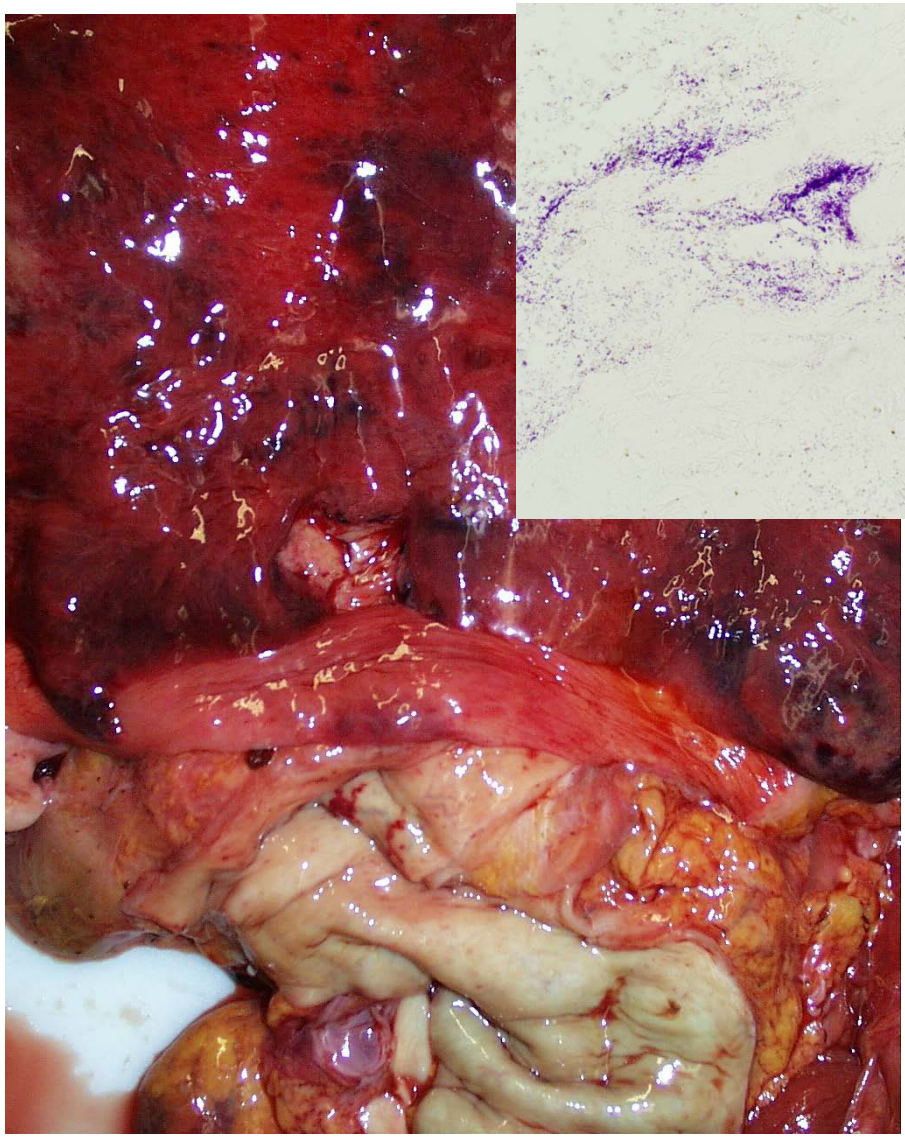
GAS

Routes of infection



Sepsis – GAS endomyometritis





New approach to pregnancy-sepsis

1. UNSAFE ABORTION

•2. PRESENTING WITH INFECTION AT TIME OF RUPTURED MEMBRANES.
•NO PRIOR OPERATIVE INTERVENTIONS

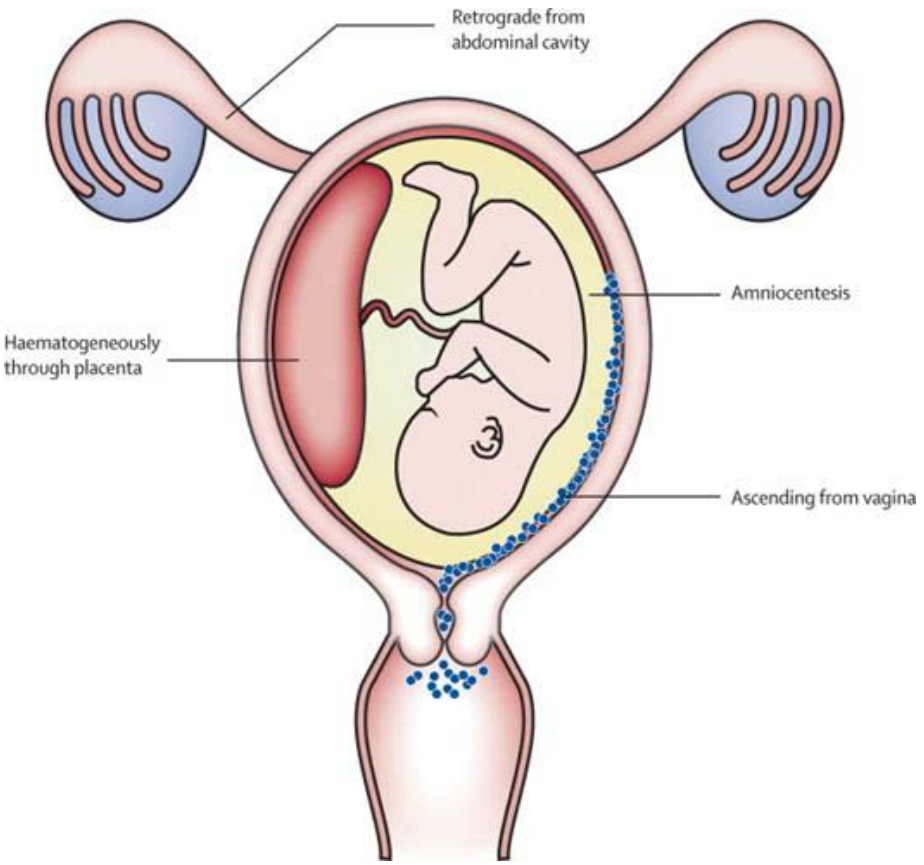
•3. SEPSIS POST-DELIVERY
•VD or CS or TOP or MISCARRIAGE
•"WELL INTERVAL" – day to weeks
•WITH GENITAL TRACT INFECTION INVOLVEMENT – clinical / microbiology / histology

•4. ADMITTED IN SEPTIC SHOCK
•MEMBRANES INTACT
•NOT IN LABOUR
•ALL COMMUNITY-ACQUIRED
•ONE THIRD OF ALL PREGNANCY-ASSOCIATED SEPSIS (UK 2006-8)

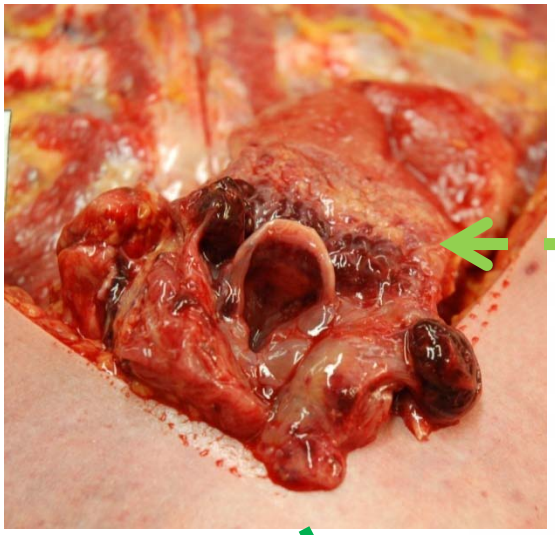
•5. SEVERE POST-PARTUM SEPSIS
•RELATED TO THE BIRTH PROCESS
    •Eg Spinal anaesthesia; CS wound infection
•GENITAL TRACT NOT INVOLVED

Sepsis at autopsy protocol

- Routine blood cultures
- Evidence for?:
  - Systemic sepsis
  - Endomyometritis
  - Chorio-amnionitis
  - Cervicitis
  - Sore throat
  - Other extra-genital focus

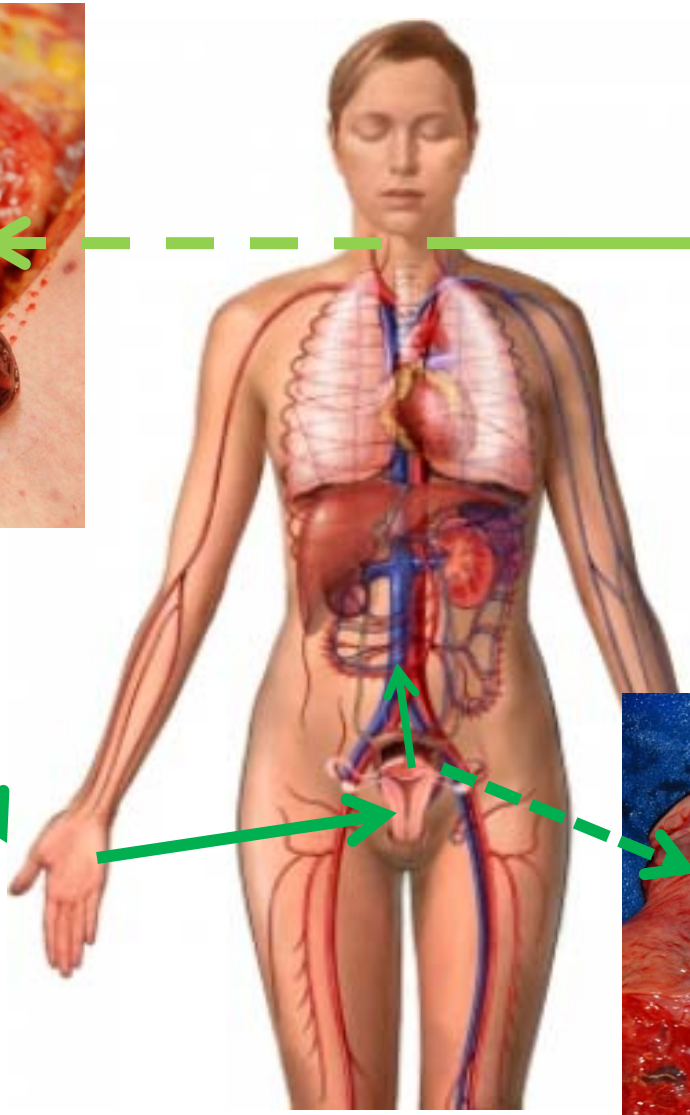


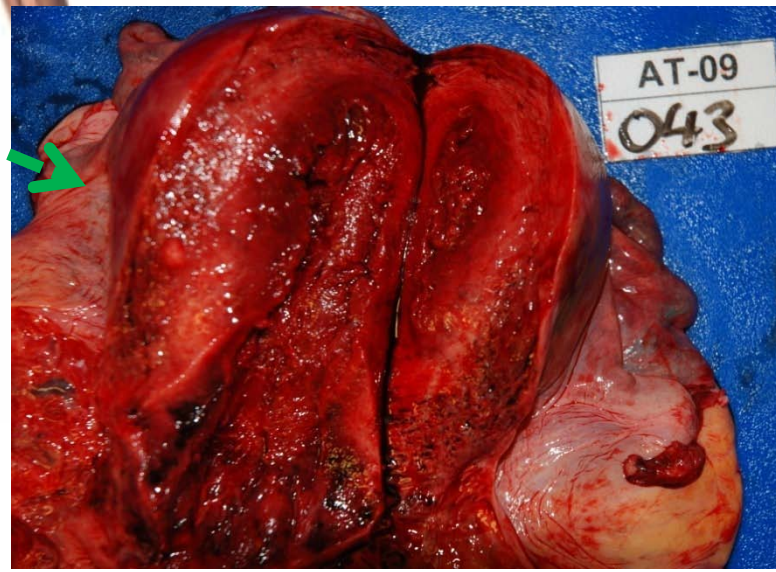
How ‘sore throat’ maternal sepsis happens?



?

BLOOD





New approach to pregnancy-sepsis

1. UNSAFE ABORTION

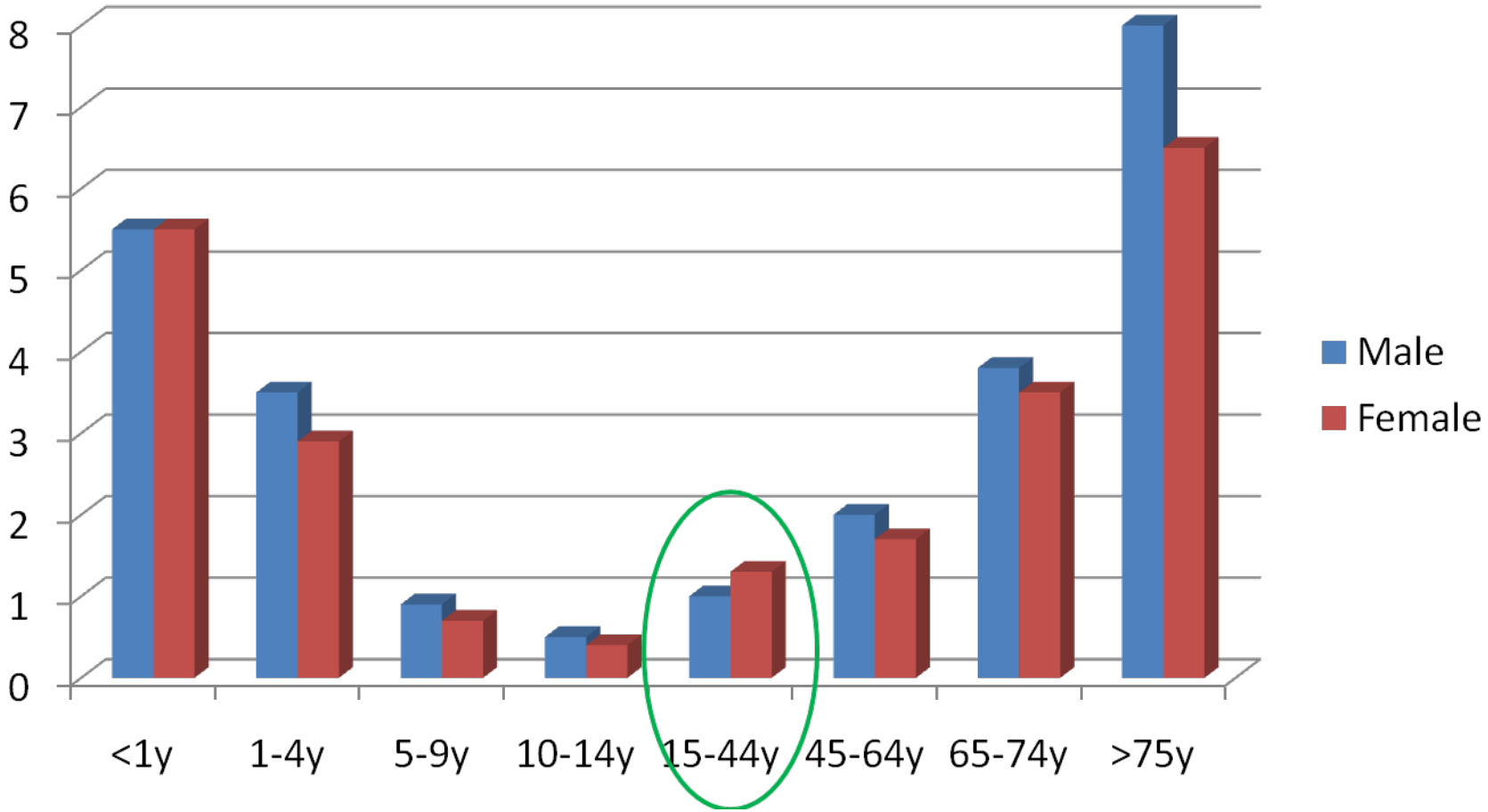
•2. PRESENTING WITH INFECTION AT TIME OF RUPTURED MEMBRANES.
•NO PRIOR OPERATIVE INTERVENTIONS

•3. SEPSIS POST-DELIVERY
•VD or CS or TOP or MISCARRIAGE
•"WELL INTERVAL" – day to weeks
•WITH GENITAL TRACT INFECTION INVOLVEMENT – clinical / microbiology / histology

•4. ADMITTED IN SEPTIC SHOCK
•MEMBRANES INTACT
•NOT IN LABOUR
•ALL COMMUNITY-ACQUIRED
•ONE THIRD OF ALL PREGNANCY-ASSOCIATED SEPSIS (UK 2006-8)

•5. SEVERE POST-PARTUM SEPSIS
•RELATED TO THE BIRTH PROCESS
    •Eg Spinal anaesthesia; CS wound infection
•GENITAL TRACT NOT INVOLVED

Age specific rates of GAS bacteraemia reports, E,W & NI – 2007 [Health Protection Agency]



Problem: notifications are not stratified for pregnancy

Sepsis research questions

Academic

1. Does pregnancy per se increase susceptibility to bacterial infection if membranes intact?
2. How does GAS get into the mother?
3. Variation in Host Response genes to infection

Practical

1. Source of infection: *Health Care* the vs *Community*?
2. Better method of distinguishing early sepsis from trivial symptoms
3. ...quicker diagnosis and management
4. Screening for GAS?

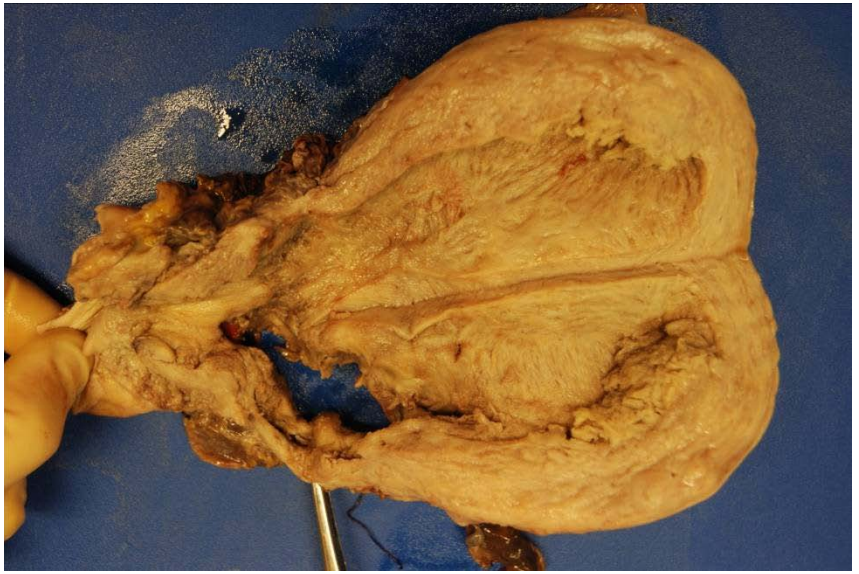
Medical termination

14 weeks gestation
Medical termination

Mifepristone
- Dilate the cervix

Misoprostol
- Expell the contents

Lateral tear of the uterus



Vaginal trauma and haemorrhage

Forceps delivery

- Inexperienced registrar
- Immediate catastrophic haemorrhage

Autopsy

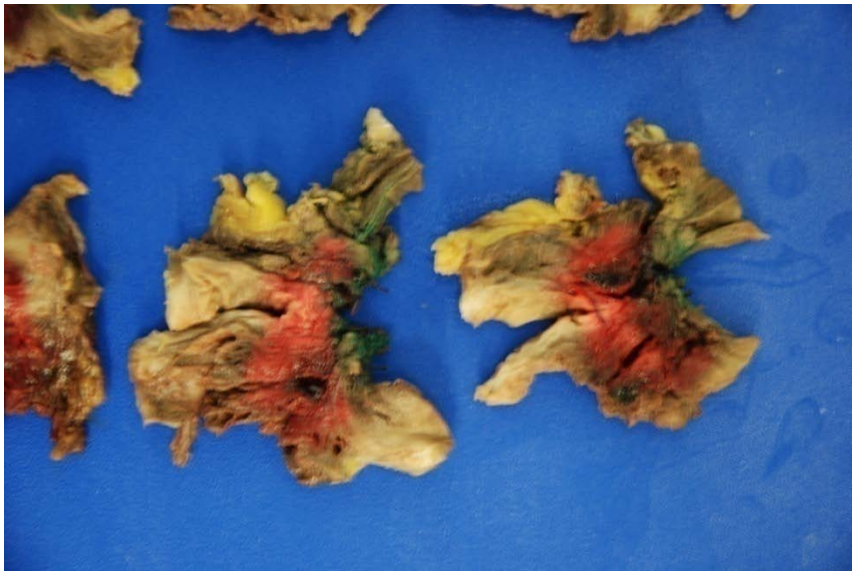
Remove the whole genital tract en bloc

Fix in formalin

Serial transverse slice

Numerous tissue blocks

Search for the torn vessels



Conclusion

Rich country perspective

- Obstetrics generally good
- Indirect deaths dominate
- Multifactorial pathogenesis
- Collaborative work
  - Clinical
  - Pathological
  - Microbiological

LICs

- HIV complications
  - tuberculosis
- Obstetric complications
- Unsafe TOP
- *But not many pathologists*
- *...do we believe the WHO stats on cause of death?*