Association of Anaesthetists

CORE TOPICS Wessex

Anaesthesia for non-obstetric surgery during pregnancy

DR JAMES ELDRIDGE

QUEEN ALEXANDRA HOSPITAL PORTSMOUTH

18TH OCTOBER 2019

Gemma

GP referral to surgeons

33 weeks gestation with RUQ pain and “unwell”

25 years old

Primip

Uncomplicated pregnancy

Nausea and vomiting

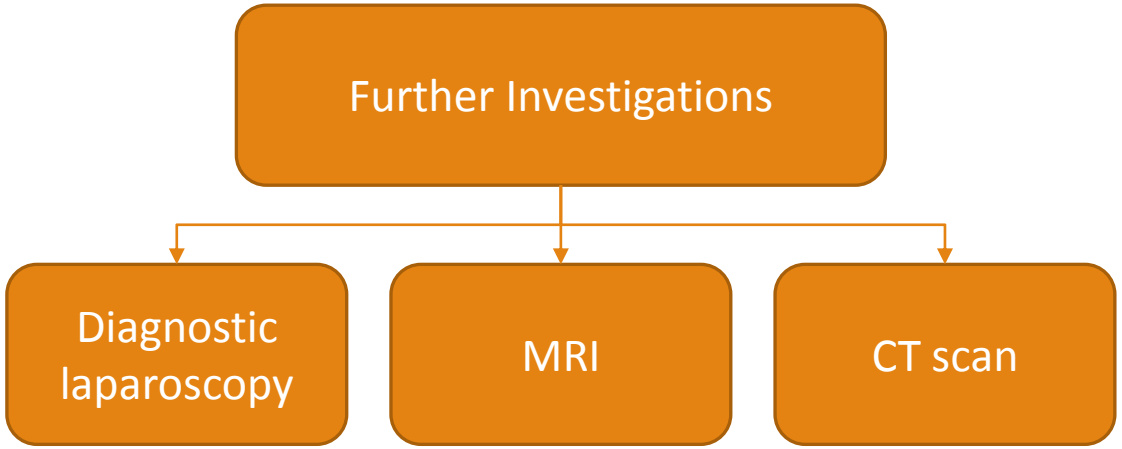
Temp 38.4 ^{o}C

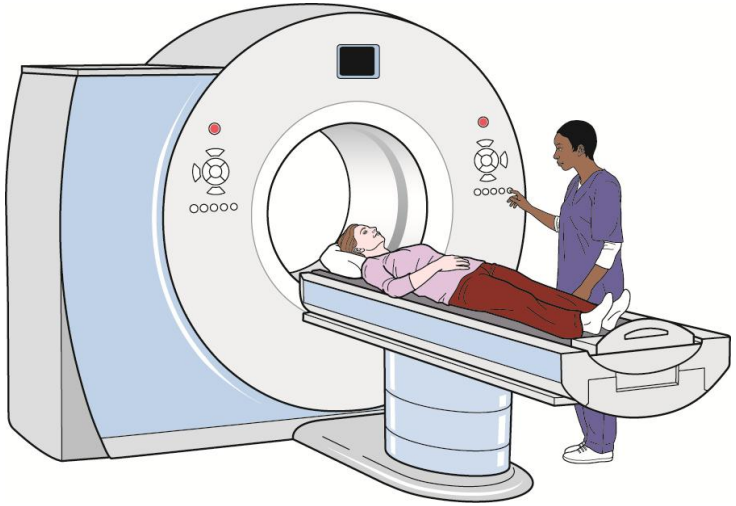
Raised CRP

Mike – General Surgeon

Abdominal US

- Probable appendix mass
- Poor views





Further Investigations

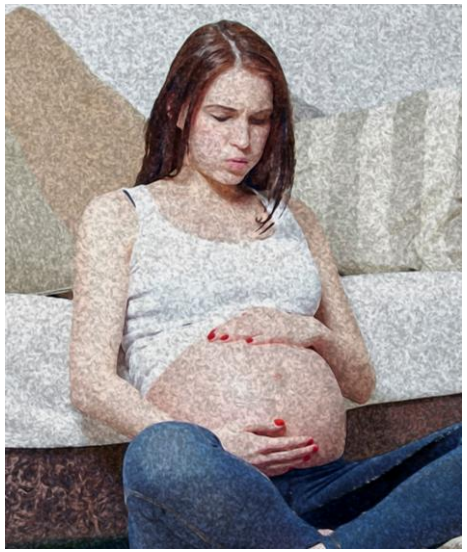
MRI should avoid gadolinium (crosses placenta and potentially teratogenic)

Radiation effects

- Risk of childhood malignancy ↑ 0.06% / 10mGy
- 5mGy increases risk of fetal loss, major abnormality by 1 per 6000 exposures
- Cumulative radiation dosage should be limited to 50-100 mGy during pregnancy.

Radiation exposure to fetus in common radiological studies	
Abdo X-ray	1-3 mGy
Fluoroscopy	200 mGY/min
Intraoperative cholangiography	2 mGy
Intravenous pyelogram	6 mGy
Barium enema	7 mGy
CT of pelvis	10-50 mGy
ERCP (without shielding)	20-125 mGy

Pearl JP 2017 SAGES



Surgeon

Anaesthetist

- What drugs to avoid?
  - Laparoscopy
  - Cardiac
  - Neuro surgery
  - Neonatal surgery
- What monitoring?
- When to intubate?
- Investigations
  - Xray
  - CT
  - MRI
- When to deliver?

Surgery during pregnancy

Open access Research

BMJ Open

Obstetric and non-obstetric surgery during pregnancy: A 20-year Danish population-based prevalence study

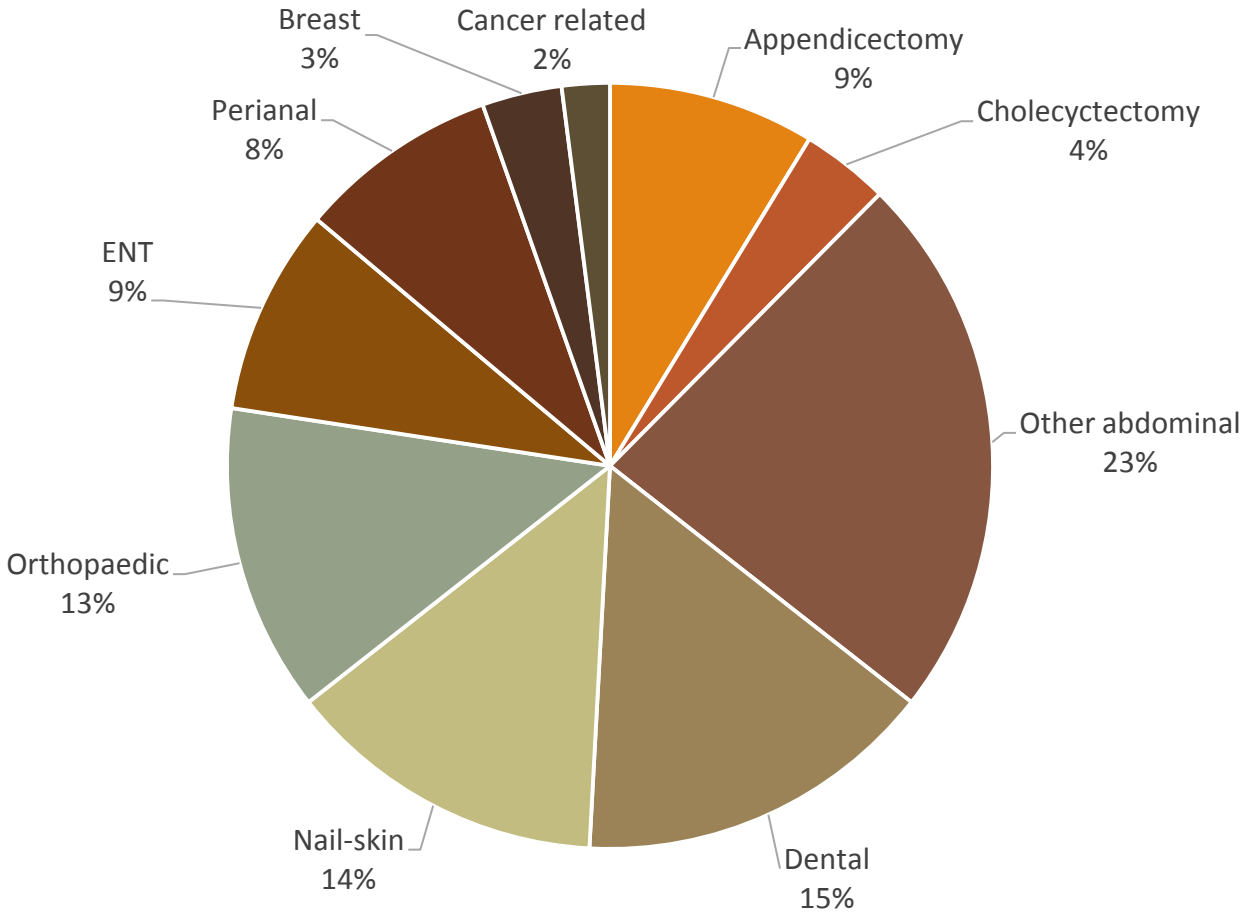
Anne Staub Rasmussen,[1] Christian Fynbo Christiansen,[2] Niels Uldbjerg,[3] Mette Nørgaard[2]

1,687,176 pregnancies

117,424 surgical procedures – 6.4% of pregnancies

23,694 non-obstetric procedures – 1.4% of pregnancies

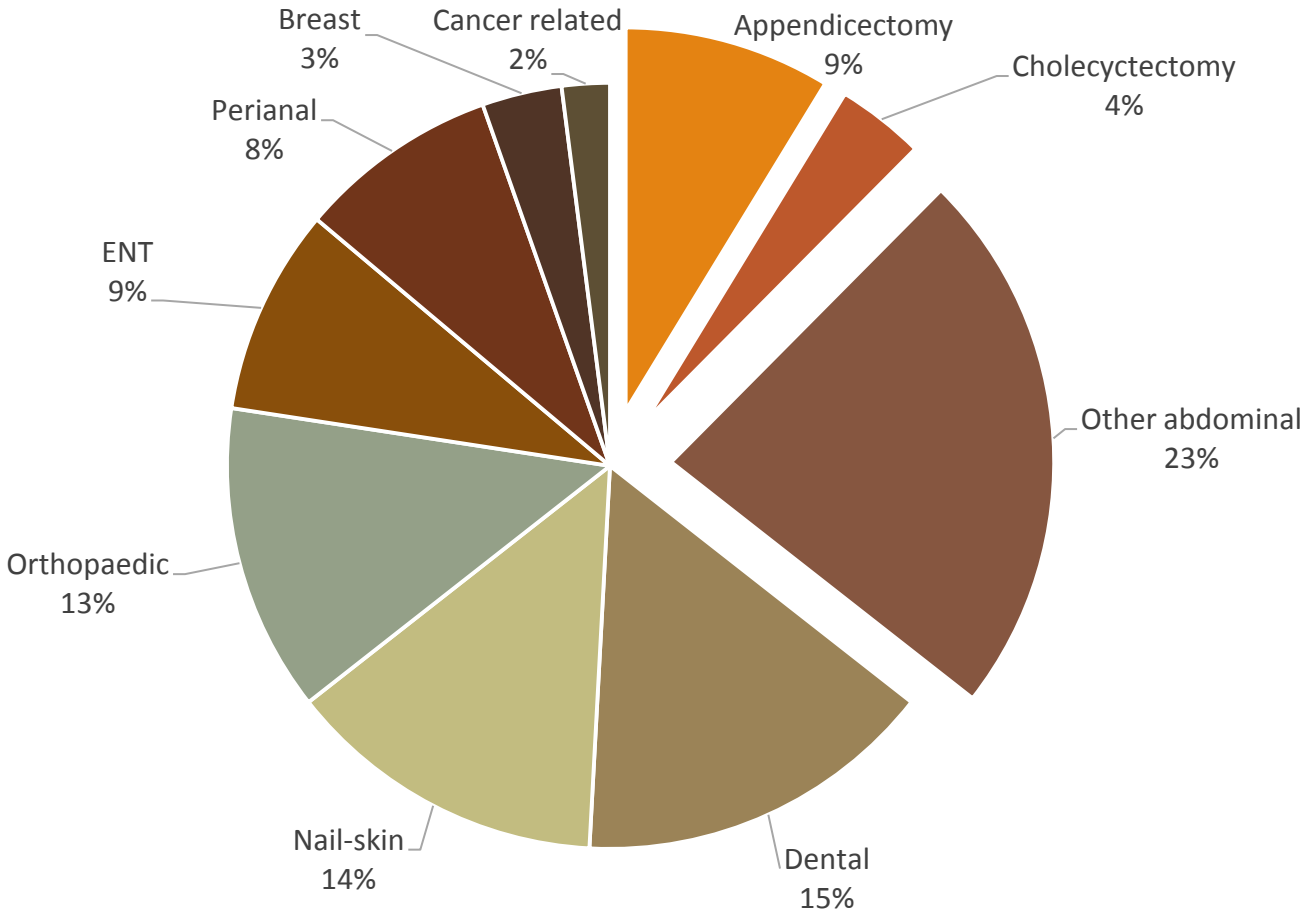
Type of non-obstetric surgery



6,486,280 pregnancies in UK 2002 - 2012

47,628 (0.74%) underwent non-obstetric surgery

Type of non-obstetric surgery



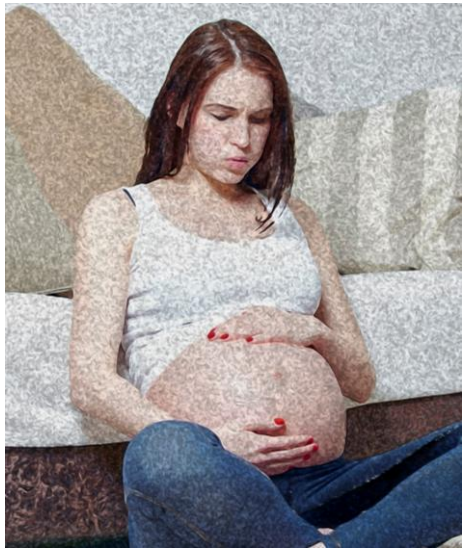
6,486,280 pregnancies in UK 2002 - 2012

47,628 (0.74%) underwent non-obstetric surgery

2/3 of all abdominal surgery was laparoscopic.

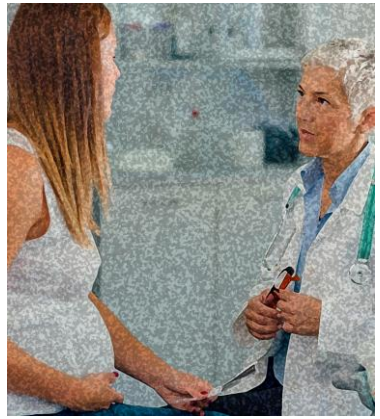
How do we achieve a good outcome?

- Multidisciplinary approach



Surgeon

Anaesthetist



Obstetrician

Midwife

Neonatologist

How do we achieve a good outcome?

- Multidisciplinary approach
- Decide on need for surgery and timing of surgery
  - Maternal risk / benefit
  - Fetal risk / benefit

Maternal risk / benefit

BENEFIT

Underlying condition and surgical outcomes

RISK

Physiological changes in pregnancy

- Modified immune system
- Thrombophilia
- Increased oxygen demand
- ? More difficult airway
- Direct trauma to uterus
- Aorto-caval occlusion

Maternal risk of surgery in pregnancy

- MBRRACE 2009-2014 - 1 death associated with anaesthesia during pregnancy
- 1 death associated with lap. cholecystectomy during pregnancy (USA)
- Prolonged inpatient stay - attributable risk 2% (1.7-2.4)

1 extra mortality per 7692 procedures

Barone 1999 Am J Surg Balinskaite 2017 Ann. Surg

Fetal risk / benefit

BENEFIT

Fetal well being intimately tied to maternal well being

RISK

Fetal loss

Stillbirth

Premature labour

Low birth weight

Teratogenicity

Risk of adverse pregnancy outcomes

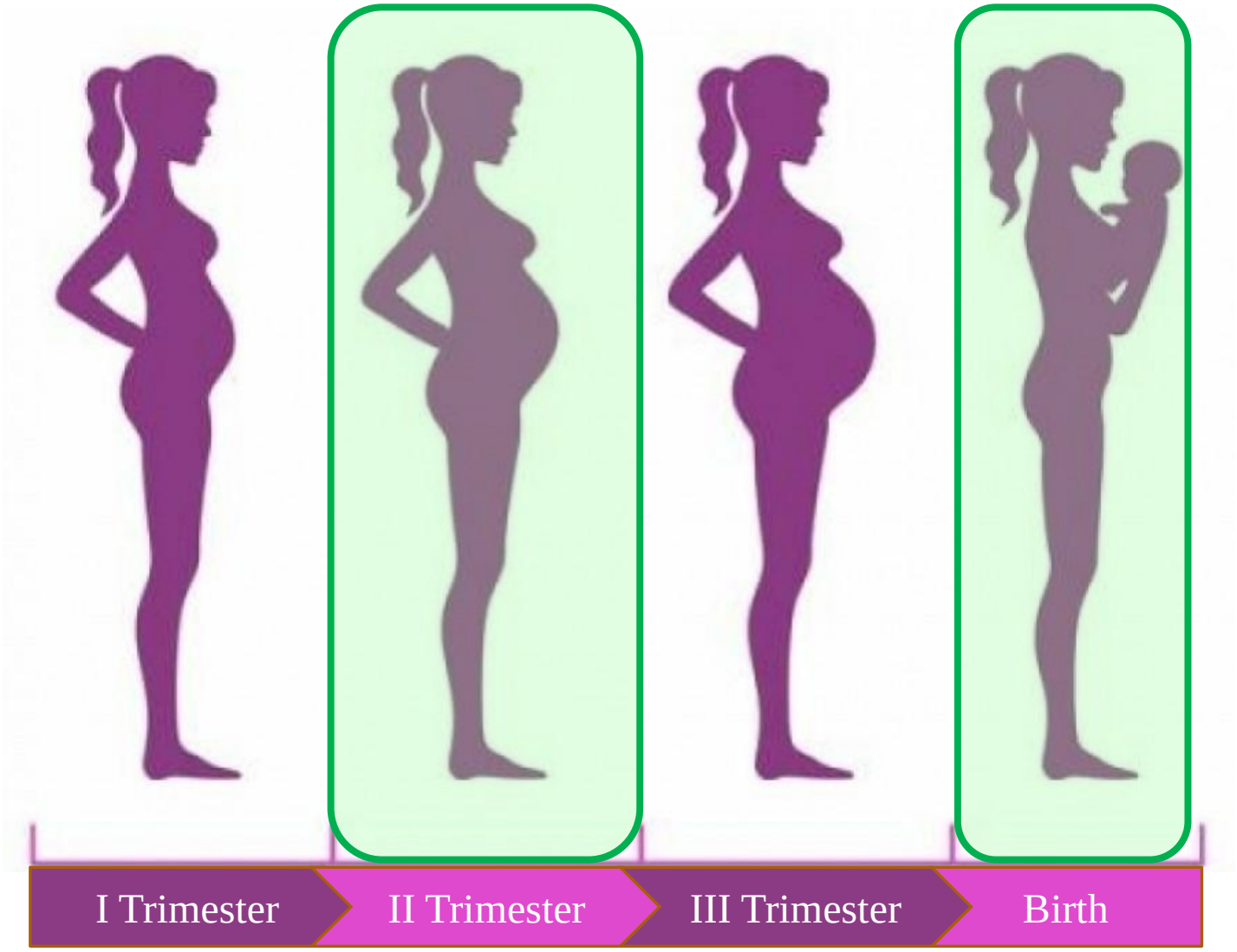
Overall risks considered to be low, but:

1 in 25 surgeries associated with 1 additional caesarean section

1 in 31 surgeries associated with 1 additional preterm delivery

1 in 39 surgeries associated with 1 additional low birth weight baby

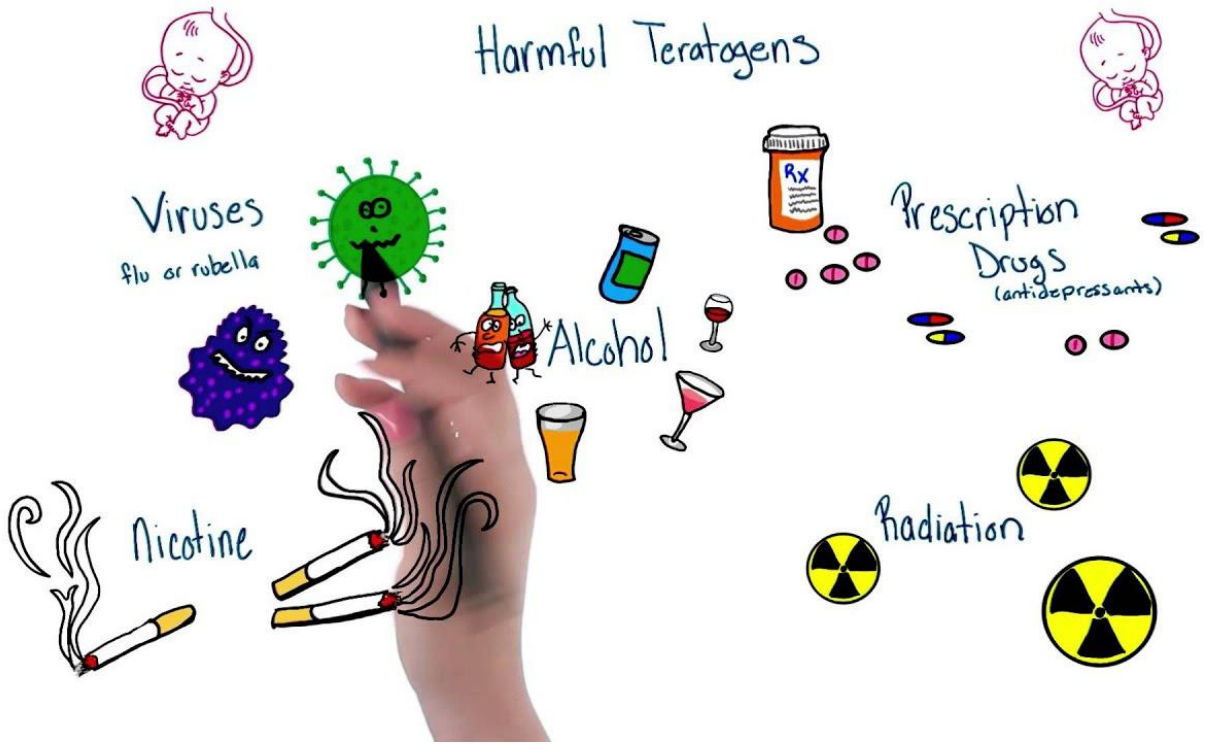
1 in 287 surgeries associated with 1 additional still birth



Timing of surgery

Delay to postnatal period

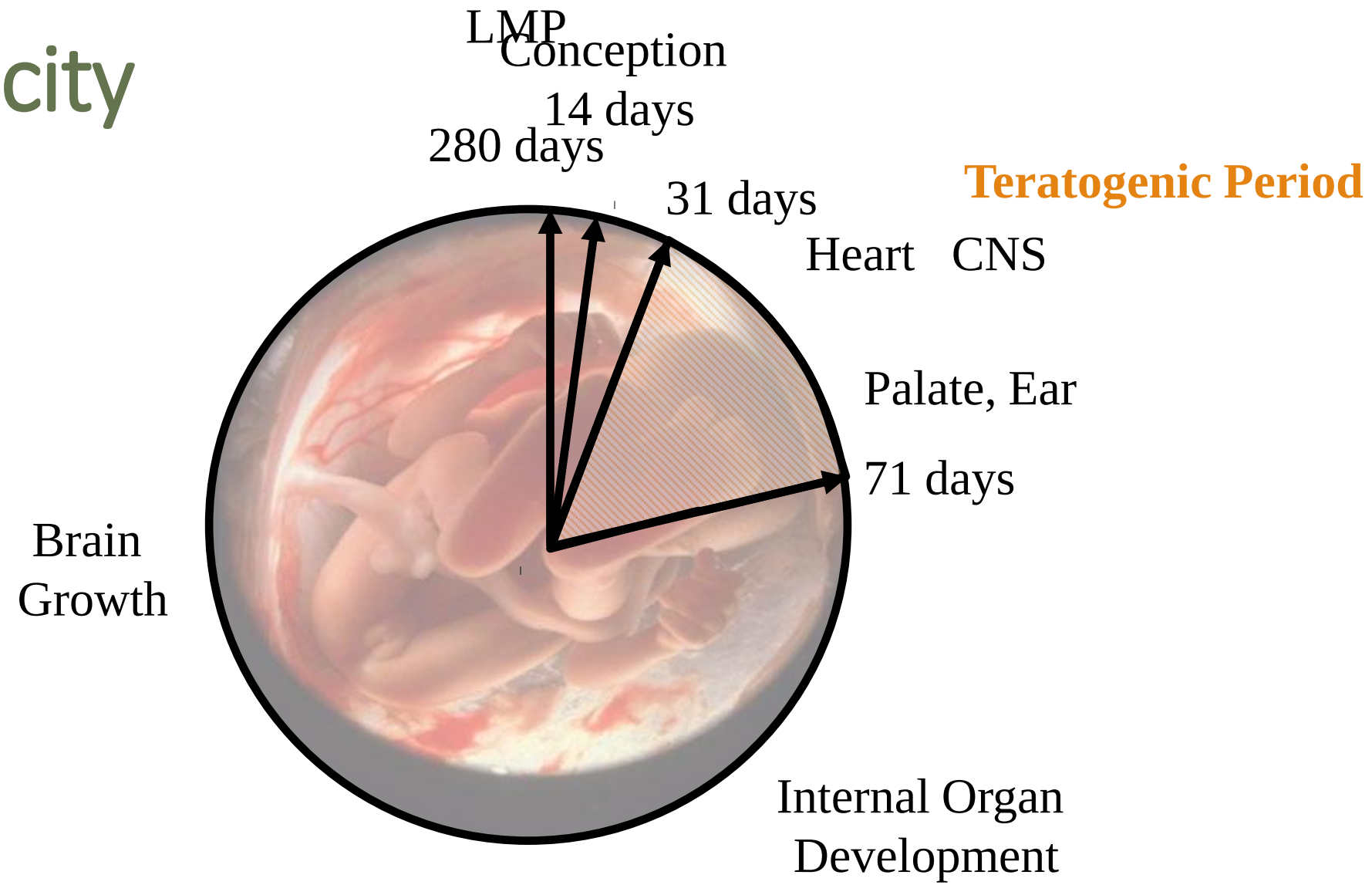
Traditionally try to avoid 1st and 3rd trimesters

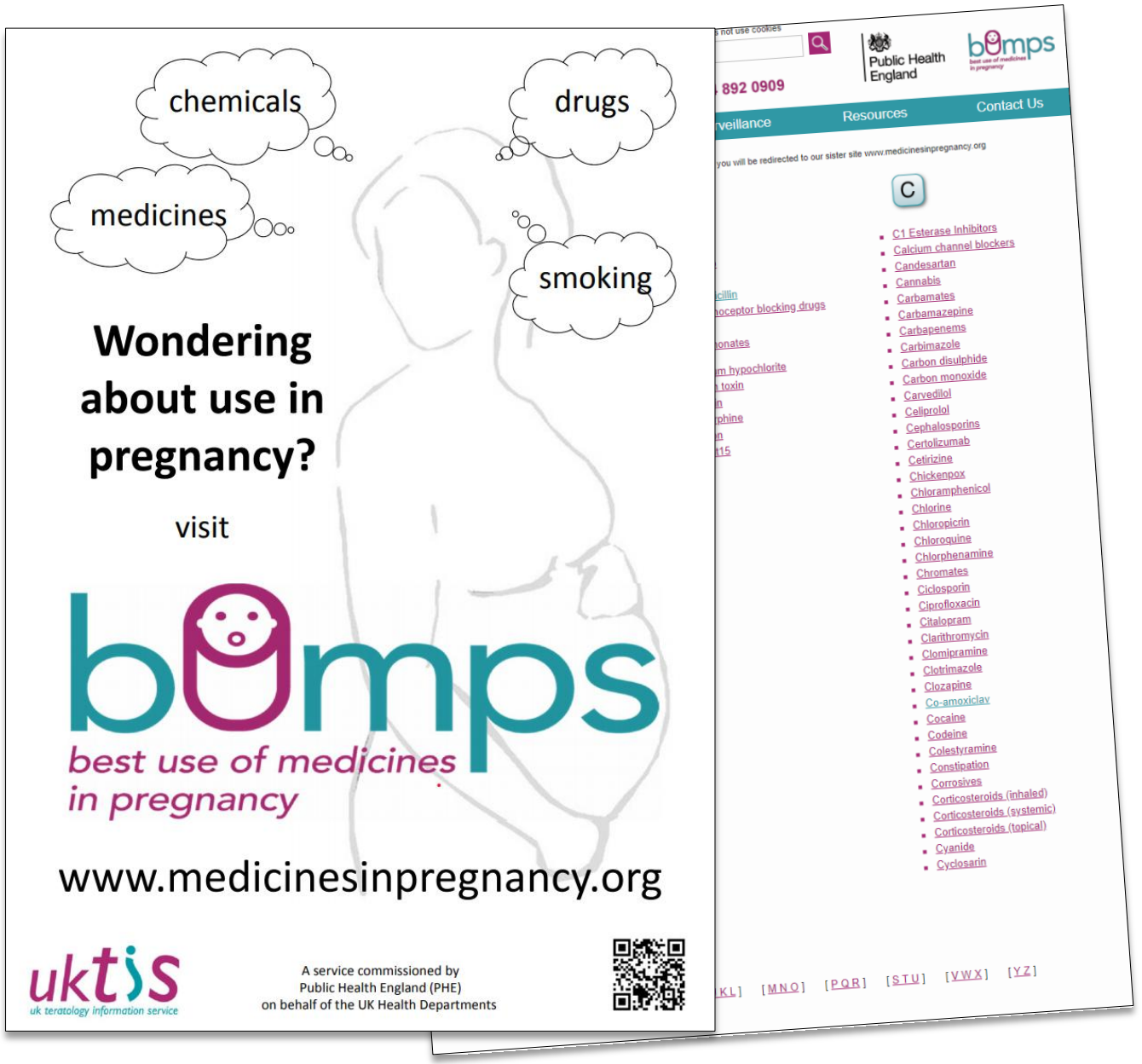


Teratogens

"Any agent that can disturb the development of an embryo or fetus."

Teratogenicity





Information Services

UK Teratology Information Service

http://www.uktis.org/

European Network of Teratology Information Services (ENTIS)

https://www.**entis**-org.eu

Organisation of Teratology Information Specialists (OTIS) (USA and Canada)

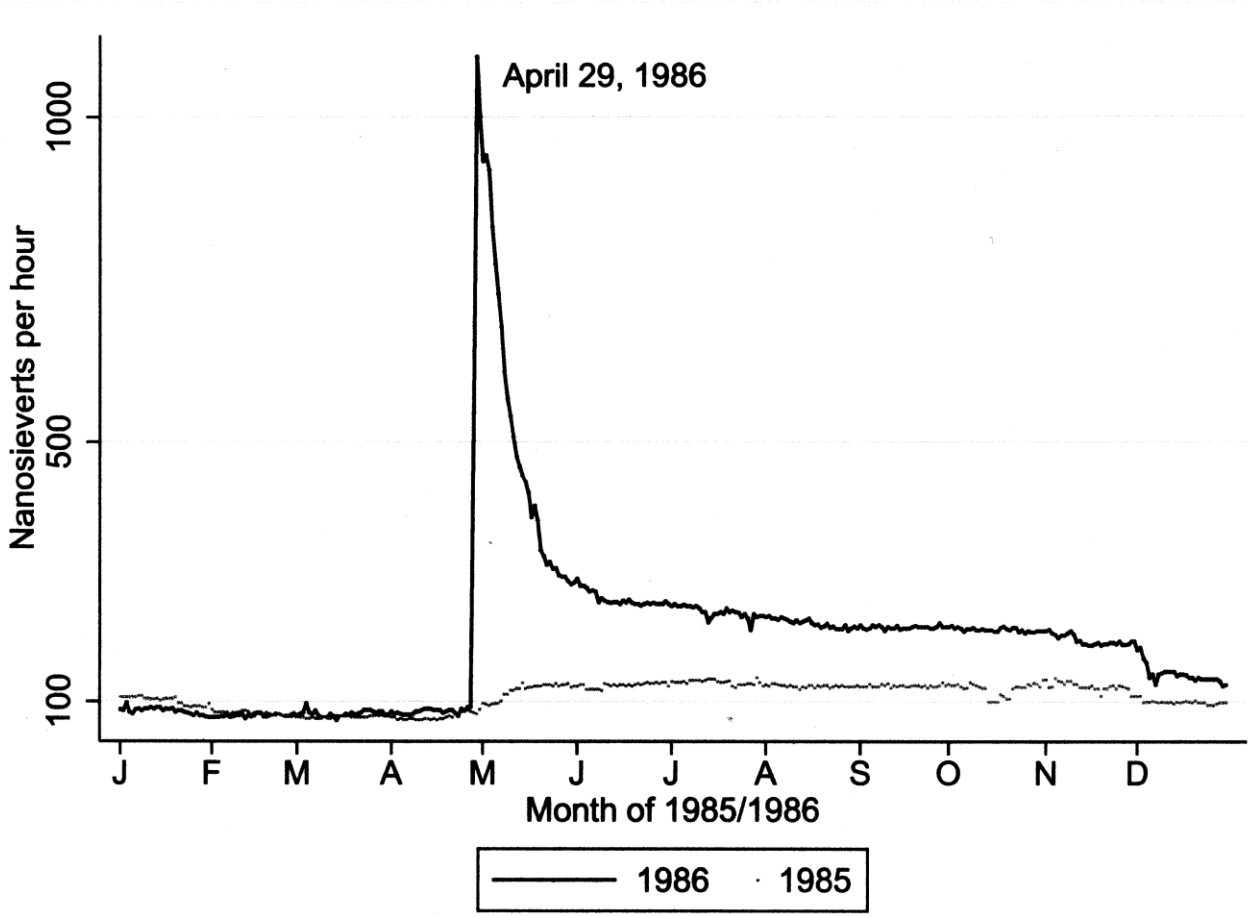
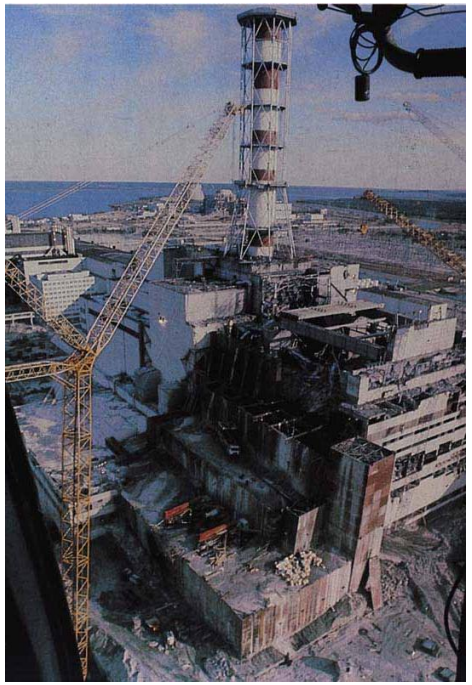


Figure I: Daily Gamma Radiation in Njurunda, Sweden


HBO
CHERNOBYL



STOCKHOLM, Sweden, Aug. 17 2009

Swedish children born in the months following the 1986 Chernobyl disaster suffered mental impairment from the radioactive fallout, a study found.

The report by researchers from Stockholm University and New York's Columbia University found that children born in the eight municipalities experiencing the highest levels of radiation were 3.6 percent less likely than others to qualify for high school, The Local said Thursday.

The researchers said it appears prenatal exposure to radiation levels previously considered safe was actually damaging to cognitive ability.

Dexamethasone & Betamethasone

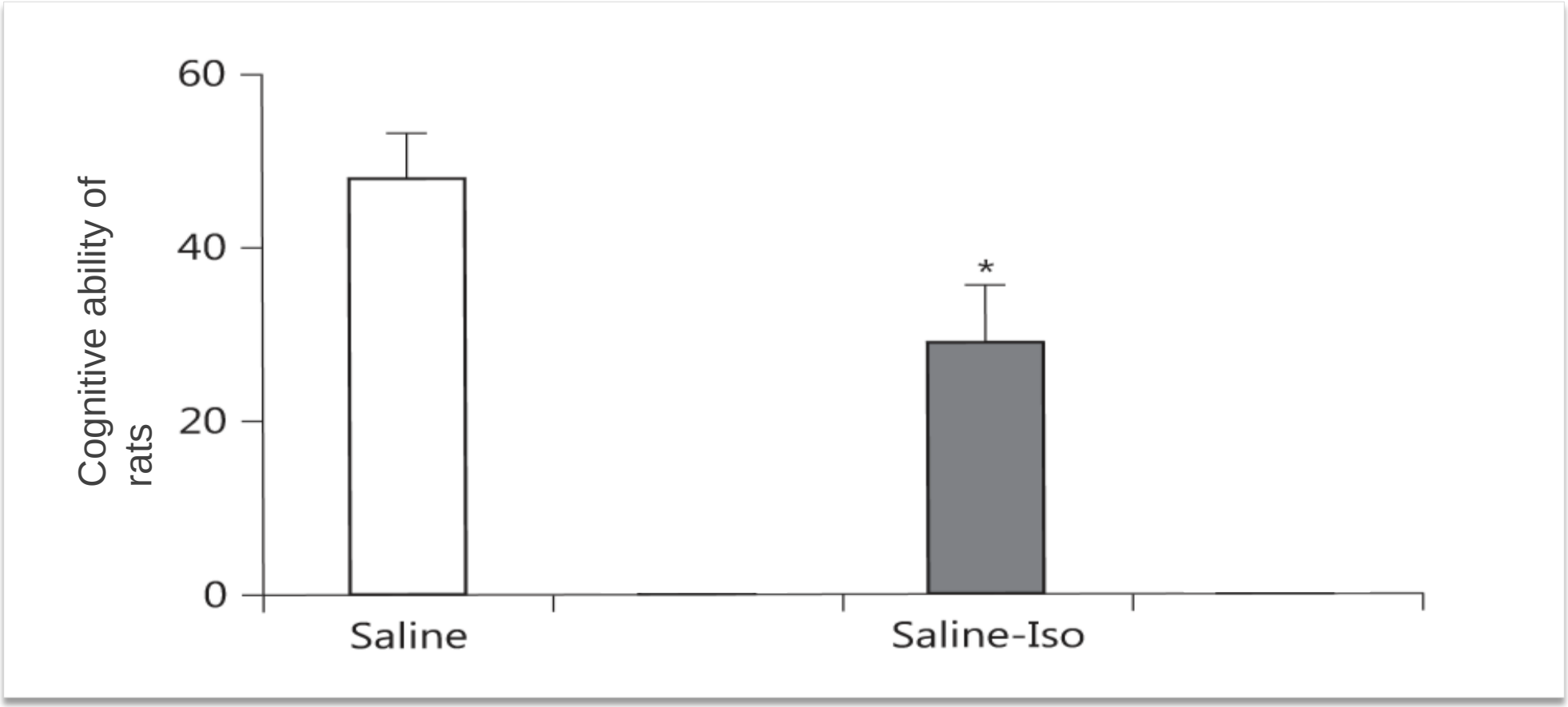
- Concern about repeated dose
- Possible association with reduced cognitive achievement in animal models
- No good evidence in humans

Recommendations

- Clear benefit for fetal lung maturation and reduced cerebral palsy
- Avoid repeated courses
- Betamethasone has reduced risk compared to dexamethasone (animal studies)

Anaesthesia and the developing brain

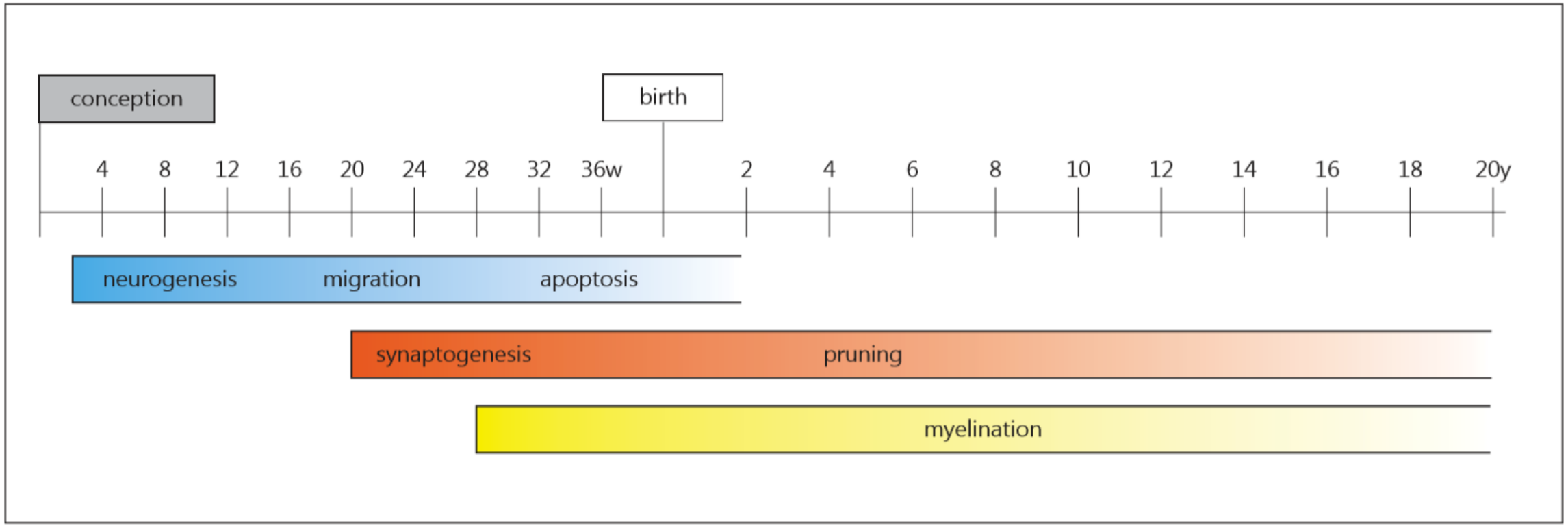
6 hr rat neonatal exposure to isoflurane



Sanders Anesthesiology 2009

Anaesthesia and cognitive impairment

Ikonomidou *et al*	Science 1999.	Blockade of NMDA receptors and apoptotic neurodegeneration in the developing brain
Jevtovic-Todorovic	J Neurosci 2003	Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits
Paule *et al*	Neurotoxicol Teratol 2011	Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys
Creeley *et al*	Anesthesiology 2014	Isoflurane-induced apoptosis of neurons and oligodendrocytes in the fetal rhesus macaque brain
Rappaport *et al*	N Engl J Med 2015	Anesthetic neurotoxicity - clinical implications of animal models
Wilder *et al*	Anesthesiology 2009	Early exposure to anesthesia and learning disabilities in a population-based birth cohort
DiMaggio *et al*	J Neurosurg Anesthesiol 2012	Pediatric anesthesia and neurodevelopmental impairments: a Bayesian meta-analysis


conception
birth
4
8
12
16
20
24
28
32
36w
2
4
6
8
10
12
14
16
18
20y
neurogenesis
migration
apoptosis
synaptogenesis
pruning
myelination

Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial

Andrew J Davidson, Nicola Disma, Jurgen C de Graaff, Davinia E Withington, Liam Dorris, Graham Bell, Robyn Stargatt, David C Bellinger,

Spinal vs sevoflurane GA (less than 1 hour) in 363 infants < 60 weeks post conceptual age undergoing inguinal hernia repair.

No difference in cognitive composite score

Research

Association Between a Single General Anesthesia Exposure Before Age 36 Months and Neurocognitive Outcomes in Later Childhood

Lena S. Sun, MD; Guohua Li, MD, DrPH; Tonya L. K. Miller, MD; Cynthia Salorio, PhD; Mary W. Byrne, PhD, MPH;

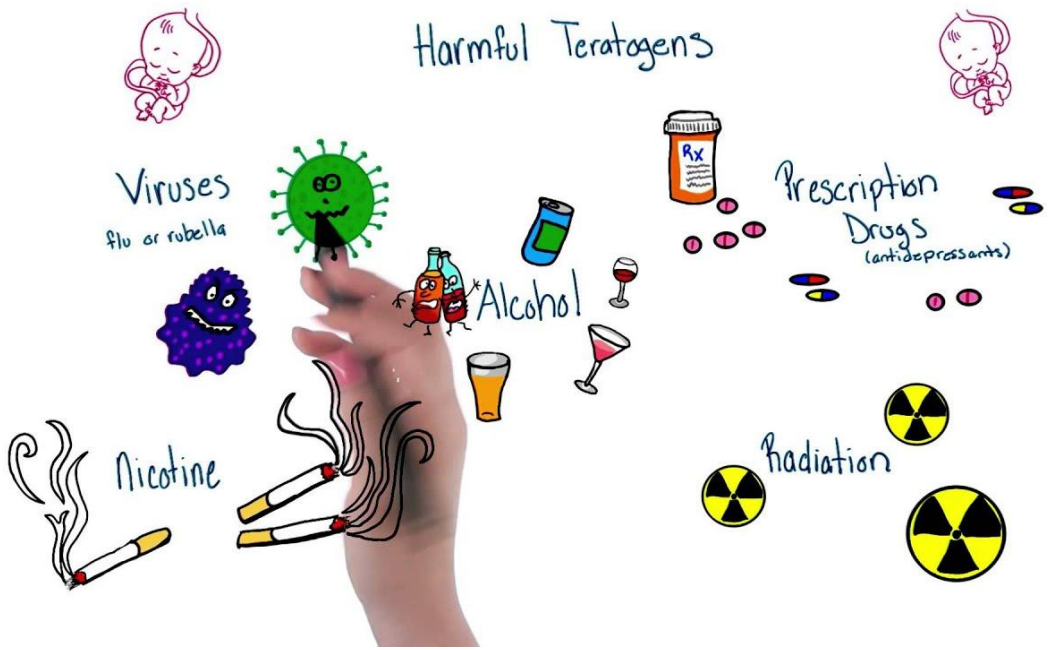
105 sibling pairs – 1 given single 20-240 min inhaled anaesthetic intervention age < 36 months

No difference in IQ aged 8-15 years

FDA Drug Safety Communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women

Health care professionals should balance the benefits of appropriate anesthesia in young children and pregnant women against the potential risks, especially for procedures that may last longer than 3 hours or if multiple procedures are required in children under 3 years. Discuss with parents, caregivers, and pregnant women the benefits, risks, and appropriate timing of surgery or procedures requiring anesthetic and sedation drugs.

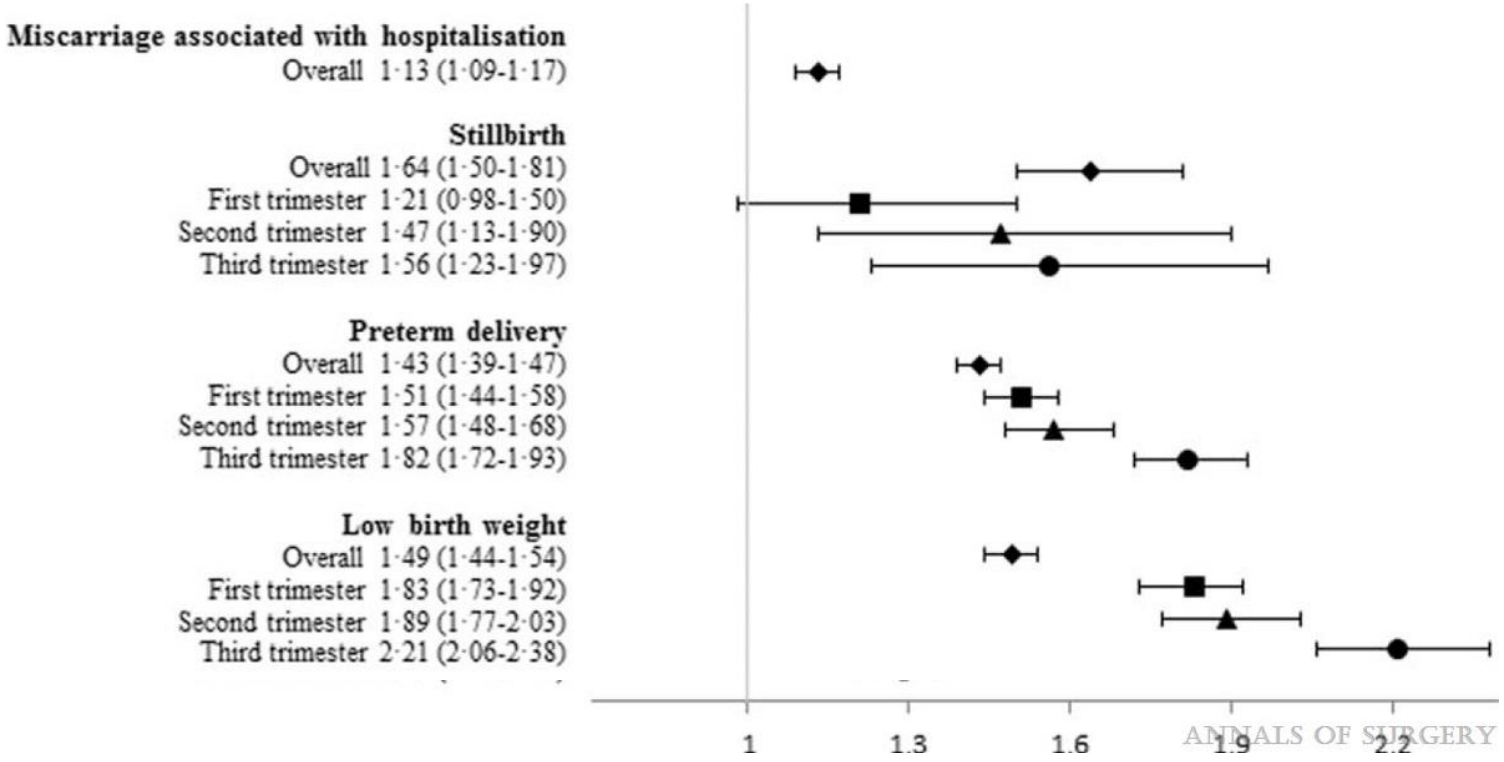
Consistent with animal studies, recent human data suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure might affect children's brain development, particularly for more lengthy or repeated exposures and in more vulnerable children.



Teratogens

"Any agent that can disturb the development of an embryo or fetus."

- Drugs / medicines
- Ionizing radiation
- Maternal pyrexia (>38.9 ^{o}C)
- Severe hypoglycaemia
- Infections
  - CMV
  - Herpes virus
  - Parvovirus
  - Rubella
  - Zika virus
  - Toxoplasmosis
  - Syphilis



The risk of adverse pregnancy outcomes following non-obstetric surgery during pregnancy

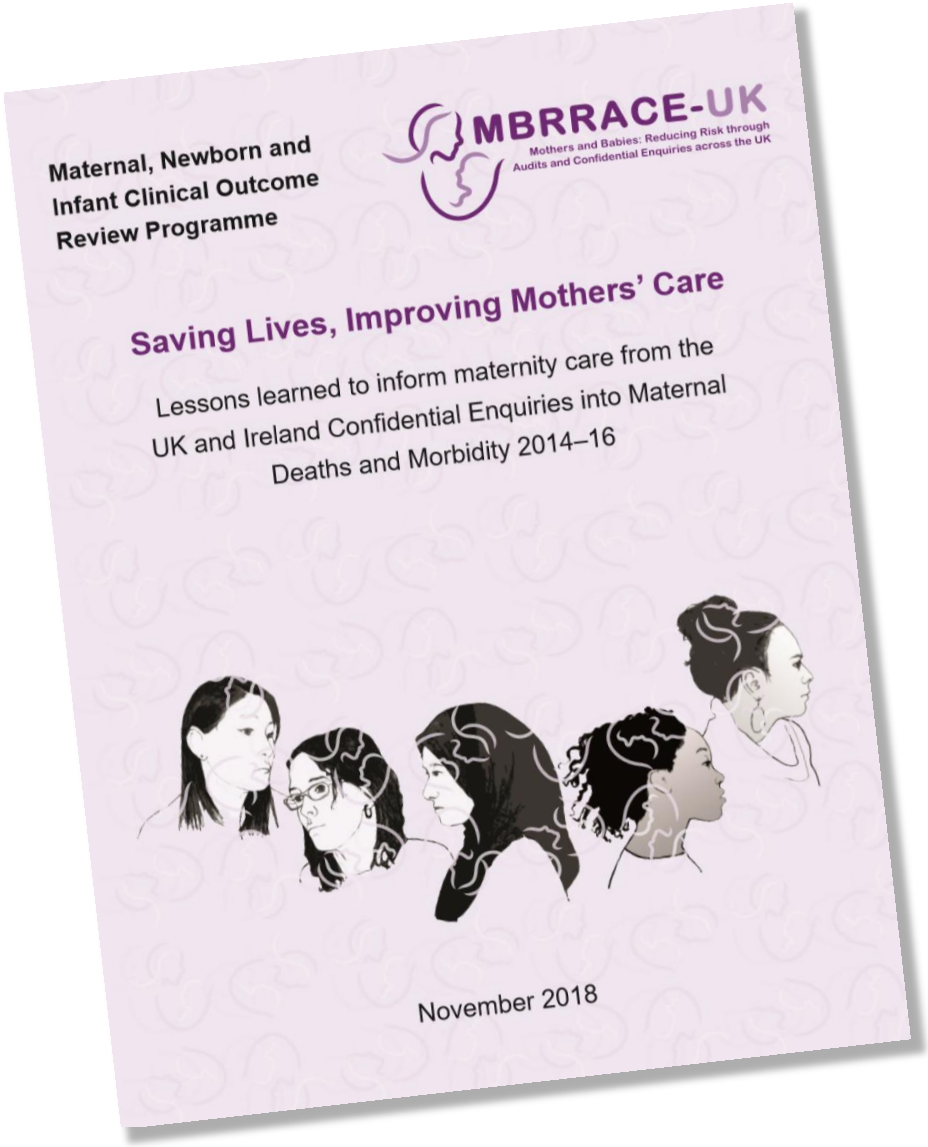
Balinskaite 2017 Annals of Surgery

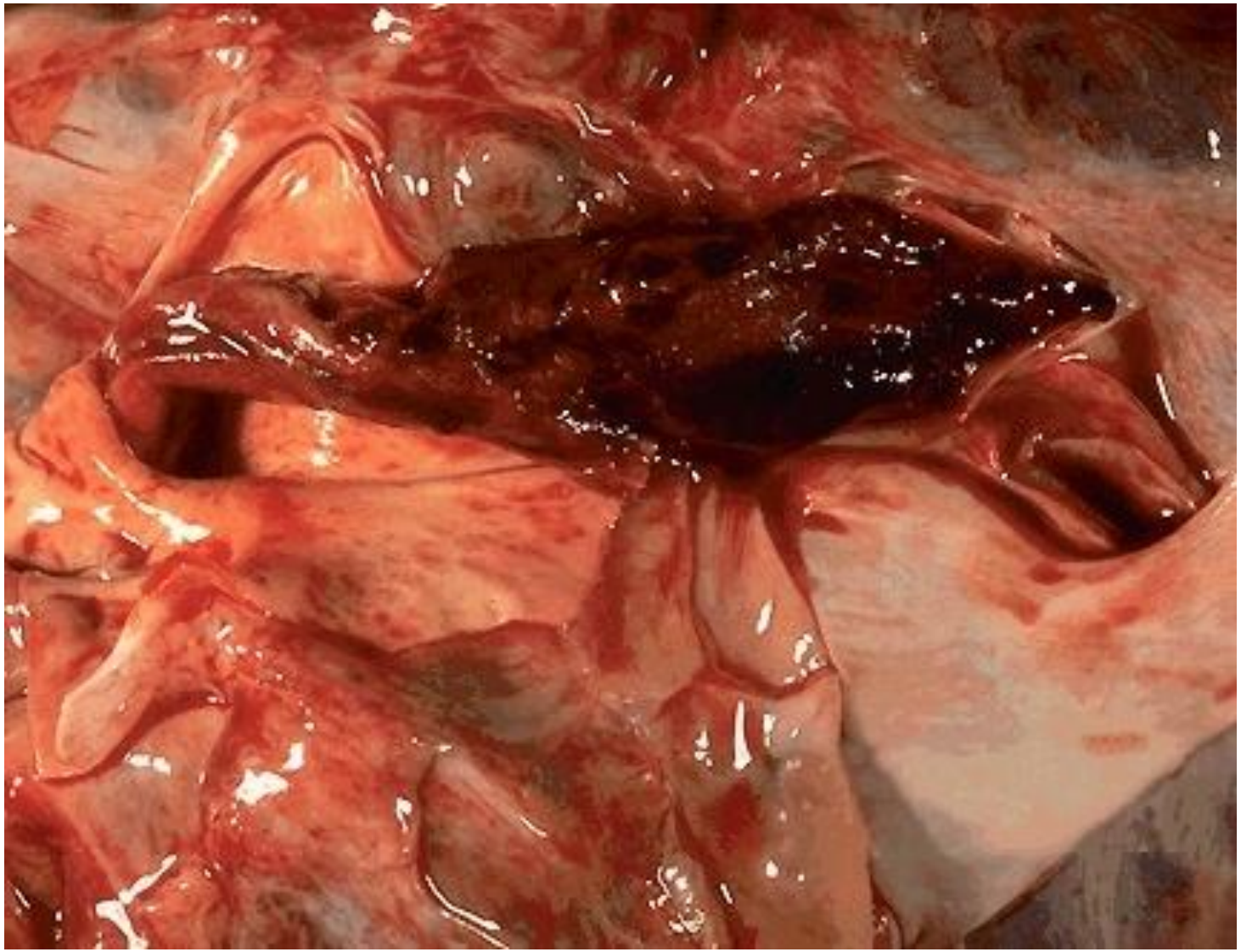
After a woman with known substance dependence had surgical management of an ectopic pregnancy …

She presented with shortness of breath and tachycardia.

After a woman with known substance dependence had surgical management of an ectopic pregnancy no risk assessment for VTE was carried out.

When she presented with shortness of breath and tachycardia the focus was on concern about possible withdrawal symptoms though the cause of her symptoms was the pulmonary embolism from which she died.

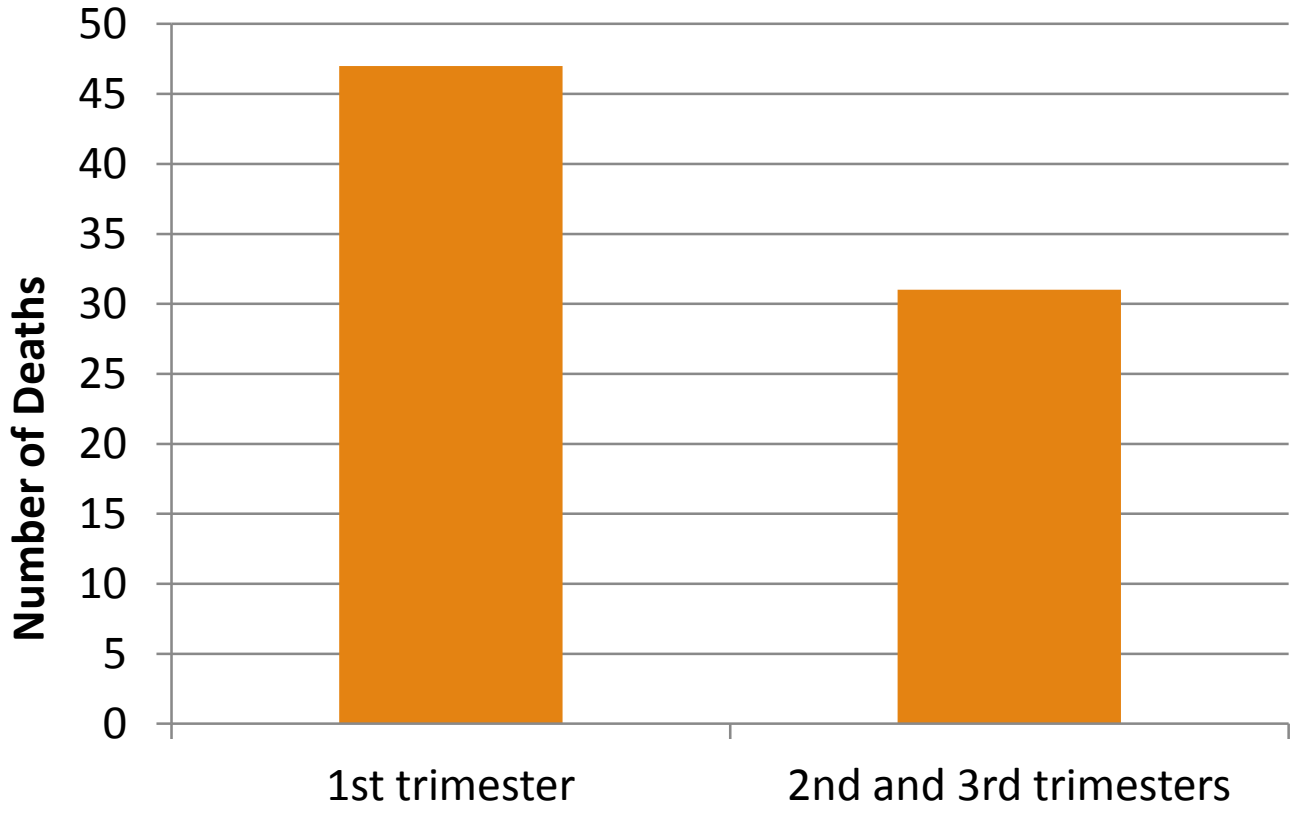




Thrombosis and Thromboembolism

Reassessment of VTE risk after miscarriage and ectopic pregnancy … is as important as reassessment … after giving birth.

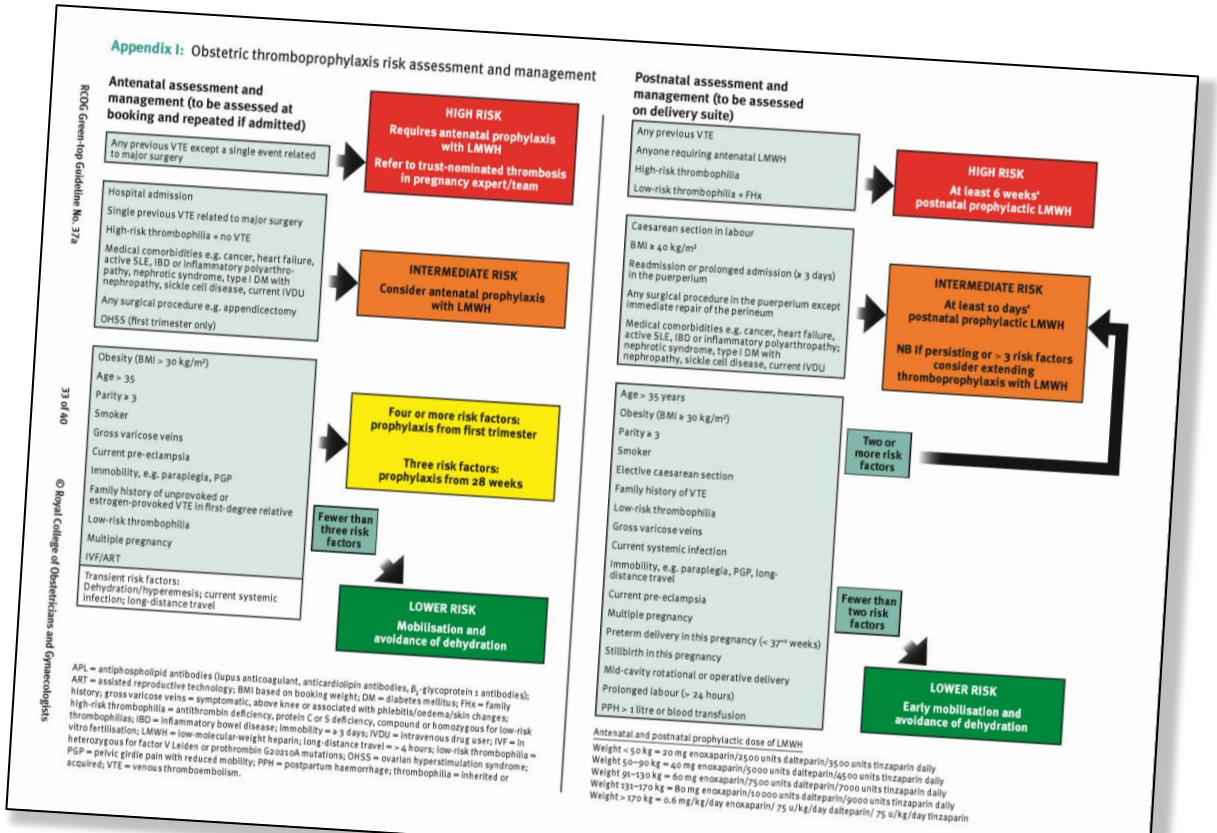
Antenatal deaths due to Thromboembolism 1997-2016



- Clear pathways for women who need thromboprophylaxis as soon as they become pregnant
- Reassessment of VTE risk after miscarriage and ectopic pregnancy
- Any surgical procedure in pregnancy or puerperium should consider thromboprophylaxis.

(RCOG Green-top Guideline 37a 2015)

CEMD 1997-2014



Appendix I: Obstetric thromboprophylaxis risk assessment and management

RCOG Green-top Guideline No. 37a

33 of 40

© Royal College of Obstetricians and Gynaecologists

Antenatal assessment and management (to be assessed at booking and repeated if admitted)

Any previous VTE except a single event related to major surgery

→ **HIGH RISK** — Requires antenatal prophylaxis with LMWH. Refer to trust-nominated thrombosis in pregnancy expert/team

Hospital admission
Single previous VTE related to major surgery
High-risk thrombophilia + no VTE
Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU
Any surgical procedure e.g. appendicectomy
OHSS (first trimester only)

→ **INTERMEDIATE RISK** — Consider antenatal prophylaxis with LMWH

Obesity (BMI > 30 kg/m²)
Age > 35
Parity ≥ 3
Smoker
Gross varicose veins
Current pre-eclampsia
Immobility, e.g. paraplegia, PGP
Family history of unprovoked or estrogen-provoked VTE in first-degree relative
Low-risk thrombophilia
Multiple pregnancy
IVF/ART

Transient risk factors: Dehydration/hyperemesis; current systemic infection; long-distance travel

→ **Four or more risk factors:** prophylaxis from first trimester
Three risk factors: prophylaxis from 28 weeks

Fewer than three risk factors → **LOWER RISK** — Mobilisation and avoidance of dehydration

Postnatal assessment and management (to be assessed on delivery suite)

Any previous VTE
Anyone requiring antenatal LMWH
High-risk thrombophilia
Low-risk thrombophilia + FHx

→ **HIGH RISK** — At least 6 weeks' postnatal prophylactic LMWH

Caesarean section in labour
BMI ≥ 40 kg/m²
Readmission or prolonged admission (≥ 3 days) in the puerperium
Any surgical procedure in the puerperium except immediate repair of the perineum
Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy; nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU

→ **INTERMEDIATE RISK** — At least 10 days' postnatal prophylactic LMWH
NB If persisting or > 3 risk factors consider extending thromboprophylaxis with LMWH

Age > 35 years
Obesity (BMI ≥ 30 kg/m²)
Parity ≥ 3
Smoker
Elective caesarean section
Family history of VTE
Low-risk thrombophilia
Gross varicose veins
Current systemic infection
Immobility, e.g. paraplegia, PGP, long-distance travel
Current pre-eclampsia
Multiple pregnancy
Preterm delivery in this pregnancy (< 37+0 weeks)
Stillbirth in this pregnancy
Mid-cavity rotational or operative delivery
Prolonged labour (> 24 hours)
PPH > 1 litre or blood transfusion

Two or more risk factors → **LOWER RISK** — Early mobilisation and avoidance of dehydration

Fewer than two risk factors

Antenatal and postnatal prophylactic dose of LMWH
Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10 000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, β_2-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = > 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or acquired; VTE = venous thromboembolism.

Attach Addressograph label

Patient name: _____

D.O.B.: _____

Hosp no.: _____

Portsmouth Hospitals NHS
NHS Trust

Actual body weight	
Weight:	Weight:
BMI	BMI
Date:	Date:

Weight should be recorded on each admission

Antenatal Risk Assessment for Venous Thromboembolism (VTE) Prophylaxis

Pre-existing risk factors	Risk Factors for VTE	Tick	Score
Previous VTE (except a single event related to major surgery)		☐	4
Previous VTE provoked by major surgery		☐	3
Known high-risk thrombophilia		☐	3
Medical comorbidities e.g. Cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type 1 diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		☐	3
Family history of unprovoked or oestrogen-related VTE in first-degree relative		☐	1
Age (>35 years)		☐	1
Obesity		☐	1 or 2[b]
Parity ≥3		☐	1
Smoker		☐	1
Gross varicose veins		☐	1
Obstetric risk f…			

…air of the

	☐	3
	☐	3
	☐	4
	☐	1
	☐	1

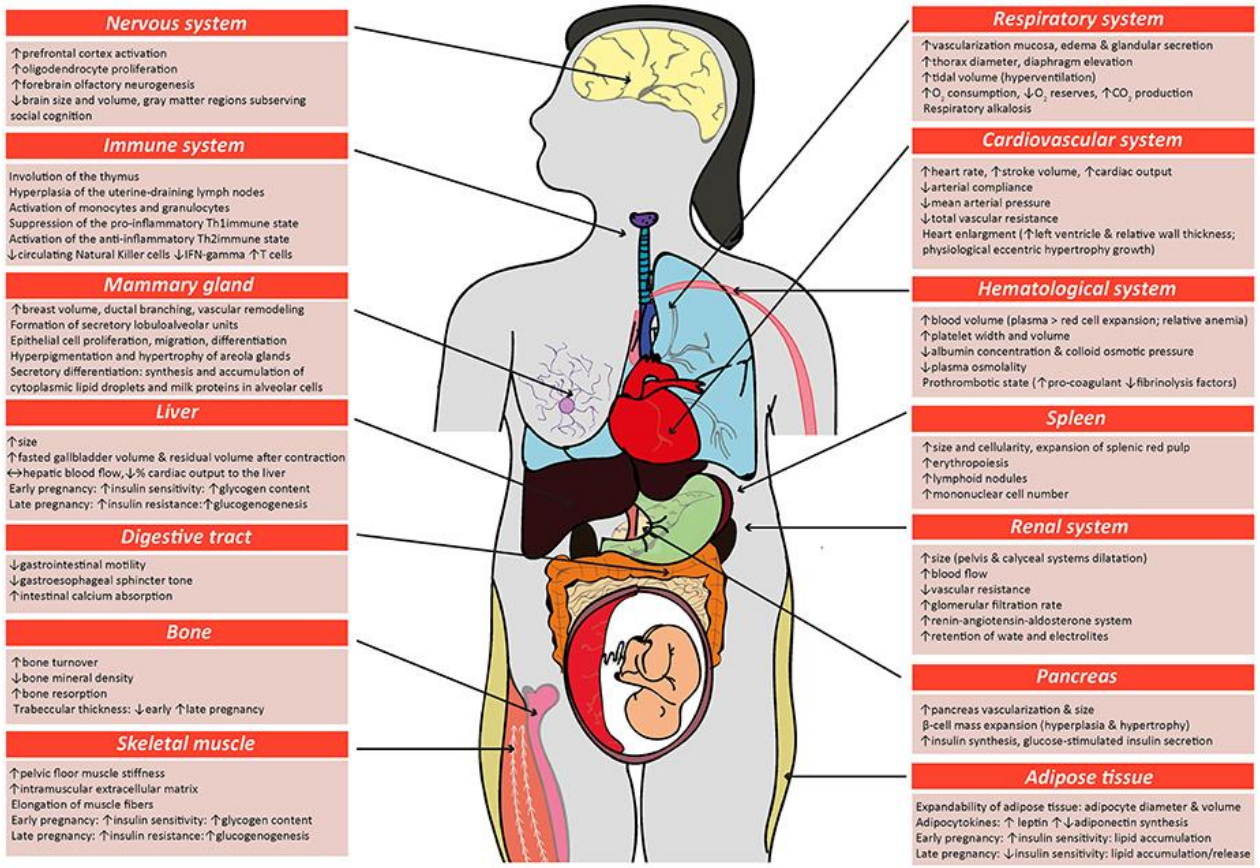
…ro fertilisation; OHSS ovarian hyperstimulation syndome; VTE venous

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks, discuss with doctor
- If admitted to hospital antenatally consider thromboprophylaxis, irrespective of score
- If prolonged admission ≥ 3 days discuss thromboprophylaxis with obstetrician

For women with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed with a haematologist with expertise in thrombosis and bleeding in pregnancy.

How do we achieve a good outcome?

- Multidisciplinary approach
- Decide on need for surgery and timing of surgery
  - Maternal risk / benefit
  - Fetal risk / benefit
- Understand physiological changes of pregnancy



Changes in maternal physiology

Modified immune system

Hypercoagulable

Increased O_2 consumption and reduced FRC

Reduced $PaCO_2$

Aortocaval compression
- 20 weeks

Prone to regurgitation

Slower whole gut transit time
- Minimal effect on gastric emptying

How do we achieve a good outcome?

- Multidisciplinary approach
- Decide on need for surgery and timing of surgery
  - Maternal risk / benefit
  - Fetal risk / benefit
- Understand physiological changes of pregnancy
- Pre-operative preparation

Pre-operative preparation

Communication with obstetrician

- Fetus viable?
- Fetus needs delivering for maternal / fetal reasons?
  - Usually “No”
  - If “yes” - Should surgery be delayed 48 hours for fetal lung maturation?

Communication with midwifery staff

- Fetal monitoring pre and post surgery to confirm presence of fetal heart beat.

Communication with mother

- Risks / benefits of surgery
- Risks / benefits of regional or GA

Antacid prophylaxis

Regional or GA?

GA: Induction Agents

Agent	Use	Comments
Thiopentone	Probably OK	
Propofol	Probably OK	
Ketamine	Avoid in 1st trimester	Assoc with ↑intrauterine pressure in 1st trimester
Benzodiazepines	Care in 1st trimester	Possible association with cleft palate
Etomidate	Avoid	Fetal and maternal steroid suppression

GA: Maintenance

Agent	Use	Comments
Inhalational agents	Probably OK	Single short (< 3hr) exposure OK. Uterine relaxation useful
Nitrous Oxide	Probably OK	Probably avoid because of methionine synthetase inhibition
Propofol TIVA	Probably OK	Uncertain of effects maternal and fetal lipid load in pregnancy

Analgesic agents

Agent	Use	Comments
Opiates	Probably OK	Prolonged exposure risks withdrawal pre or post delivery
Paracetamol	Probably OK	Possible association with childhood asthma but conflicting results
Local anaesthetic agents	Probably OK	Fetal trapping with most local anaesthetics. However total fetal exposure is small
NSAIDs	Probably avoid	↑ 1st trimester loss ↑ Premature closure of DA in 3rd trimester
Tramadol	Possibly OK	Data regarding malformation following exposure in 1st trimester is conflicting. Manufacturer recommends avoid in pregnancy and breast feeding.

Antiemetic agents

Agent	Use	Comments
Cyclizine and other anti H1 histamines	Probably OK	1st line drug for hyperemesis*
Metoclopramide	Probably OK	2nd line drug for hyperemesis gravidarum* (extrapyramidal SFX)
Prochlorperazine	Probably OK	2nd line drug for hyperemesis gravidarum* (extrapyramidal SFX)
Ondansetron	Probably OK	July 2019 warning from EMA because risk of cleft lip increased from 11/10,000 to 14/10,000 pregnancies after use in 1st trimester for hyperemesis. Risk remains low. Still suggested as 2nd line drug for hyperemesis**
Dexamethasone	Probably avoid	Repeated courses of steroids in pregnancy may be associated with cognitive impairment

*Green-top Guideline No. 69 June 2016

**UKTIS September 2019

Reversal agents

Agent	Use	Comments
Sugamadex	Probably OK	Does not cross the placenta. No evidence of harm but limited data
Neostigmine	Probably OK	Crosses the placenta and may cause fetal bradycardia
Glycopyrrolate	Probably OK	Does not cross the placenta (and so does not protect fetus from bradycardias)
Atropine	Probably OK	Crosses the placenta (and so will protect fetus from bradycardias)

Intra-operative technique

- Positioning
  - > 20/40 vena caval occlusion
  - Care with surgical retractors / leaning on uterus
- Airway
  - RSI > 18 weeks to +48 hours post delivery
- Avoid hypoxia
- Moderate hypocarbia
- Maintain blood pressure
  - Phenylephrine, metaraminol or ephedrine
- Avoid light anaesthesia
  - Catecholamines
  - Increased uterine tone
- Effective postoperative analgesia

Fetal Monitoring peri-operatively

Liaise with obstetric service

Confirm fetal heart beat pre and post operatively

Inform mother of risk of preterm labour and to report symptoms

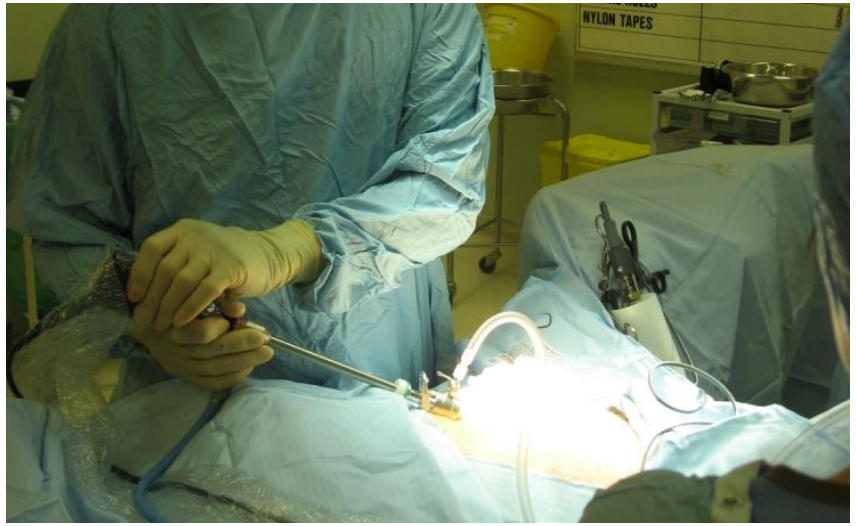
Fetal monitoring during surgery

CTG possible after 18-22 weeks

FHR variability develops after 27 weeks

But:

- Intra-operative monitoring may be difficult
- Interpretation is difficult
  - Loss of FHR variability common with anaesthetic agents & opioids



Laparoscopic surgery

Concerns

- Gravid uterus
  - Direct injury with trocar placement
  - Limited access

  But laparoscopic surgery has been performed in all trimesters

- Insufflation pressure
  - ↓ FRC
  - ↓ Uterine perfusion

  Poor evidence

- ↑ CO2
  - Fetal acidosis (animal studies)
  - No evidence of harm
  - Beware prolonged surgery

How do we achieve a good outcome?

- Multidisciplinary approach
- Decide on need for surgery and timing of surgery
  - Maternal risk / benefit
  - Fetal risk / benefit
- Understand physiological changes of pregnancy
- Pre-operative preparation
- Intraoperative concerns
  - Anaesthetics
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Postoperative Care

Analgesics

- Regular paracetamol
- Local anaesthetic
- Opioids
- Avoid NSAIDs

DVT Prophylaxis

- Risk stratify and discuss with obstetric team

Location

- Usually on surgical ward (discuss with obstetric team)

Ask mother to report contractions

- Beware premature labour
- No prophylactic tocolysis

Major Trauma in pregnancy

Usual ABC principles

Do not withhold normal investigations including CT

Beware ruptured uterus / placental abruption in (even minor) abdominal trauma

- Imaging
- Fetal distress

Remember Feto-maternal haemorrhage

- Kleihauer-Bekte test in all pregnancy women
- Anti-D (advice from haematology / midwife)

Be alert to non-accidental injury

How do we achieve a good outcome?

- Multidisciplinary approach
- Decide on need for surgery and timing of surgery
  - Maternal risk / benefit
  - Fetal risk / benefit
- Understand physiological changes of pregnancy
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Questions

OooooO

Non-conventional analgesic agents

Agent	Use	Comments
Magnesium	Probably OK	Neuroprotective for fetus Care with hypotension
Gabapentin and pregabalin	Probably avoid	Insufficient evidence for malformations. Possible association with low birth weight.
Clonidine	Possibly OK	Insufficient information Care with hypotension

Antibiotic agents

Agent	Use	Comments
Tetracyclines	Avoid	Dental discolouration, teratogenicity
Fluroquinolones	Avoid	Ciprofloxacin (and levofloxacin) causes muscle and skeletal growth problems.
Penicillins	Probably OK	
Erthyromycin	Probably OK	
Cepahlosporins	Probably OK	
Clindamycin	Probably OK	
Metronidazole	Probably OK	
Gentamicin	Probably OK	Potential for ototoxicity. Avoid if possible.