OXCOG

OXCOG.CO.UK

Screening & FASP

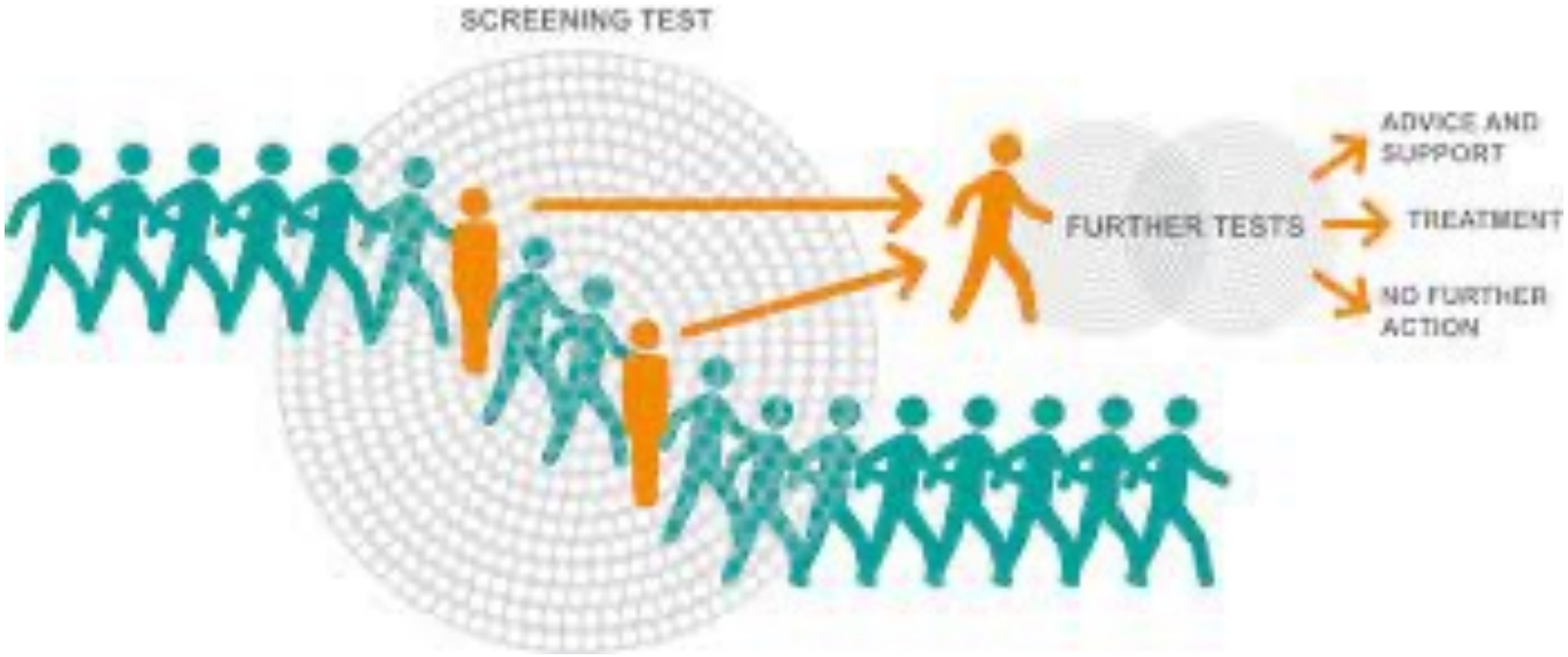
MRCOG Part 2 Online Revision Course

Miss Kit Robertson – Consultant in Obstetrics and Maternal-Fetal Medicine, Oxford University Hospitals

Aims & Objectives

- What is screening?
- Principles of Screening Tests
- NHS Antenatal Screening Programmes
  - FASP
  - Infectious Diseases in Pregnancy
  - Sickle Cell and Thalassaemia
- What the NHS does not screen for antenatally
- Non-invasive Prenatal Testing (NIPT)
- Invasive Prenatal Testing

What is screening?



- Screening is the process of identifying healthy people who may have an increased chance of a disease or condition so they can be offered information, further tests and / or treatment
- **Screening is always a choice**
- People should be able to access the information they need to help them make a decision about the offer of screening

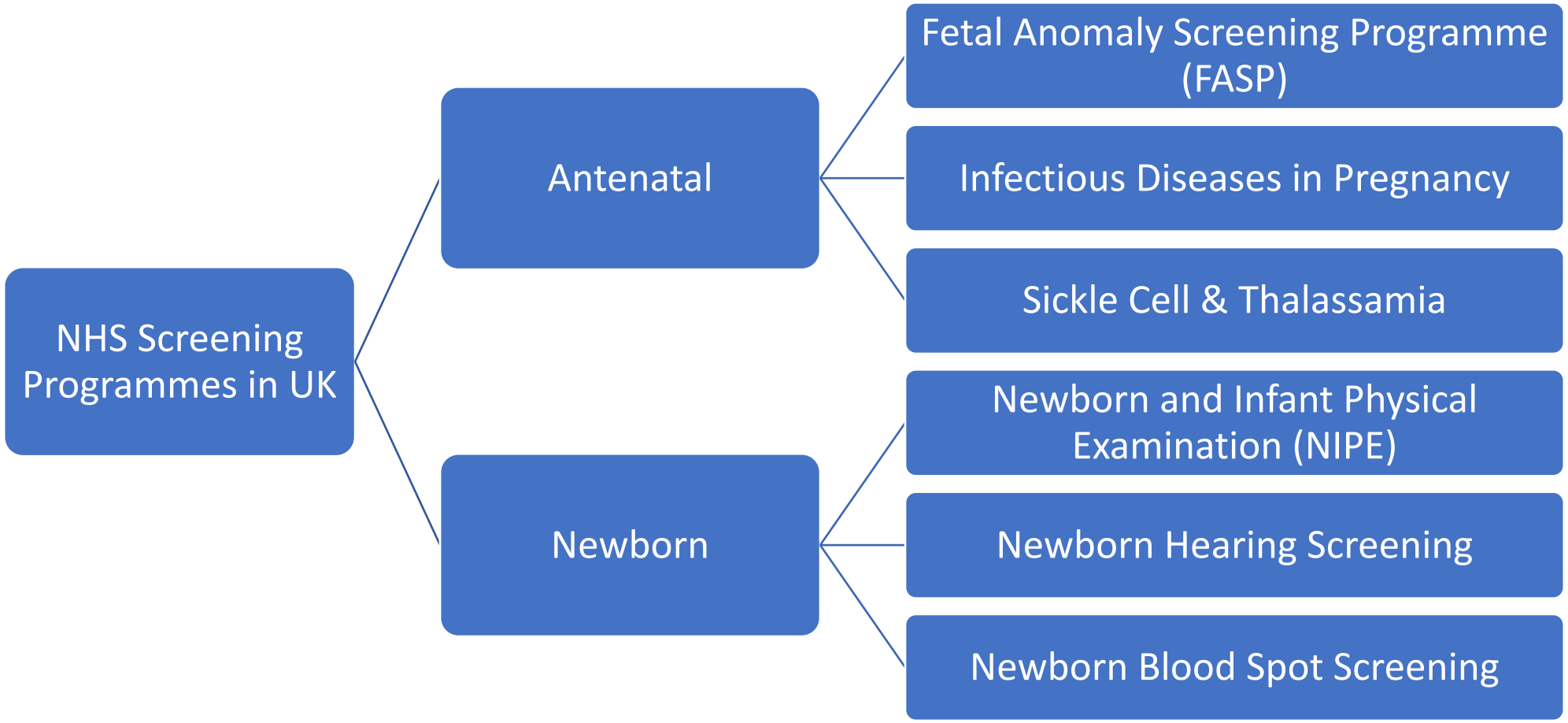
Who runs screening programmes in the UK?

- National population screening programmes are implemented in the NHS on the advice of the **UK National Screening Committee (UK NSC)** which makes independent evidence-based recommendations to ministers in the 4 UK countries
- **Public Health England (PHE)** advises the government and the NHS so England has safe high quality screening programmes that reflect the best available evidence the UK NSC recommendations
- PHE also develops standards and provides specific services that help the local NHS implement and run screening services consistently across the country

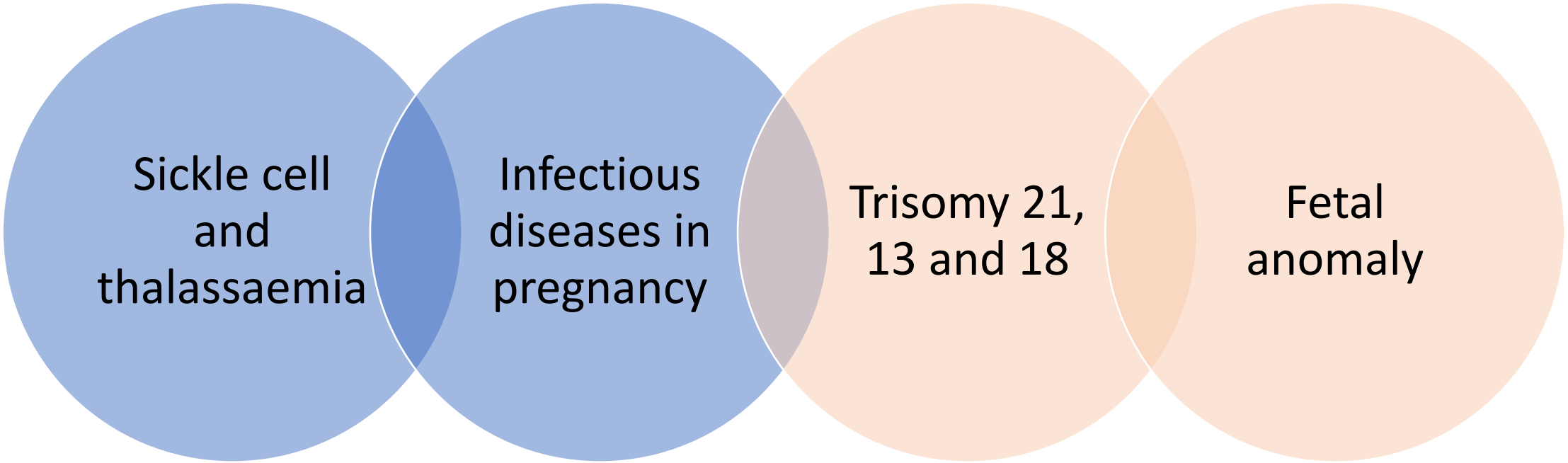
Principles of screening (WHO 2008)

1. Condition should be clinically well defined
2. Incidence should be known
3. Associated with significant morbidity or mortality
4. Effective treatment should be available
5. There should be a latent period during which intervention is possible
6. There should be an ethical, safe, simple and robust screening test
7. Screening should be cost-effective

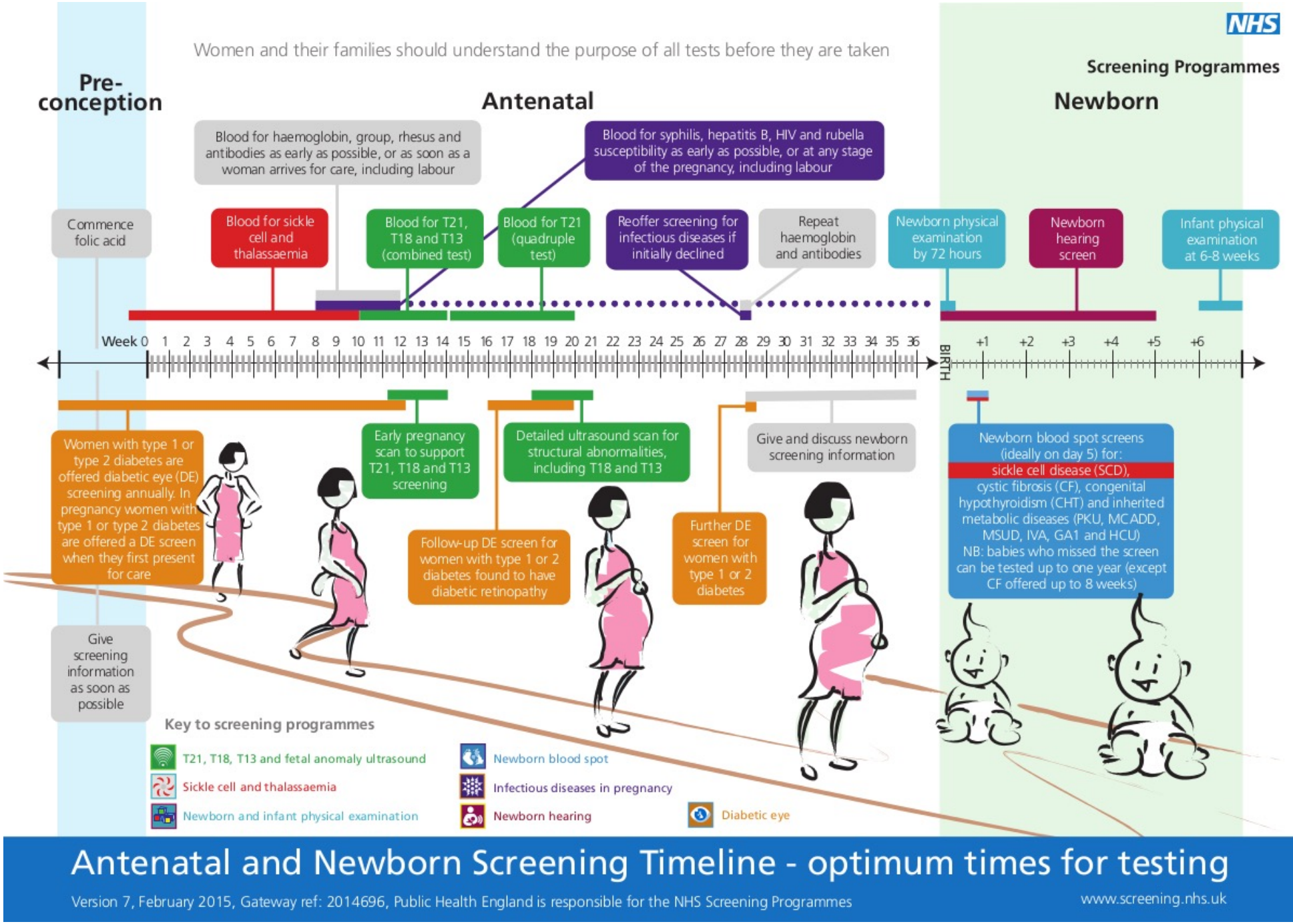
NHS Antenatal Screening Programmes in the UK



NHS Antenatal Screening Programmes in the UK



Structure of antenatal screening in UK

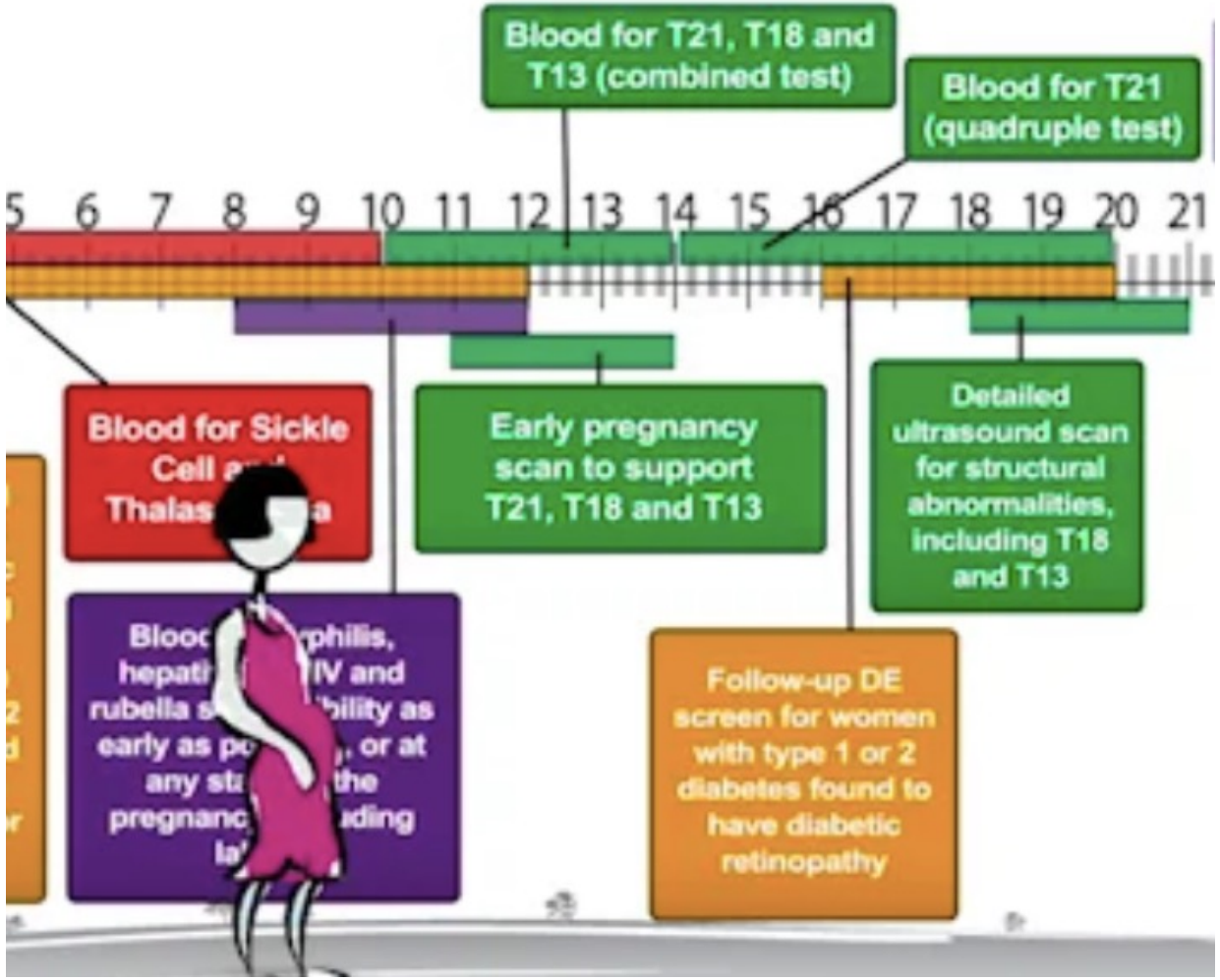


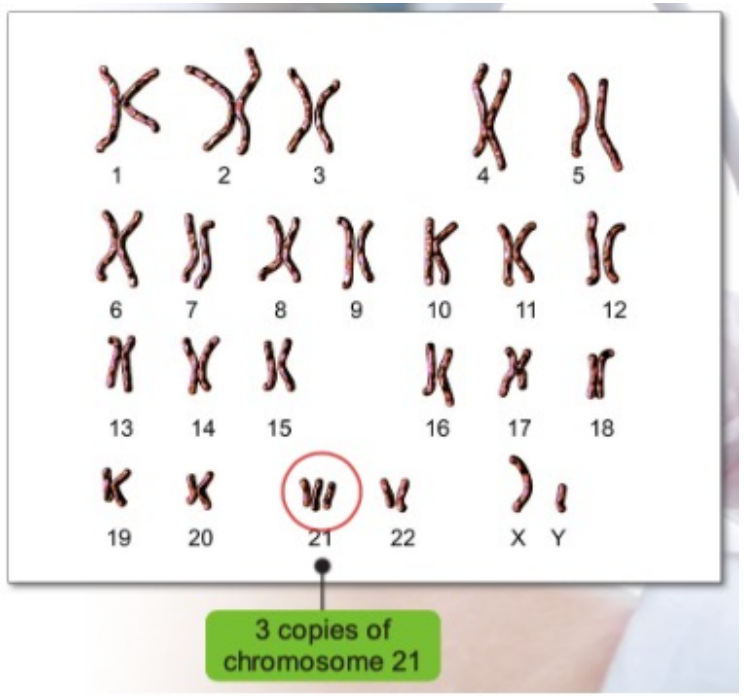
Fetal Anomaly Screening Programme (FASP)

- The **NHS Fetal Anomaly Screening Programme (FASP)** offers screening to all eligible pregnant women to assess the chance of the baby being born with Down's syndrome and / or Edwards' and Patau's Syndrome
- The test of choice for both singleton and twin pregnancies is **first trimester combined screening (CST)**
- Women with singleton or twin pregnancies who book too late for combined testing or when a nuchal translucency (NT) measurement cannot be obtained in the first trimester, should be offered **quad testing** in the second trimester

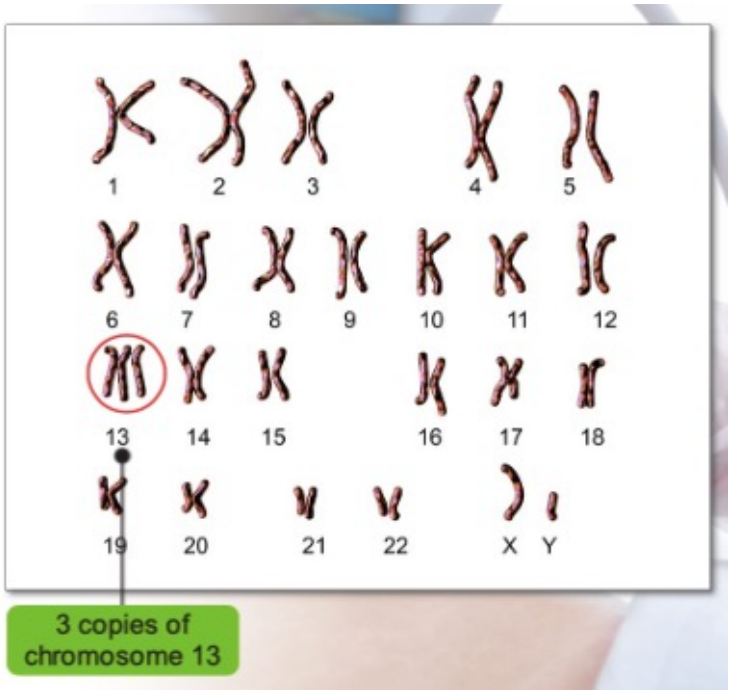
Combined screening for trisomies

- Down's Syndrome – Trisomy 21
- Edwards' Syndrome – Trisomy 18
- Patau's Syndrome – Trisomy 13

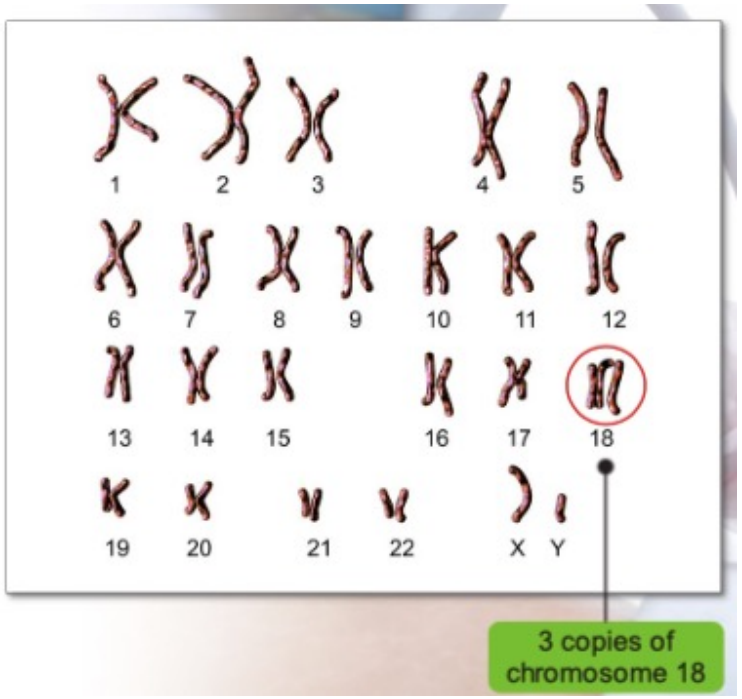




- Down's Syndrome
  - Life expectancy 20 years less than average
  - May need assistance with independent life, some neurodevelopmental delay
  - Characteristic facies
  - Specific health concerns: congenital heart disease, higher risk of haematological malignancy, hearing and visual problems



- Patau's Syndrome
  - 11% survival to 1 year of age
  - Multiple congenital abnormalities: holoprosencephaly, microcephaly,facial abnormalities meningomyelocele, polydactyly, cardiac defects, renal abnormalities, overlapping finger/thumb



- Edwards' Syndrome
  - 13% survival to 1 year of age
  - Multiple congenital abnormalities: cardiac defects, renal abnormalities, omphalocele, micrognathia, cleft lip/palate, talipes or rocker-bottom foot, clenched hands

Combined Screening for Trisomy 21/18/13

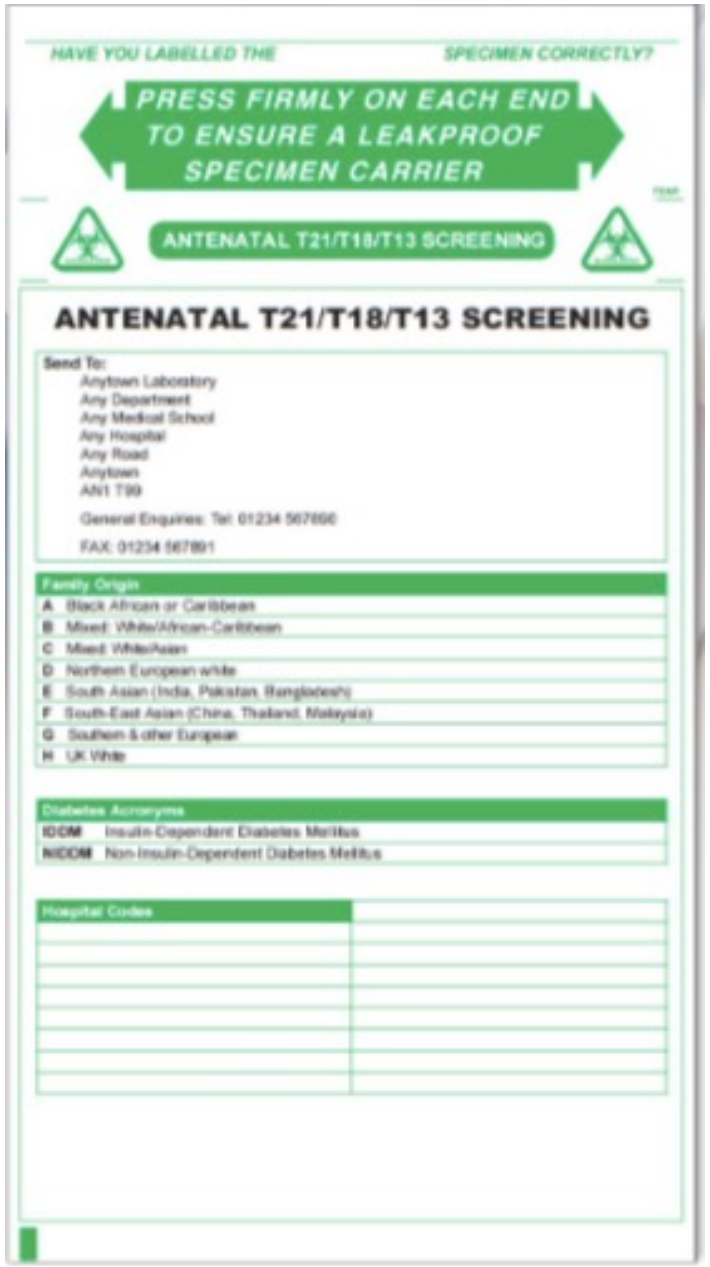
- Maternal age
- Ultrasound to measure:
  - Crown rump length (CRL) to calculate gestational age
  - Nuchal translucency (NT)
- Maternal serum screening for two biochemical markers
  - Free beta human chorionic gonadotrophin (hCG)
  - Pregnancy Associated Plasma Protein-A (PAPP-A)

Combined Screening for Trisomy 21/18/13

- Women can choose
  - Not to have screening
  - To have screening for Down's / Edward's / Patau's syndrome
  - To have screening from Down's syndrome only
  - To have screening for Edwards' / Patau's syndrome only

Combined Screening Models

- Two models
  - Serum at 10 weeks with result available at time of USS scan
  - Serum at time of USS ** Current UK practice **
- Biochemical markers are affected by:
  - Maternal weight
  - Gestational age
  - Smoking status
  - Diabetic status
  - Family origin
  - Singleton / twin pregnancies
  - Second sac with non-viable fetus (vanishing twin)



Nuchal Translucency (NT)

- Increased NT is associated with an increased chance of Trisomy 21/13/18 and may also be associated with fetal cardiac abnormalities
- NT is measured when fetal CRL is between 45 and 85mm (11+2 to 14+1 weeks of pregnancy)
- Cut off for NT is 3.0mm
  - Above this, invasive testing is offered and additional fetal echocardiography at 16 weeks

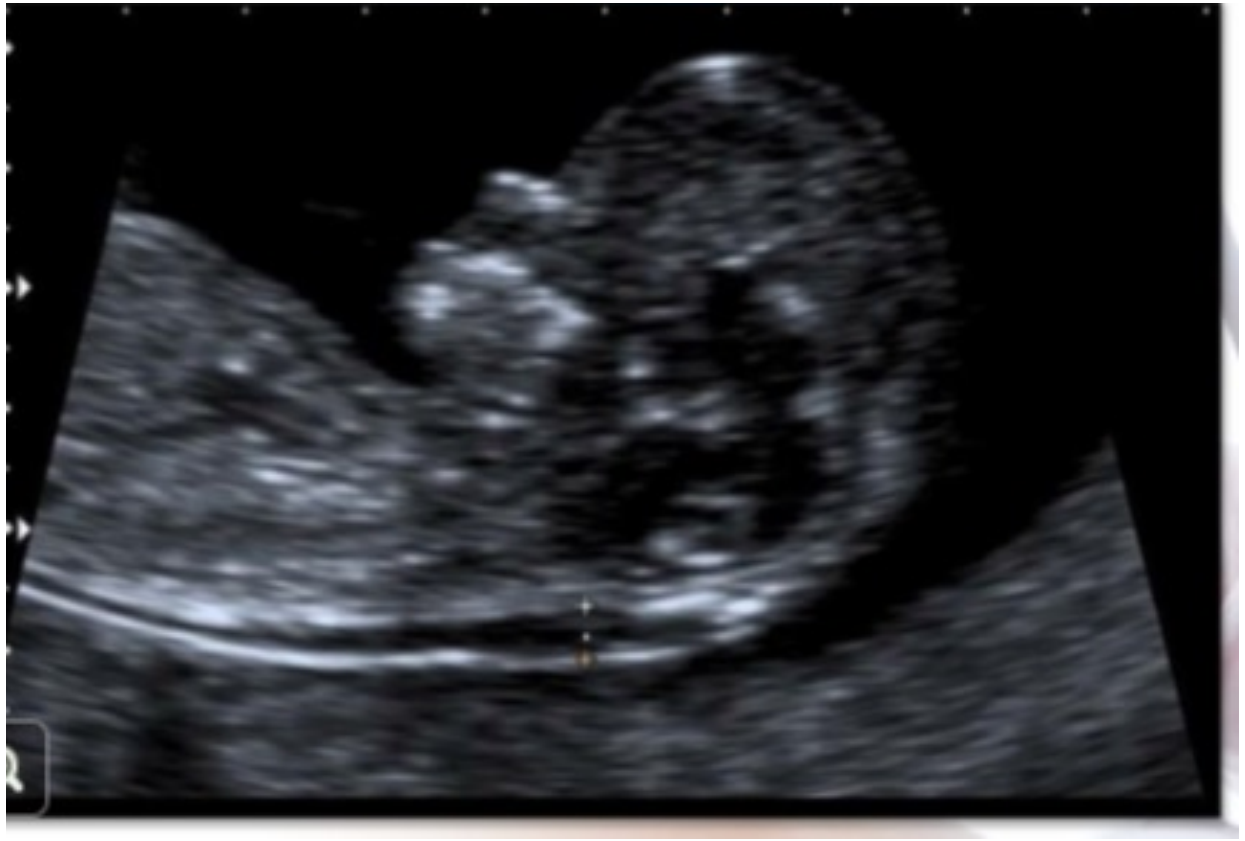


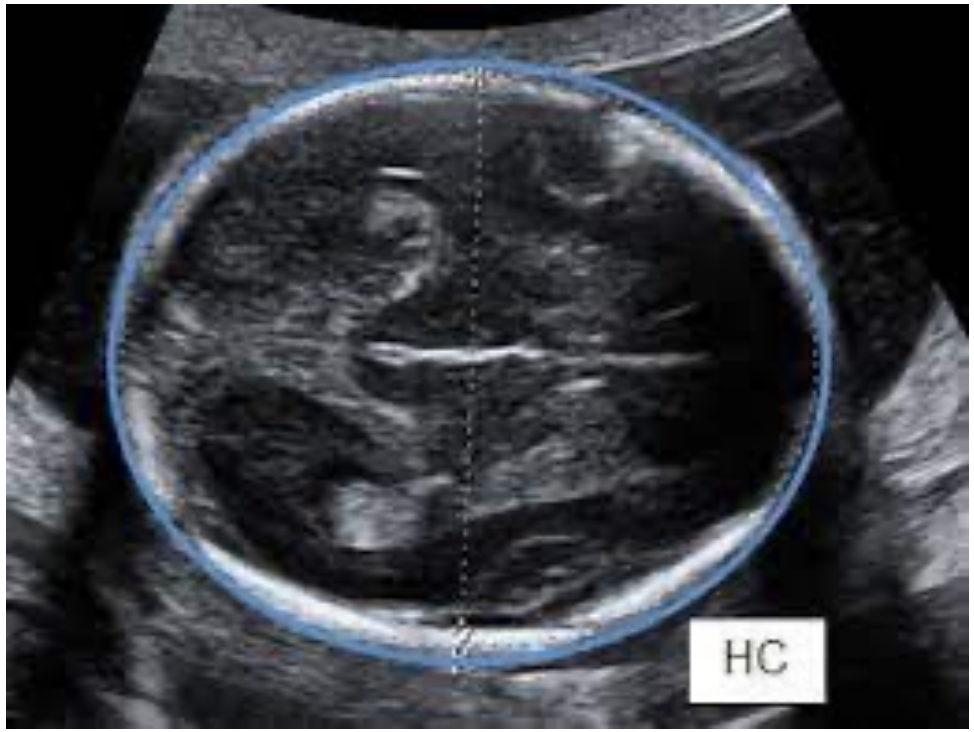
Table 8.1 Relation between Nuchal Translucency Thickness and Prevalence of Chromosomal Defects, Miscarriage or Fetal Death, and Major Fetal Abnormalities

Nuchal Translucency	Chromosomal Defects (%)	Fetal Death (%)	Major Fetal Abnormalities (%)	Alive and Well[a] (%)
<95th centile	0.2	1.3	1.6	97
95th–99th centiles	3.7	1.3	2.5	93
3.5–4.4 mm	21.1	2.7	10.0	70
4.5–5.4 mm	33.3	3.4	18.5	50
5.5–6.4 mm	50.5	10.1	24.2	30
≥6.5 mm	64.5	19.0	46.2	15

[a]Estimated prevalence of delivery of a healthy baby with no major abnormalities.

Quadruple Screening

- Second trimester screening for women who book too late for first trimester screening or when an NT measurement cannot be obtained
- Head circumference (HC) is the recommended measurement for women presenting in second trimester
- Quad offered when HC between 101 and 172mm (i.e. 14+2 to 20+0 weeks gestation)
- Maternal blood test:
  - Alpha fetoprotein (AFP)
  - hCG
  - Unconjugated oestriol (UE3)
  - Inhibin A
- Lower detection and higher screen positive rate than combined test



Second trimester screening for Edwards / Patau's Syndrome

- Recommended screening strategy: anomaly scan between 18+0 and 23+0 weeks gestation
- Rationale: fetuses affected by T13/18 will usually have specific features visible on ultrasound that will allow antenatal detection

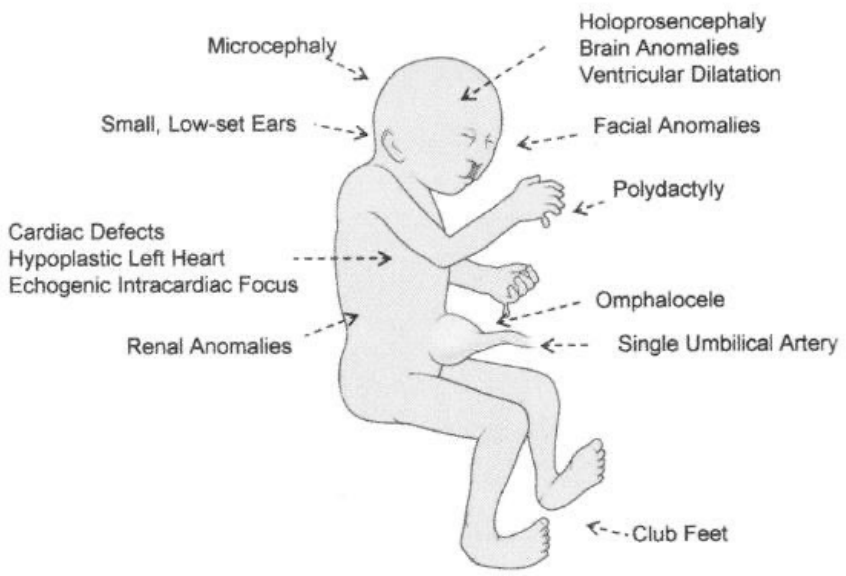


FIGURE 30-15 Common feature of trisomy 13.

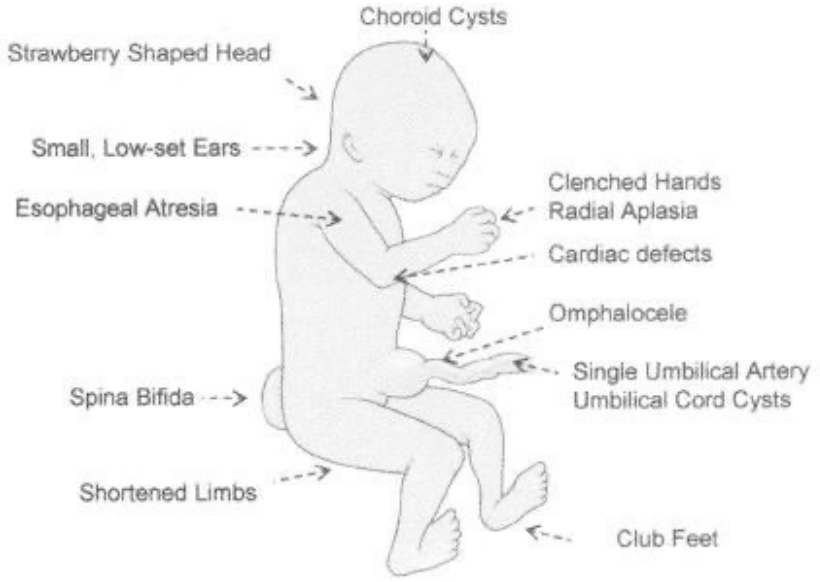


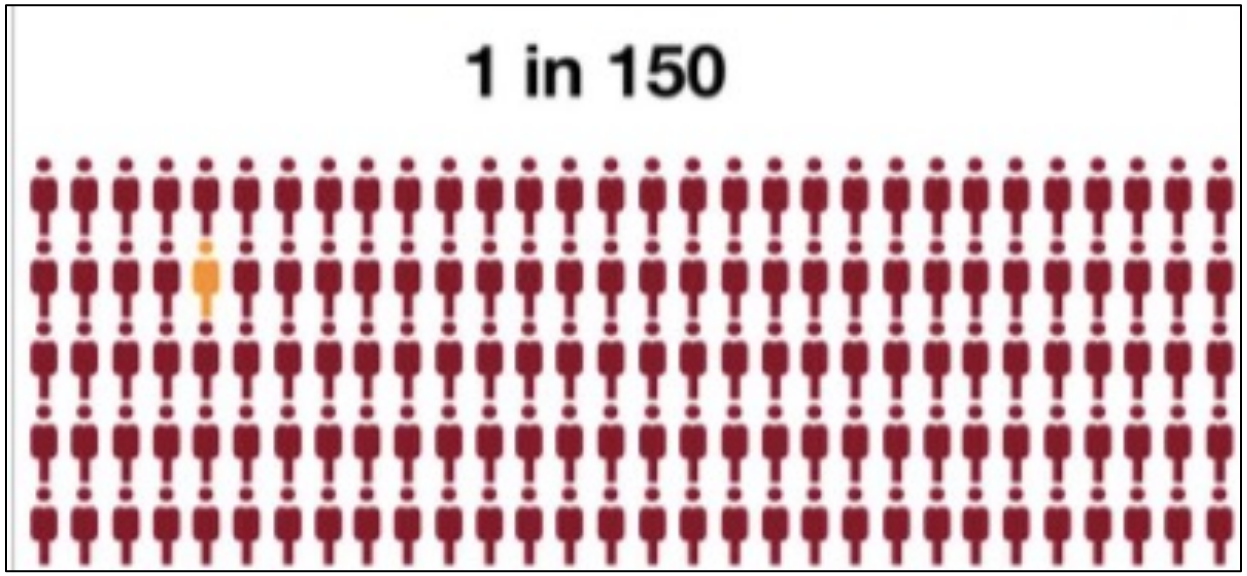
FIGURE 30-9 Common feature of trisomy 18.

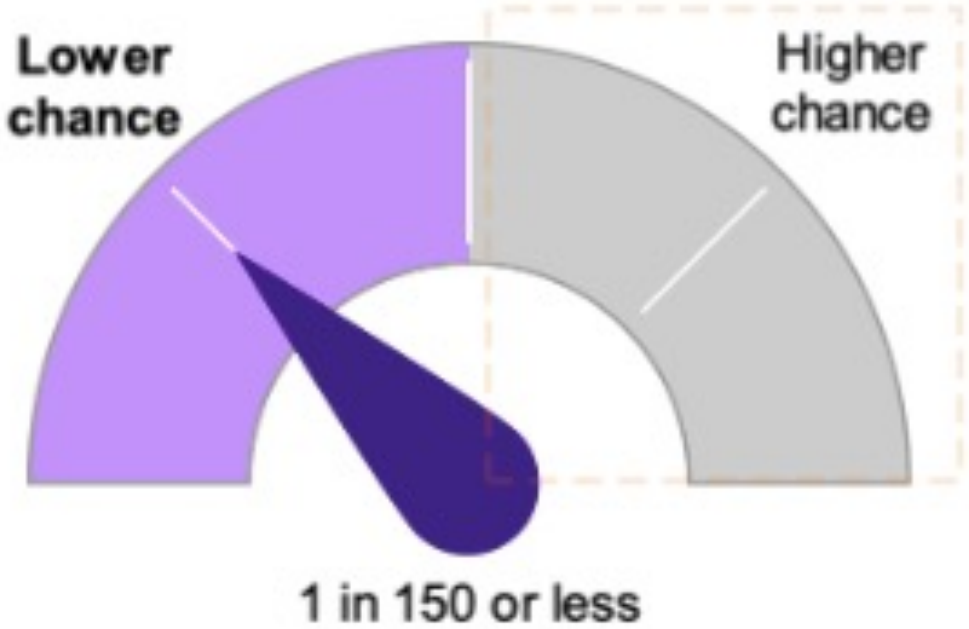
Screening in Twin Pregnancies

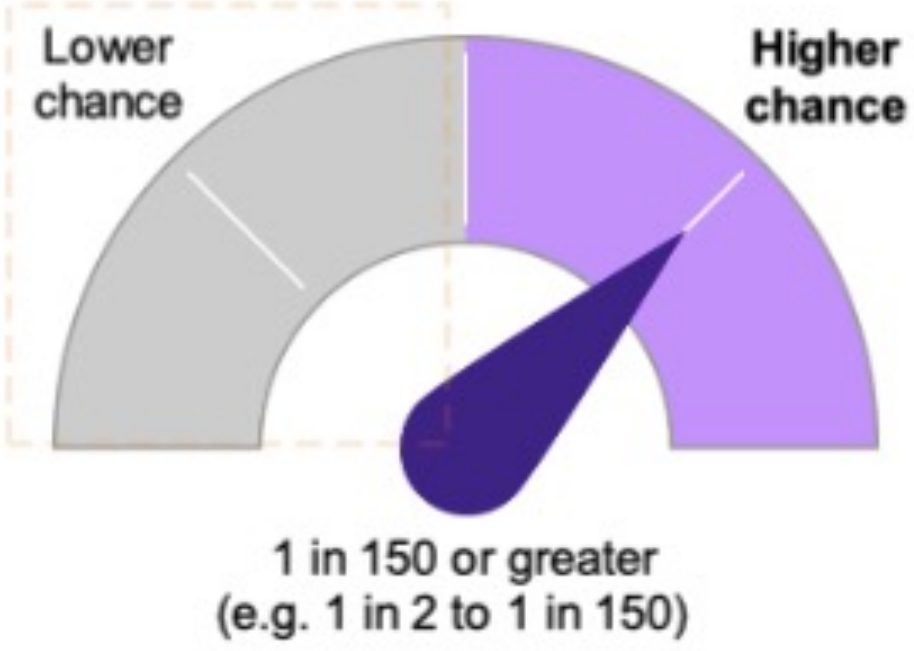
- First choice: CST for all twin pregnancies
  - DC twins: reported as chance per twin, higher chance of T21 than singleton but performance poorer as biochemical markers less discriminatory (40-50% detection for screen positive rate of 3%)
  - MC twins: reported as single chance, similar performance to singleton (80% detection for screen positive rate of 3%), lower chance of T21 as higher miscarriage rate
- Second trimester: quad test but less sensitive and delays decisions on PND and selective TOP to later gestation

Chance Cut Off

- NHS FASP defines the national cut-off
  - Currently set at 1 in 150 at term for both first and second trimester screening tests





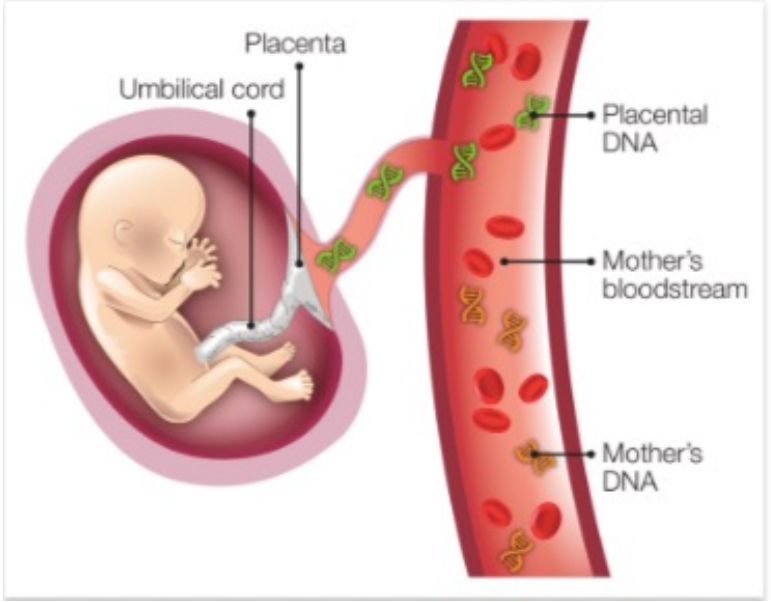


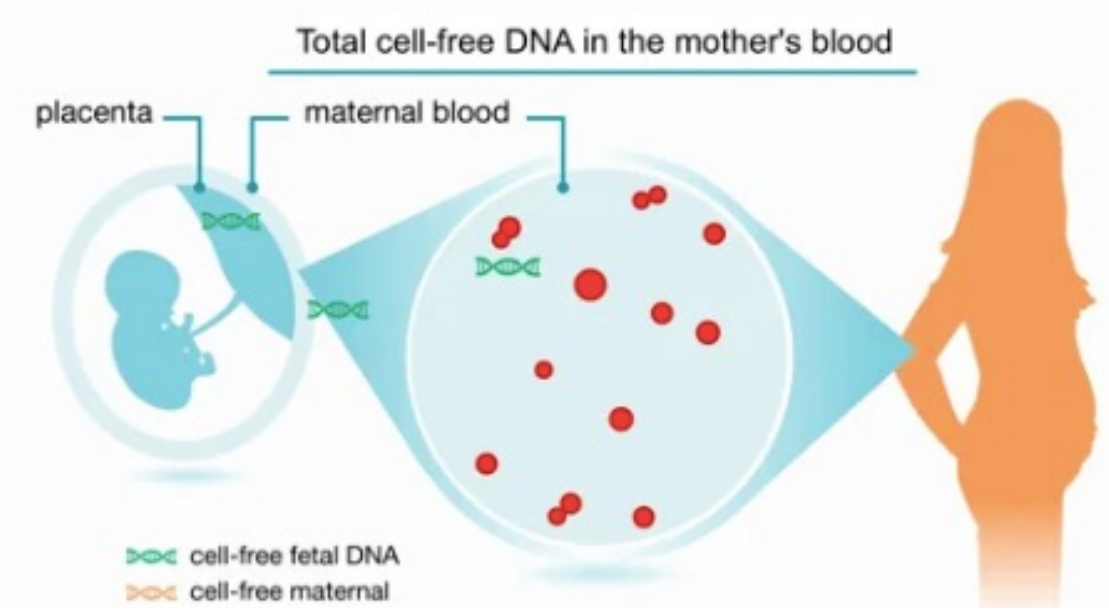
Chance Cut Off

- If higher chance results, options are:
  - No further testing
  - Non Invasive Prenatal Testing (NIPT)
  - Prenatal Diagnosis (PND)
- Regardless of previous screening test choices, can have testing for:
  - All three conditions (T13/18/21)
  - T21 only
  - T13/18 only

What is NIPT?

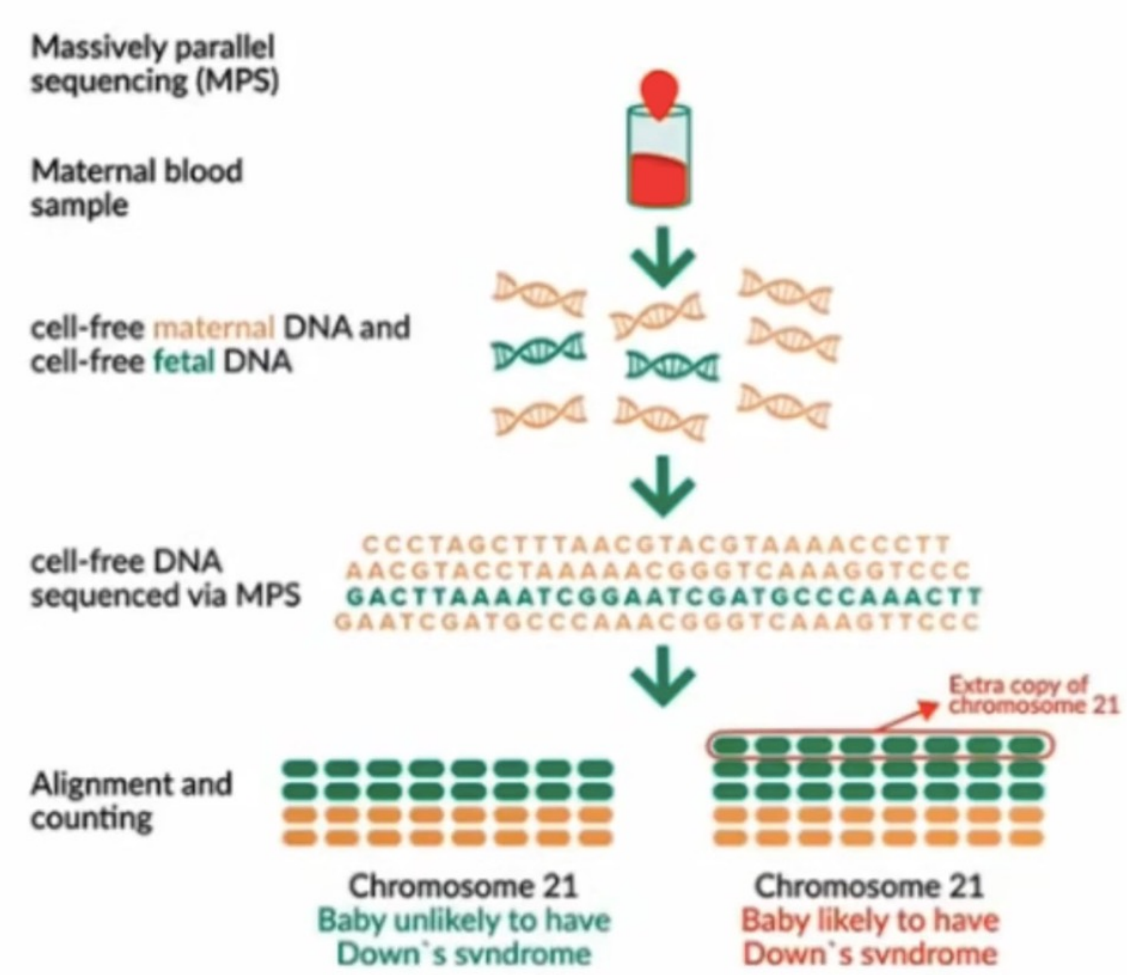
- NIPT is a screening test that assesses whether the fetus has a higher chance of T13/18/21
- Maternal blood contains maternal and placental DNA – cell free fetal DNA (cfDNA) – which increase with gestation and is pregnancy specific





How NIPT works

- Two main NIPT technologies:
  - Next generation sequency (NGS)
  - Micro-array



NIPT Performance

- Screening test – therefore can be false positive and false negative results but most NIPT will confirm lower chance result
- NIPT less accurate in twin pregnancies
- >90% higher chance NIPT for T21 -> affected baby – i.e. 1 in 10 is wrong
- >80% higher chance NIPT for T13/18 -> affected baby – i.e. 1 in 5 is wrong
- False negative NIPT results happen more often in women with very high chance result from CST or quad (e.g. between 1 in 2 and 1 in 10) and this is more common with T13/18

NIPT is not suitable for women with…

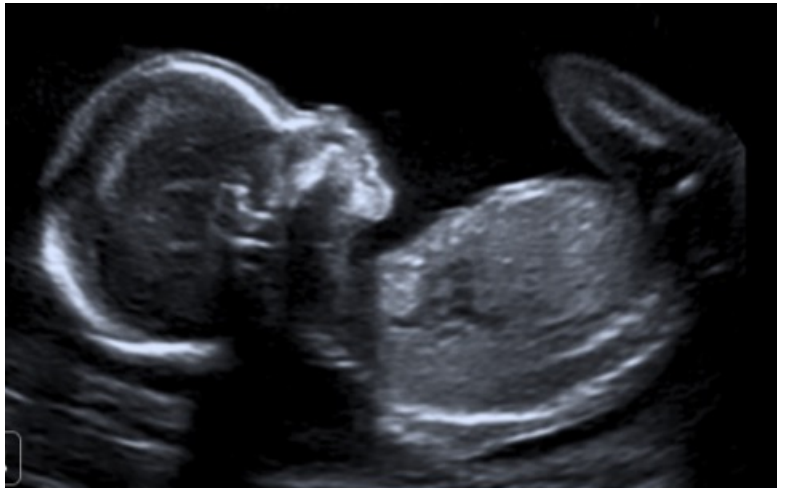
- Triplet or higher order multiple pregnancies
- Current cancer
- Blood transfusion in previous 4 months
- Bone marrow or organ transplants
- Previous stem cell therapy
- Current immunotherapy
- Vanished twin pregnancy (empty sac or sac with non-viable fetus)
- Maternal T21 or balanced translocation or mosaicism of T13/18/21

Non invasive prenatal testing (NIPT)

- Routine fetal grouping in all Rh negative women
- Molecular diagnosis of fetal skeletal dysplasias, craniosynostoses and cystic fibrosis
- Commercially available for aneuploidy screening

Anomaly screening scan

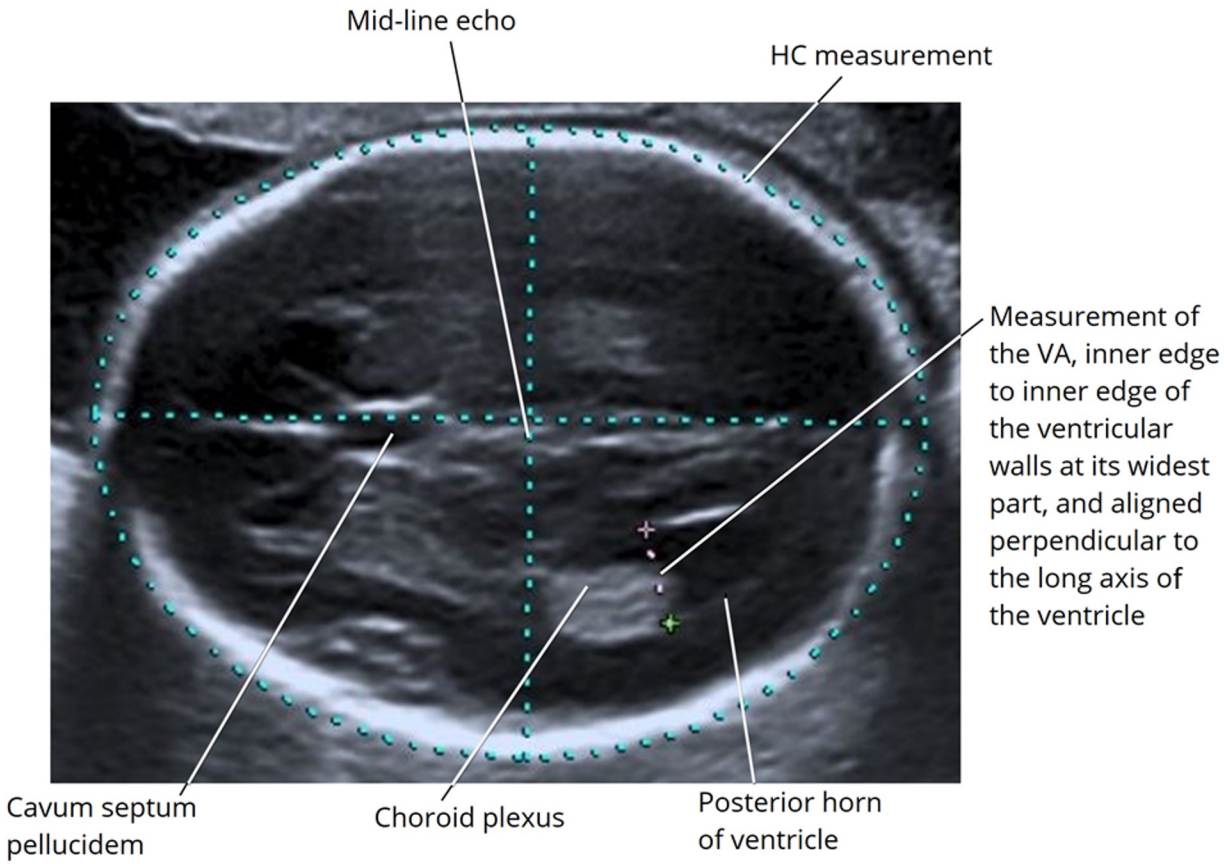
- Routinely between 18+0 and 20+6 weeks gestation, occasionally up to 23+0
- NHS Fetal Anomaly Screening Programme (FASP) requirements
- Screens for 11 major conditions with detection rates of >50%

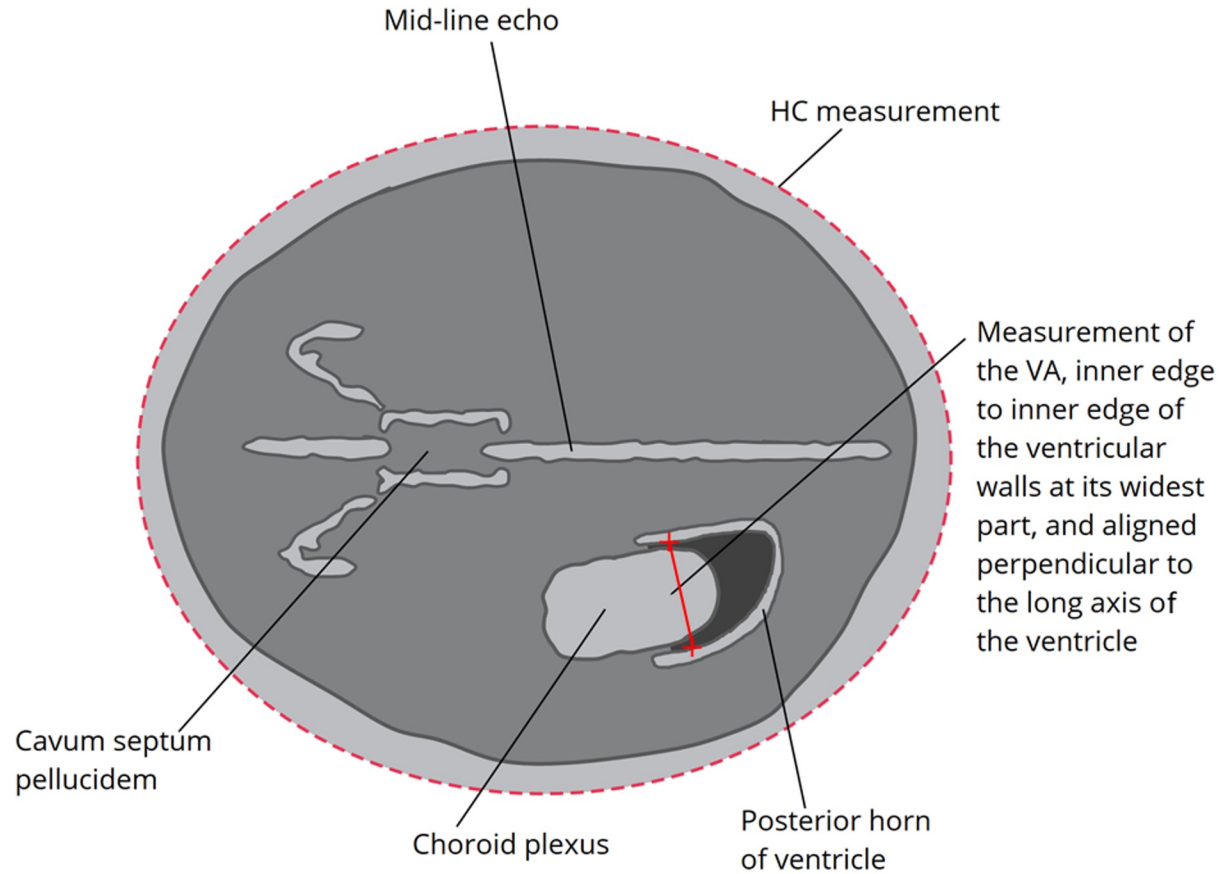


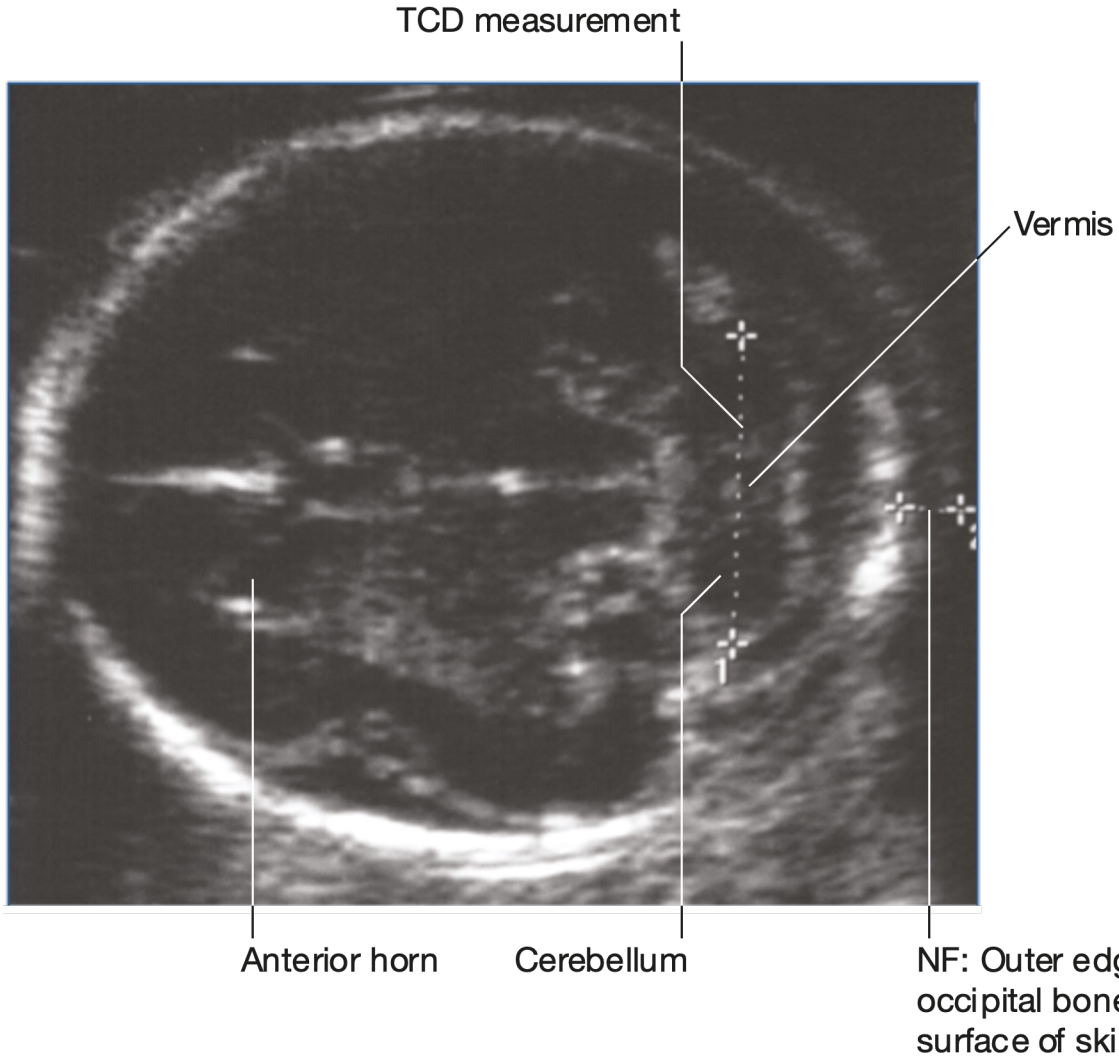
Condition	Detection rate %
Anencephaly	98
Open spina bifida	90
Cleft lip	75
Diaphragmatic hernia	60
Gastroschisis	98
Exomphalos	80
Serious cardiac anomalies	50
Bilateral renal agenesis	84
Lethal skeletal dysplasia	60
Edwards' syndrome (Trisomy 18)	95*
Patau's syndrome (Trisomy 13)	95*

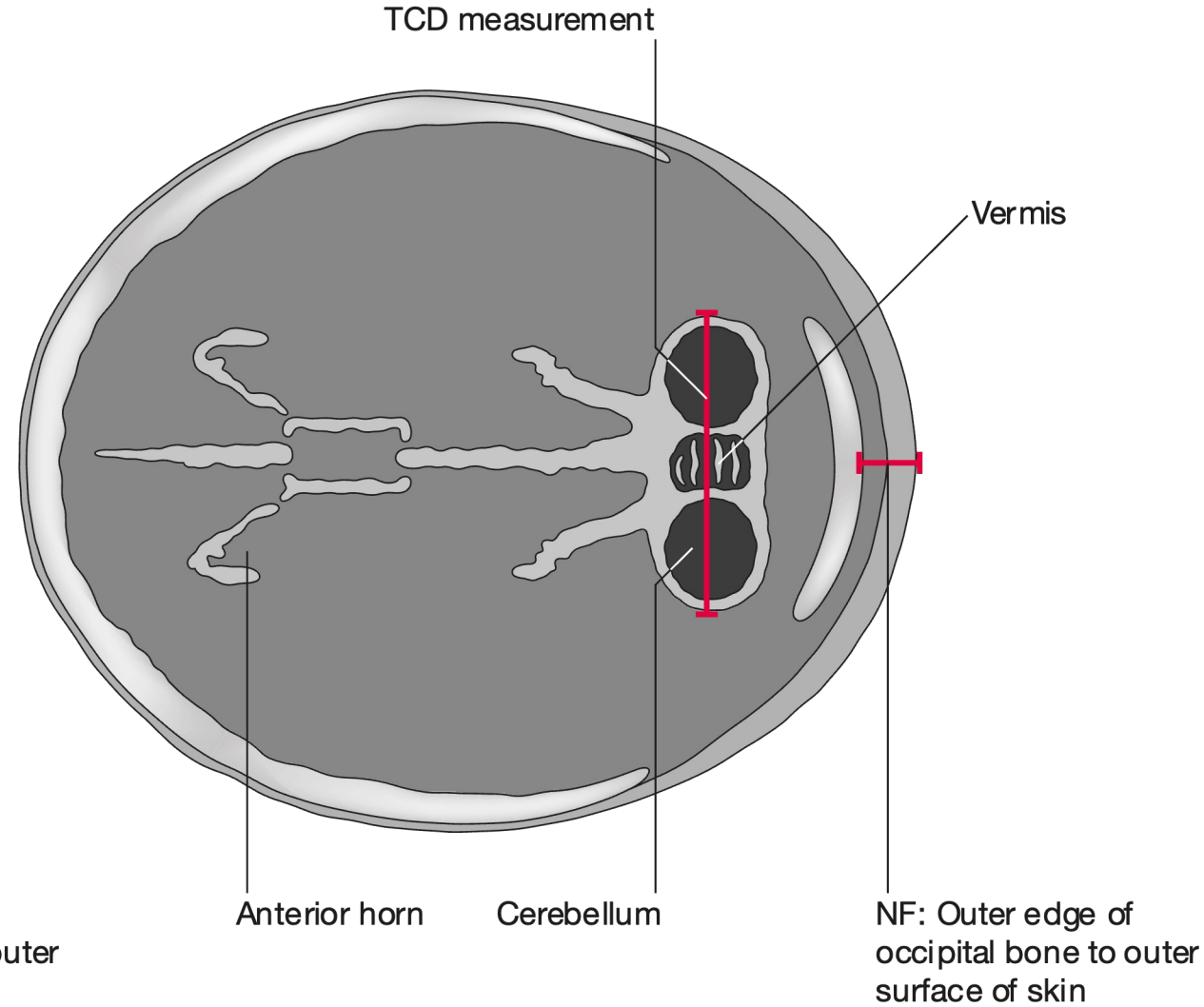
Limitations of Anomaly Scan

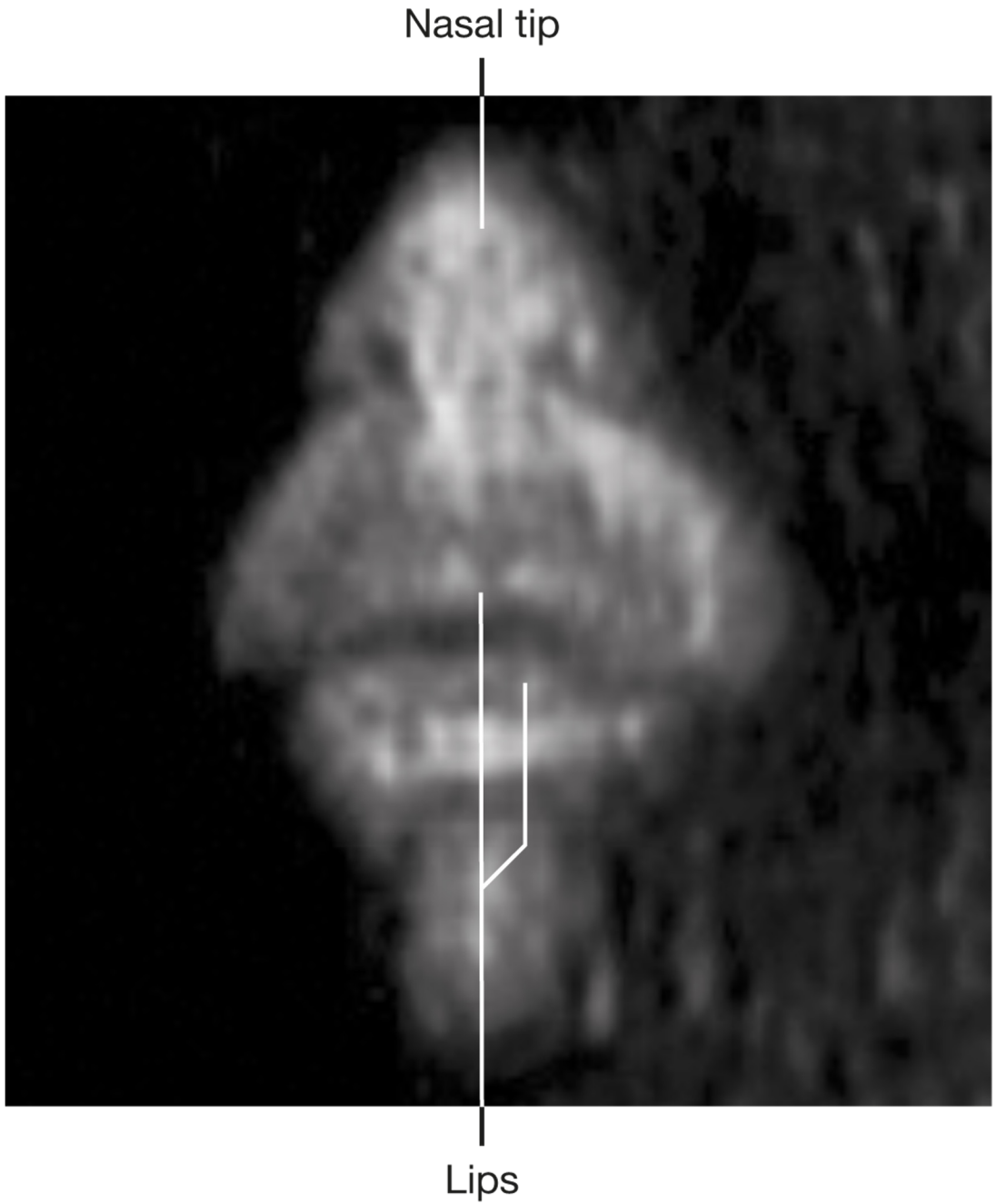
- Will not detect all conditions
- Single repeat scan offered if first examination is incomplete (e.g. due to maternal BMI, fibroids or sub-optimal fetal position) – same day or in following 2-3 weeks in practice
- If second scan incomplete, no requirement for further scanning – inform woman that screening is incomplete

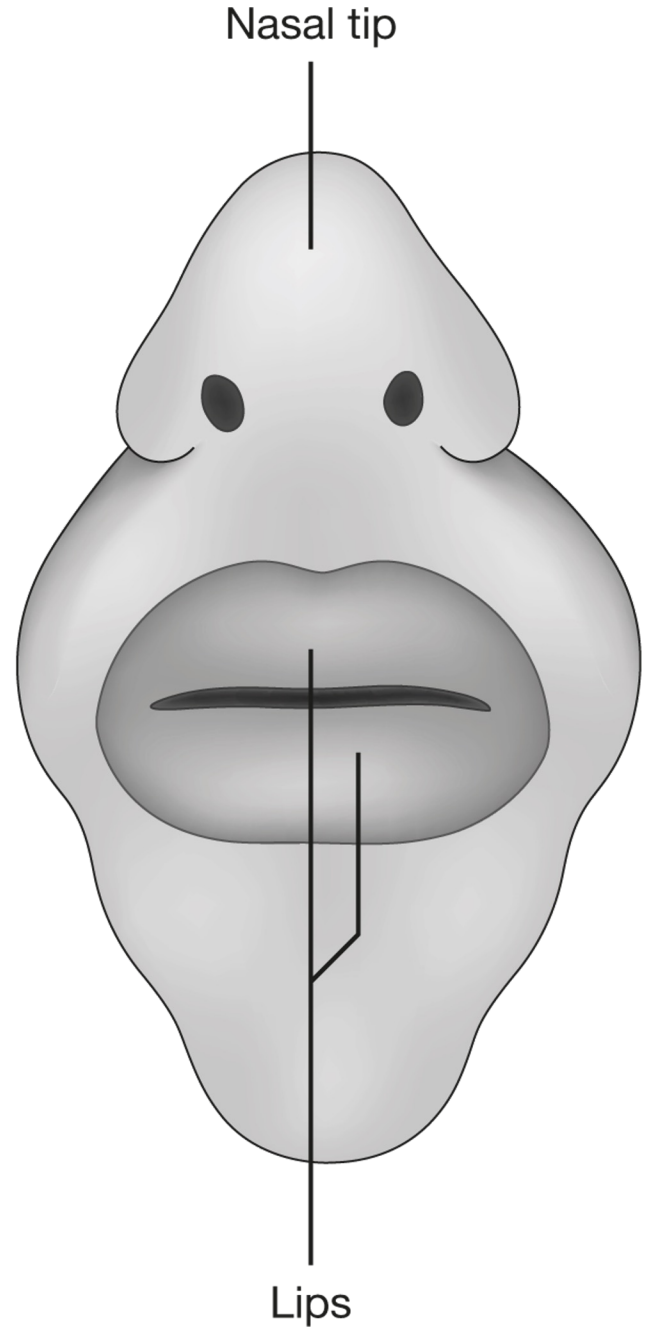

Mid-line echo
HC measurement
Measurement of the VA, inner edge to inner edge of the ventricular walls at its widest part, and aligned perpendicular to the long axis of the ventricle
Cavum septum pellucidem
Choroid plexus
Posterior horn of ventricle

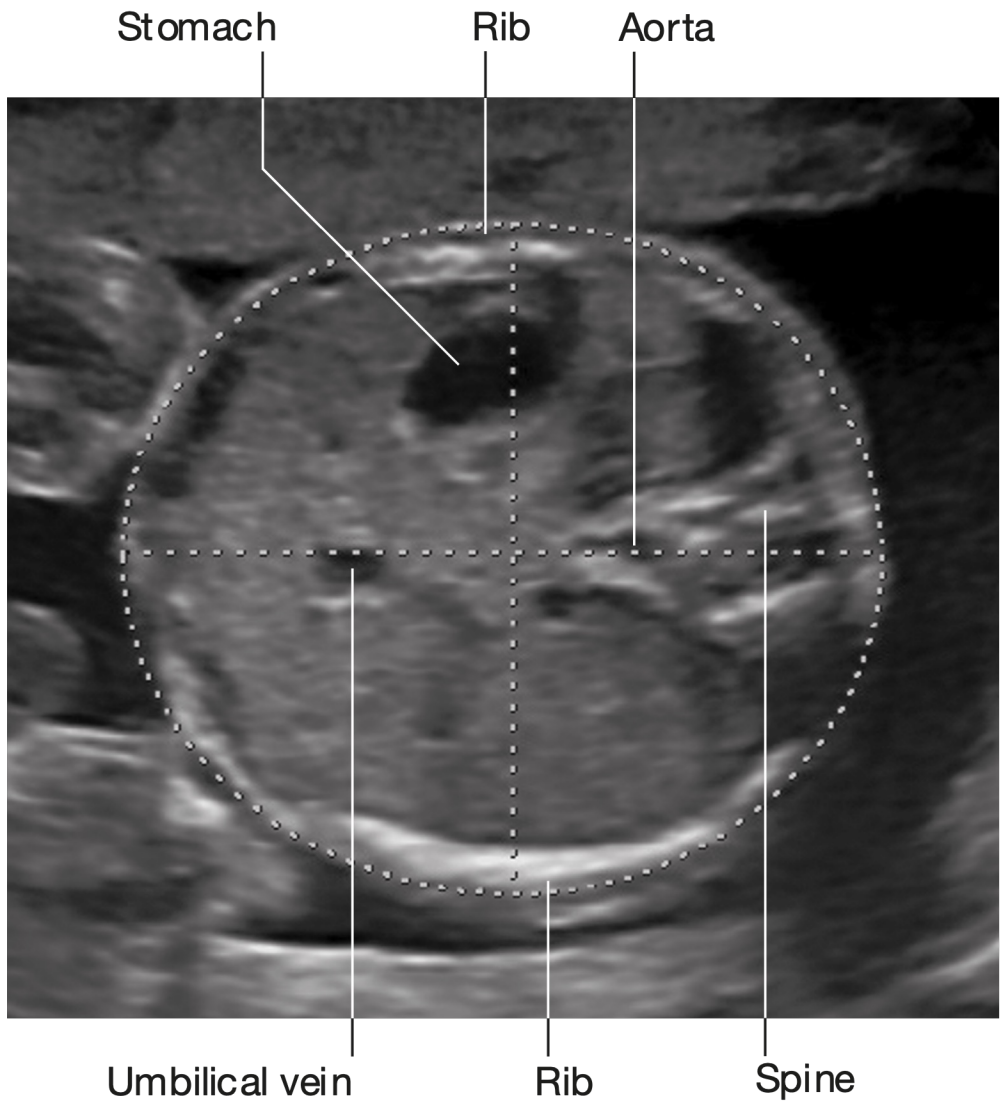

Mid-line echo
HC measurement
Measurement of the VA, inner edge to inner edge of the ventricular walls at its widest part, and aligned perpendicular to the long axis of the ventricle
Cavum septum pellucidem
Choroid plexus
Posterior horn of ventricle

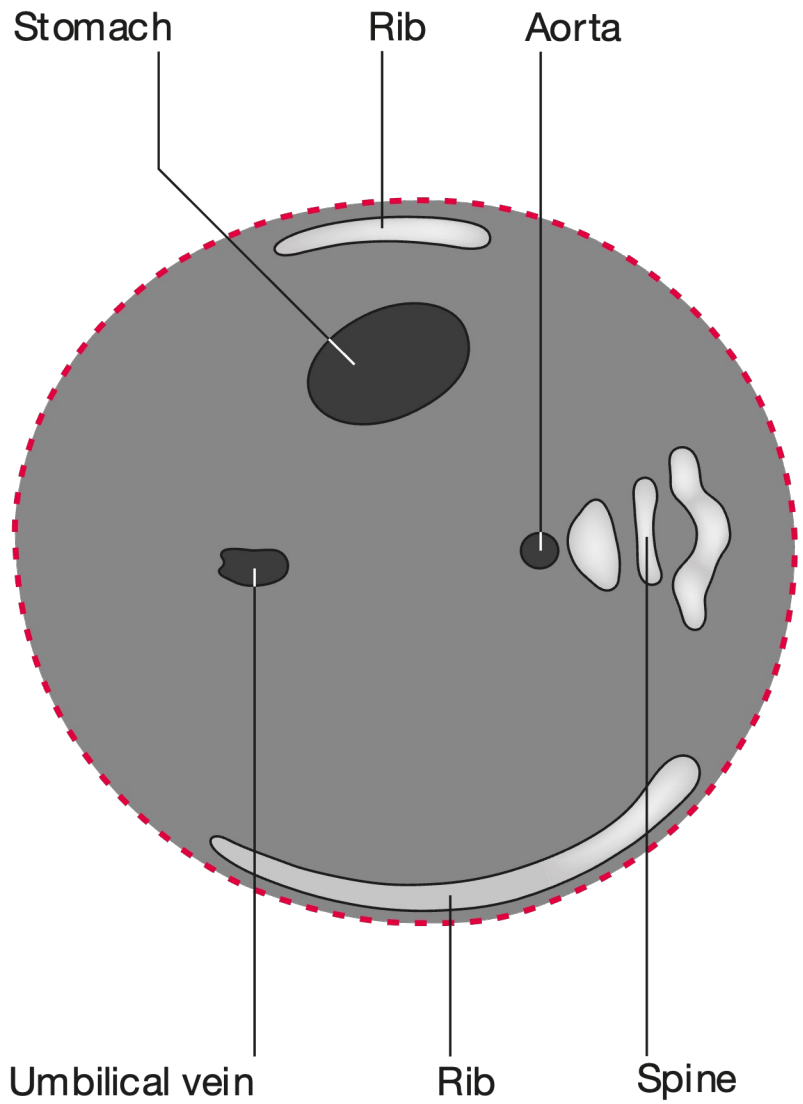

TCD measurement
Vermis
Anterior horn
Cerebellum
NF: Outer edge of occipital bone to outer surface of skin

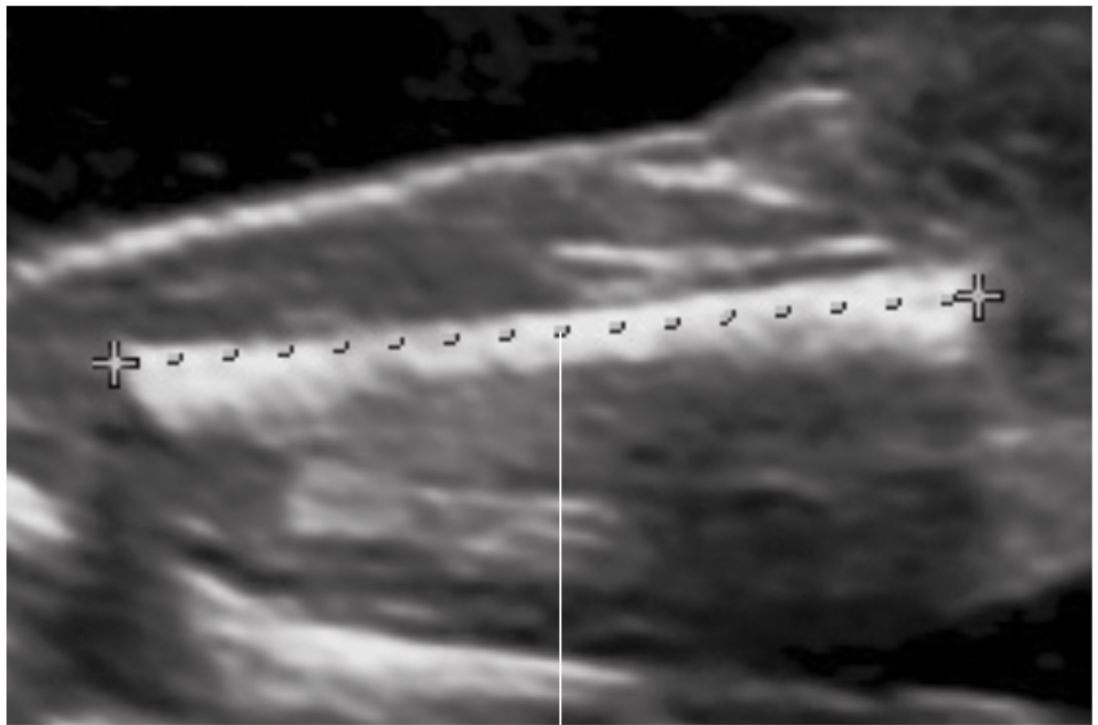

TCD measurement
Vermis
Anterior horn
Cerebellum
NF: Outer edge of occipital bone to outer surface of skin


Nasal tip
Lips

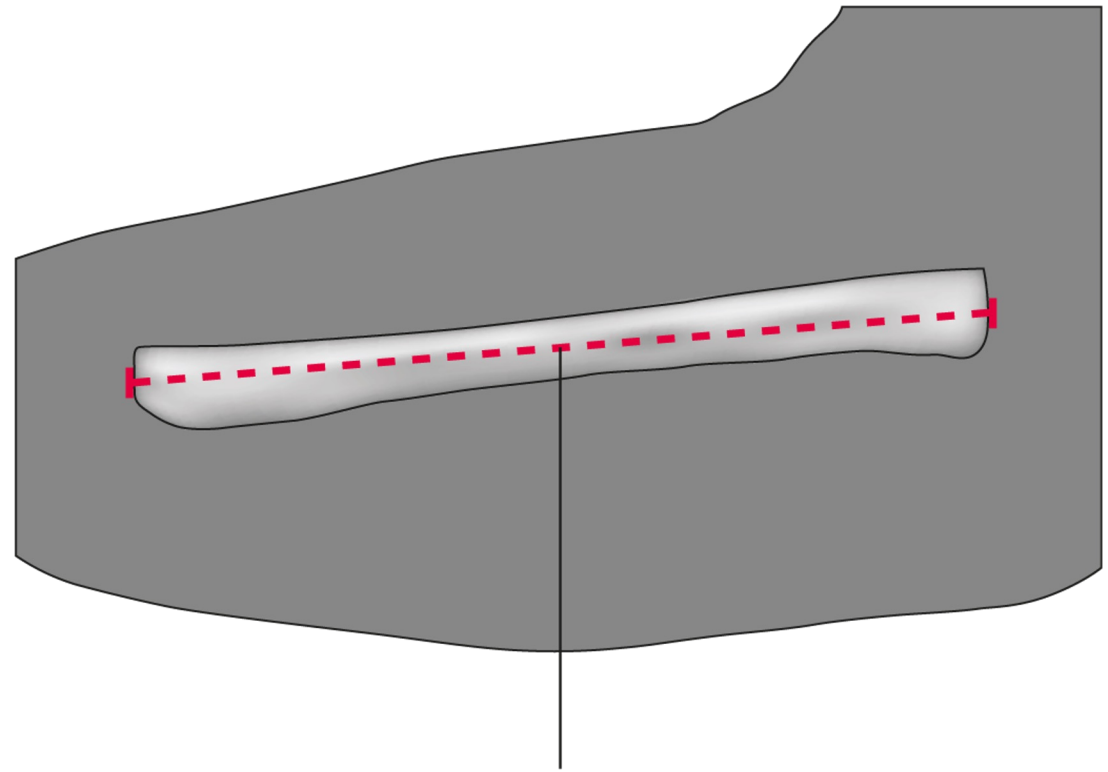

Nasal tip
Lips


Stomach
Rib
Aorta
Umbilical vein
Rib
Spine

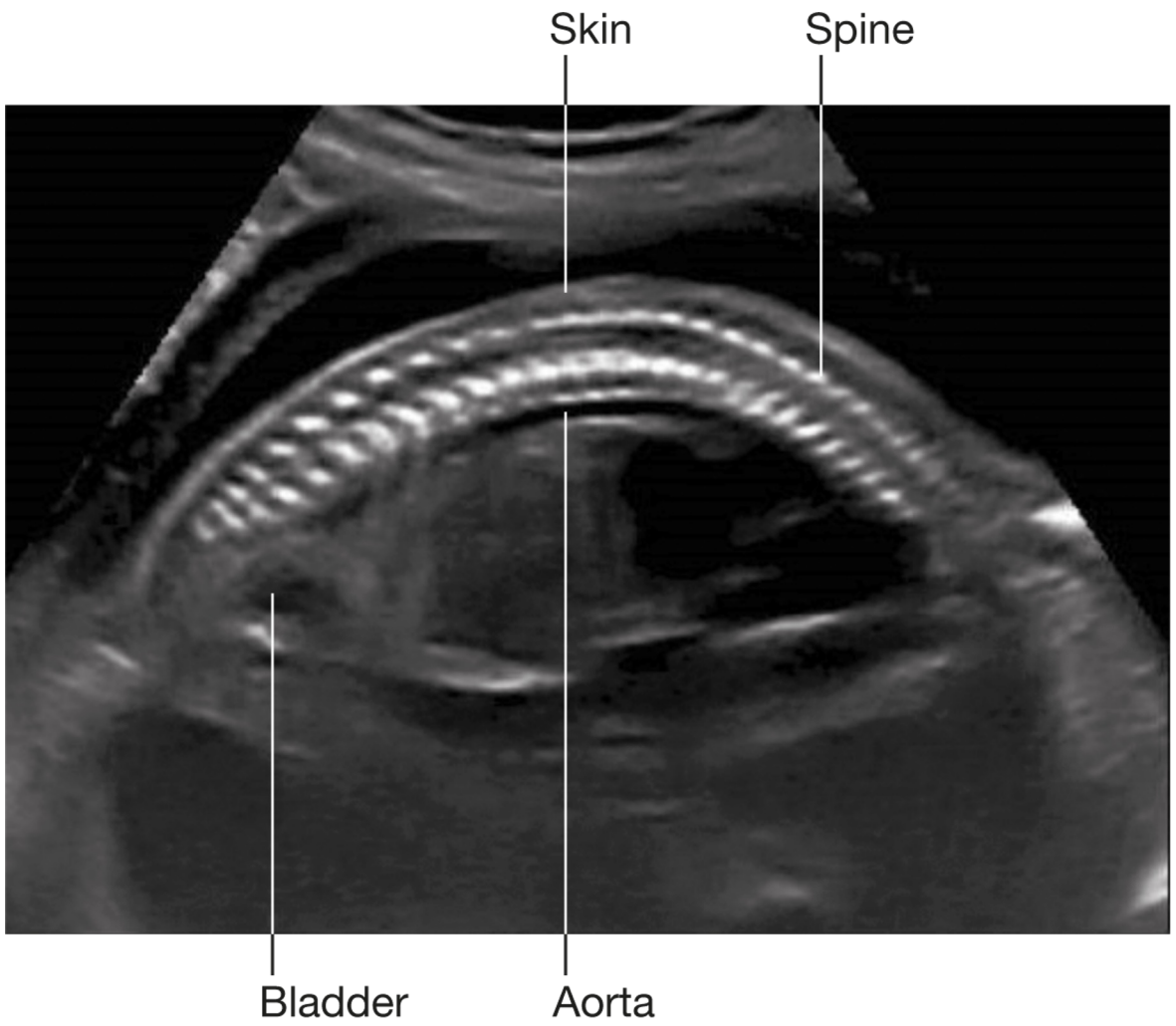

Stomach
Rib
Aorta
Umbilical vein
Rib
Spine

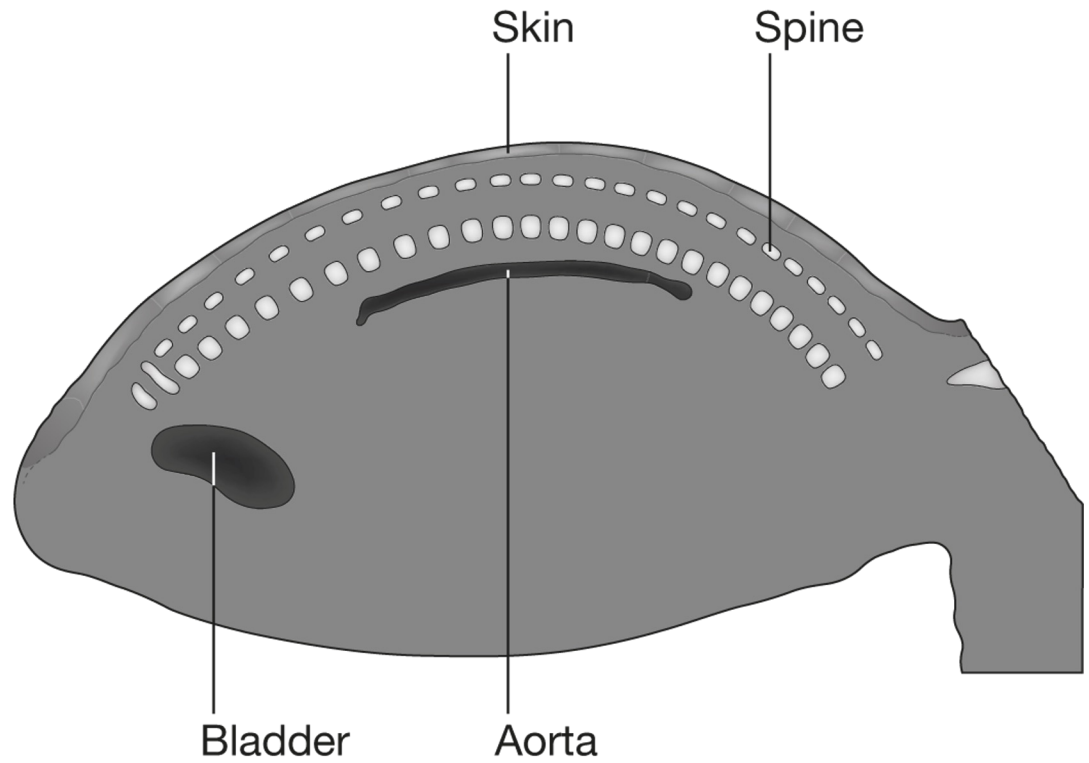


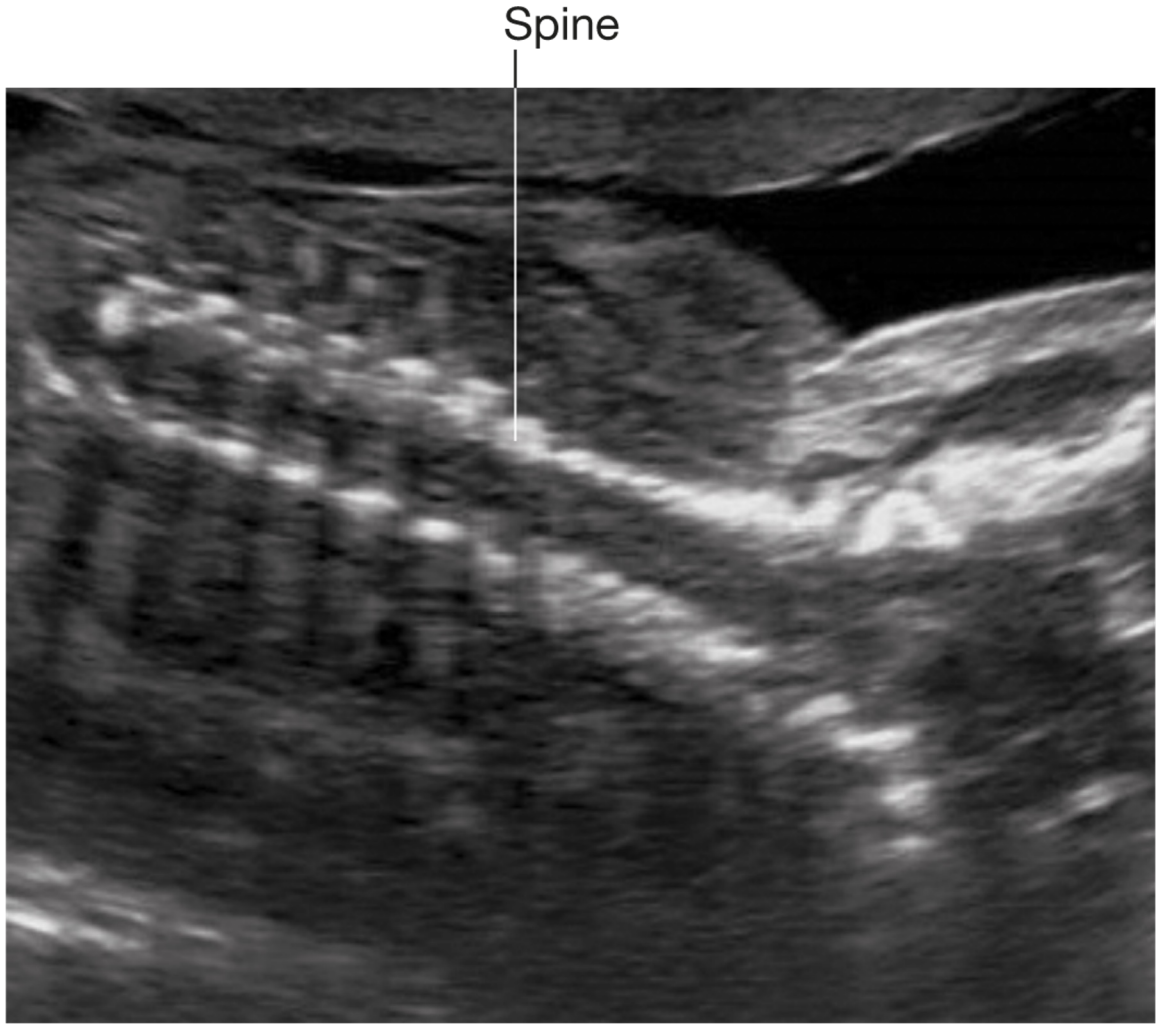
Femur length

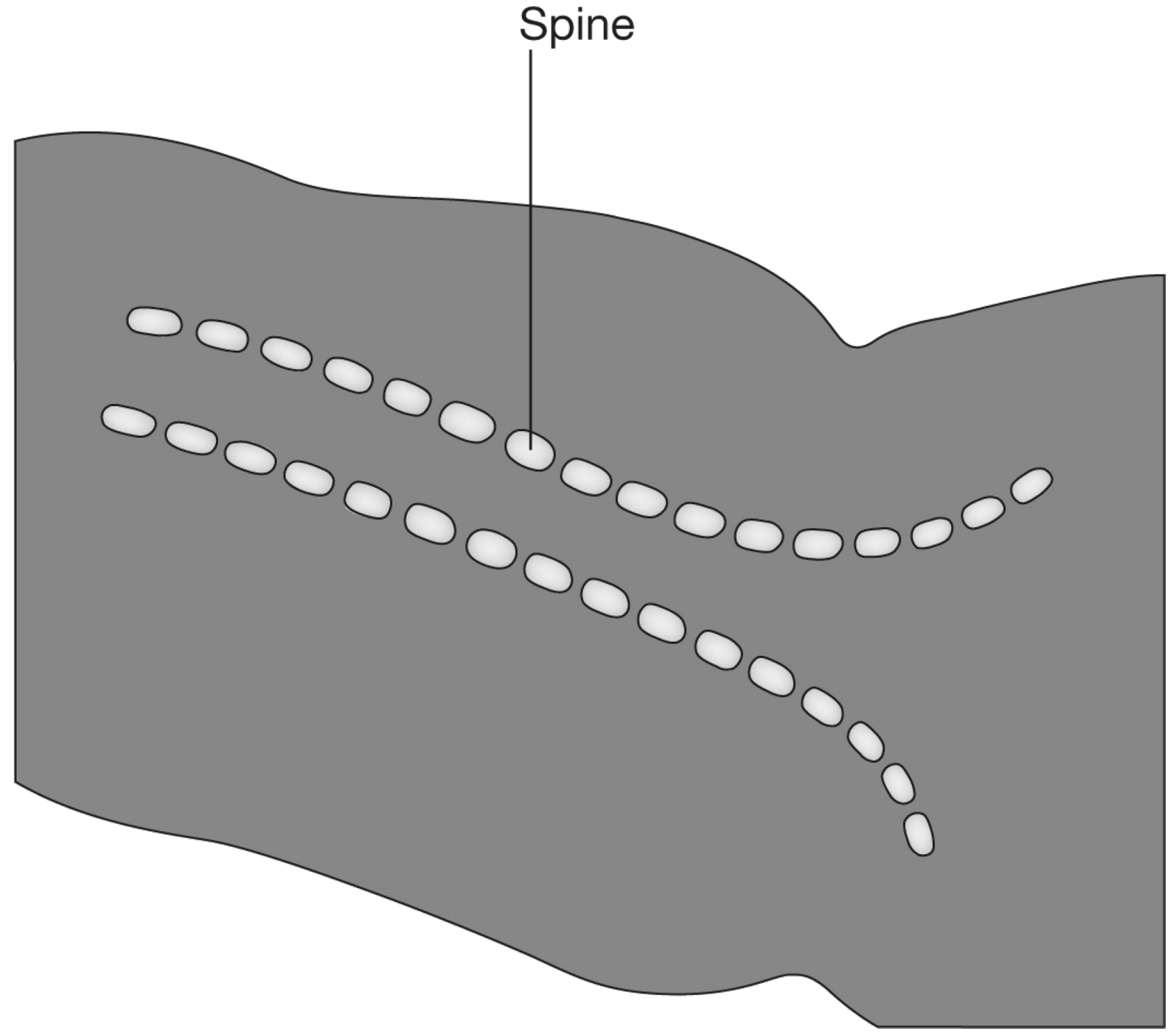


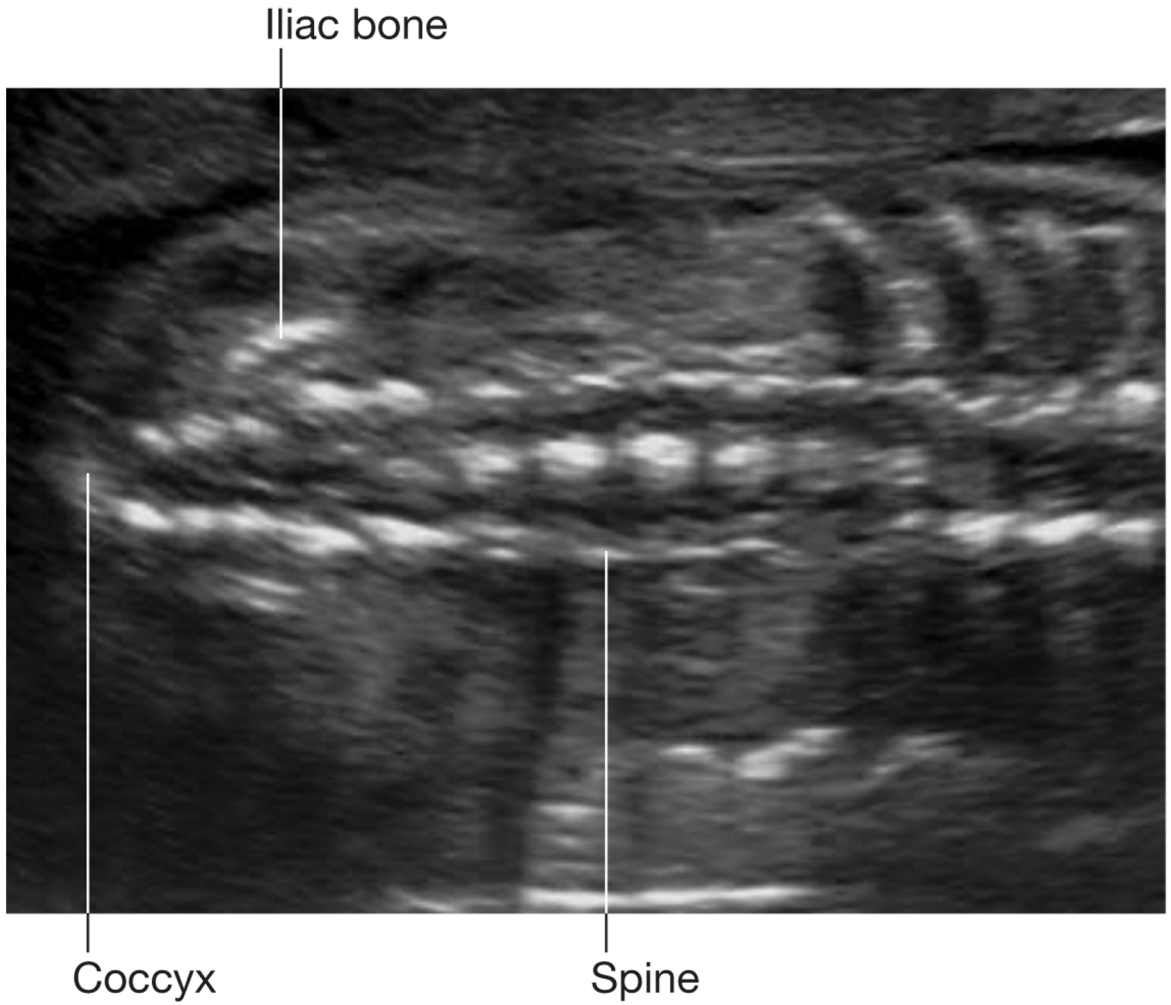
Femur length

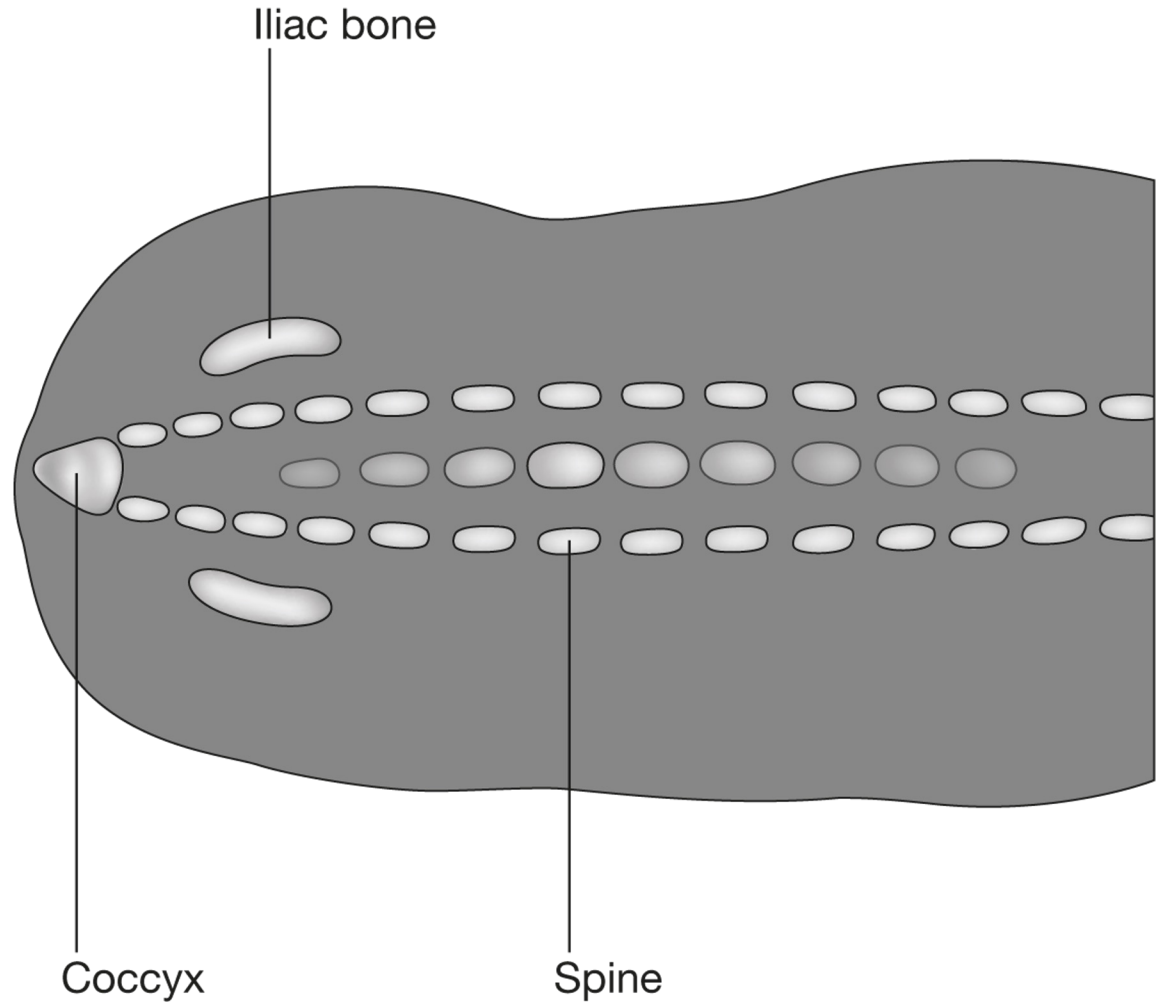

Skin
Spine
Bladder
Aorta

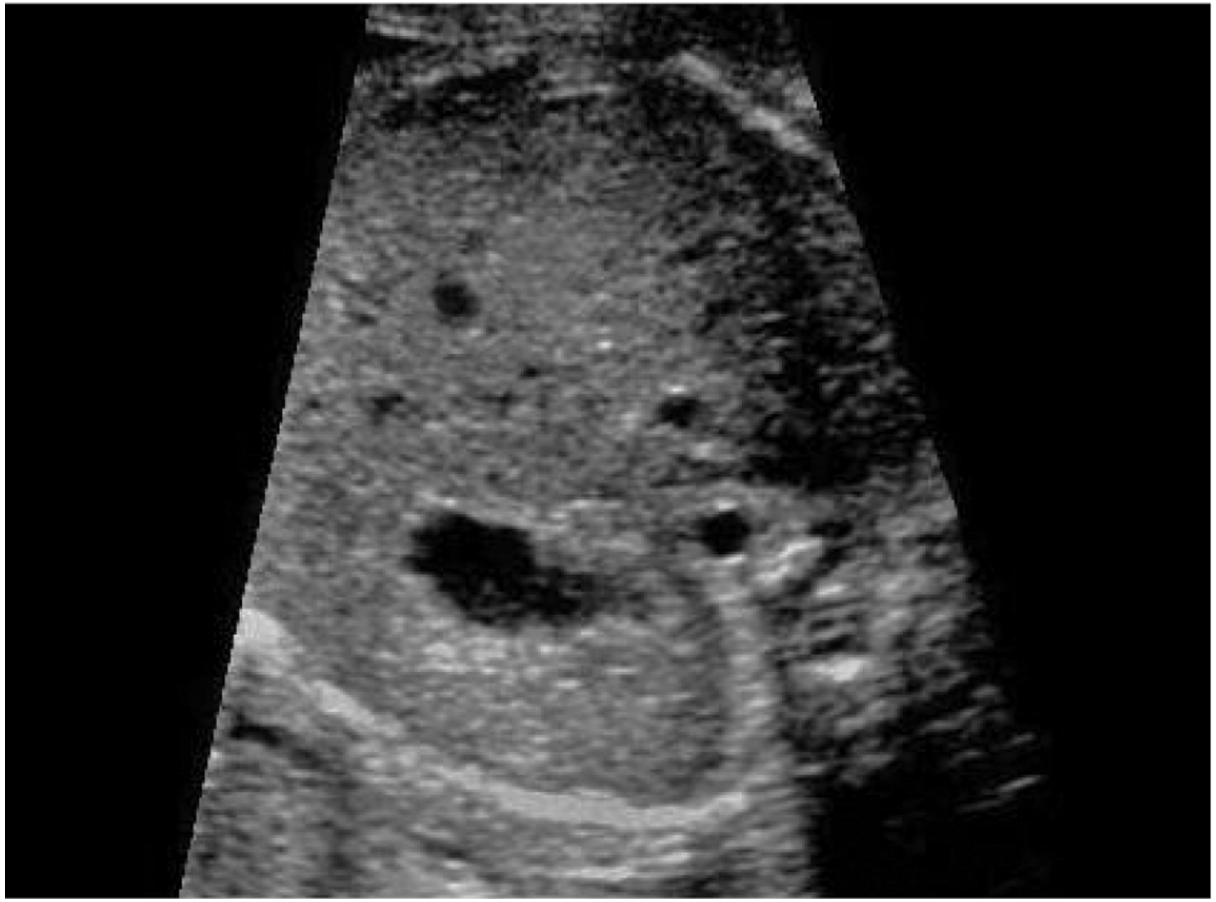

Skin
Spine
Bladder
Aorta

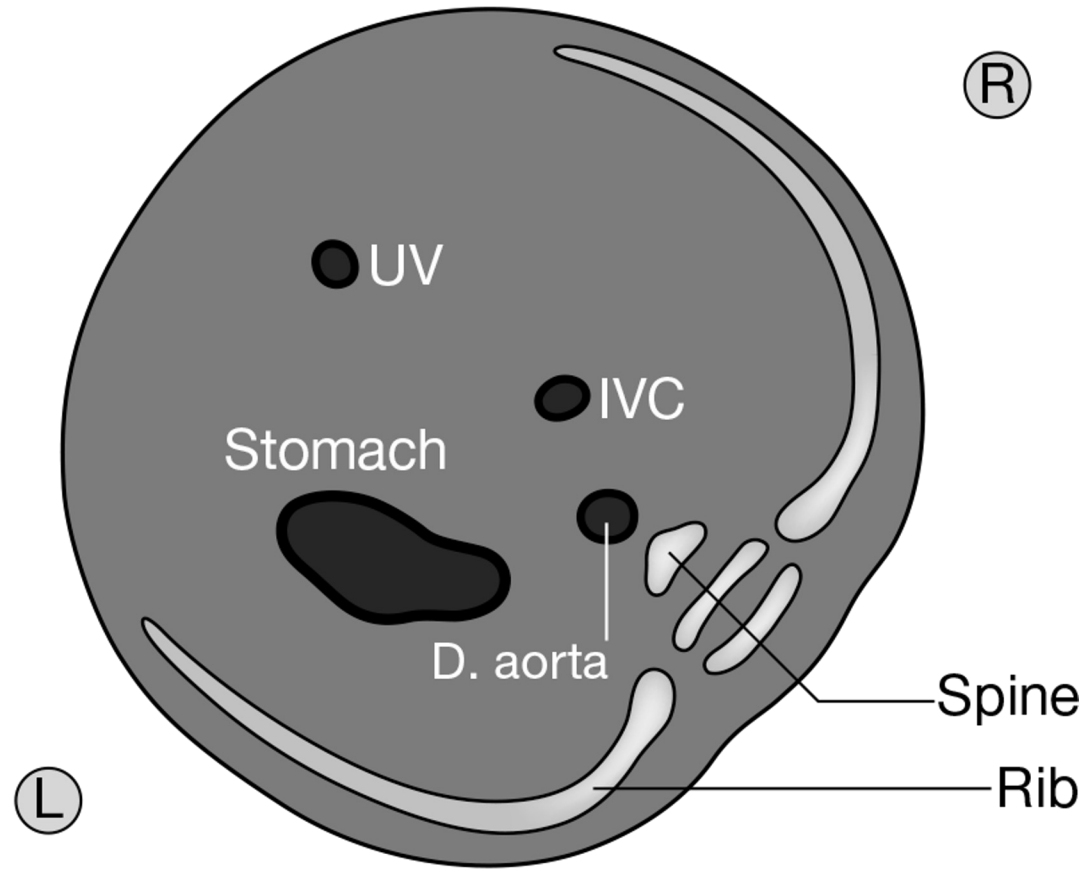

Spine

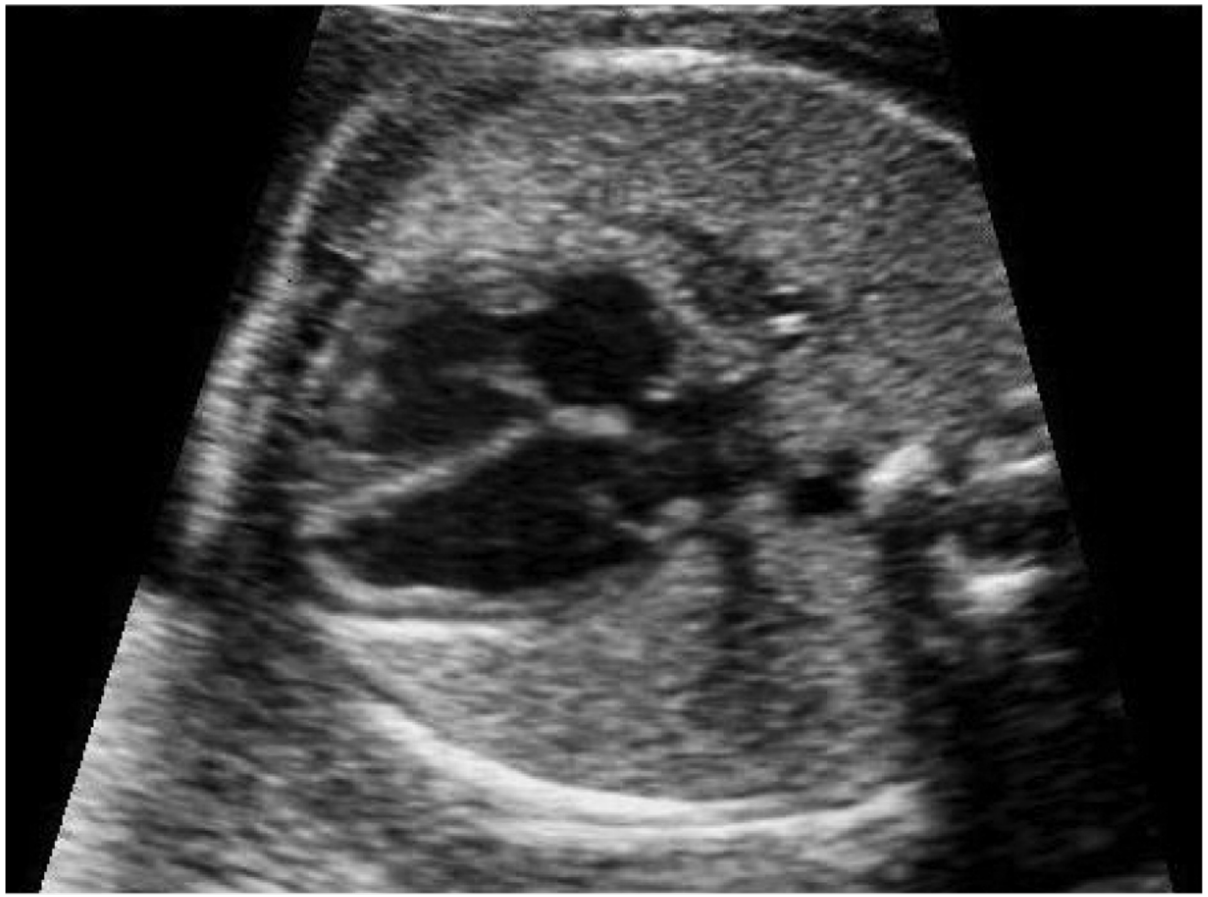

Spine

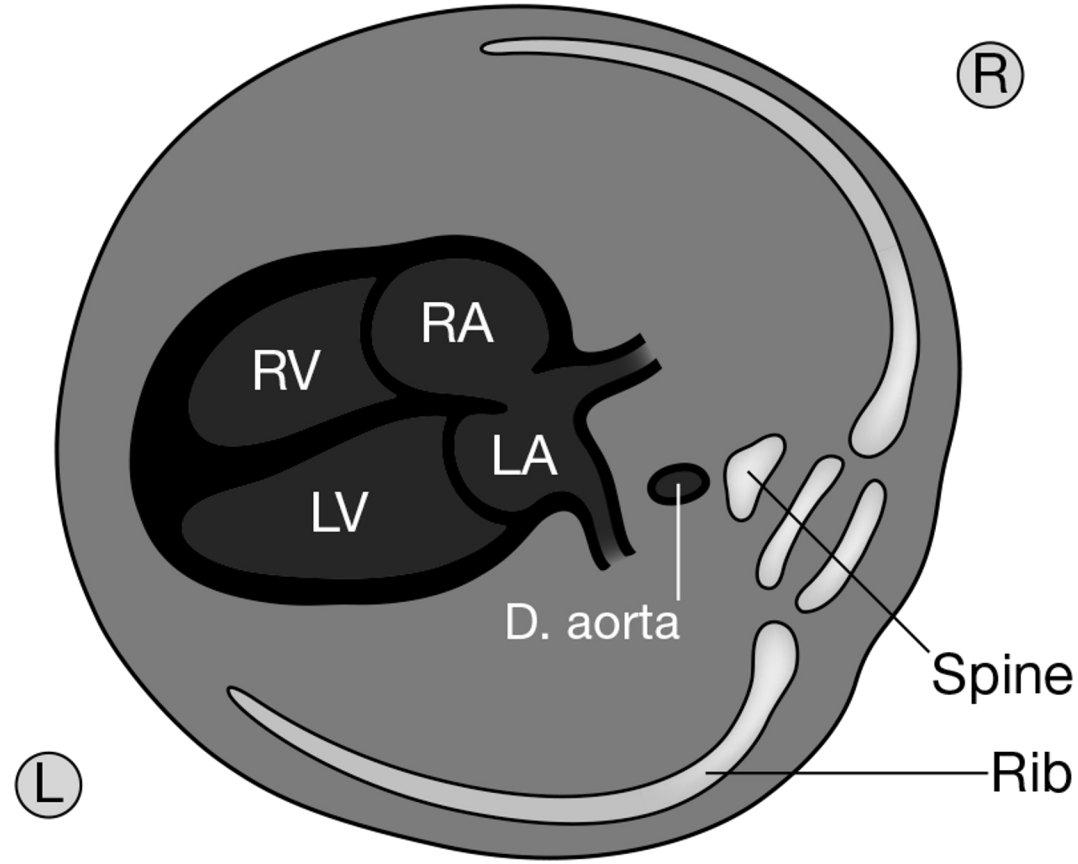

Iliac bone
Coccyx
Spine

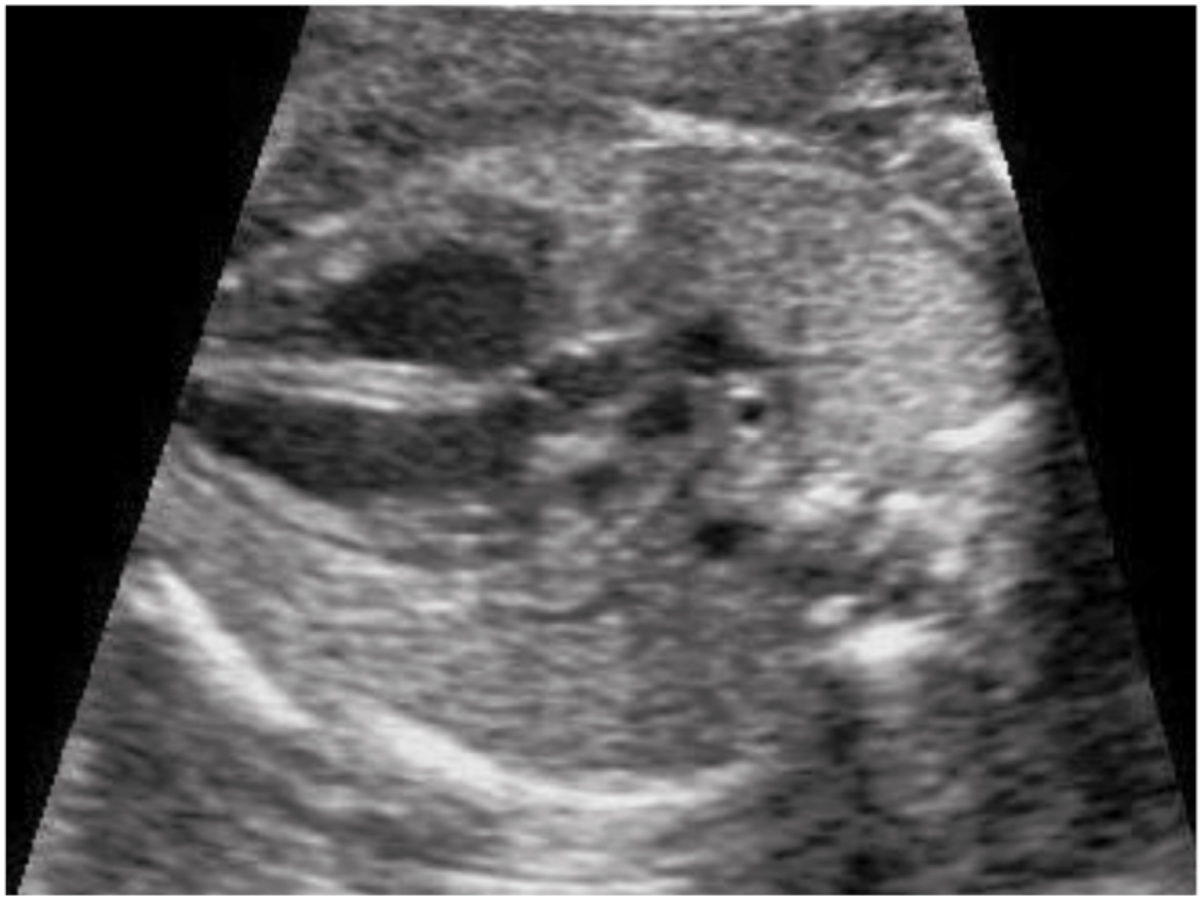

Iliac bone
Coccyx
Spine

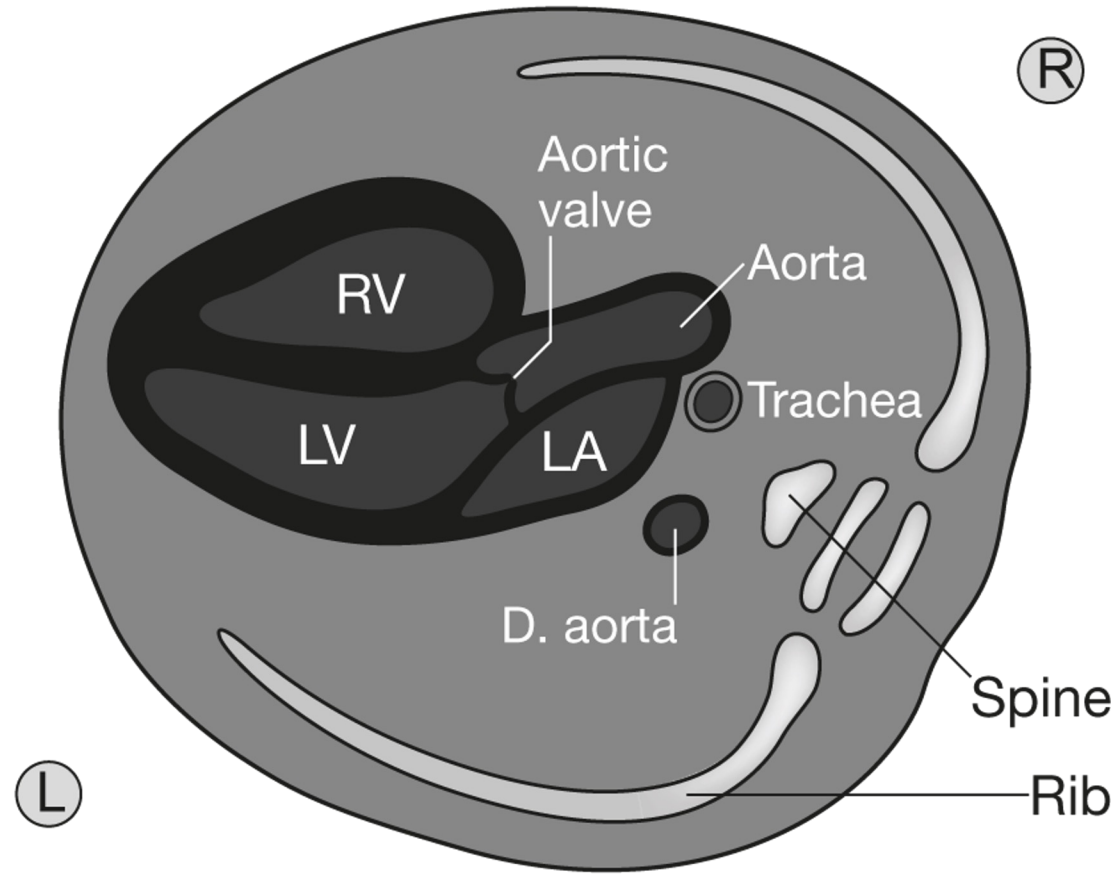


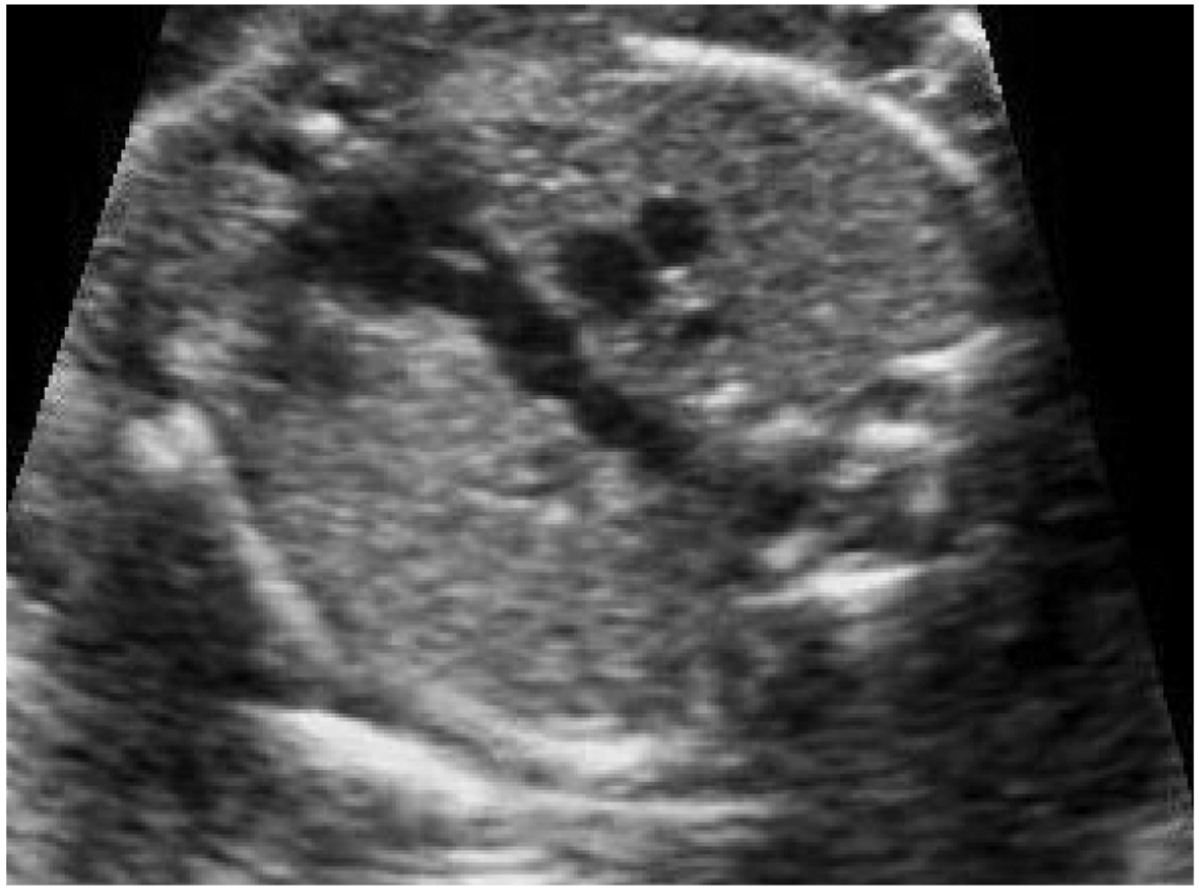

R
UV
IVC
Stomach
D. aorta
Spine
Rib
L

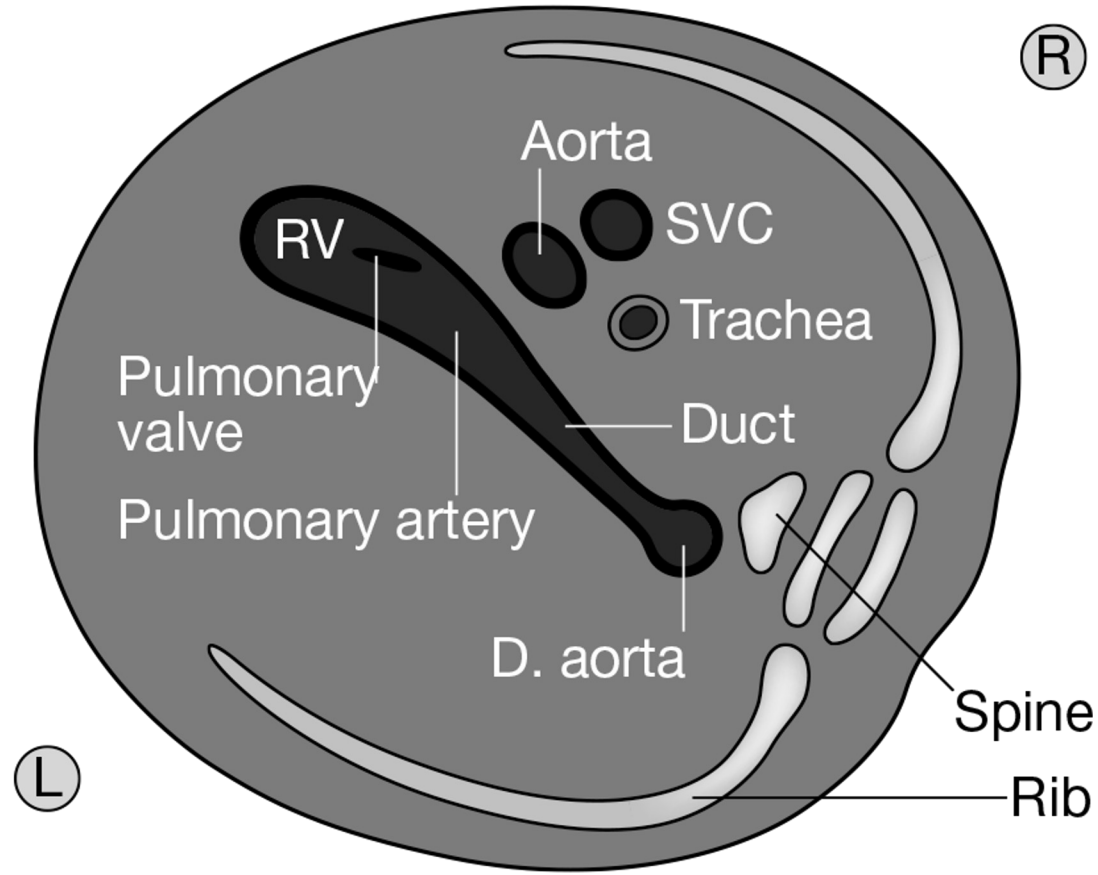


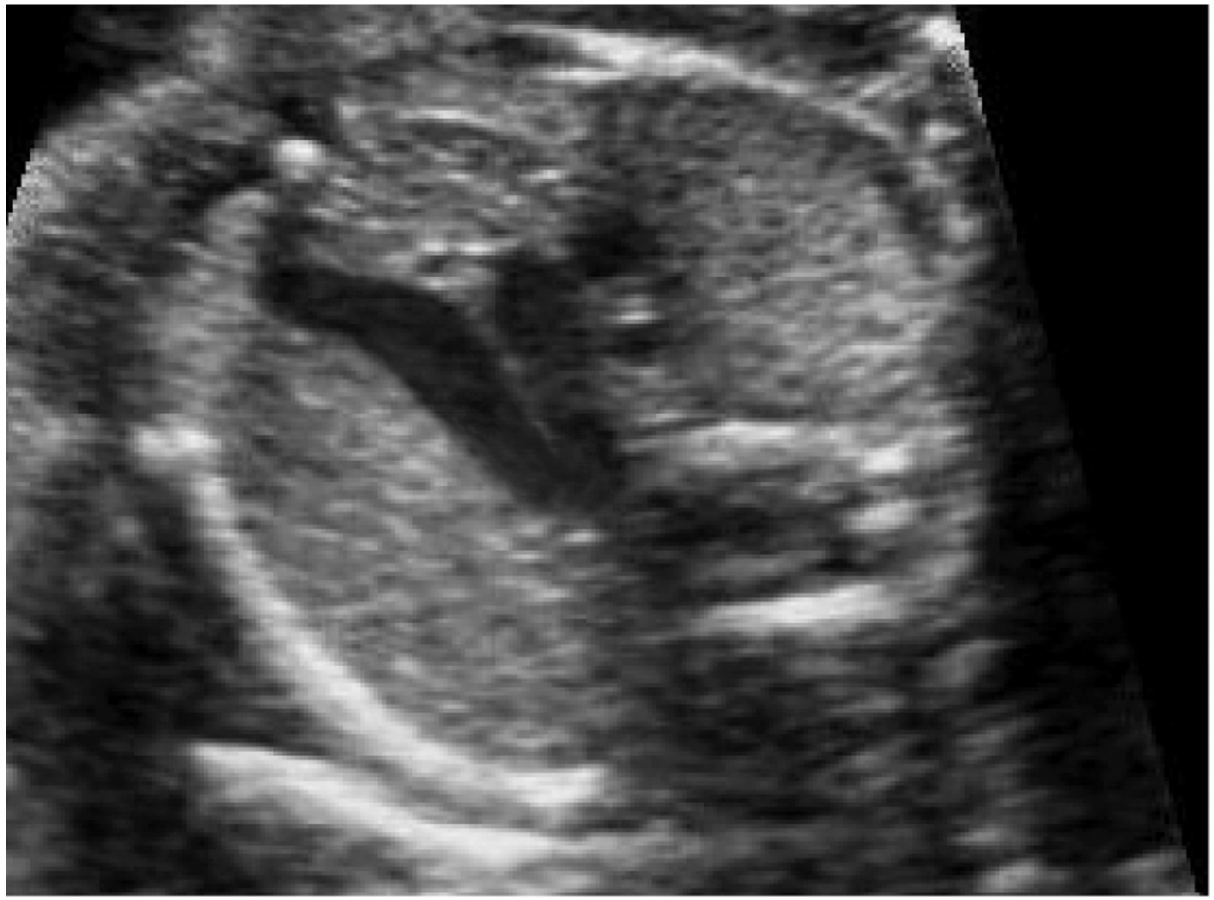

R
RV
RA
LA
LV
D. aorta
Spine
Rib
L

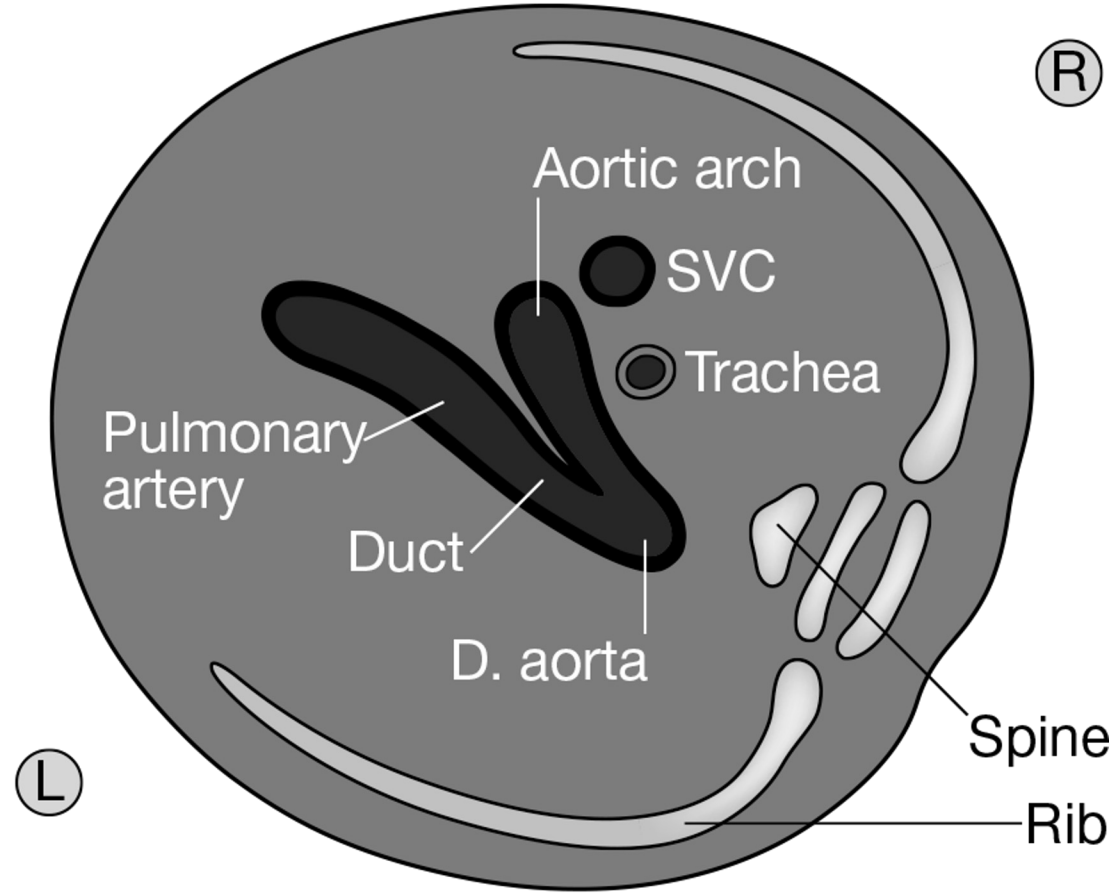


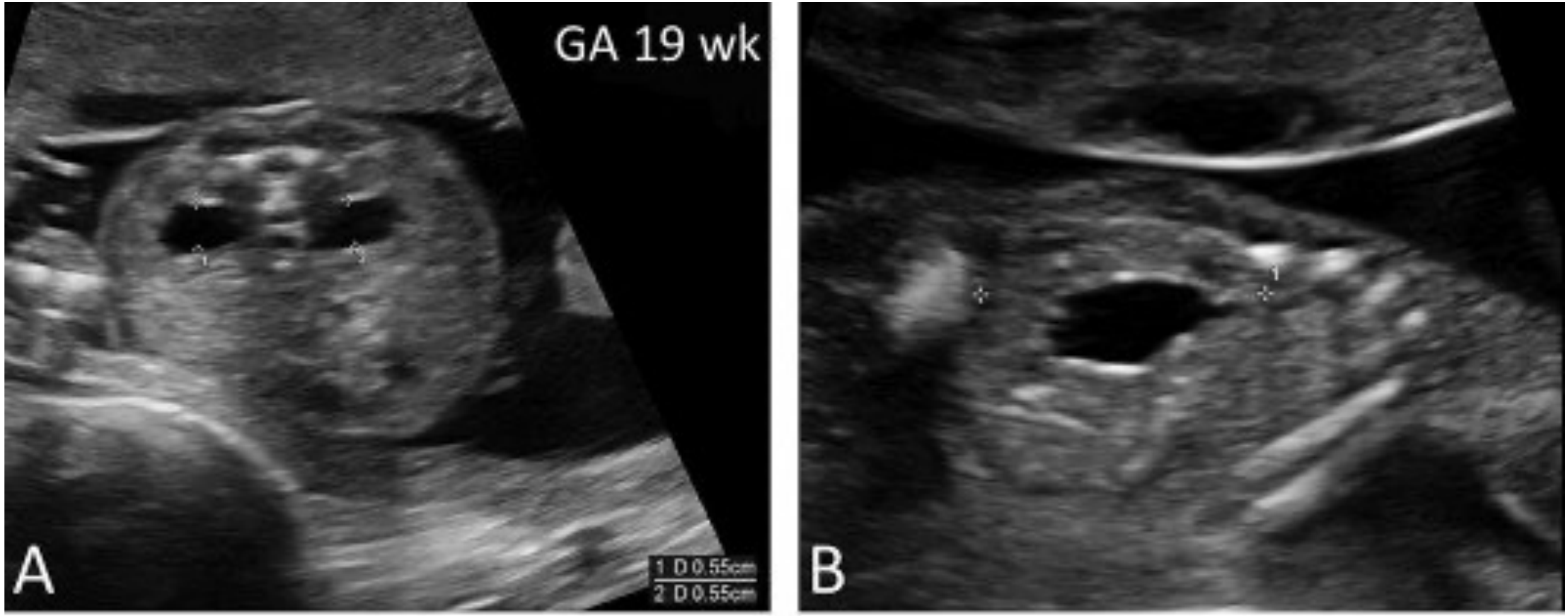

R
Aortic valve
RV
Aorta
Trachea
LV
LA
D. aorta
Spine
L
Rib

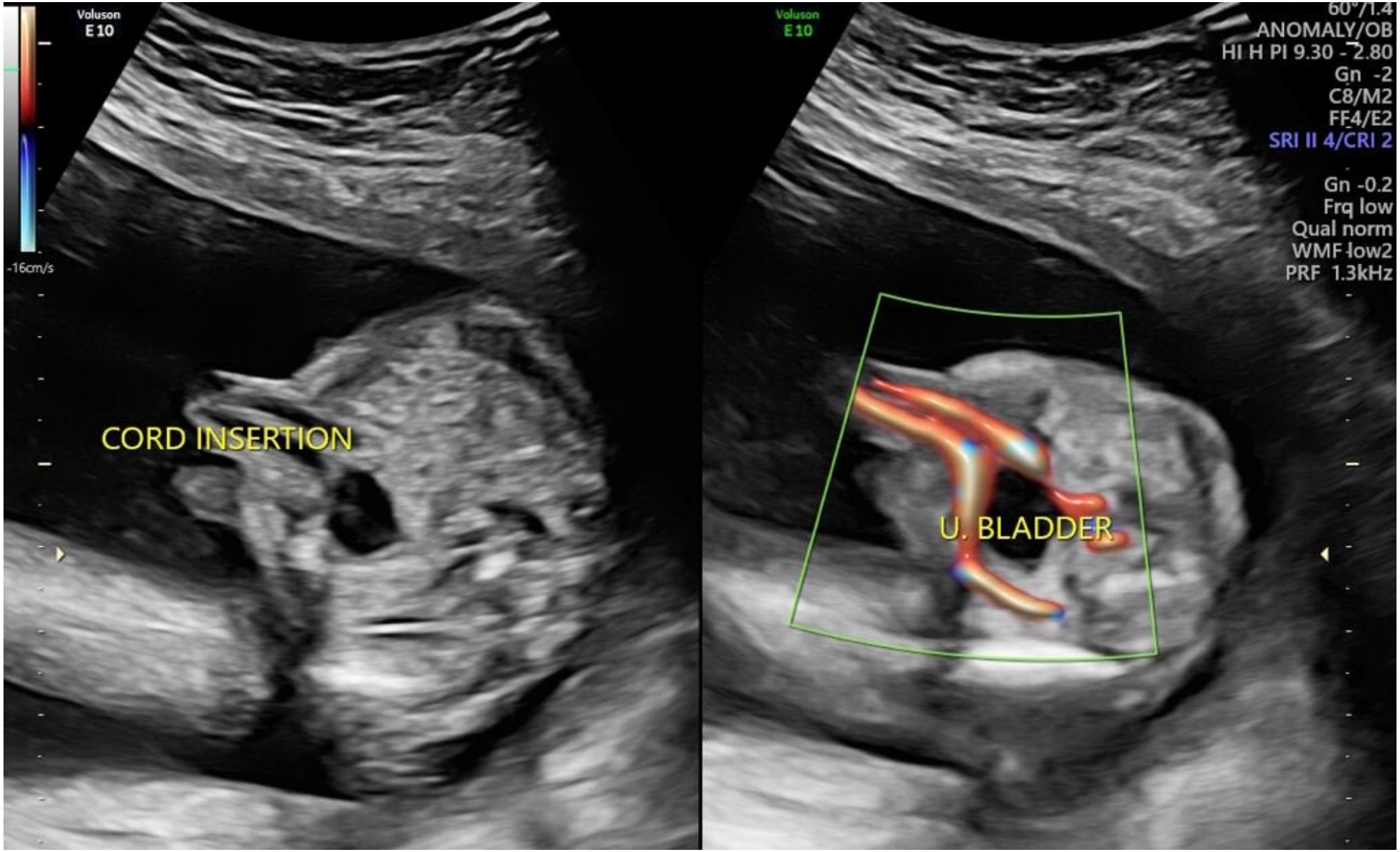


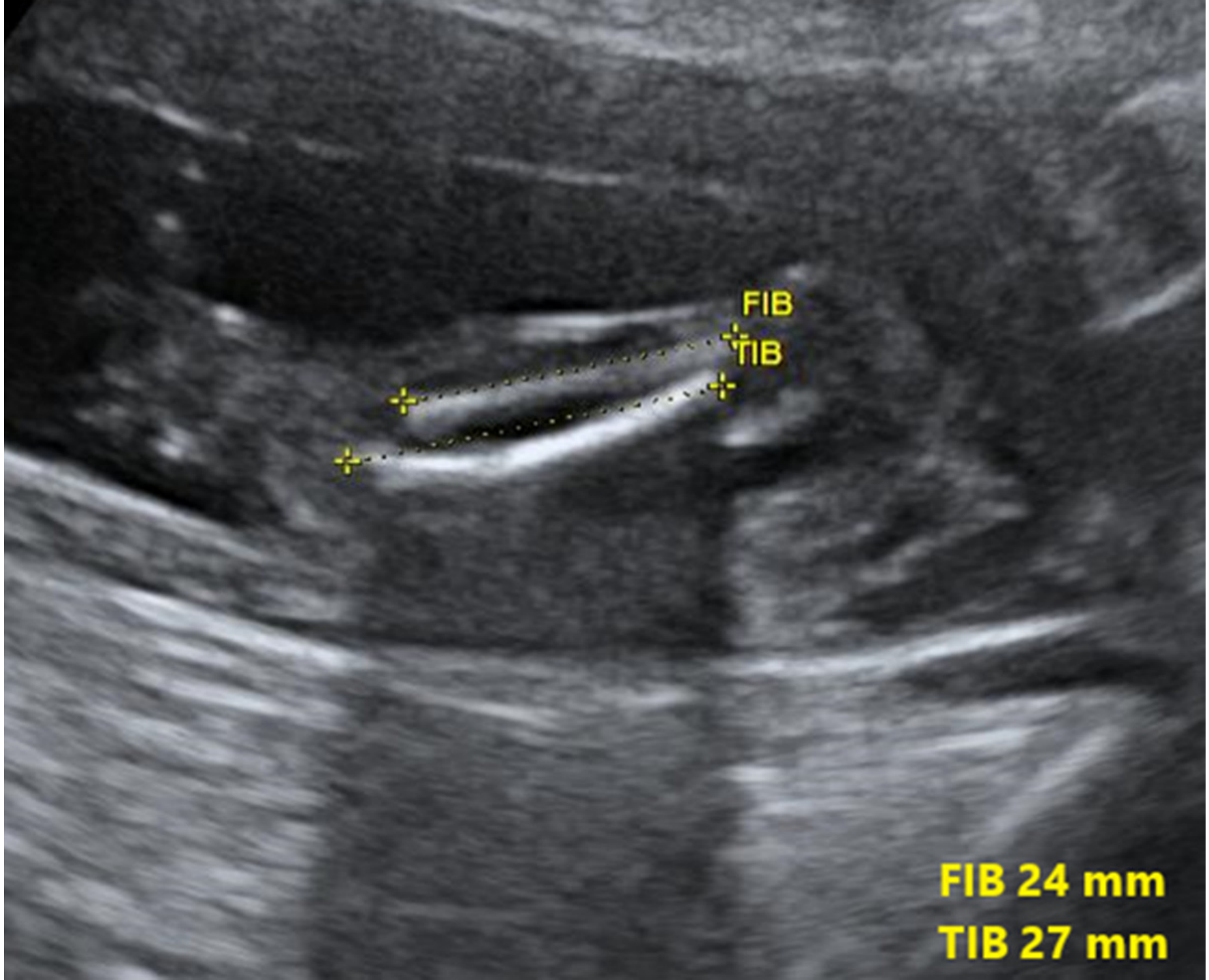

R
Aorta
SVC
RV
Trachea
Pulmonary valve
Duct
Pulmonary artery
D. aorta
Spine
L
Rib

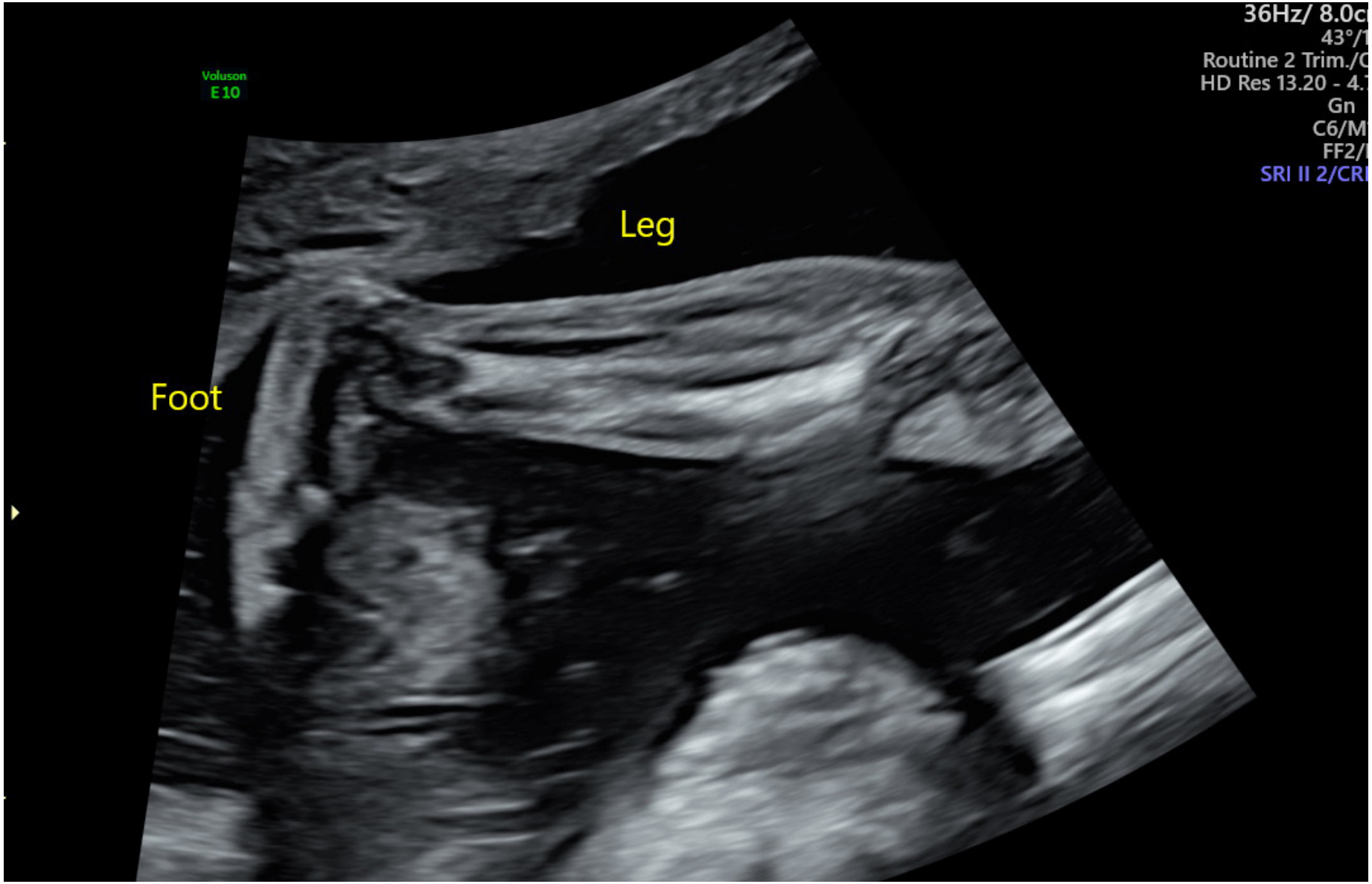


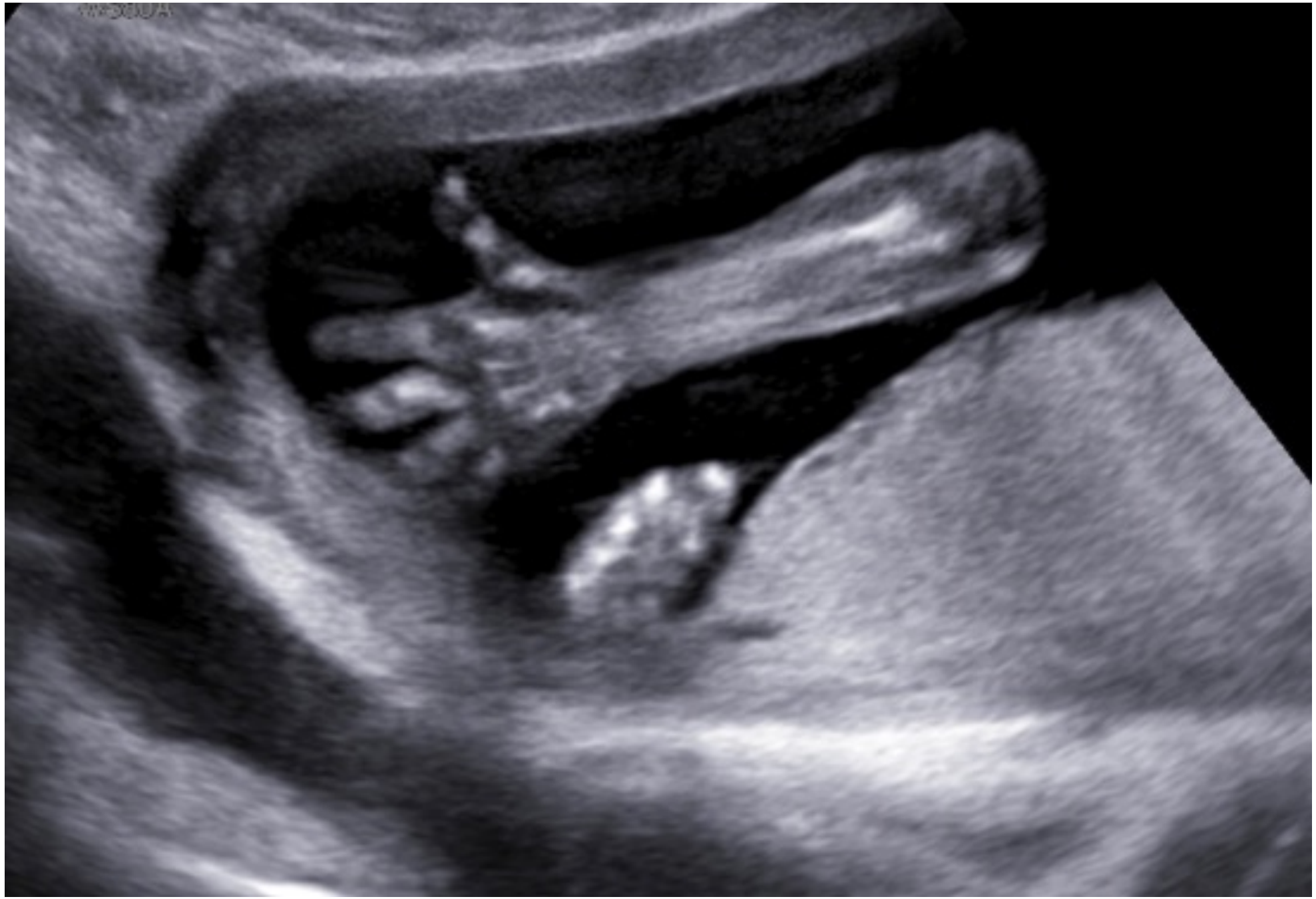

R
Aortic arch
SVC
Trachea
Pulmonary artery
Duct
D. aorta
Spine
Rib
L

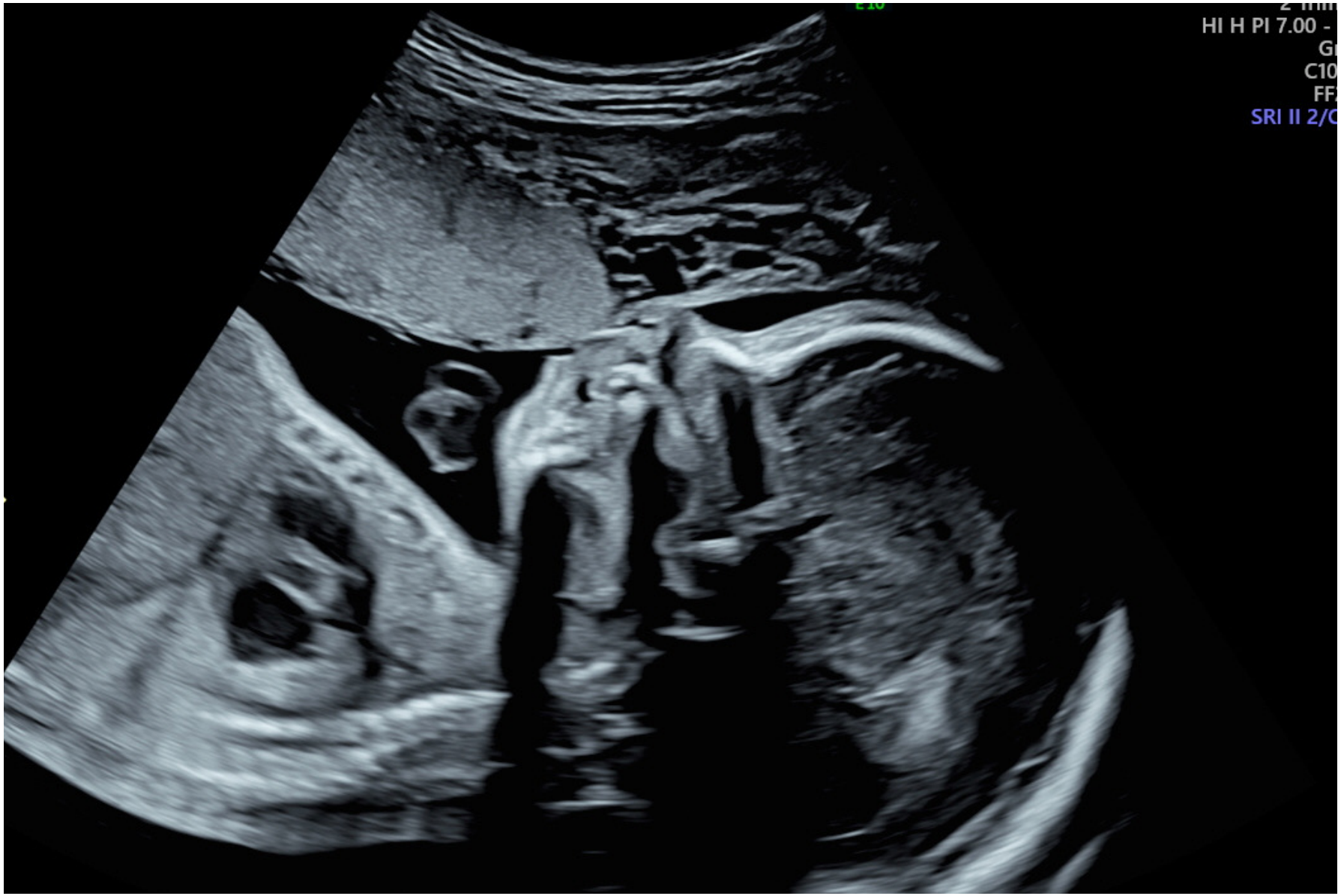

GA 19 wk
A
1 D 0.55cm
2 D 0.55cm
B


Voluson
E10
-16cm/s
CORD INSERTION
Voluson
E10
60°/1.4
ANOMALY/OB
HI H PI 9.30 - 2.80
Gn -2
C8/M2
FF4/E2
SRI II 4/CRI 2
Gn -0.2
Frq low
Qual norm
WMF low2
PRF 1.3kHz
U. BLADDER


FIB
TIB
FIB 24 mm
TIB 27 mm


Voluson
E10
Leg
Foot
36Hz/ 8.0c
43°/1
Routine 2 Trim./C
HD Res 13.20 - 4.7
Gn
C6/M
FF2/
SRI II 2/CRI




HI H PI 7.00 -
C10
SRI II 2/C

Antenatal Sickle Cell & Thalassaemia Screening (SCT)

- **WHAT** – genetic screening programme to identify pregnant women and biological fathers who have or are carriers of sickle cell disease (SCD) or thalassaemia
- **WHO** – SCT screening is offered to all pregnant women and biological fathers where antenatal screening shows the mother is a genetic carrier
- **WHY** – if both biological parents are identified as carriers, there is a 1 in 4 chance (or higher if the parent has the condition) that their baby will inherit a haemoglobinopathy

Antenatal Sickle Cell & Thalassaemia Screening (SCT)

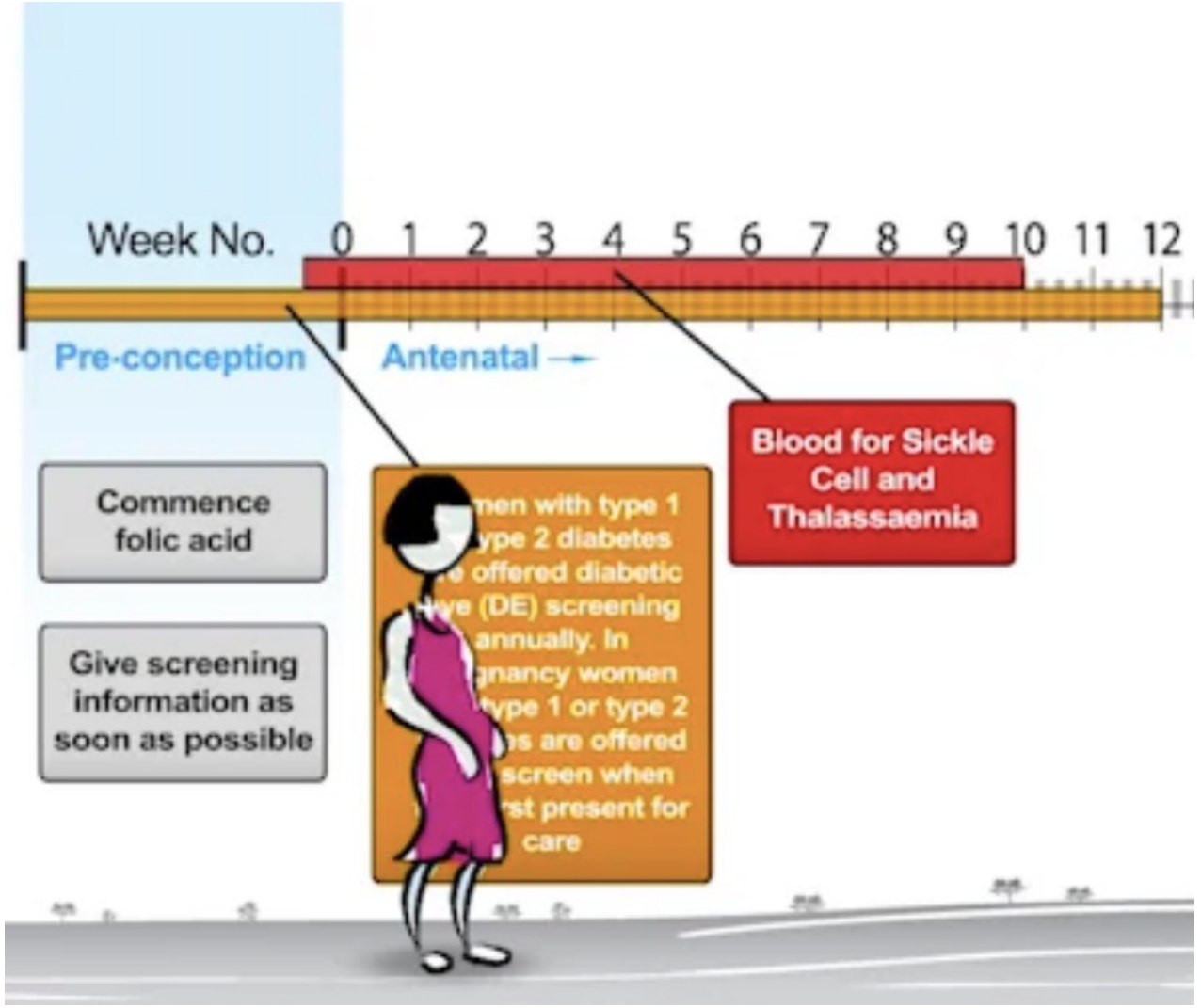
- **WHY** – therefore early antenatal screening is important to facilitate:
  - Timely biological father counselling
  - Timely offer of counselling and diagnostic test for the fetus, known as prenatal diagnosis (PND)
  - Support for parents to make personal informed decisions about their pregnancy (including continuation or termination of pregnancy where the baby has the condition screened for)

Newborn Sickle Cell & Thalassaemia Screening (SCT)

- **WHAT –** screening for SCD in newborns is offered as part of the newborn blood spot (NBS) screening programme which also identifies carriers of the sickle cell gene
  - There is no routine screen for babies at risk of inheriting beta thalassaemia major – most cases are detected during NBS but carriers are not
- **WHO –** all babies under 1 year of age are eligible for NBS screening
- **WHY –** babies with SCD are vulnerable to life-threatening infections. By identifying them promptly after birth, they can be offered potentially life saving prophylactic antibiotics and referred for specialist care
  - Linking the results of parents and babies is particularly important for SCT screening as it helps laboratories interpret newborn results and make a diagnosis

SCT Screening Standards

- The SCT Screening standards define the what, why and how standards that are measured and reported
- The SCT screening programme aims for pregnant women to have completed antenatal screening by 10 weeks gestation and prenatal diagnosis (PND) by 12+6
- An early offer of screening and PND is very important as it help give women and couples time to make personal choices



Who should be fast-tracked?

- Women / couples with **carrier status known** before the current pregnancy should be fast-tracked and immediately offered a counselling appointment to discuss their options as soon as they present in pregnancy
- Confirmatory carrier screening should still be offered – the referral should be concurrent

Useful Links

- https://www.e-lfh.org.uk/programmes/nhs-screening-programmes/
- UK Thalassaemia Society (UKTS) and Sickle Cell Society (SCS) – patient counselling resources
- Fetal Medicine Foundation – for combined screening and FASP

OXCOG

OXCOG.CO.UK

Screening & FASP

MRCOG Part 2 Online Revision Course

Miss Kit Robertson – Consultant in Obstetrics and Maternal-Fetal Medicine, Oxford University Hospitals