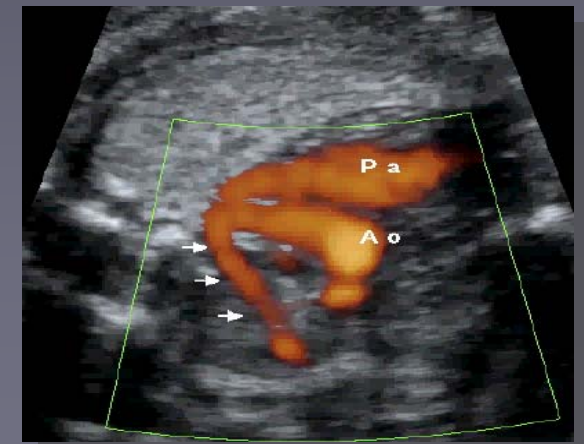


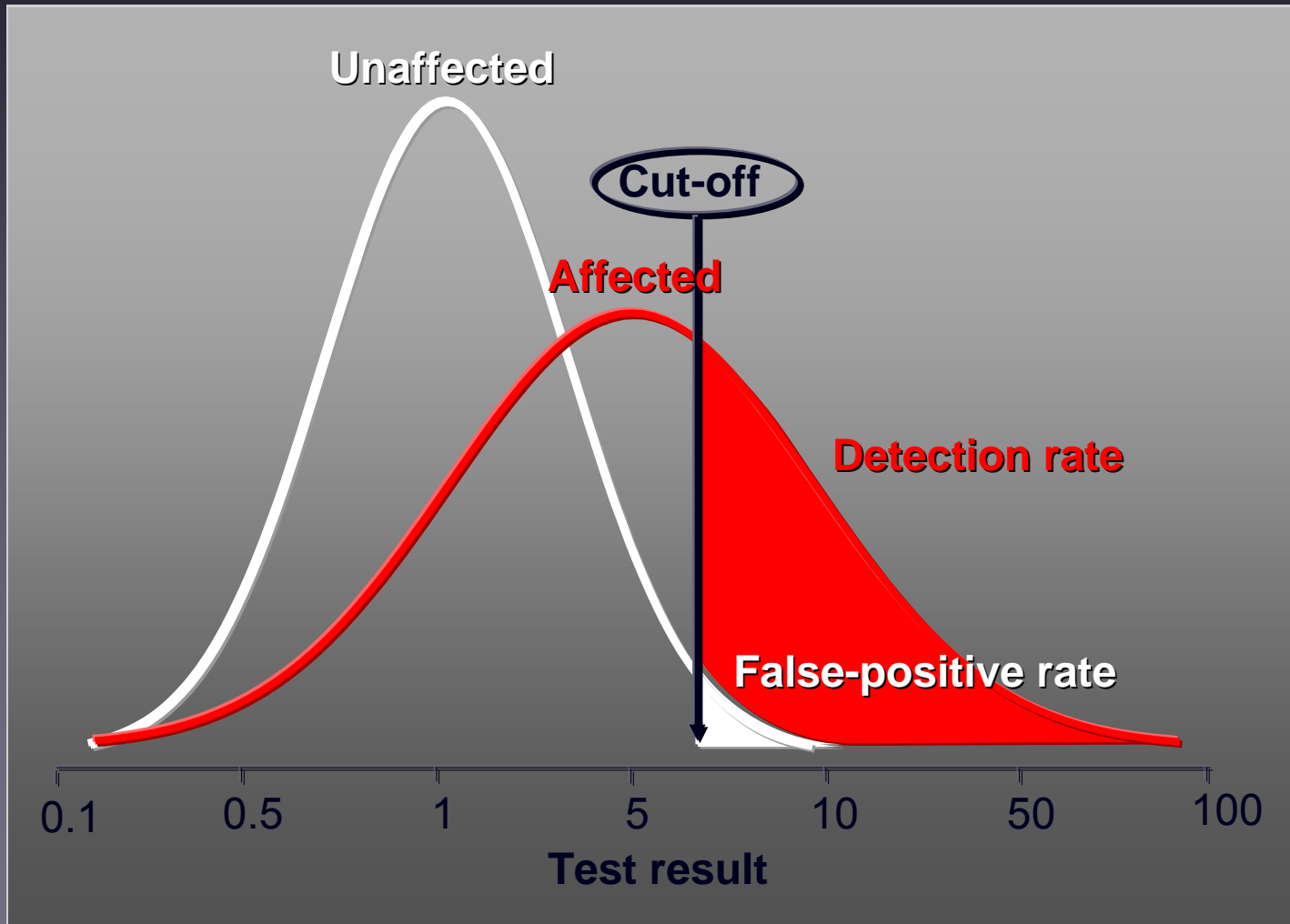
Screening for trisomy 21



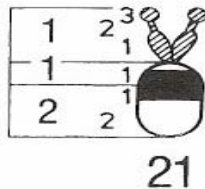
2nd trimester markers



Screening



2nd trimester DS markers



DOWN SYNDROME

(Trisomy 21 Syndrome)

Hypotonia, Flat Facies, Slanted Palpebral Fissures, Small Ears

Down's report of 1866 on the ethnic classification of idiots stated that a "large number of congenital idiots are typical Mongols," and he set forth the clinical description of the Down syndrome. The textbook by Penrose and Smith provides an overall appraisal of this disorder that has an incidence of 1 in 660 newborns, making it the most common pattern of malformation in man.

ABNORMALITIES

General. Hypotonia with tendency to keep mouth open and protrude the tongue; distasis recti. Hyperflexibility of joints. Relatively small stature with awkward gait. Increased weight in adolescence.

Central Nervous System. Mental deficiency.

Craniofacial. Brachycephaly with relatively flat occiput and tendency toward midline parietal hair whorl. Mild microcephaly with up-slanting palpebral fissures. Thin cranium with late closure of fontanel. Hypoplasia of aplasia of frontal sinuses, short hard palate.

Small nose with low nasal bridge and tendency to have inner epicanthal folds.

Eyes. Speckling of iris (Brushfield spots) with peripheral hypoplasia of iris. Fine lens opacities by slit lamp examination (59 per cent). Refractive error, mostly myopia (70 per cent); nystagmus (35 per cent); strabismus (45 per cent); blocked tear duct (20 per cent). Acquired cataracts in adults (30 to 60 per cent).

Ears. Small; overfolding of angulated upper helix; sometimes prominent; small or absent earlobes. Hearing loss (66 per cent) of conductive, mixed, or sensorineural type. Fluid accumulation in middle ear (60 to 80 per cent).

Dentition. Hypoplasia, irregular placement, fewer caries than usual. Periodontal disease.

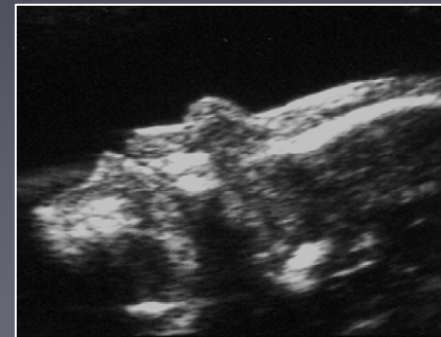
Neck. Appears short.

Hands. Relatively short metacarpals and phalanges. Fifth finger: hypoplasia of midphalanx of fifth finger (60 per cent) with clinodactyly (50 per cent), a single crease (40 per cent).

2nd trimester DS markers

Trisomy 21

- Brachycephaly
- Mild ventriculomegaly
- Nasal hypoplasia
- Nuchal edema
- Cardiac defects (AVSD)
- Echogenic focus
- Duodenal atresia
- Hyperechogenic bowel
- Shortening of femur
- Shortening of humerus
- Saldal gap
- Clinodactily



2nd trimester DS markers

Marker is a defect that is more common in chromosomally abnormal fetuses than in normal fetuses

	Normal	Trisomy 21
Mild hydronephrosis	2.6%	17.1%
Echogenic foci	4.4%	30.3%
Short femur	5.2%	42.0%
Echogenic bowel	0.6%	17.3%
Nuchal fold >6 mm	0.6%	41.1%
Major defect	0.7%	21.4%

Nyberg et al 2001, Benacerraf et al 2002

Nicolaides Ultrasound Obstet Gynecol 2003

2nd trimester markers

The importance of a marker depends on its relative frequency in the abnormal group compared to the normal group

	Normal	Tr 21	Likelihood ratio
Mild hydronephrosis	2.6%	17.1%	6.8
Echogenic foci	4.4%	30.3%	6.4
Short femur	5.2%	42.0%	7.9
Echogenic bowel	0.6%	17.3%	21.2
Nuchal fold >6 mm	0.6%	41.1%	53.1
Major defect	0.7%	21.4%	33.0

2nd trimester markers

If a marker is present the risk goes up,
if it is absent the risk goes down

	Normal	Tr 21	LR+	LR-
Mild hydronephrosis	2.6%	17.1%	6.8	0.85
Echogenic foci	4.4%	30.3%	6.4	0.75
Short femur	5.2%	42.0%	7.9	0.62
Echogenic bowel	0.6%	17.3%	21.2	0.87
Nuchal fold >6 mm	0.6%	41.1%	53.1	0.67
Major defect	0.7%	21.4%	33.0	0.79



If a marker is present the risk goes up & if it is absent the risk goes down

	Normal	Tr 21	LR+	LR-	LRc
Mild hydronephrosis	2.6%	17.1%	6.8	0.85	1.0
Echogenic foci	4.4%	30.3%	6.4	0.75	1.0
Short femur	5.2%	42.0%	7.9	0.62	1.5
Echogenic bowel	0.6%	17.3%	21.2	0.87	3.0
Nuchal fold >6 mm	0.6%	41.1%	53.1	0.67	10.0
Major defect	0.7%	21.4%	33.0	0.79	5.0

STRONG 2nd trimester markers

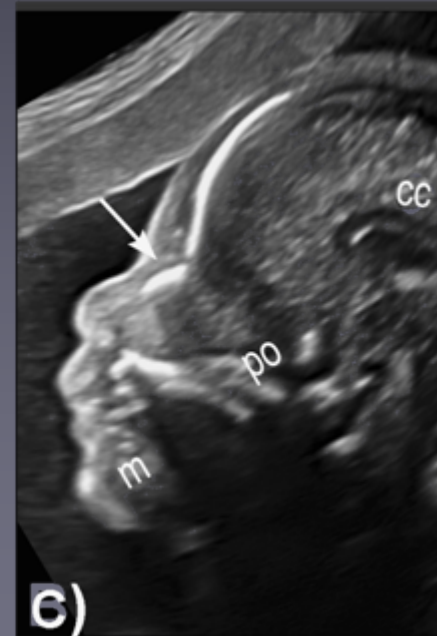
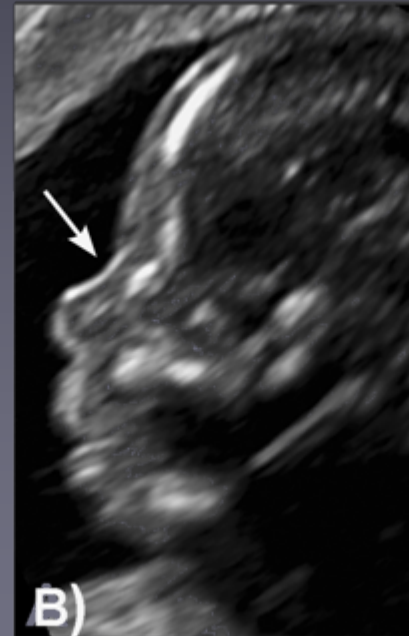
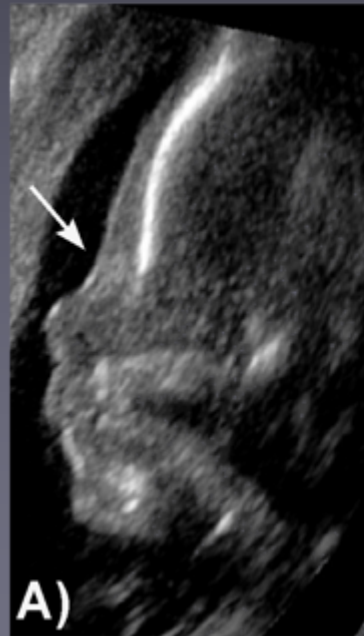
1. Nuchal Fold

- Measured on TCD plane:
> 5 or 6 mms



STRONG 2nd trimester markers

2. Nasal Bone





Nasal bone – 1. Incidence

Author	Absent nasal bone		Likelihood ratio	
	Trisomy 21	Normal	+ve	-ve
Bromley etal 2002	6/16 (37.5%)	1/233 (0.4%)	93.8	0.63
Cicero etal 2003	11/34 (32.4%)	6/982 (0.6%)	54.0	0.68
Vintzileos etal 2003	12/29 (41.3%)	0/102 (0%)	-	-
Odibo etal 2004	5/18 (27.8%)	14/583 (2.4%)	11.6	0.74
Cusick etal 2004	1/4 (25%)	3/814 (0.4%)	69.4	0.75
Tran etal 2005	11/31 (35.5%)	1/136 (0.7%)	50.7	0.65
Benoit etal 2005	8/14 (57.1%)	0/18 (0%)	-	-
Total	55/152 (37.0%)	25/2,868 (0.9%)	41.1	0.64

Abnormal nasal bone	Likelihood ratio	
	Trisomy 21	Normal
Short	40/83 (48.2%)	136/5643 (2.4%)
Absent or short	51/85 (60.0%)	31/2155 (1.4%)

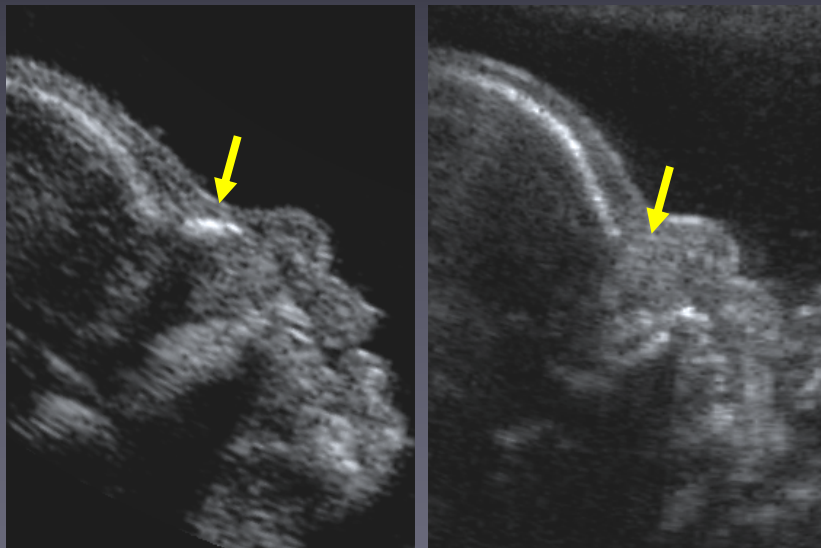


Short nose (2.5th centile): 12 wks 1.5 mm; 16 wks 3.0 mm; 20 wks 4.5 mm

Trisomy 21:

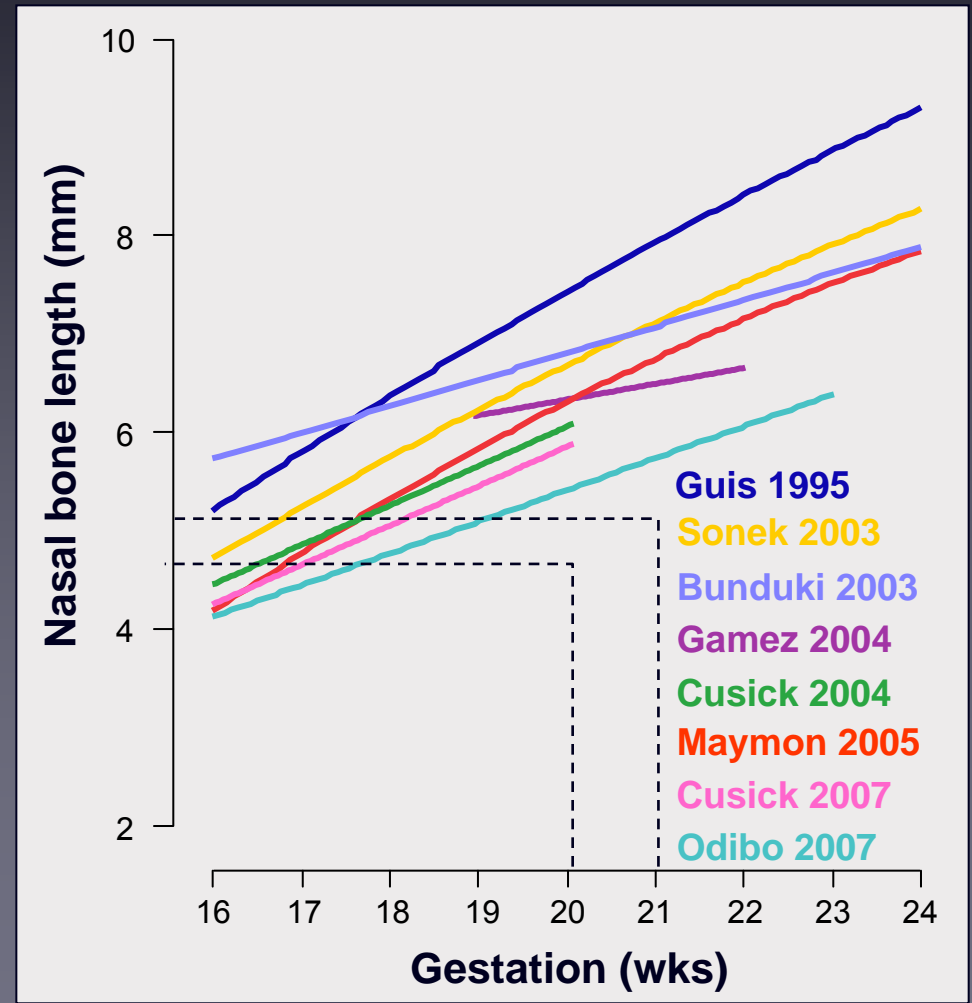
Absent 30%

Short 30%



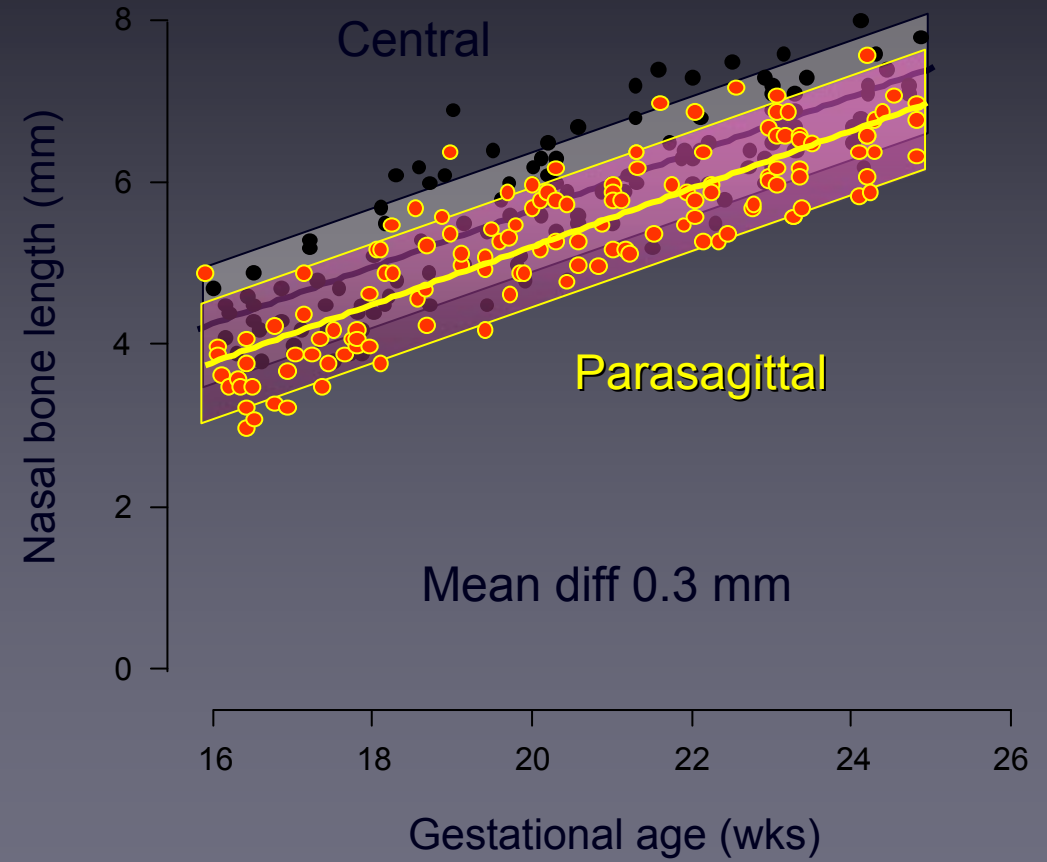
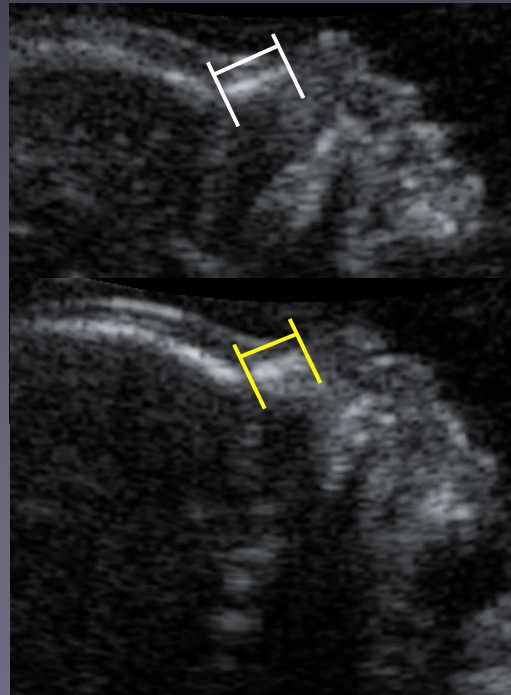
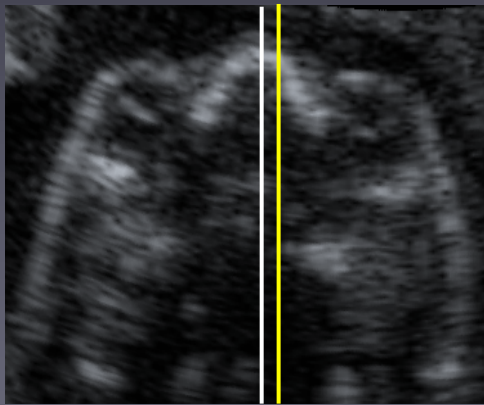
Sonek et al AJOG 2006

Nasal bone – 2. Length

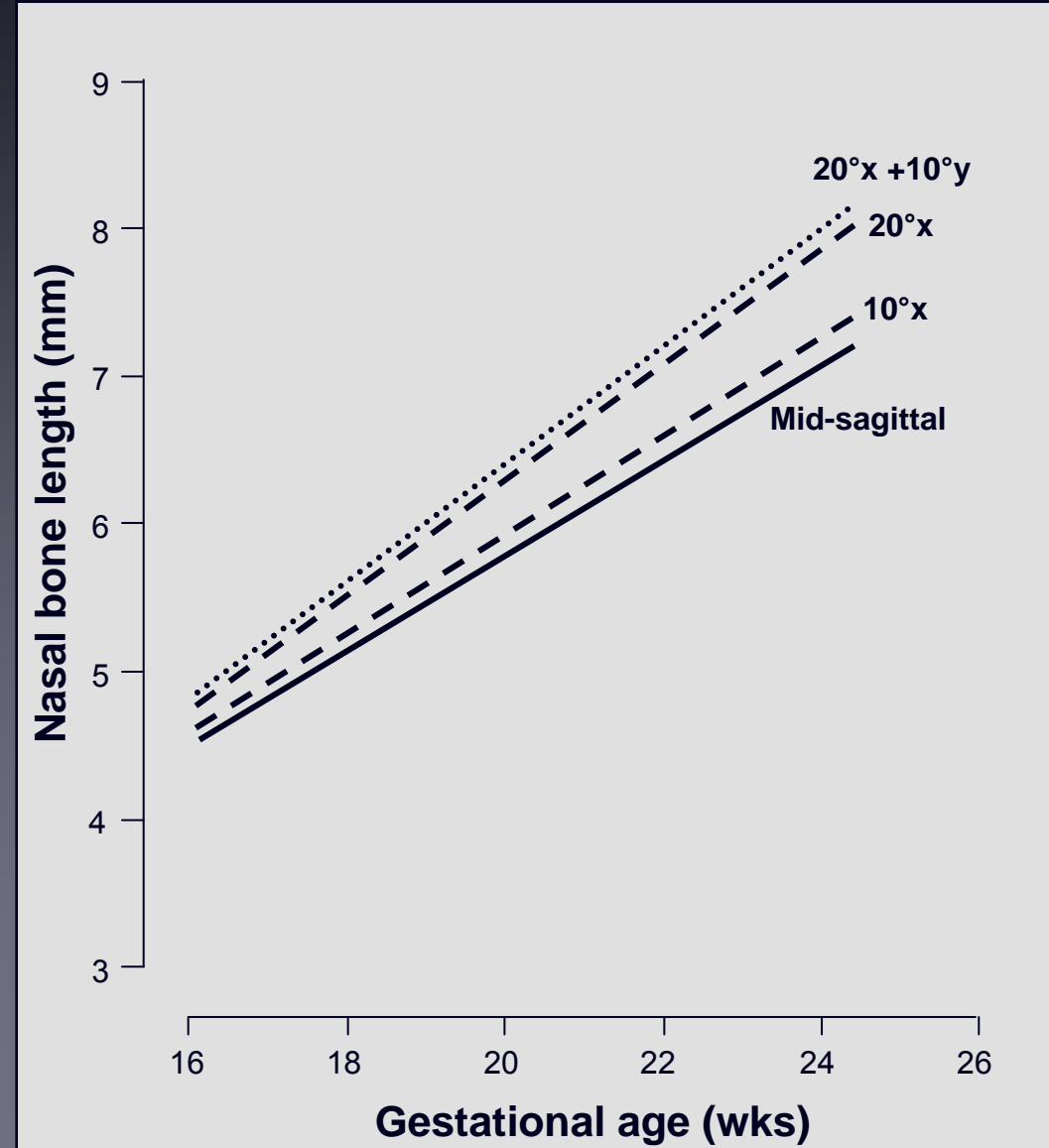
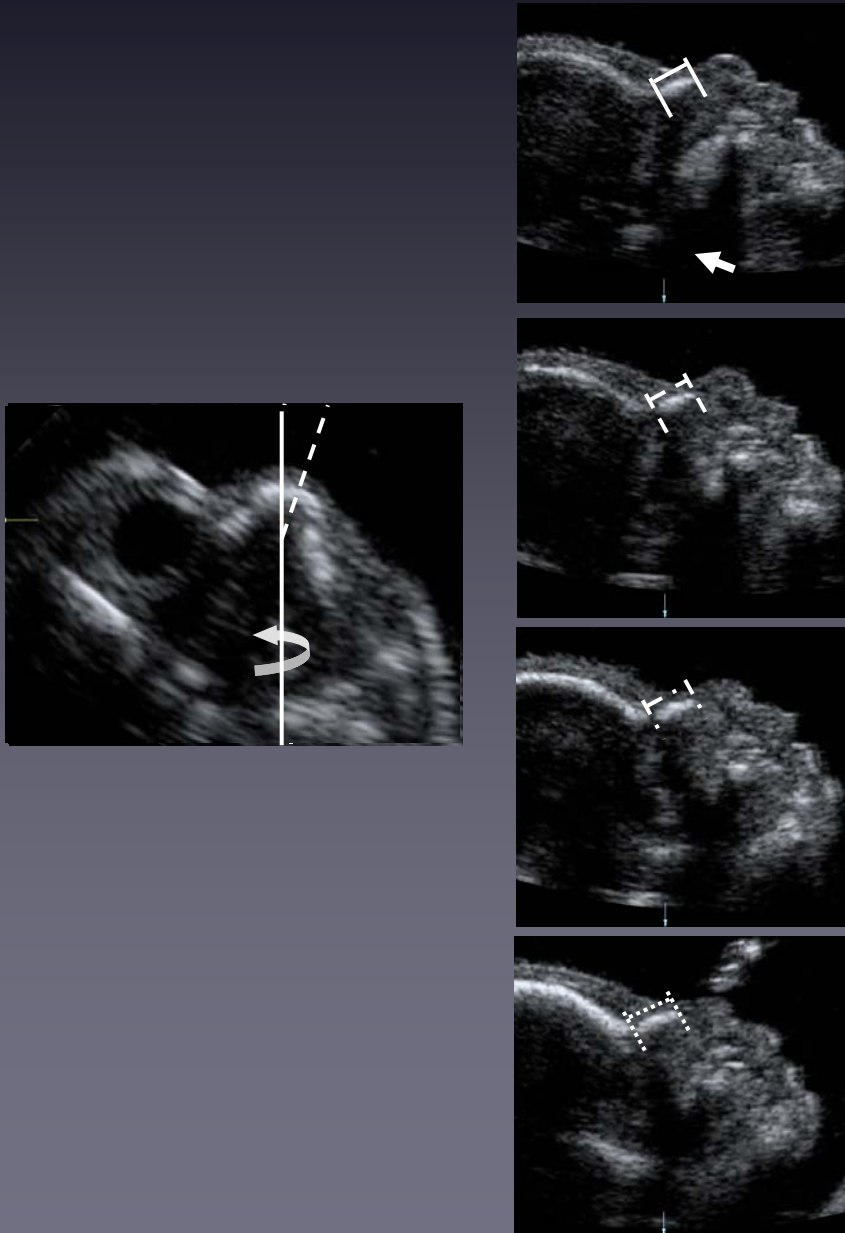


- @ 20-22 weeks, 2.5° and 5° centiles are:
4.5 and 5.0 mms

Nasal bone – 3. Plane

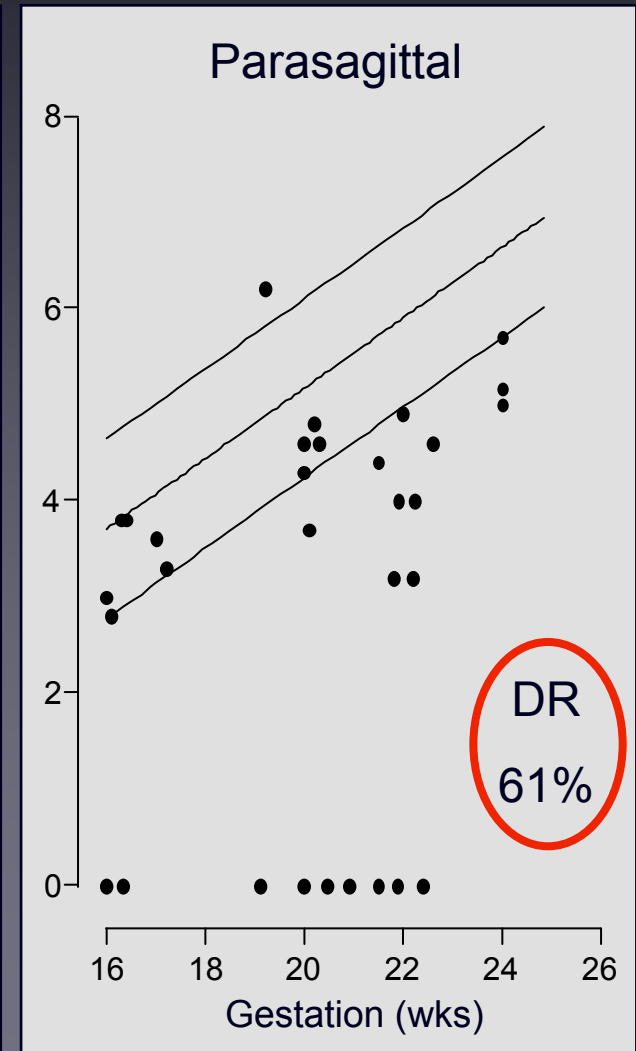
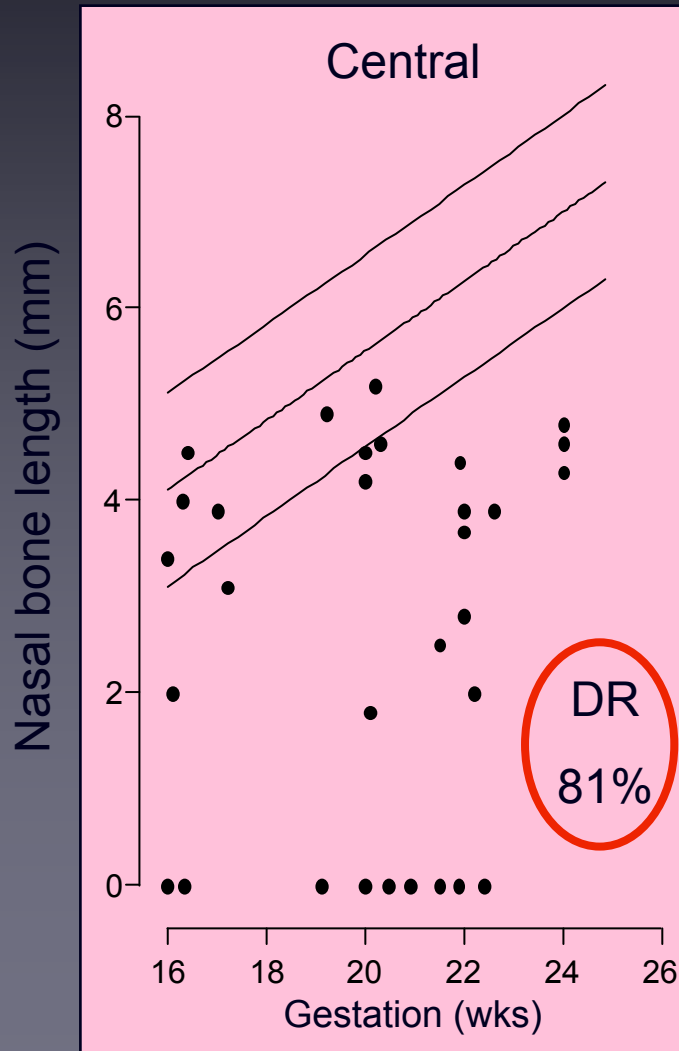
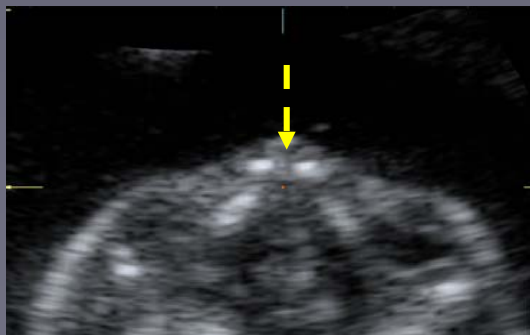
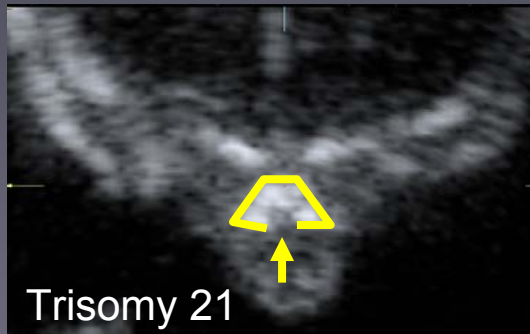
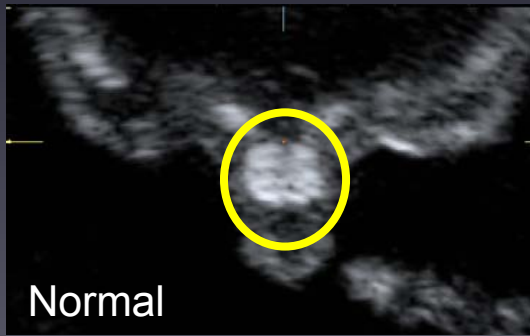


Nasal bone – 4. Angle (3D)



Nasal bone

20 weeks





(Pre-Nasal Thickness)

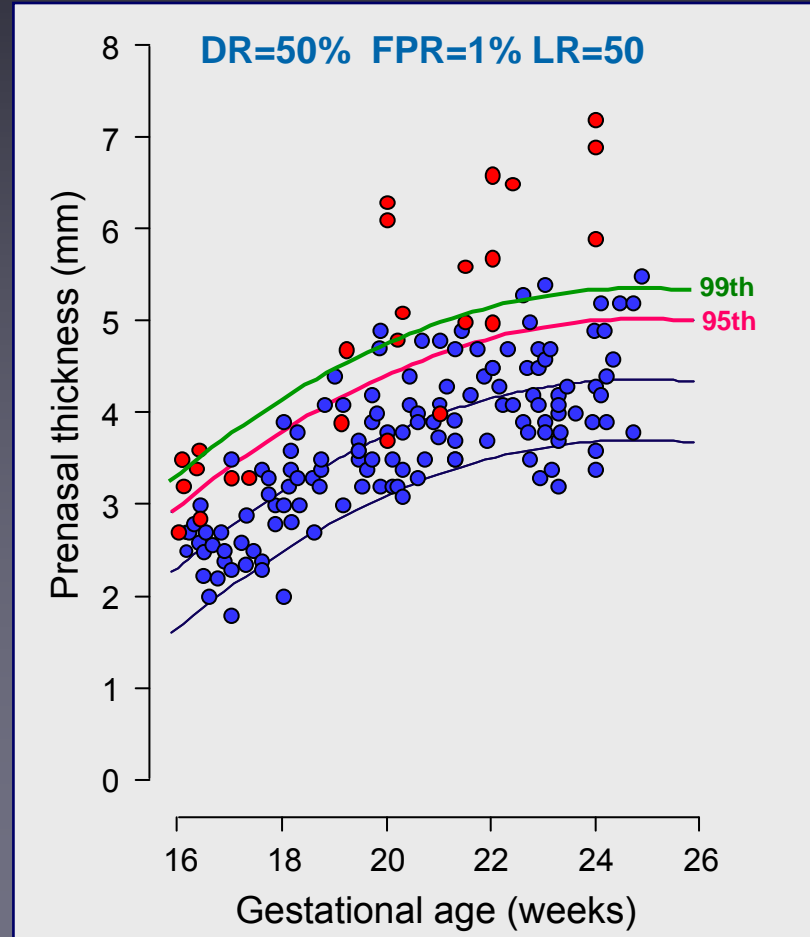
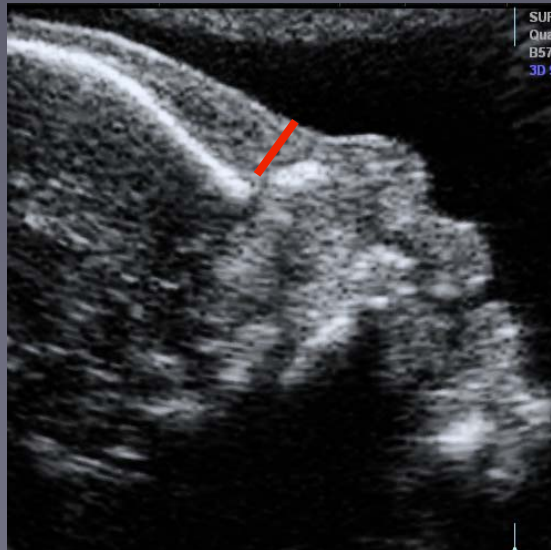
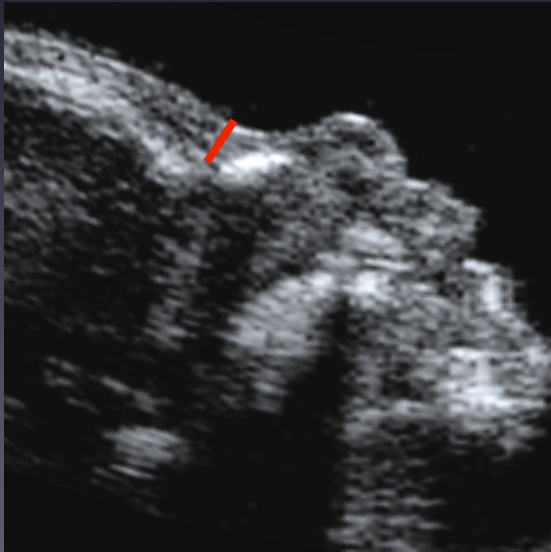
An excessive amount of skin is a common feature in Trisomy 21:

- increased nuchal translucency thickness 1st trimester
- increased nuchal fold thickness 2nd trimester
- Increased prenasal thickness 2nd trimester



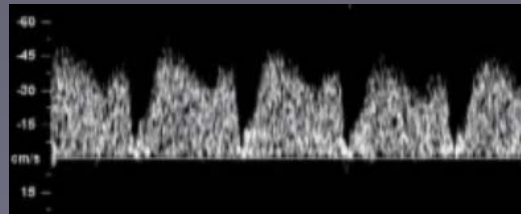
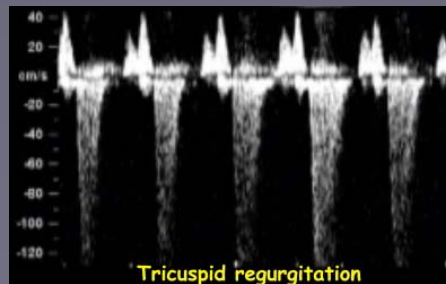
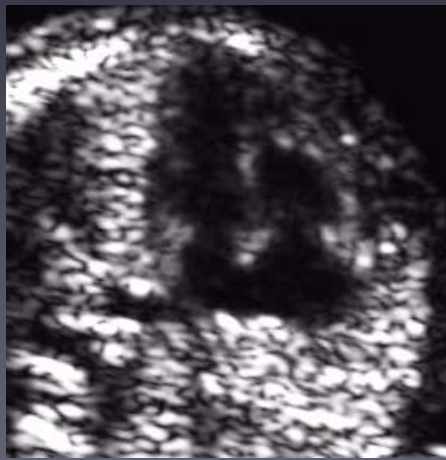


Prenasal edema

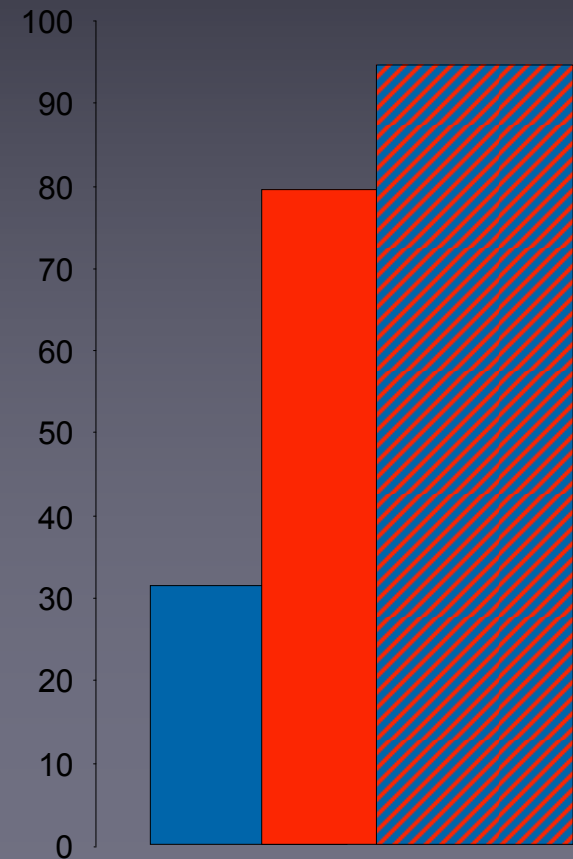


Screening for trisomy 21

Maternal age & β -hCG / PAPP-A & NT, NB, TR, DV

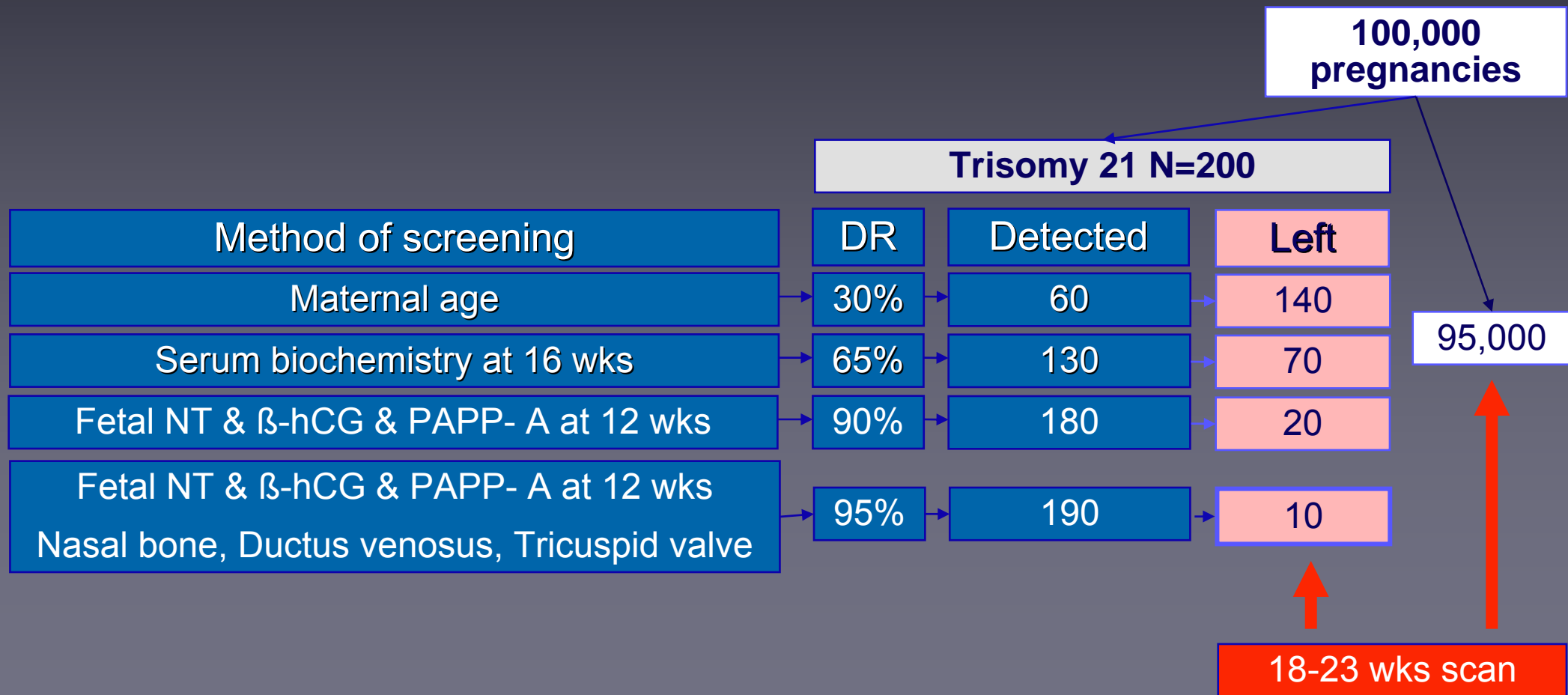


Detection rate for **FPR 5%**



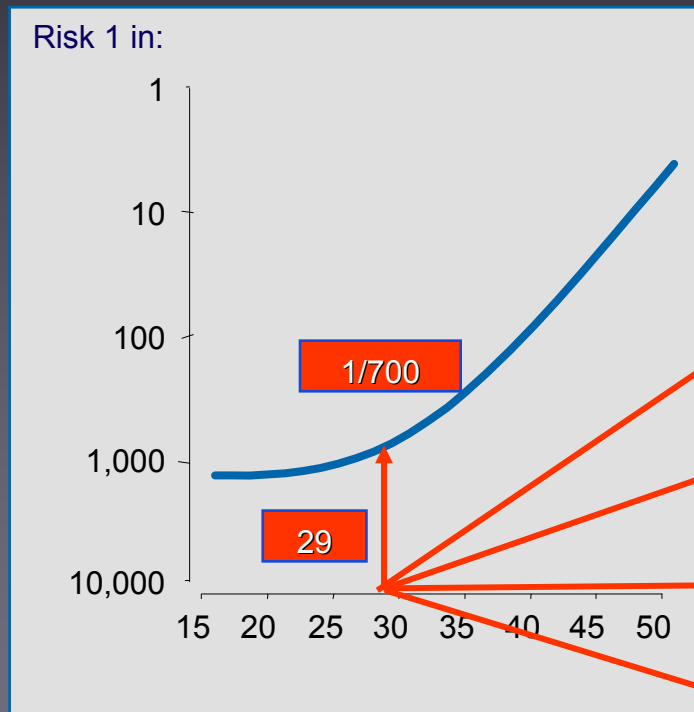
2nd trimester markers

The effect of previous screening

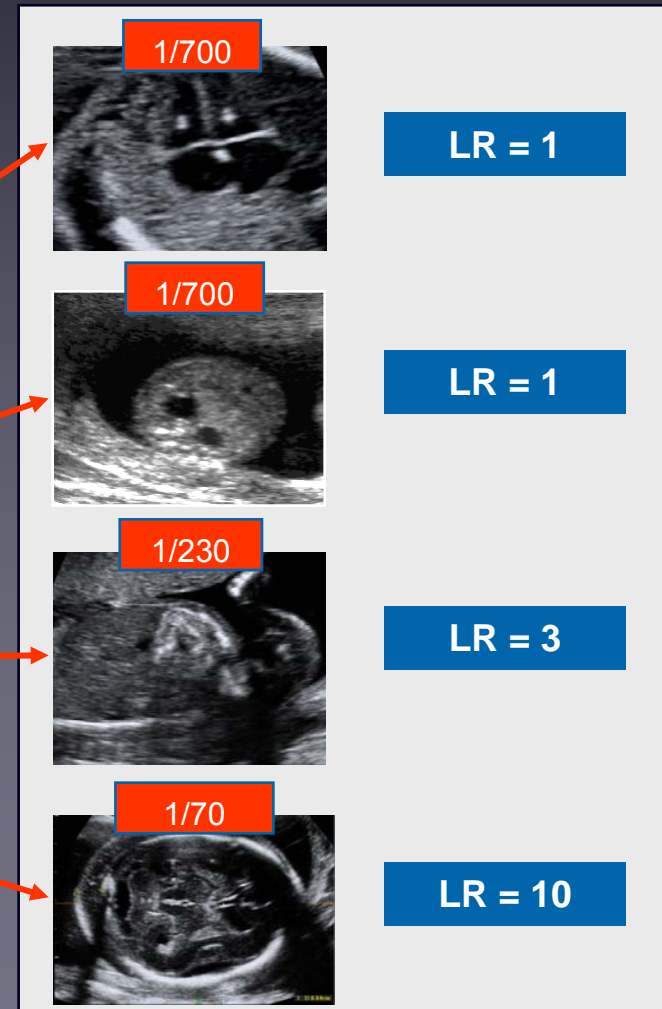


2nd trimester markers

Maternal age: 29 yrs; Fetal CRL: 65 mm; Age-risk: 1 in 700

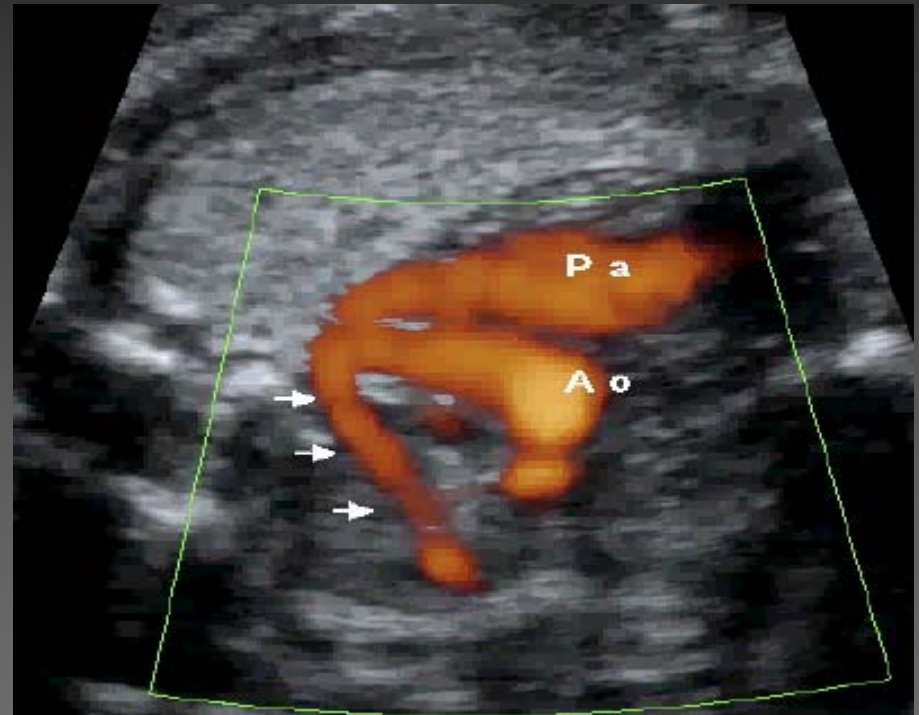


• Normal scan: risk 1 in 2100



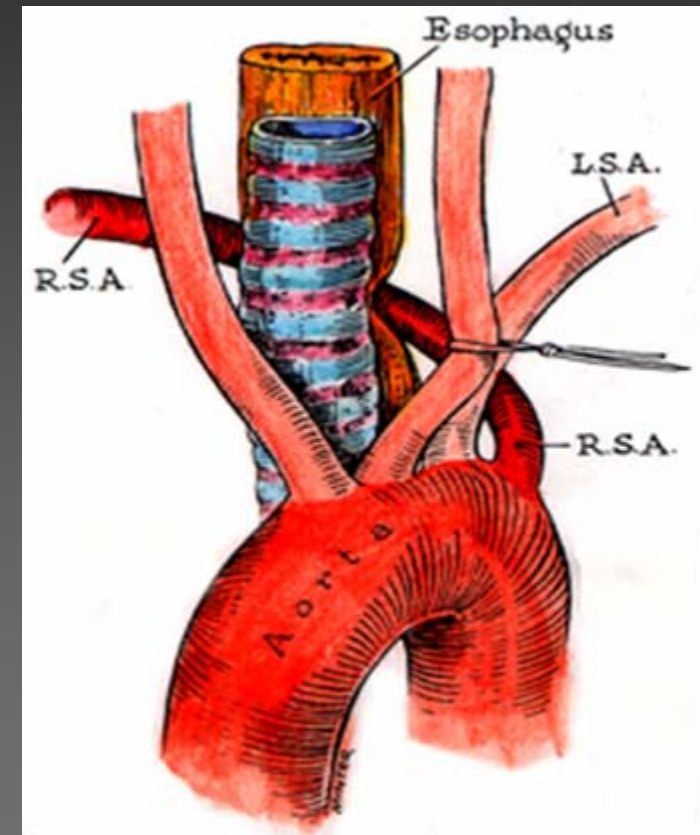
Aberrant Right Subclavian Artery. Active search or occasional finding...

D.Paladini



ARSA - Definition

- ✓ Right subclavian artery departing as 4^o vessel from aortic arch
- ✓ Coursing behind the trachea
- ✓ Reaching the right shoulder



ARSA in DS by CHD *after birth*

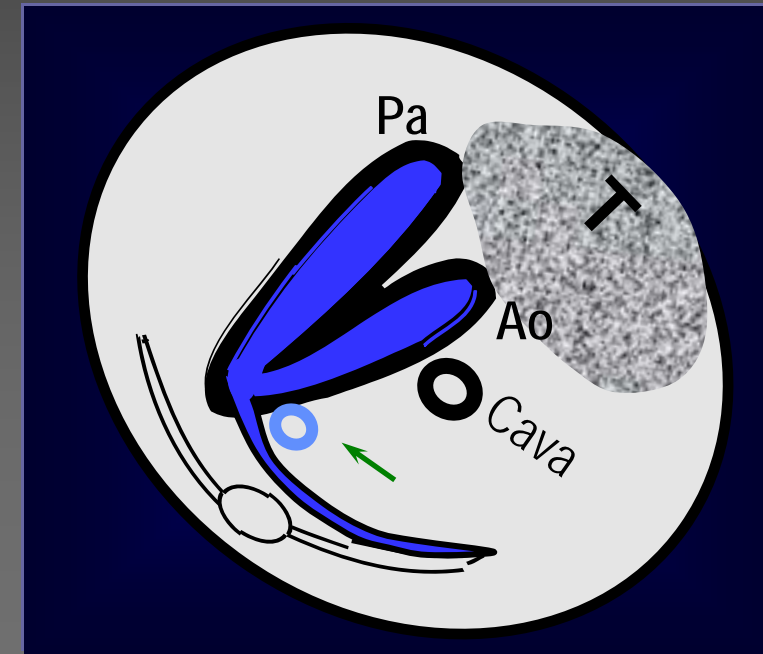
Reference	Type of study	Aberrant right subclavian artery (n (%))	
		CHD	No CHD
Evans, 1950	Postmortem	1/28 (3.6)	0/35 (0)
Strauss, 1953	Postmortem	1/6 (16.7)	0/6 (0)
Molz, 1978	Postmortem	3/3 (100)	—
Rowe, 1961	Radiol., postmortem	2/70 (2.9)	5/92 (5.4)
Goldstein, 1965	Radiological	10/27 (37.0)	0/1 (0)
Lo et al. 1989	Radiol., postmortem	24/149 (16.1)	—
Rathore, 1989	Radiological	16/45 (35.6)	—
Total		57/328 (17.4)	5/134 (3.7)

ARSA in DS vs Normals *in the fetus*

Reference	No. of cases	GA	Aberrant right subclavian artery (n (%))	
			Normal k.	DS
Chaoui, 2005 ¹	54	18-33	0/40 (0)	5/14 (36)
Chaoui, 2005 ²	906	15-34	13/905 (1.4)	1/1 (100)
Chaoui, 2006	14	< 14	--	4/14 (29)
Zalel, 2007	932	13-26	13/924 (1.4)	3/8 (37.5%)
Allan, 2008	425	11-14	2/353 (0.6)	4/51 (8)
Total			28/2222 (1.3)	17/88 (19)
Paladini, 2010	80DS	13-37	--	19/80 (24)

ARSA – *How to look for it*

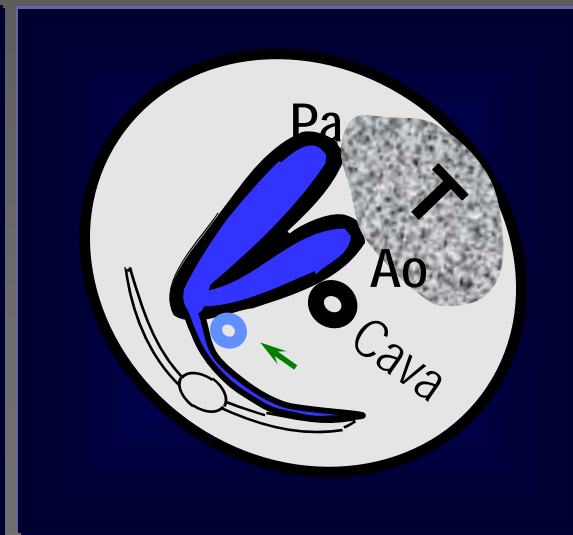
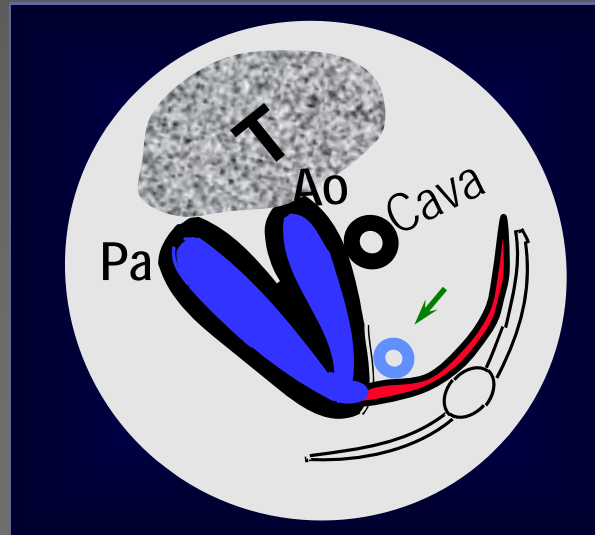
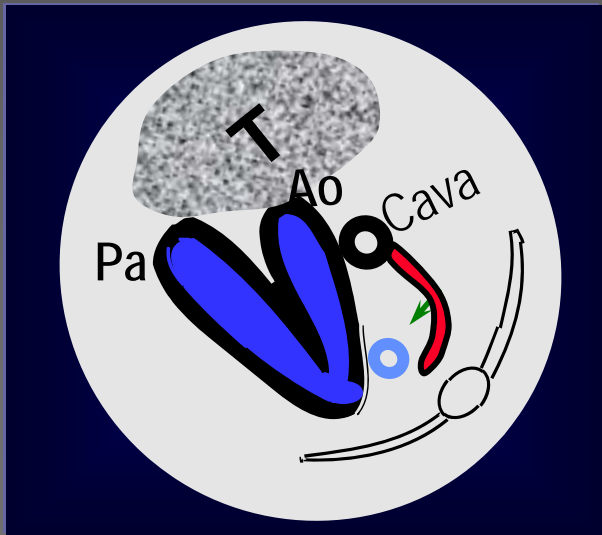
1. Three-vessel view
2. At least 30° angle with expected course of ARSA
3. Reduce PRF to ~20 cm/sec
4. Or, use Power Doppler
5. Departing from the “V”
6. Coursing behind the trachea
7. Towards the right shoulder



ARSA – *How to look for it*

➤ Three-vessel view

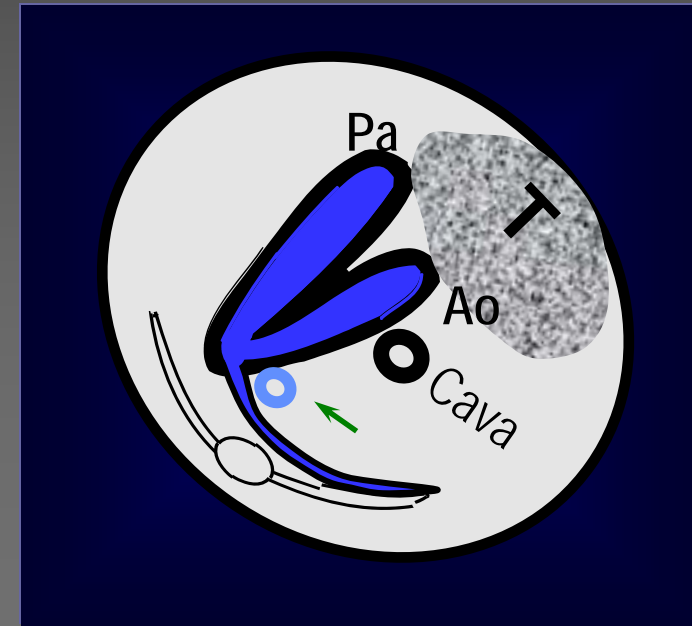
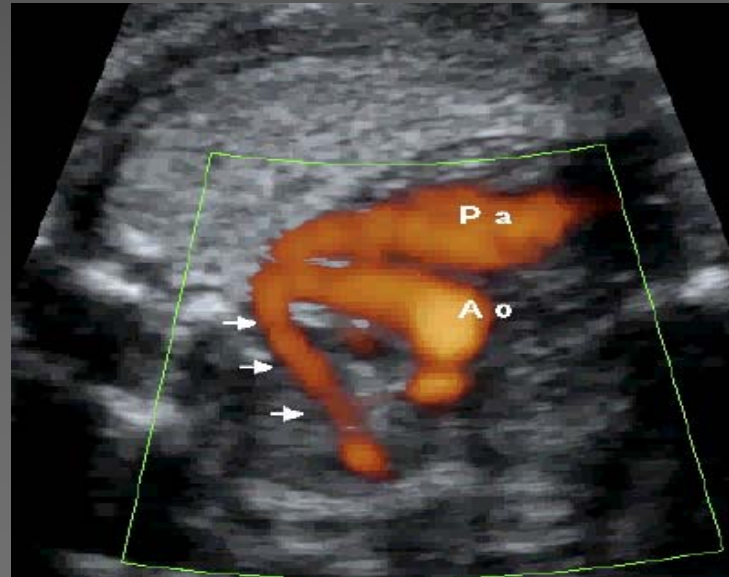
- Fetus lying on right side → *ARSA blue*
- Fetus lying on left side → *ARSA red*
- Do not be misled by azygos-SVC connection



ARSA – *How to look for it*

- Three-vessel view
 - Fetus lying on right side

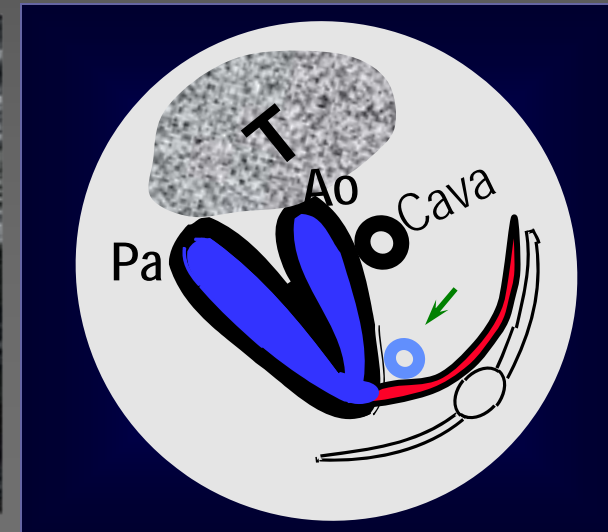
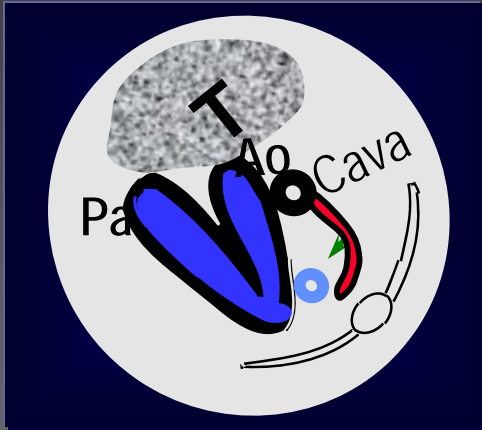
➔ *ARSA blue*



ARSA – *How to look for it*

- Three-vessel view
 - Fetus lying on left side

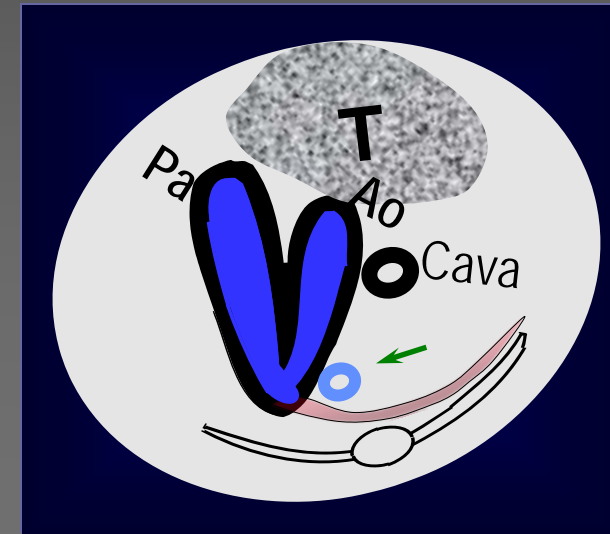
➔ *ARSA red*



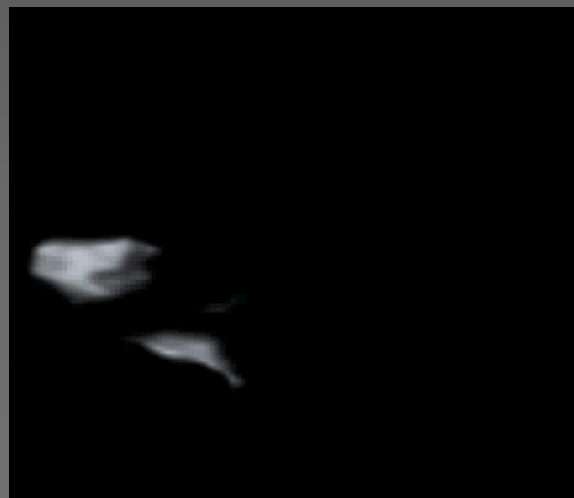
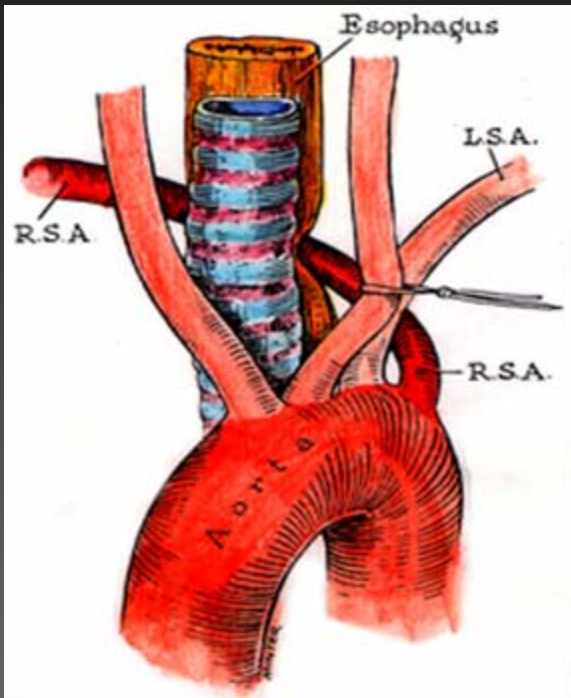
ARSA – *How NOT to look for it*

➤ Three-vessel view

- Fetus lying with spine posterior
- ARSA at 90° with insonation beam → no flow detected at CD

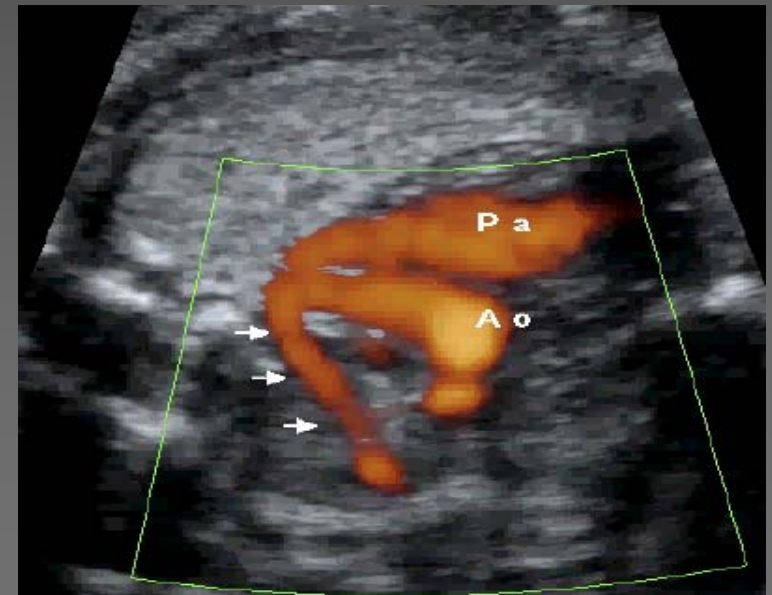


ARSA – *4D B-flow diagnosis*



ARSA – *Conclusions*

- Simple enough to be actively searched on 3vv
- In case of detection, the LR is probably high enough to warrant karyotyping, also if isolated
- Let alone if associated with other strong markers such as NB- or NF, or CHD

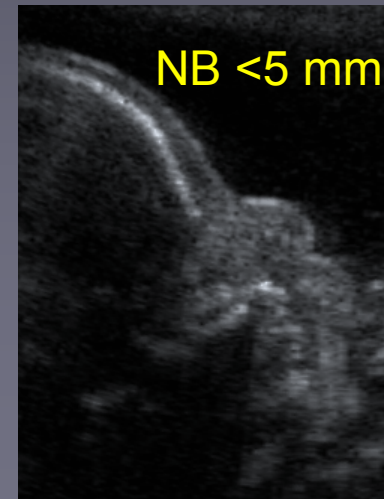
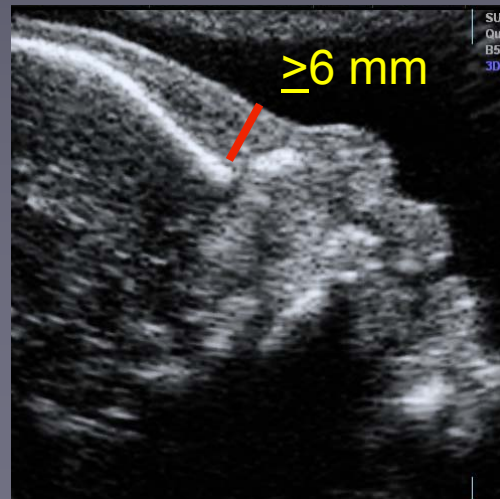
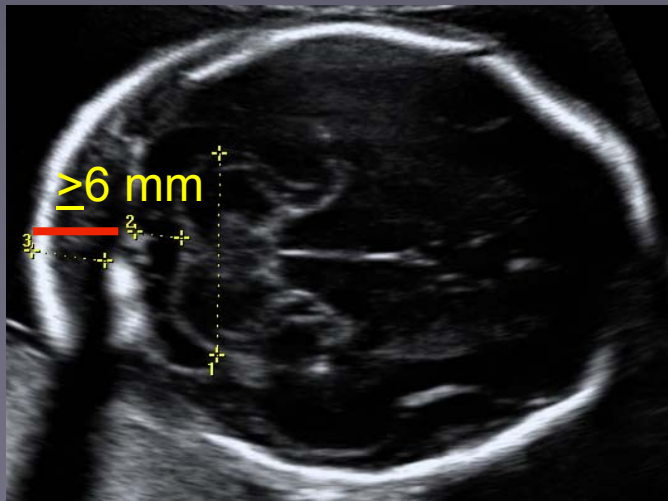


Screening for Trisomy 21

Second trimester features of chromosomal defects

Minor abnormalities or soft markers

- They are common. Not associated with handicap. Invasive testing has major implications
- Estimated risk for trisomy 21: *a priori* risk X LR of the isolated marker:
 - **About 1:** choroid plexus cysts, echogenic endocardiac foci, pyelectasia, short femur
 - **About 10:** nuchal (or prenasal?) edema, hypoplastic nasal bone & ARSA?



Thank you