**Structural foetal evaluation**
Including foetal echocardiography & foetal neurosonography

This protocol is a translation with some modifications of a protocol developed in the University Medical Centre, Utrecht, together with its satellite ultrasound clinics between 2010 and 2013, and adapted for use in South Africa. It is a guide to common conditions, not a foetal medicine textbook. Although it has been scrutinized by different professionals, please use this with discretion and let us know if you find any inaccuracies, discrepancies or new insights.

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**Orientation**

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</table>
| **Orientation** | • Number & position of foetuses  
• Foetal heart activity  
• Foetal movements  
• Amniotic fluid  
• Placental position  
• Cord insertion  
• Umbilical vessels |


Central nervous system

Axial:

a) Transventricular
   - Evaluation:
     - Skull oval shape
     - Symmetrical midline echo
     - Falx central
     - Cavum septum pellucidum 1/3 from front (always visible 16–37w)
     - Anterior & poster horns lateral ventricles
   - Measurements:
     - Head Circumference (HC): ellipse on outside of skull (excluding soft tissue) (Chitty curves)
     - Ventricular atrium in distal hemisphere (<10mm)

b) Transthalamic
   - Additional evaluation:
     - Thalami
     - Hippocampal gyrus

c) Transcerebellar
   - Additional evaluation:
     - Cerebellar hemispheres & vermis
   - Measurements:
     - Transverse cerebellar diameter
     - Cisterna magna (2-10mm)

Measurement ventricular atrium
Coronal (a-c via ant fontanel)

a  Transfrontal
   o  Interhemispheric fissure
   o  Frontal lobe cortex anterior to ventricles
   o  Orbitae
   o  Sphenoid

b  Transcaudate
   o  Genu corpus callosum
   o  Cavum septi pellucidi
   o  Anterior horn lateral ventricles
   o  Nucleus caudatus
   o  Sulcus Sylvius

c  Transthalamic
   o  Thalami
   o  Thirde ventricle
   o  Atrium lateral ventricle met choroid plexus

d  Transcerebellar (via post fontanel)
   o  Achterhoorn lateral ventricles
   o  Tentorium
   o  Cerebellum hemispheren & vermis

Sagittal

a  Mid sagittal
   o  Corpus callosum
   o  Cavum septi pellucidi
   o  Brain stem, pons
   o  4th ventricle
   o  Vermis

b  Parasagittal
   o  Lateral ventricle
   o  Choroid plexus
   o  Periventricular weefsel
   o  Cortex
Spine

Axial plane cranial to transventricular plane for evaluation cortical development

Sagittal till sacrum; skin intact
Coronal if risk skeletal abnormality (hemivertebrae)

In case of spina bifida:
Look for associated abnormalities.
Consider karyotyping; especially in presence of associated abnormality (5% chromosomal abnormality).

Highest lesion document with lowest rib visible
(quote height as lowest intact vertebra)

Encephalocele
Prognosis depends on:
- content (e.g. ventricle / nothing), asymmetry
- Associated malformation (present in 40% aanwezig) (e.g chromosomal, Meckel Gruber: occipital encephalocele, renal dysplasia, postaxial polydactily)

Ventriculomegaly
Ventriculomegaly is a description, geen diagnosis; try to get to a differential / working diagnosis.

Diagnosis van ventriculomegaly:
- Measurement ventricular atrium; >10mm = ventriculomegaly
  - Remember:
    - 10mm = 4 standard deviations above mean
    - Proximal hemisphere not (always) well visible
    - Boys have bigger ventricles than girls
  - Isolated ventriculomegaly:
- 11-12mm (mild ventriculomegaly): Prognosis good (98% survival, of whom >90% normal development)
- 13-15mm (moderate ventriculomegaly): 80% survival of whom 75% normal development
- > 15mm (severe ventriculomegaly): 33% survival of whom 60% normal neurological development
  - Good prognosis: boy, ventricle size normalizes
- Associated signs:
  - "Dangling" of choroid plexus (> 3mm between choroid plexus and medial ventricle wall)
  - Hydrocephalus = combination obstruction & increased intracranial pressure (increased HC & PI mca)

Differential diagnosis:
- Impaired cerebrospinal fluid circulation:
  - Abnormal posterior fossa:
    - Chiari malformation (neural tube defect)
    - Persisting Blake’s pouch (large cisterna magna)
    - Dandy-Walker malformation (high tentorium – evaluate sagittal / coronal & 3D)
  - Bleeding (clot visible in ventricle, ventricle wall echogenic, often asymmetrical)
  - Aqueduct stenosis (small 4th ventricle) (diagnosis at exclusion)
- Ex vacuo ventriculomegaly:
  - Corpus callosum agenesis (colpocephaly, midsagittal complete / partial agenesis, Doppler evaluation of pericallosal arteries)
  - Infection (CMV: periventricular echogenicity with/ without cysts; echogenicities in parenchyma, intraventricular adhesions, abnormal gyral development, cerebellar hypoplasia & echogenicities)
  - Lissencephaly
- Other
  - Holoprosencephaly
  - Porencephaly / schizencephaly
  - Hidranencephaly

Thus in case of ventriculomegaly:
- Look for extracranial abnormalities (present in 1/3; regardless of degree of ventriculomegaly); complete neurosonography
- Karyotype (risk chromosomal abnormality 2% in case of mild ventriculomegaly or LR 7.9, 10% in moderate / severe vm)
- TORCH, Parvo if suspicion according to history / imaging
- Screening anti-thrombocyte antibodies if bleeding suspected
- Consider MRI.
- Follow-up: repeat US after 2w; if stable, repeat /2w from 30w. At repeat US: measure atrium, HC, mca Vmax & PI, (sup sagit sinus (abnormal indien pulsations disappear; PI < 0.1)
- Consider delivery if dramatic increase ventriculomegaly or abnormal Dopplers

Holoprosencephaly
Types:
- alobar: no midline
- semi-lobar: partial fusion thalami
- lobar: absent csp

Causes:
- monogenic: syndromal / non-syndromal
- chromosomal 25-50% (trisomy 13, 18, triploidy)
- teratogens (diabetes, alcohol)

Recurrence 10% (highest of all intracranial abnormalities)
Genetic counselling important.
**Posterior fossa abnormalities**

Characteristics of normal posterior fossa:

- Cisterna magna ≤ 10 mm
- TCD normal for gestational age
- Normal cerebellar anatomy:
  - Vermis + hemispheres
  - No communication between 4\textsuperscript{th} ventricle & cisterna magna

Differential diagnosis in case of increase fluid cisterna magna:

- Tentorium high (NB sagittal view & 3D!)
  - Dandy-Walker malformation: triad of large posterior fossa, raised tentorium, complete / partial aplasia vermis & cystic dilation 4\textsuperscript{th} ventricle
- Tentorium normal:
  - Normal anatomy & biometry cerebellum and vermis:
    - Hydrocephaly; rotation vermis
    - DD megacisterna magna, arachnoid cyst, persisting Blake’s pouch (see article Volpe; measure angle between vermis & brain stem)
  - Normal anatomy, biometry abnormal:
    - Generally small: cerebellar / pontocerebellar hypoplasia
    - Focally small: dysplasia / ischemia / bleeding
  - Anatomy abnormal:
    - Complete / partial vermis aplasia
    - Rhombencephalosynapsis

In case of cerebellar abnormalities & hydrocephaly: beware of lissencephaly!

Measure brainstem-vermis (1) & brainstem-tentorium (2) angle:
**Face**

<table>
<thead>
<tr>
<th>Sagittal:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profile – note forehead, nasal bone, maxilla, upper &amp; lower lip, tongue, mandible. Corpus callosum and vermis visible if midsagittal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Axial:</th>
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<tr>
<td><img src="image.png" alt="Axial Image" /></td>
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<table>
<thead>
<tr>
<th>Coronal:</th>
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<tbody>
<tr>
<td>- Orbitae + lenses</td>
</tr>
<tr>
<td>- Nostrils</td>
</tr>
<tr>
<td>- Upper lip</td>
</tr>
</tbody>
</table>
Facial lines & angles:
Frontal bone in line or slightly (<3.6mm after 27w) in front of facial profile line (through nasion & anterior border mandible)
MNM angle (other line: front of maxilla & nasion) 10 – 17°

Cleft:
- Most important question: associated abnormalities? (present in about 50%)
- Cleft:
  - Uni / bilateral?
  - Lip / jaw / palate? (more nasal deviation if cleft jaw & palate)
- Risk of chromosomal abnormality:
  - No other abnormalities: 1-2% (especially if bilateral & palate; esp. 22q11 & trisomy 21)
  - Other abnormalities: 50% (especially trisomy 18, 13, 21)
- 3D images:
  - Start: head extended, scan from below (avoid shadow from palate & maxilla)
  - Rotate to standard (A=coronal, B=sagittal, C=axial)
<table>
<thead>
<tr>
<th>Render left to right for profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
</tr>
<tr>
<td>Render down to up for palate</td>
</tr>
<tr>
<td><img src="image2.png" alt="Image" /></td>
</tr>
</tbody>
</table>
**Thorax**

**Sagittal:**
- Shape thorax
- Echogenicity lungs
- Diaphragm (sagittal); heart above, stomach below

**If possible skeletal abnormality:**
- Measure thorax circumference (TC) (axial)
- (Scapulae length measure)
- (Claviculae length measure)
- Shape (& number) ribs

**Lungs**

Echogenic lesion:
- CHAOS (congenital high airway obstruction) – bilateral echogenic lungs, low diaphragm, poor prognosis
- Tracheal / bronchial obstruction – can be transient
- CPAM: microcystic / macrocystic / mixed
  - Antenatal progress:
    - 20% smaller
    - 40% unchanged
    - 10% bigger; mediastinal shift with risk of polyhydramnios, pulmonary hypoplasia, hydrops
  - Therefore US every 4 weeks; earlier if symptomatic
  - Aspiration macrocysts can be considered if complications arise
- Pulmonary sequester
  - Appearance like microcystic CPAM, but blood supply from aorta
  - Intra / extralobular; above or below diaphragm
  - Risk of cardiac decompensation (recirculation blood aorta – sequester – pulmonary veins – left atrium & ventricle)
  - Therefore US every 2 weeks with attention left ventricular function

Pulmonary agenesis:
- Mediastinal shift
- Usually small residual lung volume
- Beware of scimitar syndrome (together with partial anomalous pulmonary venous circulation) if agenesis right lung, therefore always foetal echocardiography
**Heart**

**General**
Prevalence congenital cardiac abnormality around 8:1000 liveborn. 80% multifactorial origin.

**Technical**
- Motion-mode (M-mode):  
  - foetal heart rhythm  
  - wall thickness

<table>
<thead>
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<th>Measurement</th>
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<tr>
<td>through atrium and ventricle for temporal relationship</td>
</tr>
<tr>
<td>through both ventricles to measure walls</td>
</tr>
<tr>
<td>peed 60/30</td>
</tr>
<tr>
<td>heart rate over 4 cycles</td>
</tr>
</tbody>
</table>

- Pulsed wave doppler:  
  - Flow rate over valves and through large vessels
- Colour Doppler:  
  - patency cardiac connections
  - direction blood flow
  - detection ventricular septal defect
  - evaluation of turbulence and insufficiency

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<th>Abdomen</th>
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<td>Foetal position</td>
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<td>Stomach left</td>
</tr>
<tr>
<td>Aorta anterior and left to spine</td>
</tr>
<tr>
<td>Vein cava inferior right of spine and anterior to the aorta</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Size</th>
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<td>Heart:thorax area ratio normal 1:3</td>
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</table>
### Position (heart axis)
- Angle between:
  - Line from spine to sternum
  - Line through ventricle septum
    - angle is $45^\circ \pm 15^\circ$
- 1st line through left atrium and right ventricle

### 4-chamber image
- Symmetry ventricles and atria
- Right ventricle moderator band
- Crux: septal insertion tricuspid valve more apical
- Crux: septum primum of atrial septum present
- AV-valves & connections

### Interventricular septum
- Patency foramen ovale
- Valve foramen ovale opens into left atrium
- AV-valves & connections
- Pulmonary veins drain into left atrium (low PRF)

### Outflow tracts heart (with colour doppler)

- Watch out for drop out phenomenon (apical approach); lateral approach preferable
- Evaluate with flow (low PRF)
Crossing great vessels
- Aorta and pulmonary artery crossing
Additional:
- Splitting pulmonary artery

Three vessel view
- Equal diameter van pulmonary artery and aorta
- Flow direction similar

Moving clip of about 10 seconds with 4-chamber view & outflow tracts

Aortic & ductal arch
- Coarctatio?
**Long and short axis**
- Front wall aortic root continuous with ventricle septum
- Mitral valve continuous with aorta

**Short axis & left chamber**
- Apple (left chamber) and pear (right chamber)
- Also with flow

**Vein cava inferior and superior**
- In sagittal plane

**Cardial measurements (on indication):**

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<th>Atria</th>
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<tr>
<td>• End systolic (ventricle systole)</td>
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<tr>
<td>• In 4-chamber image: transverse measurement from lateral atrial wall to imaginary line between two parts atrial septum (foramen ovale)</td>
</tr>
</tbody>
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**Ventricles**
- End diastolic
- Transverse: in 4-chamber image, directly below closed valve leaflets
- Length: in 4-chamber image, from apex of ventricle to tip of closed valve leaflets

**Interventricular septum**
- End diastolic
- In 4-chamber image: directly below off-set of closed valve leaflets

**Thickness ventricle wall**
- End diastolic
- In 4-chamber image: directly below off-set of closed valve leaflets

**Aorta**
- End systolic (ventricle systole)
- Short-axis image
- Aorta ascendens directly above sinuses of Valsalva
- Aorta descendens (isthmus) between branch of a subclavia sinistra and connection ductus arteriosus

**Pulmonary artery**
- End systolic (ventricle systole)
- Short-axis image
- Sinotubular junction

**In case of abnormality:**
- Discuss karyotyping; remember 22q11 deletion. Karyotyping strongly recommended in case of AVSD, conotruncal abnormalities or associated abnormalities (e.g., thick nuchal fold or hydrops, radius/thumb/other skeletal abnormalities).
- Cardiac abnormalities commonly occurring in case of 22q11 deletion: tetralogy of Fallot, pulmonary atresia, truncus arteriosus and interrupted aortic arch
**Diaphragmatic hernia**

**General:**
- US image usually abnormal position heart, stomach sometimes visible above diaphragm, position of liver confirm with colour Doppler (sagittal / coronal planes)
- Dd cpam, bronchial or laryngeal atresia, intralobular pulmonary sequester, teratoma
- Look for other abnormalities: 50% associated chromosomal, structural or genetic abnormalities: esp. trisomy 13 & 18, mosaic tetrasomy 12p, therefore always karyotyping)
- Prognosis: 50% survival if isolated diaphragmatic hernia (i.e. 25% survival at diagnosis); improves to 65% if live born
- Worse prognosis: right sided hernia, liver in thorax, small lung-head ratio (LHR) (to calculate: area **contralateral** lung on 4-chamber view in mm⁴ / HC in mm) – see [http://www.totaltrial.eu/?id=6](http://www.totaltrial.eu/?id=6)
- Prediction prognosis:
  - O/E LHR ≥ 25% survival > 60%
  - O/E LHR 15-25% survival 15%
  - O/E LHR < 15% survival unlikely
**Abdomen**

<table>
<thead>
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<th>Abdominal Circumference (AC)</th>
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<tr>
<td>• Axial plane</td>
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<tr>
<td>• Umbilical vein visible 1/3 from anterior abdominal wall</td>
</tr>
<tr>
<td>• Stomach visible</td>
</tr>
<tr>
<td>• Measurement: ellipse around outside diameter (including soft tissue)</td>
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<table>
<thead>
<tr>
<th>Evaluation abdominal wall</th>
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<tr>
<td>• Stomach &amp; bladder filling</td>
</tr>
<tr>
<td>• Bowel</td>
</tr>
<tr>
<td>• Both kidneys, evaluation of echodensity &amp; measurement of pyela if subjectively wide in anterior-posterior diameter:</td>
</tr>
<tr>
<td>- 20w: &lt; 5mm = normal</td>
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<tr>
<td>- 30w: &lt; 10mm = normal</td>
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| Coronal/ sagittal (on indication): |
| measurement length (without adrenal) |

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<thead>
<tr>
<th>Umbilical arteries</th>
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</table>
Kidneys

Pyelectasis:
- pyelum 5-10mm at 20w
  - check for indications of hydronephrosis (dilated ureters and/or calyces), oligohydramnion, thick-walled bladder of increased echodensity kidneys
  - dd double system
  - repeat scan at 32w
- pyelum >10mm at 32w:
  - pyelum 10-15mm:
    - no dilated calyces, echodensity or small cysts (high frequency scanning), normal amniotic fluid, normal bladder: repeat scan after 4w.
    - Dilated ureter; start Monotrim 0.2 ml/kg of 10 mg/ml solution (i.e. 2 mg/kg) daily after delivery. Renal ultrasound d3-10 post partum.
  - Pyelum > 15 mm individualize.

First trimester megacystis
- 7-15 mm length:
  - 20% chance chromosomal abnormalities (esp. trisomy 13, 18)
  - If no chromosomal abnormality, 90% resolution megacystis
- > 15mm:
  - 10% chance chromosomal abnormalities
  - If no chromosomal abnormality, always obstructive uropathy

MCKD:
- unilateral; scan 30 and 34 wk to check healthy kidney
- bilateral: lethal

Polycystic kidneys:
- bilateral, kidneys enlarged; small cysts (echogenic kidneys)
- family history & scan parents?

LUTO (Lower urinary tract obstruction):
- thick-walled bladder, bilateral hydronephrosis & megaureter
- dd megacystis megacolon intestinal hypomotility syndrome (dilated urinary tracts & bowel)
- discuss stent

Omphalocoele
- Prevalence 3-10:10.000
- Physiologic until 11w3d
- Associated abnormalities:
  - cardiac 50%
  - limbs 30%
  - chromosomal 25% (40% @12w, 28% @20w, 15% @40w)
  - polyhydramnion 30%
  - Beckwith-Wiedeman (macrosomia, macroglossia, polycystic kidneys)
- Always: karyotyping and echocardiography

Gastroschisis
- Prevalence 2-4:10.000
- No increased risk of chromosomal abnormalities
- Increased risk of:
  - Bowel complications 10-20%
  - IUGR
  - IUD / foetal distress
  - iatrogenic / spontaneous premature labour
- Mean gestation at delivery 36-37 weeks
- Neonatal survival 90-95%
**Skeleton and limbs**

**Femur length (FL)**
- Skin thigh parallel to femur
- Measure only bony part of diaphysis without cartilage of epiphysis

**Limbs**
- Upper and lower limbs; 4 x 3 bones
  - Presence & position hands and feet
  - Stand handen and voeten
  - Fingers count (picture with fingers stretched or in neutral position)

If risk skeletal abnormality:
- Also measure humerus, radius, ulna, tibia, fibula & foot length
- Measure both left & right if visually suspicious of different length
- Count toes

**Extended evaluation skeleton**

**When?**
Family history skeletal problem
Abnormal findings:
- Abnormal shape skull
- Club foot (feet)
- Short femur
- Bowed femur, decreased ossification, fractures
- Abnormal ossification

Missing bones

As above (including “at risk”) and additionally:
Thorough search for possible associated abnormalities (esp. renal (cysts?), cardiac, CNS, genitalia

**Vertebral column**
Coronal evaluation to exclude hemivertebrae
3D / 4D (skeletal rendering; High 2; 55°)

**Face**
Cataracts?
Measure BiOD and IOD (binocular & interocular diameter)
Profile with 3D / 4D (multiplane, High 2, 55°), note forehead, mandibula, facial angle
<table>
<thead>
<tr>
<th>Thorax</th>
<th>Placental insufficiency?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement thorax circumference (TC)</td>
<td>Doppler a. umb / a. uterina to exclude (severe) growth restriction due to placentar insufficiency</td>
</tr>
<tr>
<td>Shape sagittal (bell-shaped)</td>
<td></td>
</tr>
<tr>
<td>Claviculae:</td>
<td></td>
</tr>
<tr>
<td>Present? Ossification? Measure length</td>
<td></td>
</tr>
<tr>
<td>Scapulae:</td>
<td></td>
</tr>
<tr>
<td>Shape? Measure length</td>
<td></td>
</tr>
<tr>
<td>Ribben:</td>
<td></td>
</tr>
<tr>
<td>Number? (difficult, try 3D / 4D skelet settings)</td>
<td></td>
</tr>
<tr>
<td>Fractures / ossification, shape</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- TC: AC < 0.6 and FL:AC < 0.16 indicative of lethal abnormality
- Beware of population and individual variation, incorrect gestational age
- Beware of chromosomal abnormalities if short bones (see soft marker protocol)
- If club feet and no other abnormalities (including position conus medullaris low risk of chromosomal abnormality
**Monochorionic twins**

12 weeks  
- NT measurement even if no desire for Down screening  
  - If NT discrepancy < 20% risk of complications such as TTTS < 10%  
  - If NT discrepancy > 20% risk of complications such as TTTS > 30%

**From 14 weeks**  
2-weekly US with evaluation of:  
- Biometry, lie  
- Amniotic fluid: deepest pocket  
- Bladder filling  
- Doppler PI umbilical artery, check for at least 30 sec for intermittent absent/reverse flow  
- From 26 weeks also vmax arteria cerebri media to exclude TAPS (twin anemia-polycythemia sequence)  
- Consult if abnormalities or growth discordance > 20%

20 weeks  
- Anatomical evaluation including echocardiography & neurosonography  
- Cord insertions and distance between cord insertions  
- Check 1st trimester pictures, gender

30 weeks  
- Anatomical evaluation including echocardiography & neurosonography

**Twin to twin transfusion syndrome (TTTS):**

<table>
<thead>
<tr>
<th>Quintero stage</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Polyhydramnion, deepest vertical pocket (DVP) &gt; 80 mm and oligohydramnion, DVP &lt; 20 mm, without additional abnormalities</td>
<td>Follow closely, depending on size / dopplers etc 2x /w</td>
</tr>
<tr>
<td>II. Additional empty bladder donor</td>
<td>Laser</td>
</tr>
<tr>
<td>III. AERDV in umbilical artery, reverse flow ductus venosus or pulsatile flow in umbilical vein</td>
<td>Emergency laser</td>
</tr>
<tr>
<td>IV. At least 1 foetus hydropic</td>
<td></td>
</tr>
<tr>
<td>V. At least 1 IUD</td>
<td>Neurosonography, MRI</td>
</tr>
</tbody>
</table>

**Acardiac / TRAP syndrome**

2 management strategies: all obliteration at 16 weeks (50% overtreatment) or watchful expectancy

Look for poor prognostic factors:  
- Acardiac weight (volume per 3D) > 70% of pump twin or snell growth acardiac  
- Signs of decompensation (abnormal ductus venosus, pulsational flow umbilical vein; tricuspid insufficiency)  
- Polyhydramnion  
- Acardiac anceps (arms present)  
- Ratio diameter umbilical vein pump twin : acardiac  
- High Vmax umbilical vein of pump twin and acardiac

Follow up:  
- US /2w with evaluation poor prognostic factors  
- Poor prognostic factors present, obliteration cord acardiac
**Foetal hydrops**

**Definition**
Fluid collection in more than one foetal compartment (including amniotic fluid)

**Causes**
- Haemolytic anemia due to anti-erythrocyte antibodies
- Cardiovascular: * anatomical abnormalities (e.g. Ebstein anomaly)
  * tachy- of bradycardia
  * cardiomyopathy or myocarditis
  * intracardiac tumors (tuberous sclerosis)
- Chromosomal: * Trisomy 21 or other trisomies
  * Turner syndrome
  * Triploidy
- Infections:
  * Parvo B19
  * CMV
  * toxoplasmosis
- Anaemie foetus due to α-thalassemia
- Pulmonary:
  * CPAM
  * diaphragmatic hernia
  * extralobar pulmonary sequester
  * congenital hydro- or chylothorax
- Placenta and cord:
  * chorangioma
  * foeto-maternal transfusion
- TTTS
- Cystic hygroma with or without aneuploidy
- Metabolic disturbances, esp consanguinous relationships
- Noonan syndrome
- Sacrococcygeal teratoma

**Diagnosis**
- Blood group, rhesus and irregular antibodies
- Kleihauer
- Hb-electrophoresis if possible thalassemia
- Infection serology: Parvo B19, CMV, toxoplasmosis
- Detailed US including echocardiography
- Dopplers: a umbilicalis, a cerebri media with Vmax, ductus venosus, v umbilicalis
- Amniocentese for karyotyping (qfPCR) and PCR a verdening infection
- Refer to clinical geneticist

**Treatment and Prognosis**
- Intra-uterine transfusion if possible foetal anemia
- Poor prognosis if no treatable cause, better prognosis if disappears
Polyhydramnios

**Definition:**
- deepest pocket > 8cm, or
- AFI > 24cm or > p95

**Risk of associated abnormalities:**
- Develops during 2\textsuperscript{nd} trimester: 50%
- Develops during 3\textsuperscript{rd} trimester: no macrosomie: 30%
  Macrosomie presente: rare

**Evaluation:**
- Serology: TORCH, Parvo B19, irregular erythrocyte antibodies
- Detailed US, with attention to:
  - Heart
  - Face (cleft, retrognathia)
  - Limbs & movement
    - Club feet: poor prognosis (dd trisomy 18 / muscular dystrophy / SMA); evaluation parents for possibly muscular dystrophy (clinical genetics)
- If macrosomia: GTT
- If development in 2\textsuperscript{nd} trimester; or 3\textsuperscript{rd} trimester without macrosomia:
  - Foetal echocardiography
  - Karyotyping
    - Always if other abnormalities
    - 5% risk if no other abnormalities esp. trisomy 21/18
  - Postnatal evaluation paediatrician (dd tracheo-oesophageal fistula)
**Soft markers**

**Definition:**
- Non-specific, often transient incidental finding
- In itself no effect on pregnancy outcome
- More commonly seen in fetuses with chromosomal and other abnormalities

**Soft markers:**
Group 1: mainly associated with chromosomal abnormalities

<table>
<thead>
<tr>
<th><strong>Echogenic focus (trisomy 21)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Plexus cysts regardless of size; uni-of bilateral (trisomy 18)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Group 2: associated with chromosomal and other abnormalities

<table>
<thead>
<tr>
<th><strong>Nuchal fold &gt; 6mm</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image2.png" alt="Image" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Echogenic bowel grade III (more echogenic than bone with decreased gain)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3.png" alt="Image" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mild ventriculomegaly (10-12mm atrium)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Group 3: mainly associated with non-chromosomal abnormalities

<table>
<thead>
<tr>
<th><strong>Pyelectasis &gt;5mm in anterior-posterior direction</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image5.png" alt="Image" /></td>
</tr>
</tbody>
</table>
Single retrospective study:
- If PT:NB > 1.0, “all” trisomy 21
- If PT:NB < 0.8, “all” normal

Policy:
- 20 week scan is a poor screening method for chromosomal abnormalities
- Isolated choroid plexus cyst or single umbilical artery in the absence of other abnormalities: risk Down syndrome unchanged (LR=1)
- Others: offer risk calculation if wanted; given that compared to first trimester screen, second trimester risk evaluation is less well validated, lower sensitivity, higher false positive
- Isolated pyelectasis: see renal section
- Absence of soft markers reduces risk by about 60%

<table>
<thead>
<tr>
<th>Soft marker</th>
<th>Associated abnormalities</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuchal fold &gt; 6mm LR = 17</td>
<td>Cardiac abnormalities, Infection, Genetic syndromes</td>
<td>Repeat echocardiography at 30 – 32w</td>
</tr>
<tr>
<td>Echogenic bowel LR = 6.1</td>
<td>Retroplacental bleeding, CMV infection, IUGR (also dopplers a. uterina), Bowel pathology, Cystic fibrosis</td>
<td>Genetical counseling CF, Repeat US at 26 weeks (growth &amp; bowel)</td>
</tr>
<tr>
<td>Mild ventriculomegaly LR = 7.9</td>
<td>Impaired circulation CSF: abnormal posterior fossa, bleeding, aqueduct stenosis, Ex vacuo ventriculomegaly: corpus callosum agenesis, infection, lissencephaly</td>
<td>Verwijzing WKZ - zie artikel 2 protocol CZS</td>
</tr>
<tr>
<td>Femur &lt; P3 LR = 2.7</td>
<td>Skeletal dysplasia, IUGR (also dopplers a. uterina)</td>
<td>Fetal growth</td>
</tr>
<tr>
<td>Echogenic focus LR = 2.4</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Plexus cysts LR = 1</td>
<td>Association met trisomy 18, LR = 7.1</td>
<td>None</td>
</tr>
<tr>
<td>SUA LR = 1</td>
<td>Cardiac abnormalities, Renal abnormalities, IUGR (also dopplers a. uterina)</td>
<td>Fetal growth</td>
</tr>
</tbody>
</table>
**Chromosomal abnormalities at prenatal ultrasound abnormalities:**

**Important:**

- Percentages are given as guide for counseling and do not replace genetic counseling
- Take into account:
  - Background risk, e.g. previous pregnancies, repeated miscarriages, subfertility, maternal (and paternal) age, first trimester screening
  - Family history: repeated miscarriages, stillbirth, mental retardation, consanguinity
  - Parental karyotyping higher resolution than prenatal karyotyping
  - Gestational age: higher percentage earlier in pregnancy due to spontaneous foetal demise
  - Explicitly discuss large chance of normal karyotyping
  - Discuss follow-up in case of abnormal finding (e.g. TOP / palliative care for lethal chromosomal abnormality); and normal chromosome: sometimes small residual risk (e.g. soft markers); sometimes genetical counseling very important (e.g. holoprosencephaly)
- Table only mentions most commonly occurring chromosomal abnormalities, no other syndromes / genetic mutations / teratogenic infections
- Array CGH abnormalities found in about 5% of fetuses with chromosomal abnormalities with normal classical karyotyping
- Where possible distinction between isolated finding, or finding in presence of other visible abnormalities

<table>
<thead>
<tr>
<th>US abnormality</th>
<th>Risk of chromosomal abnormality if isolated</th>
<th>Risk of chromosomal abnormality if isolated other abnormalities present on ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neural tube defect</td>
<td></td>
<td>Trisomy 13 &amp; 18, triploidy, translocation</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>5%</td>
<td>2% if mild (10-12mm)</td>
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<tr>
<td></td>
<td></td>
<td>10% if &gt;12mm</td>
</tr>
<tr>
<td>Holoprosencephaly</td>
<td>25-50%</td>
<td>trisomy 13, 18, triploidy</td>
</tr>
<tr>
<td>Corpus callosum agenesis</td>
<td>20%</td>
<td>trisomy 13, 18</td>
</tr>
<tr>
<td>Dandy-Walker malformation</td>
<td>15-30%</td>
<td>trisomy 9, 13, 18, 18, triploidy, deletions &amp; duplications</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>Trisomy 13, 18, 22, deletions (4p-, 5p- 18p-, 18q-)</td>
<td></td>
</tr>
<tr>
<td><strong>Face:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleft</td>
<td>1-2%</td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td>22q11</td>
<td>Trisomy 13, 18, 21; 4p, 4p-, 4q, 7q, 22q11</td>
</tr>
<tr>
<td><strong>Thorax:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diaphragmatic hernia</td>
<td>10-20%</td>
<td>trisomy 18, 13, 21 also 4p-, 15q-, tetrasomy 12p (Pallister Kilian, only in amniotic fluid, not in blood or chorionic villi)</td>
</tr>
<tr>
<td>CPAM</td>
<td>No increased risk</td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>3%</td>
<td>Minor (e.g. soft markers, IUGR) 24%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Major / suspect (e.g. hydrops, abnormalities suggestive for trisomy) 62%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trisomy 13, 18, 21, 45XO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22q11 deletion esp with ToF (10-20%), pulmonary atresia (10%), truncus arteriosus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(20-35%), interrupted aortic arch (50-60%), malalignment VSD (30%)</td>
</tr>
<tr>
<td>US abnormality</td>
<td>Risk of chromosomal abnormality if isolated</td>
<td>Risk of chromosomal abnormality if isolated other abnormalities present on ultrasound</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Abdominal wall:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omphalocele</td>
<td>25% According to gestational age: 40% at 12w; 28% at 20w; 15% at 40w Trisomy 18, 13, 21, 45X, triploidy</td>
<td></td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>No increased risk</td>
<td></td>
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<tr>
<td><strong>Gastro-intestinal:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tracheo-oesophageal fistula</td>
<td>10-20% Trisomy 21 &amp; 18,22q11</td>
<td></td>
</tr>
<tr>
<td>Duodenal atresia:</td>
<td>30-40% trisomy 21, 9</td>
<td></td>
</tr>
<tr>
<td>Jejenum / ileum atresia</td>
<td>No increased risk</td>
<td></td>
</tr>
<tr>
<td>Echogenic bowel grade III</td>
<td>zie soft markers</td>
<td></td>
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<tr>
<td><strong>Urorenal:</strong></td>
<td></td>
<td></td>
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<tr>
<td>LUTO (lower urinary tract obstruction = posterior urethral valves)</td>
<td>12w: megacystis 7-15mm 20%; &gt;15mm 10% 20w: 20% trisomies</td>
<td></td>
</tr>
<tr>
<td>MCKD</td>
<td>No increased risk</td>
<td></td>
</tr>
<tr>
<td><strong>General:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrops</td>
<td>10-35% trisomy 21 &amp; other trisomies; 45X0, triploidy</td>
<td></td>
</tr>
<tr>
<td>IUD &lt; 28w</td>
<td>33% trisomie, 45X; tri/tetraploidy, deletion / translocation</td>
<td></td>
</tr>
<tr>
<td><strong>Soft markers:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild ventriculomegaly</td>
<td>Likelihood ratio (LR) 7,9</td>
<td></td>
</tr>
<tr>
<td>Short femur</td>
<td>LR 2,7</td>
<td></td>
</tr>
<tr>
<td>Nuchal skin &gt;6mm at 20w</td>
<td>LR 17</td>
<td></td>
</tr>
<tr>
<td>Echogenic bowel grade III</td>
<td>LR 6,1</td>
<td></td>
</tr>
<tr>
<td>Echogenic focus heart</td>
<td>LR 2,4</td>
<td></td>
</tr>
</tbody>
</table>