Fetal thoracic abnormalities

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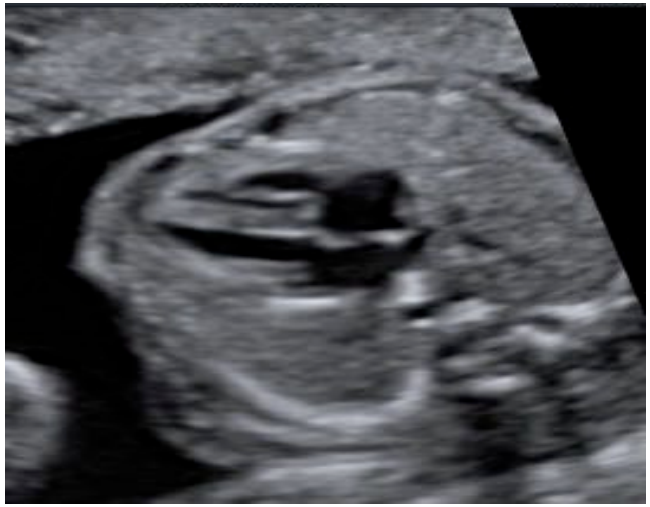
Outline

- Normal fetal chest imaging
- Fetal pleural effusions
- Echogenic lung lesions
  - Solid/cystic
- Congenital diaphragmatic hernia

Normal fetal chest imaging

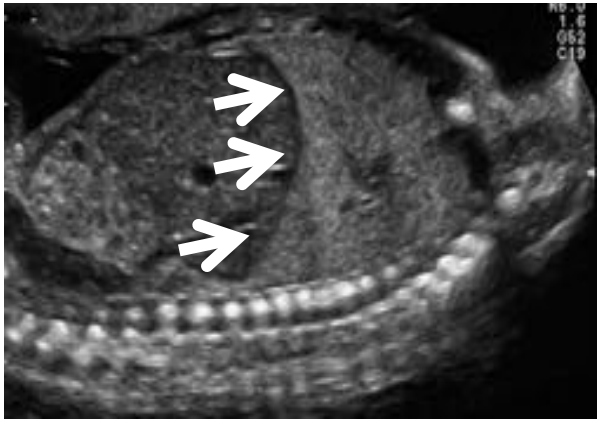
4-chamber view

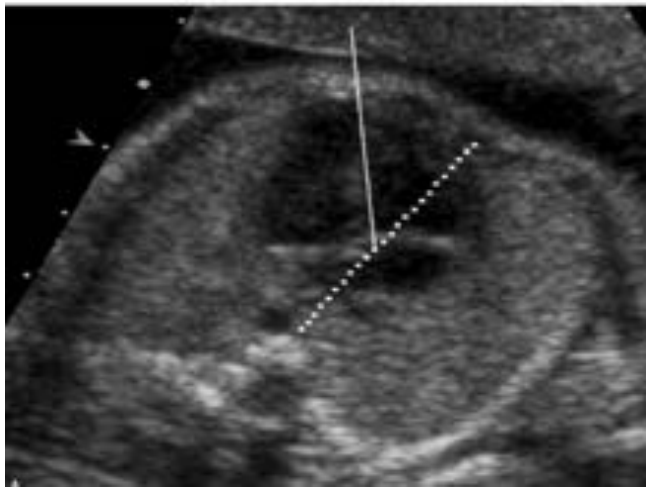
- Axial (single ribs)
- Cardiac axis/mediastinal shift
- Echogenicity (lung>liver)
- Anechoic/cystic structures



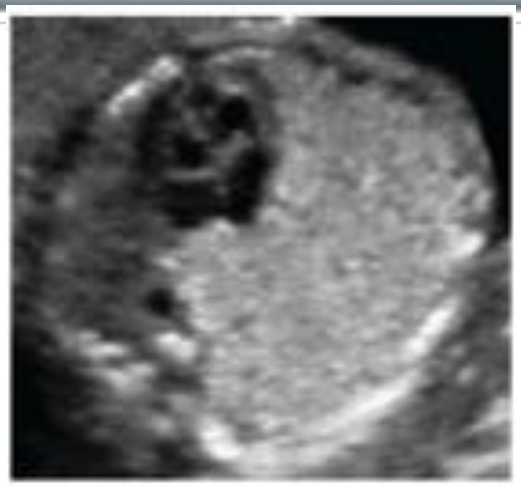
Sagittal view

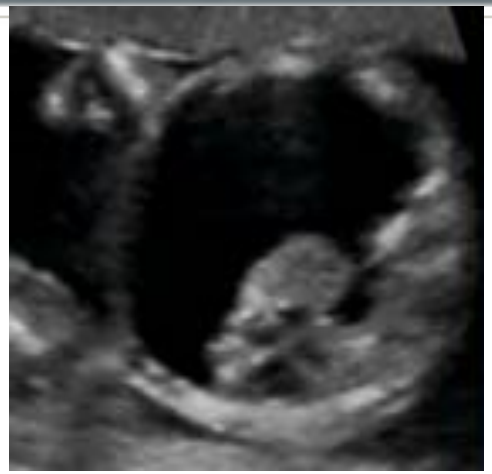
- Hypoechoic/dome-shaped diaphragm



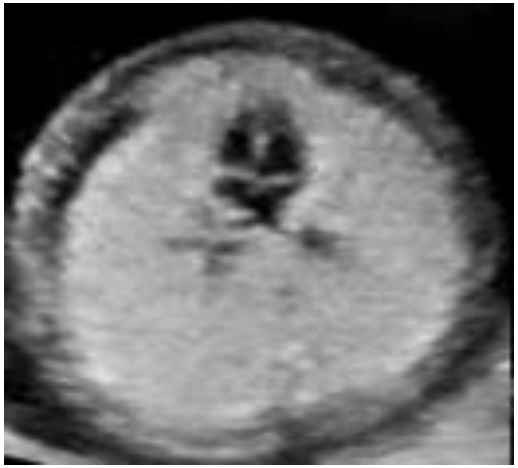


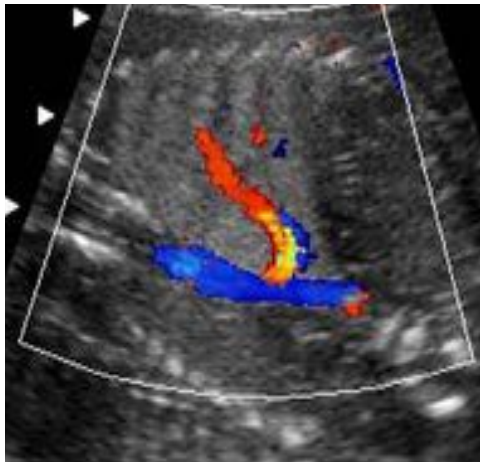
1. Mediastinal shift



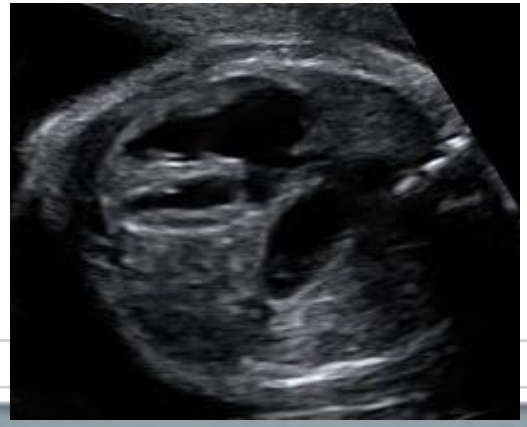


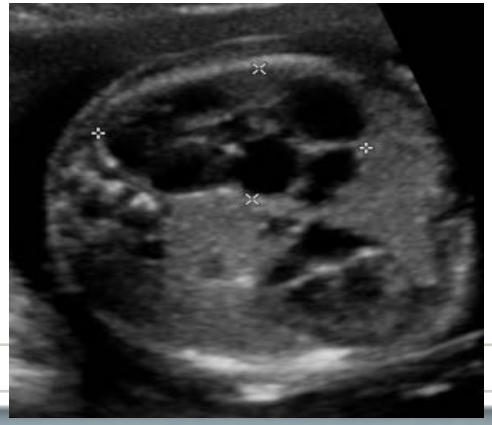
2. Abnormal echogenicity





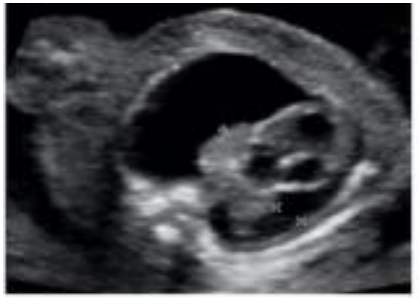
3. Cystic lesions/ fluid collections

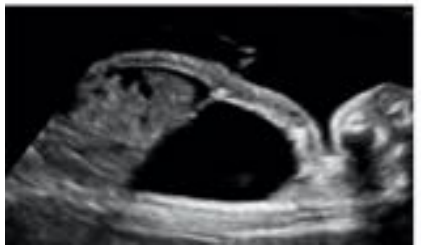




Pleural effusions

Antenatal Evaluation





1: 15 000

Primary effusions (chylothorax)

Exclude secondary causes

- Immune/non-immune hydrops
- Genetic/structural abnormalities
- Infections
- Fetal anemia

Maternal	**Fetal**
CBC, Group & screen, Hb electrophoresis Betke-Kleihauer TORCH, PB_{19} serologies	Detailed anatomical survey • Structural malformations (10-15%) • Congenital infection • Anemia (MCA PSV) Echocardiogram Karyotype, microarray, Noonan syndrome • Aneuploidy ~ 4.5-9.5% (T21, 45 X0) Thoracocentesis/ shunt • Lymphocytes >80%? • Genetic testing, TORCH PCR

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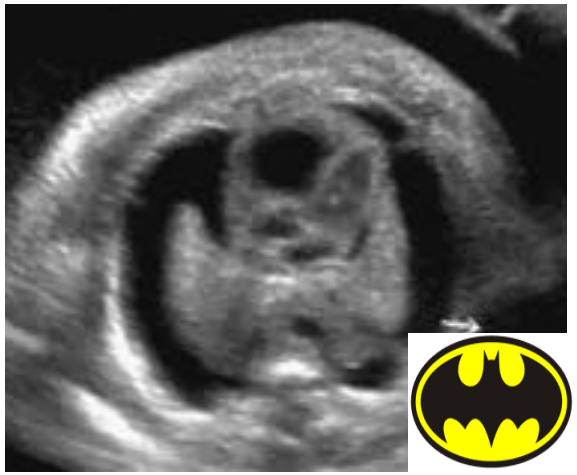
U/S features

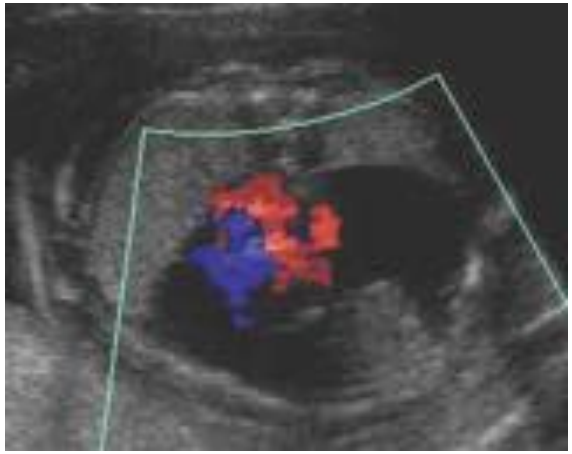
- **Freely floating lungs ("bat wing")**
- **Unilateral vs. bilateral**
- **Mediastinal shift**
- **Hydrops (60-70%)-** 2ry to pleural effusions?
  - Serial progression
  - Upper body edema
  - Pleural fluid> other compartments
  - No placentamegaly/ structural abnormalities

Poor prognostic indicators:

Rapid progression
Significant mediastinal shift
Hydrops
Associated structural/genetic malformations

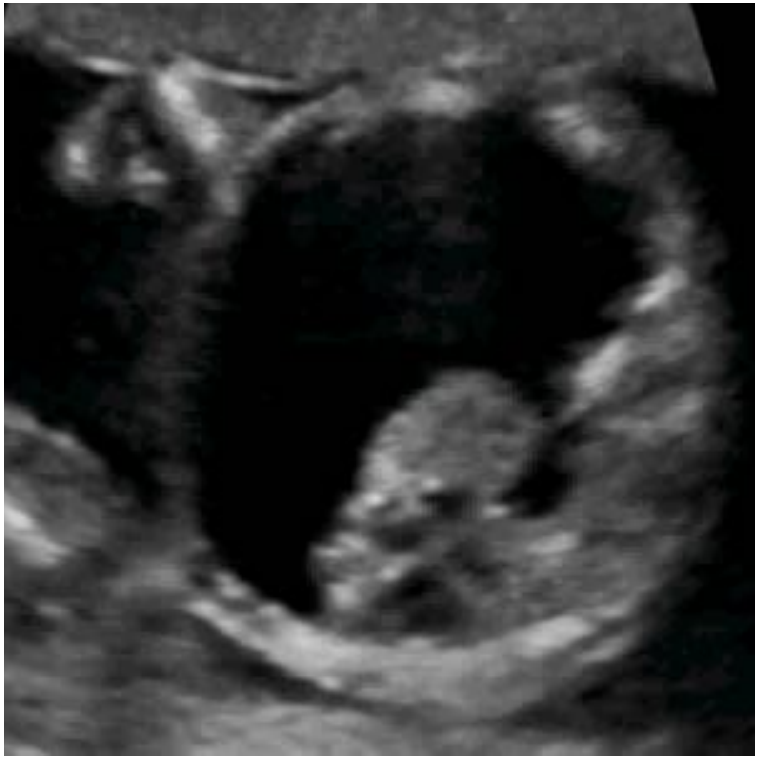


Pleural effusion



Pericardial effusion

Primary pleural effusions: Outcomes



Spontaneous resolution (~20%)[1]

- Small, unilateral, no hydrops

Progression (↑ intrathoracic pressure)

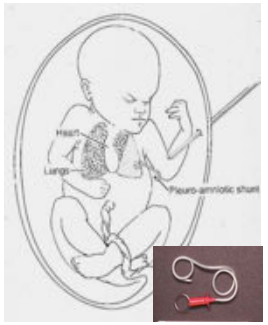
- Pulmonary hypoplasia
  - Predictors? Duration/onset of effusion?
- Esophageal compression
  - Polyhydramnios → PPROM/PTL
- Fetal hydrops
  - Cardiac/mediastinal compression & ↓ venous return→ heart failure → death

Without treatment, overall survival ~60%[2]

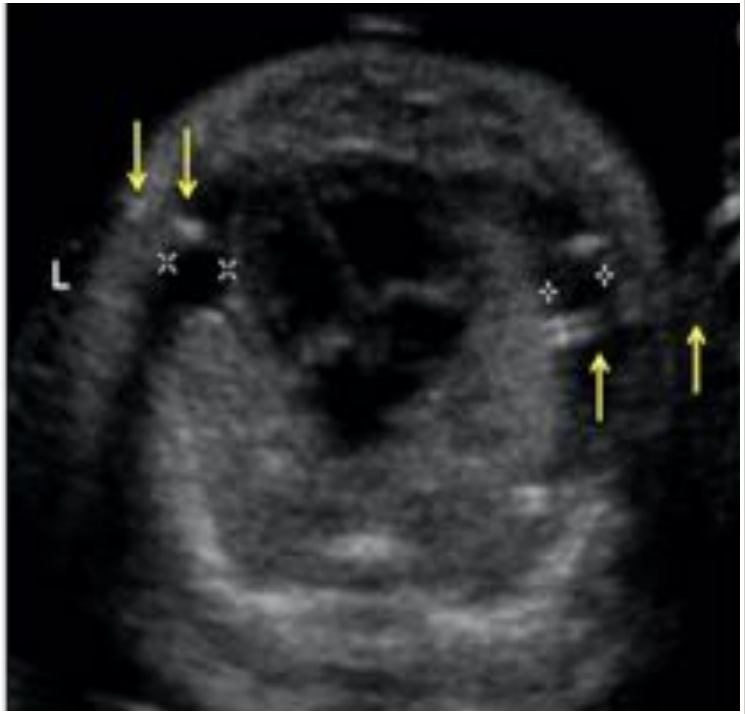
- ~75% in non-hydropic fetuses
- ~ 35% in hydropic fetuses

[1]Aubard et al. Fetal Diagn Ther 1998; 13: 325-33
[2] Rustico et al. Prenat Diagn 2007; 27: 793-799

Management: Primary pleural effusions



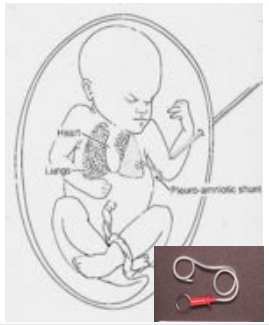
- Expectant management
  - Small, primary effusions
  - Minimal mediastinal shift/ no hydrops
  - **WEEKLY US surveillance**
- Pleural decompression
  - Thoracocentesis (re-accumulate ~75%)
  - Pleuroamniotic shunting (PAS) (↑ survival)
  - *Pleurodesis (0K-432)[2]
- Predictors of survival:
  - Hydrops reversal, GA at delivery



Hydrops *or* severe mediastinal shift, polyhydramnios

[1]Aubard et al. Fetal Diagn Ther 1998; 13: 325-33
[2] Rustico et al. Prenat Diagn 2007; 27: 793-799
[3] O'Brien et al. Fetal Diagn Ther 2015; 37(4): 259-66

Management



Comparison of outcomes between large single-center pleural shunt series for primary pleural effusions.

References	Number of cases		GA at delivery (weeks)	Hydrops resolution %	Perinatal survival		
	Total	Hydropic %			Overall %	Hydropic %	Nonhydropic %
Pettersen et al. (1997) [38]	69	59	36 (23–41)	46	68	46	100
Picone et al. (2004) [37]	47	100	34 (22–40)	89	66	66	–
Smith et al. (2005) [36]	21	76	32 (22–40)	N/A	48	44	60
Rustico et al. (2007) [11]	53	81	N/A	N/A	64	58	90
Yinon et al. (2010) ([12] & unpublished data)	132	62	34 (19–42)	47.5	65.2	38	62
Walsh et al. (2011) [43]	15	60	N/A	N/A	53	33	83
Pellegrinelli et al. (2012) [39]	27	74	31 (27–35)	78	52	47	85
Miyoshi et al. (2013) [44]	15	73	NA	N/A	60	46	100
Total	**335**	**59-100%**	**32.7**	**46-89%**	**48-68%**	**33-66%**	**60-100%**

Predictors of survival:

- **↑ GA at delivery**
- **Hydrops resolution**

Complications (~9%)

- PTB <37 wks 80%
- PPROM 6-15%, chorioamnionitis ~9%
- Shunt dislodgment 7-15%

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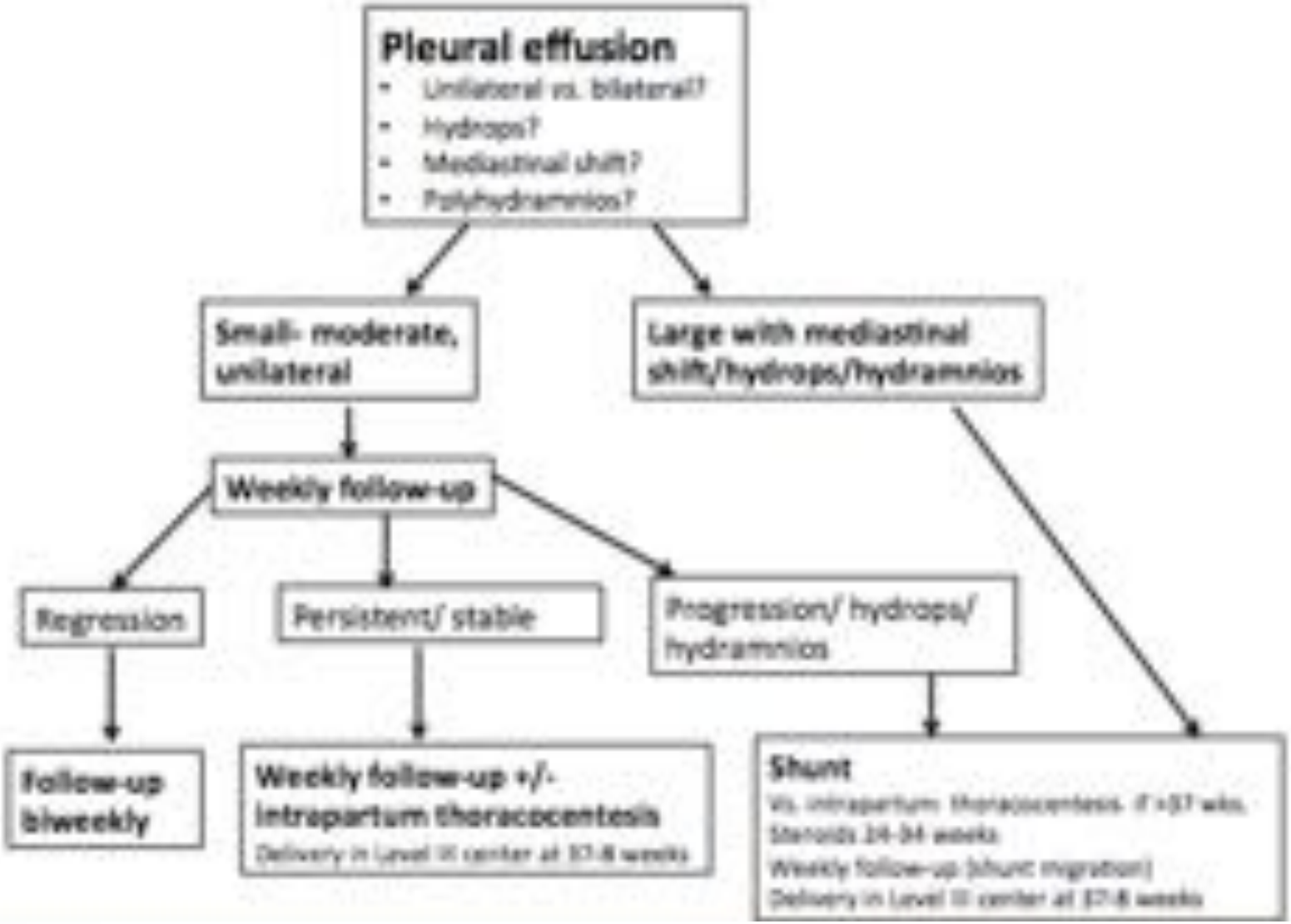
Pleural effusions: Summary



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Echogenic lung lesions

Echogenic lung lesions

Solid lesions	Cystic lesions
Cystic adenomatoid malformation (microcystic)	Cystic adenomatoid malformation (macrocystic)
Bronchopulmonary sequestration	Bronchogenic cyst
Mediastinal teratoma	Mediastinal encephalocele
Rhabdomyoma	Congenital diaphragmatic hernia
Right sided congenital diaphragmatic hernia	Pericardial and pleural effusions
Tracheal/laryngeal atresia	Congenital lobar emphysema

Bush *et al.* Prenat Diagn. 2008; 28: 604-611

Most common lesions:

1. Congenital cystic adenomatoid malformations (CCAM)
2. Pulmonary sequestration (PS)
3. Congenital high airway obstruction (CHAOS)

Although prenatal prediction of pathologic diagnosis (CCAM/ BPS) is poor, management of echogenic lung lesions is similar

CCAM/Congenital pulmonary airway malformation (CPAM)

- Bronchiolar-like airspace proliferation
- Lack normal alveoli/vascular supply
- Tracheobronchial tree communication

Histological (Stocker)[1]

Type I Few large cysts

Type II Multiple small cysts

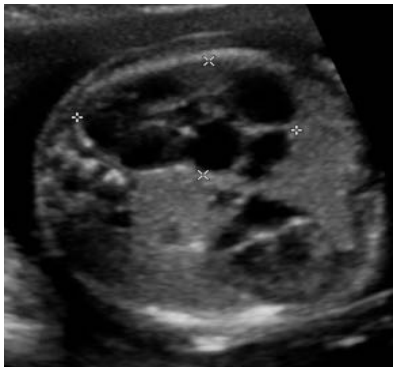
Type III Large "solid" mass

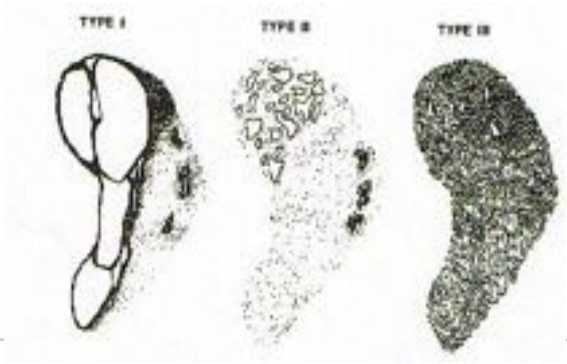
Ultrasound[2]

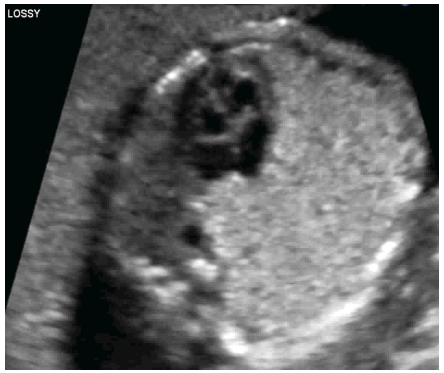
Macrocystic (22%)
- Single/multiple cysts > 5mm

Microcystic (53%)
- Cysts < 5mm/solid echogenic mass

Mixed (~25%)



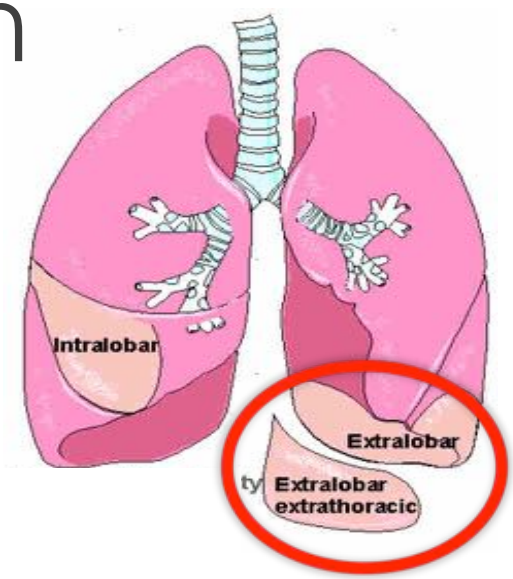


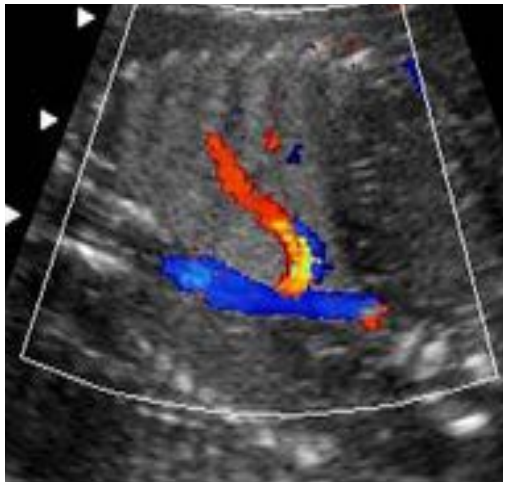


[1] Stocker JT. Hum Pathol. 1977;8(2):155-71
[2] Adzick S. J Ped Surg 1985;20;483

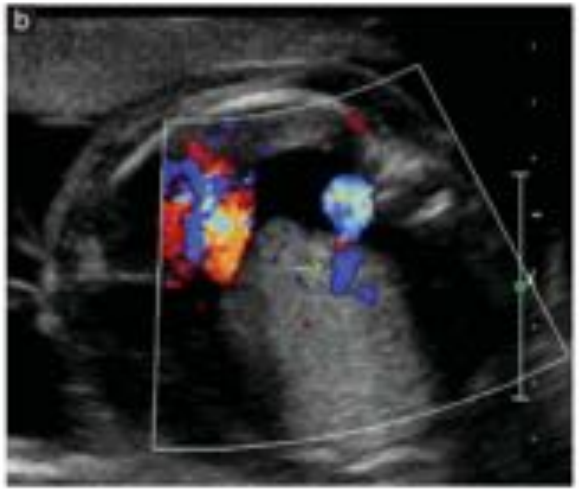
Pulmonary sequestration

- Non-functioning bronchopulmonary tissue
- No communication to tracheobrochial tree
- Solid, triangular, echogenic mass
  - Left>Right
  - Supradiaphragmatic (90%)
- Associated anomalies (CDH*, bronchopulmonary foregut malformations)

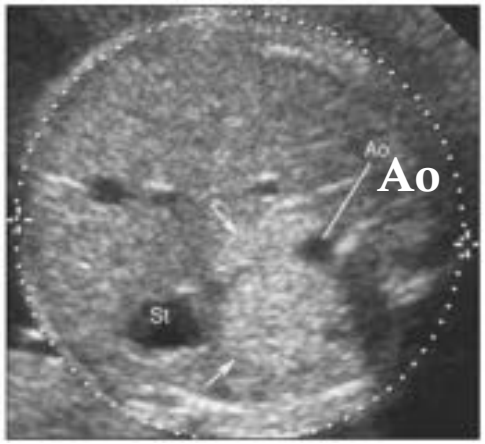




Systemic feeding vessel



Pleural effusion (6-10%)



Subdiaphragmatic PS

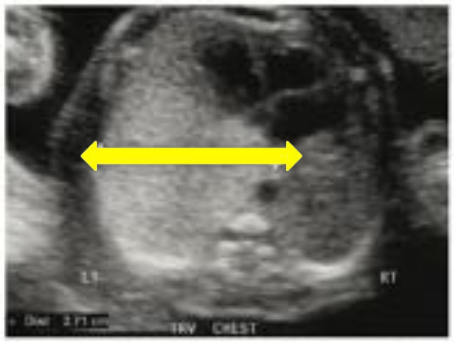
Dhingsa et al. AJR:180, February 2003

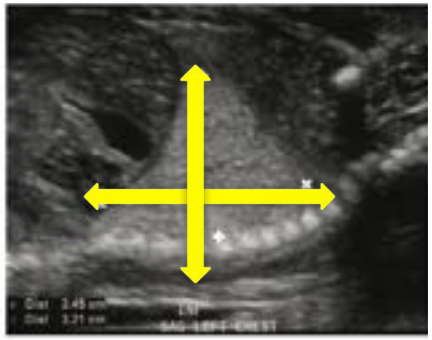
CCAM & PS: Natural history

	Antenatal regression	Overall survival (no treatment)
PS (n=95)	40%	96%
CCAM (n=645)	~30% (mostly microcystic)	97% Postnatal Sx ~60%

Cavoretto et al. UOG 2008; 32:769-783

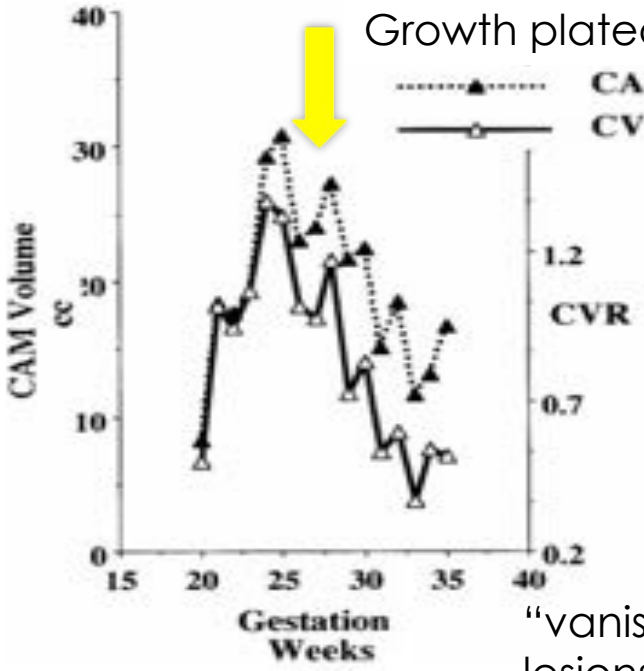
CCAM volume ratio (CVR)





$$CVR = \frac{AP \times TRV \times length \times 0.523}{\text{Head circumference}}$$

(all measurements taken in centimeters)



Growth plateaus 26-8 wks.

"vanishing" lesions 32-4 wks.

CVR ≤ 1.6:
3% risk of hydrops in absence of a dominant cyst*

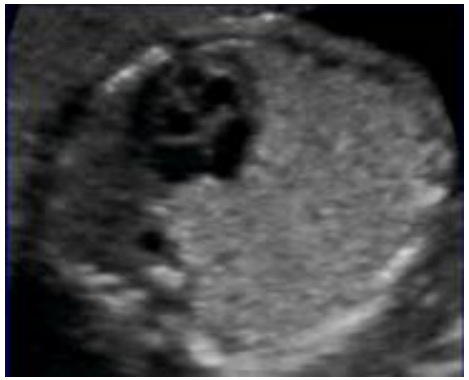
CVR >1.6:
~75% hydrops

***Macrocystic CCAM:**
Differing growth of cystic components & sudden increase in cyst size less well tolerated

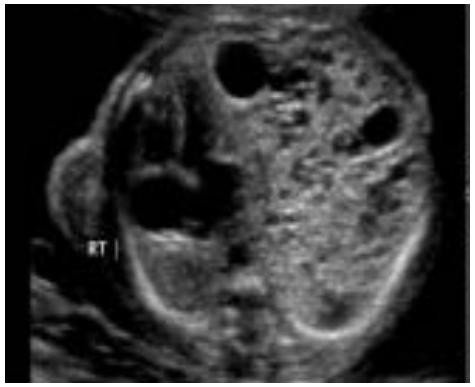
Crombleholme T *et al.* J Pediatr Surg 37:331-338.

US Assessment

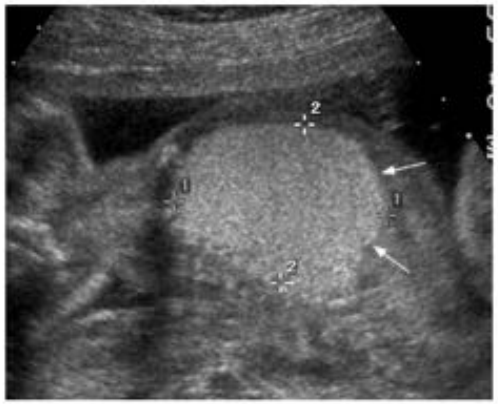
- **Micro- *vs.* macrocystic vs. mixed**
- **Vascularity** (pulmonary vs. systemic)
- **Mass effect**
  - Mediastinal shift
  - Flattening/inversion of diaphragm
  - Polyhydramnios
  - CVR
- **Hydrops**
- **Structural anomalies (*PS)**

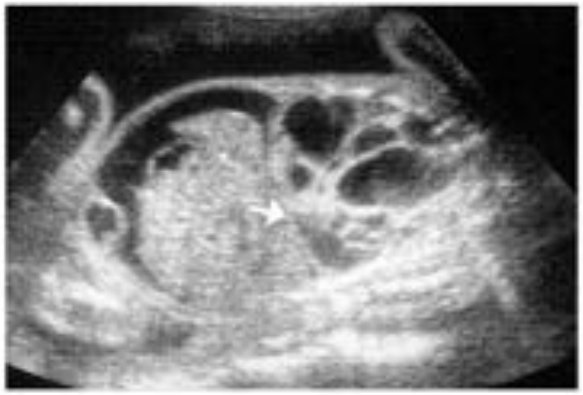


Microcystic

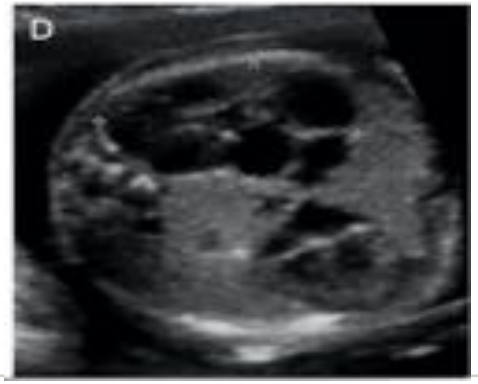


Mixed





Flattening/inversion of diaphragm



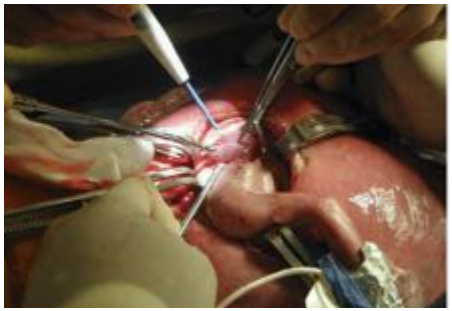
Macrocystic

Prenatal management: CCAM & PS

Hydrops *or* severe mediastinal shift, CVR>1.6, polyhydramnios

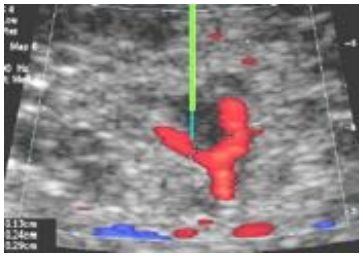
Fetal lobectomy[1]

- Survival 52% (28/54)
- *Risks PPROM, PTL, abruption, pulmonary edema, hemorrhage, uterine rupture/dehiscence



Steroids[2]

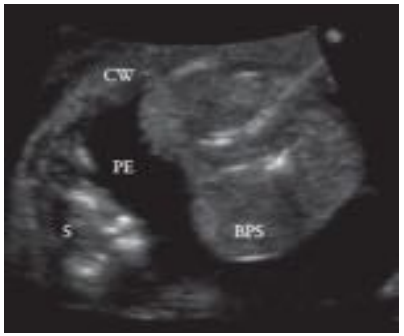
- Induce maturation of pulmonary cells/ interrupt lesion growth
- Survival 93% (single course) vs. 86% (multiple)



600 μ Nd:YAG laser fibre

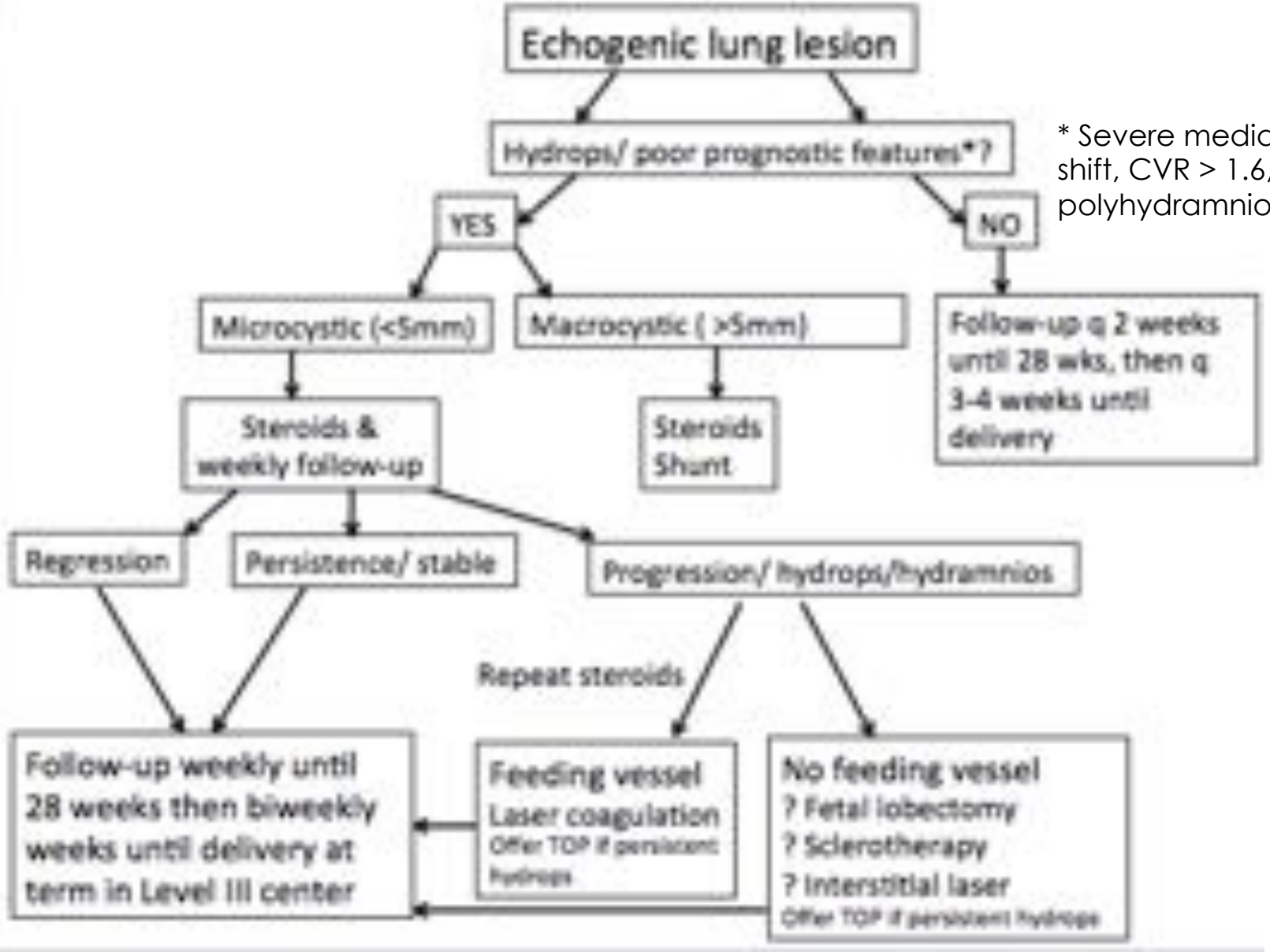
Minimally invasive therapy[3]

- Shunts (macrocystic CCAM, PS + effusion)
- Laser, RFA, sclerotherapy



Radiofrequency ablation (RFA)

[2]Cass et al. J Ped Surg (2011) 46, 292–298 [1]Peranteau et al. J Ped Surg (2016) 51, 28–32; [3]Baud et al. UOG 2013; **42**: 440–448

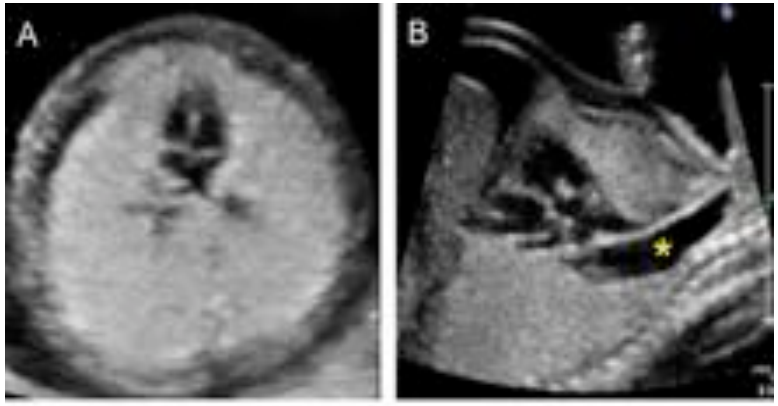


* Severe mediastinal shift, CVR > 1.6, polyhydramnios

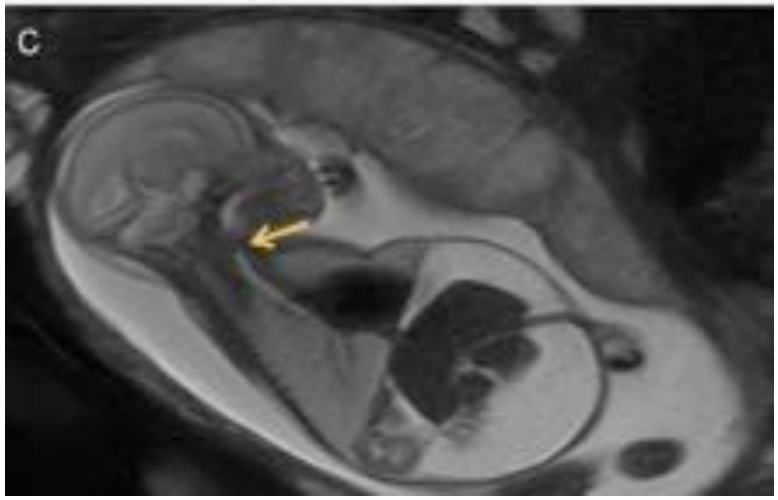
Abbasi N & Ryan G Fetal Therapy 2nd Ed.; Fetal lung pathology (in press) 2019

Congenital High Airway Obstruction (CHAOS)

- Laryngeal/tracheal atresia/ stenosis
- Laryngeal webs/ cysts
- US features:
  - Enlarged, echogenic lungs
  - Dilated tracheobronchial tree
  - Anteriorly, displaced heart
  - Hydrops/polyhydramnios/ "mirror"
- Highly lethal



Central heart Dilated trachea



Inverted diaphragm, ascites

Congenital diaphragmatic hernia

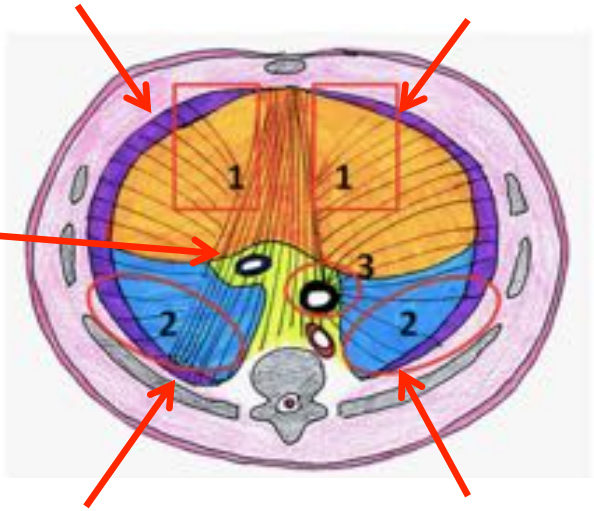
CDH- background

1/2500-1/5000 (*hidden mortality)

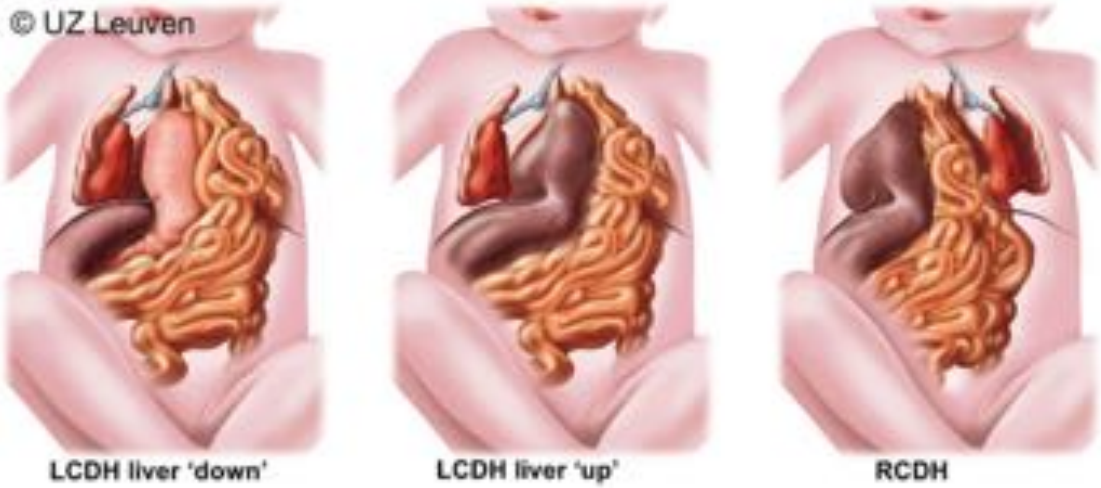
- ~85% left sided
- 13% right sided
- 2 % bilateral
- Rarely: eventration/ complete diaphragmatic agenesis

Anterior Morgagni hernia(12-15%)

Central hiatal hernia (2-5%)



Posterior Bochdalek hernia (70-90%)
Small bowel, stomach spleen, liver



[1]Russo *et al.* Prenatal Diagnosis. 2018;38:629–637

Associated abnormalities

Genetic abnormalities[1]

Chromosomal Anomalies	
1. Aneuploidies	
Tetrasomy 12p (Pallister-Killian syndrome)	CDH, cardiac defects, shortened limb, central nervous system anomalies, craniofacial dysmorphism, nuchal skin edema, skin pigmentation, hydrops, polyhydramnios[11]
Full trisomies	Trisomy 21, 18, 13, 22, 16
Translocation der (22) t(11; 22) (q23; q11)	CDH, cardiac defects, craniofacial dysmorphism, growth restriction[48]
Monosomy 15q	CDH, cardiac defects, growth restriction, pulmonary hypoplasia, facial dysmorphism, clinodactyly and brachydactyly, talipes and a single umbilical artery[12]
Partial deletion/monosomy 4p (Wolf-Hirschhorn syndrome)	CDH, facial dysmorphism, microcephaly, cardiac defects, growth restriction[49]
Deletions	Chromosome 8p23.1, chromosome 1q41-1q42,[14] Xpter-Xp22[15]
Microdeletion syndromes	16p11.2 deletions,[16] 15q24 deletions[17]
2. Mendelian disorders	
GPC3: Xq26 (Simpson-Golabi-Behmel syndrome)	CDH, macrosomia, craniofacial dysmorfism, postaxial polydactyly, hypoplastic nails, developmental delay[18]
IGF2/H19/p57KIP2 and other genes: 11p15.5 Beckwith-Wiedemann syndrome	CDH, macrosomia, omphalocele, macroglossia, neonatal hypoglycemia[19]
HCCS: Xp Microphthalmia with linear skin defects	CDH, cardiomyopathy, microphthalmia, dermal aplasia[59]
PORCN: Xp22 Goltz syndrome	CDH, focal dermal hypoplasia, dental hypoplasia, syndactyly[60]
EFNB1: Xp22 Craniofrontonasal syndrome	CDH, coronal synostosis, hypertelorism; digital anomalies[61]
WT1: 11p13 Denys-Drash syndrome	CDH, nephromegaly, glomerulopathy, growth 90th centile, male pseudohermaphroditism[61]
Syndromes with unknown genes	
Fryn's syndrome	Left-sided CDH, pulmonary hypoplasia, hypoplasia of the distal phalanges and nails, facial dysmorphism, orofacial clefting, hydrocephalus and neuronal heterotopias, cardiac defects, renal dysplasia and genitourinary malformations[62]
Gershoni-Baruch syndrome	CDH, omphalocele and radial ray malformations[63]
Cantrell's pentalogy	Anterior CDH, omphalocele, bifid sternum, ectopia cordis and congenital heart defects as ventricular septal defects and ventricular dilatation[64]

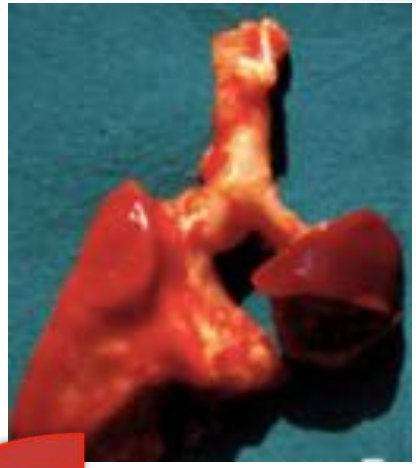
- Isolated ~ 60-70%, survival ~60%
- Associated structural and genetic abnormalities in 30-40%, survival ~15%[1]
  - Cardiovascular (25-50%)
  - GU (5-10%)
  - CNS (1-10%)
  - MSK (1-15%)
  - GI (2-10%)
  - Chest (BPS/CCAM 2-5%)

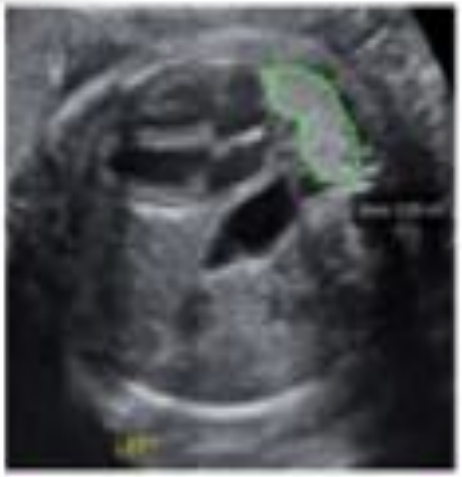
Largest CDH series (n=256 CDH), chromosome & subchromosome abnormalities in ~6%[2]

[1]Russo *et al.* Prenatal Diagnosis. 2018;38:629–637
[2] Yu *et al.* J Med Genet 2012; 49: 650-59

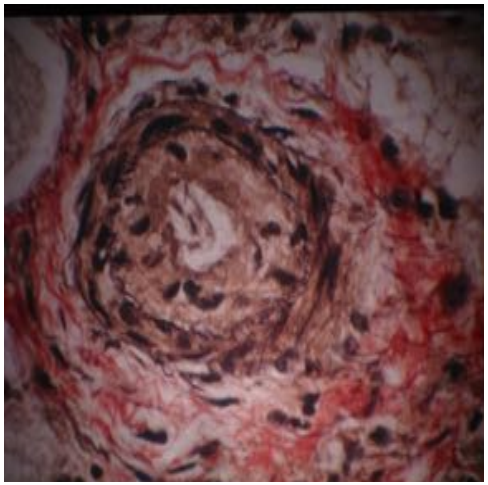
Neonatal morbidity & mortality

Pulmonary hypoplasia



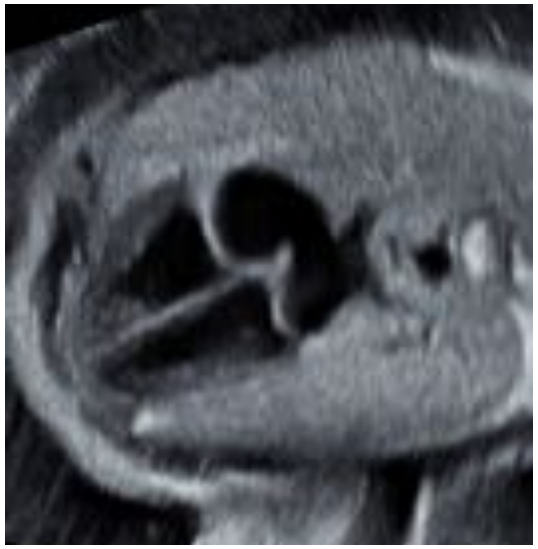


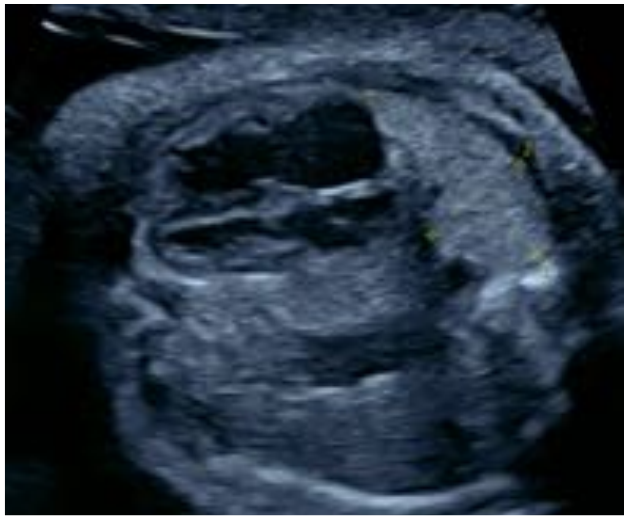
Pulmonary hypertension



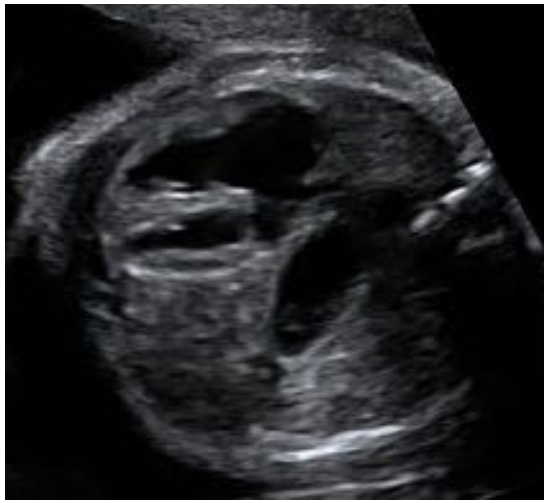
Antenatal prognostication

Mediastinal shift

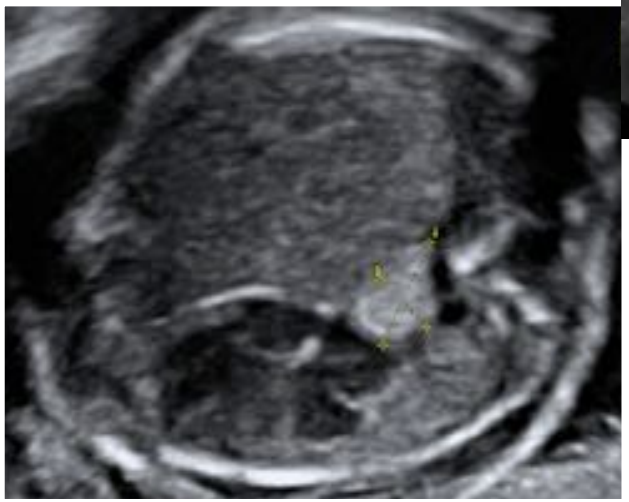




Left CDH (isolated "dextrocardia"/dextroposition)

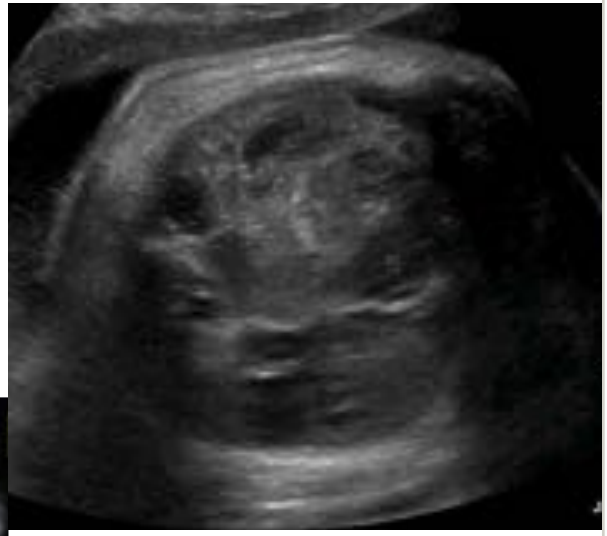


Left CDH- Stomach up

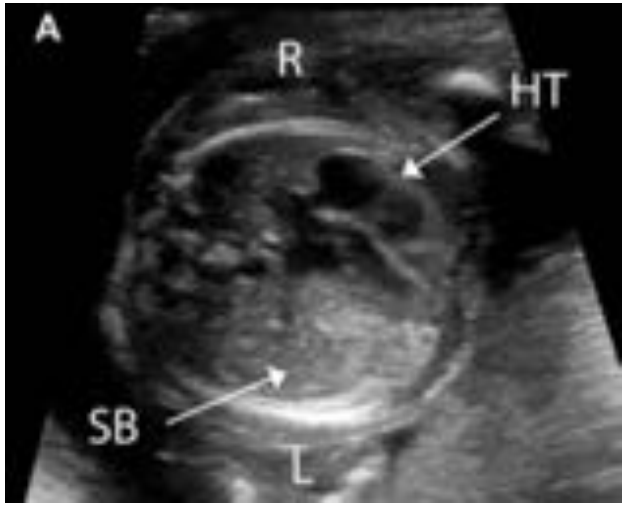


Right CDH

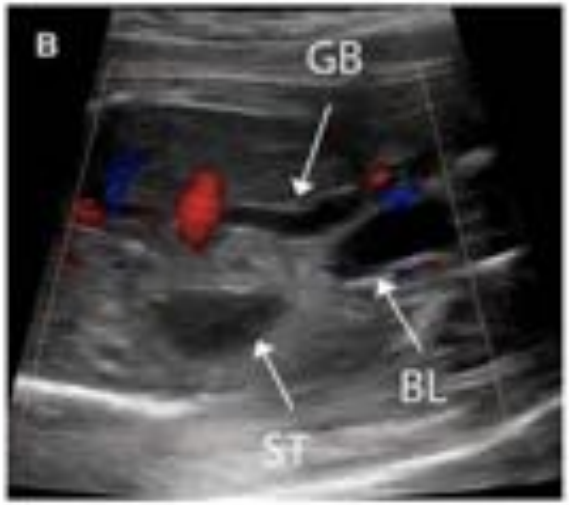
Abnormal echogenicity



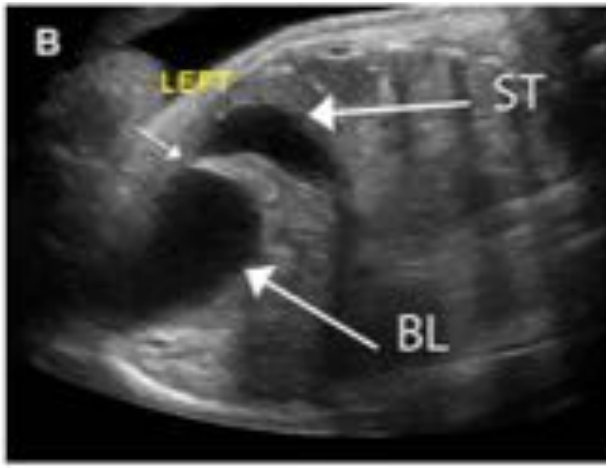
Left CDH- Stomach down



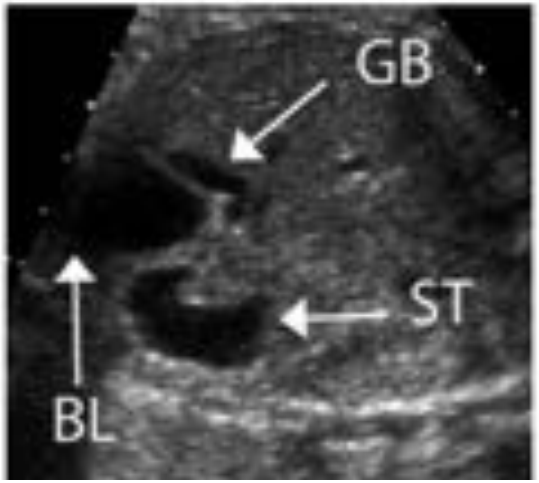
Dextrocardia/ dextroposition



Gall bladder & bladder



Stomach & bladder

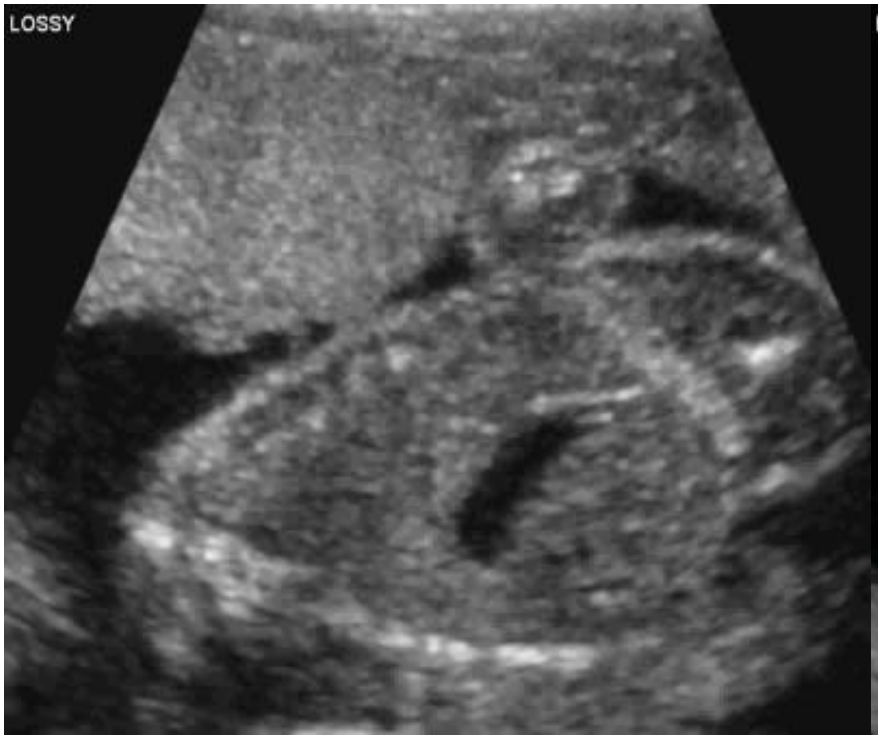


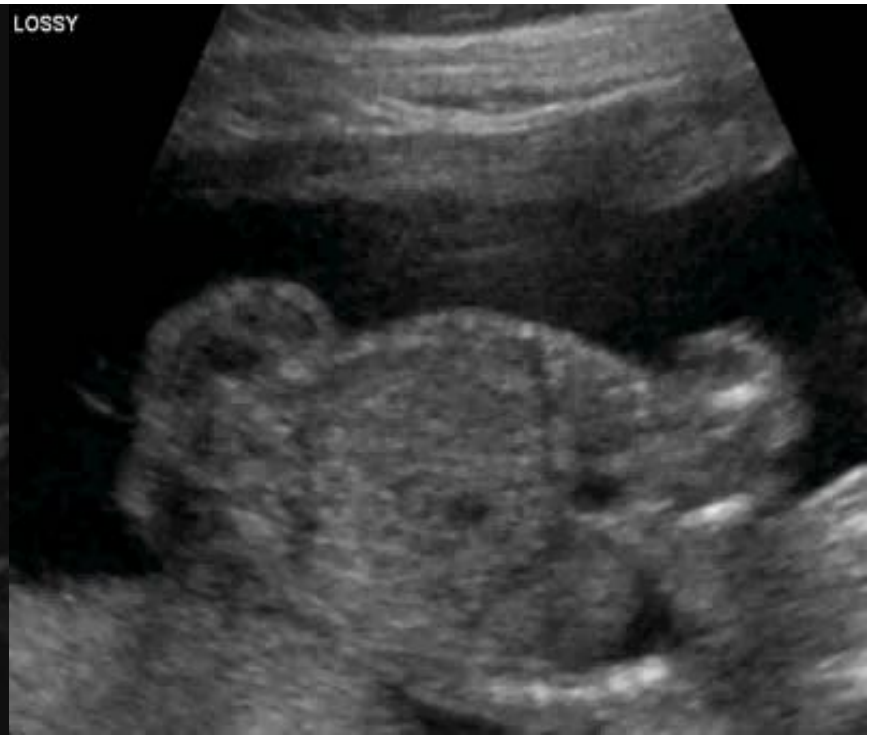
Gall bladder, stomach & bladder

Morgan T *et al.* J Ultrasound Med 2016

Normal fetal breathing

Paradoxical Respiration

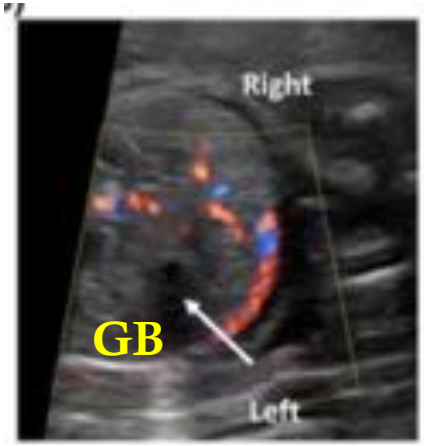


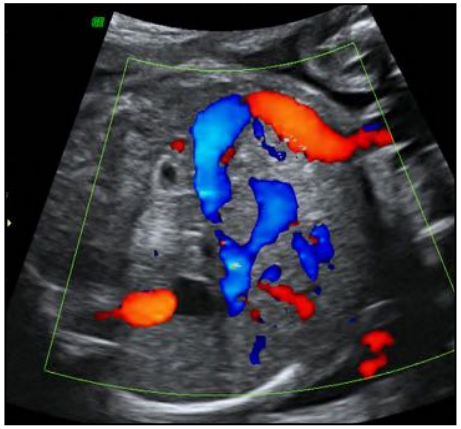


Normal Diaphragm

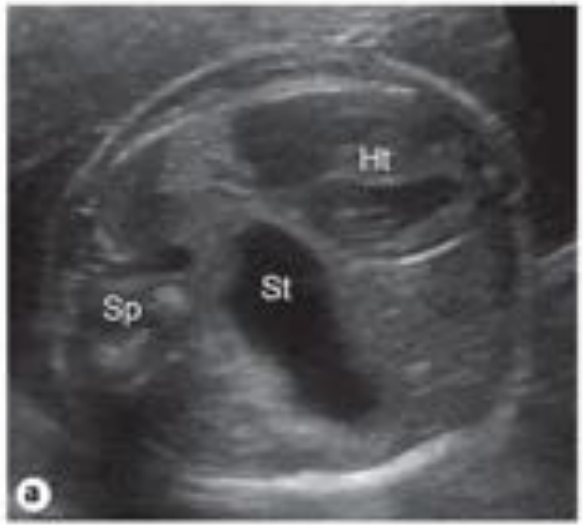
Left CDH

Liver herniation

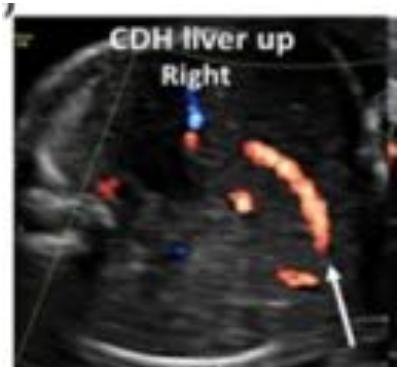




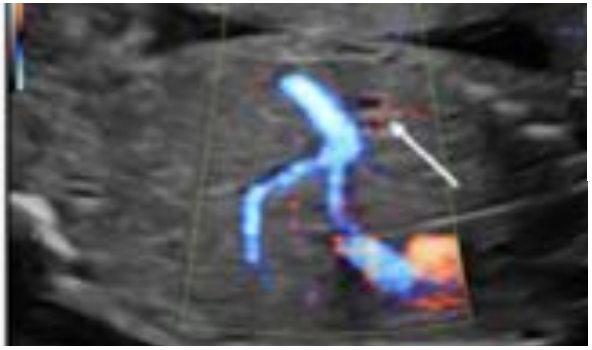
Abnormal gall bladder & ductus venosus position



Retrocardiac stomach position



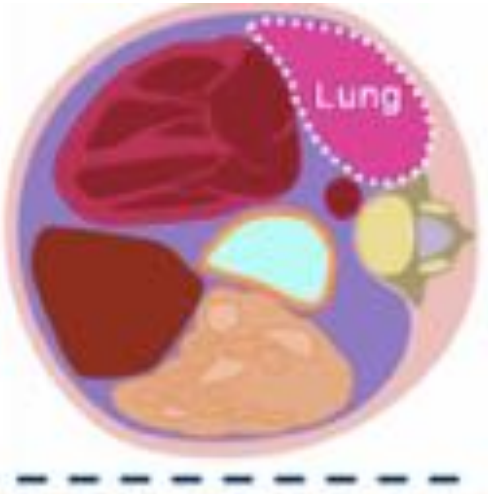
Bowing of portal vein



Hepatic vessels up toward diaphragmatic ridge

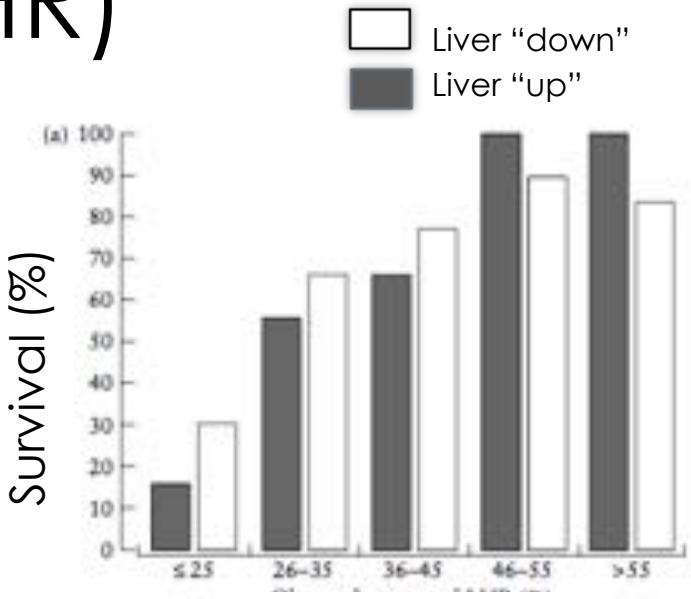
Russo F et al. *Prenatal Diagnosis*. 2018;38:629–637.
Metkus A *et al.* J Pediatr Surg 31:1; 148-52, 1996
Bootstaylor B *et al.* JUltrasound Med 14:515-520, 1995

observed-to-expected LHR (o/e LHR)

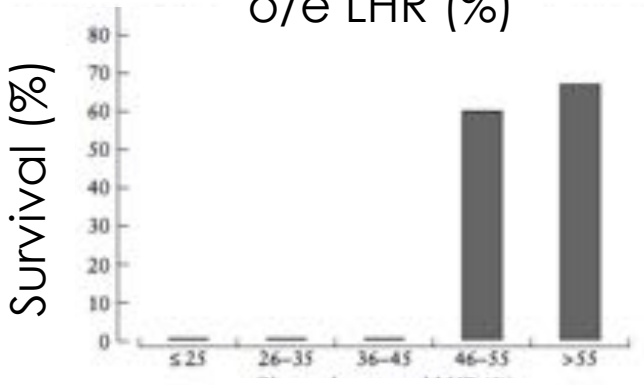


www.totaltrial.eu

Lung-to-head ratio (LHR)



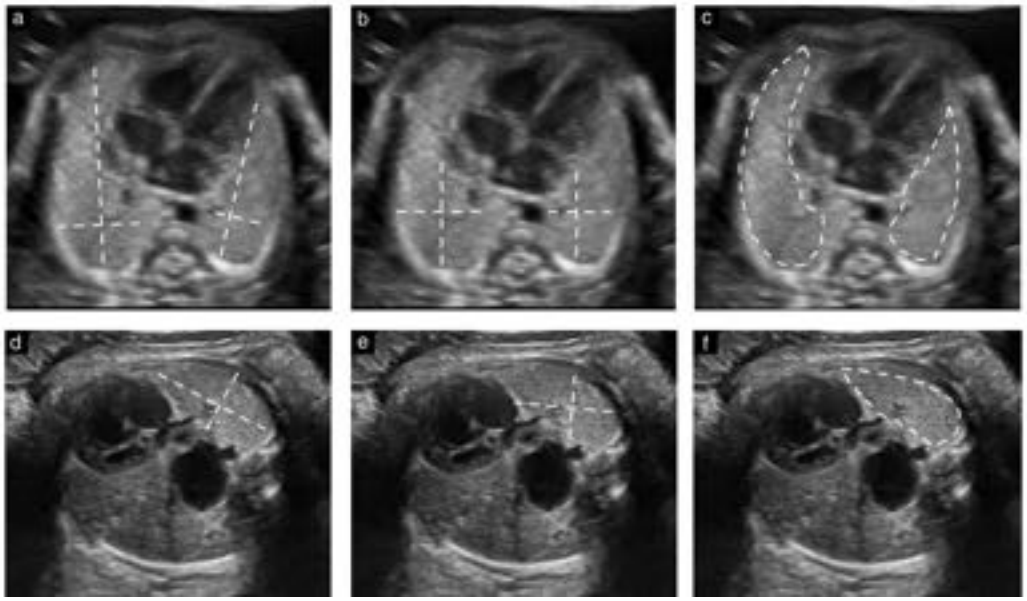
o/e LHR (%)



o/e LHR (%)

Ultrasound Obstet Gynecol 2007; **30**: 67–71.

The problem with o/e LHR…



Longest | Antero-posterior (AP) | Trace

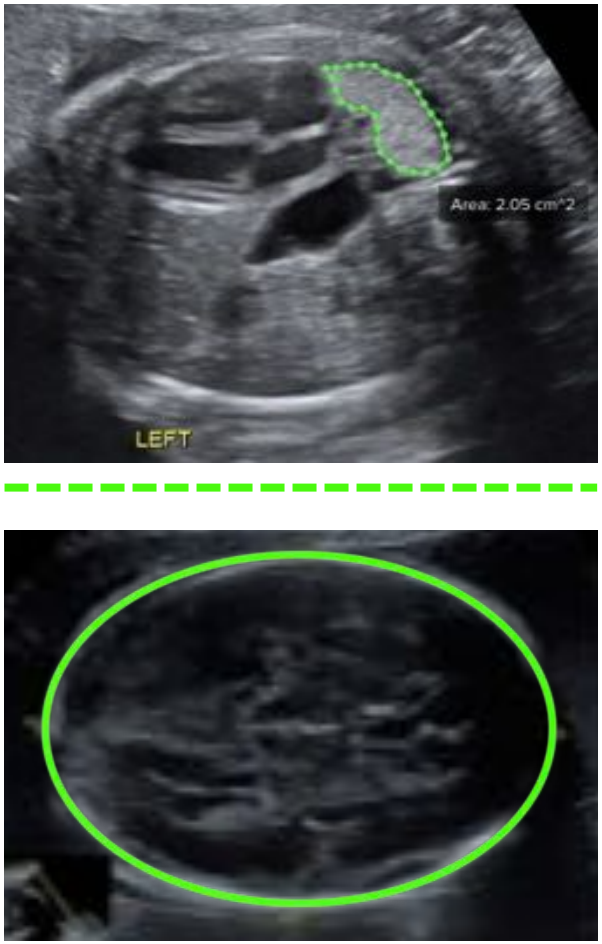
Standardization?

		AP	Longest	Trace
Agreement (ICC)	FETO centers†	0.83 (95% CI 0.67, 0.94)	0.89 (95% CI 0.75, 0.97)	0.94 (95% CI 0.83, 0.98)
	Non-FETO centers¶	0.54 (95% CI 0.1, 0.91)	0.57 (95% CI 0.12, 0.90)	0.86 (95% CI 0.79, 0.93)

Abbasi N *et al.* Prenat Diag. 2019

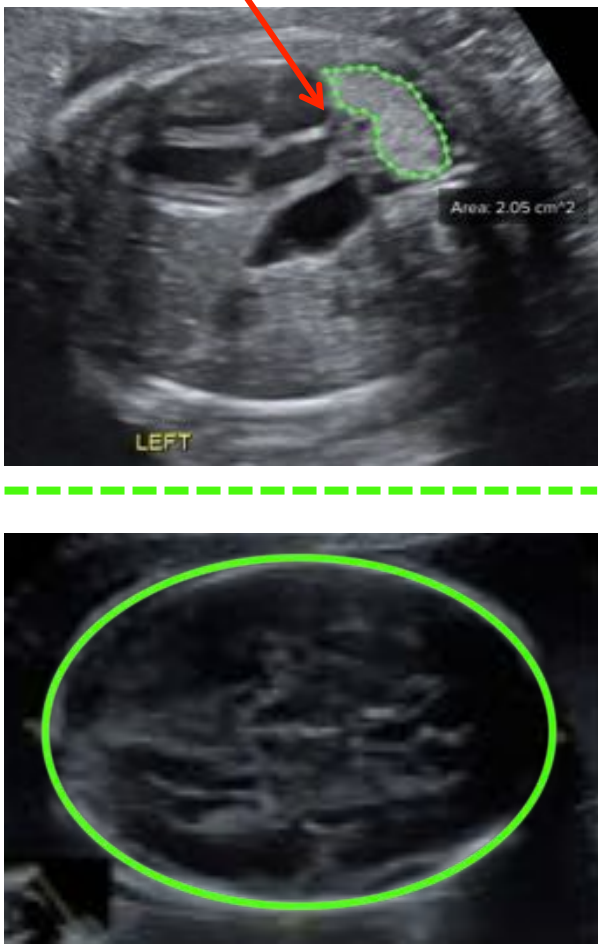
How to measure o/e LHR: Image selection

- **Axial section** (single rib, 4 chamber view * valves) & **take sweep**
- **Spine at 3 or 6 o'clock** with contralateral lung to CDH closest to transducer
- Scan through intercostal space (avoid rib shadow)
- **Optimize image** (i.e.: depth, focus, high frequency probe 5-9MHz)
- **Magnification (chest ~75% of screen)**

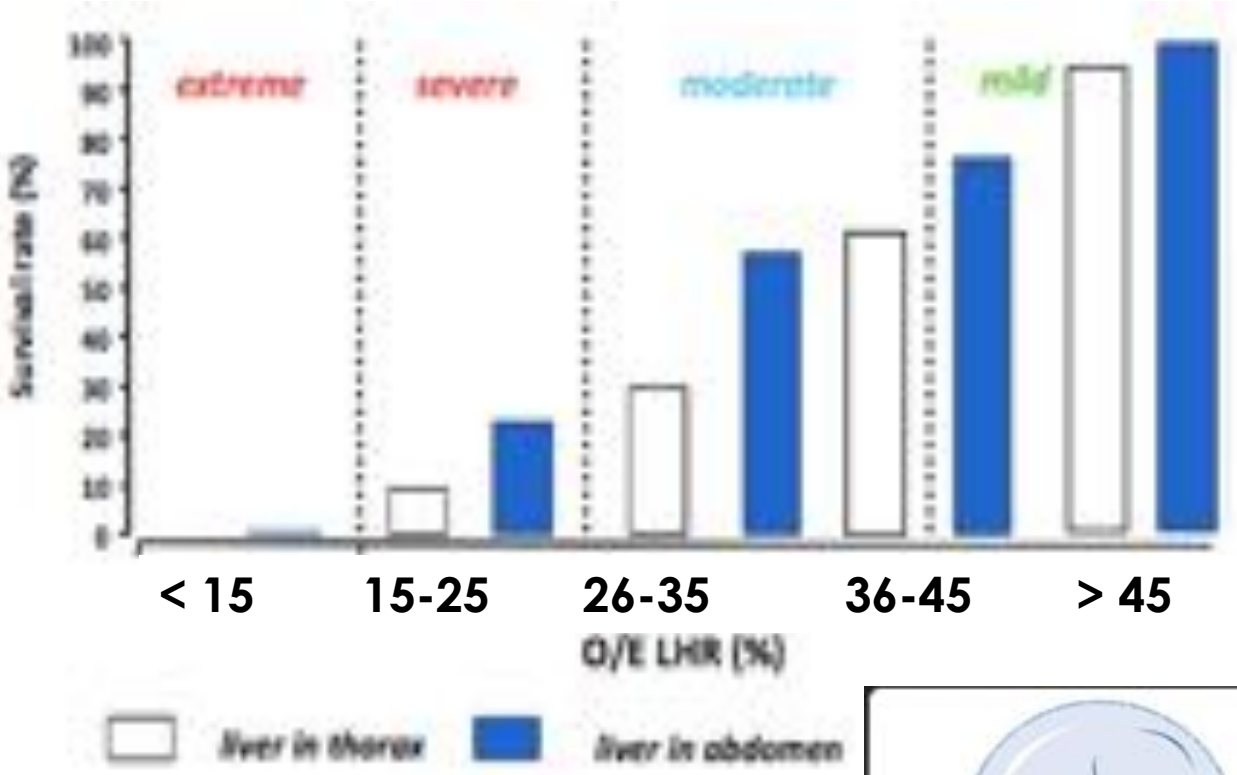


How to measure o/e LHR

- **Measure contralateral lung using the TRACE method**
  - Do **NOT** include cardiovascular structures or mediastinal vessels, bony structures (ribs/vertebrae)
- 2-3 measurements
  - **Use qualitatively best image**
- **Measure head circumference** (ellipse)
  - CSP, thalami, posterior horns of lateral ventricles & midline falx dividing brain into 2 symmetrical hemispheres.
  - NO cerebellum/posterior fossa.
- **Calculate o/e LHR (www.totaltrial.eu)**



Prognostication and management



- Standard postnatal repair
- Termination of pregnancy
- Fetal intervention?

Fetal
Endoscopic
Tracheal
Occlusion
vs. postnatal surgery
for mod-severe CDH

J. Deprest et al. / Seminars in Fetal & Neonatal Medicine 19 (2014) 338–348

Conclusion

- Suspect fetal thoracic pathology on 4CH view
  - Mediastinal shift
  - Abnormal echogenicity
  - Cystic lesions/fluid collection
- Increased intrathoracic pressure →
  - Pulmonary hypoplasia
  - Polyhydramnios/prematurity
  - Hydrops/death
- Prognostic indicators
  - Hydrops, CVR (CCAM/BPS), o/e LHR (CDH)
- Role of prenatal intervention