# Congenital diaphragmatic hernia

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# Introduction

- **2.3–2.4 per 10,000 live births** in Europe and USA
- "hidden mortality" 1/3 of prenatally diagnosed are still births
- left side hernia more common on (80%)
- Posterolateral hernia/Boschdalek more common (90%)
- Significant mortality (20-30%) and long term morbidity despite advances
- Only one paper from Ethiopia….

*Miliard Derbew.* ***Congenital diaphragmatic hernia outcomes in East Africa: The Ethiopian Experience****. East Cent. Afr. J. Surg. Vol 21. no 3. December 2016*

- **Study duration**: 4 years (2012-2016)
- **Sample** : 12 patients (3/15 charts lost)
- **Epidemiology**
  - M:F = 3:1
  - Age = 10 hours – 18 month (75% after neonatal age)
  - Side = Left 6/12 (50%), right 6/12 (50%)
  - Type = boschdalek 9/12 (75%), Morgagni 2/12 (16 %), diaphragmatic eventration 1/12 (8%)
  - Ass anomaly = downs syndrome 2/12 (16%)
- **Presentation**: 83.3% initially misdiagnosed
- **Surgery**: all repaired primarily through abdominal approach
- **Complications** = (each in 1 patient) SSI , incisional hernia, intussuception, partial SBO
- **Mortality** = 2/12 (16%)

# Outline

1. Embryology
2. Prenatal management
3. Clinical Presentation
4. Neonatal management
5. Surgical technique

# 1. Embryology

# Embryology of diaphragm

- **septum transversum** (in young embryos, is identical to the floor of the Pericardium)
- structures that surround the pleural cavity
  - **Post Hepatic Mesenchymal Plate** (covers the dorsal aspect of the liver)
    - *the most important role in normal diaphragmatic development
  - **pleuro-peritoneal fold** (separates the pleura from the peritoneal cavity).
  - **mediastinum** (esophagus, the trachea and the Aorta)

# Embryologic theories

- **Failure of fusion** of the pleuro-peritoneal membrane with septum transversum
  - *PPF Develops 6$^{th}$ wk,* ***closes 8$^{th}$ wk****. right side closes before left*
- **Failure of muscularization** of the lumbocostal trigone and pleuro-peritoneal
- **Pushing of intestine** through postero-lateral part (foramen of Bochdalek)
- **Premature return of the intestines** into the abdominal cavity with canal still open
- **Abnormal development of the lung** preventing proper closure of pleuro-peritoneal canals (lung hypoplasia is a primary problem= two hit theory)

# Applied embryology

**Nitrofen rat model**

- **CDH not due to failure of fusion of pleuroperitoneal memb**
  - Single embryonic gut loop requires at least an opening of 450 µm size to herniate. None have this size even with delayed/inhibited closure of canal.
  - Found defective development of the post-hepatic mesenchymal plate (too short)
  - region of the diaphragmatic defect was a distinct entity separated from that part of the diaphragm where the pleuro-peritoneal 'canals' are localized
- **Lung hypoplasia is not due to compression**
  - Liver herniates through defect early (grows faster and occupy space so lung can't grow)
  - Herniated gut found late (after hypoplasia occurred)

# Applied embryology

- **Retinoic acid deficiency**
  - Vitamin a deficient rodents gave offsprings with CDH
  - Retinoic acid receptor knockout mice developed CDH
  - Nitrofen affects retinoic acid synthesis pathway
  - Low plasma level of retinoic acid and its binding protein found in infants with CDH
- **PPF derived muscel connective tissue fibroblasts**
  - Mutation in GATA4 (strongly expressed in PPF) resulted in CDH
  - Herniated tissue shown to physical impede lung dev't

# Embryology of lung development

- Fetal lung development is divided into five overlapping stages.
  - ***embryonic stage*** *(*3rd wk – 6th wk) = lung bud - lobar structures)
  - ***Pseudoglandular stage*** *(*5th - 17th wk) = formal lung buds – terminal bronchi
  - ***Canalicular stage*** *(16-25 wk) =* **pulmonary vessels**, respiratory bronchioles, and alveolar ducts develop between weeks with type 1 & 2 pneumocytes
  - ***saccular stage*** *(*24 – term) = maturation of alveolar sacs.
  - ***alveolar stage*** (after birth) = increase and development of alveoli

# Embryology of lungs in CDH

- **Bilateral** Hypoplastic lungs in CDH infants with a decreased number of airways and smaller alveolar airspaces. (?uncorrectable)
- **Decreased cross sectional area** + **inc muscularization** of vessels>> persistent pulmonary hypertension (?potentially reversible)

# Etiology

- Environmental trigger
  - Thin or underweight mothers
  - vitamin A deficiency
  - thalidomide, anticonvulsants, quinine
- Genetic
  - 2% in 1st degree relative
  - ass with syndromes
  - chromosomal anomalies identified in sporadic case)

# 2. Prenatal management

# 2.1. Diagnosis

*50-70% antenatal diagnosis with ultrasound as early as 11 wk*

- Lt side
  - rt mediastinal shift, stomach in chest (next to or behind the heart)
  - absence of stomach below diaphragm, small abdominal circumference
- Rt side
  - lt mediastinal shift, homogenous mass (liver)/gall bladder in chest at level of heart
  - echogenicity of liver similar to lung (difficult to d/t CCAM / BPS)
- Polyhydraminos (80%) – kinking of GEJ
- Hydrops fetalis – mediastinal shift and compression of great vessels

# 2.2. Workup (prognostication)

- Ultrasound
  - Lung to head ratio: LHR (<1, <0.85 or O/E <25%)
  - Rt sided lesion,  liver herniation (Doppler)
- Fetal MRI
  - Total fetal lung volume lung volume (O/E <30% expected)
  - liver herniation (>20%)
- Fetal Echocardiography (ass. Anomalies)
- Fetal Karyotype (chromosomal abn)
- Genetic studies (aCGH)

# 2.3. Antenatal monitoring

*IUFD in 3-8%, higher if ass anomalies*

- **NST/BPP** (2x/wk starting 33-34 wk)
- **fetal growth & amniotic fluid** (wks 28, 30, 32, 34-35)
- **? Antenatal corticosteroids** – role is undetermined (awaits RCT)

# 2.4. Fetal intervention

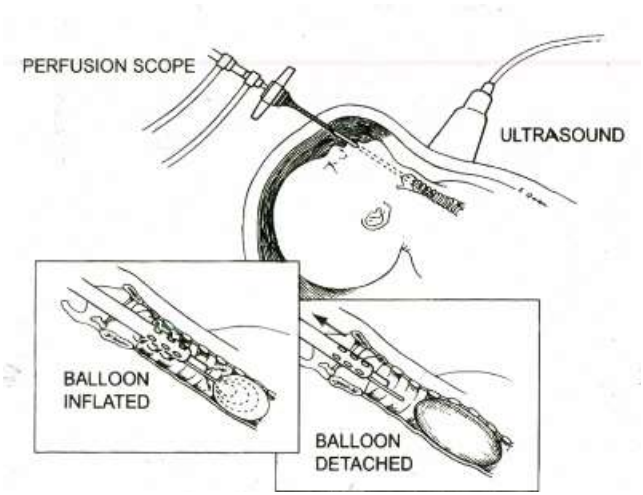
*The 2003 trial showed comparable survival but methods were different*

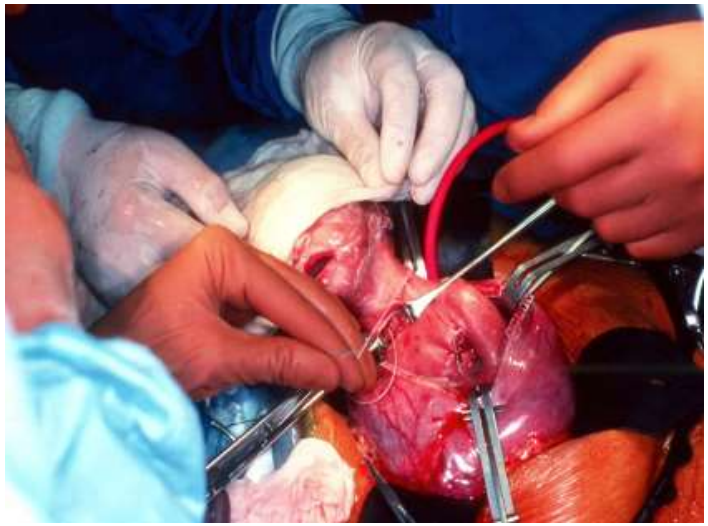
*The 2012 trial found decreased pulmonary hypertension and improved long term survival*

*Currently, "TOTAL trial" (Tracheal Occlusion to Accelerate Lung growth) is conducting in Europe and USA*

- **FETO** (fetal endoscopic tracheal occlusion)
  - The lung produces ~ 100ml/kg/d. Therfore, obstructing outflow will stimulate expansion
  - 24-28 wk - intubating fetus (endoscopic) and placing a detachable balloon in the trachea
  - 34 wk – deflated/removed
- **EXIT** (Exutero intrapartum treatment)
  - Baby partially delivered (remains attached to placenta) while the surgeon reverse airway obst.
  - Used in the case of premature labor prior to de-occlusion

# 2.4. Fetal intervention



- Fetal endoscopic tracheal occlusion and reversal. Alternatively reversal can be done by EXIT procedure if labor occurs prior to fetoscopic de-occlusion

# 2.5. Delivery

- ? SVD
- Planned induction
  - Early term induction between 38-39 wk
  - to monitor labor & prepare peds team

# 3. Clinical Presentation

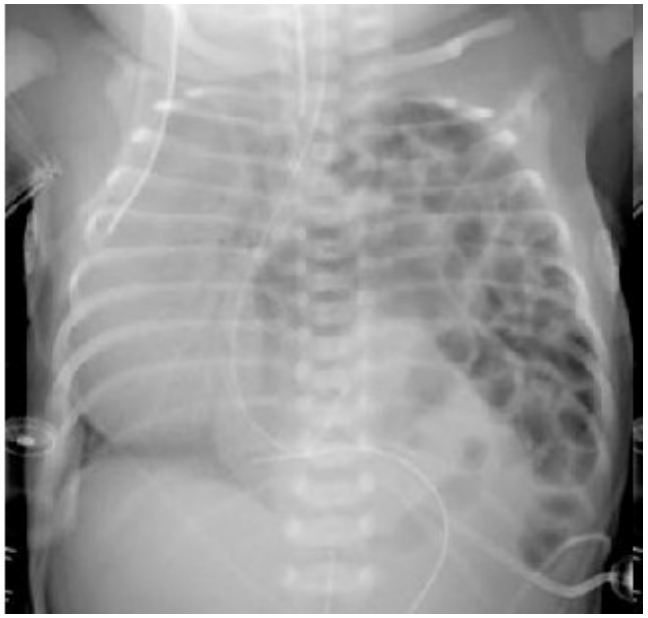
# Associated anomalies

- Isolated CDH (60%)
  - Significant survival advantage (80% vs 20%)
- Complex CDH (40%)
  - 60% of neonatal deaths have ass anomalies, only 10% of survivors have anomalies
  - Major structural anomalies – CVS (27.5%), urogenital (17.7%), MSK (15.7%), and CNS(9.8%)
  - Chromosomal anomalies (10-20%)
  - Underlying syndrome (10%)
  - Genetic variation is detected in 1/3

# Signs and symptoms

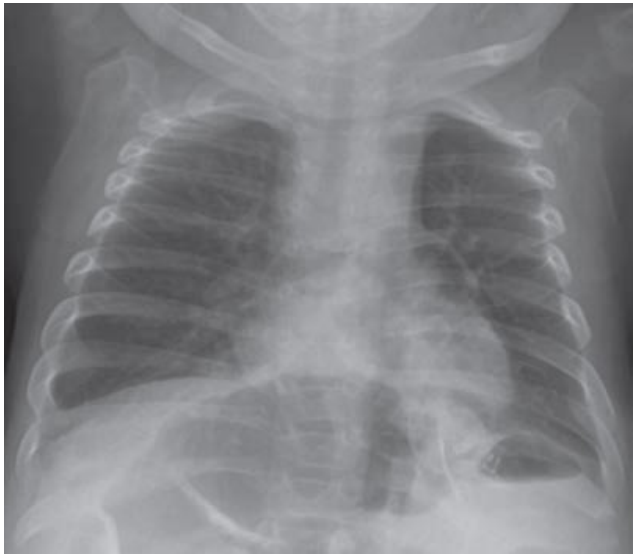
- Majority present in first 24 hrours of life
  - immediate, profound respiratory distress  (majority present in 24 hrs of life
  - Assymetric chest, scaphoid abdomen, mislocated PMI, absent breath sounds
- Some initial stable period with delayed respiratory distress
- 20% may present outside the neonatal period.
  - chronic pulmonary infections, pleural effusions, pneumonias
  - feeding intolerance, gastric volvulus
  - malrotation – obstruction/volvulus

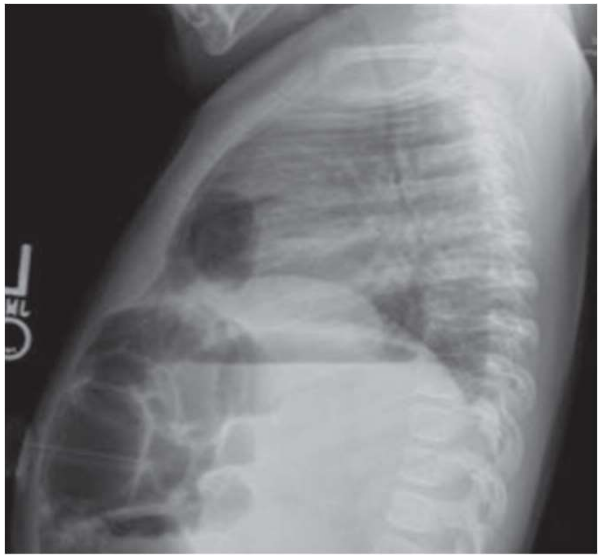
# Chest x-ray



- intestinal loops within the hemithorax
- displacement of the stomach/orogastric tube
- mediastinal shift

# Chest x-ray





- Anterior hernia/Morgagni (<2%): air filled loops of bowel seen above diaphragm, posterior to sternum. Sometimes is small and may require contrast study or CT to confirm diagnosis.

# 4. Neonatal management

# 4.1. Initial treatment

- Endotracheal intubation (*avoid mask ventilation)
- Gastric decompression
- Sedation & pain management
- Blood gas/ SO2 (Monitoring + estimating lung capacity)
- temp-glucose-volume status-acidosis

# 4.2. Optimizing ventilation

*Gentle ventilation (maintain oxygenation while limiting the risks of ventilator-induced lung injury)*

- Conventional ventilation (low press-inc rate, permissive hypercarbia, spontaneous respirations)
- High frequency oscillating ventilator (when PIP reaches 25 cmH2O with and targets not achieved)
- ECMO (failure to respond to alternative therapies)
  - ECMO may not be offered if preductal so2 < 85% is overwhelming hypoplasia
- ?Pulmonary vasodilator ( Inhaled nitric oxide, sildenafil) – benefit shown in PPHN but not in CDH
- ?Ionotropes (milrinone) to decrease shunting
- ? Surfactant (continues to be used despite the lack of proven efficacy,)

# 4.3. Workup

- Echo
  - degree of pul HTN
  - shunt flow
  - ventricle performance

# 4.4. Surgery

- Timing = early (48hr) vs delayed
  - ? Repair while on ECMO (dec ECMO requirement but inc edema & bleeding)
- Anesthesia = NICU vs OR
- Approach = abdominal vs thoracic, open vs minimally invasive
- Extent = abd wall flap, appendectomy
- ? Chest drain = if used at all remove early and avoid suction

# 4.5. Outcome

- Prognosis = defect size, associated anomalies, prematurity
- Survival = 55-80% (<10% for complex CDH)
- Late death = 10%
- Recurrence (future pregnancy) = 1-2%
- Complications (CDH survivors)
  - Recurrence - recurrent hernia
  - Pulmonary - infection, BPD,
  - GI – GERD (~50%), intestinal obst (malrotation)
  - Neurologic – cerebral palsy, Subtle cognitive problems, hearing impaiment
  - MSK – chest wall abnormality, scoliosis

# 5. Surgical technique

# Diaphragmatic replacements

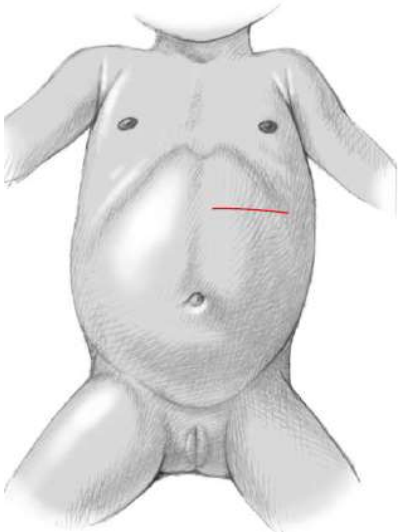
*Required for repair of large diaphragmatic defects Irrespective of the operative approach*

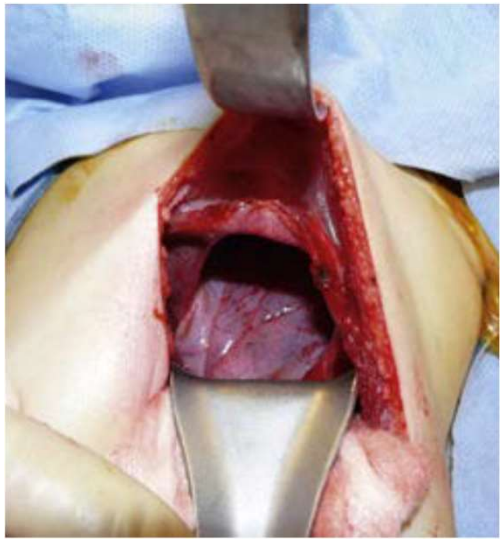
- **Non absorbable synthetic patches** – PTFE (Gore-Tex®), polypropylene (Marlex®)
  - Less tissue dissection, reducing risk of hemorrhage especially for those on ECMO
  - Anchored to chest wall so can result in chest wall deformity, bowel obstruction, patch infection
  - Early recurrence (6%) due to lack of tissue adhesion
- **Absorbable bio-synthetic patches** – Surgisis®, Permacol®, AlloDerm®, Surgimend®
  - Lower risk of infection and ability to grow with the patient
  - No diff in other complication with synthetic patch
  - Thinning of patch and incomplete muscular ingrowth, have been found**.**
- **Autologus tissue patches** - internal oblique /transversus abdominis, latissimus dorsi, serratus
  - vascularized tissue that will grow with the infant and has a minimal inflammatory response
  - Procedures are too long and complex for critically ill patients and can lead to unsightly chest deformities.
  - denervation of the graft may lead to lack of movement and atrophy overtime.

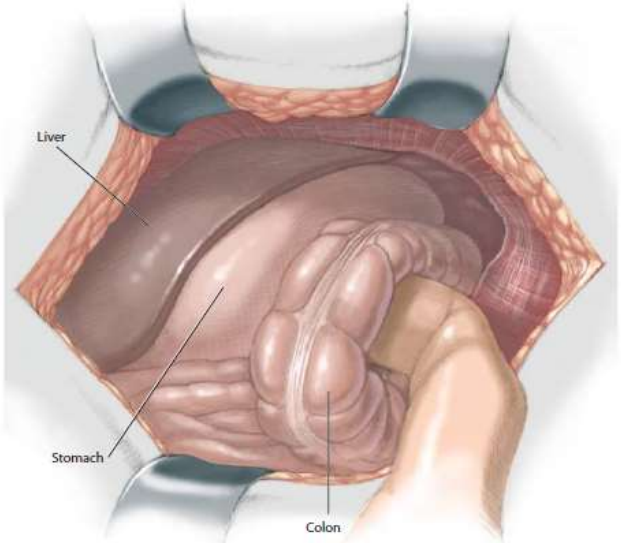
# Open CDH repair

- Open Abdominal approach preferred than thoracic
  - Easier reduction
  - ability to mobilize posterior rim of diaphragm
  - Able to deal with malrotation
  - Avoid sequelae of thoracotomy
- Care on reducing spleen not to cause laceration
- hernia sac (<20%) composed of pleura and peritoneum should be excised to avoid loculated space
- Thoracic and abdominal cavities should be inspected for sequestration
- Careful attention to peak airway pressures as the abdominal fascia is closed.
  - A large patch that bows into hemithorax can minimize risk
  - Consider temporary closure (silo, vacuum-assisted closure, skin-only closure)

# Open CDH repair

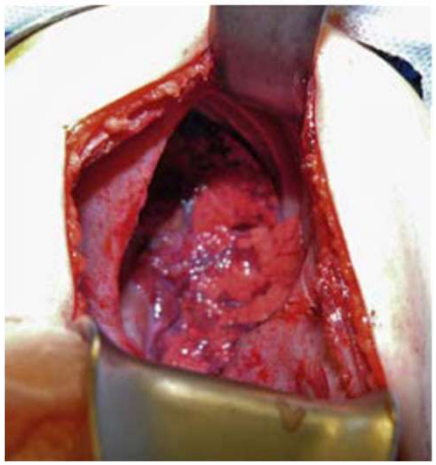


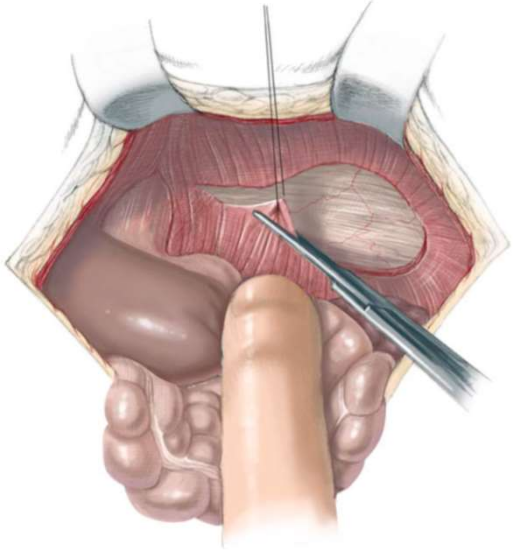


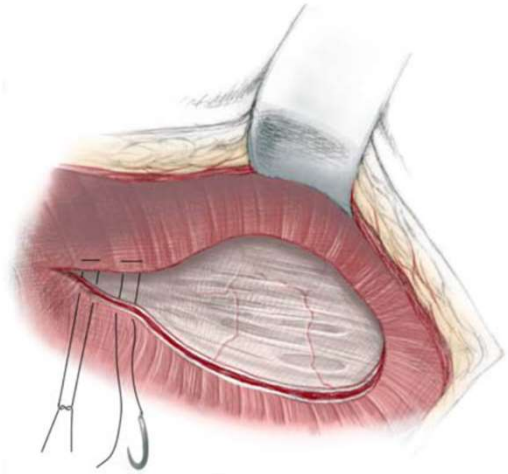



- Abdomen entered via left subcostal incision and CDH exposed. The contents of the hernia are gently reduced in the abdomen.

# Open CDH repair

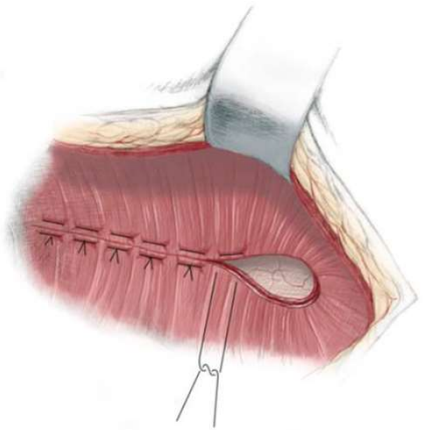


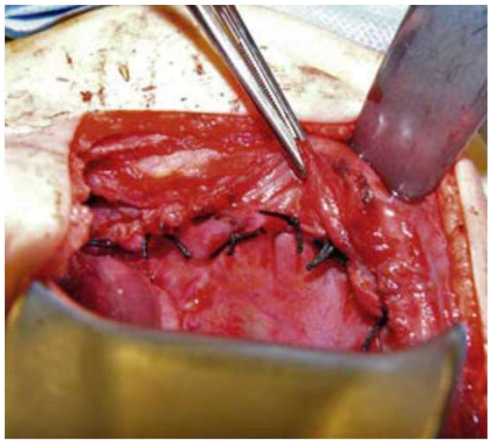


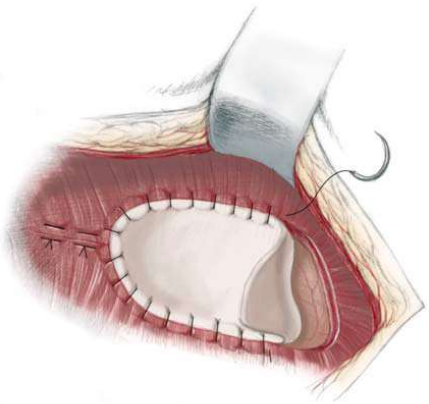


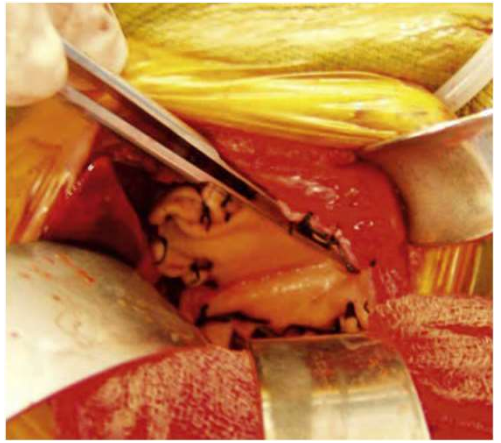
- hernia sac excised and defect visualized. Anterior rim of diaphragm is evident, posterior rim may require mobilization by incising over peritoneum.

# Open CDH repair



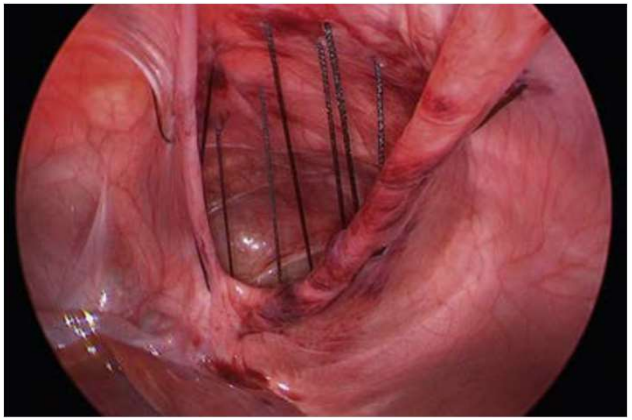


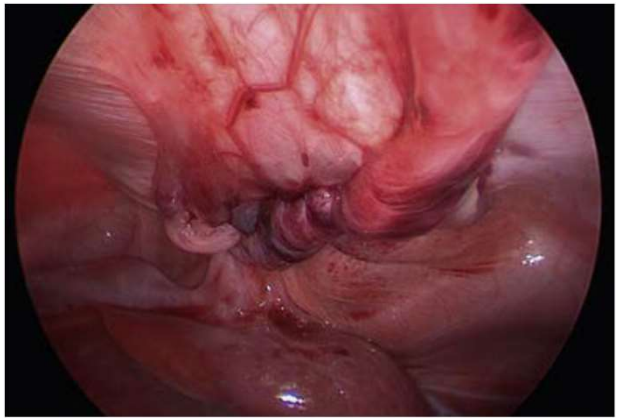




- Most diaphragmatic defects can closed primarily by interrupted silk sutures on the edges of the defect. Alternatively patch may be placed to close a larger defect.

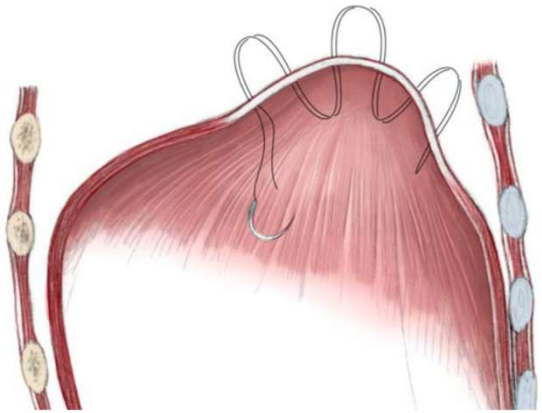
# *repair of Morgagni hernia

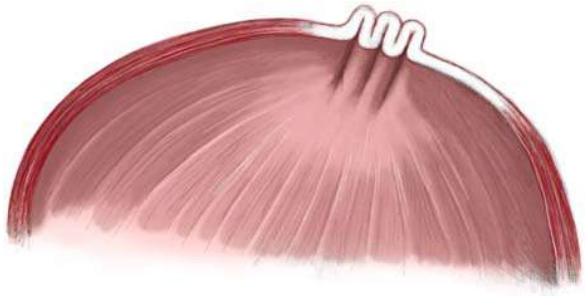


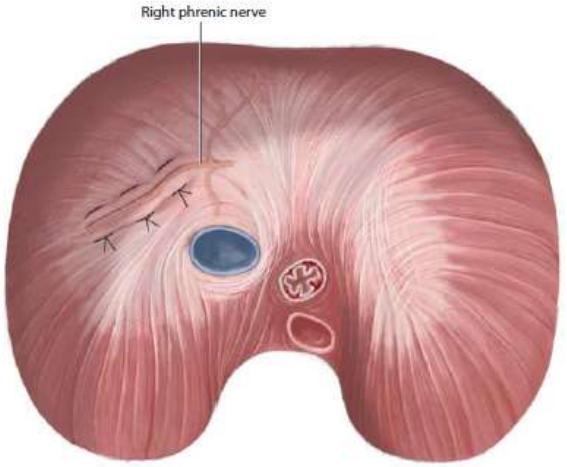


- Repair of Morgagni hernia entails approximation of the diaphragm to the posterior rectus sheath at the costal margin. 2-0 silk sutures have been placed transabdominally around the edges of the defect to bring the muscular rim anteriorly and repair the hernia. The sutures will be tied at the same time. When defect is closed, knots are in the soft tissue of the anterior abdominal wall.

# *Plication for congential diaphragmatic eventration





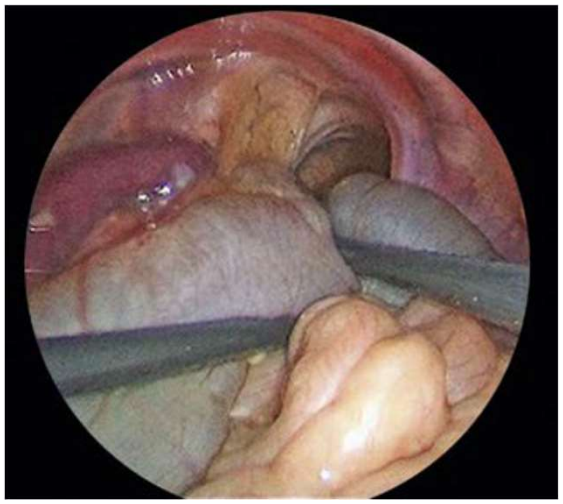


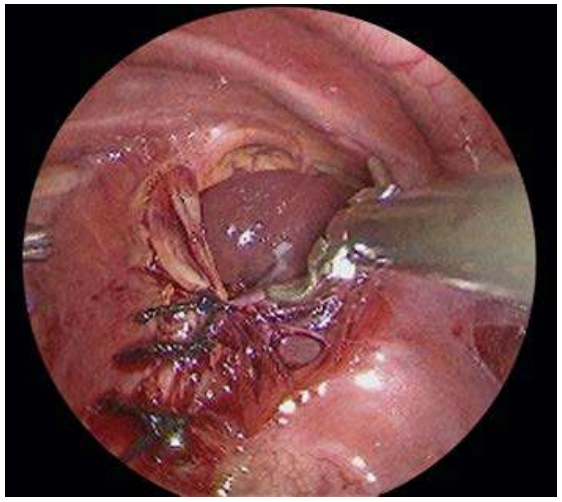

- In congenital eventration, the diaphragm muscle is usually thin and may be indistinguishable from a hernia sac seen in CDH. Plication can be done using nonabsorbable sutures, avoiding injury to the phrenic nerve.

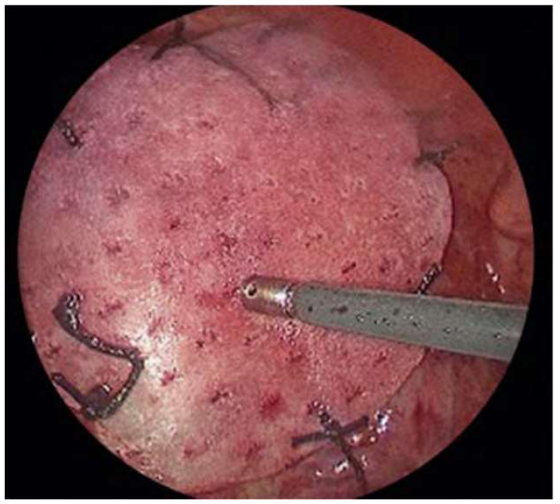
# Minimally invasive repair

- MIS has advantages (less hospital stay…)
- However, higher recurrence (6% vs 3%)
- Issue of insufflation causes concerns
  - CDH patient are sensitive to hypercapnia (may absorb CO2)
  - intrathoracic pressure inc further (limit venous return and tidal volume)

# Minimally invasive CDH repair







- thoracoscopic approach reveals colon and spleen in left chest. Abdominal contents reduced and diaphragmatic defect partially closed. A Permacol® mesh has been sewn over the partial diaphragmatic closure and ribs with silk. Patch should be placed in a dome/cone shape to be more physiologic and inc. abdominal domain.

# Summary: Controversies in CDH

**RESOLVED ISSUES**

- There is a high incidence of associated malformations.
- Delivery at a tertiary center improves survival for antenatally diagnosed patients.
- Agenesis of the diaphragm and herniation of the liver are poor prognostic signs.
- Multidisciplinary approach using gentle ventilation improves outcome.
- Survivors need long-term follow-up and management of associated complications.

**UNRESOLVED ISSUES**

- The utility of antenatal ultrasound and magnetic resonance imaging markers to predict survival
- The role of antenatal steroids, surfactant, and inhaled nitric oxide in management
- Surgical approach
- Benefit of extracorporeal membrane oxygenation (ECMO) and use of chest tube

**RECOMMENDATIONS**

- Accept preductal saturations greater than or equal to 85%, $PaCO_2$ less than or equal to 65 mm Hg, and pH greater than or equal to 7.25.
- Identify preset ventilatory limits that are not to be exceeded.
- Use high-frequency oscillatory ventilation if, conventional mechanical ventilation, fails.
- Use ECMO per preset criteria.
- Delay surgery until persistent pulmonary hypertension improves.

# References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- Uptodate articles
  - Congenital diaphragmatic hernia: prenatal diagnosis and management (updated Jan 11, 2013)
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