Ebstein Anomaly

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1

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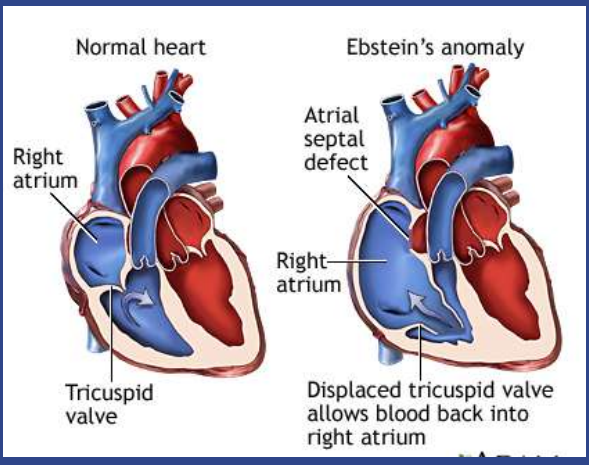
Objective:

- Understanding the pathophysiology of Ebstein anomaly
- Learn key fetal echo findings
- Be able to assess severity and associated anomalies

3

Ebstein Anomaly



Singh DP, Hussain K, Horenstein MS, et al. Ebstein Anomaly and Malformation. [Updated 2024 Feb 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK534824/

4

First Description of Ebstein Anomaly

- On June 28th, 1864, A 19-year-old laborer whose childhood dyspnea and palpitation had worsened with age was admitted to the hospital Dr. Ebstein worked at.
- The patient's attending physician described the patient's cachexia; severe cyanosis; jugular veins that throbbed in synchrony with the heart's rhythm; a systolic cardiac murmur; and an enlarged cardiac silhouette, detected during cardiac percussion. This clinical picture indicated congenital heart disease
- Patient died eight days later and Dr. Ebstein performed the autopsy.
- In 1866, Dr. Wilhelm Ebstein was the first to publish a case study "A very rate case of tricuspid regurgitation".

Mazurak M, Kusa J. The Two Anomalies of Wilhelm Ebstein. *Tex Heart Inst J.* 2017;44(3):198-201. Published 2017 Jun 1. doi:10.14503/THIJ-16-6063

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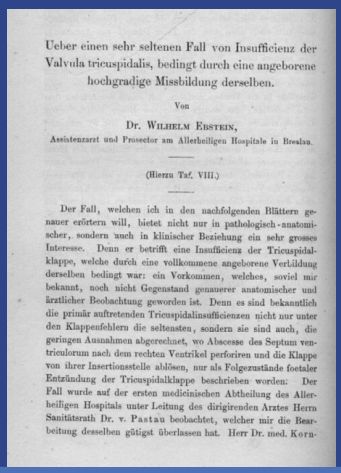
Key Findings from Dr. Ebstein's paper from 1866



Ueber einen sehr seltenen Fall von Insufficienz der Valvula tricuspidalis, bedingt durch eine angeborene hochgradige Missbildung derselben.

Von

Dr. Wilhelm Ebstein,

Assistenzarzt und Prosector am Allerheiligen Hospitale in Breslau.

(Hierzu Taf. VIII.)

Der Fall, welchen ich in den nachfolgenden Blättern genauer erörtern will, bietet nicht nur in pathologisch-anatomischer, sondern auch in klinischer Beziehung ein sehr grosses Interesse. Denn er betrifft eine Insufficienz der Tricuspidalklappe, welche durch eine vollkommene angeborene Verbildung derselben bedingt war: ein Vorkommen, welches, soviel mir bekannt, noch nicht Gegenstand genauerer anatomischer und ärztlicher Beobachtung geworden ist. Denn es sind bekanntlich die primär auftretenden Tricuspidalinsufficienzen nicht nur unter den Klappenfehlern die seltensten, sondern sie sind auch, die geringen Ausnahmen abgerechnet, wo Abscesse des Septum ventriculorum nach dem rechten Ventrikel perforiren und die Klappe von ihrer Insertionsstelle ablösen, nur als Folgezustände foetaler Entzündung der Tricuspidalklappe beschrieben worden. Der Fall wurde auf der ersten medicinischen Abtheilung des Allerheiligen Hospitals unter Leitung des dirigirenden Arztes Herrn Sanitätsrath Dr. v. Pastau beobachtet, welcher mir die Bearbeitung desselben gütigst überlassen hat. Herr Dr. med. Korn-

- Meticulous illustrations by his colleague, Dr. Wyss
- Description of anatomic and pathologic factors
- Connection between the clinical findings and cardiac pathologic conditions suggesting embryonic defects as a likely cause of the patient's anomaly.
- Observed that the TV was extremely malformed
  - Anterior leaflet was elongated with numerous fenestrations
  - Hypoplastic, thickened poster and septal leaflets adhered to the right ventricle.
  - Atrialized part of the right ventricular wall was thing
  - Right atrium was enlarged

Mazurak M, Kusa J. The Two Anomalies of Wilhelm Ebstein. *Tex Heart Inst J.* 2017;44(3):198-201. Published 2017 Jun 1. doi:10.14503/THIJ-16-6063

6

History of Ebstein Anomaly

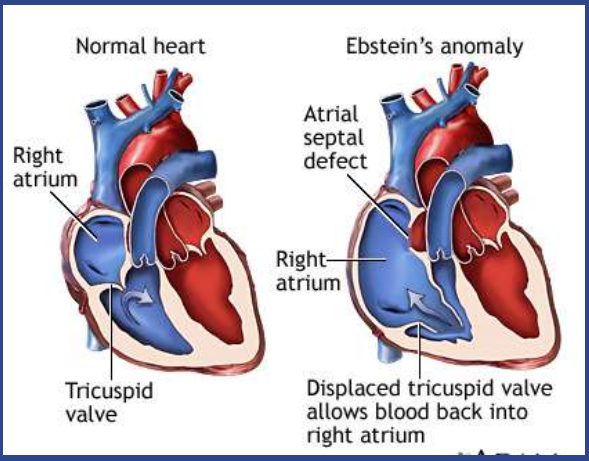
- The term Ebstein's disease did not appear in medical literature until 1927.
- Until the 1950s a mere handful of cases of patient with Ebstein anomaly had been reported.
- In 1951 Soloff and colleagues report the case of a living patient in whom cardiac catheterization and angiography revealed Ebstein anomaly.
- In 1962 Christiaan Barnard surgically replaced an affected TV with a bioprosthesis in 1962

Mazurak M, Kusa J. The Two Anomalies of Wilhelm Ebstein. *Tex Heart Inst J.* 2017;44(3):198-201. Published 2017 Jun 1. doi:10.14503/THIJ-16-6063

7

Defining Characteristics

- Apical displacement of the tricuspid valve
- Adherence of the septal and posterior leaflets to the myocardium
- Apical displacement and dilation of the tricuspid annulus
- Dilation of the Atrialized portion of the right ventricle
- Redundancy, fenestrations, and tethering of the anterior tricuspid valve leaflets



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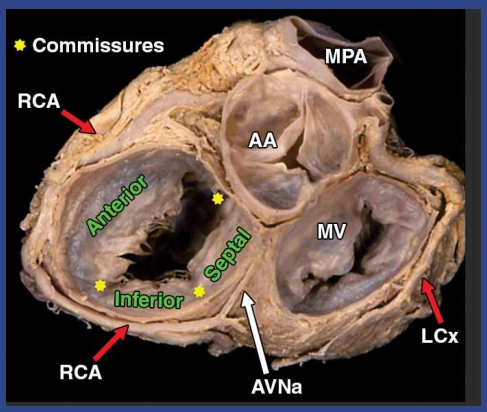
8

What is Ebstein anomaly:

- Tricuspid valve has three leaflets
  - Anterior
  - Septal
  - Inferior (a.k.a. posterior)

- In Ebstein anomaly
  - The septal leaflet is displaced towards the cardiac apex
  - The anterior leaflet is usually large and redundant and described as “Sail-like”

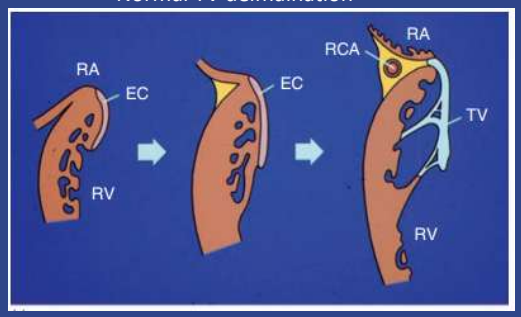


Ebstein anomaly: MedlinePlus Medical Encyclopedia

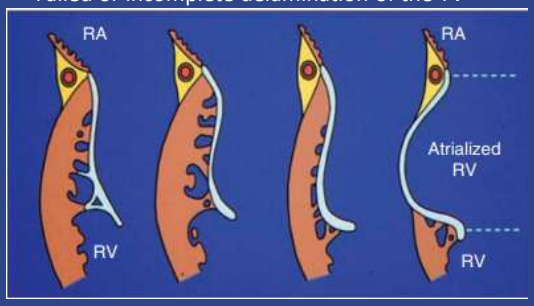
9

Embryology

Normal TV delmaination



Failed or incomplete delamination of the TV



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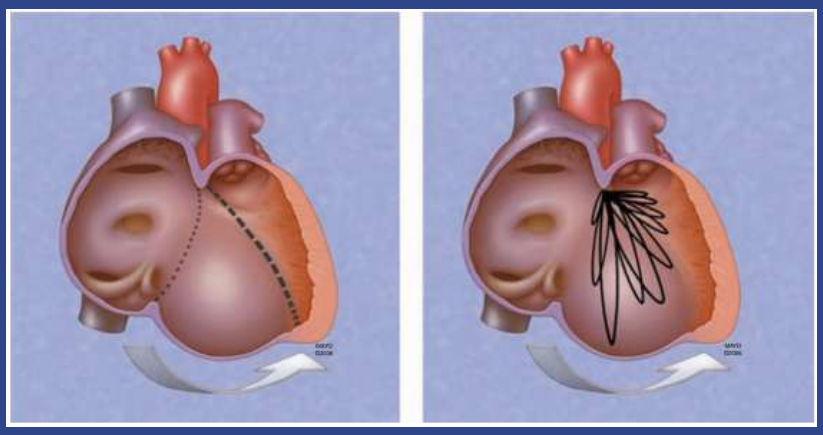
10

Embryology



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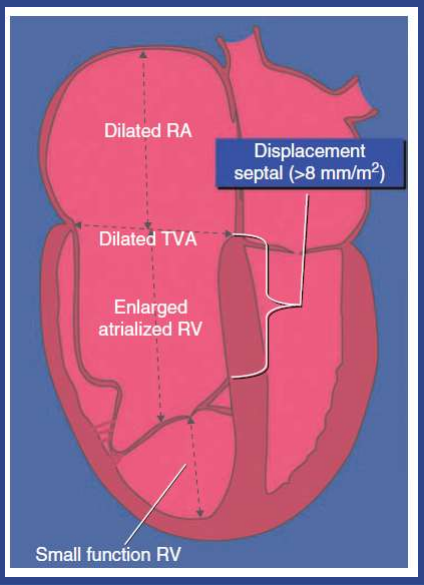
11

Diagnostic Criteria

- Distance from the hinge point of the anterior mitral leaflet is measured to the hinge point of the delaminated septal tricuspid valve leaflet.
- This measurement divided by the body surface area equals the displacement index.
- A displacement index of >8mm/m^2 is diagnostic of Ebstein anomaly.



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12

Incidence of Ebstein Anomaly

- One of the less common congenital heart defects, accounting for 3% - 7% of cases in the fetal population.
- 1 in 20,000 live births and makes up 0.5% of congenital cardiac cases
- Equal distribution between the sexes
- Risk of occurrence when on sibling is affected is ~1%
- More common in prenatal series as it accounts for 3% - 7% of congenital heart disease in fetus[2]

1. Drose, Julia A. *Fetal Echocardiography*. Saunders, 2010.
2. Abuhamad, A., & Chaoui, R. (2010). *A Practical Guide to Fetal Echocardiography: Normal and Abnormal Hearts*. Lippincott Williams & Wilkins.

13

Associated Anomalies

- Pulmonary stenosis or pulmonary atresia (functional)
  - Hypoplasia of the RVOT is thought to be secondary to chronic reduced antegrade RV flow in fetal life.
- Interatrial communication is present in over 90% of patients, often with right – to left shunting (resulting in cyanosis)
- Prominent Eustachian valve, likely secondary to abnormal flow patterns in the right atrium.
- Tetralogy of Fallot
- Isolated ventricular septal defects

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

14

Associated Anomalies

- Congenitally corrected transposition of the great arteries (ccTGA)
  - (up to 50% of ccTGA present with variable tricuspid valve morphology which could be classified as Ebstein anomaly
- Abnormalities of the left ventricle in up to 39% of patients
  - Abnormal LV morphology, volume and function.
- Left ventricular non-compaction can also be present in up to 19% of patients
- Mitral valve abnormalities including mitral valve prolapse, mitral cleft, double orifice mitral valve and parachute mitral valve.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

15

Arrythmias

- Ebstein anomaly harbours substrate for the entire sepctrum of atrial and ventricular arrhythmias.
- Supraventricular arrhythmias are common and include
  - atrial tachycardia
  - atrial flutter
  - atrial fibrillation
  - AV node-dependent re-entrant tachycardias.
- The need for permanent pacemaker in Ebstein is ~4.7% of patients, most commonly for AV block, followed by sinus node dysfunction.

Gupta A, Prabhu MA, Anderson RD, et al. Ebstein's anomaly: an electrophysiological perspective. *J Interv Card Electrophysiol*. 2024;67(4):887-900. doi:10.1007/s10840-024-01744-8

16

Extracardiac Anomalies

- Lung hypoplasia
  - Secondary to severe right atrial/ventricular dilation and cardiomegaly.
  - Heart can occupy >55% of the chest circumference with compression of the lungs and influencing lung development.
- Impaired cardiac output leads to redistribution of blood flow as seen in fetal hypoxemia where blood flow to the brain and heart is prioritized, at the expense of flow to placenta and other organs.
  - This can contribute to limited intrauterine growth, a risk factor for fetal demise.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

17

Genetics

- Majority are not inherited, and genetic testing is not always performed.
- Familial Ebstein Cases with reports of genetic variants in the MYH7, TPM1, and NKX2-5 genes.
- It's important to note that MYH7 and TPM1 variants are commonly present in cardiomyopathies and so these patients may be more likely to have a co-existing cardiomyopathy including left ventricular non compaction.
- Variants in NKX2.5 in addition to Ebstein, can also produce a phenotype of atrio-ventricular block, VSD and tetralogy of Fallot.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

18

Fetal presentation

- Severe Ebstein can have significant hemodynamic impact increasing the risk of in-utero demise or neonatal mortality.
- Severe displacement of the valve results in increased atrialization of the RV, influencing the RV's ability to generate adequate pressure for antegrade flow across the pulmonary valve.
- If there is significant atrialization of the RV and severe TR, the pressure generated by the RV may be inadequate
- RV pressures are proportional to gestational age
  - 29-week fetus should have an RV pressure $\geq$ 29mmHg

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

19

Fetal presentation

- Severe tricuspid regurgitation results in right atrial and ventricular dilation and may cause septal deviation impeding LV diastolic filling which raises left atrial pressure.
- Increased left atrial pressure can lead to changes in foramen ovale size and flow, along with changes in right atrial and systemic venous pressures with consequential changes in ductus venosus, umbilical vein and placental flow increasing the risk for hydrops.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

20

Fetal mortality

- Fetal risk factors for mortality at <30 days of age include
  - Abnormal right ventricular function predicted by low tricuspid regurgitation velocity
  - Increase cardiothoracic ration >0.53
- Fetal predictors of motrality at time of diagnosis include
  - Detection at <32 weeks gestation,
  - Increased tricuspid valve annulus Z-score
  - Presnece of pulmonary regurgitation
  - Pericardial effusion
- Non-survivors were more likely to have pumomnary regurgitation at any gestation and lower gestational age and weight at birth.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

21

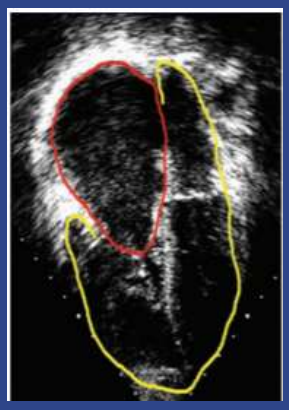
Prognosis

- Several prenatal series of Ebstein anomaly reported poor prognosis, with ~45% of fetuses dying in utero and an overall 80% - 90% mortality.
- Poor prognostic markers prenatally include
  - Massive cardiomegaly
  - Decreased right ventricular outflow due to pulmonary stenosis
  - Fetal hydrops
  - Compression of the lungs may contribute to pulmonary hypoplasia
- Celermajer Index
  - Echo grading score involves calculating the ratio of the combined area of the right atrium and atrialized right ventricle to that of the functional right ventricle and left heart in a four-chamber view at end diastole

Abuhamad, A., & Chaoui, R. (2010). *A Practical Guide to Fetal Echocardiography: Normal and Abnormal Hearts*. Lippincott Williams & Wilkins.

22

Celermajer Index


[1]

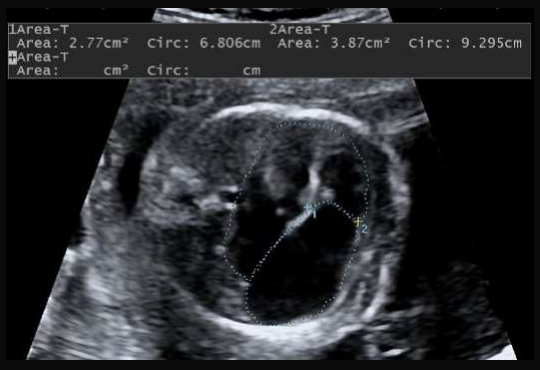
[2]

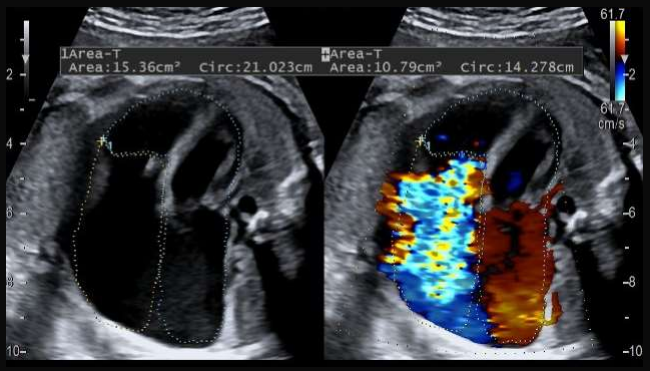
Echo Prognostic Score for Fetuses and Infants with Ebstein Anomaly	
Score	Outcome
Grade I = ratio <0.5	Very good
Grade II = ratio 0.5 - 0.99	Good – up to 92% survival
Grade III = ratio 1 – 1.49	Poor – early mortality of 10% Childhood mortality 45%
Grade IV = ratio >1.5	Very poor – 100% mortality likely

1. Lai, Wyman W., et al., editors. *Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult*. Third edition, Wiley-Blackwell, 2021.
2. Abuhamad, A., & Chaoui, R. (2010). *A Practical Guide to Fetal Echocardiography: Normal and Abnormal Hearts*. Lippincott Williams & Wilkins.

23

Celermajer Index





24

Fetal management

- Unless there is antenatal SVT, requiring transplacental (maternal) therapy with antiarrhythmics, most programs proceed with expectant management.
- Some centers advocate for increased surveillance once fetus reach 32-week gestation.
  - Weekly surveillance with non-stress test, biophysical profile and/or fetal echocardiogram.

- Ramcharan TKW, Goff DA, Greenleaf CE, Shebani SO, Salazar JD, Corno AF. Ebstein's Anomaly: From Fetus to Adult-Literature Review and Pathway for Patient Care. *Pediatr Cardiol*. 2022;43(7):1409-1428. doi:10.1007/s00246-022-02908-x.

25

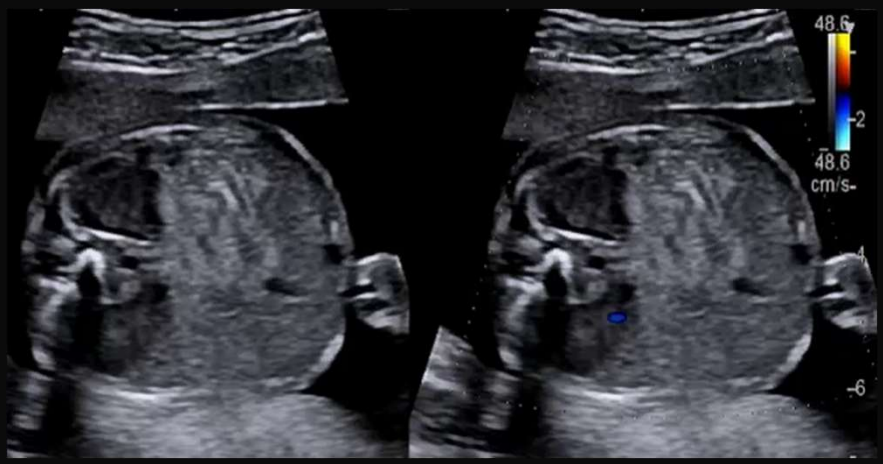
26

Case #1

- 32-year-old female
- 22w4d gestation referred for abnormal ultrasound
  - Referral: AVSD versus Transposition

27

20w6d



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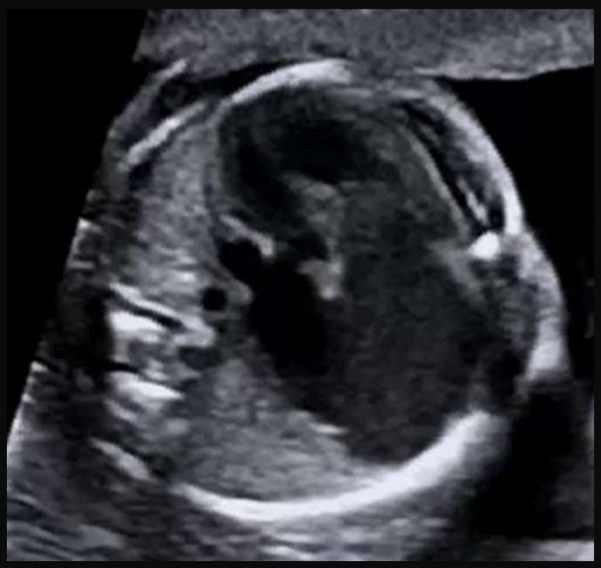
20w6d



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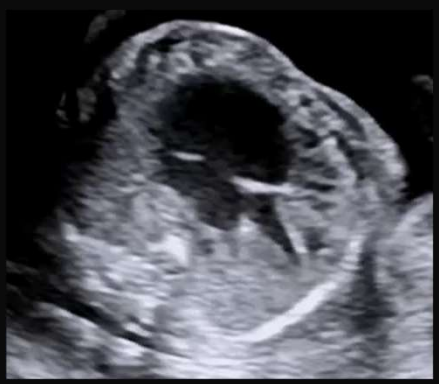
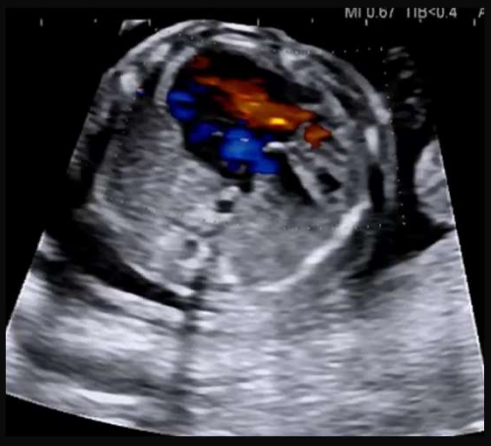
22w4d





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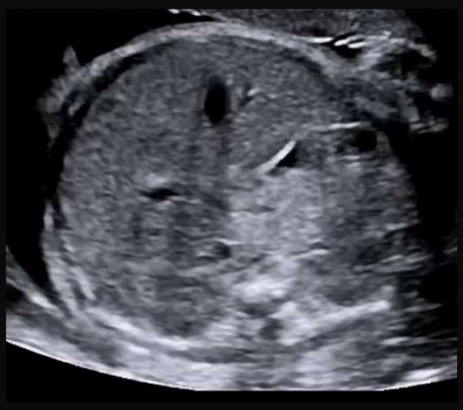
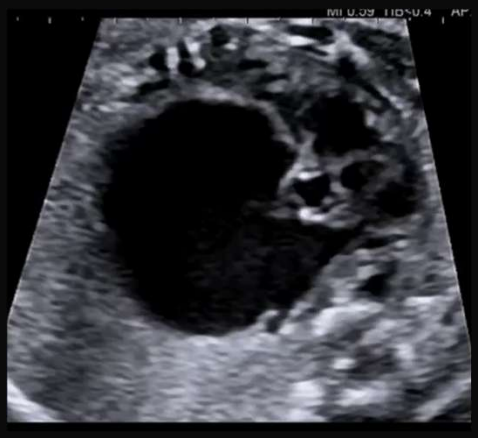
30w3d





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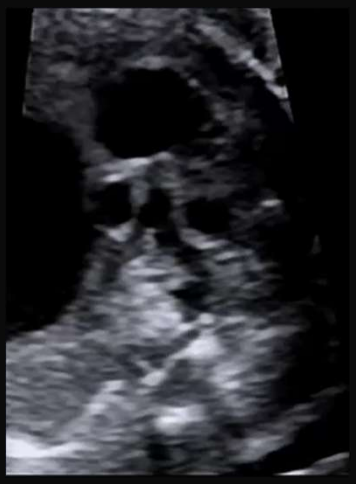
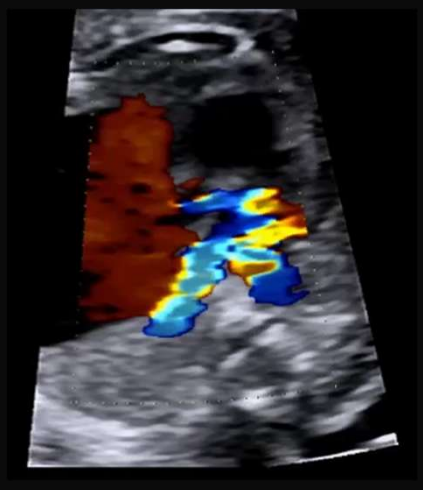
30w3d





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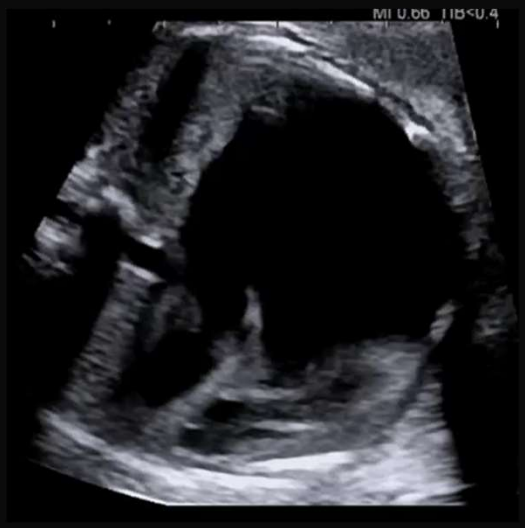
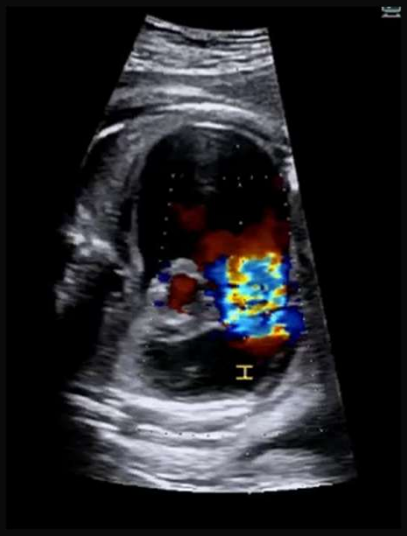
34w3d





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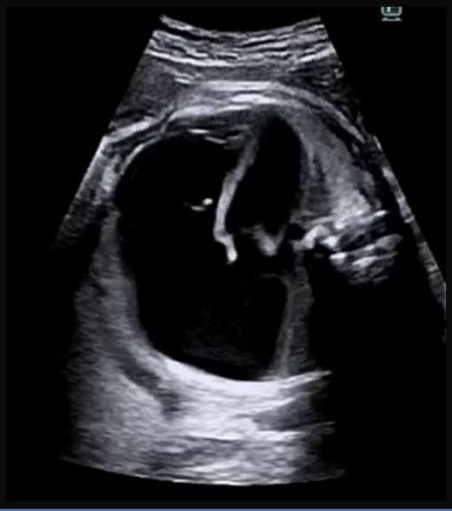
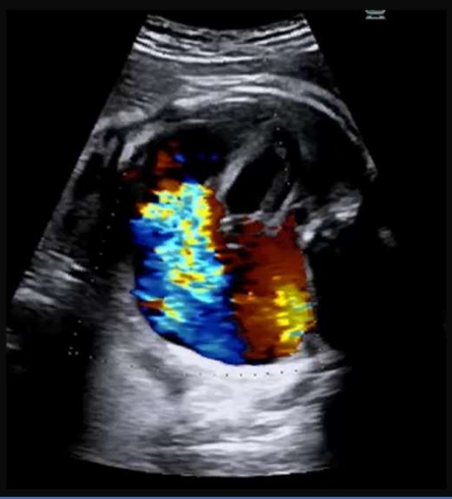
36w3d





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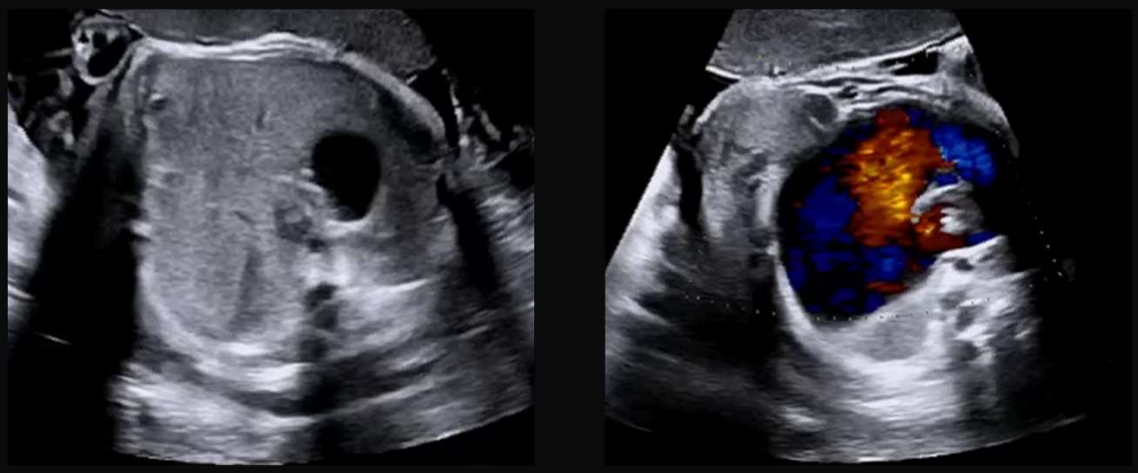
38w3d



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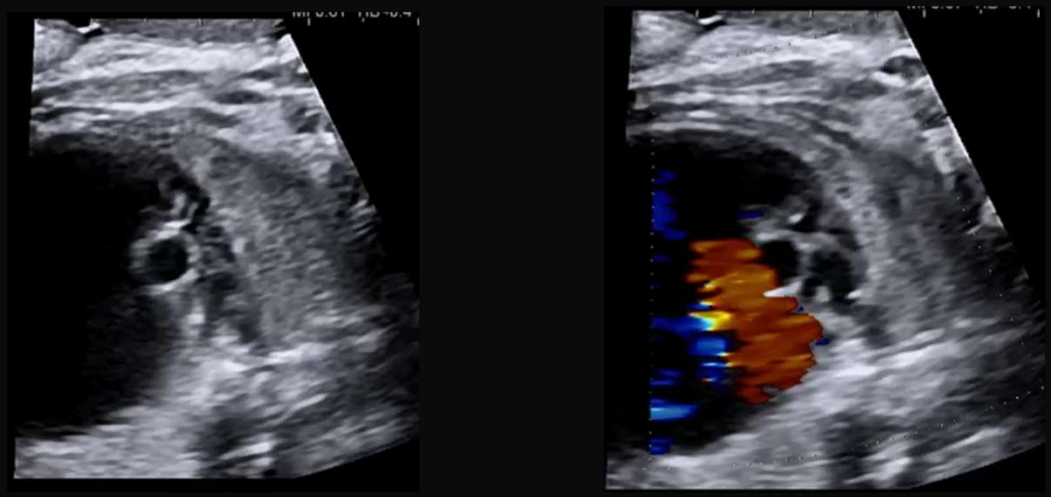
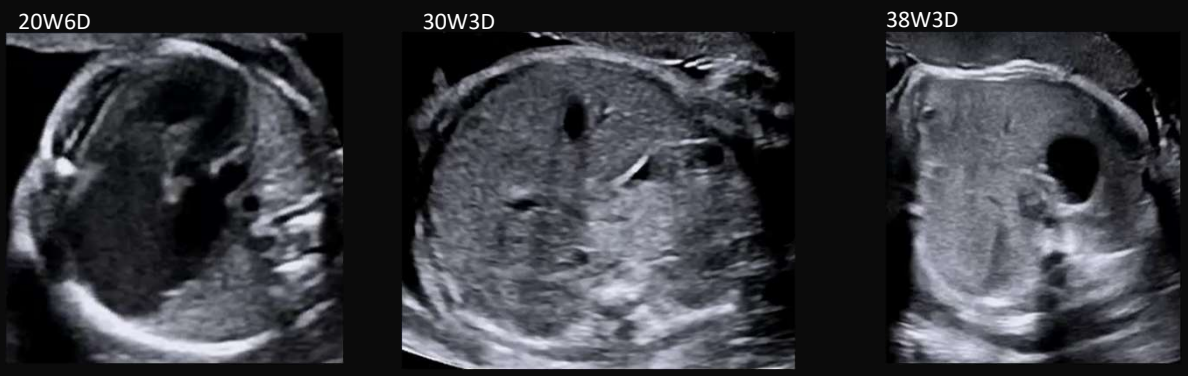


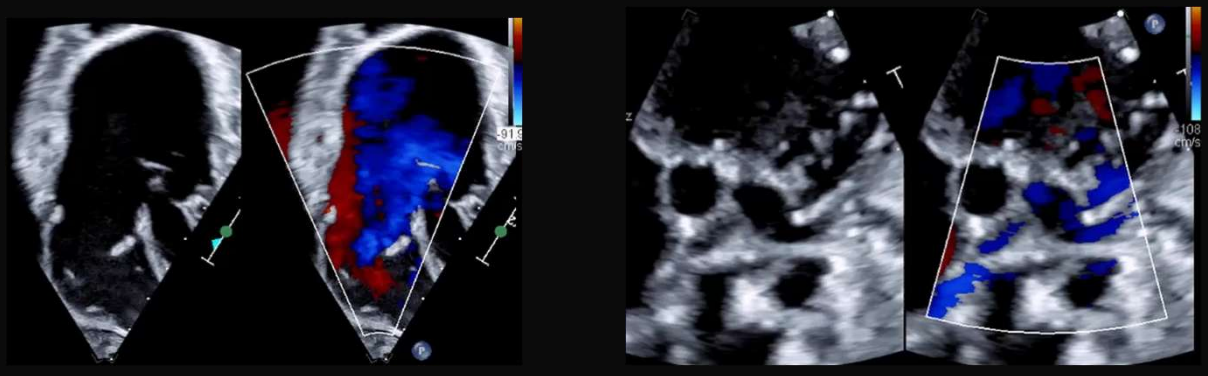
36

Progression During Fetal Life



37

2 day old



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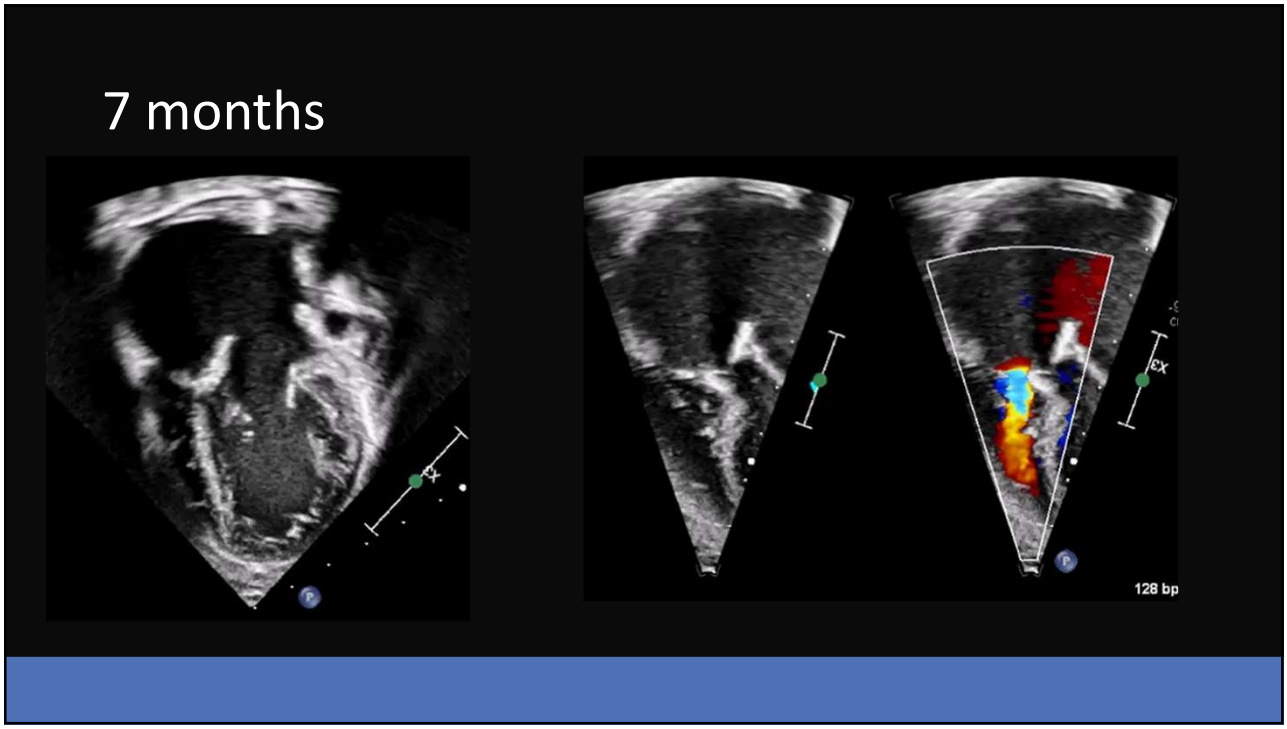
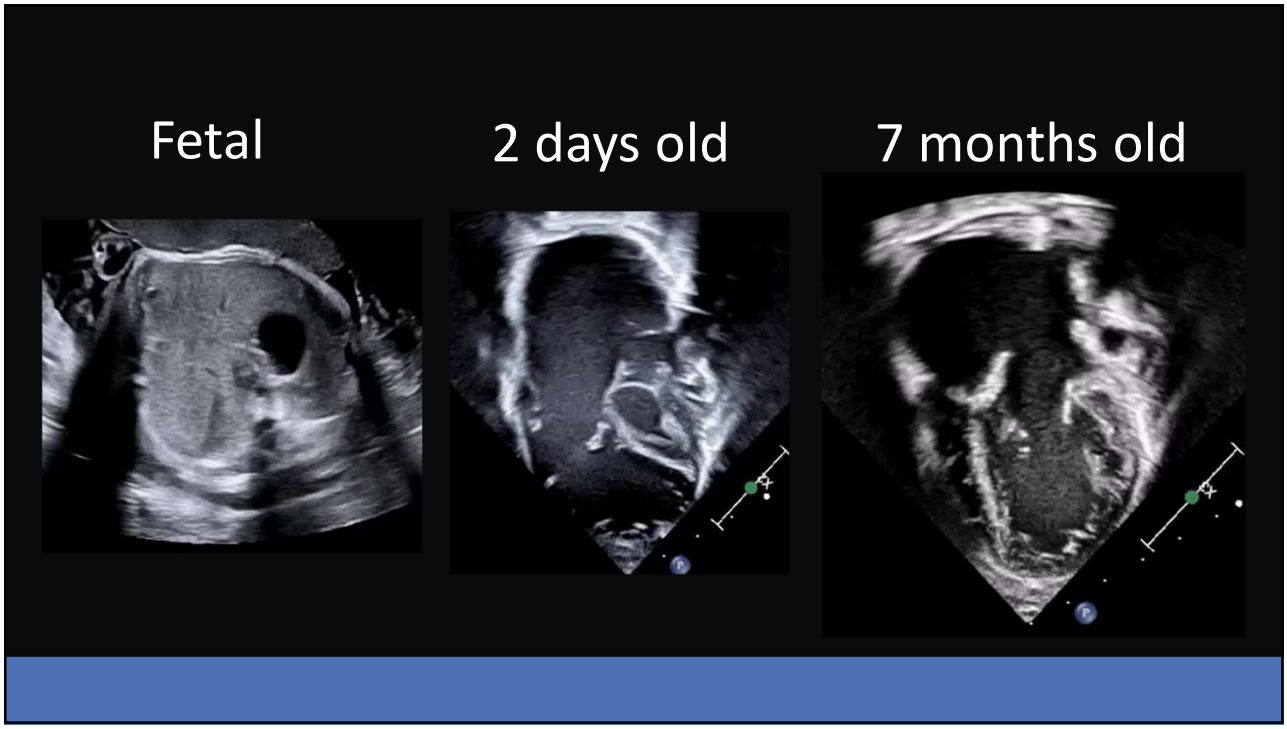


39



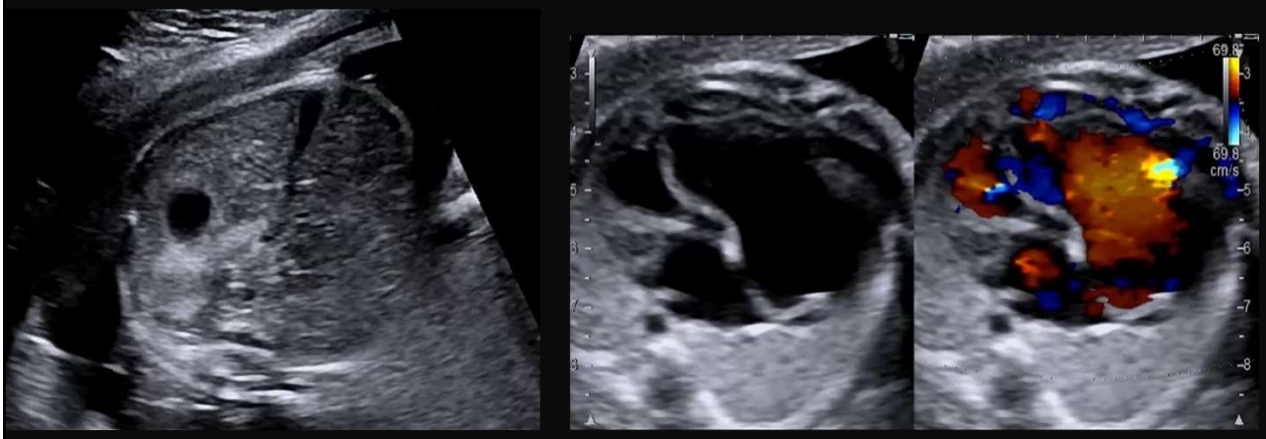
40

Case #2

- 24-Year-Old Female
- 22W5D gestation
- Most recent obstetric ultrasound showed normal interval growth and dilated right atrium and displacement of tricuspid valve.

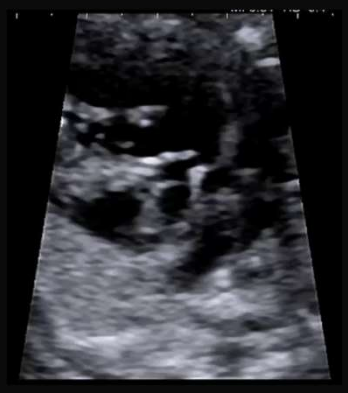
41

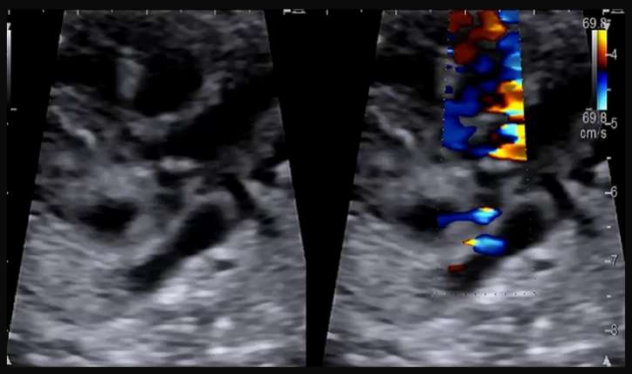
28w4d



42

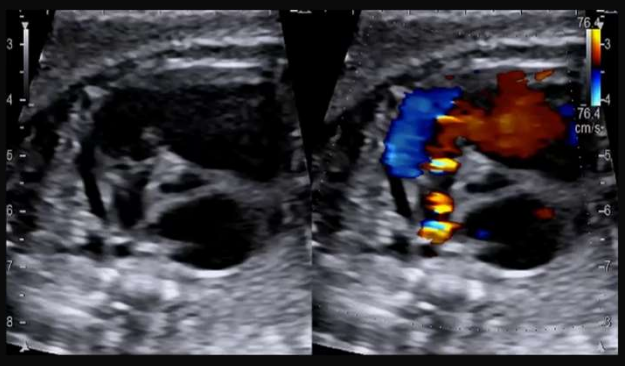
28w4d

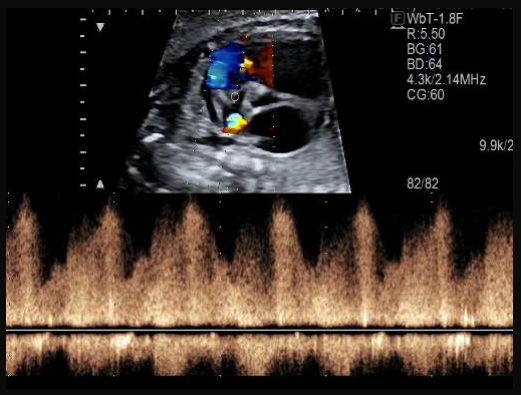




43

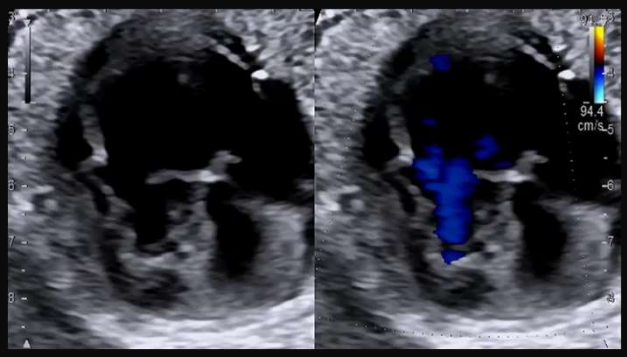
28w4d

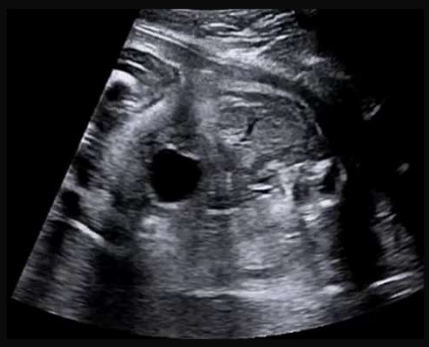




44

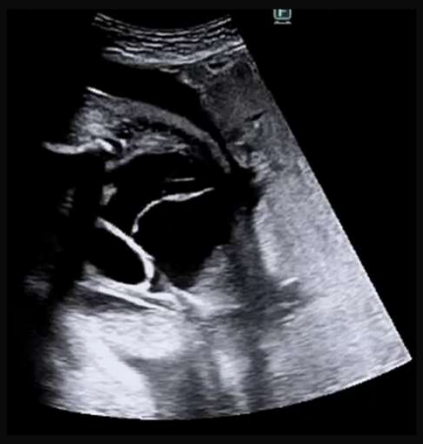
30w4d

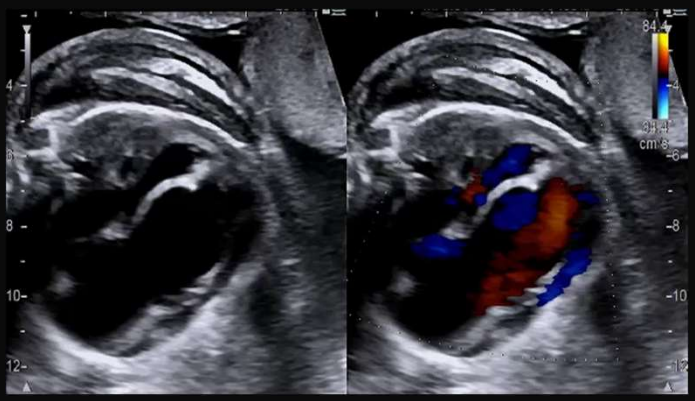




45

34w4d





46

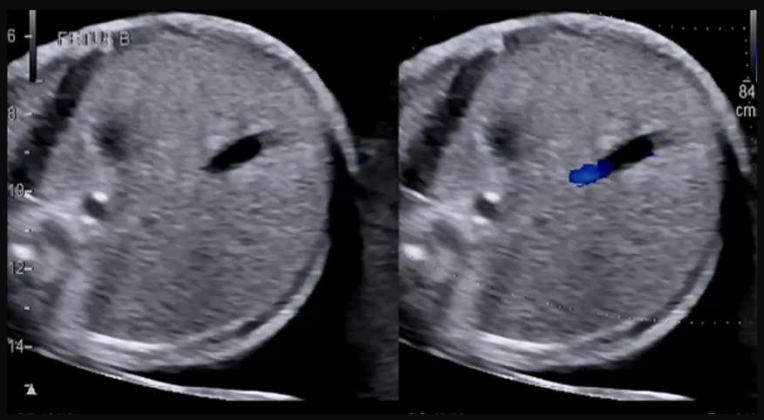
Differential Diagnosis: Tricuspid Valve Dysplasia

- Hinge point of the septal leaflet is not displaced from the level of the true annulus.
- Leaflets are thickened and the chordal apparatus is foreshortened
- Myocardium of the RV is more normal than in Ebstein anomaly

Lai, Wyman W., et al., editors. *Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult*. Third edition, Wiley-Blackwell, 2021.

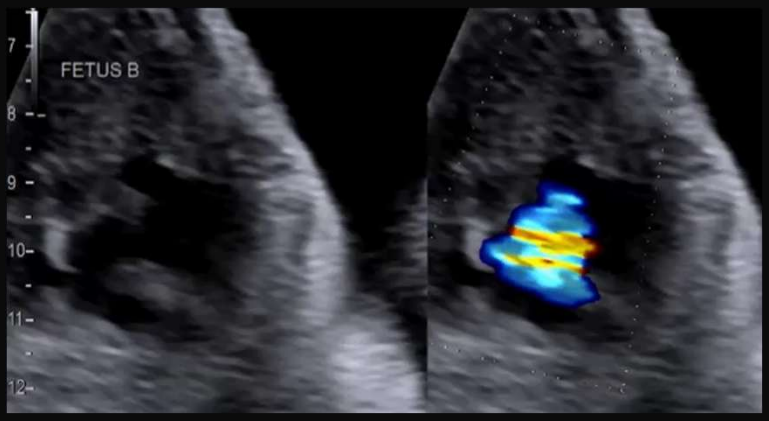
47

TV Dysplasia



48

TV Dysplasia



49

Where are we now

- 159 years later we are talking about diagnosing Ebstein anomaly in the fetus.
- Remarkable progress has been made in its repair.
- Since the introduction of various corrective surgical techniques, operative mortality rates have decreased.
- Diagnosis and treatment of Ebstein anomaly can still be challenging

Mazurak M, Kusa J. The Two Anomalies of Wilhelm Ebstein. *Tex Heart Inst J.* 2017;44(3):198-201. Published 2017 Jun 1. doi:10.14503/THIJ-16-6063

50

Key Points

- Septal and posterior leaflets of the tricuspid valve are displaced inferiorly form the TV annulus, toward the apex of the heart and originate from the RV myocardium
- Anterior tricuspid leaflet maintains is normal attachment to the TV annulus
- Proximal portion of the RV is continuous with the true RA and forms an "atrialized portion" of the RV
- Color Doppler helps in the detection of severe tricuspid regurgitation even prior to the enlargement of the RA
- Tricuspid regurgitation is holosystolic with high peak velocities and typically arises from the middle of the RV

Abuhamad, A., & Chaoui, R. (2010). *A Practical Guide to Fetal Echocardiography: Normal and Abnormal Hearts*. Lippincott Williams & Wilkins.

51

Key Points

- Common associated cardiac abnormalities include an obstruction of the RV outflow tract and atrial septal defects in more than 60% of cases
- Pulmonary hypoplasia can occur with severe cardiomegaly
- Prenatal series report poor prognosis with about 45% of fetuses dying in utero and an overall 80%-90% mortality.
- Poor prognostic markers prenatally include massive cardiomegaly, decreased RV outflow due to pulmonary stenosis, and fetal hydrops.

Abuhamad, A., & Chaoui, R. (2010). *A Practical Guide to Fetal Echocardiography: Normal and Abnormal Hearts*. Lippincott Williams & Wilkins.

52