

# Heterotaxy

## Epidemiology in the era of prenatal diagnosis

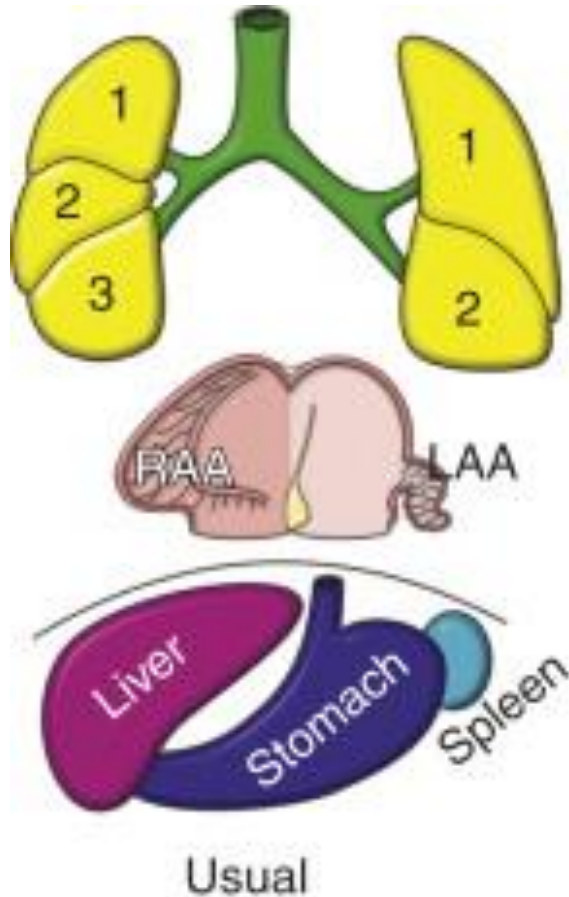
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# Fetal Heterotaxy

- **definition**
- **prenatal incidence**
- **key features**
  - cardiac findings
- **intrauterine course**

# Normal body configuration „Lateralization“



**Thoracal and abdominal  
organs are orientated to  
right or left side**

# Definition of Heterotaxy\*

**Abnormal arrangement of thoracic and abdominal organs across the left-right axis of the body.**

Associated with complex cardiac and extracardiac disease.

„\* heteros“ = different „taxis“ = arrangement

# Idealized Heterotaxy Subsets

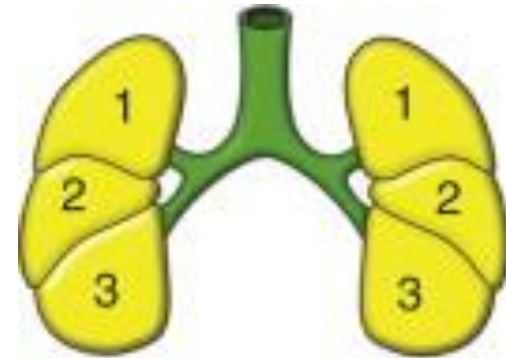


Mid-line liver

Malrotated gut

*Genova Press*

**Left atrial Isomerism**



Mid-line liver

Malrotated gut

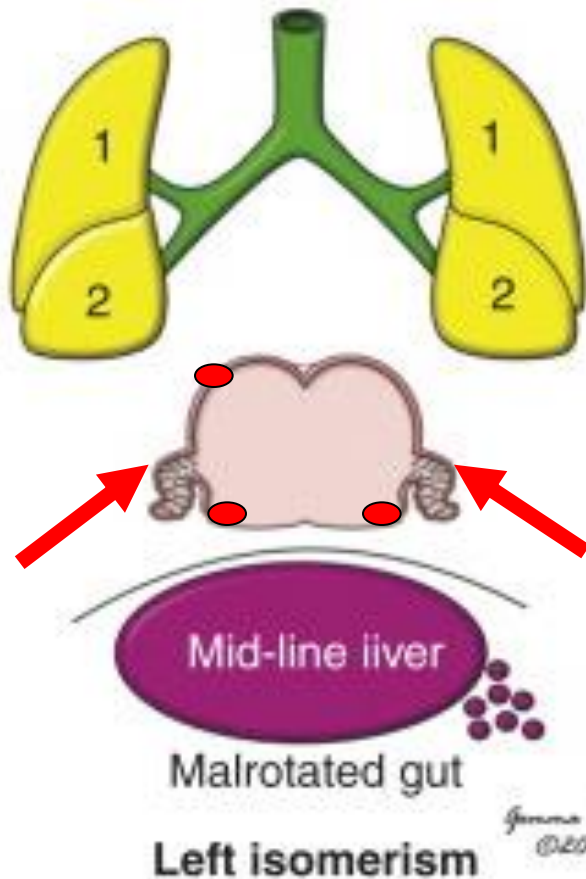
**Right atrial Isomerism**

# Incidence of Heterotaxy

- Incidence of heterotaxy 1-1.44/10.000 births
- 2-4.2% of all infants with congenital heart disease
- **at least 6%** of the cardiac defects detected in utero
- recurrence 5-10% of siblings

*Lim, Circulation 2005; Lin, Genet Med 2000; Freedom, Card Young 2005, Hsiao 2007; overview Yoo 2009 in Yagel, Fetal Cardiology, 2nd Ed. Fasslova 2014*

# Typical findings on left atrial isomerism LAI



## Bilateral left atria

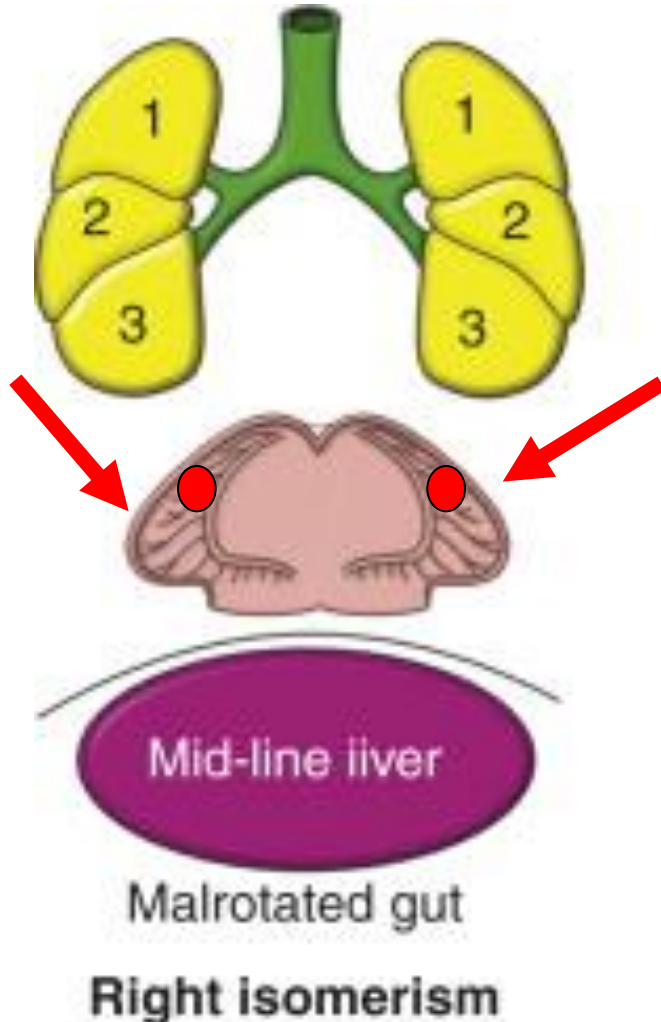
- Abnormal sinus node and atrioventricular conduction  
→ *Bradycardia, AV-Block*
- Anomalies of systemic veins (interrupted IVC)

## Bilateral „left lungs“

## Abdomen: Situs ambiguus

- **Polysplenia**
- Intestinal obstruction
- hypoplastic gallbladder 20%
- **Biliary atresia 7%**

# Typical findings on right atrial isomerism



## **Bilateral right atrial appendages**

- dual sinus nodes
  - Rhythm disturbances
  - Tachycardia
- **Total anomalous pulmonary venous return**

## **Bilateral right lungs**

## **Situs ambiguus**

- Intestinal obstruction
- Asplenia



# Prenatal Epidemiology

165 Fetus with prenatal diagnosis of heterotaxy  
1991-2011

Gestational age at first presentation:

LAI 23.35 ± 6.3  
n= 111

RAI 25.65 ± 7.18 wks  
n=54

# CHD and Heterotaxy

	<i>Left isomerism N=111</i>	<i>Right isomerism N=54</i>
CHD in Heterotaxy	86.5%	98.1%
Total pulmonary venous connection	Rare 4.5%	31.5 % +/- obstruction
Partial pulmonary venous connection	9.9%	9.3%
<b>AVSD unbalanced</b>	<b>71.2%</b>	<b>66.7%</b>
<b>DORV</b>	<b>22.5%</b>	<b>35.2%</b>
<b>Univentricular</b>	<b>+</b>	<b>+++</b>
<b>Ventriculoarterial connection</b>	<b>Discordant 11.7%</b>	<b>Discordant 35.2%*</b>
Pulmonary atresia or stenosis	37.8%	63.8%*
Left sided obstructive lesion	11%	13%

\* p<0.05

# Heterotaxie Syndrom



## Left atrial isomerism

- „better“ CHD
- 2/3 two ventricles
- biliary malformation\*\*



## Right atrial isomerism

- „worse“ CHD
- most single ventricle
- Total abnormal pulmonary venous return

# „AV-Block“ in Heterotaxy

	<i>Left isomerism</i> <i>N=111</i>	<i>Right isomerism</i> <i>N=54</i>
<b>AV-Block prenatal n= 44</b>	<b>44 (40%)</b>	<b>0 (0%)</b> p<0.001
Fetal hydrops n=38	33 (30%)	5 (9.4%) p=0.002
Spontaneous IUFD	8	3
Spontaneous IUFD with AV-Block	6	0

**fetal heart disease +  
AV-Block  
high risk of fetal demise**

# Perinatal Outcome in Fetuses with Heterotaxy Syndrome and Atrioventricular Block or Bradycardia

Maria C. Escobar-Diaz · Wayne Tworetzky · Kevin Friedman · Terra Lafranchi · Francis Fynn-Thompson · Mark E. Alexander · Douglas Y. Mah

Pediat Cardiol Febr. 2014

22/91 fetuses with LAI  
 9 fetal AV-Block II-III at presentation  
 13 sinus bradycardia

**Table 2** Risk factors for fetal death ( $n = 19$ )

Risk factors	Surviving patients ( $n = 15$ )	Non surviving patients ( $n = 4$ )	$p$
First ventricular rate <55 bpm (in utero)	2	1	0.530
Last ventricular rate <55 bpm (in utero)	2	2	0.178
<b>Hydrops</b>	<b>3</b>	<b>4</b>	<b>0.009</b>
<b>Cardiac dysfunction in utero</b>	<b>0</b>	<b>2</b>	<b>0.035</b>
AV block in utero	5	2	0.603

Data in bold represents statistically significant data ( $p < 0.05$ )

AV atrioventricular

**Predictors of IUFD**



# Counselling



## Left atrial isomerism

- „better“ CHD
- 2/3 two ventricles
- biliary malformation?
- AV-Block → risk of IUFD

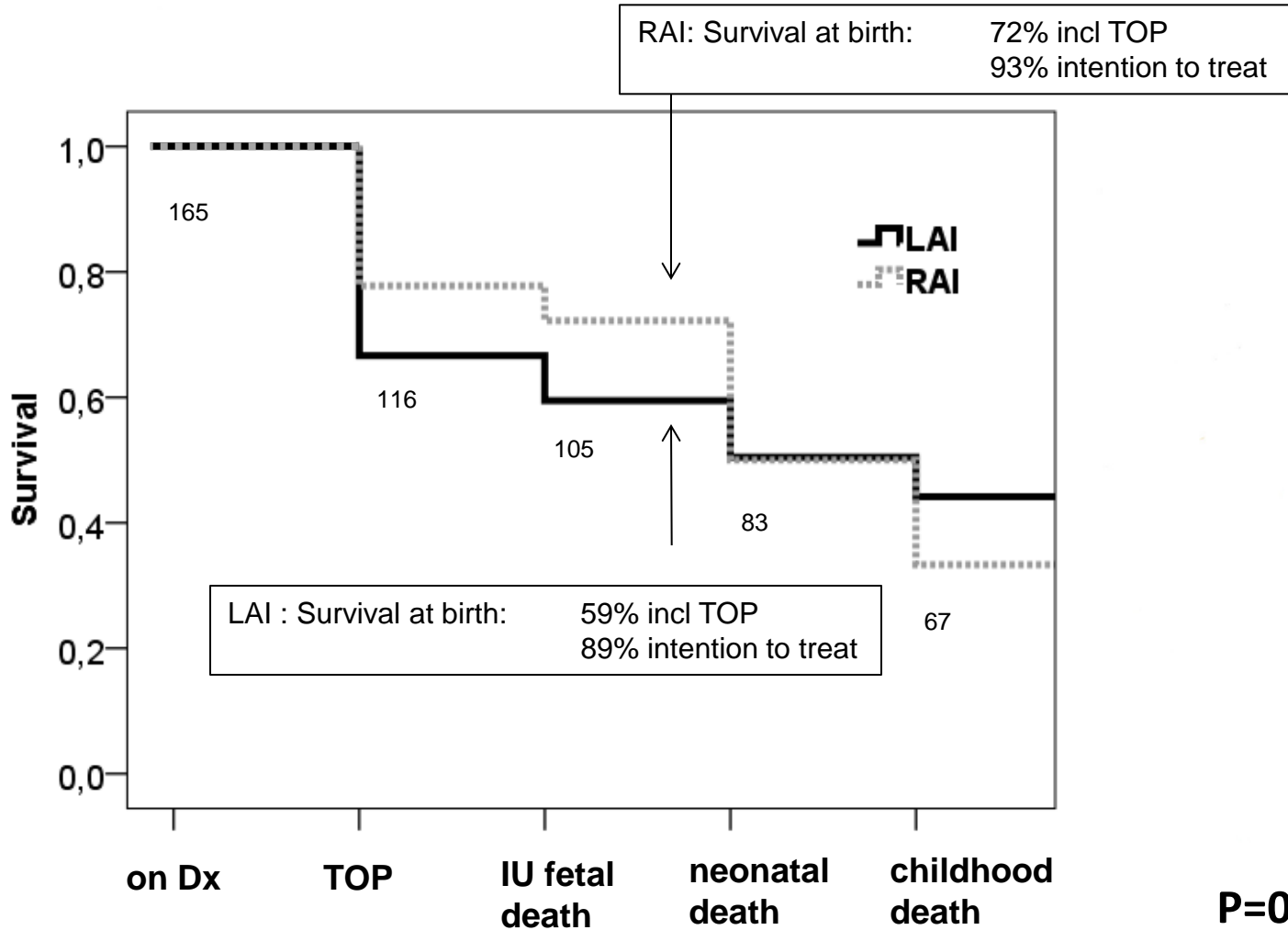


## Right atrial isomerism

- „worse“ CHD
- most single ventricle
- Total abnormal pulmonary venous return

**Parental decision?**

# Survival



# „Fetal Outcome“ of Heterotaxy

	<i>n=</i>	<i>Interruption</i>	<i>Intrauterine death</i>	<i>Total survival</i>	<i>Survivors Excluding interruptions</i>
<b>Left Isomerism</b>	<b>111</b>	<b>37</b>	<b>8</b>	<b>59%</b>	<b>89%</b>
<b>Our data</b>					
<b>Lim 2005</b>	<b>52</b>	<b>20</b>	<b>2</b>	<b>60%</b>	<b>96%</b>
<i>Pepes 2009</i>	41	22	7	29%	63%
<i>Taketazu 2006</i>	48	13	2	73%	94%
<b>Right Isomerism</b>	<b>54</b>	<b>12</b>	<b>3</b>	<b>72%</b>	<b>93%</b>
<b>Lim</b>	<b>31</b>	<b>7</b>	<b>1</b>	<b>74%</b>	<b>95%</b>
<i>Taketazu 2006</i>	23	7	1	65%	93%

*Berg et al. 2014; Pepes 2009; Taketazu 2006, Lim 2005*





# Summary

- The incidence of heterotaxy syndrome in utero is higher than postnatally
- Intrauterine fetal death is mostly related to fetal cardiac dysfunction and fetal AV-Block (LAI)
- the epidemiology of fetal heterotaxy is significantly influenced by a high rate of TOP in Western Countries

# Summary

- LAI
  - „better“ CHD
  - relevant intrauterine mortality due to fetal AV-block and hydrops
  - associated with biliary atresia
  - postnatally LAI carries a significant better prognosis than RAI
- RAI is associated with
  - more complex CHD
  - favourable intrauterine course
  - relevant postnatal mortality