PREVALANCE OF FETAL HEART DEFECTS

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Importance of CHD

- *Major CHD*: Lethal
  Requiring intervention
- ***> 20% of prenatal deaths*** resulting from congenital malformation
- ***> 50% of deaths*** from lethal malformations during childhood

Young ID, Clarke M. Br Med J 1987; 295: 89-91.

Prenatal detection rate of CHD

- Major CHD: 38.8%, Minor CHD:20.8%
- Major CHD: 23 %

Eurofetus Study. Am J Obstet Gynecol 1999
Bull C. Lancet 1999

Does Prenatal Detection of Heart Defects Make a Difference?

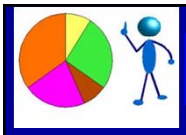
- Helps for diagnosis of genetic disorders
- Provides the option of termination or in utero treatment
- May improve neonatal mortality and surgical outcome in specific cardiac anomalies such as TGA & HLHS

The knowledge of prevalance of CHD would help for:

- *Better understanding of the underlying pathology of cardiac defects*
- *Increased identification of fetuses with CHD*

Etiology of Congenital Heart Disease (CHD)

Cause	Percent
Primary genetic causes	
Chromosome abnormalities	8-10
Monogenic defects	3-5
Primary exogenous factors	
Infections (e.g. rubella)	1
Others (teratogenic effects, maternal illness)	1
Multifactorial inheritance	85



Incidence of CHD

- In liveborn infants: 4-8 per 1000
- In stillborn infants: 10 x live births
- True incidence among fetuses is difficult to evaluate

Hunter S et al. Heart 2000

Young ID, Clarke M. Br Med J 1987

Baltimore-Washington Infant study between 1981 and 1989

- 60% of cases with CHD diagnosed by 4 weeks of age
- 80% by 12 weeks
- 90% by 24 weeks

Perry LW et al. In: Epidemiology of Congenital Heart Disease. C Ferenz, JD Rubin, CA Loffredo, CA Magee, eds. The Baltimore-Washington Infant Study 1981-1989. Perspectives in pediatric cardiology. 1993; 4: 33-62.

The reported incidence rate per 1000 liveborn infants:

- **3.3 at birth**

  4.0 at the end of 1st week of neonatal life

  5.2 by the end of 1st month

- **7.8 by the end of the first year**

True incidence of CHD: ???

- ***Need for a medical system:***

✓Pediatric cardiologists or obstetricians can diagnose CHD accurately

✓Whole population can reach these cardiologists easily

The barriers for ascertainment of the disease to be incomplete:

- Some CHD causes death in the first few days of life after birth
- Children with very mild lesions such as minimal PS or ASD / VSD might never be diagnosed

Other barriers

1) An unknown number of maturational disorders such as PDA might be included in any published series

2) Many serious forms of CHD are now detected by fetal ECHO and these parents might choose to abort these fetuses

3) The incidence of CHD depends upon how many of asypmtomatic tiny muscular VSDs are included in the series

- *If included, CHD incidence: 4-5%*
- *If not: 1%*

CONGENITAL HEART DISEASE

Improving the effectiveness of routine prenatal screening for major congenital heart defects

J S Carvalho, E Mavrides, E A Shinebourne, S Campbell, B Thilaganathan

Heart 2002;88:387–391

Prevalance for major CHD: 4.3 / 1000 pregnancies

Single center study that included:

- ✓ Pathologic examinations
- ✓ Neonatal echocardiography
- ✓ Long term paediatric follow-up

ACCURATE ESTIMATE

- Prevalance for major CHD: 2.1 / 1000 pregnancies

✓ Underreporting of fetal diagnosis & necropsy results

UNDERESTIMATION

Bull C. Lancet 1999

Incidence of CHD in liveborn children

Lesion	*Median percentage of all CHD*
VSD	**32.4**
PDA	**7.1**
ASD	**7.8**
AVSD	**3.7**
Pulmonary stenosis	**7.0**
Aortic stenosis	**4.1**
Coarctation of aorta	**5.0**
Transposition of great arteries	**4.5**
Tetralogy of Fallot	**5.1**
Truncus arteriosus	**1.4**
Hypoplastic left heart	**2.8**
Hypoplastic right heart	**2.2**
Double inlet left ventricle	**1.4**
Double outlet right ventricle	**1.2**
Total anomalous pulmonary venous connection	**1.0**
Miscellanous	**11.6**

Heart 1999;82:34–39

Spectrum of congenital heart defects and extracardiac malformations associated with chromosomal abnormalities: results of a seven year necropsy study

C Tennstedt, R Chaoui, H Körner, M Dietel

Table 1 Incidence of congenital heart defects, other cardiovascular (CV) and extracardiac malformations, and cases with chromosome anomalies (1991-97)

Diagnostic group	Total	No other CV or extracardiac malformations	With other CV malformations	With extracardiac malformations	Chromosome anomalies	Trisomy 21	Trisomy 18	Trisomy 13	Monosomy X	Triploidy N	Other structural anomalies
VSD	36 (28)	–	20	31	15	8	4	1	–	1	1
AVSD	21 (16)	–	17	17	13	9	3	–	–	–	1
HLH	21 (16)	8 (38)	7	8	2	–	1	1	–	–	–
DORV	15 (12)	–	14	11	5	–	3	2	–	–	–
[illegible]	7 (6)	–	2	7	3	1	–	–	2	–	–
TGA	5 (4)	2 (40)	4	1	–	–	–	–	–	–	–
AoVS	5 (4)	1 (20)	4	1	1	–	–	–	1	–	–
TOF	4 (3)	–	4	3	2	1	–	1	–	–	–
TAC	4 (3)	–	4	3	1	–	–	–	–	1	–
PaVS/PaVA	4 (3)	–	3	–	–	–	–	–	–	–	–
TA	4 (3)	–	3	2	–	–	–	–	–	–	–
SV	2 (1.5)	–	2	–	–	–	–	–	–	–	–
ASD	1 (0.5)	–	1	1	1	–	–	1	–	–	–
Total	129 (100)	11 (9)	85 (66)	85 (66)	43 (33)	19 (15)	11 (9)	6 (5)	3 (2)	2 (1.5)	2 (1.5)

Values are n or n (%).

MOST COMMON DEFECT: **VSD**

The most frequent cardiac defect **BOTH** in necropsy studies of live births and stillbirths

Isolated or associated with other CHD

- The spectrum and frequency of the individual lesions differ between necropsy studies and liveborn series
- Severe heart defects which are usually lethal are more commonly found in necropsy studies

PREVALANCE OF CHD IN RISK GROUPS

Ultrasound Obstet Gynecol 2008; 32: 239–242
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.6115

ISUOG consensus statement: what constitutes a fetal echocardiogram?

Table 1 Common indications for fetal echocardiography

Maternal indications	*Fetal indications*
First-degree relative of proband (mother or father) with CHD	Increased nuchal translucency thickness
Prior child with CHD born to mother and/or father	Abnormal ductus venosus waveform
Pre-existing metabolic disease	Abnormal fetal cardiac screening exam
Type 1 diabetes	Major extracardiac abnormality
Phenylketonuria	Abnormal fetal karyotype
Infections	Hydrops
Parvovirus B19	Effusion
Rubella	Fetal cardiac dysrhythmias
Coxsackie	Persistent bradycardia or tachycardia
Autoimmune antibodies	
Anti-Ro (SSA)	
Anti-La (SSB)	
Teratogen exposure	
Retinoids	
Phenytoin	
Carbamazepine	
Lithium carbonate	
Valproic acid	
Paroxetine	

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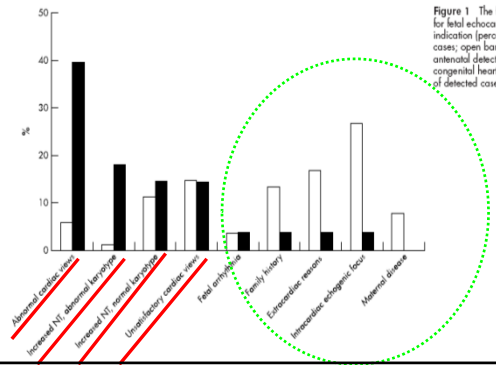
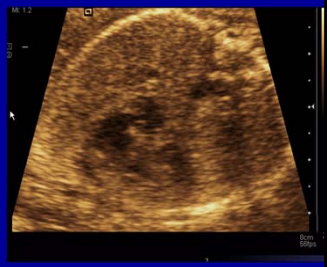


Figure 1 The frequency of referral for fetal echocardiography by indication (percentage of referred cases; open bars) and subsequent antenatal detection of major congenital heart defects (percentage of detected cases; solid bars).

Suspected Cardiac Defect

- The highest risk factor for diagnosing CHD
- FETAL RISK: 50-70%
- *"Routine prenatal screening for major CHD can be highly effective in low risk population"*



Gembruch U et al. 1997

Carvalho JS et al. 2002

Echogenic Focus & CHD

TABLE 2 Cardiac malformations and ICEF in euploid fetuses

Author (Ref.)	Frequency of Cardiac Malformation	Malformation	Method of Ascertainment
Schechter et al. (1)	0/25		Prenatal US and echocardiogram, postnatal physical exam
How et al. (2)	1/24	Transposition of great vessels	Prenatal US and postnatal echocardiogram
Simpson et al. (6)	1/226	VSD	Postnatal echocardiogram, questionnaire
Achiron et al. (7)	0/66		Postnatal echocardiogram
Manning et al. (8)	0/23		Prenatal US
Petrikovsky et al. (13)	0/41		Prenatal echocardiogram, postnatal physical exam
Wax et al. (14)	0/27		Prenatal US, postnatal physical exam, postnatal echocardiogram
Dildy et al. (15)	1/25	ASD, VSD, left SVC	Prenatal US, postnatal echocardiogram
Merati et al. (16)	0/37		Prenatal US, postnatal echocardiogram
Bromley et al. (18)	0/62		Prenatal US, postnatal physical exam

US, ultrasound; VSD, ventricular septal defect; ASD, atrial septal defect; SVC, superior vena cava.

Wax J et al. Obstetrical & Gynecological Survey 2000

Increased NT

- Increased NT above the 99th centile should mandate referral for detailed fetal ECHO
- FETAL RISK: 5%

PRENATAL DIAGNOSIS
Prenat Diagn 2002; **22**: 864–868.
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/pd.413

INVITED COMMENTARY:
CURRENT ISSUES IN OBSTETRICS AND GENETICS

Increased nuchal translucency in fetuses with a normal karyotype

Jon A. Hyett*

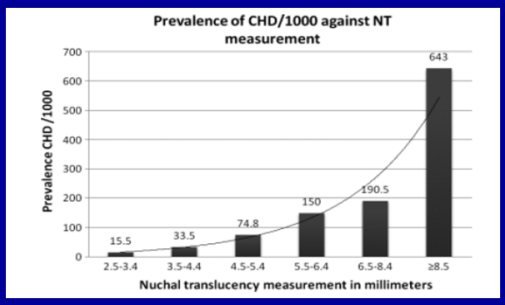
Author	NT cut-off (centile)	Detection rate
Hyett *et al.* (1999)	95th	28/50 (56%)
	99th	20/50 (40%)
Michailidis and Economides (2001)	95th	4/11 (36%)
	99th	3/11 (27%)
Mavrides *et al.* (2001)	95th	4/26 (15%)
	99th	3/26 (12%)
Total	95th	36/87 (41%)
	99th	26/87 (30%)

PRENATAL DIAGNOSIS
Prenat Diagn 2009; **29**: 739–748.
Published online 27 April 2009 in Wiley InterScience
(www.interscience.wiley.com) DOI: 10.1002/pd.2281

REVIEW

The nuchal translucency and the fetal heart: a literature review

S. A. Clur[1,2]*, J. Ottenkamp[1,2] and C. M. Bilardo[3]



Extracardiac anomaly

- FETAL RISK: 13-14%
- AVSD, ToF are more frequently associated with extracardiac anomalies than other CHD

Table 2 Frequency of malformations of the systems associated with heart defects

Organ system	*Heart defect (n = 129) n (%)*
Central nervous system	40 (31)
Kidney, urinary tract, and genital system	34 (26)
Gastrointestinal system	31 (24)
Respiratory system	14 (11)
Skeletal system	10 (8)

Tennstedt C et al. Heart 1999

AbN Fetal Karyotype

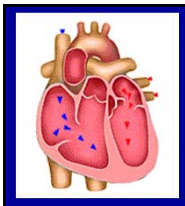
The risk of chromosomal abnormality in a fetus with CHD

- 16%: Allan et al
- 32%: Copel et al
- 22%: Chaoui et al
- 28%: Gembruch et al
- 29%: Körner et al

Frequency of chromosomal anomalies associated in single types of CHD

Type of CHD	Chromosomal anomaly (%)
AVSD*	35 - 47
VSD*	37 - 48
ASD	3
ToF*	27
DORV*	12 - 45
HLH	4
Truncus arteriosus*	14 - 29
TGA	3
CoA*	21 - 29
Tricuspid atresia	2 - 9
Ebstein's anomaly	5 - 6
Aortic stenosis	0.2 - 17
Pulmonary stenosis/atresia	4 - 5

Karyotype	Associated CHD	Risk (%)
Trisomy 21	AVSD, VSD, ASD, ToF, CoA	50%
Trisomy 18	VSD,ToF,DORV, AVSD,BiAv,AS,BiPv, PS,HLH	99
Trisomy 13	VSD,ASD,HLH,ToF	90
Partial trisomy 22	TAPVC, VSD,ASD	40
Triploidy	VSD	60
Turner syndr.	CoA,AS,HLH,ASD	30-40
Monosomy 22q11	VSD,ToF,DORV,TAC,CoA, IAA	85-95



Incidence of CHD: 50-56%

- AVSD & VSD: 76%
- ToF & DORV: 7%
- CoA: 2%

Paladini D et al. Ultrasound Obstet Gynecol 2000

Trisomy 21: Atrioventricular septal defect

45,XO: Coarctation of Aorta

22q11 deletion: Conotruncal Abnormalities

FETAL ARRYTHMIAS

CHD may be present in:

- 30-50 % of cases with complete AV block
- 2-5% of cases with tachyarrythmias

FAMILY HISTORY & CHD

- *The most common indication for fetal ECHO*

FETAL RISK:

- **2%** if one previous child affected
- **10%** if two previous siblings affected
- **4%** if maternal CHD
- **2%** if paternal CHD

Some lesions:

- *Left heart obstructive lesions*
- *Heterotaxy syndromes*

have a slightly higher recurrence rate than other CHD

Allan LD et al. Am J Cardiol 1986

Teratogen exposure

- Risk increases when exposed between 6-8 weeks of pregnancy
- FETAL RISK: 2-3%
- Alcohol, AEDs, Lithium, Retinoic acid

A Reevaluation of Risk of In Utero Exposure to Lithium

Lee S. Cohen, MD; J. M. Friedman, MD, PhD; James W. Jefferson, MD; E. Marshall Johnson, PhD; Myra L. Weiner, PhD

Conclusion.—While initial information regarding the teratogenic risk of lithium treatment was derived from biased retrospective reports, more recent epidemiologic data indicate that the teratogenic risk of first-trimester lithium exposure is lower than previously suggested. The clinical management of women with bipolar disorder who have childbearing potential should be modified with this revised risk estimate.

(*JAMA*. 1994;271:146-150)

Table 2.—Summary of Case-Control Studies of Maternal Lithium Treatment During Pregnancy Among Children With Ebstein's Anomaly of the Heart

Source	Frequency of Maternal Lithium Treatment During Pregnancy: Ebstein's Anomaly Cases	Controls
Kallen[8]	0/25	0/28
Edmonds and Oakley[9]	0/34	0/34
Zalstein et al[10]	0/59	1/168
Sipek[11]	0/89	1/168

Pregnancy in the Woman with Epilepsy: Maternal and Fetal Outcomes

Page B. Pennell, M.D.[1]

Table 1 Major Malformations in Infants of Women with Epilepsy

Malformation	General Population	Infants of Women with Epilepsy
Congenital heart	0.5%	1.5–2%
Cleft lip/palate	0.15%	1.4%
Neural tube defect	0.1%	1–2% (VPA)
		0.5–1% (CBZ)

CBZ, carbamazepine; VPA, valproate.

Maternal Diseases & CHD

- Good periconceptional metabolic control might decrease the risk to near the level of N population
- Maternal DM ~ Conotruncal lesions

In poor metabolic control, FETAL RISK:

- ***4-6% in IDDM***
- ***14% in PKU***

Shields LF et al. Obstet Gynecol 1993

Thank you for your attention…