

Prenatal diagnosis

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PRENATAL DIAGNOSIS INFORMATION SOURCES

- **TROPHOBLAST / PLACENTA**
CARYOTYPE, ADN, BIOCHEMISTRY
- **AMNIOTIC FLUID**
CELLS: CARYOTYPE, ADN, BIOCHEMISTRY
FLUID: BIOCHEMISTRY
- **FETAL BLOOD**
CARYOTYPE, ADN, SEROLOGY, HEMATOLOGY,
BIOCHEMISTRY
- **FETUS**
TISSUES (BLOOD, SKIN, MUSCLE, LIVER)
"PHENOTYPE"
"WELL-BEING"
"BEHAVIOUR"
- **MATERNAL BLOOD**
FETAL CELLS, FETAL DNA

PRENATAL DIAGNOSIS WHICH TEST TO USE ?

- **QUESTION TO BE ANSWERED :**
CHOICE OF THE APPROPRIATE INFORMATION SOURCE
- **GESTATIONAL AGE :**
CHOICE OF THE APPROPRIATE METHOD
- **RISK OF THE VARIOUS SAMPLING
METHODS**

PRENATAL DIAGNOSIS

CHOICE OF THE SAMPLING METHOD

GESTATIONAL AGE

- ≤ 13 WKS : CVS
- ≥ 15 WKS : AMNIOCENTESIS
- ≥ 20 WKS : AMNIOCENTESIS
FBS

PRENATAL DIAGNOSIS SAMPLING METHODS

AMNIOCENTESIS

FETAL BLOOD SAMPLING (FBS)

CHORIONIC VILLUS SAMPLING (CVS)

**FETAL TISSUES BIOPSIES (SKIN,
MUSCLE, LIVER)**

PRENATAL DIAGNOSIS AMNIOCENTESIS

INDICATIONS

DETERMINATION OF FETAL CARYOTYPE

NEURAL TUBE DEFECTS

MENDELIAN DISEASES

INFECTIONS (TOXOPLASMOSIS, CMV)

PRENATAL DIAGNOSIS AMNIOCENTESIS

DETERMINATION OF FETAL CARYOTYPE:

- **(ADVANCED MATERNAL AGE (≥ 35 YRS))**
- **HIGH RISK OF ANEUPLOIDY ON SCREENING**
- **HISTORY OF CHROMOSOMAL ANOMALY**
- **PARENTS CARRIERS OF A BALANCED TRANSLOCATION**
- **X-LINKED DISEASES**
- **ULTRASOUND-DETECTED FETAL ANOMALIES**
- **MATERNAL ANXIETY**

PRENATAL DIAGNOSIS AMNIOCENTESIS

NEURAL TUBE DEFECTS

**MEASUREMENT OF AMNIOTIC ALPHA-FETOPROTEIN AND
ACETYL-CHOLINESTERASE CONCENTRATIONS:**

ELEVATION OF MATERNAL SERUM aFP

HISTORY OF NTD

PRENATAL DIAGNOSIS AMNIOCENTESIS

MENDELIAN DISEASES

**MEASUREMENT OF ENZYME ACTIVITIES OR
METABOLITES CONCENTRATIONS IN AMNIOTIC
FLUID OR AMNIOCYTES**

ANALYSES OF FETAL DNA FROM AMNIOCYTES

PRENATAL DIAGNOSIS AMNIOCENTESIS

TECHNIQUES

BLIND SAMPLING

ULTRASOUND-DIRECTED PUNCTURE

**SAMPLING UNDER ULTRASOUND
GUIDANCE**

PRENATAL DIAGNOSIS AMNIOCENTESIS

CONTRIBUTIONS OF ULTRASOUND

CONFIRMATION OF FETAL LIFE

CONFIRMATION OF GESTATIONAL AGE

DIAGNOSIS OF MULTIPLE GESTATIONS

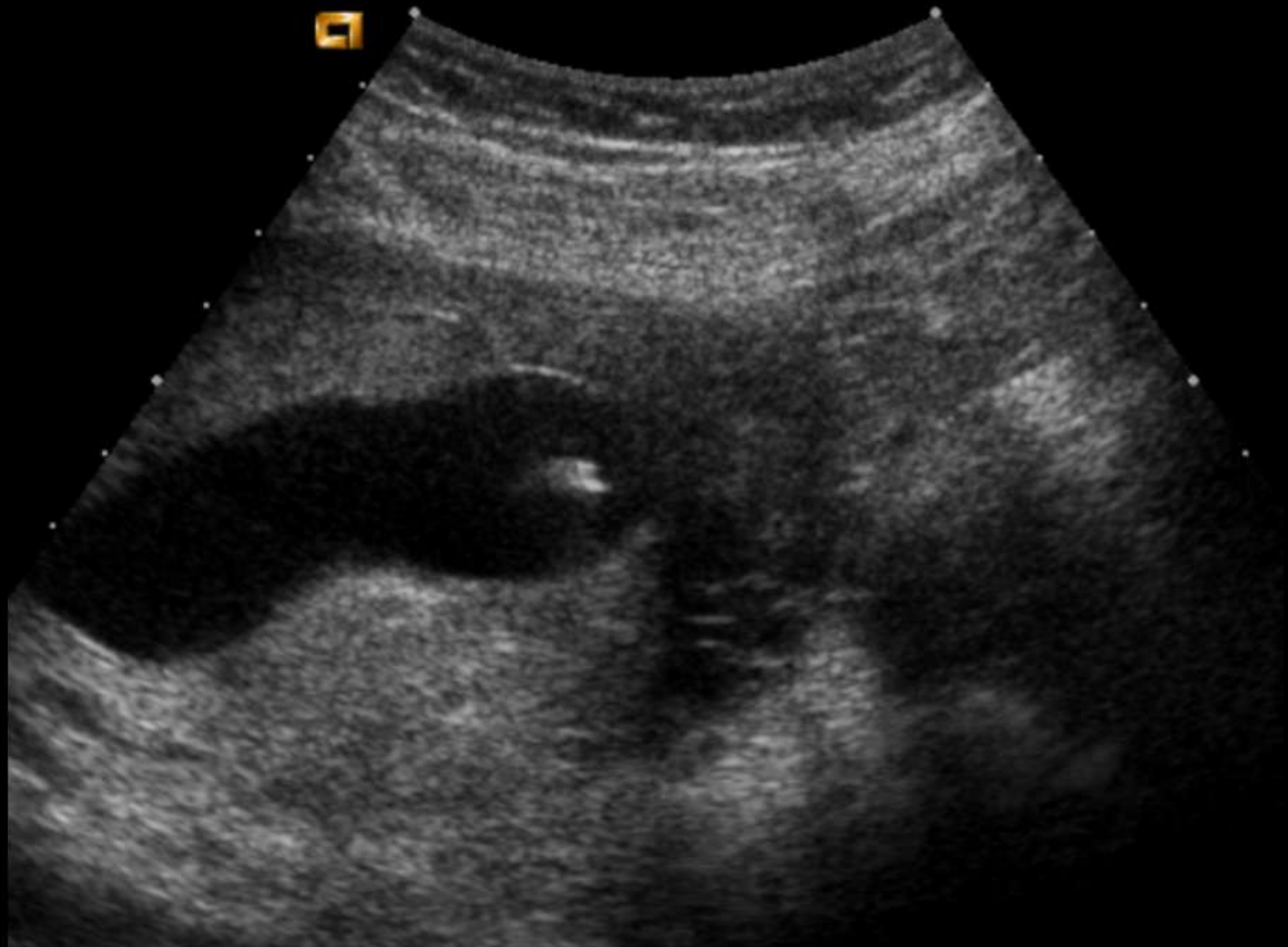
DIAGNOSIS OF FETAL ANOMALIES

SELECTION OF THE OPTIMAL SAMPLING SITE

REDUCTION OF UNSUCCESSFUL SAMPLINGS

REDUCTION OF BLOODY SAMPLES

REDUCTION OF FETAL LESIONS



PRENATAL DIAGNOSIS

AMNIOCENTESIS

COMPLICATIONS

CHORIOAMNIONITIS	< 1/1000
FETAL LESIONS	-
AMNIOTIC FLUID LEAKAGE	\leq 1/100
FETAL DEATH, MISCARRIAGE	0.5 - 1/100
RH SENSITIZATION	~ 5 %

PRENATAL DIAGNOSIS FETAL BLOOD SAMPLING

INDICATIONS

**DETERMINATION OF FETAL CARYOTYPE
MATERNAL INFECTIONS
MATERNAL ALLO-IMMUNISATION
FETAL BIOLOGY
INTRA-UTERINE TREATMENT
(FETAL DNA ANALYSIS)**

PRENATAL DIAGNOSIS FETAL BLOOD SAMPLING

TECHNIQUES

POSSIBLE FROM 18 WKS

US-GUIDED PUNCTURE OF:

1. UMBILICAL VEIN IN THE CORD

PLACENTAL INSERTION

UMBILICAL INSERTION

FREE LOOP

2. INTRA-HEPATIC PORTION OF THE UMBILICAL VEIN

3. CARDIAC CHAMBERS

PRENATAL DIAGNOSIS FETAL BLOOD SAMPLING

COMPLICATIONS

RUPTURE OF MEMBRANES

HEMORRHAGE AT PUNCTURE SITE

FETAL BRADYCARDIA (TRANSITORY)

FETAL DEATH ($\leq 1\%$)

PRENATAL DIAGNOSIS CHORIONIC VILLUS SAMPLING (CVS)

POTENTIAL ADVANTAGES:

EARLY DIAGNOSIS

DETERMINATION OF FETAL CARYOTYPE:

DIRECT PREPARATIONS

CELL CULTURES

DIRECT MEASUREMENT OF ENZYMATIC ACTIVITIES

SOURCE OF FETAL DNA

PRENATAL DIAGNOSIS CHORIONIC VILLUS SAMPLING (CVS)

TECHNIQUES

TRANSCERVICAL SAMPLING

US-GUIDED ASPIRATION OR BIOPSY

TRANSABDOMINAL SAMPLING

US-GUIDED ASPIRATION OR BIOPSY

(TRANSVAGINAL SAMPLING)

CVS VERSUS AMNIOCENTESIS META-ANALYSIS (COCHRANE DATABASE)

CVS

AMNIOCENTESIS

SAB (≤ 28 WKS):

259/3646 (7.1%)

133/2634 (5.05%)

OR 1.53 (1.16 - 2.01)

TOTAL PREGNANCY LOSS:

395/3646 (10.83%)

211/2634 (8.01%)

OR 1.49 (1.19 - 1.56)

PRENATAL DIAGNOSIS CVS VERSUS MA

- 1. TOTAL PREGNANCY LOSS AFTER CVS IS HIGHER THAN AFTER MA**
- 2. CVS IS ASSOCIATED WITH A GREATER NUMBER OF INADEQUATE SAMPLES, CULTURE FAILURES AND AMBIGUOUS RESULTS**
- 3. CVS SHOULD NOT BE PERFORMED BEFORE 10 WKS, CONSIDERING THE RISK OF LRD'S PROBABLY ASSOCIATED WITH EARLIER SAMPLINGS**

PRENATAL DIAGNOSIS EARLY AMNIOCENTESIS

DEFINITION :

- **MID-TRIMESTER AMNIOCENTESIS (MA) : ≥ 15 WKS**
- **EARLY AMNIOCENTESIS (EA) : < 15 WKS**

AREA OF CONCERN :

- **SAFETY**
- **CYTOGENETIC RELIABILITY**

PRENATAL DIAGNOSIS EA VERSUS TA-CVS

KING'S COLLEGE TRIAL:

EARLY AMNIOCENTESIS (10-13 WKS): 238

TA-CVS (10-13 WKS): 250

**EXCESS OF PREGNANCY LOSS: 4.7% (1.4-8.0)
IN THE EA GROUP**

LANCET 1994; 344: 435-9

PRENATAL DIAGNOSIS EA VERSUS TA-CVS

DANISH TRIAL:

EARLY AMNIOCENTESIS (11-13 WKS): 581

TA-CVS (10-12 WKS): 579

PREGNANCY LOSS: 5.4% VERSUS 4.8% $p = 0.66$

CLUB FOOT: 1.7% VERSUS 0% $p < 0.01$

LANCET 1997; 350: 697-703

PRENATAL DIAGNOSIS EA VERSUS MA

RANDOMISED TRIAL (CEMAT)

	EA (11+0 - 12+6)	MA (15+0 - 16+6)	p
N	2183	2185	
PREGNANCY LOSS:	7.6%	5.6%	0.012
AF LEAKAGE (<22 SEM.):	3.5%	1.7%	0.0007
CLUB FOOT:	1.3%	0.1%	0.0001
CYTOGENETIC FAILURE:	1.7%	0.2%	0.001

LANCET 1998; 351: 242-7

PRENATAL DIAGNOSIS

A. WHEN RISK FACTORS ARE ABSENT (SCREENING):

1. FIRST-TRIMESTER MATERNAL SERUM SCREENING + NT:

- PAPP-A / FREE beta-hCG:
- NT

EVALUATION OF THE RISK OF FETAL ANEUPLOIDY (T21)

2. SECOND-TRIMESTER MATERNAL SERUM SCREENING:

- aFP: NTD (OTHER FETAL ANOMALIES)
- aFP, hCG / free beta-hCG, UE3:

EVALUATION OF THE RISK OF FETAL ANEUPLOIDY (T21)

3. ULTRASOUND

PRENATAL SCREENING OF FETAL ANEUPLOIDY

CRITERIA USED	DETECTION RATE	AMNIOCENTESIS RATE
MATERNAL AGE :	30%	12-15%
MATERNAL AGE + aFP :	40%	10%
MAT. AGE + 2nd TRIM. BIOCHEM. :	>60%	5-8%
MAT. AGE+1st TRIM. BIOCHEM.+NT:	>85%	5%

RISK FACTORS FOR CONGENITAL ANOMALIES

- FAMILIAL HISTORY OF CONGENITAL ANOMALIES
- MOTHER AFFECTED BY A CONGENITAL ANOMALY
- PRIOR CHILD WITH A CONGENITAL ANOMALY
- BOTH PARENTS CARRIERS OF AN AUTOSOMAL RECESSIVE ANOMALY
- ETHNIC ORIGIN
- CONSANGUINITY
- PARENTS CARRIERS OF A BALANCED TRANSLOCATION
- MATERNAL DISEASE (EPILEPSY, DIABETES)
- EXPOSITION TO DRUGS (LITHIUM, RETINOIDS, DPH, TRIMETHADIONE, VALPROATE, COUMARINS)
- EXPOSITION TO TOXIC SUBSTANCES (ALCOHOL)
- INFECTIOUS AGENTS (RUBELLA, TOXOPLASMOSIS, CMV)
- ADVANCED MATERNAL AGE (≥ 35 YRS)
- MULTIPLE GESTATIONS
- ELEVATION OR REDUCTION OF MATERNAL SERUM α FP CONCENTRATIONS
- 1ST OR 2ND-TRIMESTER SCREENING INDICATING A HIGH RISK OF FETAL ANEUPLOIDY

PRENATAL DIAGNOSIS

B. WHEN RISK FACTORS ARE PRESENT:

1. GENETIC COUNSELING

2. SAMPLING:

**CHORIOCENTESIS, AMNIOCENTESIS,
FETAL BLOOD SAMPLING**

3. ULTRASOUND (EMBRYOSCOPY)

INFORMATION BEFORE PRENATAL DIAGNOSIS (1)

1. FETAL DISORDER

- **SEVERITY (AVERAGE AND EXTREMES)**
- **LONG-TERM CONSEQUENCES FOR CHILD, FAMILY AND COMMUNITY**
- **POSSIBILITIES OF TREATMENT AND THEIR EFFECTIVENESS**

2. RISKS

- **OCCURRENCE/RECURRENCE OF THE DISORDER**
- **RISKS OF THE DIAGNOSTIC PROCEDURE FOR MOTHER AND FETUS**
- **CHANCES OF MISDIAGNOSIS**

INFORMATION BEFORE PRENATAL DIAGNOSIS (2)

3. PROCEDURES

- WHAT THEY INVOLVE
- TIME INTERVAL BEFORE A DIAGNOSIS CAN BE MADE
- WHAT PREGNANCY TERMINATION INVOLVES

4. OPTIONS

- IGNORE A LOW RISK OF ABNORMALITY
- PROCEED WITH PRENATAL DIAGNOSIS
- SEEK OTHER OPTIONS
 - HAI
 - ADOPTION
 - AVOID FURTHER REPRODUCTION

FETAL MEDICINE MANAGEMENT OPTIONS

1. SEVERE ANOMALY / INCOMPATIBLE WITH SURVIVAL:
TERMINATION OF PREGNANCY IS AN OPTION
2. CURABLE ANOMALY:
OPTIMIZATION OF PERINATAL MANAGEMENT
3. INTRA-UTERINE TREATMENT
4. PARENTAL REASSURANCE WHEN ANOMALIES CAN
BE EXCLUDED