Prenatal diagnosis – clinical introduction

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Pregnancies

High risk

- Familial history
- Screening tests

No increased risk

Prenatal diagnosis vs Screening

Diagnosis

- Increased risk
- +/- specific condition
- Test result gives a clear answer

Screening

- “general” pregnant population
- Frequent anomalies
- Non-invasive
- Test result gives a risk estimation

Aim of diagnosis / screening

Inform future parent(s)

Allow making of informed decisions

Sometimes treatment

Termination of pregnancy

Prepare for the birth of a child with a medical condition

Prenatal screening

Ultrasound

Tests on maternal blood

- Serum markers
- cffDNA

Ultrasound

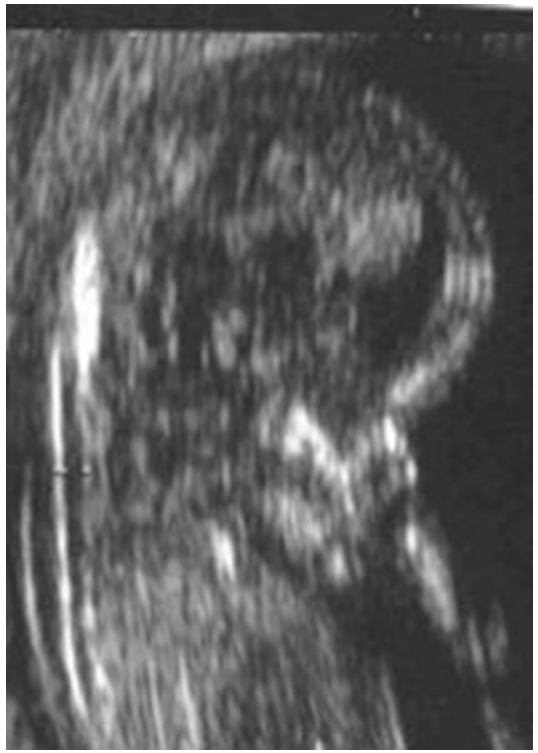
During pregnancy reimbursement of 3 US(1 per trimester)

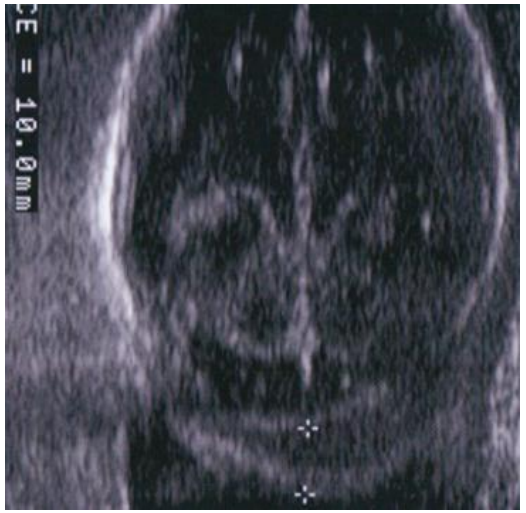
First US (+/- 8 weken) not reimbursed

High-risk pregnancies : extra US

Code	Aard prestatie	Honorarium	Tegemoetkoming	
			Normale tegemoetk.	Verhoogde tegemoetk.
460515	Basisechografie door radioloog	23,41	20,93	23,41
469895	Basisechografie door geneesheer-specialist die geen radioloog is	26,92	24,44	26,92
460530	Echografie door radioloog bij hoog obstetrisch of foetaal risico	46,16	43,68	46,16
469910	Echografie bij hoog obstetrisch of foetaal risico door geneesheer-specialist die geen radioloog is	46,16	43,68	46,16
460552	Echografie door radioloog bij ernstige aangeboren misvorming of bewezen risico	89,02	86,54	87,92
469932	Echografie bij ernstige aangeboren misvorming of bewezen risico door geneesheer-specialist die geen radioloog is	89,02	86,54	89,02

Ultrasound





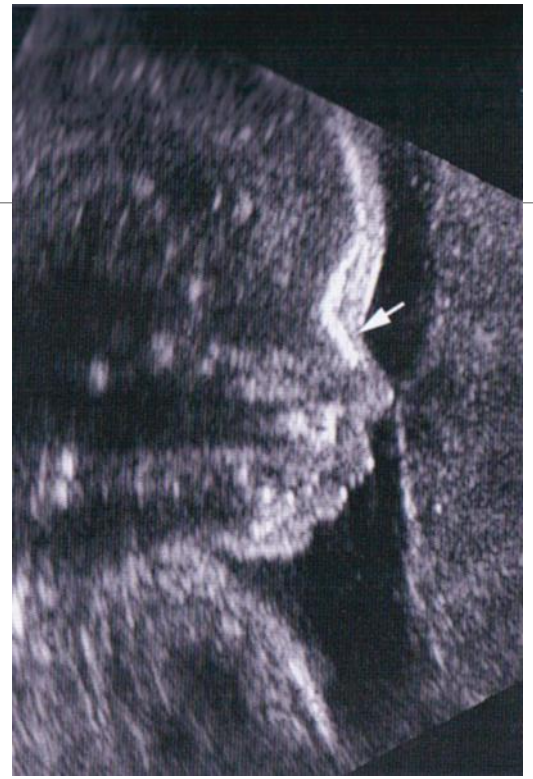
Nuchal translucency

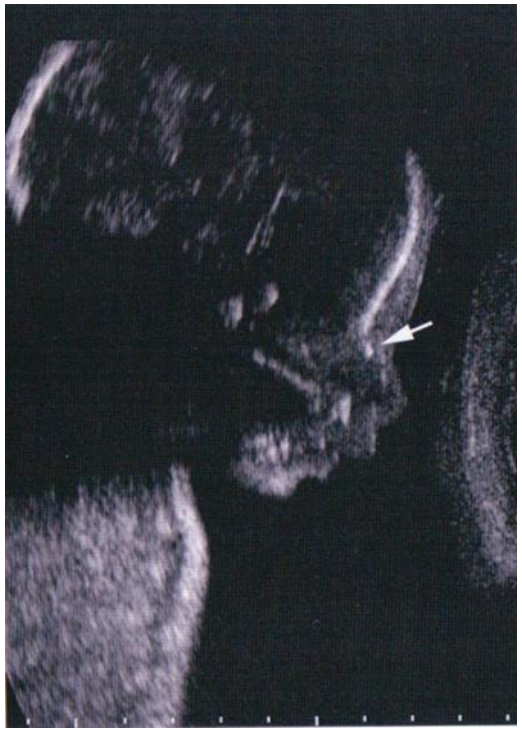
Ultrasound

Fetal NT (mm)	
Normal karyotype	2.0
Trisomy 21	3.4
Trisomy 18	5.5
Trisomy 13	4.0

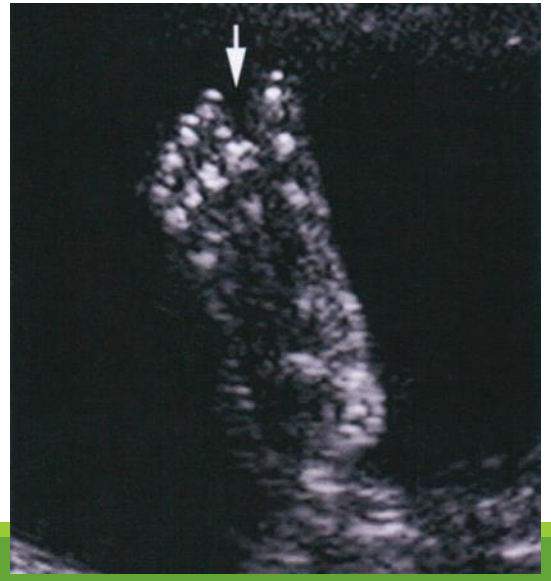
Kagan et al, Hum Reprod, 2008

Ultrasound





Hypoplasia nasal bone



Sandal gap

Ultrasound

Single-Gene Disorders

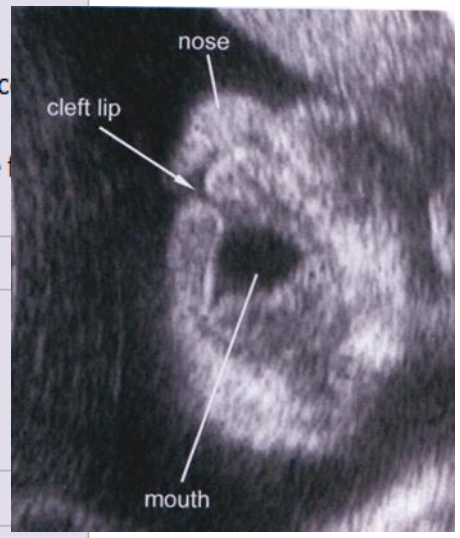
- Holoprosencephaly
- Infantile polycystic kidney disease
- Meckel-Gruber syndrome (an autosomal recessive disorder with encephaloc
  polydactyly, and polycystic kidneys)
- Fryns syndrome (an autosomal recessive disorder with abnormalities of the f
  diaphragm, limbs, genitourinary tract, and central nervous system)

Disorders Usually Thought of as Multifactorial

- Cleft lip and other facial malformations
- Clubfoot
- Congenital heart defects
- Neural tube defects

Anomalies That May Indicate a Syndrome

- Abnormal genitalia
- Cystic hygroma
- Polydactyly
- Omphalocele
- Radial ray defects



Thompson & Thompson, p354

Ultrasound

	Percent of Fetuses with Abnormal Karyotype	
Abnormality	**If Isolated Abnormality**	**If Multiple Abnormalities**
Ventriculomegaly	2	17
Choroid plexus cysts	≪1	48
Cystic hygroma	52	71
Nuchal edema	19	45
Diaphragmatic hernia	2	49
Heart defects	16	66
Duodenal atresia	38	64
Exomphalos	8	46
Renal abnormalities	3	24

Thompson &Thompson, p 354

Tests on maternal blood

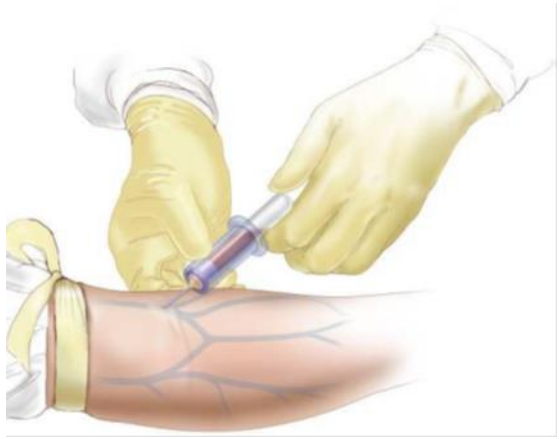
Alpha-foetoproteïn

Papp-A (pregnancy-associated plasma protein A)

hCG (totaal of B-subunit)

Unconjugated oestriol

Inhibine



Tests on maternal blood

	First-Trimester Screen			Second-Trimester Screen			
	Nuchal Translucency	PAPP-A	Free β-hCG	uE_3	AFP	hCG	Inhibin A
Trisomy 21	↑	↓	↑	↓	↓	↑	↑
Trisomy 18	↑	↓	↓	↓	↓	↓	—
Trisomy 13	↑	↓	↓	↓	↓	↓	—
Neural tube defect	—	—	—	—	↑↑	—	—

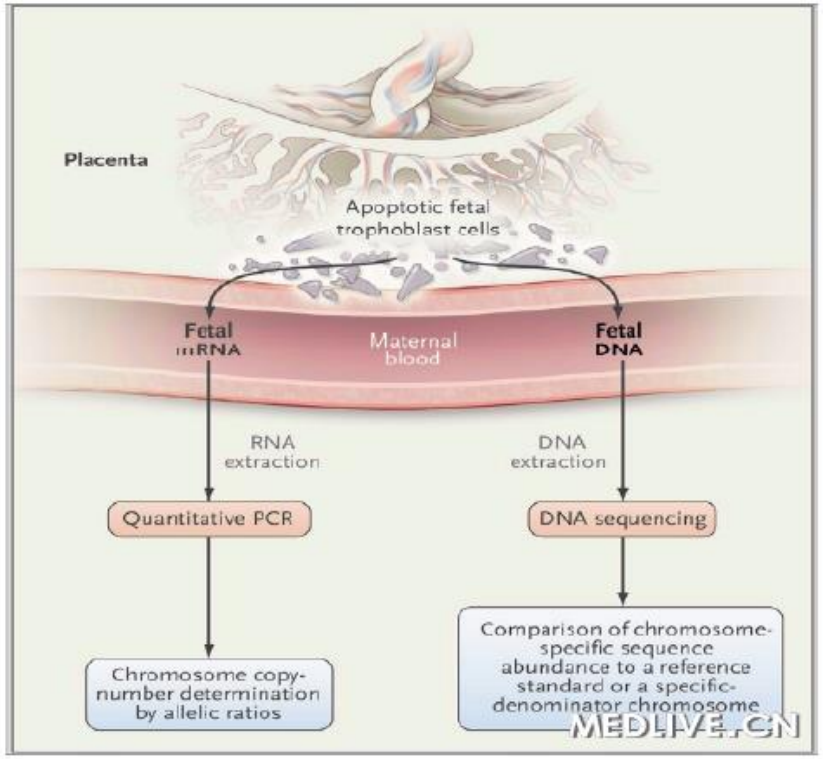
Thompson&Thompson, p358

Tests on maternal blood

NIPT (non-invasive prenatal test)

1997 Lo et al: cffDNA (cell free fetal DNA) in materneel bloed

Cfr next presentation



http://www.medlive.cn/uploadfile/2012/0109/20120109022529674.png

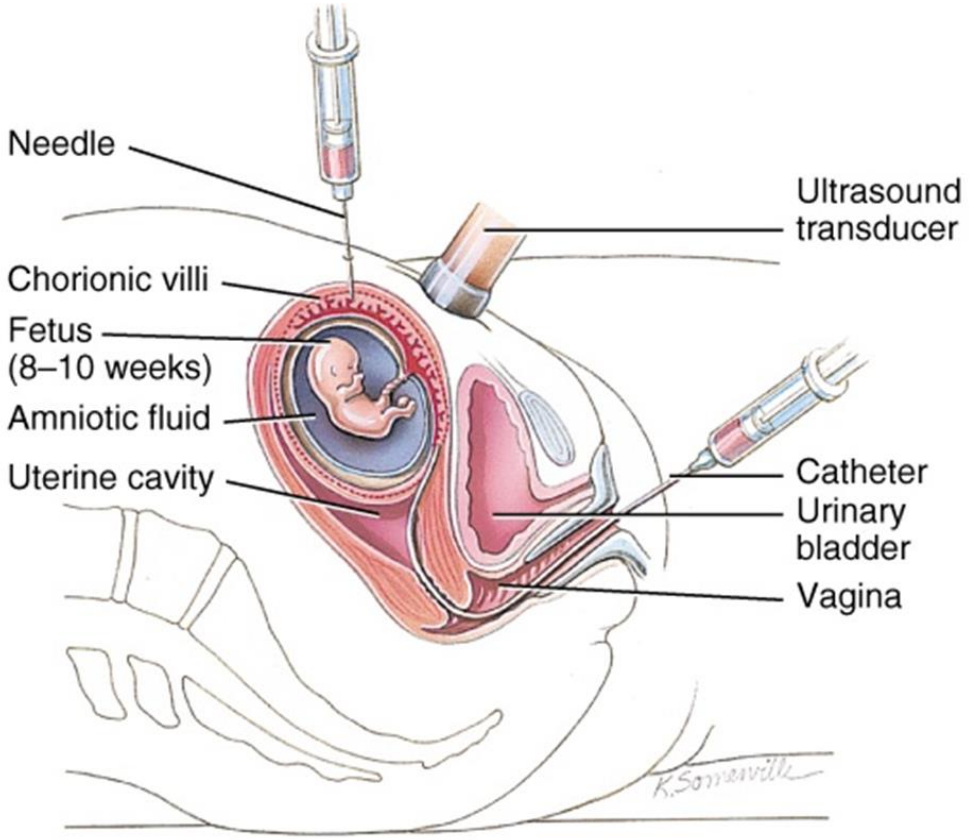
Invasive Prenatal diagnosis

Chorionic villus sampling (CVS)

Amniocentesisn(AC)

Umbilical cord puncture

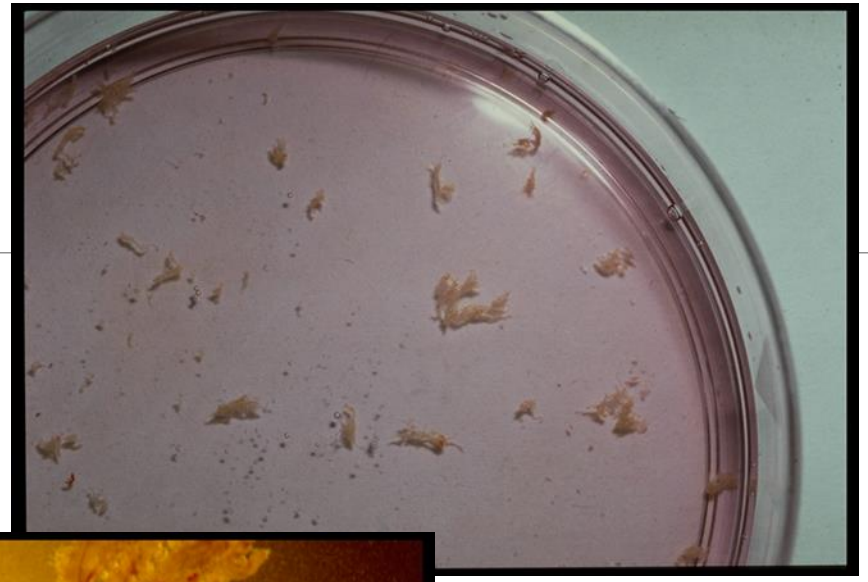
Chorionic villus sampling (CVS)

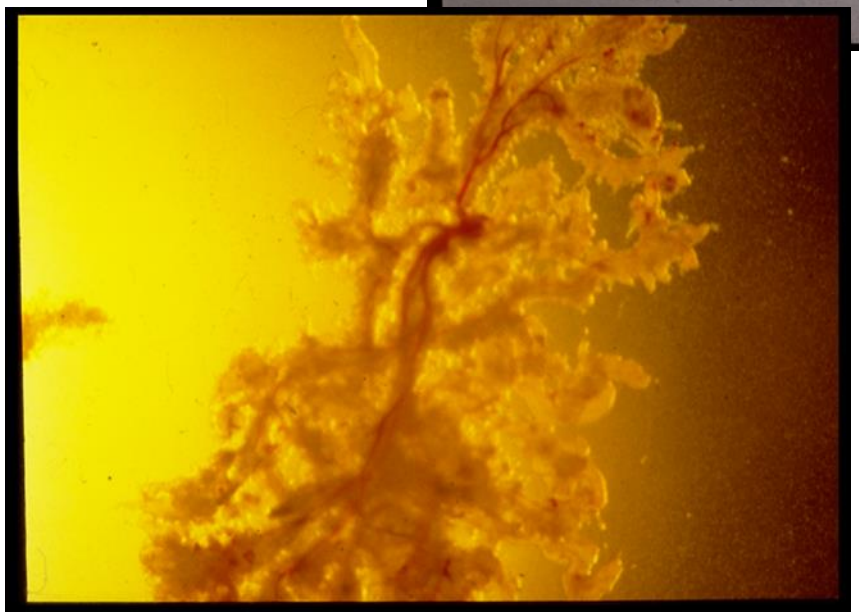


CVS

11-13 weeks

Chorionic villi





CVS

Results come earlier

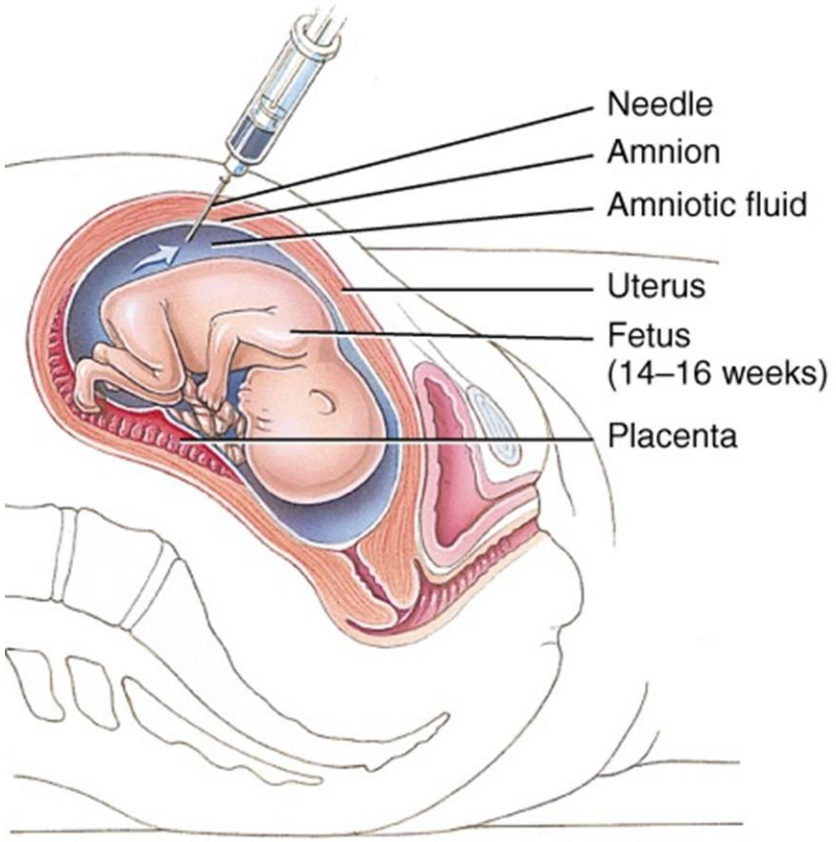
- Earlier reassurance
- Options for termination of pregnancy

Placental mozaïcism

Risk for miscarriage

- + 0,5%
- Mostly in first month after cvs

Amniocentesis



Amniocentesis

From 15 weeks

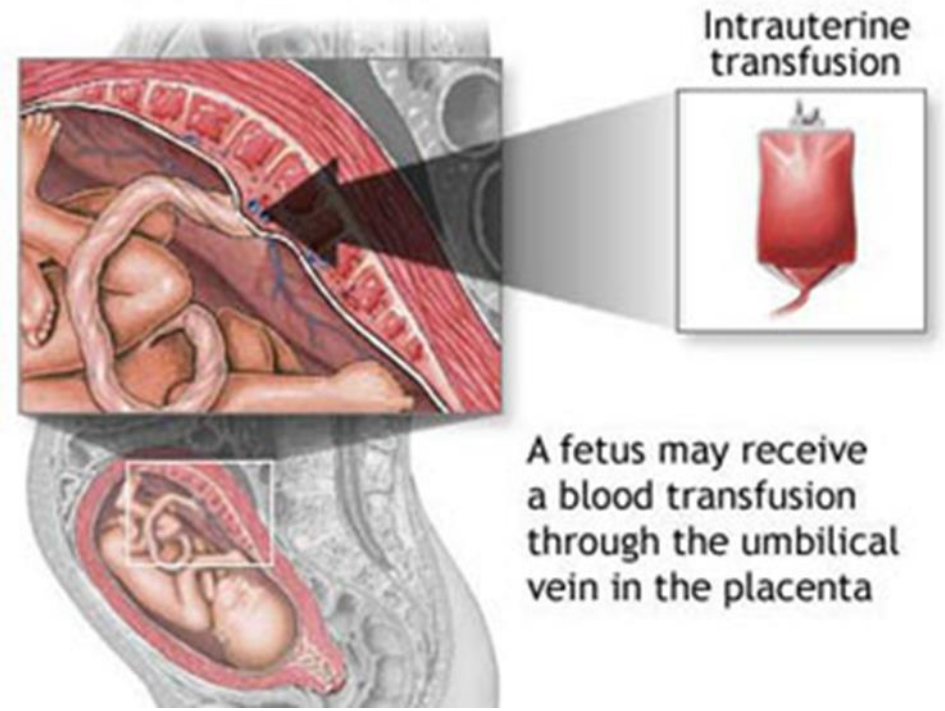
Amniocytes (mixture of cells)

Results come later

Risk for miscarriage

- +0,2%

Umbilical cord puncture



Umbilical cord puncture

From 19 weeks

Foetal blood

Seldom for genetic diagnosis

Foetal anemia

Therapeutical actions (e.g. blood transfusion)

Invasive tests

Chromosomal analysis

Monogenic conditions

- Specific gene analysis
- Gene panel
- Biochemical tests

Chromosomal analysis

See next presentations

High risk for chromosomal anomaly based on screening test (NIPT, US)

High risk for chromosomal anomaly based on abnormal karyotype in parent (e.g. balanced translocation)

Low risk but additional analysis in a prenatal diagnosis for monogenic disorder

Monogenic conditions

Familial history

- E.g. couple with known ¼ risk for cystic fibrosis (CFTR)
- E.g. couple with known ½ for neurofibromatosis (NF1)
- !! Genetic defect must be known, no prenatal diagnosis can be offered for “intellectual disability”, “autism”, …

US anomalies

- E.g. suspicion of achondroplasia
- E.g. suspicion of Beckwith Wiedemann syndrome

See next presentations

Conclusion

Prenatal screening/ diagnosis is an option for the pregnant couple

Autonomous decision (cfr non-directive counseling)

Results

- reassurance
- diagnosis
  - Prognosis
  - Option termination of pregnancy
  - Preparing the future parents and family
  - Optimizing neonatal care
  - Counseling of couple and family