ANTENATAL SCREENING FOR FETAL ABNORMALITIES IN HUNGARY

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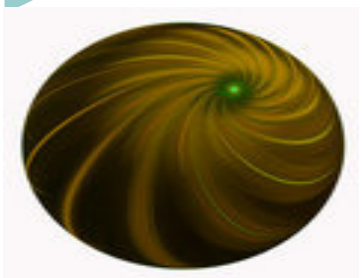
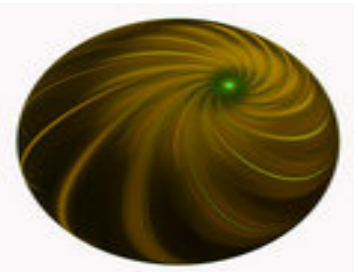




1st Central & Eastern European Summit on Preconception Health & Prevention of Birth Defects, Budapest, 29.08,2008

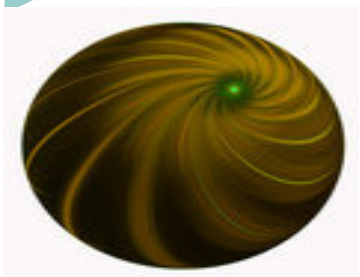
ANTENATAL SCREENING FOR FETAL ABNORMALITIES IN HUNGARY

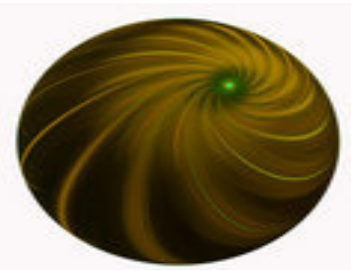
-Screening for Down syndrome

-Indications for prenatal invasive diagnosis

-Screening for structural anomalies by US

-Termination of pregnancy for fetal anomaly





1st Central & Eastern European Summit on Preconception Health & Prevention of Birth Defects, Budapest, 29.08,2008

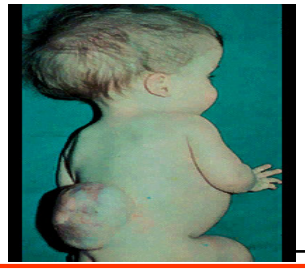
ISSUES

- **PREVALENCE**
- **Screening strategies**
- **STRUCTURAL DEFECTS**
- **CHROMOSOMAL ABNORMALITIES**
- **MATERNAL AGE!!**
- **Too many choices!**
- **FUTURE TASKS**

POPULATION FREQUENCY OF DISORDERS WITH GENETIC BACKGROUND

- At birth: 4% (5-6%!)
- At 1 year of age: 5 %
- At 25 years of age: ~8%
  - monogenic
- At 60 years of age: >90%
  - Polygenic (complex)

ANNUAL RATE OF CONGENITAL ANOMALIES IN THE EARTH (WHO)



Total no. of birth in the world:	**120 000 000**
1. Congenit. struct. anomalies:	2 890 000
2. Chromosomal anomalies:	800 000
3. Mendelian disorders:	700 000
4. Haemoglobinopathies:	200 000
Total:	4 590 000

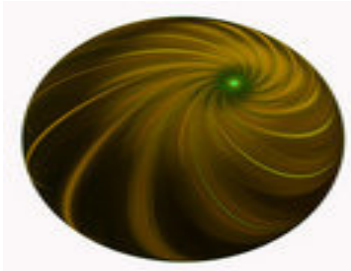
CONGENITAL AND GENETIC DISORDERS

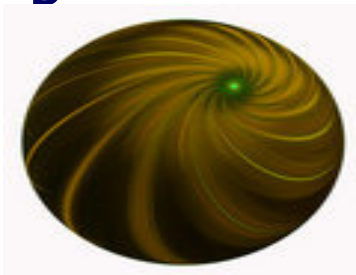
- **Primary prevention**
  - folates ⇒ **NTD, CHD**, rubella vaccinatic
- ***Preimplantation Genetic Diagnosis***
- **Secondary prevention**
  - **Prenatal screening and**
  - **Prenatal diagnostics**
  - **Prenatal counselling**
- **Aim: ⇒ Prenatal therapy!!!**

Tertiary prenatal centers with cytogenetic labs in Hungary

ANTENATAL SCREENING FOR FETAL ABNORMALITIES IN HUNGARY

- Hungary was among the first countries applying **amniocentesis** in the late 70th and
- **chorionic villus** sampling in the early 1980th and prenatal diagnosis of fetal chromosomal abnormalities started.
- **weak govermental** support and the motor of the development was mainly
- **individual ambition/efforts** and enthusiasm characterizing outstanding activity of experts (ob/gyn, pediatr).





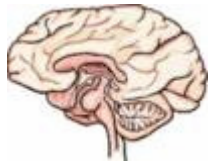
Screening for Structural Anomalies by Ultrasound

Screening for Congenital Heart Defects

- **1249 CHD out of 100 000 birth in 2005 (1,25%!)**
- *Prenatal detection rate: 2,49%*
- **Use of NT! approx: ~35-40%**

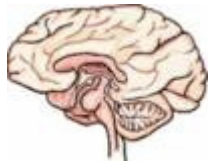
Works only in experienced hands.

Screening for Neural Tube Defects



- **Non-invasive screening for *fetal structural abnormalities* commenced in the early eighties by**
- **ultrasound and**
- **maternal serum alpha-fetoprotein (MS-AFP) determination.**

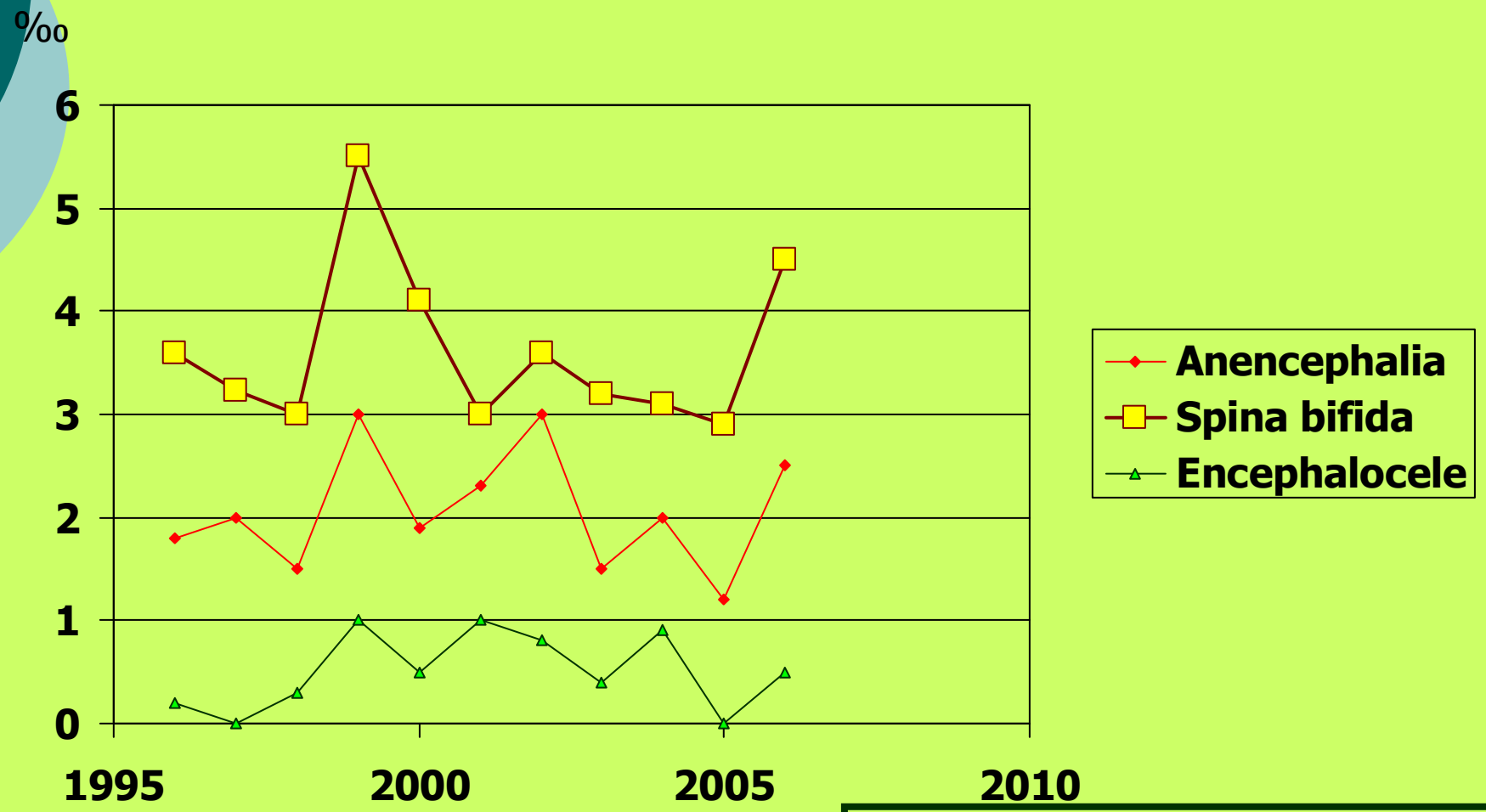
Screening for Neural Tube Defects (2004)



- **Anencephaly: 10/12 (83,3%)**
- **Spina bifida: 16/30 (53,3%)**
- **Encephalocele: 0/1**
- **Total No NTD: 26/43 (60,0%!)**
- **Prenatal detection rate: 60 %**
- **Use of MS-AFP**

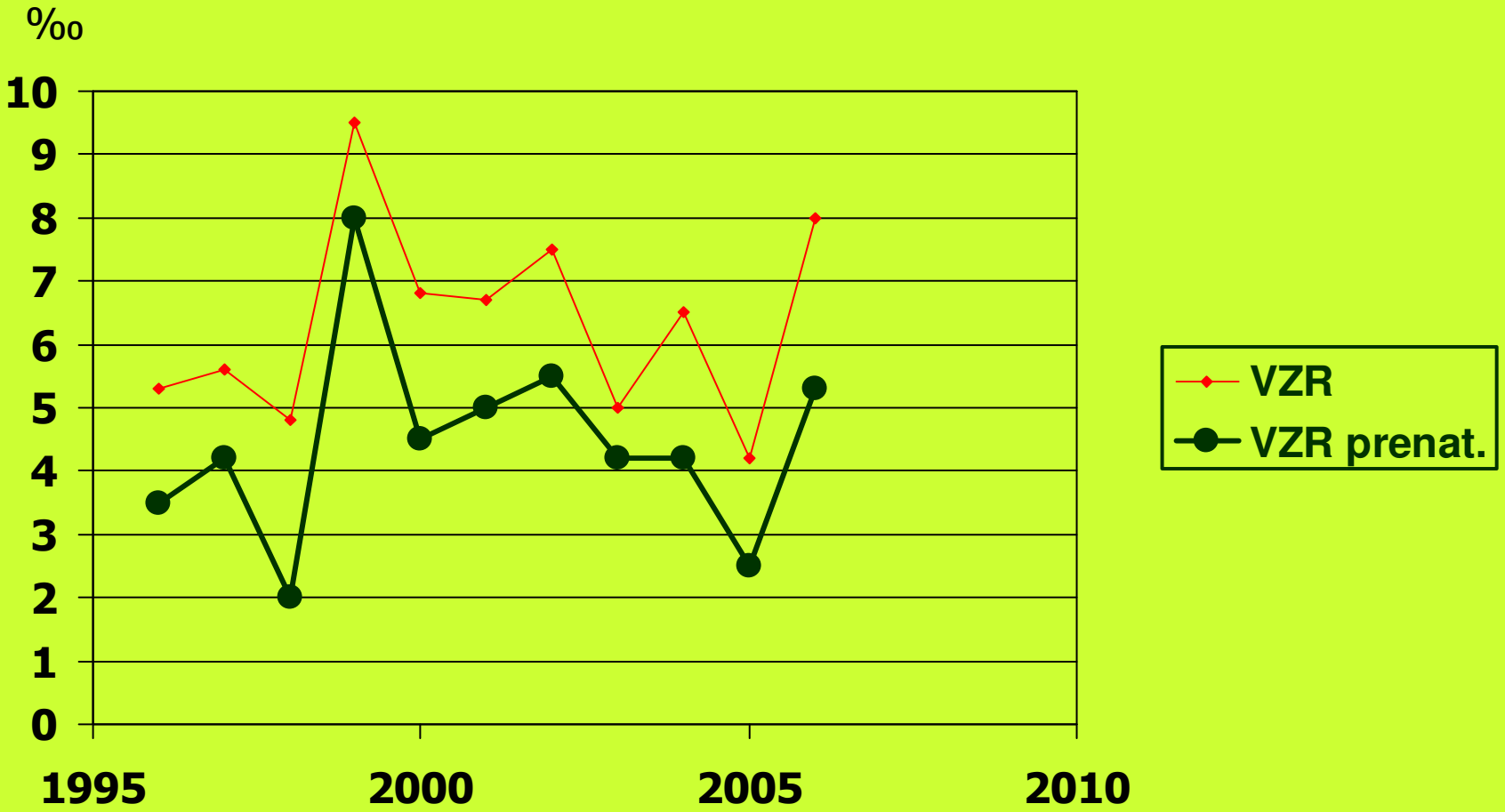
Works only in experienced hands.

Prevalence of Neural Tube Defects in Hungary (1996-2006)



HCAR(VRONY) (2008)

Rate of prenatally detected neural tube defects (1996-2006)



HCAR(VRONY) (2008)

Most efficient prenatal diagnostics

(Hungarian Congenital Abnormality Registry data, 2005)

- **Anencephaly: 92,31%**

  24 prenat.dg. out of 26 total

- **Other chromo abnorm.: 77,78%**

  35 prenat.dg. out of 45 total

- **Branchial arch abnorm: 68,75%**

  22 prenat.dg. out of 32 total

- **Spina bifida: 58,33%**
  - **28 prenat.dg. out of 48 total**

Less efficient prenatal diagnostics

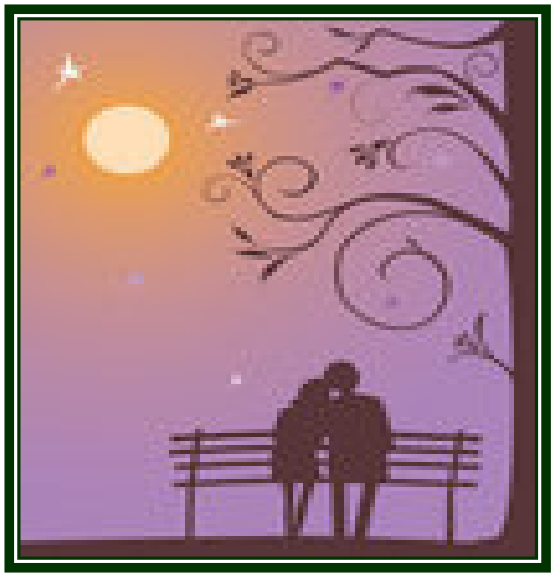
(Hungarian Congenital Abnormality Registry data, 2005)

- **Trisomy 21 65/152: 42,8%**
- **Polycystic kidney (7/35): 20%**
- **Urogenital obstr:30/317: 9,4%**
- **Limb reduction a.: 2/30: 6,7%**

SCREENING OF CHROMOSOMAL ABNORMALITIES

SCREENING OF CHROMOSOMAL ABNORMALITIES

MATERNAL AGE!!!

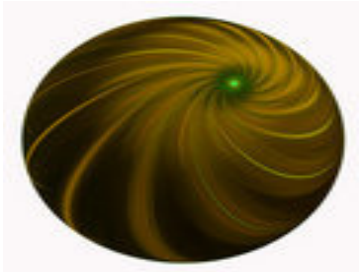


ULTRASOUND markers:

- First-trimester
- Second trimester

MATERNAL BIOCHEMISTRY

- First-trimester: PAPP-a, freeß-hCG
- Second trimester: triple, quad-test



RISK ASSESSMENT based genetic counseling!!!

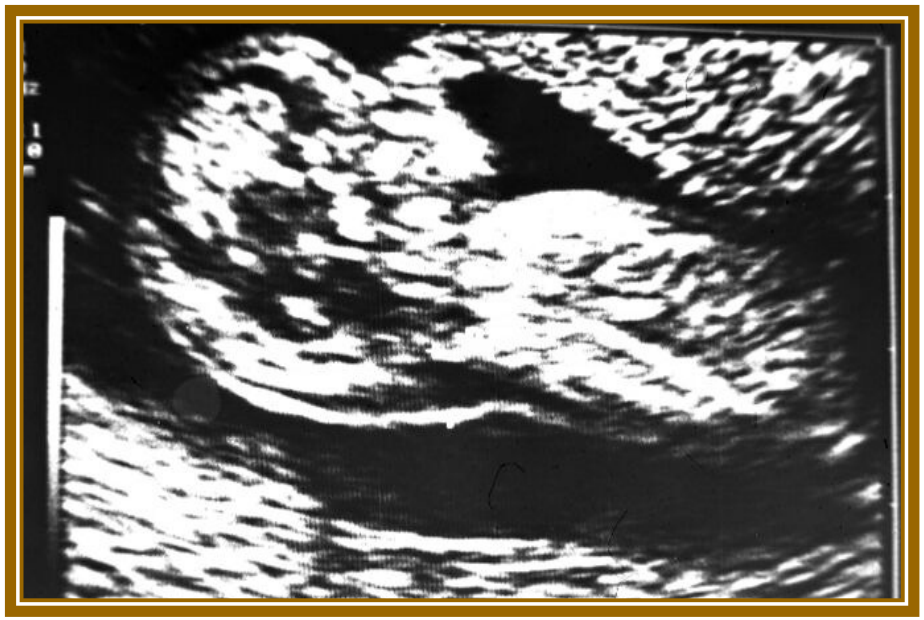
SCREENING OF CHROMOSOMAL ABNORMALITIES

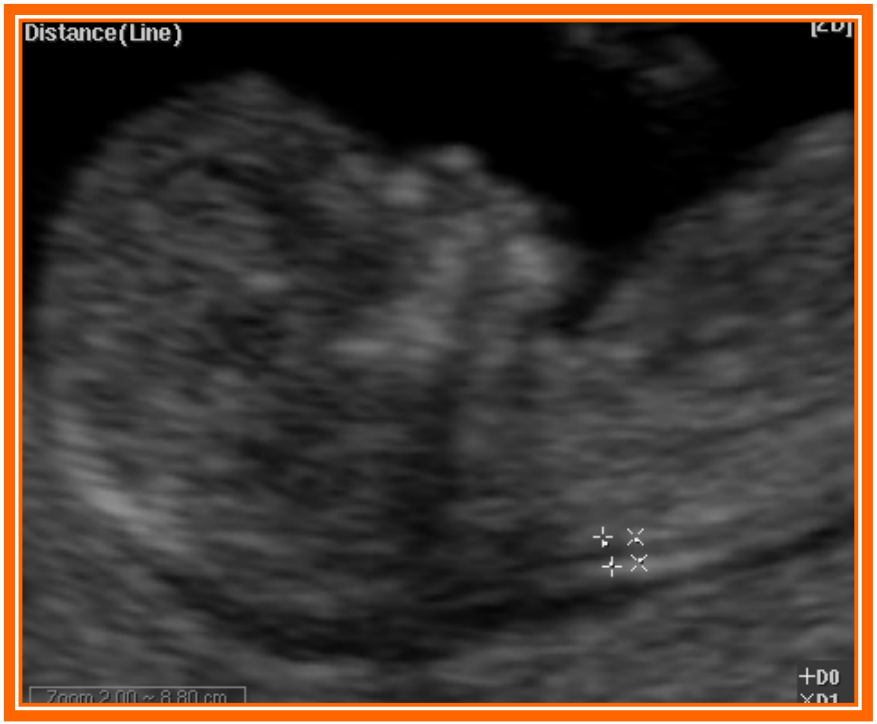
MATERNAL AGE OF ≥35!!!

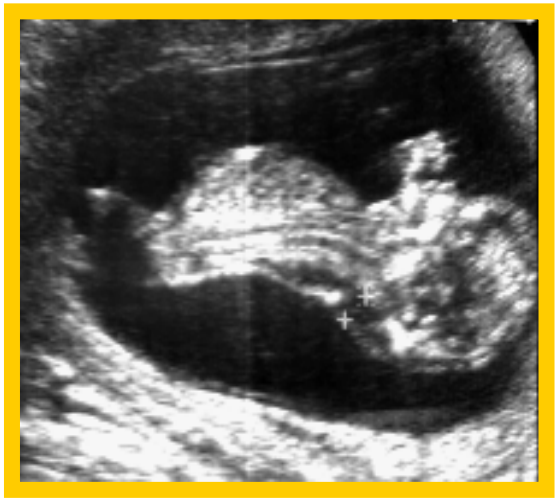
- Still present, and **strong directive** to invasive diagnostics from ob/gyn parties!
- **Irrespective of the level of risk obtained from screening studies.**

SCREENING OF FETAL CHROMOSOMAL ABNORMALITIES

FIRST-TRIMESTER: NT+NB (FROM 1990,2006)





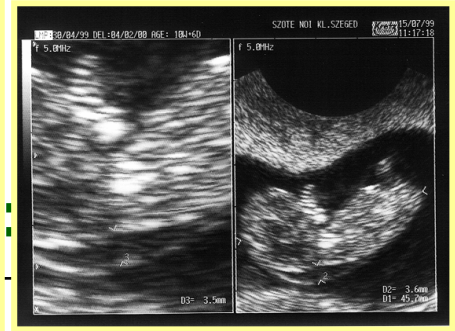


The maximum thickness of NT should be measured !

Absent Nasal Bone in Trisomy 21 and 18

Normal	469	3 (0.6%)
Trisomy 21	38	29 (6.3%)

Aim of Prenatal Screening and Diagnosis Comes True with Ultrasound:

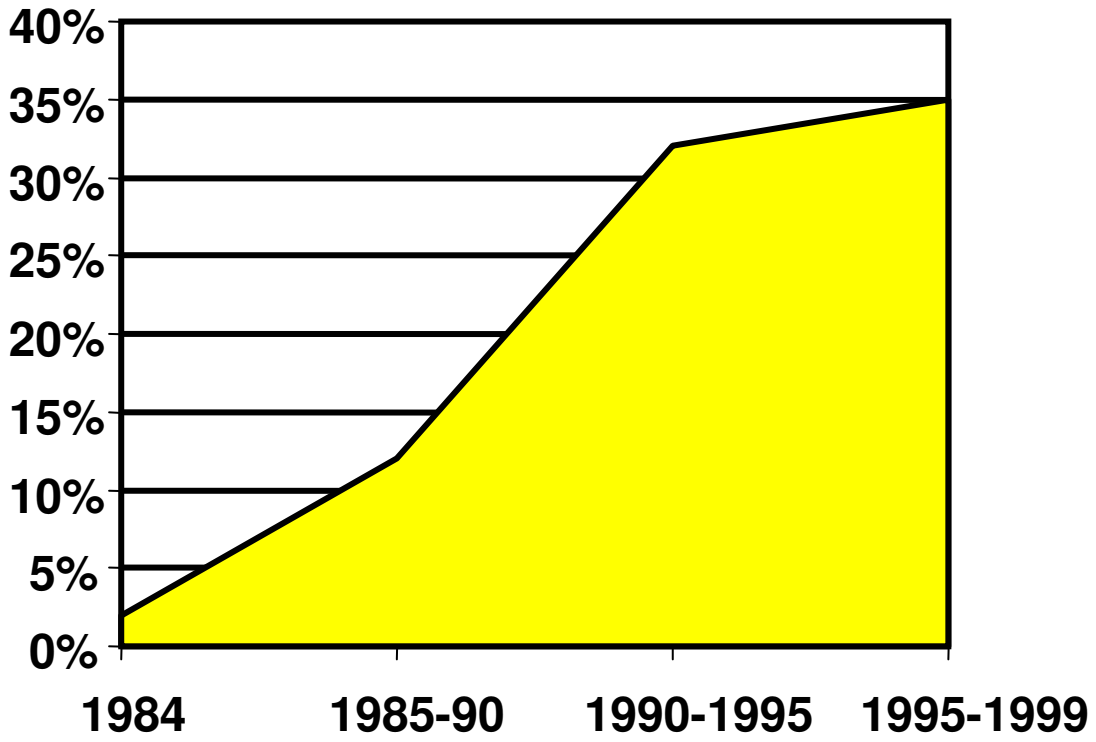


Holistic approach

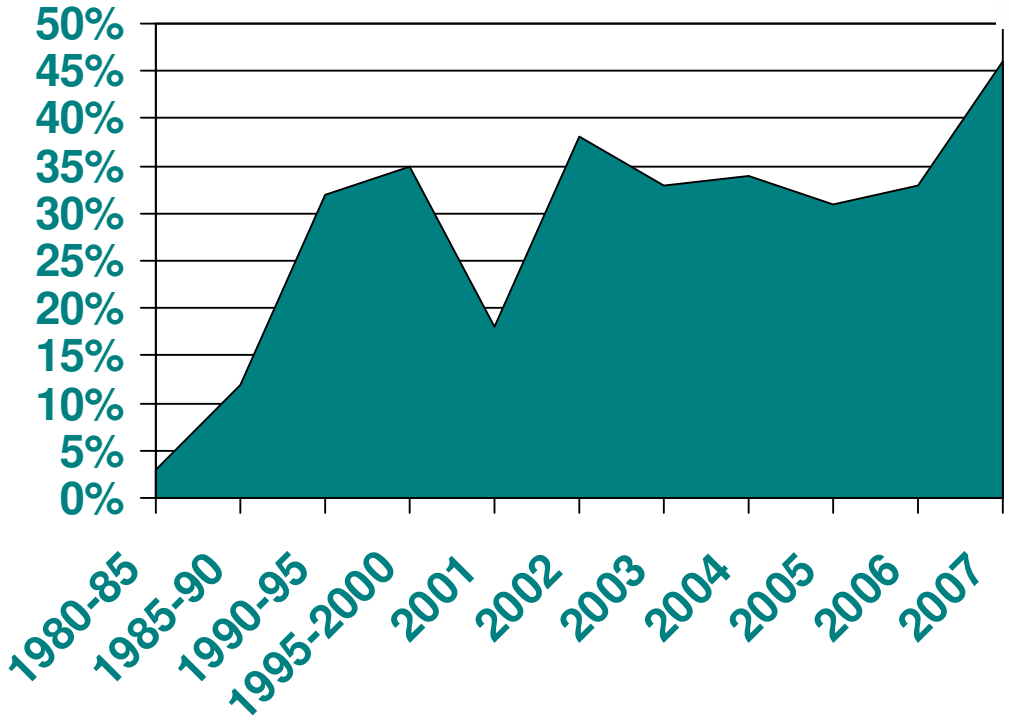
<u>TO STOP</u>

- not only RECURRENCE, but
- firts OCCURRENCE!

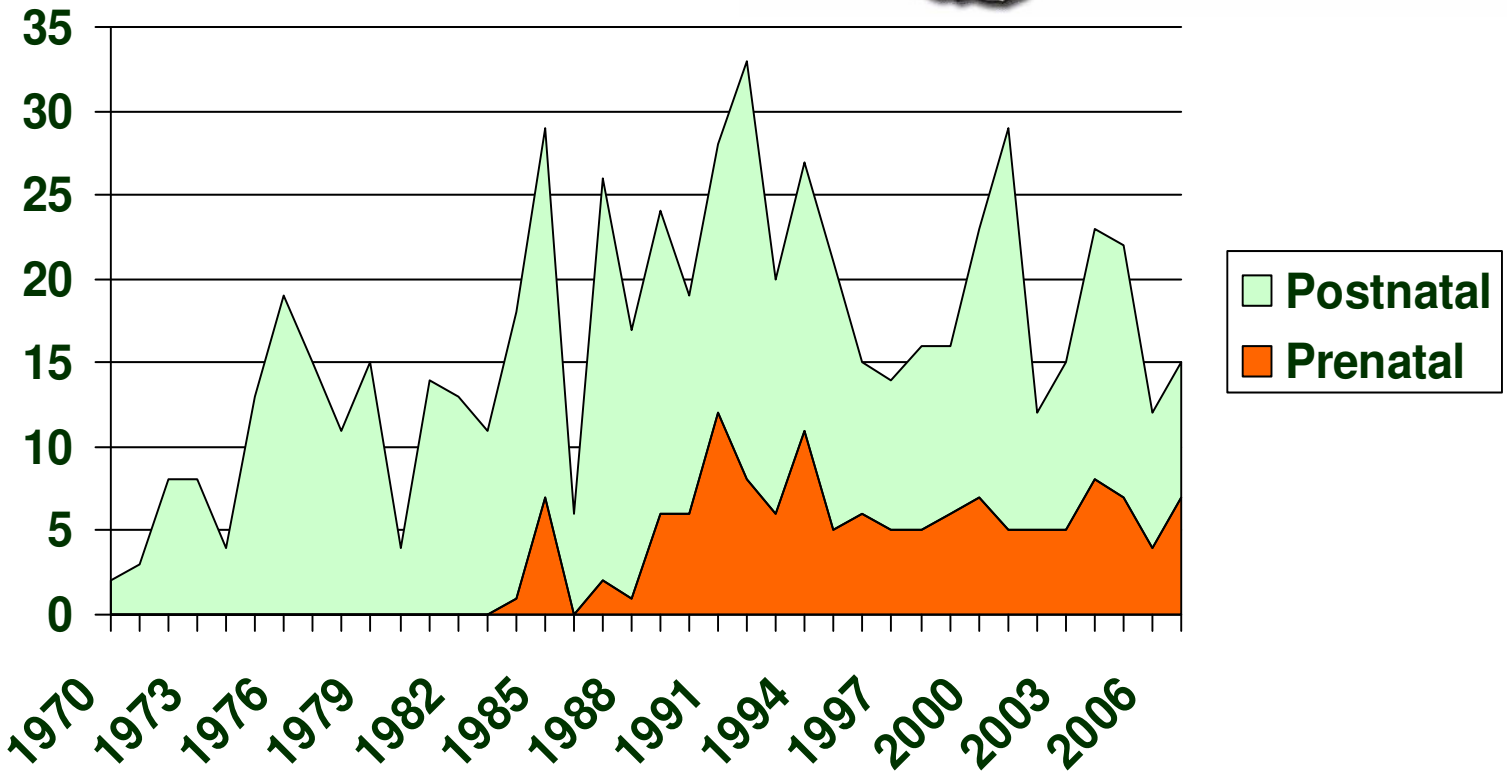
EFFECT OF NT-SCREENING ON PRENATALLY DETECTED RATE OF TRISOMY 21 (1984-1999)



Rate of Prenatally Diagnosed trisomy 21 cases between 1984-2007 in South Hungary (US screening)



Prevalence of trisomy 21 in South-Hungary (1970-2007)



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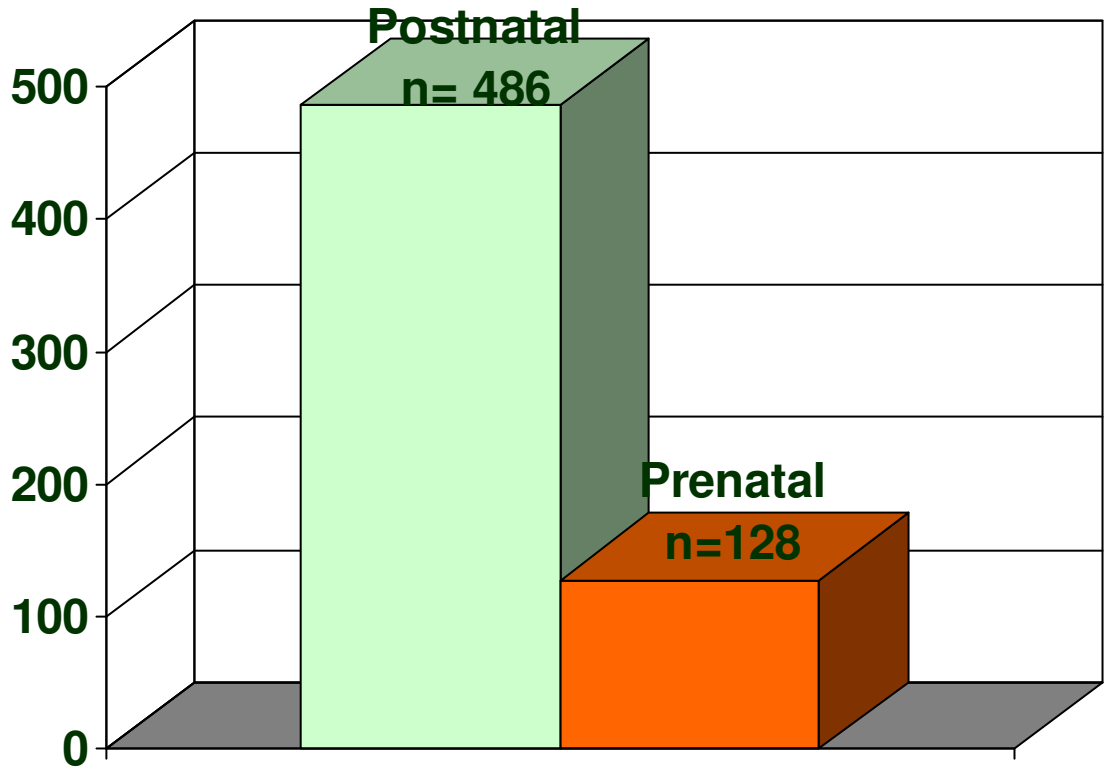


Policy offer of Hungarian Society of Ultrasound in Obstetrics and Gynecology for screening of fetal abnormalities

- **1st US: 12 weeks**
- **2nd US: 18-20 weeks**
- **3rd US: 28 weeks**
- **Works only in experienced hands. A, B, C level ultrasound examination**

Ultrasound screening for trisomies

Ultrasond markers in 1st trimester

- nuchal translucency √.
- nasal bone √?
- Frontomaxillary facial angel -
- Ductus venosus flow -
- Tricuspid regurgitation -

Ultrasond markers in 2nd trimester

- Nuchal pad √ -
- Heart defects √ -
- Nasal bone length √ -
- Dilatation of the lateral ventricle -
- Gastrointestinal tract √
- Urogenital tract. et cet. √

First-trimester maternal serum markers (at 10-12 week)

1. Free β-HCG↑

2. PAPP-A↓ (Pregnancy associated plasma protein-A)

Second-trimester screening for fetal aneuploidies

Biochemistry (16th week)

1. Free β-HCG and
2. AFP (alfa-fetoprotein)
3. Estriol
4. Inhibin-A

Quad test

MS SERUM ALPHA-FETOPROTEIN (at 16th week)

Elevated MS-AFP level:

1. NTD
2. VENTRAL WALL DEFECTS
3. MULTIPLES
4. I.U. DEATH, MISSED ABORTION
5. NEPHROSIS syndrome
6. Other

LOW MS-AFP level:

1. MISSED ABORTION
2. ANEUPLOIDIES

Screening approaches, TOO MANY CHOICES!

- Maternal age
- Combined in 1st trimester
- Contingency
- Combined in 2nd trimester
- Fully integrated test
- Sequential

Screening for fetal abnormalities

- There is a basic and fundamental principle of screening:
- a screening test may be followed by a diagnostic test,
- not another screening test!

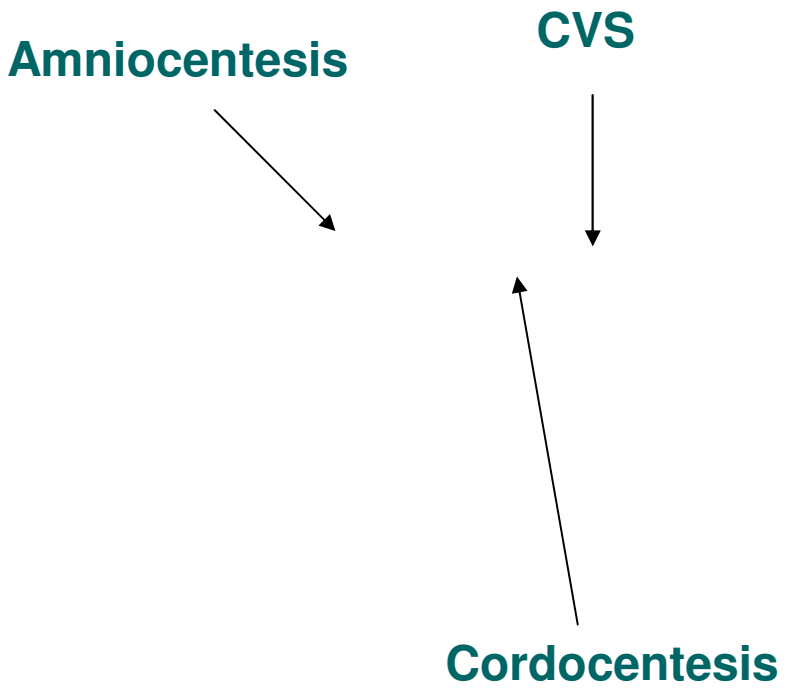
Screening should not confuse us!

Avoid!

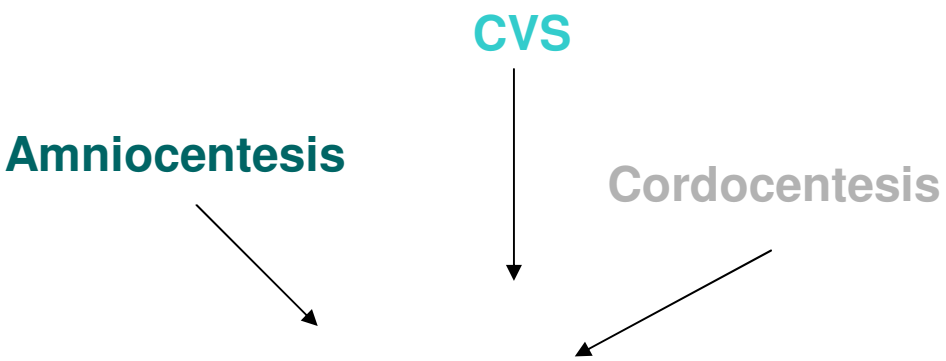
1. **Confusion: patient, obstetrician, counsellor**
2. **Lack of confidence leading anger on the part of the patient.**
3. **"Which screening test do I believe?"**

INVASIVE TESTS

Carry 1% risk of abortion!



Capacity of cytogenetic labs (increased false positive rate!).



DISTINGUISH between screening and diagnosis of Down's syndrome!

- **CVS, amnio-, or cordocentesis**
- *1% fetal loss indicates that it can be recommended only to pregnant population with high genetic risk.*
- *Consequently: the development of screening methods with high detection rate and with low false positive and negativ rate is mandatory →**FOR EACH PATIENTS***

DISTINGUISH between screening and diagnosis of Down's syndrome.

Diagnosis: **Yes or no answer**

at present by

cytogenetic-processing fetal cells obtained by

CVS, amnio-, or cordocentesis

~1% fetal loss

FETAL SAFETY!

Screening: NO HARM to the outcome of pregnancy

Fals positive rate: the % a pregnant population above the cut off

More sampling we perform, the more procedure related fetal loss will occur, in other words:

- **Increasing the no. of sampling increase the**
- **iatrogenic pregnancy loss rate**
- **FETAL SAFETY!**

Focus on safety!!

- We think along with others that prenatal **screening for Down syndrome should focus not only on cost-effectiveness but on detection rate and fetal safety, which depends on reliability of a particular screening approach.**

There are many tasks ahead us

- 1. selection and introduction of the most sensitive novel techniques,
- 2. continuous theoretical and
- 3. practical training and education,
- 4. refreshing guidelines by the clinical genetic board,
- 5. quality control.
- 6. Primary prevention

VIIth DOWN SYNDROME SYMPOSIUM
MAY 16-17, SZEGED, 2008.MAY

- **DOWN SYNDROME:COMPLEX!!!**

  -Not only an issue „to screen it out"

  -Parental party

- **Ethics**

  ***Guidelines for Gen.Couns.**

  INFORMED AND INTERPRET!

  ***Mutual understanding !!**

MAY I TEACH YOU?