Screening for carriership of recessive disorders

GENDIA

Antwerp, Belgium

Genetic diseases

1 % chromosome anomaly (eg Down syndrome)

1 % monogenic disorder (eg cystic fibrosis)

1 % malformation (eg spina bifida)

Prenatal screening (1)

We do NIPT in most pregnancies to screen for Down syndrome

- Which has a prevalence of 1 / 500
- Which is mild as compared to other genetic disorders

Prenatal screening (2)

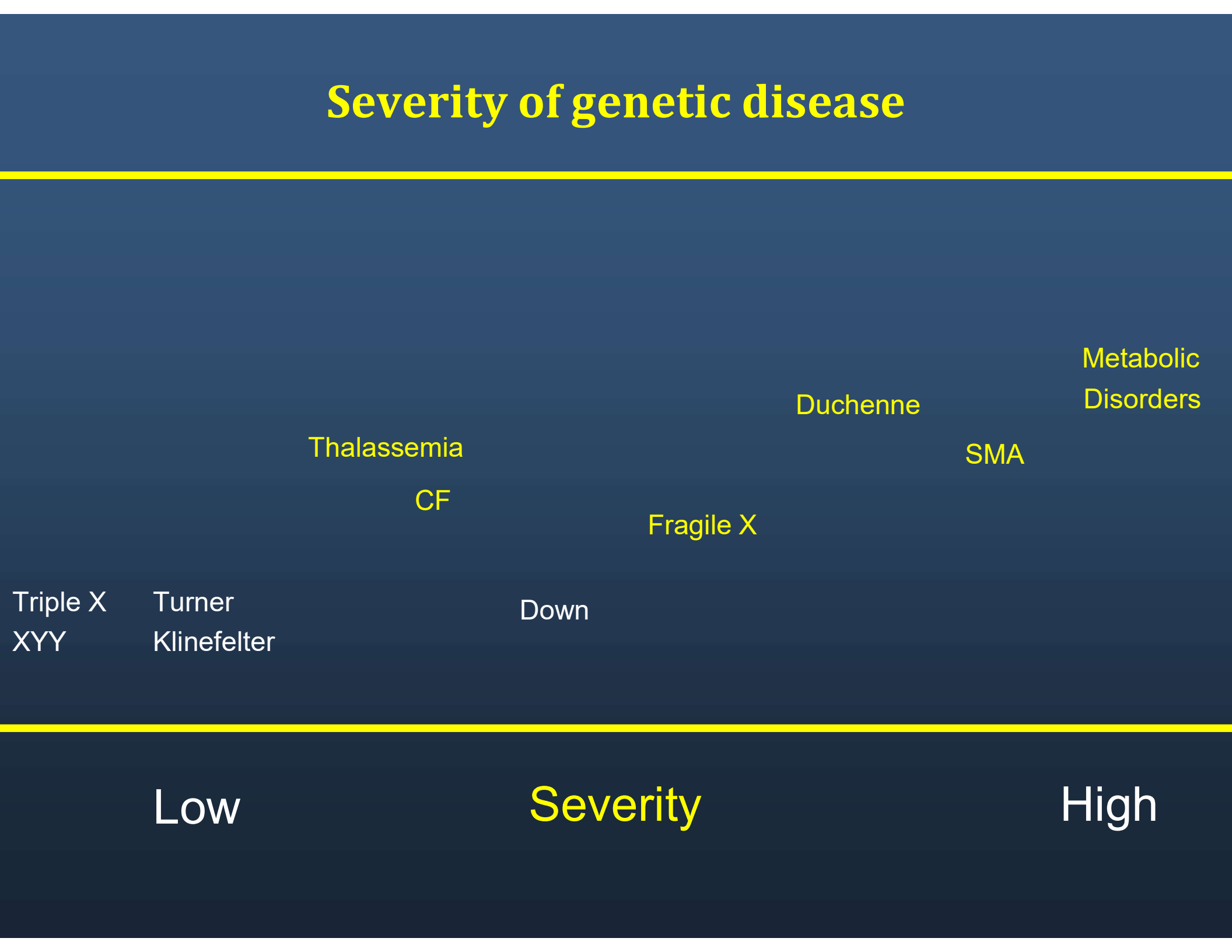
So why not screen pregnancies
for common severe monogenic disorders ?

- Which have a combined prevalence of 1 / 100
- Which are severe as compared to Down syndrome

Frequent recessive disorders

Disorder	Gene	Frequency
Cystic Fibrosis	CFTR	1/3000
Spinal muscular atrophy	SMN1	1/5000
Fragile X	FMR1	1/5000
Thalassemia	HBB	1/300 - 1/3000

Severity of genetic disease



STID carrier test

STID is a **S**creening **T**est for **I**nherited **D**iseases

to screen for carriership for the most common genetic diseases with recessive inheritance

If both parents are carriers of the same disease

the fetus has a 25 % risk of being affected

and prenatal testing can be offered by CVS/AC

STID

STID is geared toward reproductive risks in children

not personal health risks (breast cancer, Huntington)

nor children

STID

STID is worldwide

the second most frequent genetic test

after NIPT

STID Indications

Every pregnancy (no specific indication)

But especially :

- Consanguinity
- Ethnicities with high incidence of genetic diseases
- Family history of deceased children eci
- Difficult pregnancies (IVF)

Different STID

Single disease :

- Tay-Says in Jewish community
- Cystic fibrosis in Western countries
- Thallassemia in Mediterranen area

Core diseases :

- Jewish diseases in Jewish community
- Cystic fibrosis, SMA and fragile X in Western countries

Large set of diseases : up to 1000

Genetic screening in Askhenazi Jewish

- Initially : Tay-Sachs
- Dor Yeshorim program in orthodox Ashkenazi :
  Tay-Sachs, Gaucher, Niemann-Pick,
  Canavan, Bloom, Fanconi, CF
- J screen program: 40 diseases that are common in the Ashkenazi,
  Sephardic, or Mizrahi Jewish populations
- Expanded J screen : 40 diseases that are common in Jewish populations
  40 diseases that are common in the general population

Genetic screening of thalassemia

Mandatory screening :

Premarital screening

in Cyprus, Iran, Saudi Arabia

Voluntary screening :

Screening in high schools, preconceptually or prenatally

in many countries with high incidence

Genetic screening of cystic fibrosis

- 1/25 is carrier in Caucasians (1/2500 children born with CF)
- 1/65 is carrier in Africa
- 1/90 is carrier in Asia

- US : American College of Medical Genetics :
  advise of preconceptual screening

- Belgium : Screening of couples seeking prenatal diagnosis
  or genetic counseling for other reasons
  is now recommended by the Health Counsyl

- The Netherlands : Limited local screening (AMC, Groningen, GENDIA)

GENDIA STID : large set of diseases

1. TEST : NGS sequencing of 436 genes implicated in > 500 relatively common severe recessive diseases

2. OBJECTIVE : To select couples for prenatal diagnosis

3. SAMPLE : 5 ml EDTA blood, 5 ug DNA, saliva in kit

4. TURNAROUND TIME : 1 month

5. INDICATION : Each couple that wants children

6. PRICE : 390 Euro per person

STID results

1. **Both parents carrier :** Risk of affected children is 25 %

   – prenatal testing (CVS, AC)
   – preimplantation diagnostics (PGD)

2. None of the parents is carrier : residual risk for affected children usually is < 1 on 1.000.000 , and no prenatal test is necessary

3. **One of the parents is carrier :** residual risk for affected children usually is < 1 on 10.000 , and no prenatal test is necessary

STID

SCREENING TEST for INHERITED DISEASE

Testing of common recessive diseases

from parental blood before or during pregnancy

www.STID-GENDIA.net