

# The Development of Prenatal Diagnostic Tools

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## Introduction

- What limitations currently exist to regulate the prenatal genetic diagnostic tools, and what limitations should exist if at all?
- Common Prenatal Genetic Diagnostic Tools currently used:
  - Amniocentesis
  - Chorionic Villus Sampling
  - Fetal blood sampling
  - Pre-implantation genetic diagnosis with *in vitro* fertilization
  - Post-natal genetic diagnosis



## Where are all the Girls in China?

- In 1980, a one-child policy was imposed to slow the rapid population increase
- Cultural preferences for male heirs remained strong, and illegal prenatal sex selection has resulted in a gender imbalance
- The male-female ratio has risen to 130 boys for 100 girls
- Census in 2005 revealed that for those under the age of 20, males exceeded females by 35 million
- Consequences:** Societal implications where there is a lack of females for men to marry

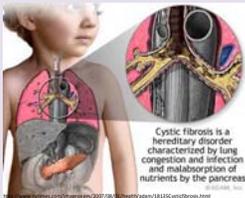


## Significance of Cystic Fibrosis (CF)

- Autosomal recessive genetic disorder
- Caused by a mutation CFTR gene on chromosome 7
- Most common cause of chronic lung disease in children and adults, and most common fatal genetic disorder in caucasians
- Symptoms:** Severe lung damage and nutritional deficiencies, failure to grow, and respiratory infections, death by age 2 without treatment
- Prevalent in those with Eastern European lineage and in Ashkenazi Jewish communities
- Carrier testing in those with a family history of CF is encouraged though the test is expensive
- Diagnostic test for infants is a Sweat Test, measuring the amount of sodium and chloride in the sweat

### Prevalence of Carrier Testing:

- Currently, just those with a family background of CF are tested if they are carriers
- Jews of Eastern European descent are regularly tested regardless of family history



Cystic fibrosis is a hereditary disorder characterized by lung congestion and infection and malabsorption of nutrients by the pancreas

## Conclusion

- In various cases, mandating or strong cultural advocacy towards carrier testing has almost entirely eliminated certain genetic disorders from some populations
  - Providing options earlier for families when a risk exists for a genetic disorder will decrease cultural, emotional, and financial burdens in the future
- However...
- Should carrier screening be mandated or just highly encouraged?
  - Should carrier screening be increased for cystic fibrosis?
  - What is the role of carrier screening and prenatal genetic screening for genetic diseases?



Skull bossing due to expansion of the red bone marrow in the skull



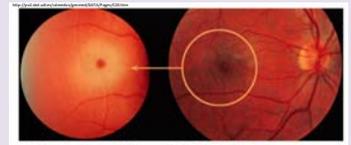
Enlarged spleen, weighing about 1 kg in a 5 year old boy due to  $\beta$ -thalassaemia

## Thalassemia-Free Cyprus

- An autosomal recessive mutation that causes either a defective  $\alpha$  hemoglobin chain or defective  $\beta$  hemoglobin chain
- Symptoms:** listless behavior, pallor, protruding abdomen, abnormal development, malformations of facial features, and death usually by age six if left untreated
- Named for its anemic-like symptoms

### Cyprus Case:

- One in seven of those of either Greek and Turkish descent on the island of Cyprus are carriers for  $\beta$ -thalassaemia
- Laws exist to mandate carrier screening for those seeking marriage licenses
- Government subsidized prenatal diagnosis and pregnancy terminations for homozygotic fetuses were available
- Consequences:** No  $\beta$ -thalassaemia births occurred within two years after the law to mandate premarital certificate screening



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## Decline of Tay-Sachs Among Ashkenazi Jews

- An autosomal genetic disorder
- Caused by a mutation in the HEXA gene on chromosome 15
- Carriers are identified with a blood test to detect  $\beta$ -hexosaminidase A (hex A) enzyme
- Diagnostic tool: An enzyme assay test is utilized to detect hex A levels
- Symptoms:** severe mental and developmental retardation, a "cherry-red spot" in the retina, paralysis and debilitation in the late stages, seizures, and death by age 4 or 5 often due to opportunistic infections

### Tay-Sachs in Ashkenazi Jews:

- 1 in 27 Ashkenazi Jews are carriers
  - Tay-Sachs occur in 1 in 2,500-3,600 births within Ashkenazi Jewish community
  - Israel offers free carrier screening since the 1970's, with prenatal genetic diagnosis and termination options for carriers.
  - Jewish communities worldwide encouraged testing
- Consequences:** Voluntary screening has decreased Tay-Sachs by 90% in Ashkenazi Jews in the United States and Canada
- Success, despite non-mandated carrier testing since Jewish communities are well educated and immersed in genetic research



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