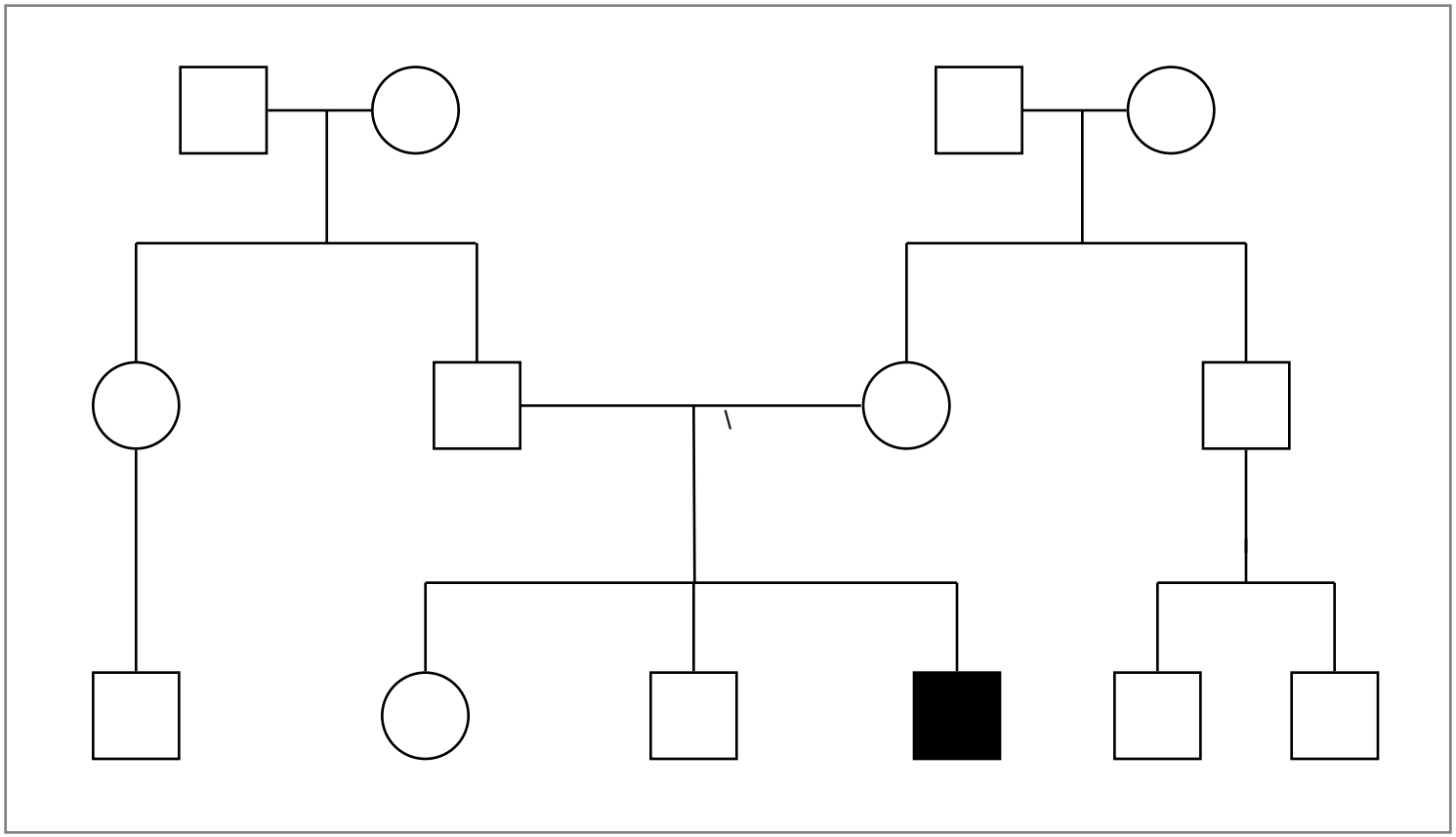
Case 1: Cleft Lip and Palate



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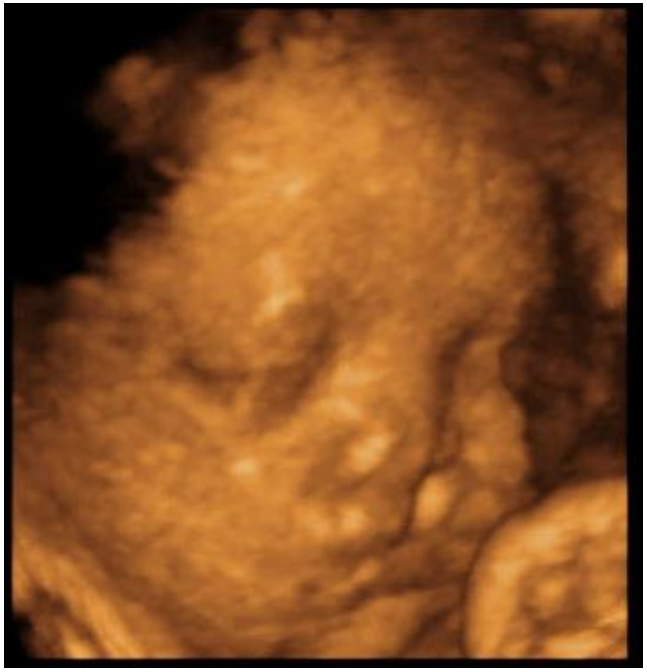
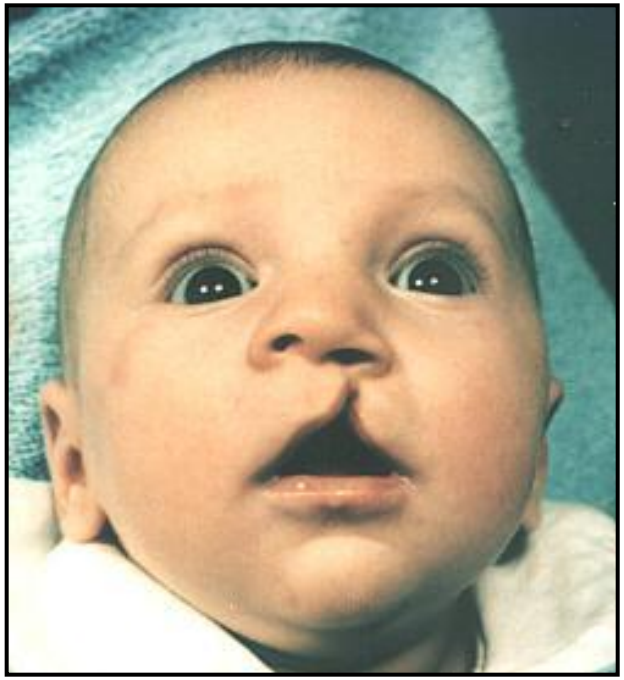
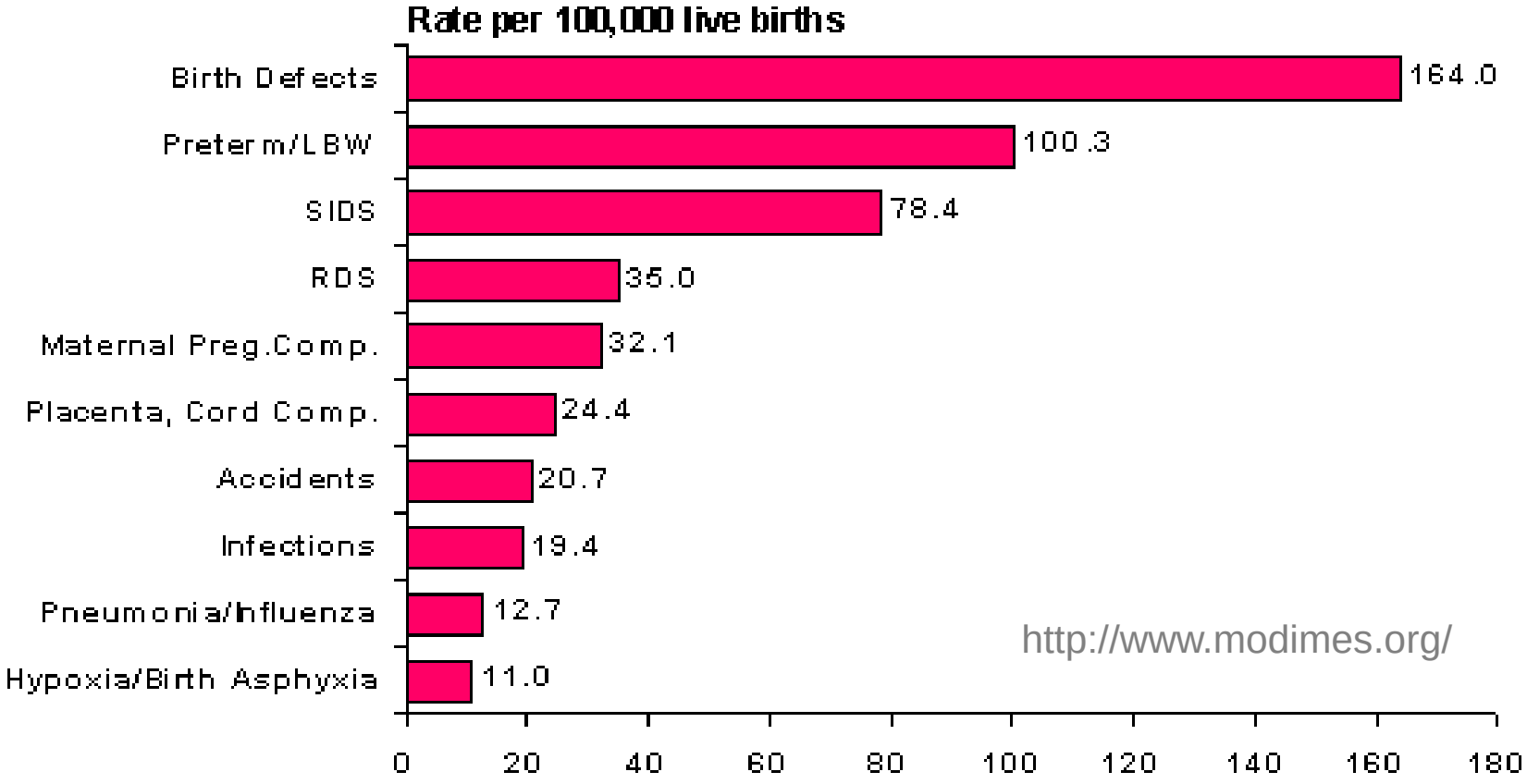




www.widesmiles.org

Birth Defects

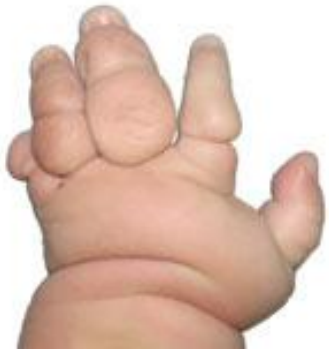


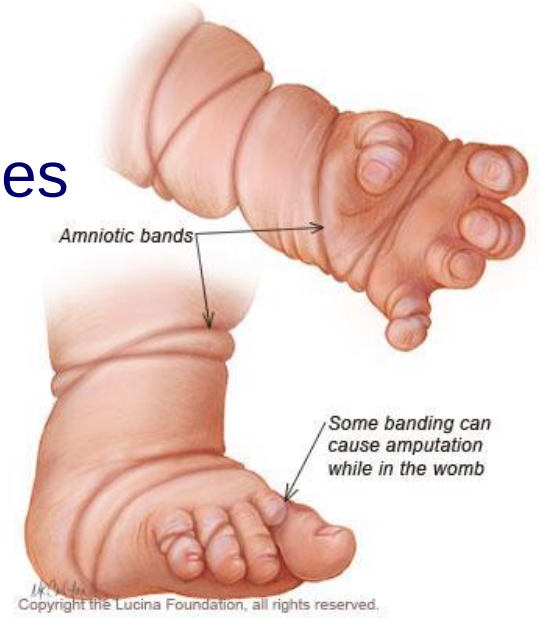
http://www.modimes.org/

Birth Defects Classification

- deformations - mechanical distortion
  - e.g. positional talipes, plagiocephaly

- disruption - distruction of normal tissues
  - e.g. amniotic bands





Birth Defects Classification

- malformation - failure of embryonic processes
  - e.g. omphalocoele, bladder extrophy

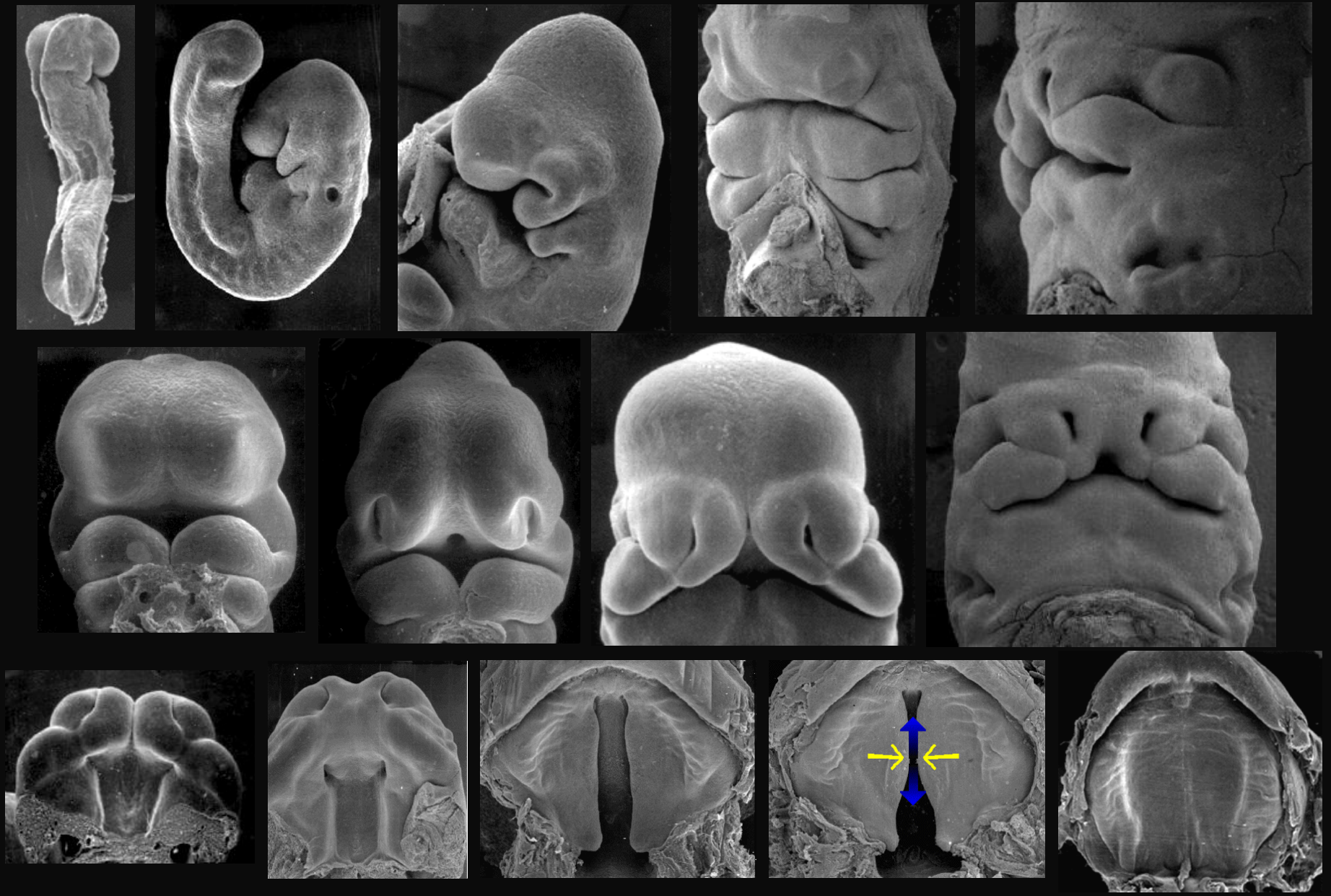
- dysmorphism - rare variants of development
  - e.g. upslanting palpebral fissures in caucasians

Causes of Birth Defects

- genetic
  - monogenic
  - chromosomal
- environmental
  - maternal infections
  - maternal illness
  - medications
  - substances
- unknown

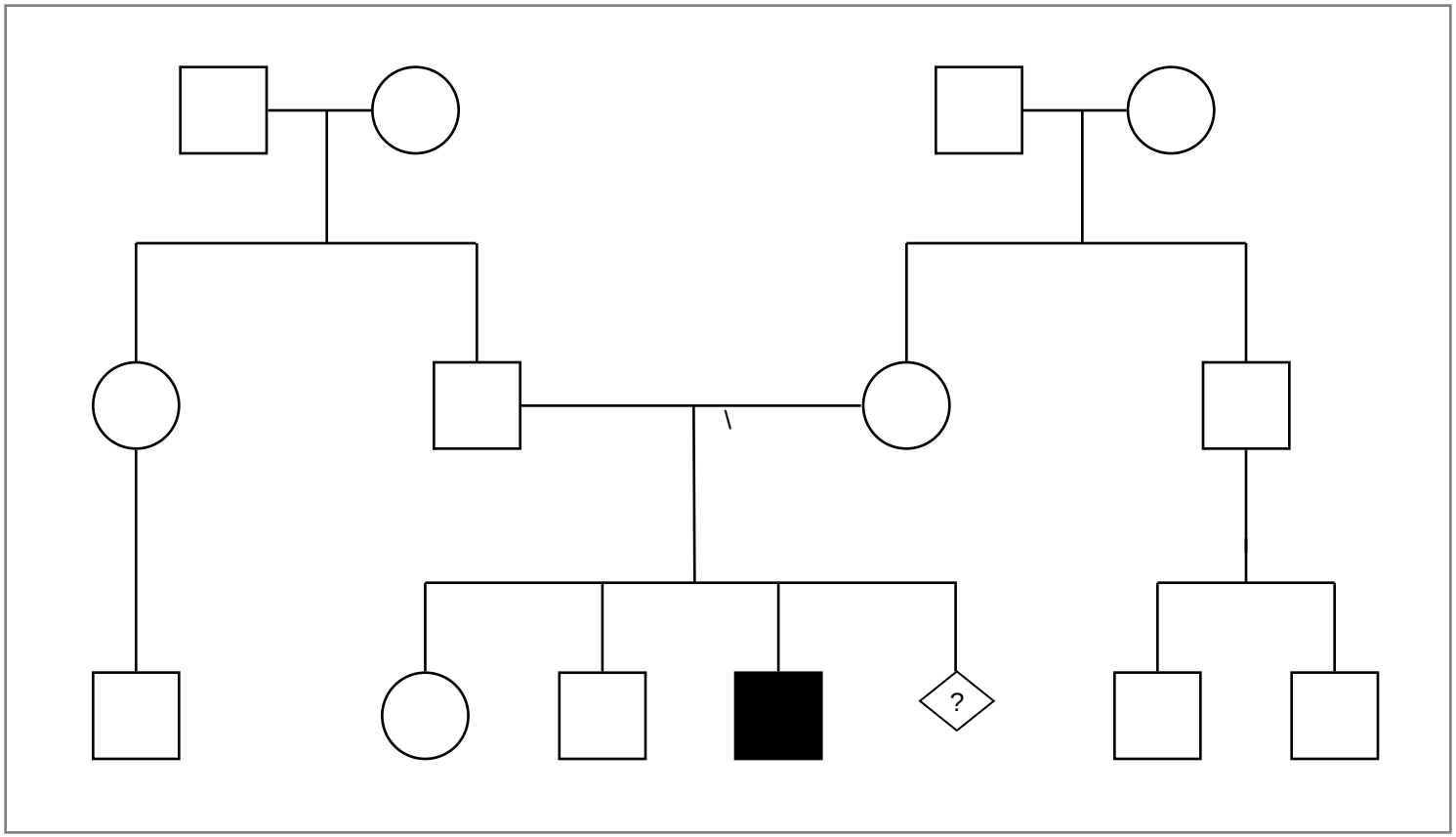
Cleft Lip: Clinical Features

- 1:1000 live births
- male > female
- left > right
- 1/3 bilateral
- 2/3 cleft palate
- 1/4 other birth defects



http://www.med.unc.edu/embryo_images

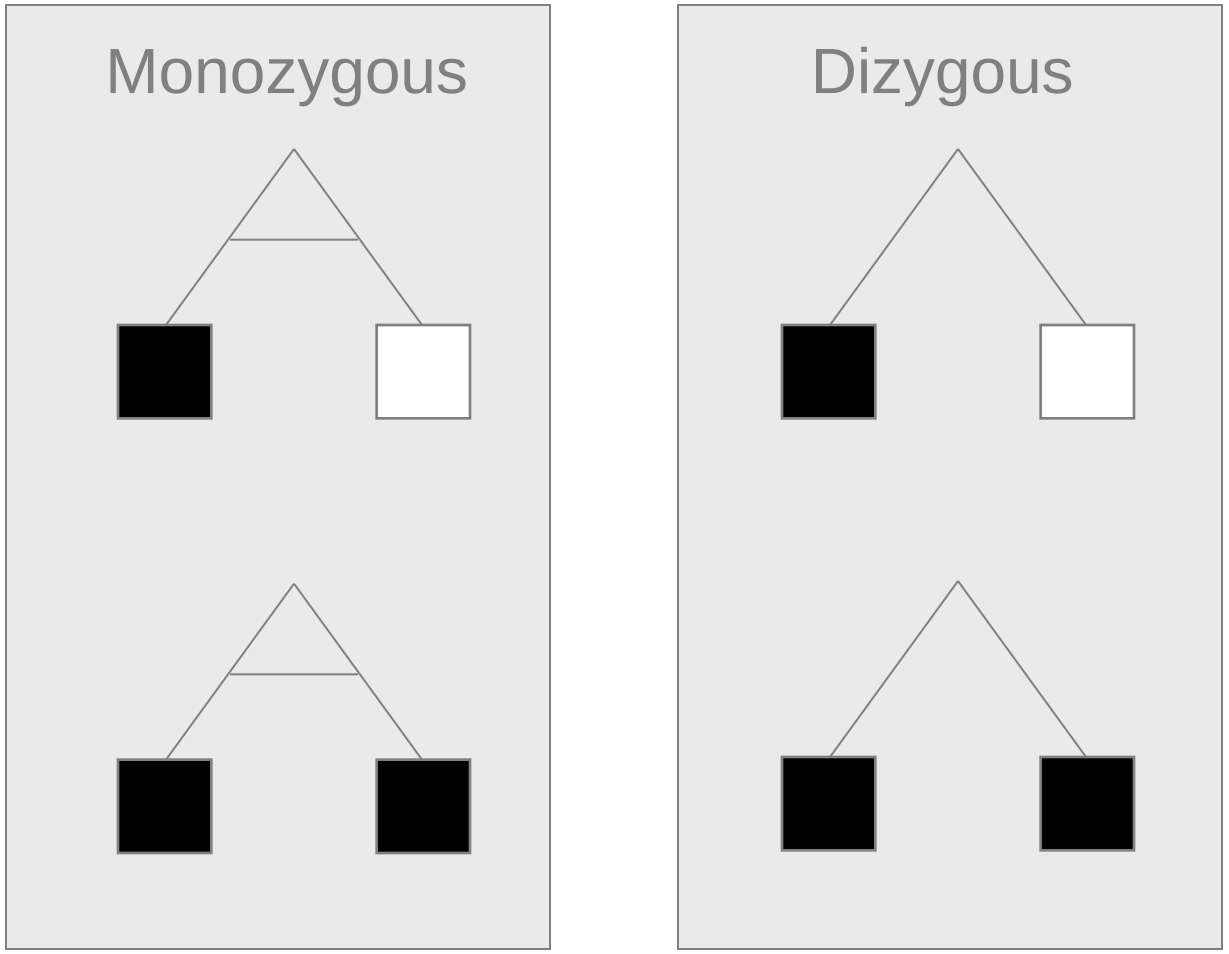
Case 1: Cleft Lip and Palate



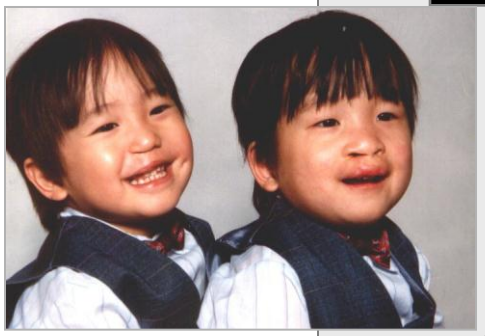
Cleft Lip: Genetic Features

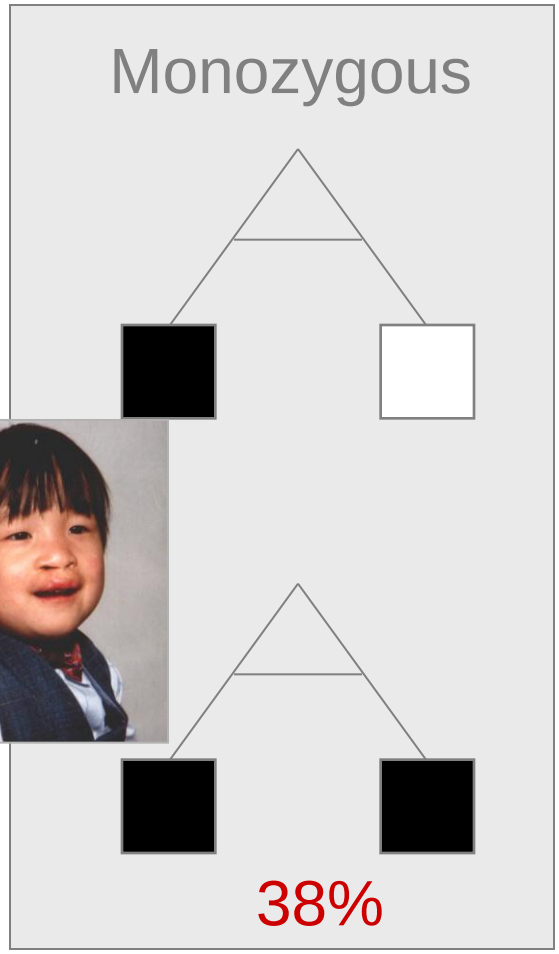
- sibling RR 2-4% (↑~30X)
- offspring RR same
- RR↑ if proband female
- RR↑ if severe defect in proband

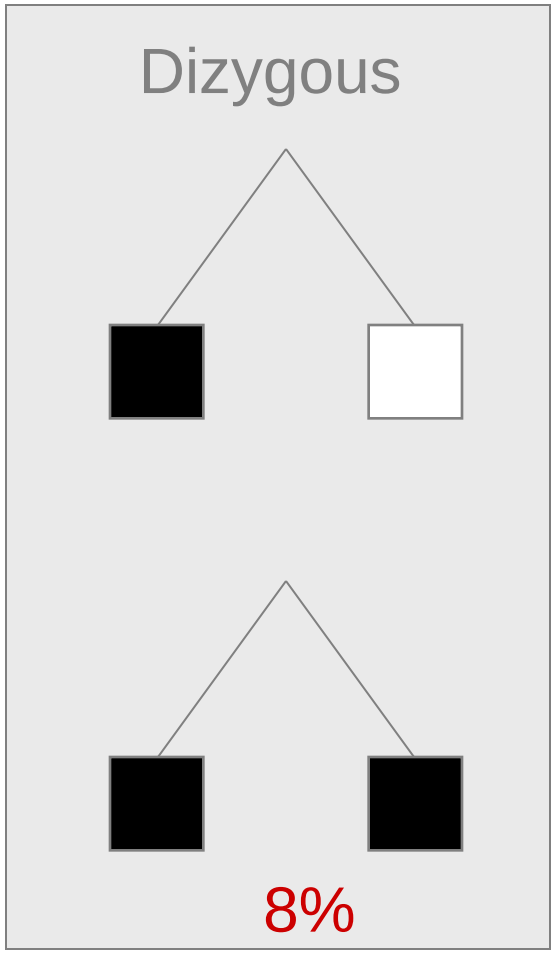
Twin Studies



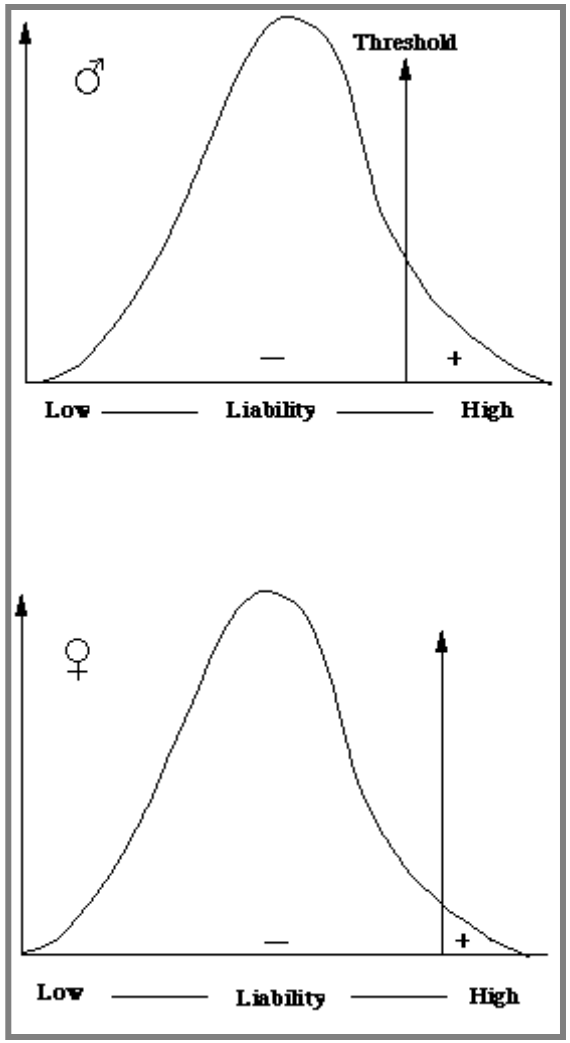
Twin Studies



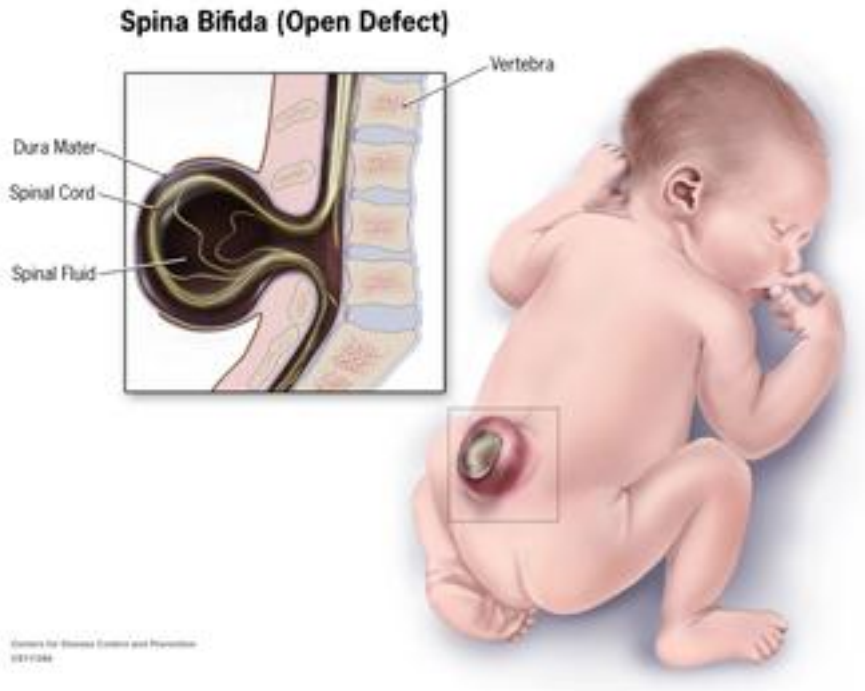


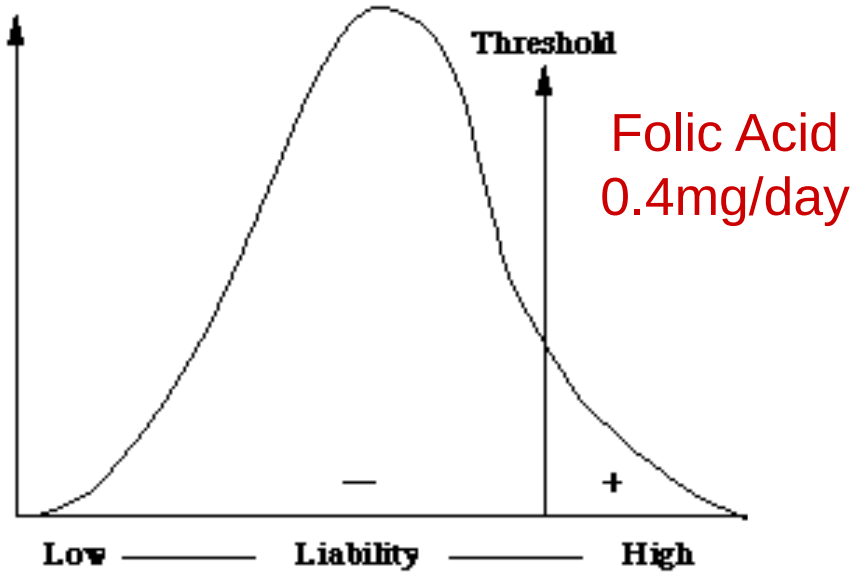


Cleft Lip: Genetic Features



Primary Prevention

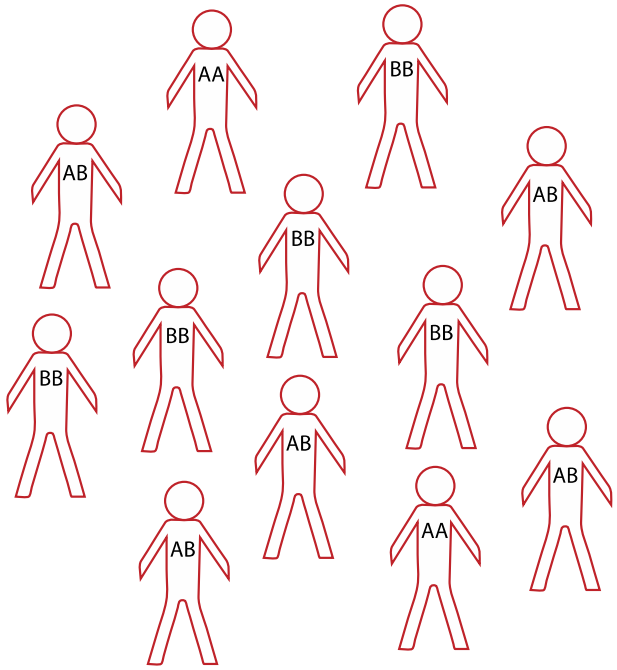




http://www.cdc.gov/ncbddd/spinabifida/

Genetic Association Studies

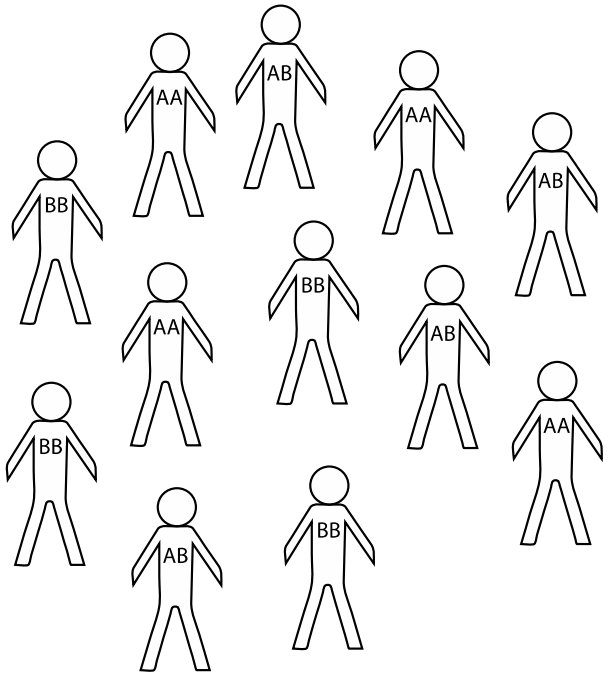
Cases



genotype: allele frequency

B>A

Controls



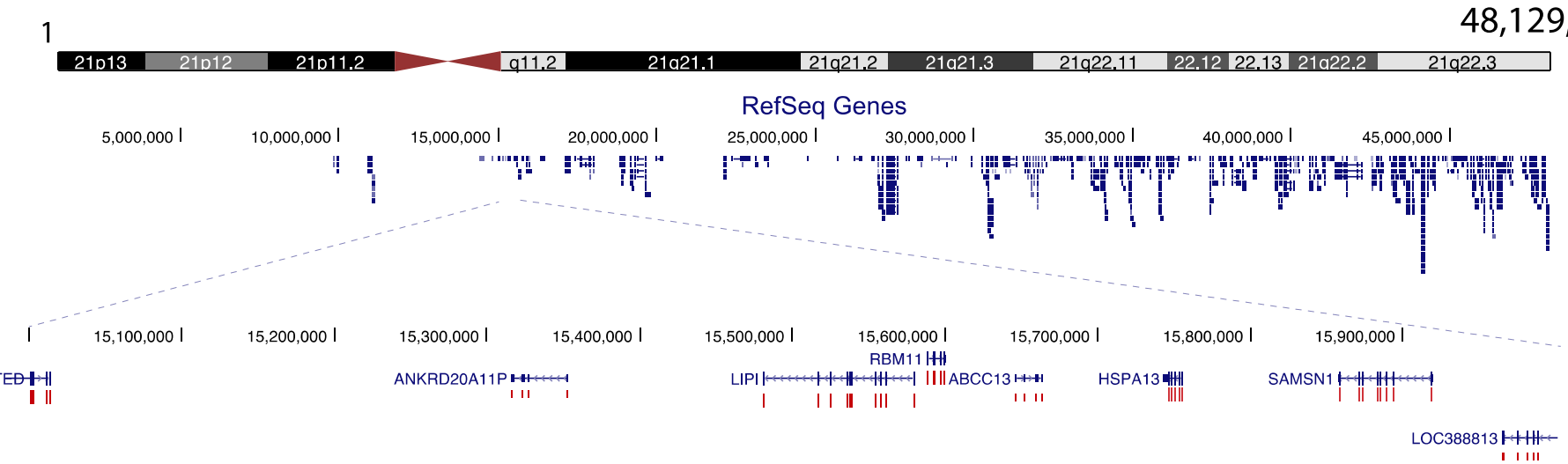
genotype: allele frequency

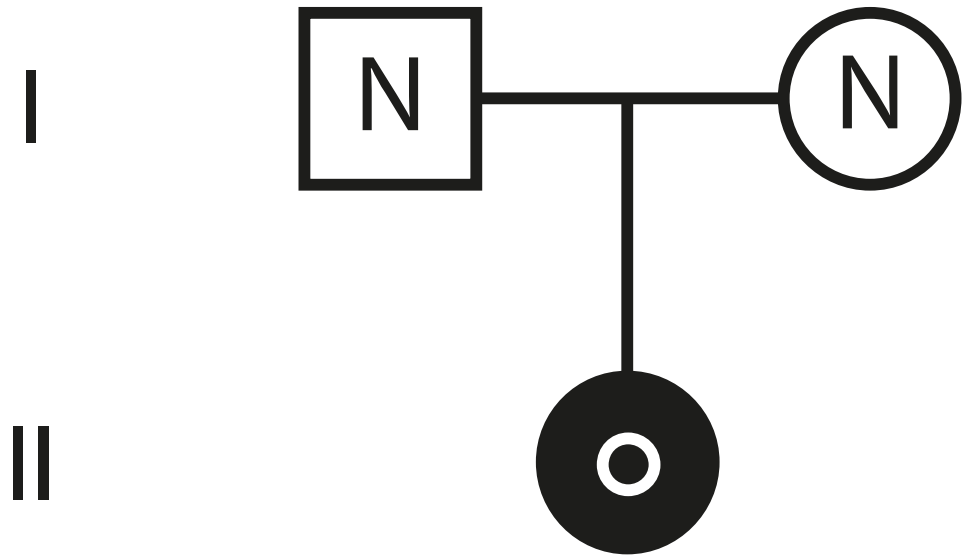
A=B

genetic of common disease
(complex genetic disease)

- familial clustering
  - non-mendelian
  - rare mendelian
    - syndromal
    - non-syndromal
- gene-environment interaction ++
- clinically useful genetic tests rare

Exome Sequencing vs Whole Genome Sequencing





70-120 *de novo* mutation in each individual

~1 *de novo* mutation in coding region

syndromal forms of clefts

van der Woude syndrome

IRF6 gene

Suspect a Syndrome if...

- birth defect associated with:
  - family history
  - craniofacial dysmorphisms
  - behavioral phenotype
  - growth disorder
  - learning disability

computer-aided diagnosis

- >2000 disorders
  - eponyms
  - acronyms
- computerised catalogue
  - photo library
  - clinical abstracts
  - reference list

unofficial learning objectives

- rare diseases are important
- find useful ways of medical thinking
- academic medicine should be the rule
- children’s medicine is the most interesting!