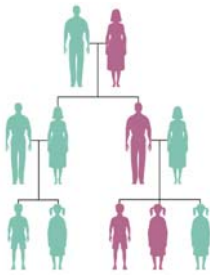
Session 3

Patterns of Inheritance

Part 1



Javad Jamshidi
Fasa University of Medical Sciences, February 2017

How are Traits passed on from Parents to Children?

Monogenic & Polygenic

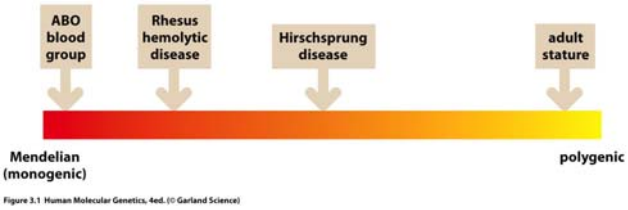
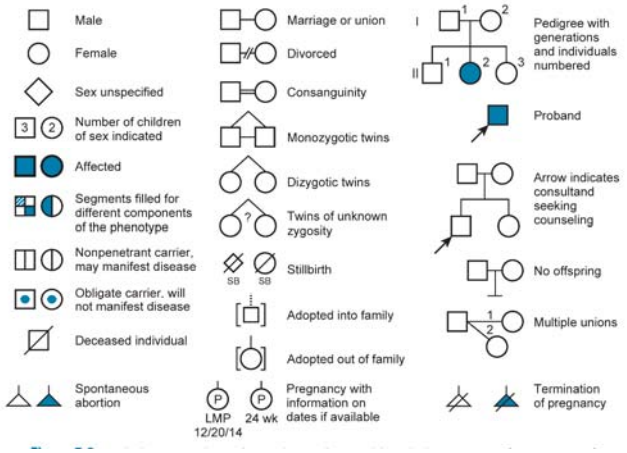


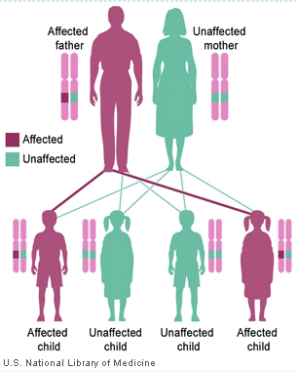
Figure 3.1 Human Molecular Genetics, 4ed. (© Garland Science)

Patterns of Inheritance

- Autosomal
  - Dominant
  - Recessive
- X-Linked
  - Dominant
  - Recessive
- Y-Linked



Autosomal Dominant Inheritance



Autosomal Dominant Inheritance Specific Features

- Affect both males and females in equal proportions
- Transmitted from one generation to the next
- All forms of transmission between the sexes
  - Affected individual usually have at least one affected parent
  - Two affected parents having unaffected offspring

Autosomal Dominant Pedigree

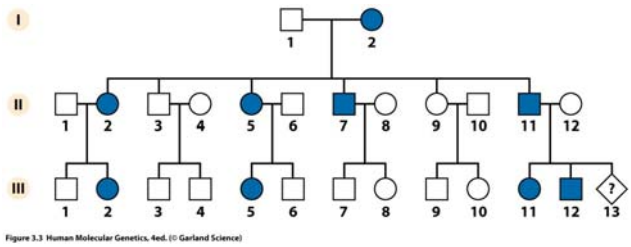
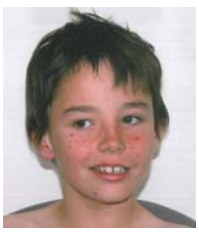


Figure 3.3 Human Molecular Genetics, 4ed. (© Garland Science)

Pleiotropy

- A single gene that may give rise to two or more apparently unrelated effects
- In tuberous sclerosis: learning difficulties, epilepsy, a facial rash known as adenoma sebaceum and subungual fibromas



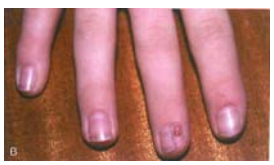


Image from: Emery's Elements of Medical Genetics, 14th Edition, by Peter D. Turnpenny and Sian Ellard, (2012)

Variable Expressivity

- The clinical features variation from person to person
- This variation can be seen even in the same family

Image from: Atlas Of Genetic Diagnosis and Counseling, 2006 Humana Press Inc.

Pedigree Shows Variable Expressivity

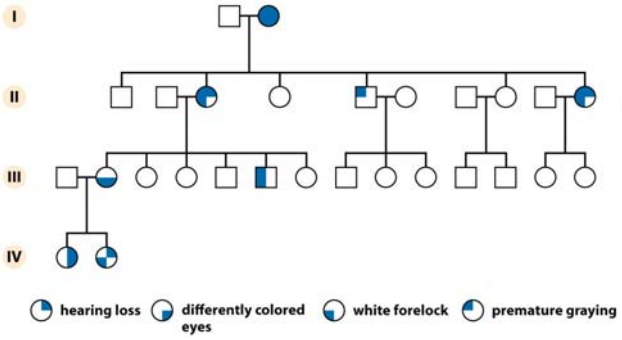
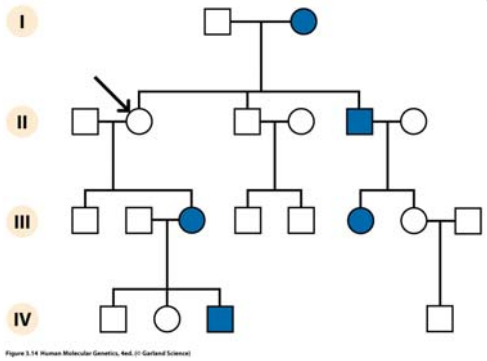


Figure 3.17 Human Molecular Genetics, 4ed. (© Garland Science)

Reduced Penetrance

- Individuals heterozygous for gene mutations of a certain autosomal dominant disorders with no abnormal clinical features
- Probably results from a combination of genetic and environmental factors
- Need to be taken into account when interpret family history information for autosomal dominant disorders

Pedigree Shows Reduced Penetrance



New Mutations

- The sudden appearance of a condition usually is a result of new mutation.
- In less dramatic conditions other explanations for the 'sudden' appearance of a disorder must be considered.
- New dominant mutations, in certain instances, have been associated with an increased age of the father

New Mutation

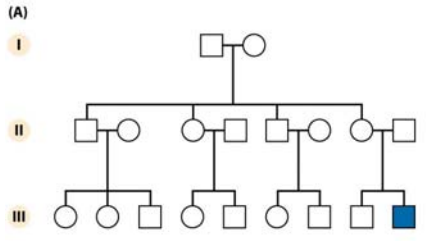
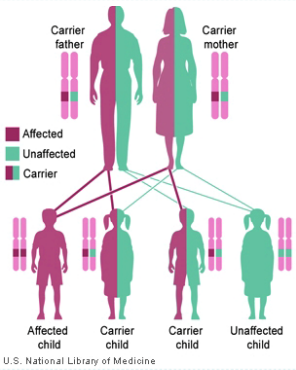


Figure 3.21 Human Molecular Genetics, 4ed. (© Garland Science)

Homozygosity for AD Traits

- In some instances, affected individuals appear either to be more severely affected, or to have an earlier age of onset
- The heterozygote with a intermediate phenotype is consistent with a haploinsufficiency loss of-function mutation
- Some dominantly inherited disorders, homozygous individuals are not more severely affected than heterozygotes

Autosomal Recessive Inheritance



Autosomal Recessive Inheritance Specific Features

- Affects males and females in equal proportions.
- Usually affects only individuals in one generation
- Consanguinity in the parents provides further support
- Affected individual usually have normal parent

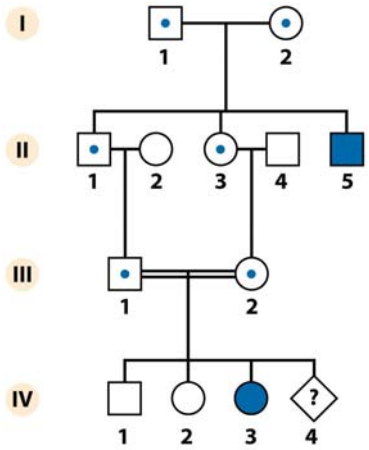


Figure 3.4 Human Molecular Genetics, 4ed. (© Garland Science)

Locus Heterogeneity

- A disorder inherited in the same manner due to mutations in more than one gene
- For example hearing impairment/deafness
- Disorders with the same phenotype from different genetic loci are known as genocopies

Double heterozygotes

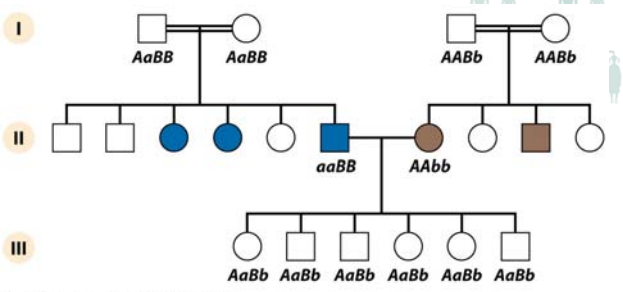


Figure 3.12 Human Molecular Genetics, 4ed. (© Garland Science)

Mutational Heterogeneity

- Different mutations in the same gene as being responsible
- Individuals who have two different mutations at the same locus and are known as **compound heterozygotes**
- Most individuals affected with an autosomal recessive disorder are probably compound heterozygotes rather than true homozygotes,