بسم الله الرحمن الرحيم

Study Sheet: Features of Autosomal Dominant and Autosomal Recessive Pedigrees

Human genetics lecture review | based on the uploaded slides

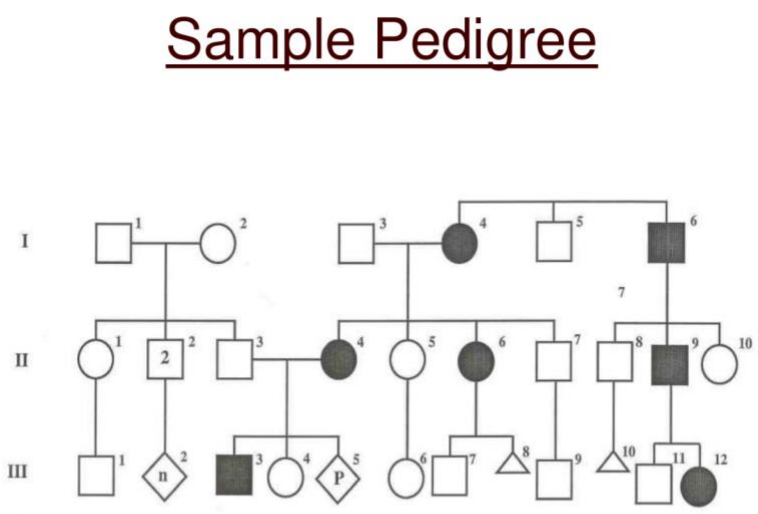
How to use this sheet

- Start with pedigree symbols and key terms, then move to dominant vs recessive patterns.
- The disease examples are the high-yield part: know the hallmark clinical features, inheritance pattern, and the classic pedigree clues.
- Photos from the lecture slides are included to make the pattern recognition stick.

اللهم ربِّ ارحمهما كما ربياني صغيرًا

1) Why pedigrees matter

- Humans are not ideal subjects for genetic research because generation time is long, families are small, and controlled breeding experiments are not ethical.
- Even so, Mendelian genetics still forms the backbone of human genetics.
- A pedigree is a family tree that shows relationships between parents and children across generations and helps trace inheritance patterns.
- Pedigrees are also used to predict future offspring probabilities using the multiplication and addition rules.



Sample pedigree from the lecture (page 4).

2) Core pedigree terminology and notation

Term	Meaning
Locus	The position of a gene on a chromosome.
Allele	Alternative forms of a gene at the same locus.

Term	Meaning
Genotype	The allele combination at a locus.
Phenotype	The observable trait produced by genotype plus environment.
Homozygous	Two identical alleles at a locus; can be two normal alleles or two mutant alleles.
Heterozygous	Two different alleles at a locus.
Compound heterozygote	Two different mutant alleles at the same gene.
Carrier "obligate heterozygote"	A heterozygote who carries a recessive disease allele but is usually clinically normal.
Penetrance	Whether a genotype is expressed at all.
Expressivity	How strongly or variably the phenotype is expressed.
Pleiotropy	One gene affects multiple phenotypic traits.
Genetic heterogeneity	Different genes or different alleles can cause a similar disease phenotype.

Another terms:
Dmominant
Codminant
Recessive
Ageof onset
X-linked
Hemizygous
Sex limited
Sex influnced
Imprinting
Trinucleutide repeat

✅ are mentioned in slides' table but not explained, to be in the safe side memorise them

Hemizygous means that a person has **only one copy of a gene instead of the usual two.**

🧬 **The simplest way to think about it:**

Normally, you inherit:

- **1 gene from mom**
- **1 gene from dad**
  → so you have **2 copies (alleles)**

But if you're **hemizygous**, you only have **ONE copy** of that gene.

🔷 1. Sex-limited traits

👉 **Definition:**
Traits that are controlled by genes present in *both sexes* BUT are **expressed in only one sex**.

🔶 2. Sex-influenced traits

👉 **Definition:**
Traits that are expressed in **both sexes**, BUT **the phenotype depends on sex**.

Genomic imprinting is a special genetic phenomenon where **the expression of a gene depends on which parent it came from.**

🧬 **Simple idea:**

Normally → you inherit **2 copies (alleles)** of a gene (one from mom, one from dad), and **both can be active**.

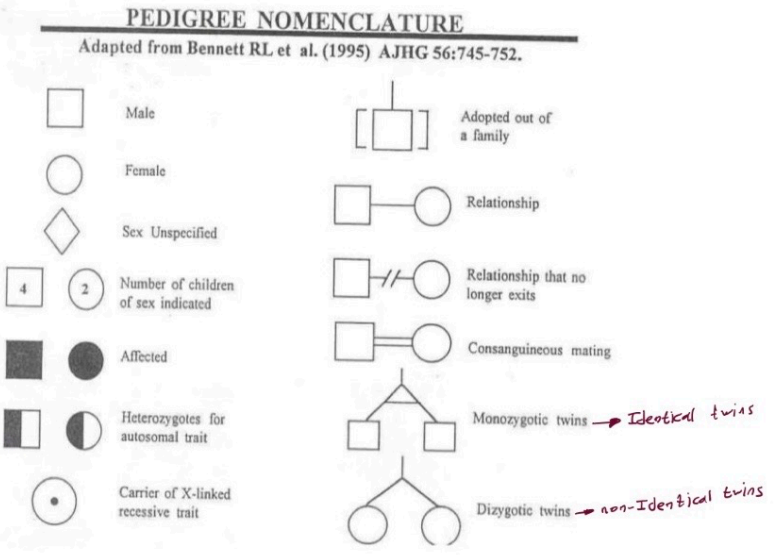
But in **imprinting**:
👉 **One copy is "silenced" (turned OFF)**
👉 Only **the other copy is expressed**

⚡ **Key point:**

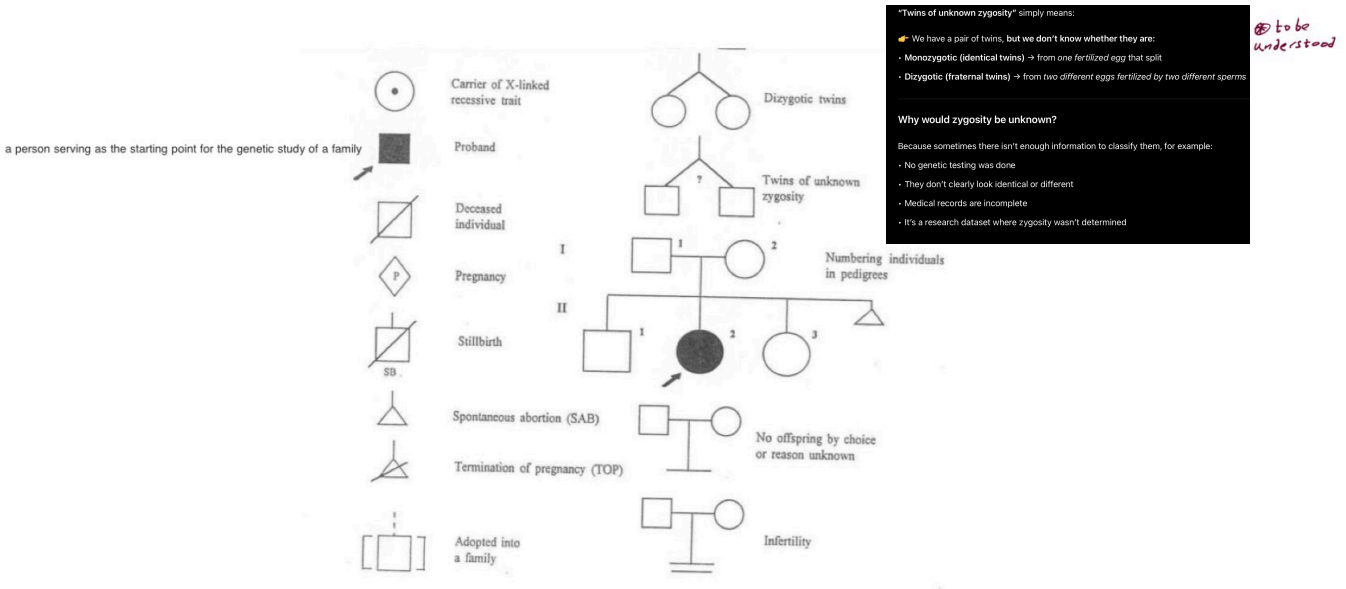
- The silencing is **parent-specific**
  - Some genes → only the **maternal copy works**
  - Others → only the **paternal copy works**

3) Reading pedigree symbols correctly

- Generations are marked with Roman numerals (I, II, III...) and individuals within a generation are numbered from left to right with Arabic numerals.
- The oldest generation is placed at the top.
- Siblings are listed from oldest to youngest, left to right.
- Male partners are usually drawn to the left of female partners.
- Shading, hatching, dots, or other fill patterns may be used to indicate medical status; always look for the legend.
- The proband is the affected person who first comes to medical attention; it is marked by an arrow.
- Pedigrees can also show adoption, infertility, pregnancy, stillbirth, spontaneous abortion, termination of pregnancy, twins, and changing relationship status.



Pedigree nomenclature and symbols (page 11).



Expanded pedigree symbols including proband, twins, pregnancy, and termination of pregnancy (page 12).

Record full name, current age and date of birth, or age at death for each individual

Record race and ethnic origin of each individual

Note health problems and/or cause of death for each individual

There are appropriate symbols to use for both adoption and assisted-reproductive technologies

- Standardization of symbols is essential to facilitate communication - See Robin Bennett's article referenced in resources at the end of the syllabus for more details if interested.

- Nomenclature is an evolving process.
- Several ethical and legal dilemmas - Potential for discrimination, issues of privacy raised, and need for guidelines.

4) Basic genetics you need before the patterns

- The gene is the unit of inheritance.
- An individual's phenotype is determined by the genotype at a locus and the environment in which it is expressed.
- Traits on the 22 autosomes are autosomal; traits on X-linked loci are X-linked; traits on the Y chromosome are Y-linked.
- Mendel's laws: unit inheritance, segregation, and independent assortment. Linkage is the major exception to independent assortment. ⊗ explained in the next slide

5) Dominant, recessive, and codominant

- For dominant traits, the mutant allele is written with a capital letter and the normal allele with a small letter in the lecture convention.
- Autosomal dominant: one mutant allele is enough for expression; heterozygote and homozygote for the dominant allele are classically affected in the same direction, although homozygotes may be more severe.
- Autosomal recessive: expression usually requires two mutant alleles.
- Codominance: the heterozygote has a different phenotype from either homozygote.

6) X-linked comparison from the lecture

- X-linked dominant: one dominant allele on the X chromosome can cause disease in either sex.
- X-linked recessive: males are affected with one mutant X because they are hemizygous; females usually need two mutant X alleles.

7) Types of genetic disease

- Chromosomal
- Single gene (Mendelian)
- Multifactorial
- Teratogenic

Gregor Mendel's Laws of Inheritance

- Law of Unit Inheritance - parental characteristics do not blend because there is a unit of inheritance. Mendel's "units" are now known as genes or alleles.

- Law of Segregation - the two alleles at a particular locus segregate into different gametes.

- Law of Independent Assortment - alleles at different loci are transmitted independently of each other. Linkage is an exception to this rule.

Dominant and Recessive Inheritance

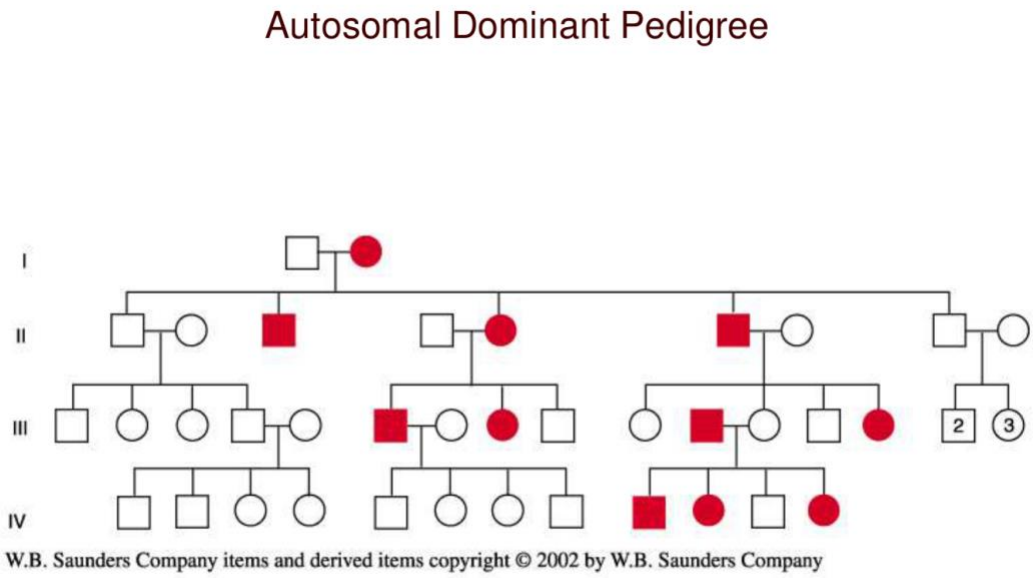
- If the heterozygote (AB) has a different phenotype than either of the homozygotes (AA or BB), then the alleles are said to be **codominant**.

- **X-linked dominant traits** are those expressed when either males or females have one copy of the dominant allele, i.e., X^AY or X^AX^a where A=dominant allele.

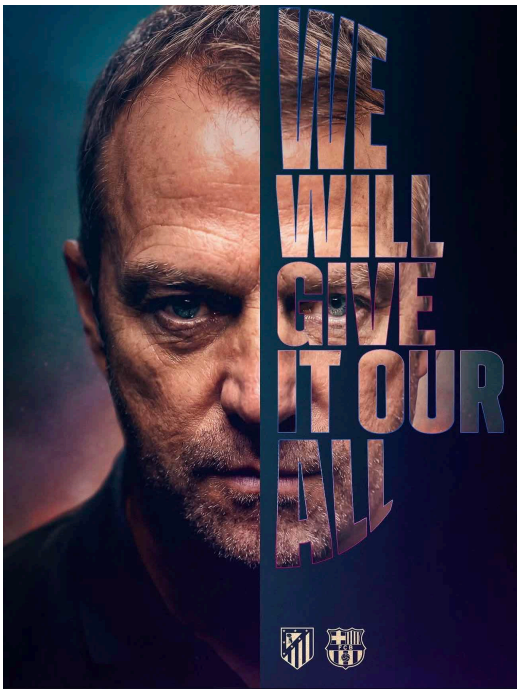
- **X-linked recessive** traits are those expressed in males who carry one copy of the recessive allele (i.e., are hemizygous, XaY where a=recessive allele). Two copies of the recessive allele are generally required for females to express the trait, i.e., XaXa.

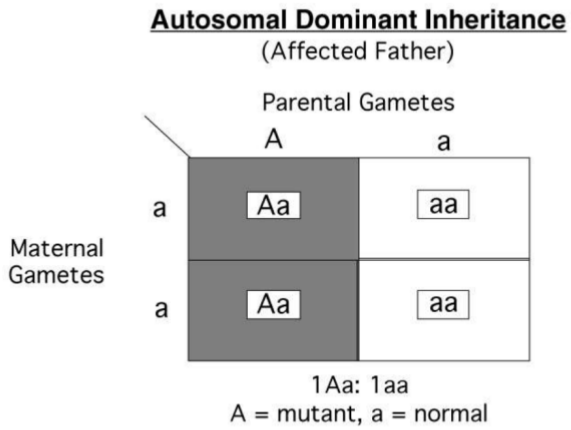
8) Autosomal dominant inheritance

- Vertical transmission: the trait usually appears in every generation and passes directly from grandparent to parent to child without skipping generations.
- Both sexes are affected in about a 1:1 ratio.
- Both sexes can transmit the trait.
- Heterozygotes are much more common than homozygotes.
- Variable expressivity and variable age of onset are common.
- Homozygotes are often more severely affected than heterozygotes.
- A new mutation can create an affected child even when parents are unaffected.
- The gene product is often a structural or non-enzymatic protein.



Autosomal dominant pedigree pattern (page 30).





Punnett square for autosomal dominant inheritance with an affected heterozygous parent (page 31).

9) Autosomal dominant probability rules

- Affected heterozygote (Aa) × unaffected (aa) → 50% affected children, 50% unaffected children.
- Affected heterozygote (Aa) × affected heterozygote (Aa) → 75% affected children, 25% unaffected children.
- In a dominant pedigree, a true unaffected person usually does not transmit the trait, unless penetrance is incomplete or the diagnosis is not yet evident.

10) Classic autosomal dominant examples

Disorder	High-yield clinical features from the slides
Familial hypercholesterolemia	Xanthomas; very high LDL; coronary heart disease in middle age in heterozygotes and childhood coronary disease in homozygotes.
Huntington disease	Progressive loss of brain neurons, dementia, and loss of motor control; late onset, typically 30-40 years, but may be earlier; unstable trinucleotide repeats.
Neurofibromatosis type 1 (NF1)	Café-au-lait spots, Lisch nodules (benign iris growths), peripheral nerve tumors; variable expressivity; high mutation rate.
Myotonic dystrophy	Facial weakness, cataracts, progressive muscular weakness; variable onset and variable expressivity.
Marfan syndrome	Tall stature with long limbs, narrow face with high narrow palate, dislocated lenses and myopia, cardiac manifestations such as aortic aneurysm; connective tissue disorder; pleiotropy.
Achondroplasia	Short-limbed dwarfism, megalocephaly, lordosis and kyphosis; about 80% are new mutations, with more mutations at increasing paternal age.

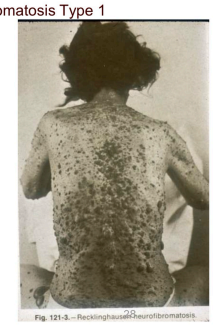
Dominantly Inherited Disorders

- Some human disorders are caused by dominant alleles
- Dominant alleles that cause a lethal disease are rare and arise by mutation
- *Achondroplasia* is a form of dwarfism caused by a rare dominant allele

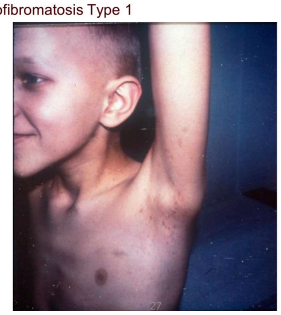
Achondroplasia example and dominant inheritance (page 23).

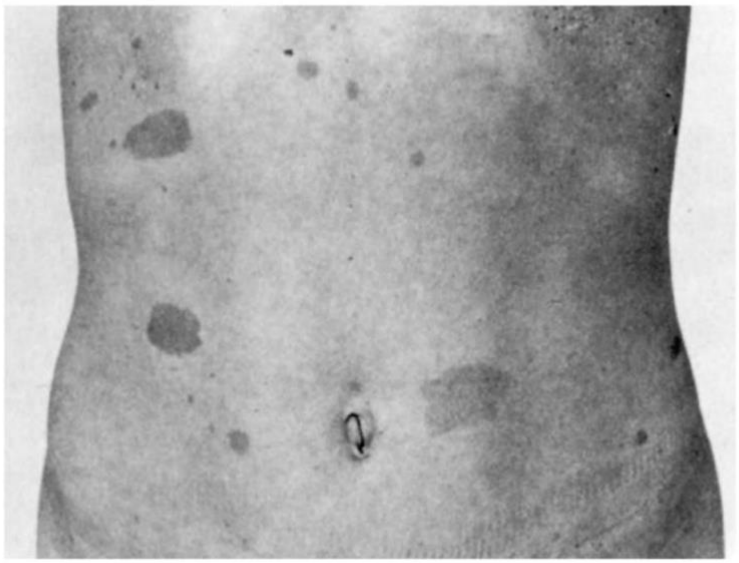
Neurofibromatosis Type 1

Neurofibromatosis Type 1



Neurofibromatosis Type 1





Neurofibromatosis type 1 clinical photos showing café-au-lait spots and skin findings (page 26).

11) Why dominant lethal disorders are rare

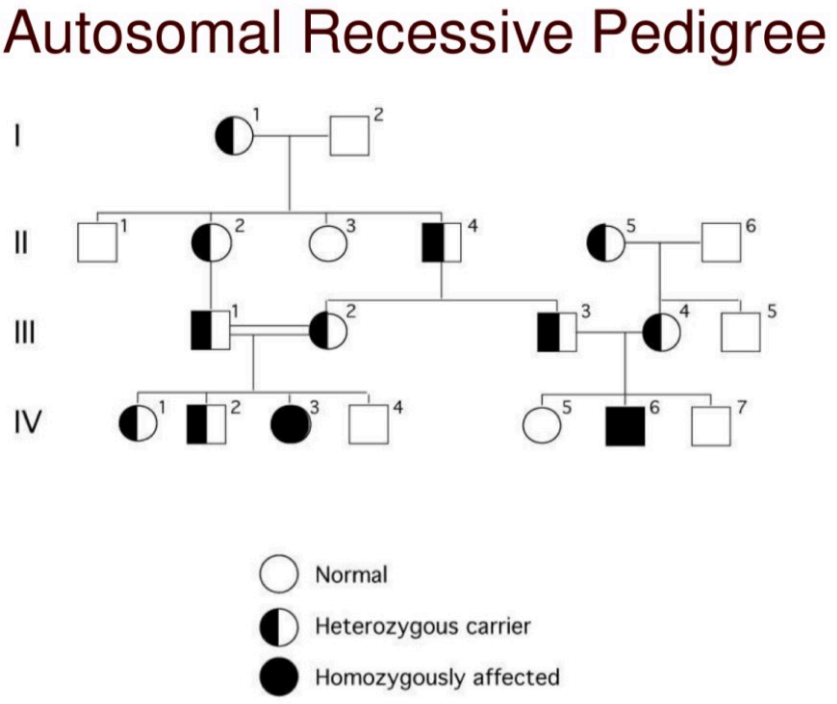
- Dominant alleles that cause lethal disease are rare because they are usually removed by selection.
- When they do appear, they often arise by mutation.
- Achondroplasia is the lecture example of a rare dominant allele causing dwarfism.

12) Autosomal recessive inheritance

- Horizontal transmission: affected individuals are often found in the same sibship or same generation rather than through every generation.

- Both sexes are affected in about a 1:1 ratio.
- Both sexes can transmit the mutant allele equally.
- Consanguinity is an important clue because close relatives are more likely to carry the same rare allele.
- The gene product is usually an enzymatic protein.

- Many genetic disorders are inherited in a recessive manner
- These range from relatively mild to life-threatening



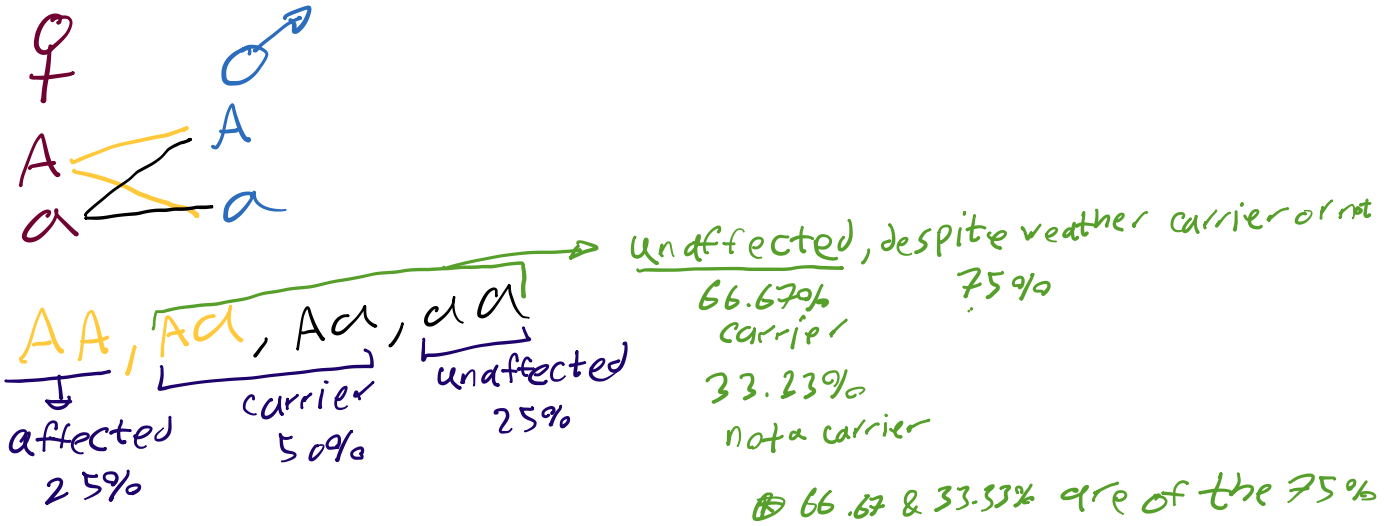
Autosomal recessive pedigree example (page 49).

13) Autosomal recessive probability rules

- Carrier × carrier (Aa × Aa) → 25% affected (aa), 50% carrier (Aa), 25% unaffected non-carrier (AA).
- Among unaffected children of carrier parents, the chance of being a carrier is two in three.
- Affected homozygotes are commonly the offspring of two heterozygote carriers.

بدل ما تبصمج الpropabilities بتذكر بالوراثة بأحياء توجيهي كنا نشوف كل حدا من الparents ايش عنده اليلات و نضربهم ببعض، و بالأخير نشوف ايش حيطلع الoffspringg

For example:
Father is Aa
Mother is Aa



14) Recessive disease examples

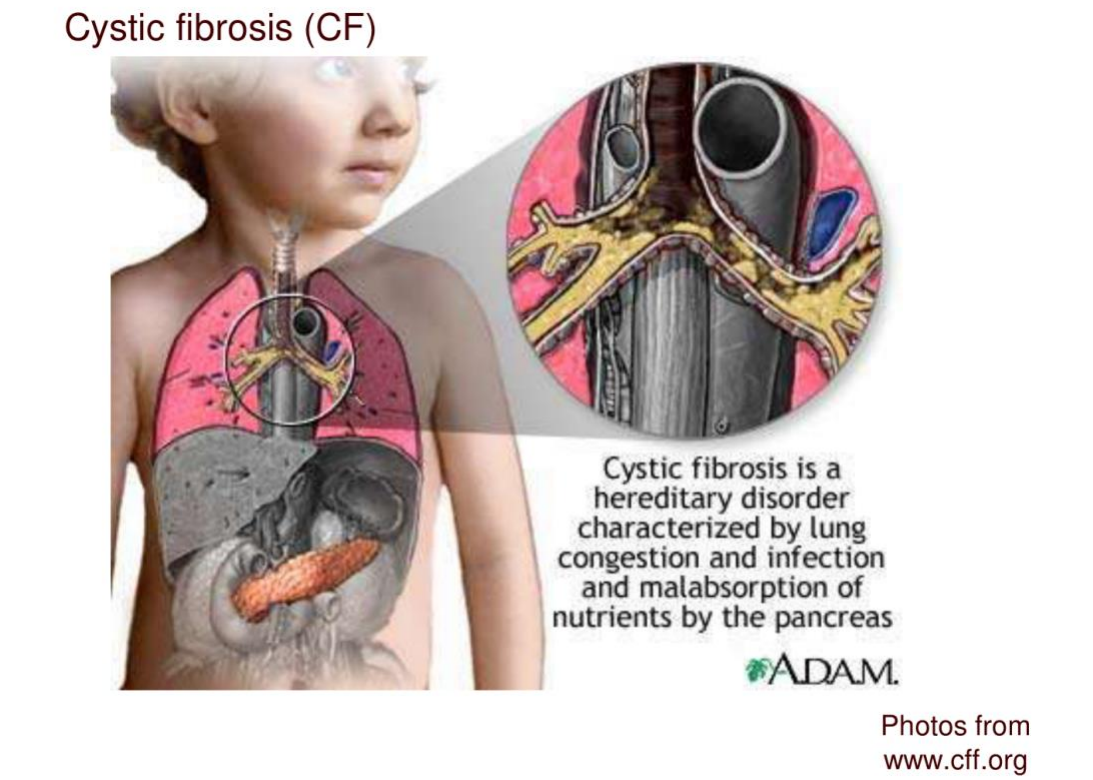
Disorder	High-yield clinical features from the slides
Cystic fibrosis	Chronic progressive pulmonary disease, pancreatic endocrine insufficiency, elevated sweat chloride, more frequent in European Caucasians.
Tay-Sachs disease	Progressive neurological abnormalities, retinal cherry-red spot, higher frequency in Ashkenazi Jewish and French Canadian populations, reduced serum hexosaminidase A, usually fatal in early childhood.
Sickle cell anemia	Failure to thrive, chronic anemia, vaso-occlusive crisis with pain, increased risk of infection, higher frequency in those of African descent, heterozygote advantage.
Phenylketonuria (PKU)	Increased phenylalanine due to defective phenylalanine hydroxylase (PAH), neurological problems, hypopigmentation, musty odor of urine.

The Behavior of Recessive Alleles

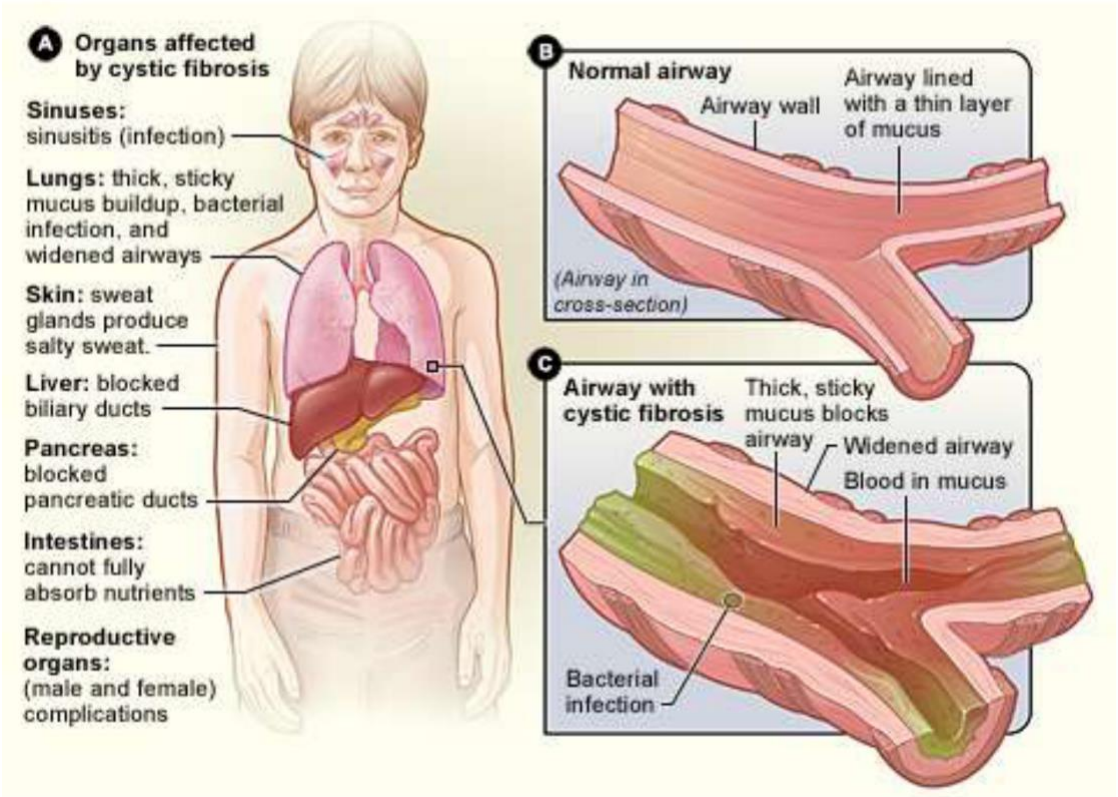
- Recessively inherited disorders show up only in individuals homozygous for the allele
- **Carriers** are heterozygous individuals who carry the recessive allele but are phenotypically normal; most individuals with recessive disorders are born to carrier parents
- **Albinism** is a recessive condition characterized by a lack of pigmentation in skin and hair and eyes

Cystic Fibrosis

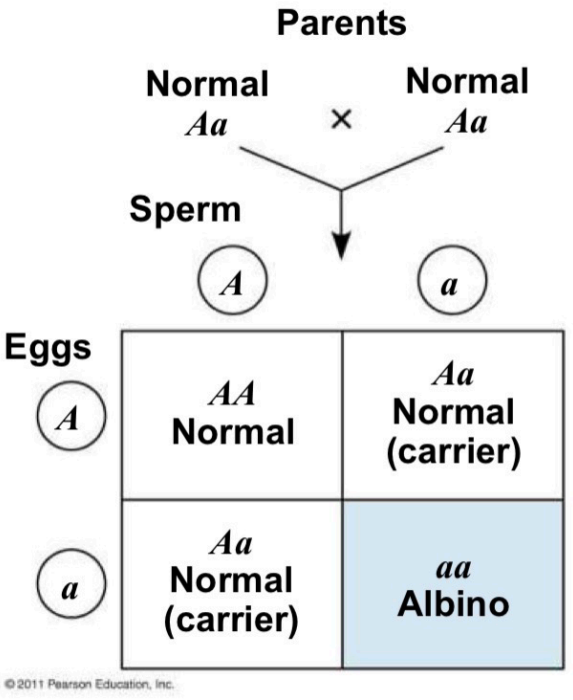
- **Cystic fibrosis** is the most common lethal genetic disease in the United States, striking one out of every 2,500 people of European descent
- The cystic fibrosis allele results in defective or absent chloride transport channels in plasma membranes leading to a buildup of chloride ions outside the cell
- Symptoms include **mucus buildup** in some internal organs and abnormal absorption of nutrients in the small intestine



Cystic fibrosis illustration of lung and organ involvement (page 39).



Cystic fibrosis affecting multiple organs and mucus obstruction in the airway (page 40).

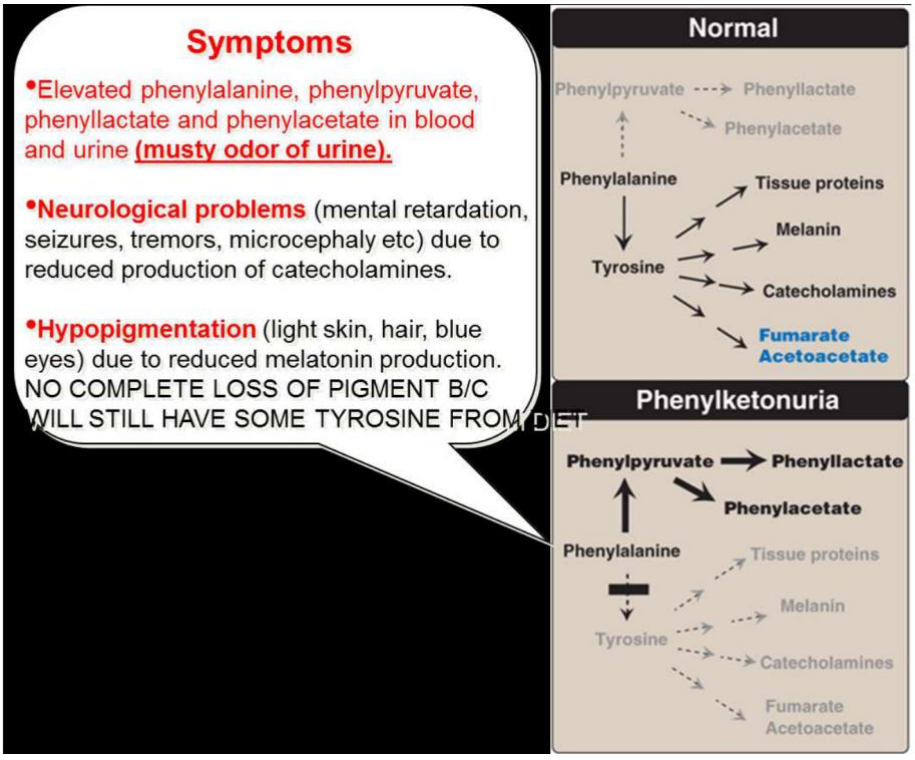


Sickle-Cell Disease: A Genetic Disorder with Evolutionary Implications

- **Sickle-cell disease** affects one out of 400 African-Americans
- The disease is caused by the substitution of a single amino acid in the hemoglobin protein in red blood cells
- In homozygous individuals, all hemoglobin is abnormal (sickle-cell)
- Symptoms include physical weakness, pain, organ damage, and even paralysis

- Heterozygotes (said to have sickle-cell trait) are usually healthy but may suffer some symptoms
- About one out of ten African Americans has sickle cell trait, an unusually high frequency of an allele with detrimental effects in homozygotes
- Heterozygotes are less susceptible to the malaria parasite, so there is an advantage to being heterozygous

Sickle cell anemia photo from the lecture (page 45).



Phenylketonuria and its metabolic consequences (page 47).

15) Carrier logic and consanguinity

- Because recessive disease alleles are usually rare, the chance that two unrelated carriers meet is low.
- Consanguineous matings increase the chance that both parents carry the same rare allele.
- Most societies have legal or cultural limits on marriages between close relatives.

16) Sickle-cell disease and heterozygote advantage

- Sickle-cell disease is caused by a single amino-acid substitution in hemoglobin.

- In homozygotes, all hemoglobin is abnormal and symptoms can include weakness, pain, organ damage, and even paralysis.
- Heterozygotes usually have sickle-cell trait and are often healthy, but they are less susceptible to malaria.
- That malaria protection is why the allele can remain relatively common despite harming homozygotes.

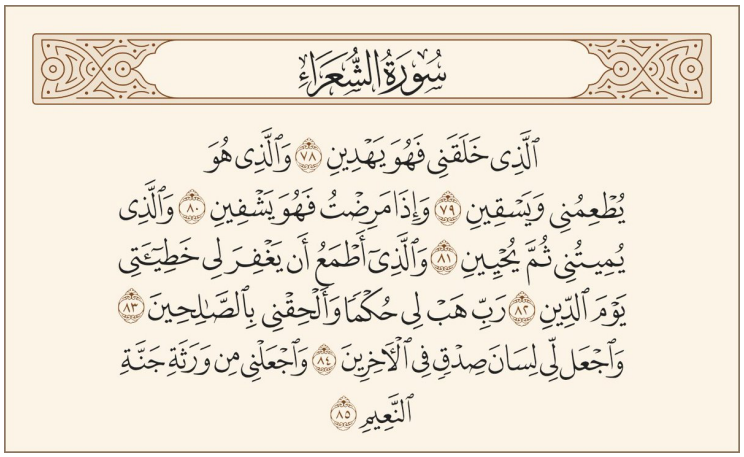
17) PKU in one glance

- PKU is due to a defective hepatic enzyme, phenylalanine hydroxylase (PAH).
- Because phenylalanine cannot be converted normally to tyrosine, phenylalanine and related metabolites build up.
- Key consequences: neurological problems, hypopigmentation, and a musty odor of urine.

18) Autosomal dominant vs autosomal recessive: rapid comparison

Feature	Autosomal dominant	Autosomal recessive
Transmission pattern	Vertical, every generation	Horizontal, same sibship/generation
Sex ratio	1:1	1:1
Who transmits?	Either sex	Either sex
Typical genotype of affected person	Usually heterozygote	Usually homozygote
Carriers	Often not emphasized	Common and usually unaffected
Consanguinity	Not a classic clue	Classic clue
Gene product	Often structural protein	Often enzymatic protein
Common pedigree clue	Affected person usually has an affected parent	Affected child may have unaffected carrier parents

Lecture coverage note: all 53 slides were incorporated into the sections above, with the key figures reproduced as slide images.



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