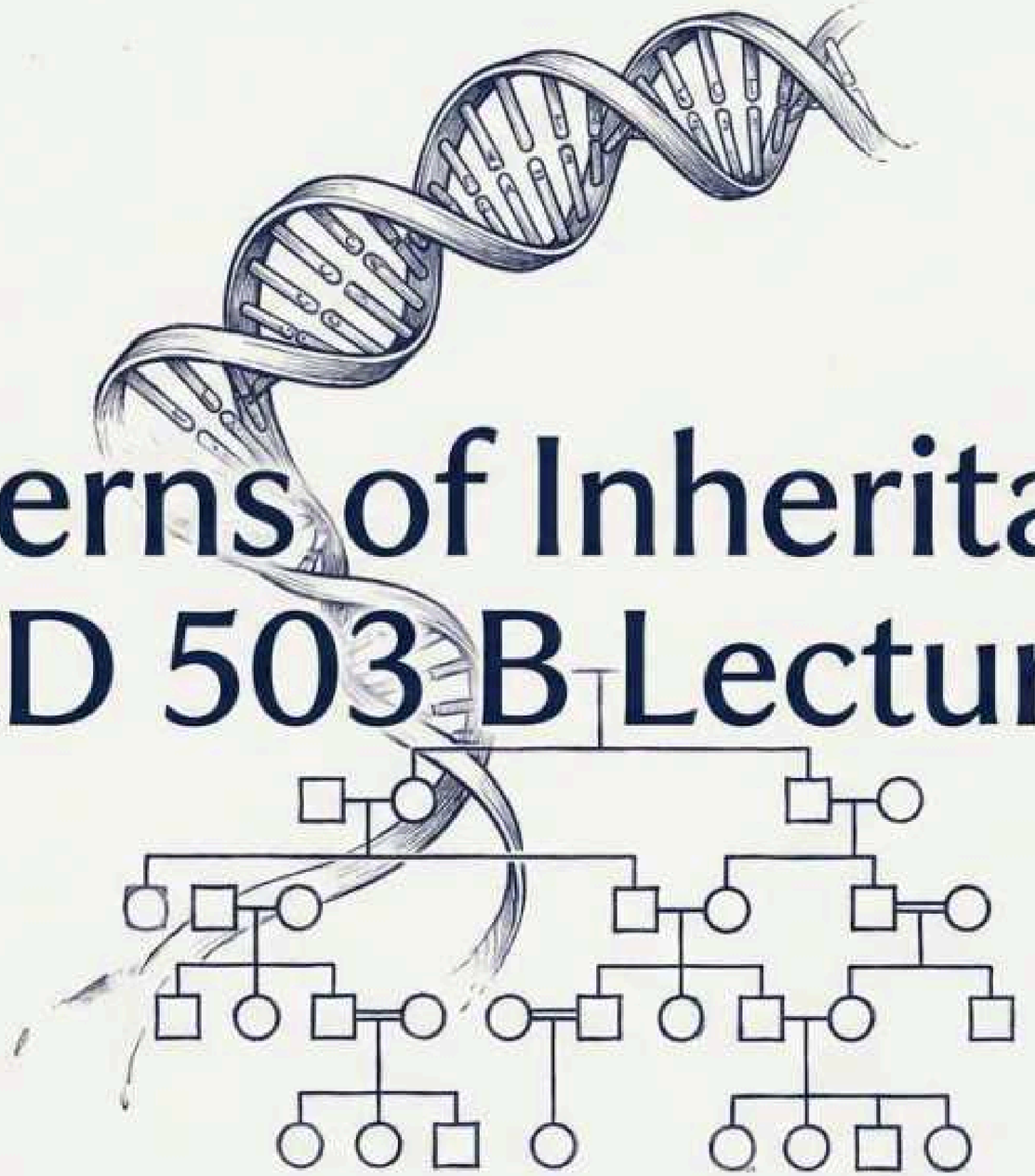


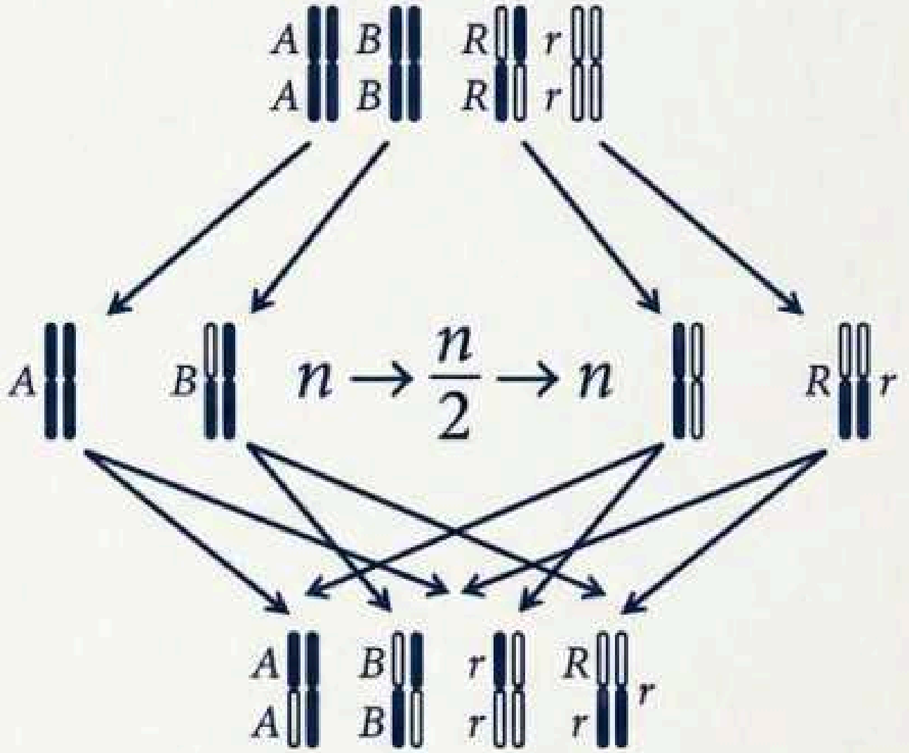
Patterns of Inheritance
MED 503 B Lecture 3

Gary Anderson, Anderson Academy | Questions: garyanderson@mail.grokbot.com | X: @garyanderson

The Backbone of Clinical Genetics



19th-century patterns remain the foundation of clinical genetics.



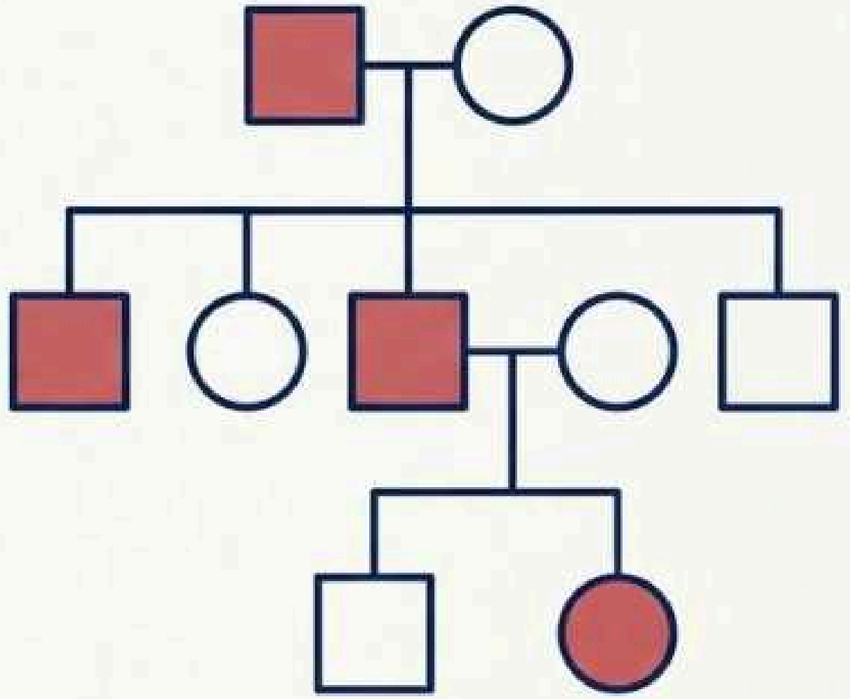
The Golden Rule:

- Two copies of each autosomal gene (one from each parent)
- Passes one copy, chosen at random, to each child

Autosomal Dominant Mechanics

	A	a
A	AA	Aa
A*	A*A	A*a

P(inheritance) = 0.5

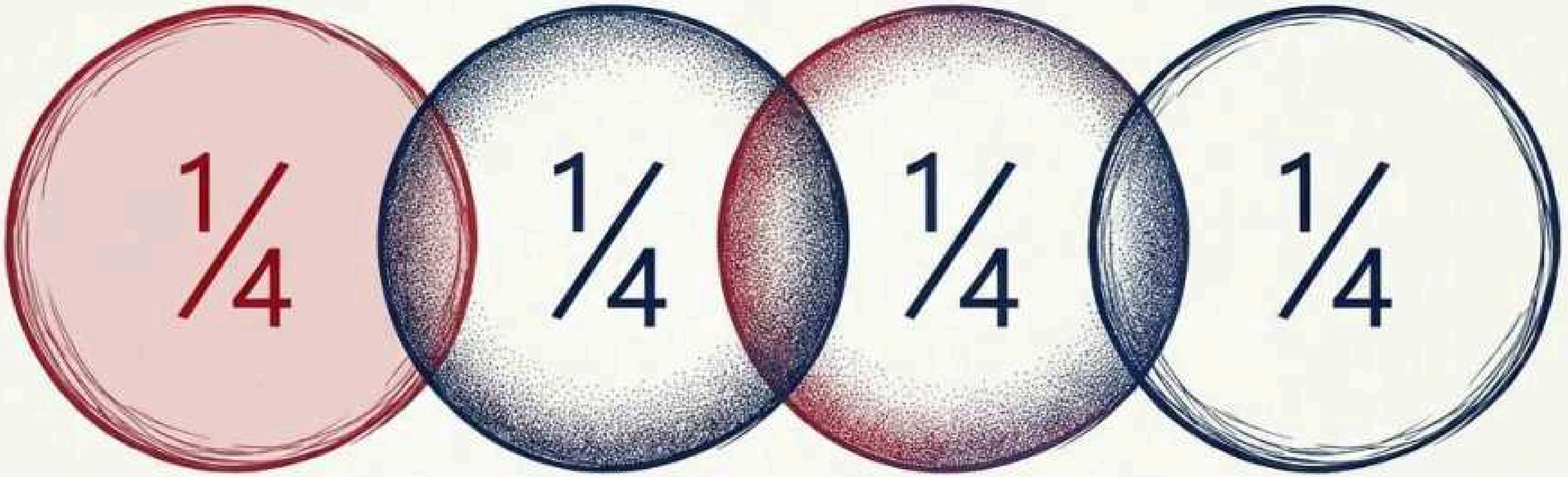


Core Rule: One altered copy is enough.

- Affected persons usually have an affected parent.
- Condition tends to appear in every generation.
- Independent of sex.

Clinical Examples: Huntington disease, Familial hypercholesterolaemia

Autosomal Recessive Mechanics



Core Rule:

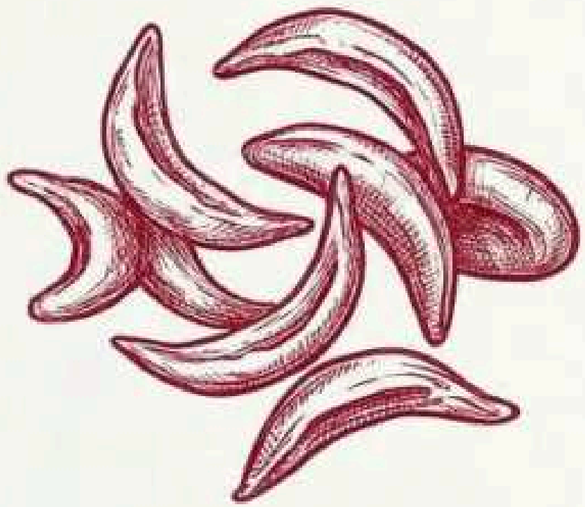
- Both copies must be altered.
- One altered copy = Carrier (healthy state).

Clinical Reality:

- Appears unexpectedly in families with zero history.
- Occurs only when two carriers reproduce together.

The Heterozygote Advantage

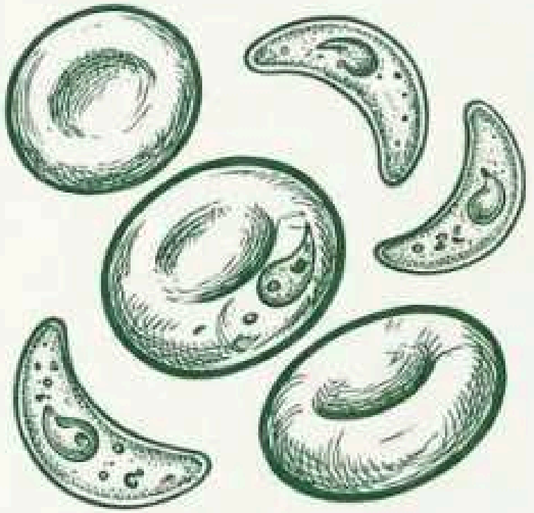
Harm in two copies



Sickle Cell Disease



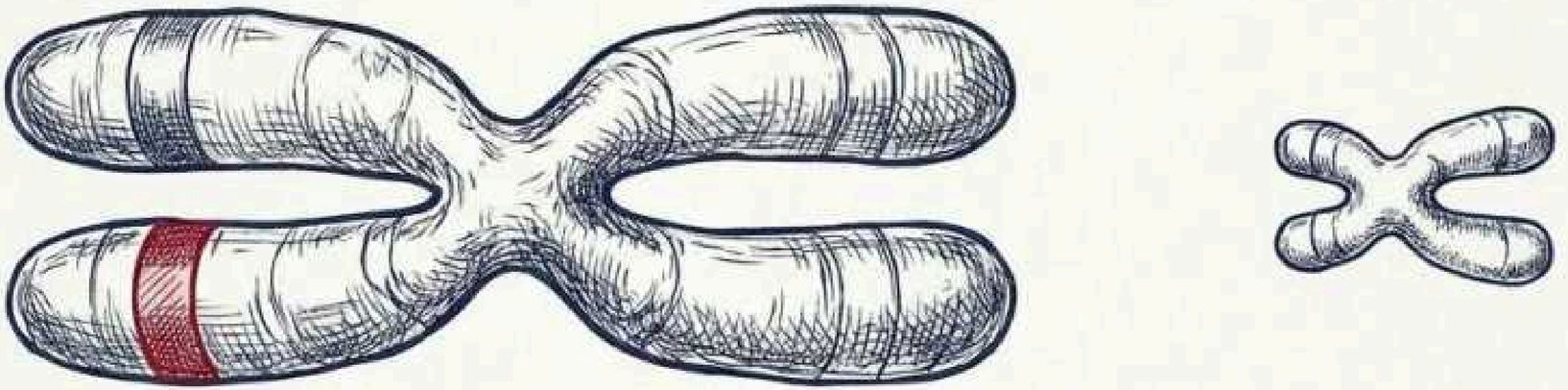
Help in one copy

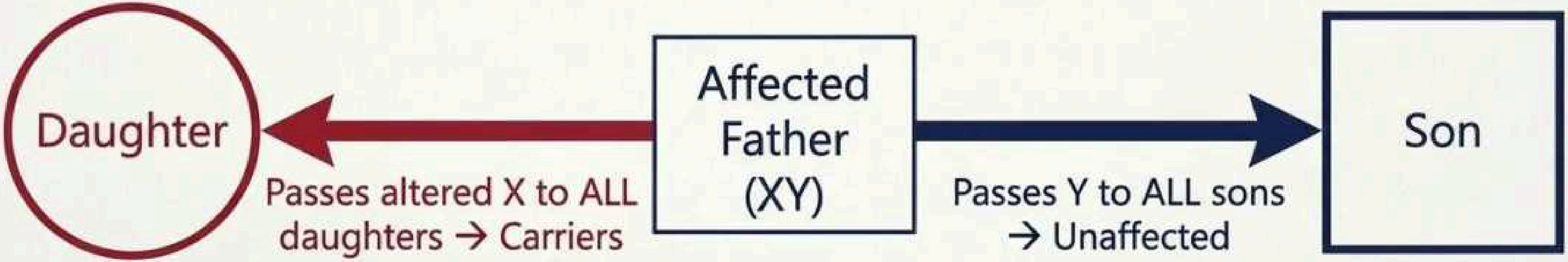


Malaria Protection

Evolutionary Insight: A variant harmful in two copies can provide protection in carriers (one copy).
Examples: Cystic fibrosis, Sickle cell disease, Phenylketonuria (PKU)

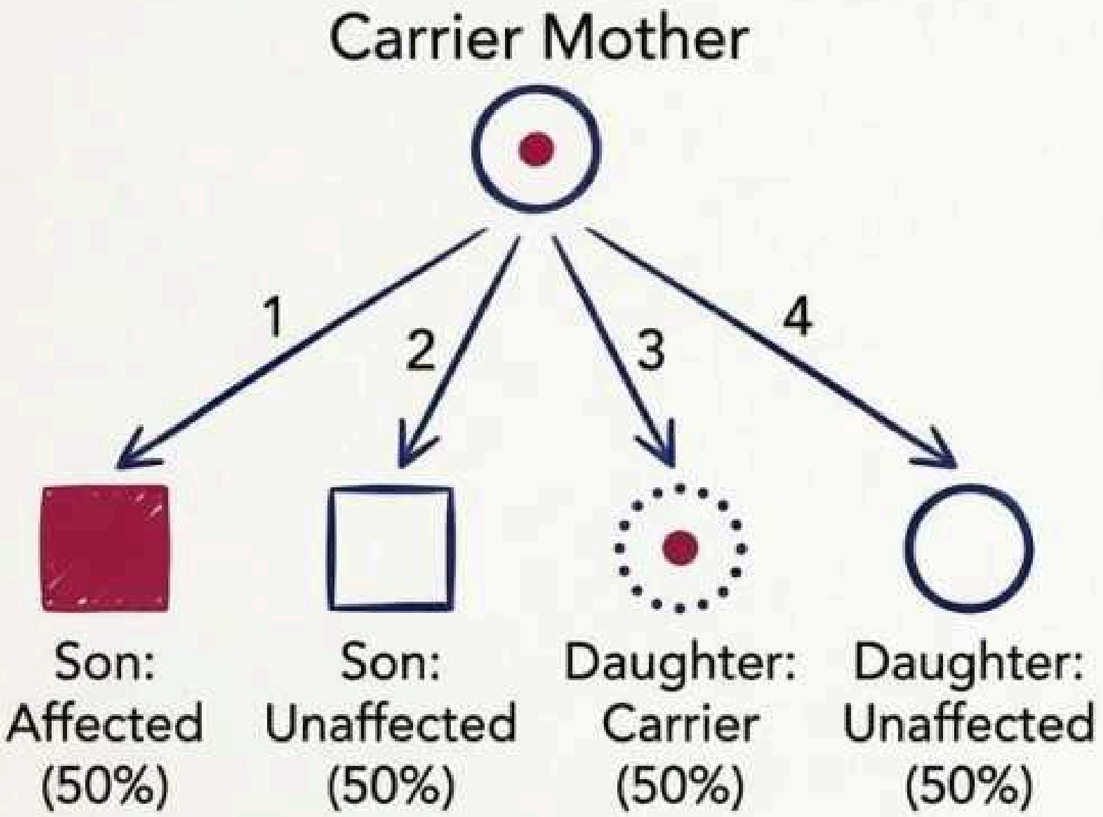
X-Linked Inheritance: The Male Vulnerability





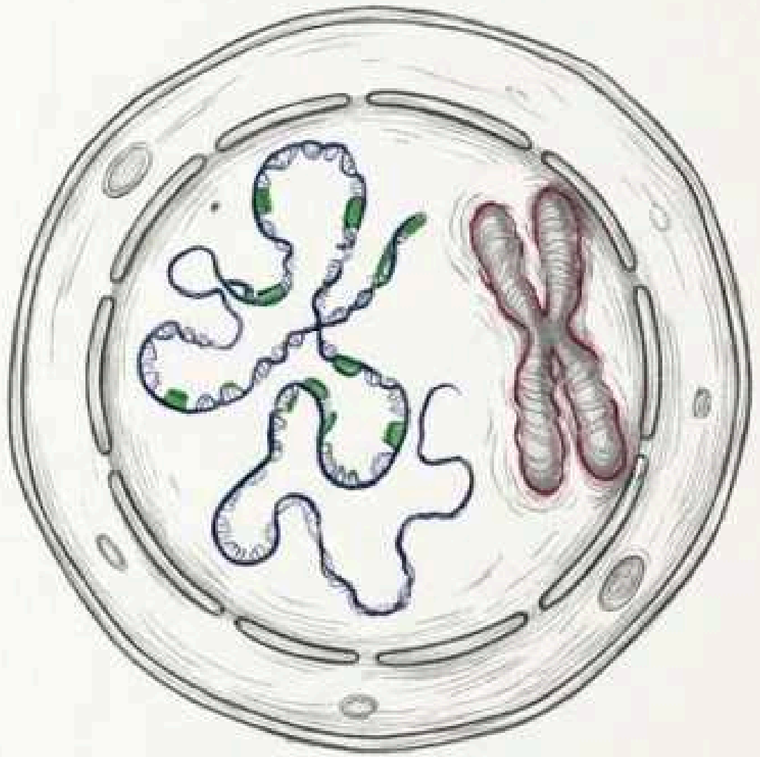
Transmission Axiom: NEVER passed from father to son.
Clinical Examples: Haemophilia, Duchenne muscular dystrophy

X-Linked Inheritance: The Maternal Line



Conditions typically affect males and appear to skip generations.

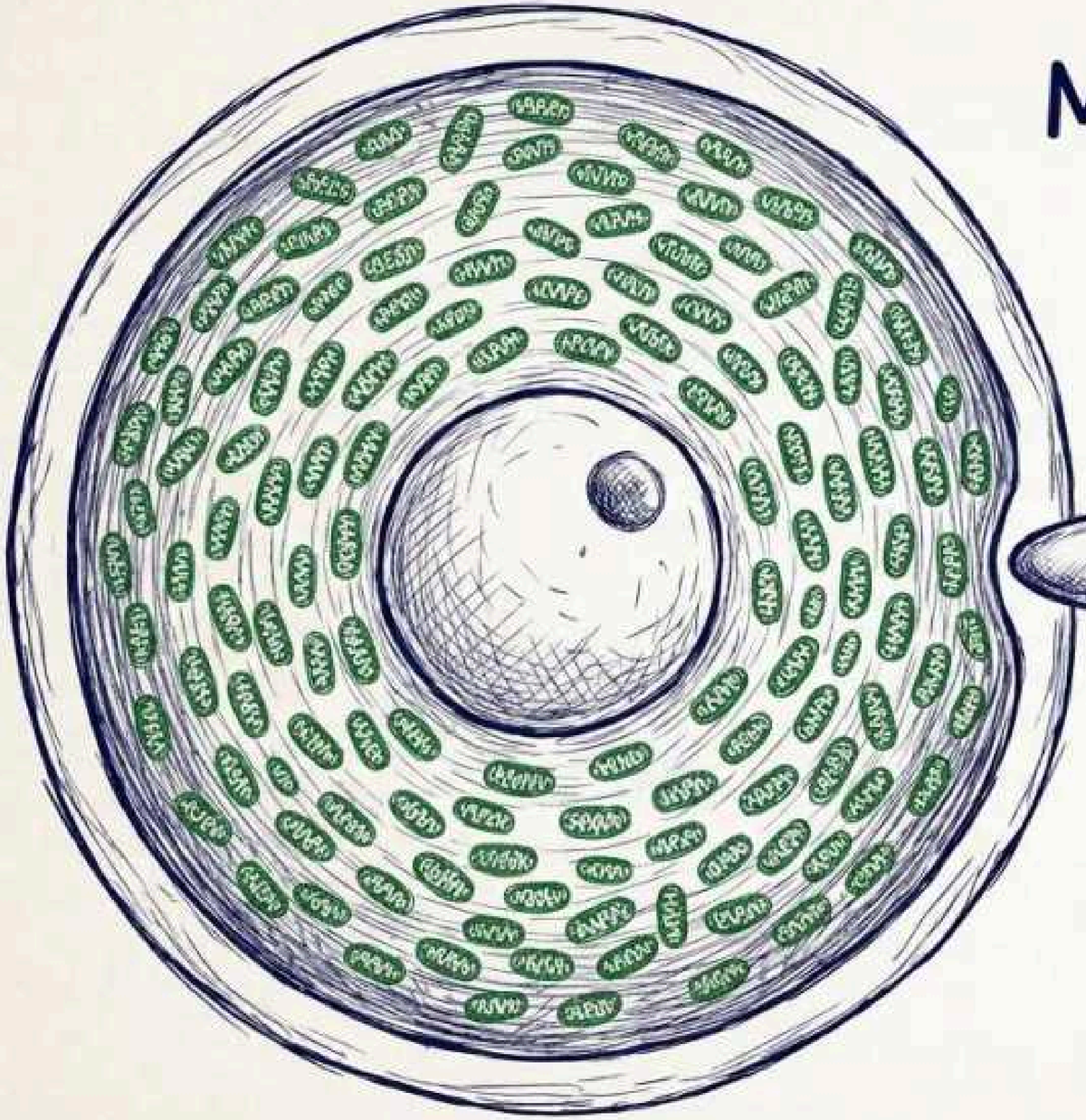
X-inactivation



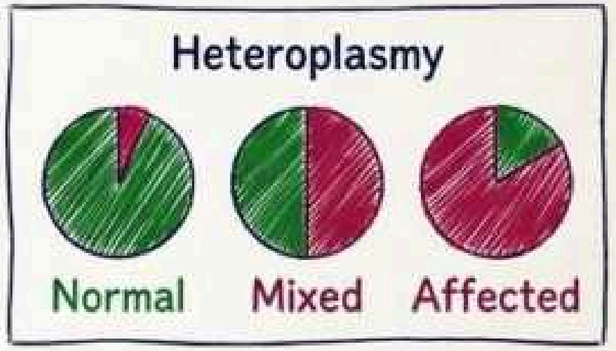
Cellular Exception: Carrier females may show mild symptoms because one X chromosome is randomly switched off per cell.

¶ 3.7

Mitochondrial Inheritance: The Maternal Engine





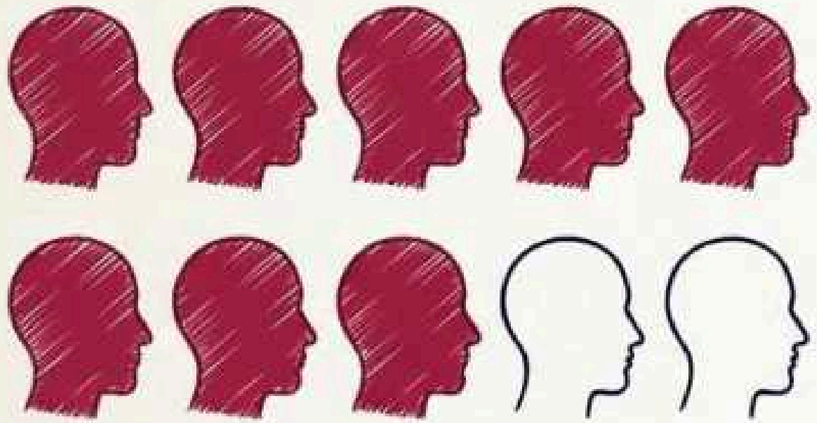


Core Rule: Passed from mother to ALL children. Affected father passes to NONE.

Variable Severity: Cells contain many copies of mitochondrial DNA. The share carrying a variant differs between tissues, explaining massive variations in severity within one family.

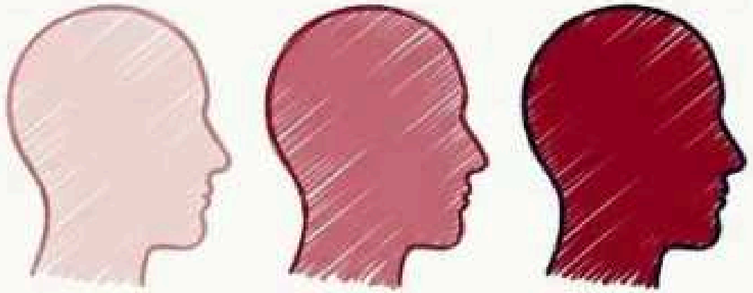
The Biological Noise

Penetrance



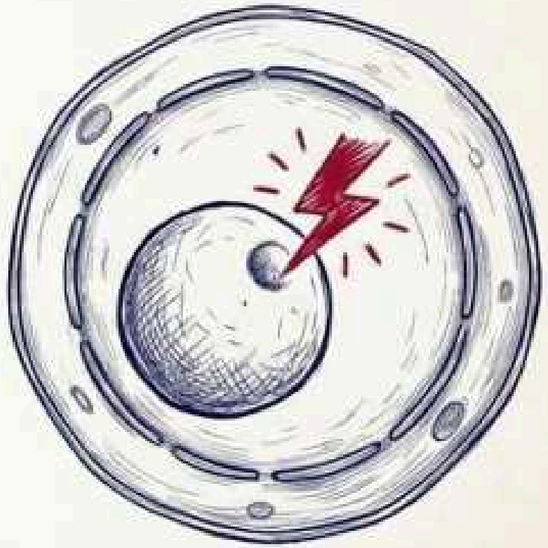
Penetrance: The proportion showing the condition at all. (Incomplete = carrying dominant variant but remaining healthy).

Variable Expressivity



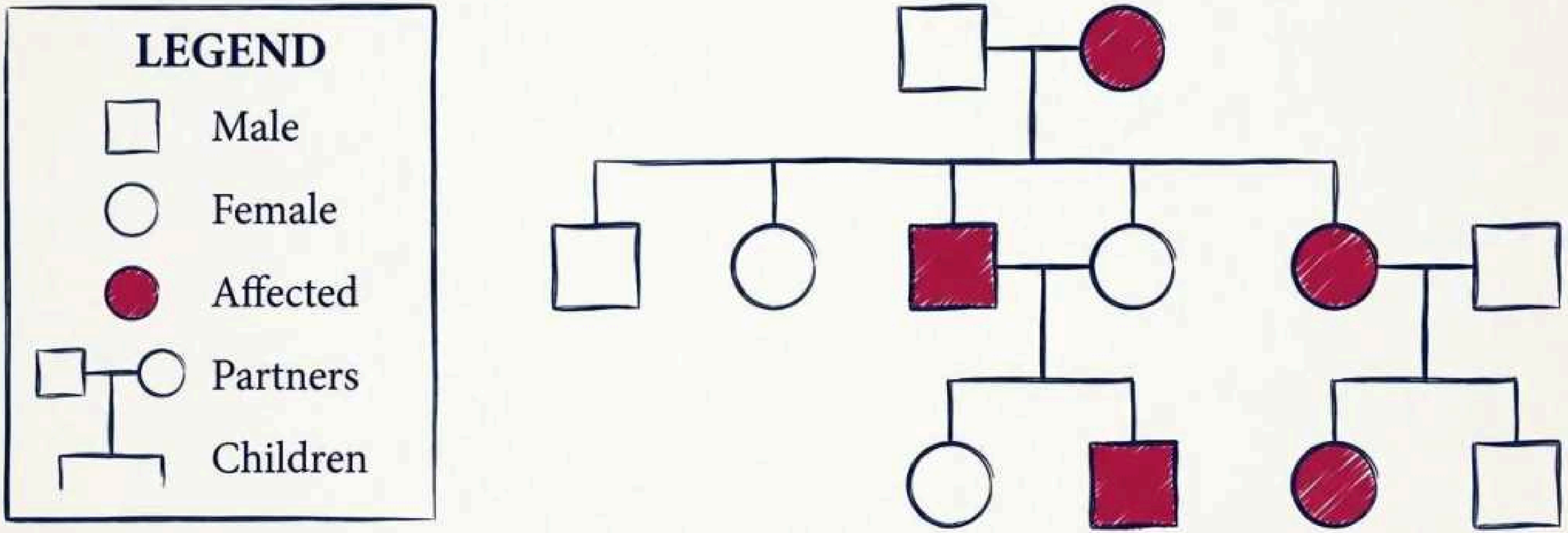
Variable Expressivity: People with the exact same variant affected to very different degrees.

De Novo Variants



De Novo Variants: Conditions appearing for the first time due to a new variant arising in the egg or sperm.

The Pedigree: The Clinician's Tool



Diagnostic Power: A careful three-generation family history is one of the most powerful tools in genetics—and it costs nothing. The visual pattern often points directly to the mode of inheritance before any laboratory test is done.

The Mathematics of Genetic Counseling

$P(\text{Child 1}) = 0.25$ $P(\text{Child 2}) = 0.25$ $P(\text{Child 3}) = 0.25$



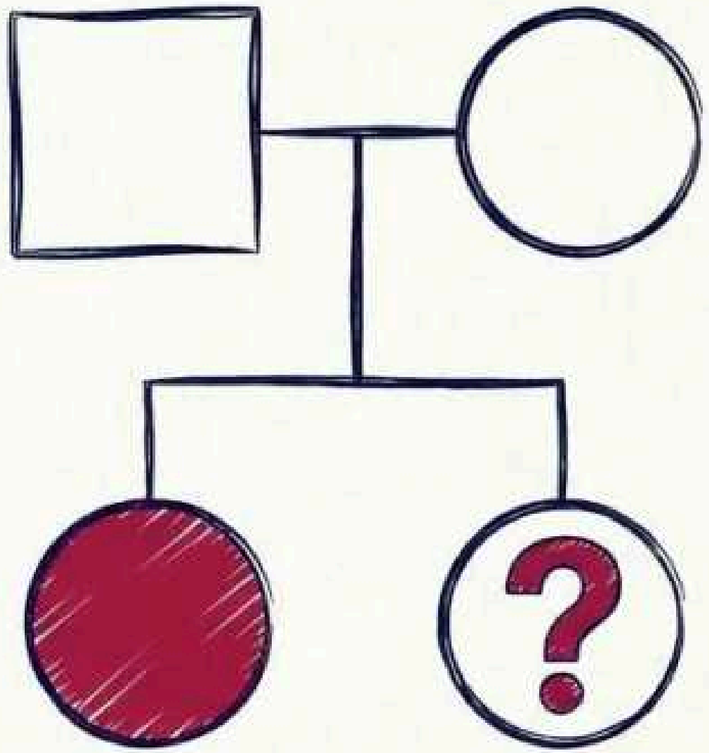
Probabilities, Not Predictions:

- Knowing the pattern allows risk estimation.
- We can calculate the chance a relative is a carrier, or a child is affected.

The Gambler's Fallacy:

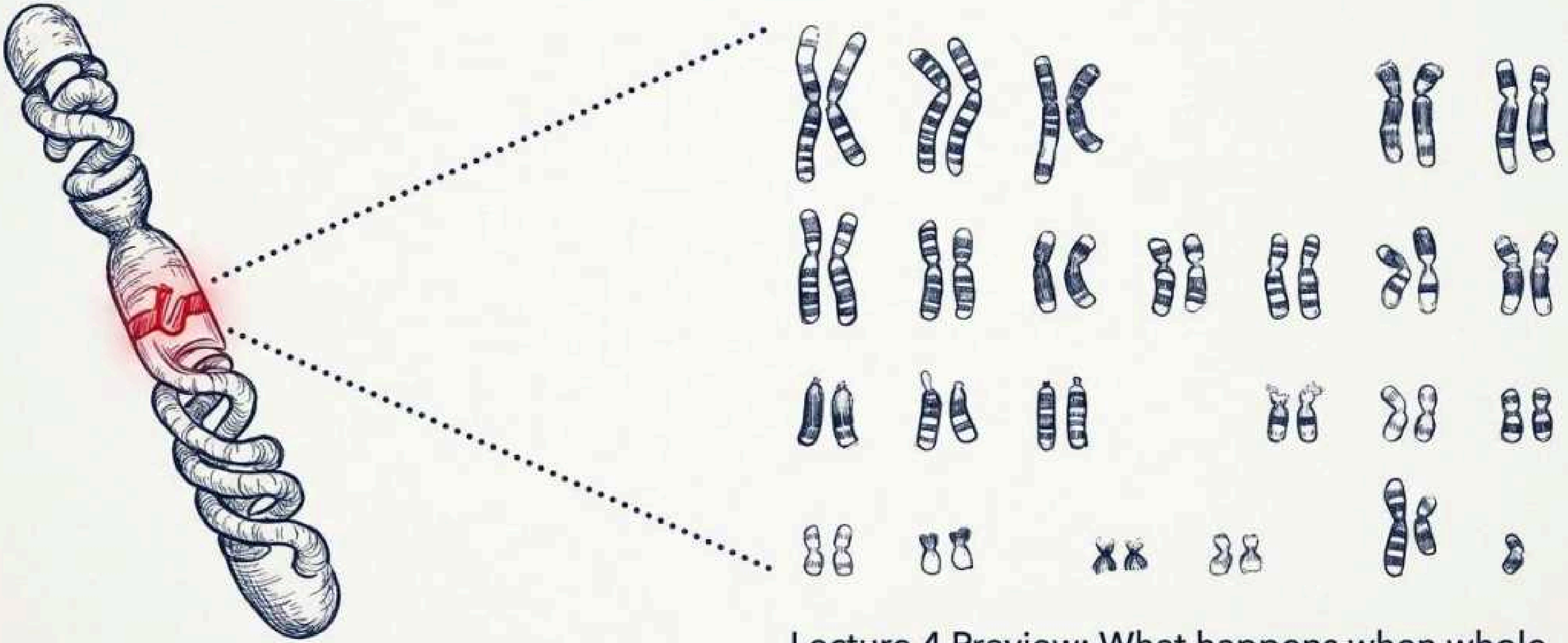
- A 1-in-4 chance applies to each pregnancy INDEPENDENTLY.
- A couple with one affected child does not have a lower chance next time.
- Explaining this kindly is the art of the profession.

Clinical Application



The Scenario: Two healthy parents have a child with an autosomal recessive condition.
Prompt 1: What can you conclude about the parents' status?
Prompt 2: What is the exact probability that their next child will be affected?

The Next Horizon



Lecture 4 Preview: What happens when whole chromosomes—rather than single genes—are affected?