The balance between the rates of synthesis and breakdown in the liver is controlled by 2 hormones:

Epinephrine/Glucagon – breakdown
Insulin – synthesis

GLYCOGEN-STORAGE DISEASES (GSDs)

- Glycogen metabolism is prone to genetic defects.
- 1929 – 1st glycogen storage disease described by Von Gierke.

TYPE	DEFECTIVE ENZYME	ORGAN AFFECTED	GLYCOGEN IN THE AFFECTED ORGAN	CLINICAL FEATURES
I Gierke's disease	G6Pase	Liver kidney	Increased amount	- Enlarged liver - Hyp. - Ketosis
II Pompe's disease (AMD)				

GSD = Glycogenosis

" Acid maltase deficiency = acid-alpha glucosidase (lysosomal)

INHERITANCE DISORDERS

1. Autosomal Recessive

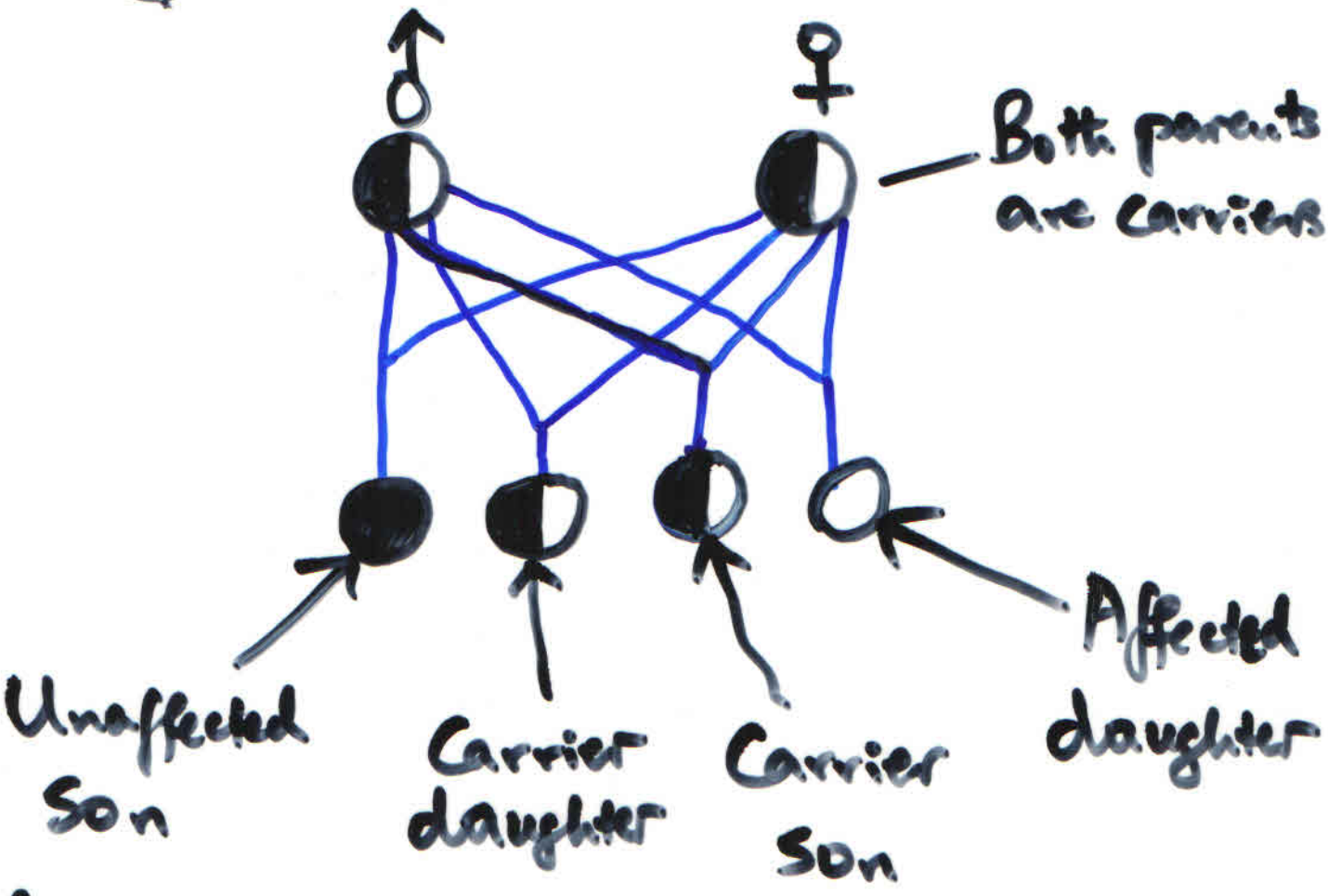
- 2 copies of an abnormal gene must be present in order for the disease or trait to develop.
- If one is born to parents who both carry an autosomal recessive change (mutation), one has a 1/4 chance of getting the "wrong" genes from both parents ⟶ disease. One has a 50% ($\frac{1}{2}$) chance of inheriting one abnormal gene.

i.e.

- If 4 children are born to a couple who both carry the gene (carriers);
  1. One child is born with two normal genes ⟶ normal child.
  2. 2 children are born with one normal and one abnormal genes (carriers).

3. One child is born with two abnormal genes → Sick child.

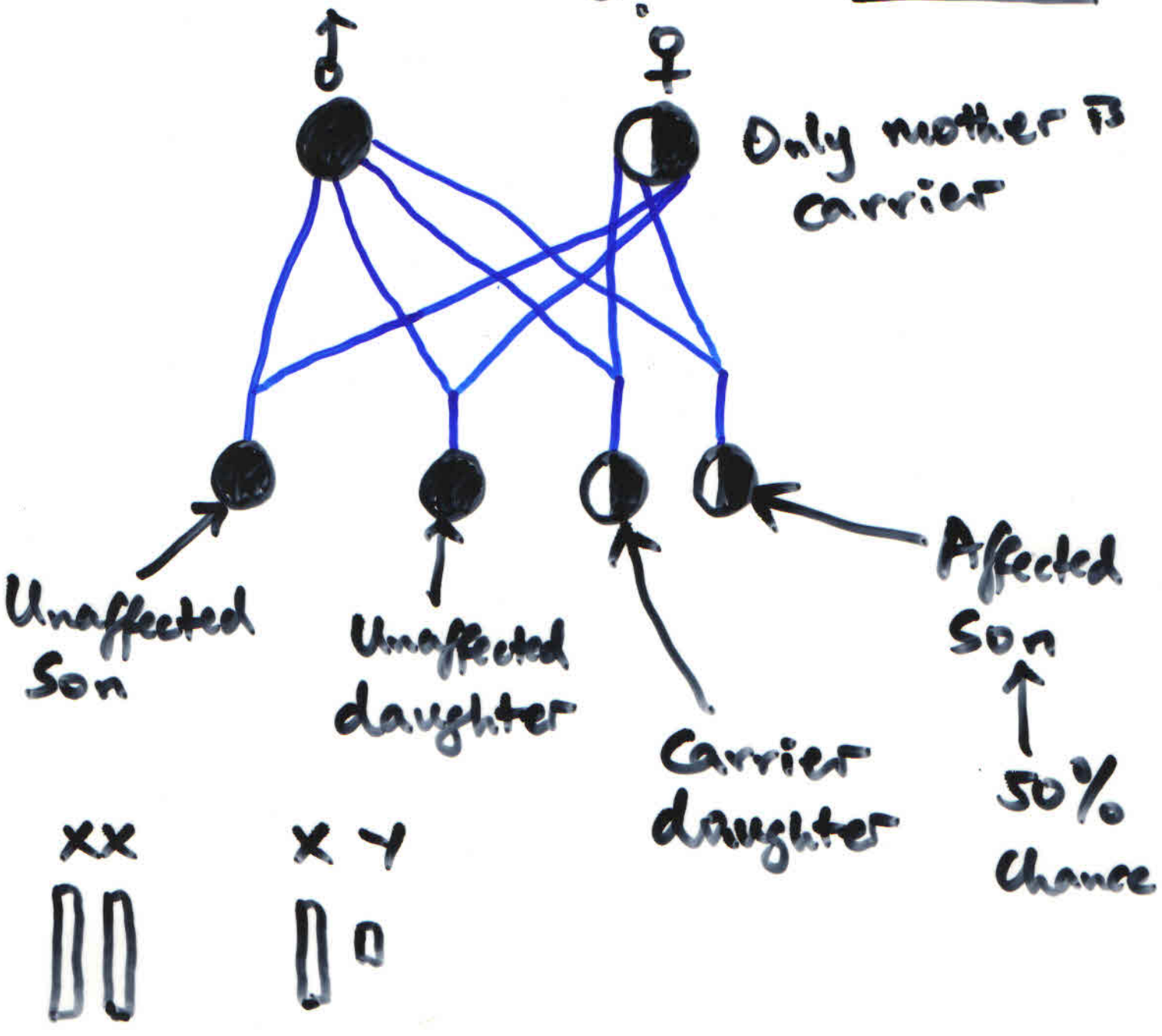
- Unaffected – $\frac{1}{4}$ chance = 25%
- Affected – $\frac{1}{4}$ chance = 25%
- Carrier – $\frac{2}{4}$ chance = 50%



NB
- Each gene is located on an autosome.
- A son or daughter has an almost equal chance of either being unaffected, affected or being a carrier.

2. X-linked Recessive

- A single gene disorder
- A genetic disease caused by a mutation on the X-chromosome.
- In X-linked recessive conditions, a normal female (carrier) passes on the mutated gene to her son.



- An X-Chromosome carries more genes than the Y chromosome.
- Males pass their X-chromosome gene(s) to their daughters and never to their sons.
- Females pass their X-chromosome to daughters and sons equally.
- An autosome is a non-sex chromosome that is the same in both sexes of a species. In humans, there are 22/23 pairs.
- Autosomal DNA is passed from both parents and controls physical traits like eye color or facial characteristics.

*- The X and Y chromosomes are not autosomal. They are sex chromosomes = Allosomes = heterosomes

GLYCOGEN STORAGE DISEASES (GSDs)

TYPE	DEFECTIVE ENZYME	ORGAN AFFECTED	GLYCOGEN IN THE AFFECTED ORGAN	CLINICAL FEATURES
I GIERKE'S	Glucose 6 – phosphatase	Liver and kidney	Increased amount	- Hepatomegaly - Severe hypoglycemia - Ketosis - Hyperlipidemia - Lactic acidosis
II POMPE'S -Infertile onset -Late onset	α 1-4 Glucosidase (lysosomal)	All organs -Heart -Muscles -Liver -Nervous system	Increased amount	- Cardiomegaly - Cardiomyopathy - Hypotonia - Cardiorespiratory stress - Cardiorespiratory failure. Death before age 2
III CORI'S/FORBE'S (GSD III a-d)	α 1-6 glucosidase (Debranching enzyme)	Muscle and Liver	-Increased amount -Short outer branches	- Like Type I but milder - Like type II but milder -
IV ANDERSEN'S	Glucosyl (4 → 6) transferase (Branching enzyme)	Liver and Spleen	Normal amount but very long outer branches	- Hepatomegaly - Splenomegaly - Cirrhosis - Hypotonia - Death before age 5

V McARDLE'S	Glycogen Phosphorylase	Muscle	Moderately increased amount	- Exercise intolerance - Painful cramps - Early fatigue - Myoglobinuria - Rhambomyolysis
VI HERS'	Glycogen Phosphorylase	Liver	Increased amount	- Like type I but milder
VII TARUI'S	PFK	Muscle RBC	Increased amount	- Like type V but more severe - Death before age 5 - Affects Glycolysis
VIII Related to VI (X-linked) Affects male only	Phosphorylase Kinase b	Liver	Increased Amount	- Mild hepatomegaly - Mild hypoglycemia
IX Related to VI and VIII	Phosphorylase Kinase a	Liver	Increased amount	- Like Type VI and VIII
X Related to VI, VIII and IX	Protein Kinase A	Liver	Increased amount	- Like type VI, VIII and IX
O	Glycogen synthase	Liver	Decreased amount	- Hypoglycemia when fasting - Drowsiness - Vomiting - Convulsions - Tired/fatigued - Muscle cramping