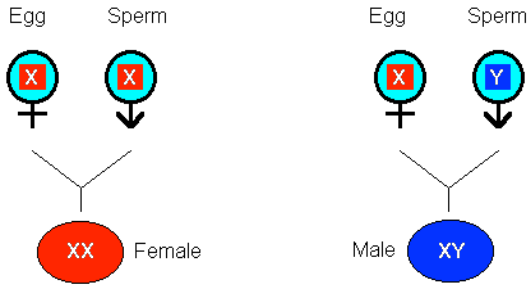
Sex Determination

Sex chromosomes determine the sex of an organism. A human somatic cell has two sex chromosomes: XY in male and XX in female. A human germ cell has one sex chromosome: X or Y in a sperm and X in an egg. When an X-sperm is combined with an egg, the resulting **zygote** (fertilized egg) will contain two X chromosomes. A person developed from the XX-zygote will have the characteristics of a female. Combination of a Y-sperm and an egg will produce a male.



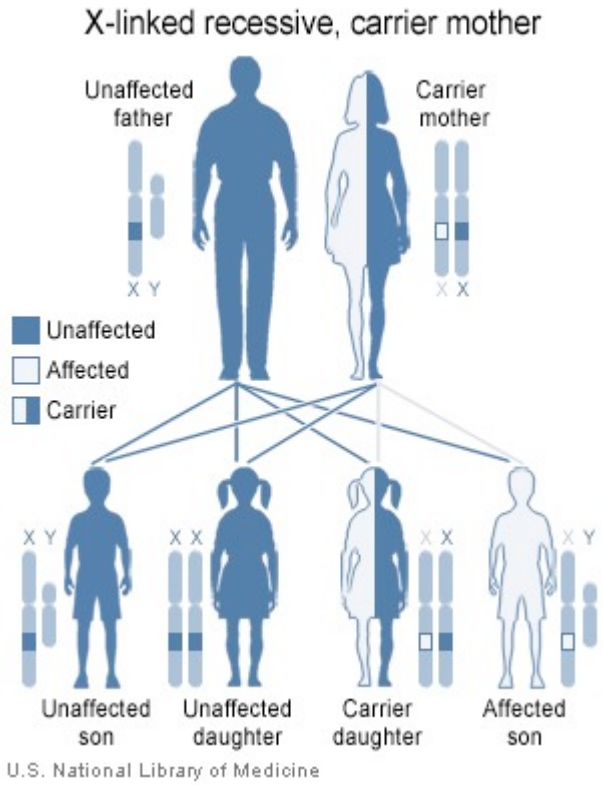
Probability of Determining Sex is quite simple.

From the table on the right, there is a 50/50 chance of getting a male or female. The X or Y chromosomes in the male are the chromosomes found in the sperm cell while the X and X chromosomes are found in the egg cells. The randomization will give rise to the sex of the offspring if there are no mutations (Turner's syndrome XO, Kleinfelter XXY)

Male → / Female ↓	X	Y
X	XX	XY
X	XX	XY

X- linked diseases

X-linked diseases are single gene disorders that reflect the presence of defective genes on the X chromosome. This chromosome is present as two copies in females but only as one copy in males. The inheritance patterns of X-linked diseases in family pedigrees are complicated by the fact that males always pass their X chromosome to their daughters but never to their sons, whereas females pass their X chromosomes to daughters and sons with equal. Like autosomal single gene disorders, X-linked diseases can be either recessive or dominant. X-linked recessive diseases include red-green colour blindness, haemophilia and the Duchenne and Becker forms of muscular dystrophy (both of which involve mutations in the DMD gene). These diseases are much more common in males than females because two copies of the mutant allele are required for the disease to occur in females, while only one copy is required in males.



Hemophilia

Hemophilia is a bleeding disorder that affects the factors that help your blood clot. Hemophilia A is an X-linked disorder that affects about 1 in every 10 000 males. When we compare that statistic to females, females' chances of being hemophilic are 1 in 100 million. The reason for this is that hemophilia is an X-linked disorder that affects the X chromosome. Males can inherit the allele for hemophilia on the X chromosome if their mothers are carriers (they have the allele but don't express the alleles themselves). You only need one recessive allele to cause hemophilia in males, while you need both recessive alleles to cause hemophilia in females.

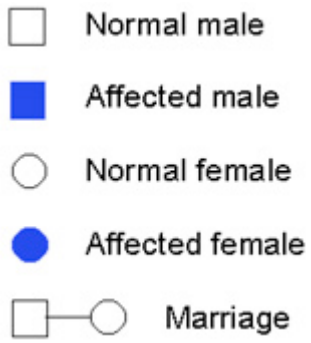
X^h – denotes hemophilia recessive gene.

Male → / Female ↓	X^h	Y
X	**XX^h**	XY
X	**XX^h**	XY

You can see from the table (left) that the females will become "carriers" of the gene. However, if the female becomes a carrier and mates with an unaffected father, you can see the chances from the Punnett Square below:

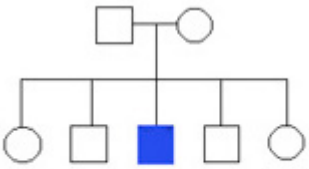
Male → / Female ↓	X	Y
X^h	X^h X	**X^h Y**
X	X^h X	**XY**

There is a 50% chance that their son will be affected by the gene since the X^h will be expressed even when it's paired up with Y. However, as for the females, they will not be affected but will become carriers of the gene.



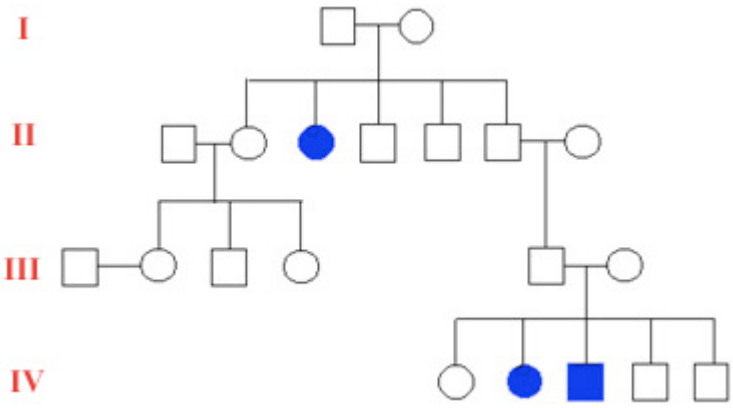
Pedigree Chart

In the royal families of Europe, the famous genetic pedigree depicts how the sex-linked hemophilia allele is introduced to the entire family. Please refer to hand out.



Eldest child ↔ Youngest child

A pedigree chart shows a record of the family of an individual. It can be used to study the transmission of a hereditary condition. It is particularly useful when there are large families and a good family record over several generations.



Left is a pedigree chart of a family showing four generations. A total of 20 individuals.

Generations are identified by Roman numerals. Individuals in each generation are identified by Arabic numerals numbered from the left. Therefore the affected individuals are **II3**, **IV2** and **IV3**.

Colour Blindness

Colour blindness is another recessive X-linked disorder that is due to an abnormal gene on the X chromosome. The inherited abnormality in Caucasian populations is about 8% of the males and 0.4% of females. Colour blindness is present in males if the X chromosome has the abnormal gene, while females only show a defect when both of the X chromosomes contain the abnormal gene. However, female children of a man with X – linked colour blindness are carriers of the colour blindness and pass the defect on to half of their sons, similar to the example above. Therefore, X-linked colour blindness skips generations and appears in males of every second generation.

Male → / Female ↓	X	Y
X^c	X^c X	X^c **Y**
X	X^c X	**XY**

X-linked disorder summary

- The vast majority of affected individuals are male.
- Affected males never pass the disease to their sons because there is no male-to-male transmission of the X chromosome.
- Affected males pass the defective X chromosome to all of their daughters, who are described as obligate carriers. This means they carry the disease-causing allele but generally show no disease symptoms since a functional copy of the gene is present on the other chromosome.
- Female carriers pass the defective X chromosome to half their sons (who are affected by the disease) and half their daughters (who are therefore also carriers). The other children inherit the normal copy of the chromosome.
- The overall pattern of the disease is therefore characterized by the transmission of the disease from affected males to male grandchildren through carrier daughters.
- Affected females, with two deficient X chromosomes, are the rare products of a marriage between an affected male and a carrier female. However, manifesting carrier females (with one deficient X chromosome and one normal one) may arise if there is a chromosome disorder or a problem with X-chromosome inactivation.

Test your Understanding

Questions:

1. What are the chromosomes found in males?
2. Draw a Punnett Square for the probability in finding the sex of an offspring.
3. What are X-linked disorders?
4. Who determines the gender in humans? Explain
5. What are autosomes?
6. How come X-linked disorders are never passed onto the sons by their father? Explain
7. List three recessive X-linked disorders and explain what they are.
8. Why are these recessive x-linked disorders more common in males than females? Explain
9. If you have a carrier mother for hemophilia and a non carrier father, what are the chances of their daughters getting the disorder? What about their sons?
10. If a daughter is a carrier for hemophilia, what are the possible genotypes for her parents?
11. John and Jessica sought genetic counseling since Jessica's brother and maternal uncle both have hemophilia. Her family does not live in Canada. John has never met them and is not familiar with the blood disorder. Draw a Pedigree Chart to show that Jessica's mother must be a carrier.