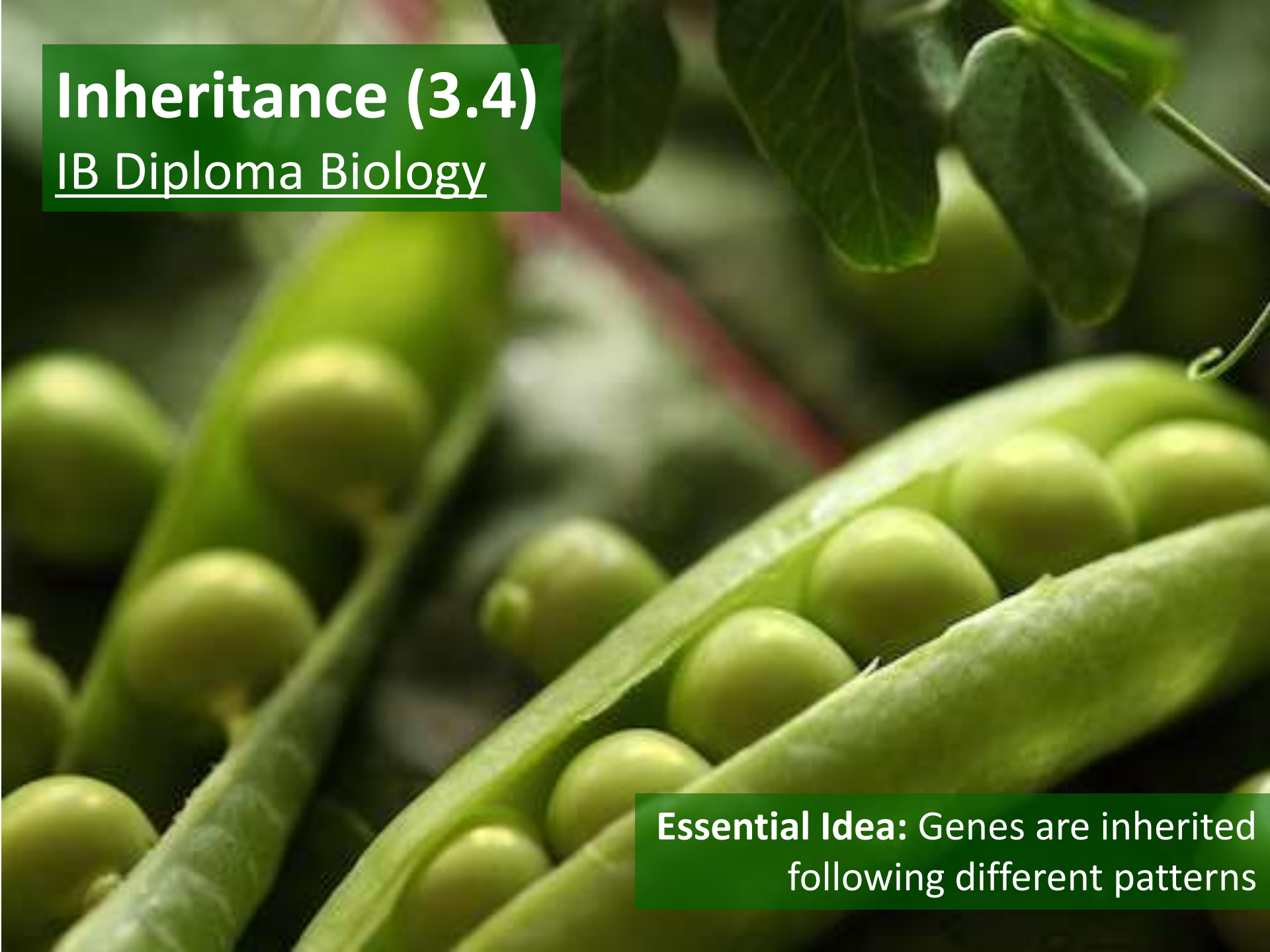
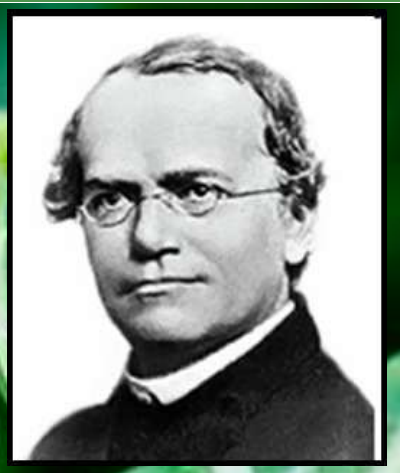
Inheritance (3.4)

IB Diploma Biology



Essential Idea: Genes are inherited following different patterns

3.4.1 Mendel discovered the principles of inheritance with experiments in which large numbers of pea plants were crossed.



Offspring inherit many traits from their parents, but the specific details of inheritance eluded scientists for centuries:

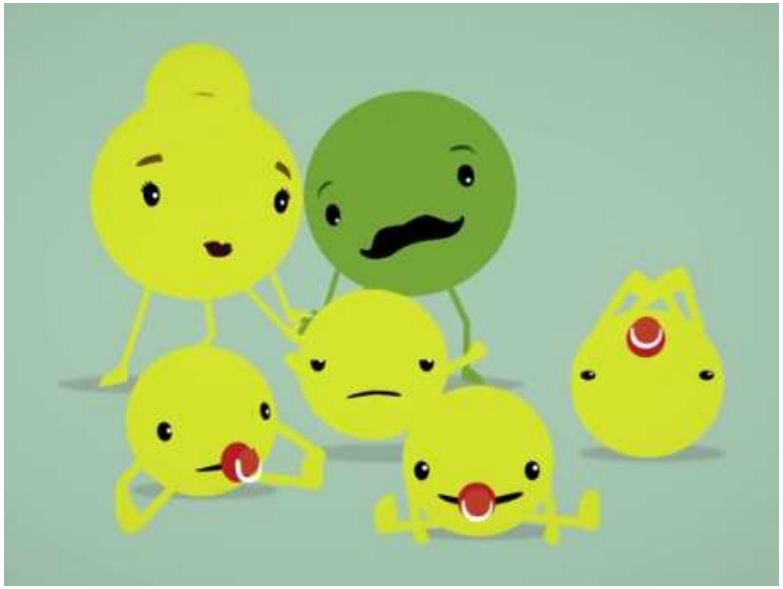
- Early theories assumed a simple blending of traits of the two parents…
- **Aristotle** noticed that offspring sometimes looked more like one parent than the other – sometimes even more like a grandparent
- In 1866, **Gregor Mendel** published his pea plant cross-breeding experiments that showed traits being inherited in specific patterns
- His work was largely ignored until the early 1900s when it was rediscovered, replicated, and became the foundation for modern genetics

3.4.1 Mendel discovered the principles of inheritance with experiments in which large numbers of pea plants were crossed.

Hybrid Parent Plant Cross	Offspring Phenotypes	Ratio
Tall stem x Dwarf stem	787 Tall : 277 Dwarf	2.84 : 1
Round seed x Wrinkled seed	5474 Round : 1850 Wrinkled	2.96 : 1
Yellow peas x Green peas	6022 Yellow : 2001 Green	3.01 : 1
Purple flowers x White flowers	705 Purple : 224 White	3.15 : 1

Mendel noticed that certain versions of a trait, such as tall height, round seeds, yellow color, and purple flowers would always show-up in a cross with a purebred plant – **He called these DOMINANT versions of the gene, or ALLELE**

Other versions of the trait only showed up in hybrid crosses or when the 'dominant trait' was not present in either parent – **He called these the RECESSIVE alleles**

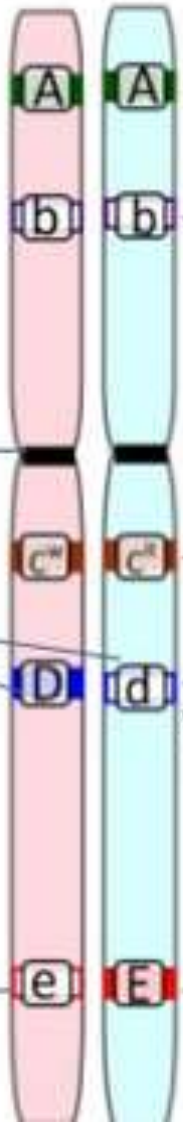


http://ed.ted.com/lessons/how-mendel-s-pea-plants-helped-us-understand-genetics-hortensia-jimenez-diaz

3.4.1 Mendel discovered the principles of inheritance with experiments in which large numbers of pea plants were crossed.

Definitions

This image shows a pair of homologous chromosomes.
Name and annotate the labeled features.



Genotype
*The **combination of alleles** of a gene carried by an organism*

Phenotype
*The **expression of alleles** of a gene carried by an organism*

Centromere
Joins chromatids in cell division

Alleles
***Different versions** of a gene*
Dominant alleles = capital letter
Recessive alleles = lower-case letter

Carrier
*Heterozygous carrier of a **recessive disease-causing** allele*

Homozygous dominant
Having two copies of the same dominant allele

Homozygous recessive
Having two copies of the same recessive allele. Recessive alleles are only expressed when homozygous.

Codominant
Pairs of alleles which are both expressed when present.

Heterozygous
Having two different alleles. The dominant allele is expressed.

Gene loci
Specific positions of genes on a chromosome

3.4.2 Gametes are haploid so contain one allele of each gene / 3.4.4 Fusion of gametes results in diploid zygotes with two alleles of each gene that may be the same allele or different alleles

Gametes are **haploid** and contain one copy of each chromosome – and therefore one allele of each gene:

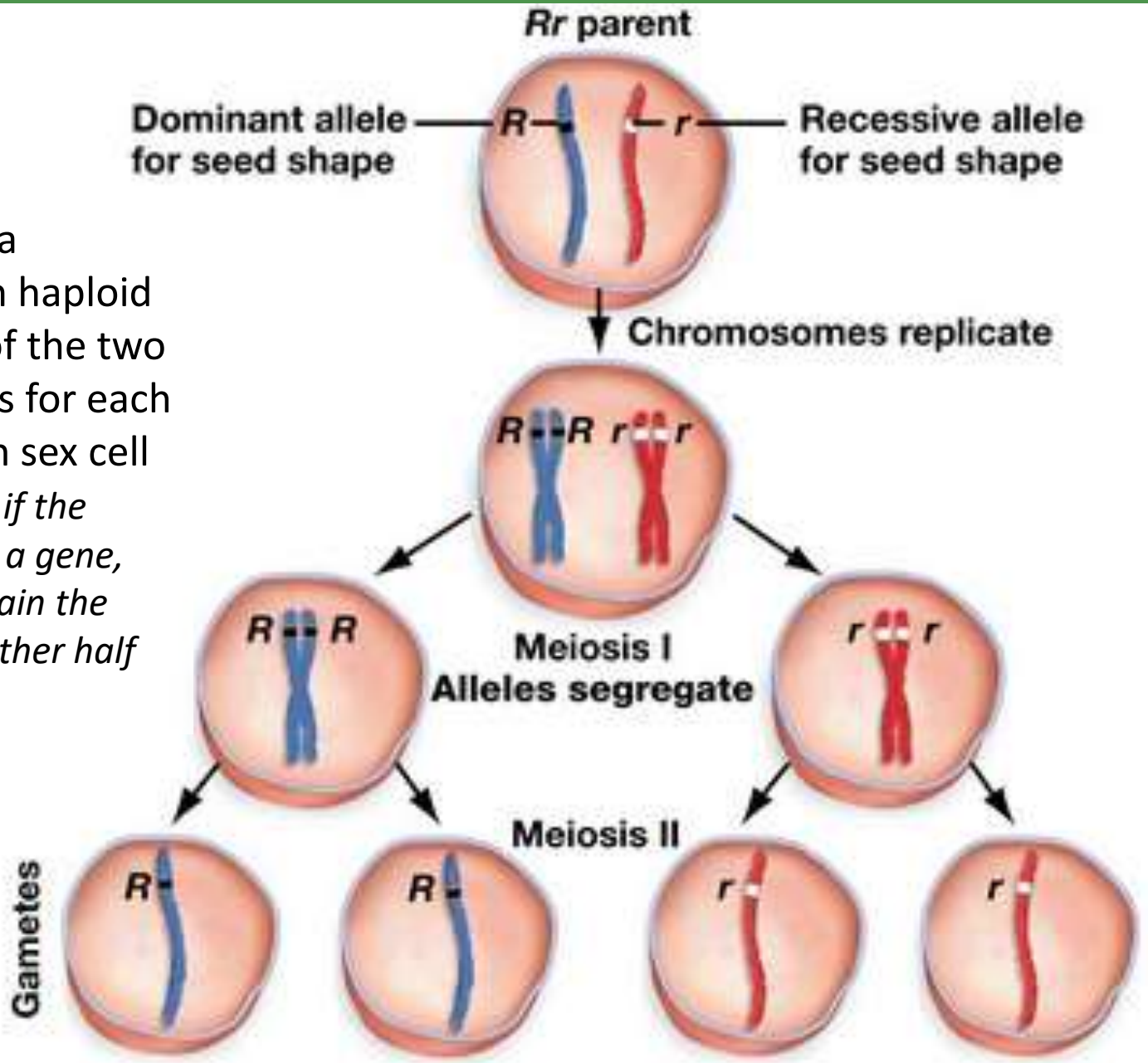
When the male and female gametes fuse in **fertilization**, the resultant diploid cell – called the **Zygote** – will have *two* alleles of each gene, one from each parent

Many genes have *two* alleles, as Mendel observed – often one is dominant, one recessive, producing three possible **genotypes**:

- **AA** = Homozygous Dominant (dominant phenotype)
- **Aa** = Heterozygous (dominant phenotype)
- **aa** = Homozygous Recessive (recessive phenotype)

3.4.3 The two alleles of each gene separate into different haploid daughter nuclei during meiosis

Since **Meiosis** involves a *reduction division*, each haploid gamete gets only one of the two alleles that a parent has for each gene. Which allele each sex cell receives is ***random*** (*i.e. if the father is heterozygous for a gene, half of his sperm will contain the dominant allele and the other half will have the recessive*)



3.4.5 Dominant alleles mask the effects of recessive alleles but co-dominant alleles have joint effects

Dominant alleles always show their encoded trait, when present in an organism (they mask recessive alleles)

Recessive alleles only express their encoded traits when no other alleles are present

- *Dominant alleles code for functional proteins, while recessive alleles code for non-functional proteins*

Codominant alleles can have joint effects if both are present*

*Patterns of inheritance, like Codominance, that do not follow Mendel's observations are called **Non-Mendelian** inheritance patterns.

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Segregation

"alleles of each gene separate into different gametes when the individual produces gametes"

F_0

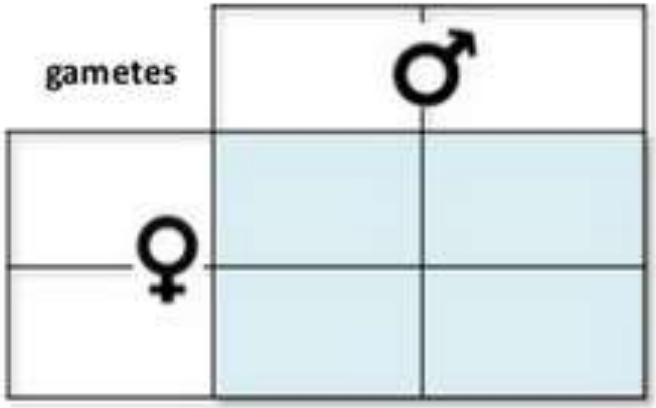
♀ X crossed with ♂

Genotype: Y y × Y y

Gametes: Y or y × Y or y

*Alleles **segregate** during **meiosis** (anaphase I) and end up in different haploid gametes.*

Punnet Grid:



F_1

Genotypes:

Phenotypes:

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

Crossing a single trait.

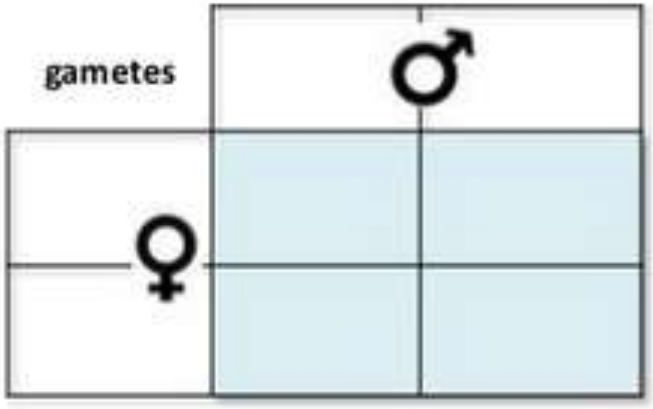
F_0

♀ X crossed with ♂

Genotype: Y y × Y y

Gametes: Y or y × Y or y

Punnet Grid:



*Alleles **segregate** during **meiosis** (anaphase I) and end up in different haploid gametes.*

Fertilisation results in diploid zygotes.

A punnet grid can be used to deduce the potential outcomes of the cross and to calculate the expected ratio of phenotypes in the next generation (F_1).

F_1

Genotypes:

Phenotypes:

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

Crossing a single trait.

F_0

♀ X crossed with ♂

Genotype: Y y × Y y

Gametes: Y or y × Y or y

Punnet Grid:

gametes	Y ♂	y
Y ♀	YY	Yy
y	Yy	yy

*Alleles **segregate** during **meiosis** (anaphase I) and end up in different haploid gametes.*

Fertilisation results in diploid zygotes.

*A **punnet grid** can be used to deduce the potential outcomes of the cross and to calculate the expected **ratio of phenotypes** in the next generation (F_1).*

F_1

Genotypes:

Phenotypes:

Phenotype ratio:

Mendel from: http://history.nih.gov/exhibits/nirenberg/popup_htm/01_mendel.htm

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

Crossing a single trait.

F_0

♀ X crossed with ♂

Genotype: Y y × Y y

Gametes: Y or y × Y or y

Punnet Grid:

gametes	Y ♂	y
Y ♀	YY	Yy
y	Yy	yy

*Alleles **segregate** during **meiosis** (anaphase I) and end up in different haploid gametes.*

Fertilisation results in diploid zygotes.

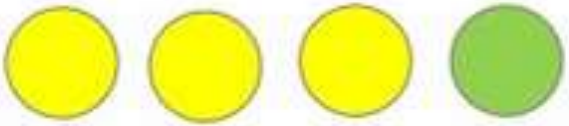
*A **punnet grid** can be used to deduce the potential outcomes of the cross and to calculate the expected **ratio of phenotypes** in the next generation (F_1).*

Ratios are written in the simplest mathematical form.

F_1

Genotypes: YY Yy Yy yy

Phenotypes:



Phenotype ratio: **3 : 1**

Mendel from: http://history.nih.gov/exhibits/nirenberg/popup_htm/01_mendel.htm

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

What is the expected ratio of phenotypes in this monohybrid cross?

F_0

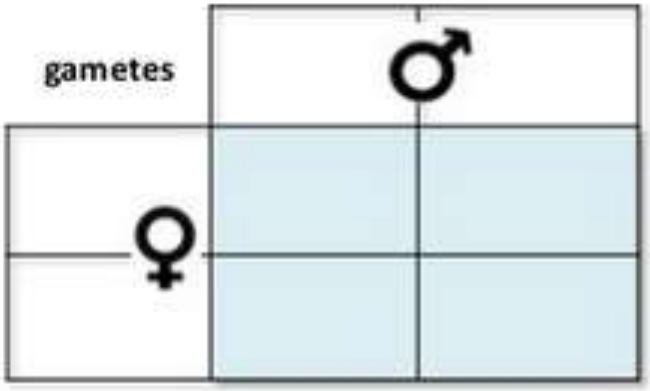
Phenotype: ♀ ○ X crossed with ○ ♂

Genotype:

Homozygous recessive *Homozygous recessive*

Key to alleles:
Y = yellow
y = green

Punnet Grid:



F_1

Genotypes:

Phenotypes: ○ ○ ○ ○

Phenotype ratio:

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

What is the expected ratio of phenotypes in this monohybrid cross?

F_0

Phenotype: ♀  X crossed with  ♂

Genotype: **y y** X **y y**

Homozygous recessive X *Homozygous recessive*

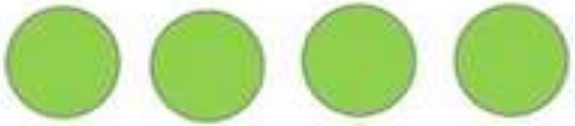
Key to alleles:
Y = yellow
y = green

Punnet Grid:

gametes	y ♂	y
y ♀	yy	yy
y	yy	yy

F_1

Genotypes: yy yy yy yy

Phenotypes: 

Phenotype ratio: **All green**

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

What is the expected ratio of phenotypes in this monohybrid cross?

F_0

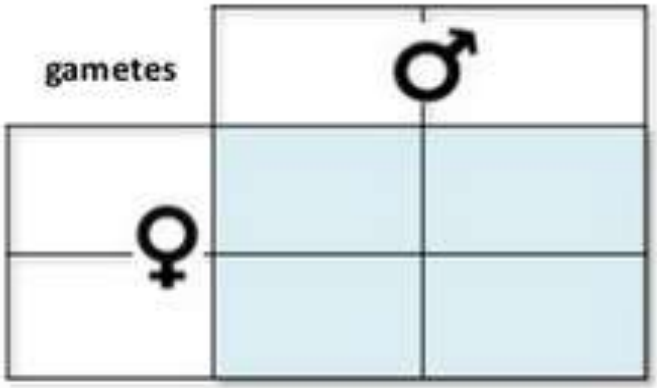
Phenotype: ♀ ○ X crossed with ○ ♂

Genotype:

Homozygous recessive *Heterozygous*

Key to alleles:
Y = yellow
y = green

Punnet Grid:



F_1

Genotypes:

Phenotypes: ○ ○ ○ ○

Phenotype ratio:

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Monohybrid Cross

What is the expected ratio of phenotypes in this monohybrid cross?

F_0

Phenotype: ♀  X crossed with  ♂

Genotype: **y y** X **Y y**

Homozygous recessive X *Heterozygous*

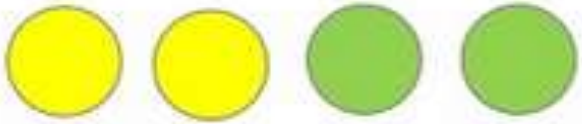
Key to alleles:
Y = yellow
y = green

Punnet Grid:

gametes	Y ♂	y
y ♀	Yy	yy
y	Yy	yy

F_1

Genotypes: Yy Yy yy yy

Phenotypes: 

Phenotype ratio: **1 : 1**

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

A Mendelian monohybrid cross:

F1 Parent Genotypes: **Tt x Tt**

F1 Parent Phenotypes: **Tall x Tall**

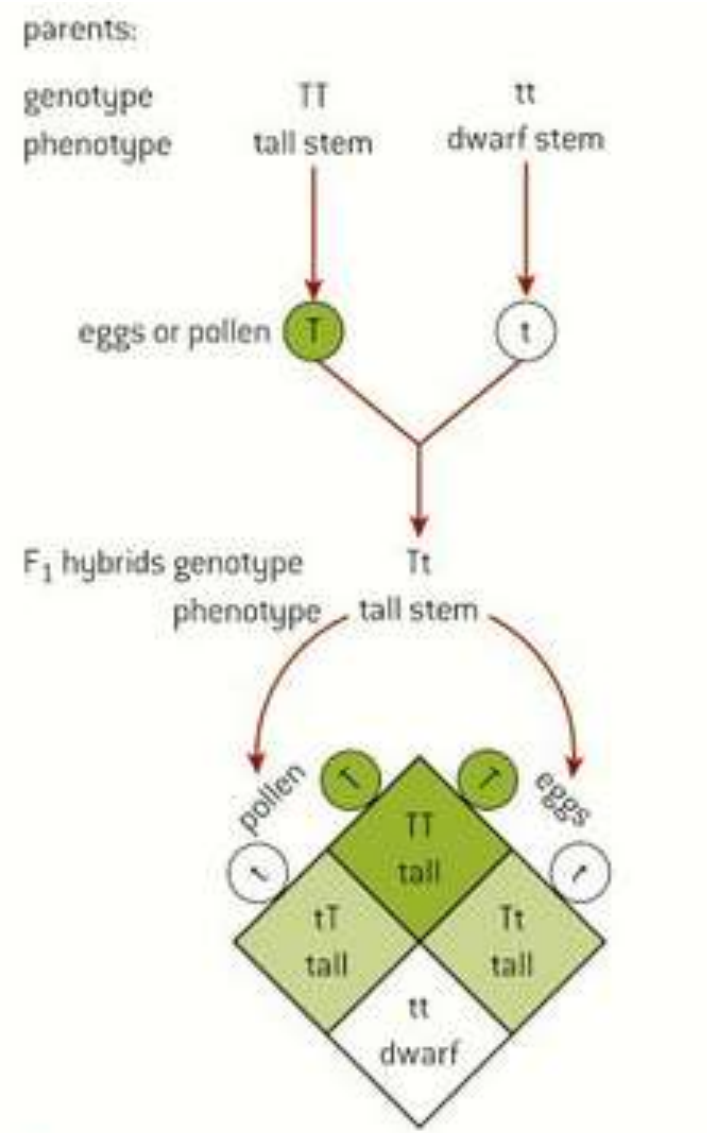
Offspring Genotype Ratio:

1 : 2 : 1 (TT : Tt : tt)

Offspring Phenotype Ratio:

3 : 1 (Tall : Dwarf)*

**Just as Mendel observed!*



▲ Figure 7 Explanation of Mendel's 3:1 ratio

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

A Non-Mendelian monohybrid cross:

F1 Parent Genotypes: **C^RC^W x C^RC^W**

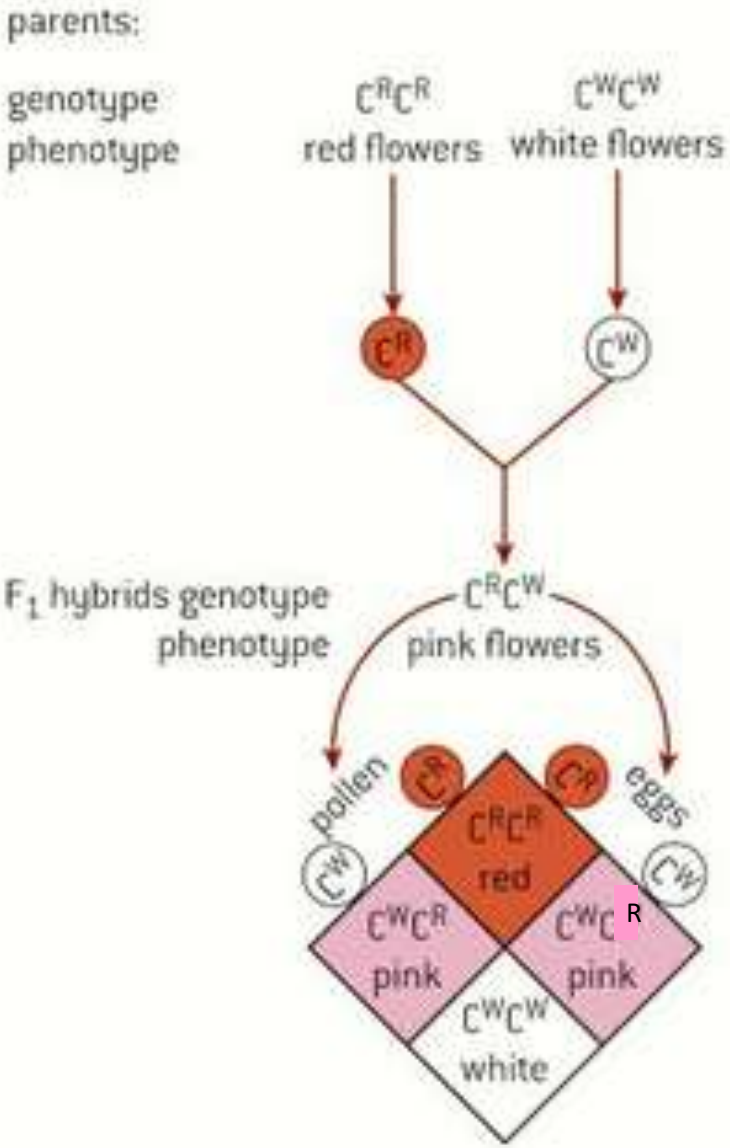
F1 Parent Phenotypes: **Pink x Pink**

Offspring Genotype Ratio:

1 : 2 : 1 (C^RC^R : C^RC^W : C^WC^W)

Offspring Phenotype Ratio:

1 : 2 : 1 (Red : Pink : White)



▲ Figure 8 A cross involving co-dominance

3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Test Cross

*Used to **determine the genotype** of an **unknown** individual.*
*The unknown is crossed with a known **homozygous recessive**.*

F_0

Phenotype: ♀  X crossed with  ♂

Genotype: **R ?** **r r**

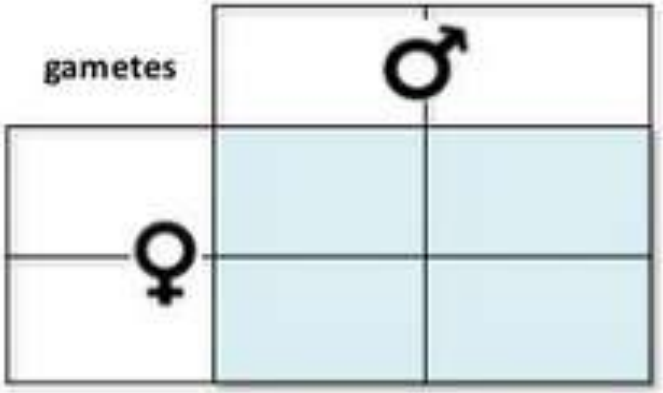
unknown *Homozygous recessive*

Key to alleles:
R = Red flower
r = white

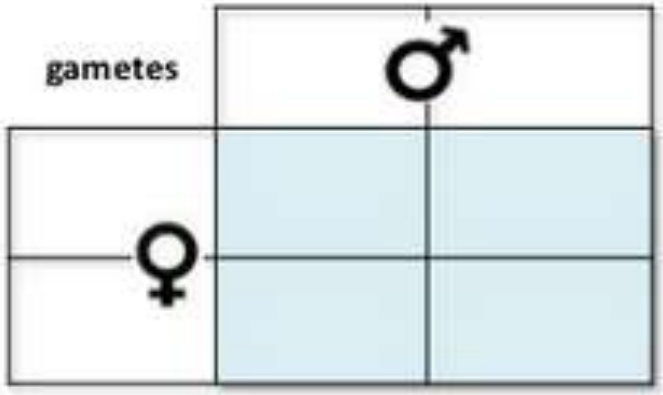
Possible outcomes:

F_1 Phenotypes:

Unknown parent = RR



Unknown parent = Rr



3.4.15 Construct Punnett grids (squares) for predicting the outcomes of monohybrid genetic crosses.

Test Cross

*Used to **determine the genotype** of an **unknown** individual.*
*The unknown is crossed with a known **homozygous recessive**.*

F_0

Phenotype: ♀  X crossed with  ♂

Genotype: **R ?** **r r**

unknown *Homozygous recessive*

Key to alleles:
R = Red flower
r = white

Possible outcomes:

F_1

Phenotypes: **All red**

Unknown parent = RR

gametes	r ♂	r
R ♀	Rr	Rr
R	Rr	Rr

Some white, some red

Unknown parent = Rr

gametes	r ♂	r
R ♀	Rr	Rr
r	rr	rr

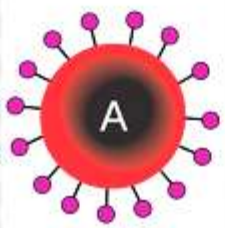
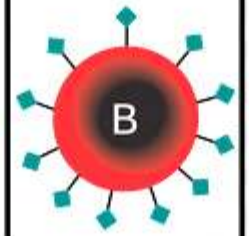
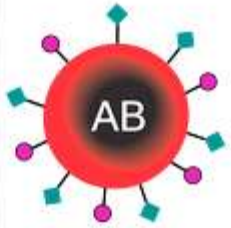
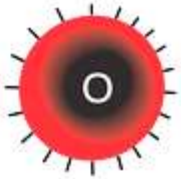

3.4.11 Inheritance of ABO blood groups

When surgeons started performing human blood transfusions in the mid-1800s, they were a very risky procedure. Doctors noticed that sometimes the blood transfusion was successful, while other times the transfused blood clumped up (clotted) inside the patient and killed them.

It was not until the early 1900s that scientists discovered humans have different glycoproteins on their red blood cells that give them different blood types. Since the immune system only recognizes certain blood types, the immune cells of patients who got mismatched blood would attack and destroy the ‘foreign’ cells, causing clots.

3.4.11 Inheritance of ABO blood groups

In humans, ABO blood group is determined by a single gene on Chromosome 9. ABO blood type is an example of '*Multiple Alleles*' and *Codominance*:

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

The gene has *three* alleles:

I^A : glycoprotein with A antigen (codominant)

I^B : glycoprotein with B antigen (codominant)

i : normal glycoprotein (recessive)

Genotypes	Phenotype
I^AI^A or I^Ai	A
I^BI^B or I^Bi	B
I^AI^B	AB
ii	O

3.4.16 Comparison of predicted and actual outcomes of genetic crosses using real data

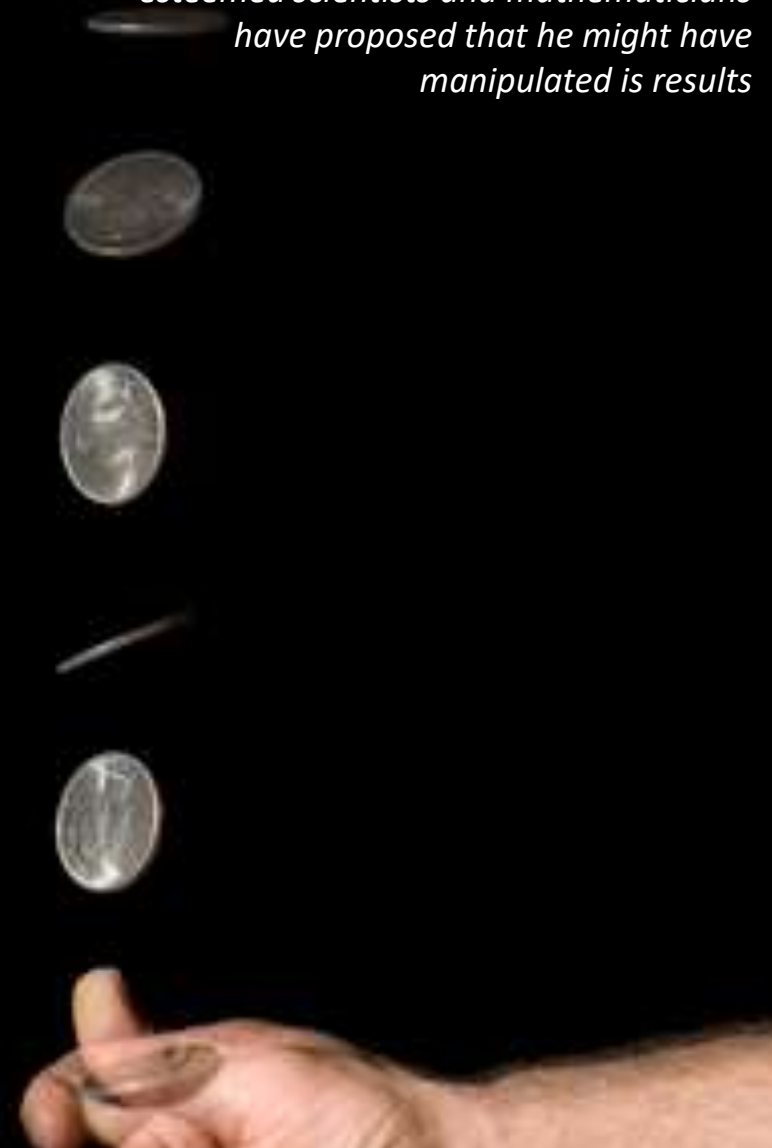
Mendel's experiments and Reginald Punnett's models allow for the prediction of genetic outcomes in offspring.*

However, predictions do not always match actual outcomes. For example, a coin tossed 100 times does not always produce 50 heads and 50 tails since each flip is a random event

With this in mind, scientists can collect large amounts of data to reduce the impact of such random fluctuations – The Law of Large Numbers (i.e. 10,000 coin flips will show a closer to 50-50 split than 10 flips)

Scientists can also use statistical tests like the **T-test** and the **Chi-Squared test** to determine if results are significant, or due to random chance!

**Mendel's actual data were so close to perfect 3:1 predicted ratios that many esteemed scientists and mathematicians have proposed that he might have manipulated is results*



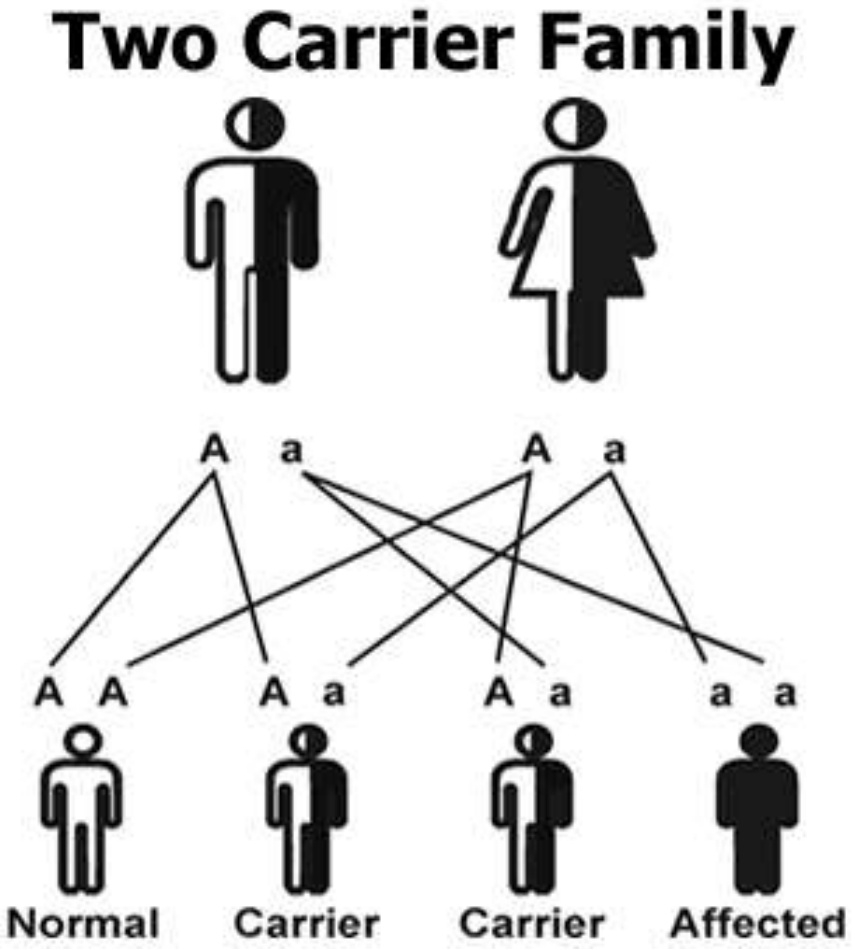
3.4.6 Many genetic diseases in humans are due to recessive alleles of autosomal genes

NOTE: An **autosomal gene** is a gene whose loci is on an autosome, not a sex chromosome

A genetic disease is a disorder caused by a gene, rather than microbes. In most cases, a mutated allele causes a protein to be altered which impairs normal cell / body function – *we have already seen an example of this in Sickle Cell Anemia*

Most disease-causing alleles are recessive – meaning an individual must inherit both copies of the disease allele to actually have the disorder

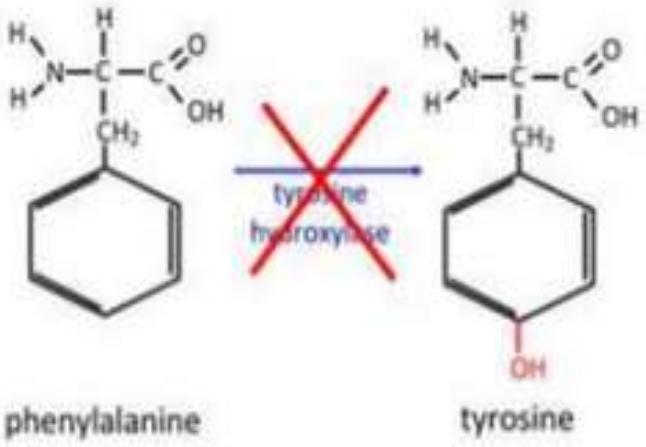
Individuals can be **carriers** for these genetic disorders, meaning they 'carry' one copy of the recessive disease allele and one dominant allele that gives them a normal phenotype.



3.4.6 Many genetic diseases in humans are due to recessive alleles of autosomal genes

Phenylketonuria (PKU)

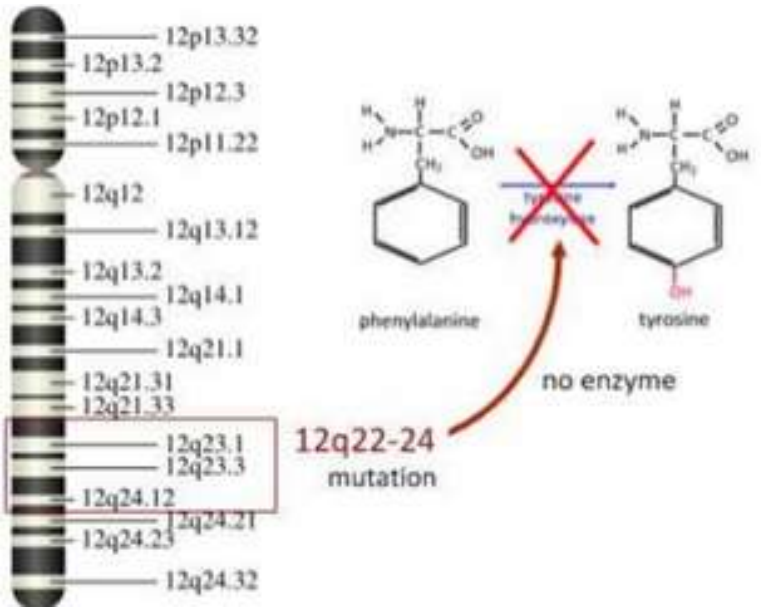
Clinical example.



A mis-sense mutation in the gene that produces tyrosine hydroxylase means that phenylalanine cannot be converted to tyrosine in the body - so it builds up.

This results in brain developmental problems and seizures. It is progressive, so it must be diagnosed and treated early.

Dairy, breastmilk, meat, nuts and aspartame must be avoided, as they are rich in phenylalanine.



Genetics review:

1. What is a missense mutation?

It is a base-substitution mutation where the change in a single base results in a different amino acid being produced in the polypeptide.

2. Is this disorder autosomal or sex-linked?

Autosomal – chromosome 12

3. What is the locus of the tyrosine hydroxlase gene?

12q22 - 24

3.4.6 Many genetic diseases in humans are due to recessive alleles of autosomal genes

Phenylketonuria (PKU)

Clinical example.

What is the probability of two parents who are both carriers of the recessive allele producing children affected by PKU?

F_0

Phenotype: ♀ carrier X carrier ♂

Genotype: T t X T t

Key to alleles:
T = Normal enzyme
t = faulty enzyme

Punnet Grid:

gametes	T ♂	t
T ♀		
t		

F_1

Genotypes:

Phenotypes:

Phenotype ratio:

3.4.6 Many genetic diseases in humans are due to recessive alleles of autosomal genes

Phenylketonuria (PKU)

Clinical example.

What is the probability of two parents who are both carriers of the recessive allele producing children affected by PKU?

F_0

Phenotype: ♀ carrier X carrier ♂

Genotype: **T t** crossed with **T t**

Key to alleles:
T = Normal enzyme
t = faulty enzyme

Punnet Grid:

gametes	T ♂	t
T ♀	TT	Tt
t	Tt	tt

F_1

Genotypes: TT Tt Tt tt

Phenotypes: Normal enzyme PKU

Phenotype ratio: **3 : 1**

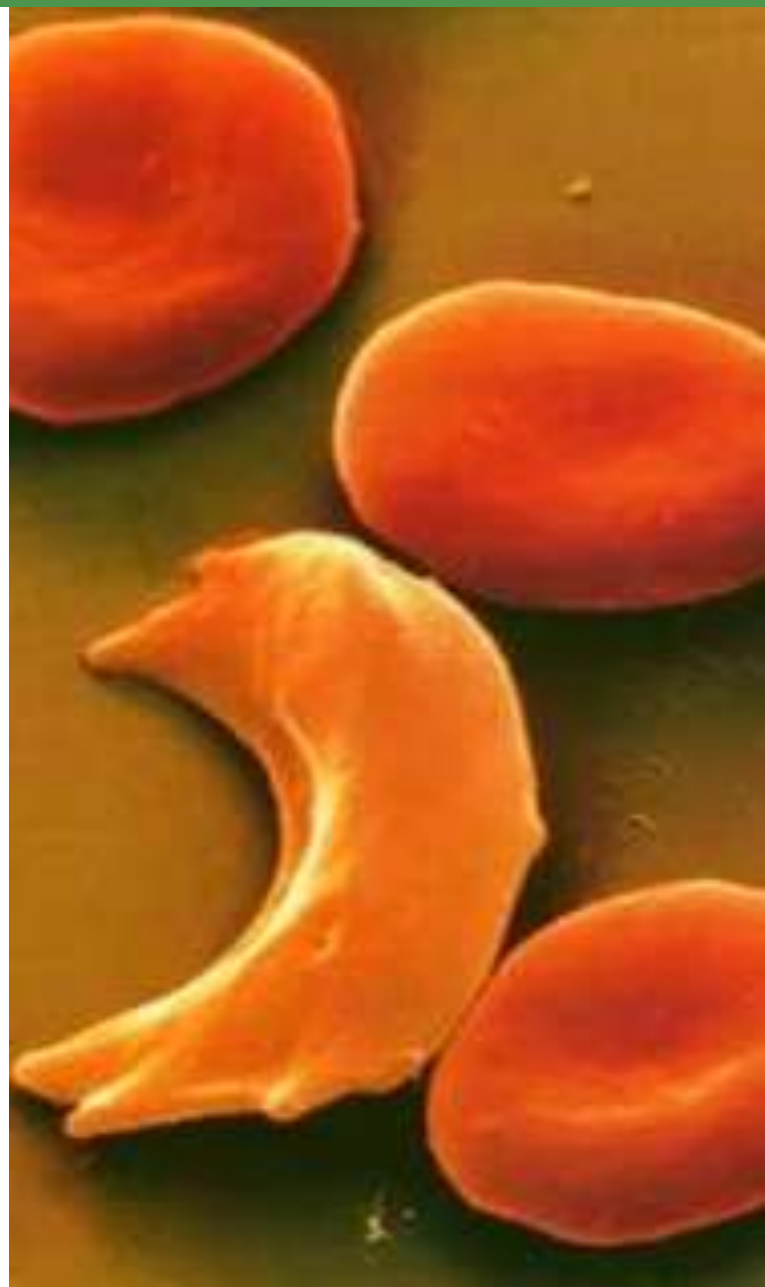
Therefore 25% chance of a child with PKU

3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

- **Huntington's disease is caused by an autosomal dominant allele:**
  - Inheriting just one mutated allele will cause this deadly neurological condition

- **Sickle Cell Anemia is caused by autosomal codominant alleles:**
  - **Hb^A Hb^A =** *Normal phenotype*
  - **Hb^A Hb^S** *= Mild anemia phenotype with malaria resistance*
  - **Hb^S Hb^S =** *Full sickle cell phenotype*

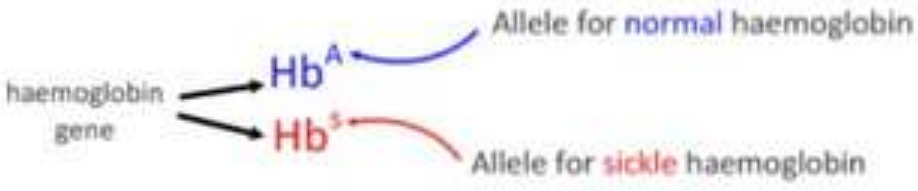
- **Color-blindness is caused by a recessive allele on the X sex chromosome** (so the gene is said to be 'sex linked'):
  - Since males only get one copy, they are more likely to express the colorblind phenotype *(a female would need to inherit two colorblind alleles to show this trait)*



3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

Sickle Cell

*Another example of **codominance**.*



Remember the notation used: superscripts represent codominant alleles.
In codominance, heterozygous individuals have a mixed phenotype.

The mixed phenotype gives protection against malaria, but does not exhibit full-blown sickle cell anemia.

Complete the table for these individuals:

Genotype	$Hb^A Hb^A$	$Hb^A Hb^S$	$Hb^S Hb^S$
Description	Homozygous Hb^A	Heterozygous	Homozygous Hb^S
Phenotype	normal	carrier	Sickle cell disease
Malaria protection?	No	Yes	Yes

3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

Sickle Cell

*Another example of **codominance**.*

Key to alleles:
Hb^A = Normal Hb
Hb^S = Sickle cell

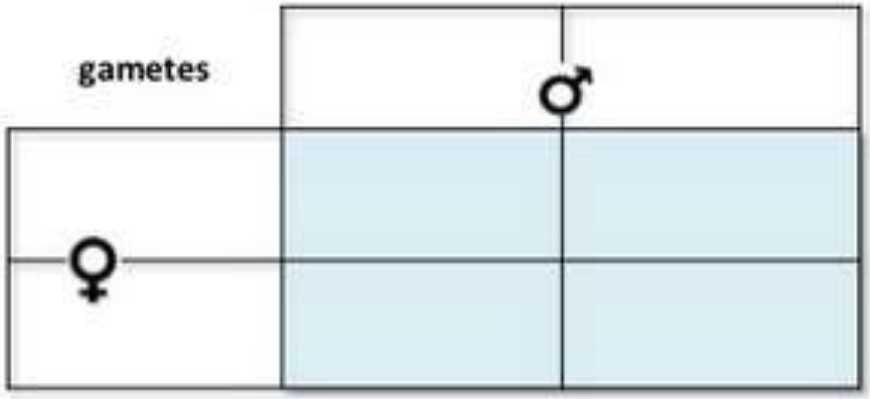
Predict the phenotype ratio in this cross:

F_0

Phenotype: ♀ carrier X affected ♂
crossed with

Genotype:

Punnet Grid:



F_1

Genotypes:

Phenotypes:

Phenotype ratio: :

Therefore 50% chance of a child with sickle cell disease.

3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

Sickle Cell

*Another example of **codominance**.*

Key to alleles:
Hb^A = Normal Hb
Hb^S = Sickle cell

Predict the phenotype ratio in this cross:

F_0

Phenotype: ♀ carrier X crossed with affected ♂

Genotype: $Hb^A Hb^s$ × $Hb^S Hb^s$

Punnet Grid:

gametes ♀ \ ♂	Hb^S	Hb^S
Hb^A	Hb^AHb^S	Hb^AHb^S
Hb^S	Hb^SHb^S	Hb^SHb^S

F_1

Genotypes: Hb^AHb^S & Hb^SHb^S

Phenotypes: Carrier & Sickle cell

Phenotype ratio: 1 : 1

Therefore 50% chance of a child with sickle cell disease.

3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

Sickle Cell

*Another example of **codominance**.*

Key to alleles:
Hb^A = Normal Hb
Hb^S = Sickle cell

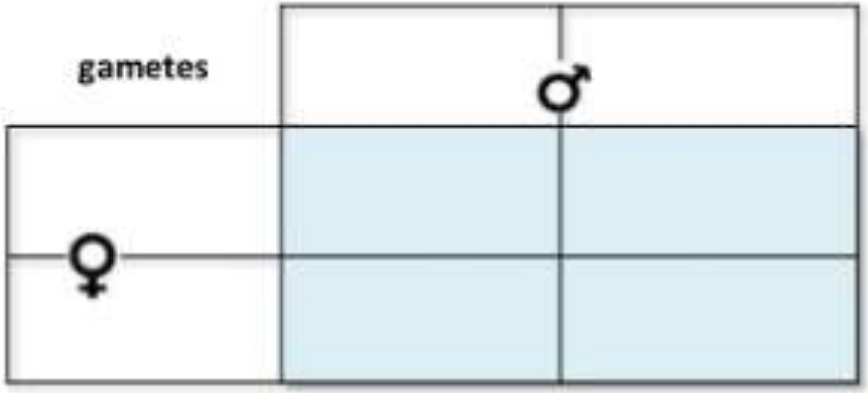
Predict the phenotype ratio in this cross:

F_0

Phenotype: ♀ carrier X crossed with carrier ♂

Genotype:

Punnet Grid:



F_1

Genotypes:

Phenotypes:

Phenotype ratio:

3.4.7 Some genetic diseases are sex-linked and some are due to dominant or co-dominant alleles

Sickle Cell

*Another example of **codominance**.*

Key to alleles:
Hb^A = Normal Hb
Hb^S = Sickle cell

Predict the phenotype ratio in this cross:

F_0

Phenotype: ♀ carrier X crossed with carrier ♂

Genotype: $Hb^A Hb^S$ X $Hb^A Hb^S$

Punnet Grid:

gametes	Hb^A ♂	Hb^S
Hb^A	Hb^AHb^A	Hb^AHb^S
♀ Hb^S	Hb^AHb^S	Hb^SHb^S

F_1

Genotypes: Hb^AHb & 2 Hb^AHb^S & Hb^SHb^S

Phenotypes: Unaffected & Carrier & Sickle cell

Phenotype ratio: **1 : 2 : 1**

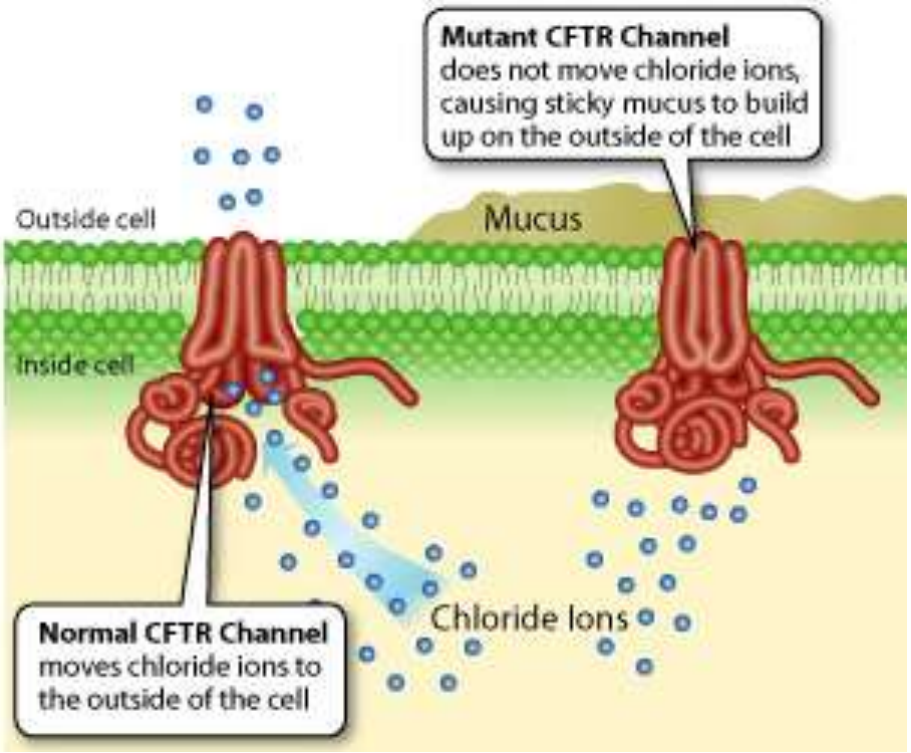
Therefore 25% chance of a child with sickle cell disease.

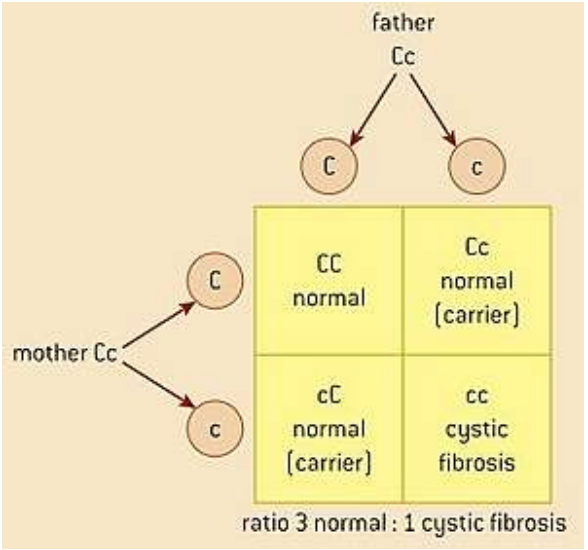
Cystic Fibrosis

An autosomal recessive genetic disease caused by a mutation of the **CFTR gene** on *Chromosome 7*

The CFTR gene encodes the production of a chloride membrane channel protein involved in secretion of sweat, mucus, and digestive juices

The mutated, disease allele produces a non-functional membrane protein that causes sticky mucus builds up in the lungs, causing infection





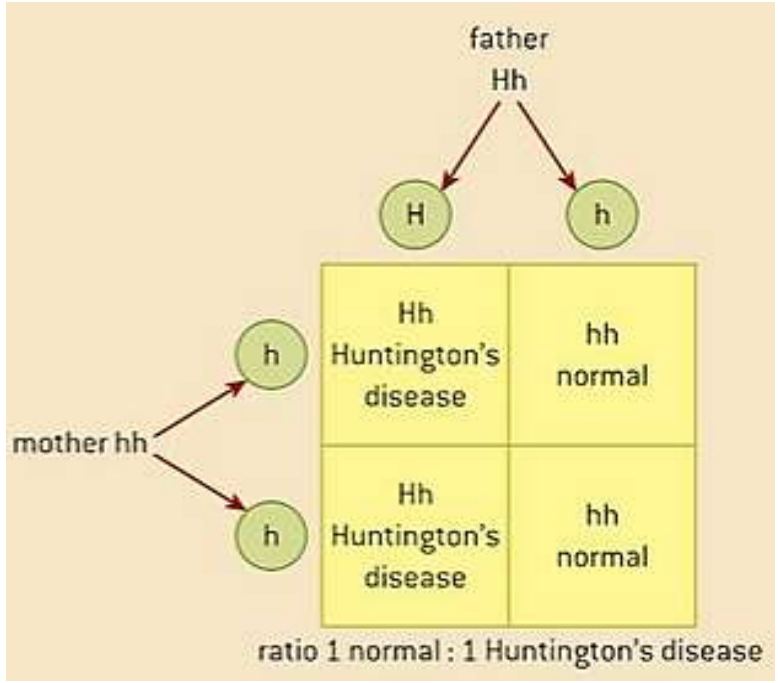
Huntington's Disease

An <u>autosomal dominant</u> genetic disease caused by a mutation of the **HTT gene** on *Chromosome 4*

The function of the normal *huntingtin* protein is still being studied, but the dominant allele causes progressive neurodegeneration beginning between ages 30 and 50.

Life expectancy is ~20 years after the onset of symptoms.

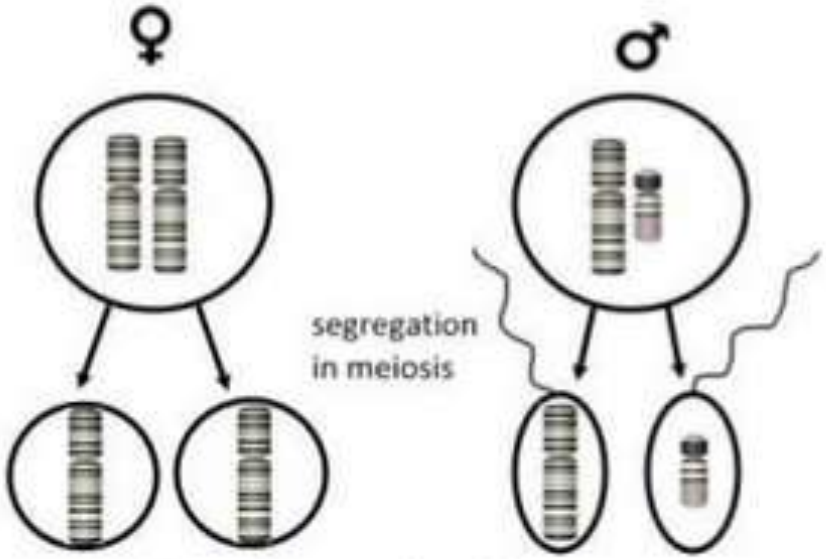
Due to the late-onset nature, most parents have already had children before they become symptomatic…



3.4.8 The pattern of inheritance is different with sex-linked genes due to their location on sex chromosomes.

Sex Determination

It's all about X and Y...



Segregation of the sex chromosomes in meiosis.

Chromosome pairs **segregate** in meiosis.

Females (XX) produce only eggs containing the X chromosome.

Males (XY) produce sperm which can contain either X or Y chromosomes.

gametes	X	Y
X	XX	XY
X	XX	XY

Therefore there is an even chance* of the offspring being male or female.

3.4.8 The pattern of inheritance is different with sex-linked genes due to their location on sex chromosomes.

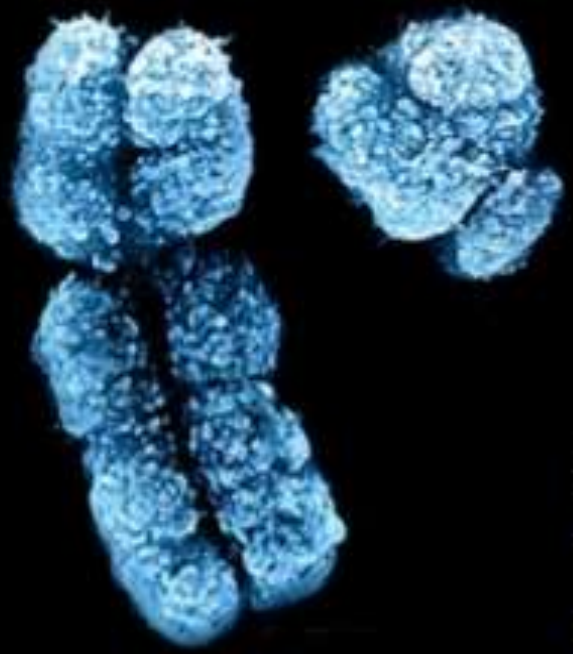
Sex Linkage

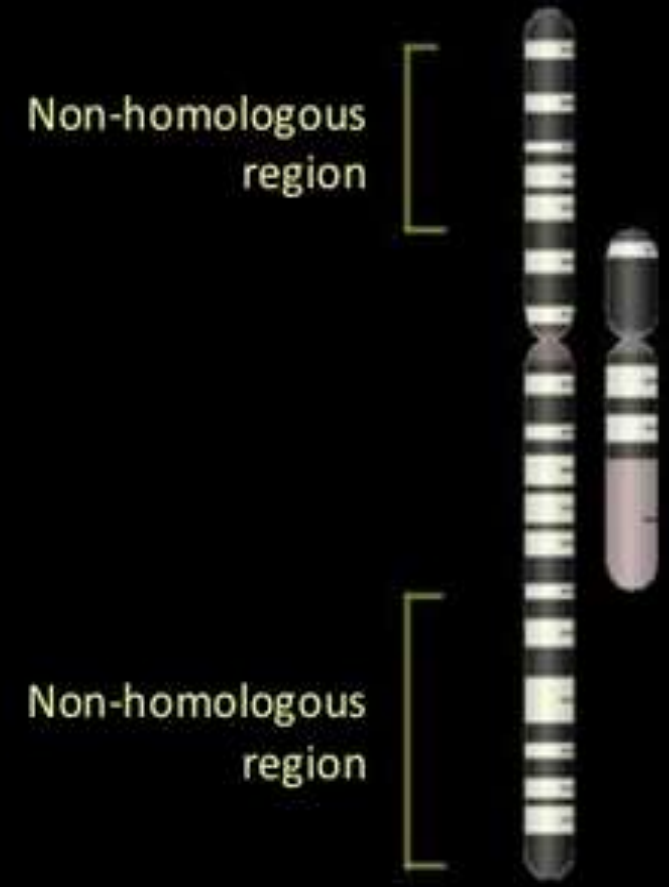
X and Y chromosomes are non-homologous.

Share

The sex chromosomes are non-homologous. *There are many genes on the X-chromosome which are not present on the Y-chromosome.*

Sex-linked traits are those which are carried on the X-chromosome in the non-homologous region. They are more common in males.





Examples of sex-linked genetic disorders:

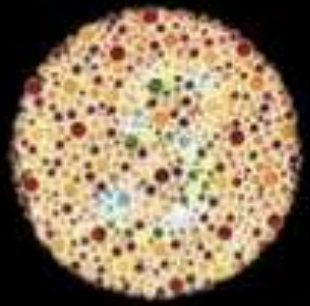
- **haemophilia**
- colour blindness

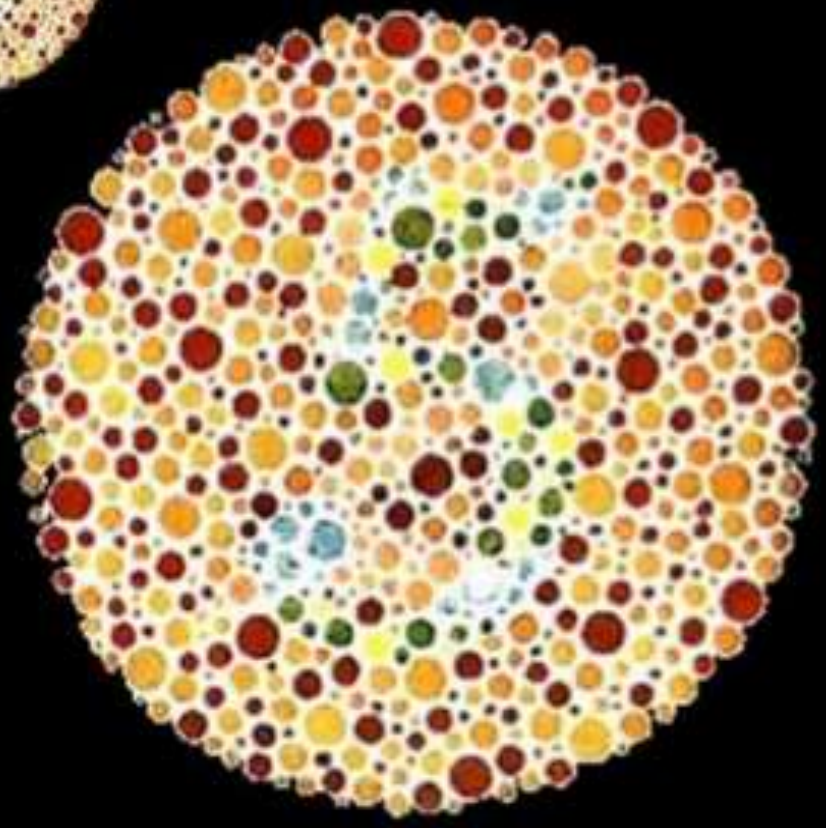
3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

X and Y chromosomes are non-homologous.

What number do you see?



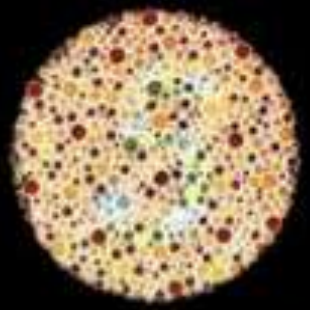


3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

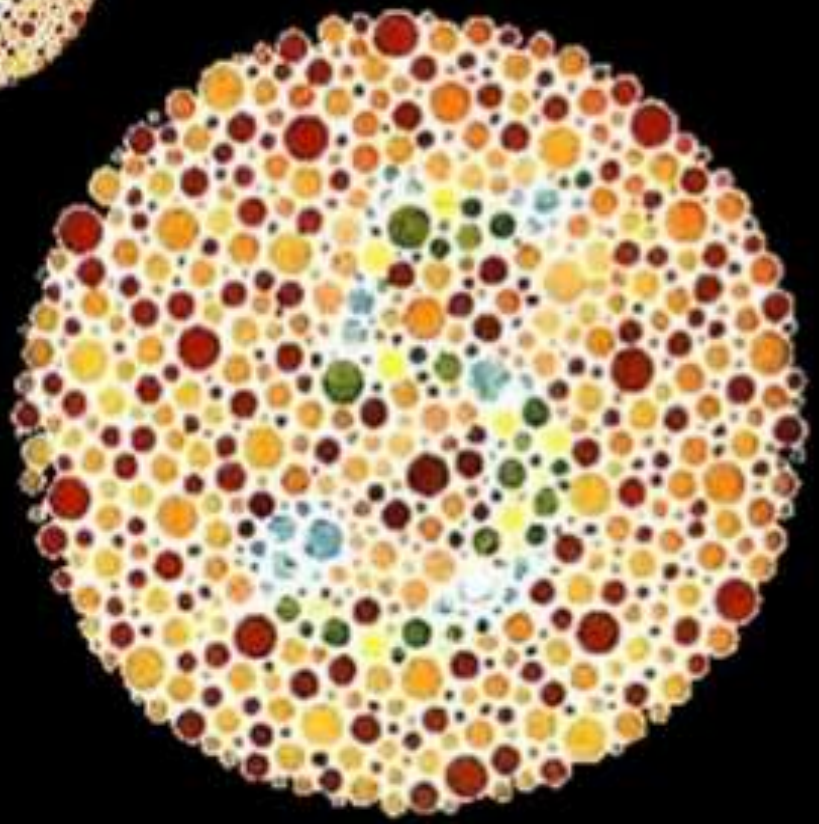
X and Y chromosomes are non-homologous.

What number do you see?



5 = normal vision

2 = red/green colour blindness

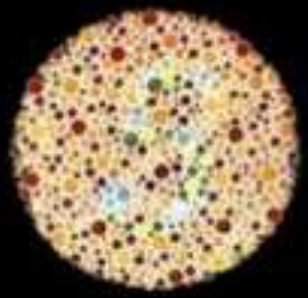


3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

X and Y chromosomes are non-homologous.

How is colour-blindness inherited?



The red-green gene is carried at locus Xq28.
This locus is in the non-homologous region, so there is no corresponding gene (or allele) on the Y chromosome.

Normal vision is dominant over colour-blindness.

$X^N X^N$ Normal female

$X^N Y$ Normal male ← no allele carried, none written

$X^n X^n$ Affected female

$X^n Y$ Affected male

Key to alleles:
N = normal vision
n = red/green colour blindness

$X^N X^n$ Carrier female

Human females can be *homozygous* or *heterozygous* with respect to *sex-linked genes*. Heterozygous females are carriers.

Chromosome images from Wikipedia:

3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

X and Y chromosomes are non-homologous.

Share

What chance of a colour-blind child in the cross between a normal male and a carrier mother?

Key to alleles:

N = normal vision

n = red/green colour blindness

F_0 Genotype: $X^N X^n$ x $X^N Y$

Phenotype: Carrier female x Normal male

Punnet Grid:

F_1

3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

X and Y chromosomes are non-homologous.

What chance of a colour-blind child in the cross between a normal male and a carrier mother?

Key to alleles:
N = normal vision
n = red/green colour blindness

F_0

Genotype: $X^N X^n$ x $X^N Y$

Phenotype: Carrier female x Normal male

Punnet Grid:

F_1

	X^N	Y
X^N	$X^N X^N$	$X^N Y$
X^n	$X^N X^n$	$X^n Y$

3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Sex Linkage

X and Y chromosomes are non-homologous.

What chance of a colour-blind child in the cross between a normal male and a carrier mother?

Key to alleles:
N = normal vision
n = red/green colour blindness

F_0

Genotype: $X^N X^n$ x $X^N Y$

Phenotype: Carrier female x Normal male

Punnet Grid:

	X^N	Y
X^N	$X^N X^N$ Normal female	$X^N Y$ Normal male
X^n	$X^N X^n$ Carrier female	$X^n Y$ Affected male

F_1

There is a 1 in 4 (25%) chance of an affected child.

3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Hemophilia

Another sex-linked disorder.

Blood clotting is an example of a metabolic pathway – a series of enzyme-controlled biochemical reactions.

It requires *globular proteins* called **clotting factors**.
A recessive X-linked mutation in hemophiliacs results in one of these factors not being produced. Therefore, the clotting response to injury does not work and the patient can bleed to death.

$X^H X^H$
Normal female

$X^H Y$ ← no allele carried, none written
Normal male

Key to alleles:
X^H = healthy clotting factors
X^h = no clotting factor

$X^h X^h$
Affected female

$X^h Y$
Affected male

$X^H X^h$
Carrier female

Human females can be *homozygous* or *heterozygous* with respect to *sex-linked genes*.
Heterozygous females are *carriers*.

3.4.12 Red-green color-blindness and hemophilia as examples of sex-linked inheritance

Hemophilia

results from a lack of clotting factors. These are globular proteins, which act as enzymes in the clotting pathway.

Cell/ tissue damage

↓

Clotting factors

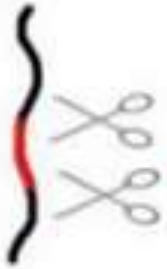
prothrombin → thrombin

fibrinogen → fibrin

fibrin → clot

One potential treatment for haemophilia is to use injections of clotting factors produced industrially through gene transfer:

Find gene
for healthy human clotting factors



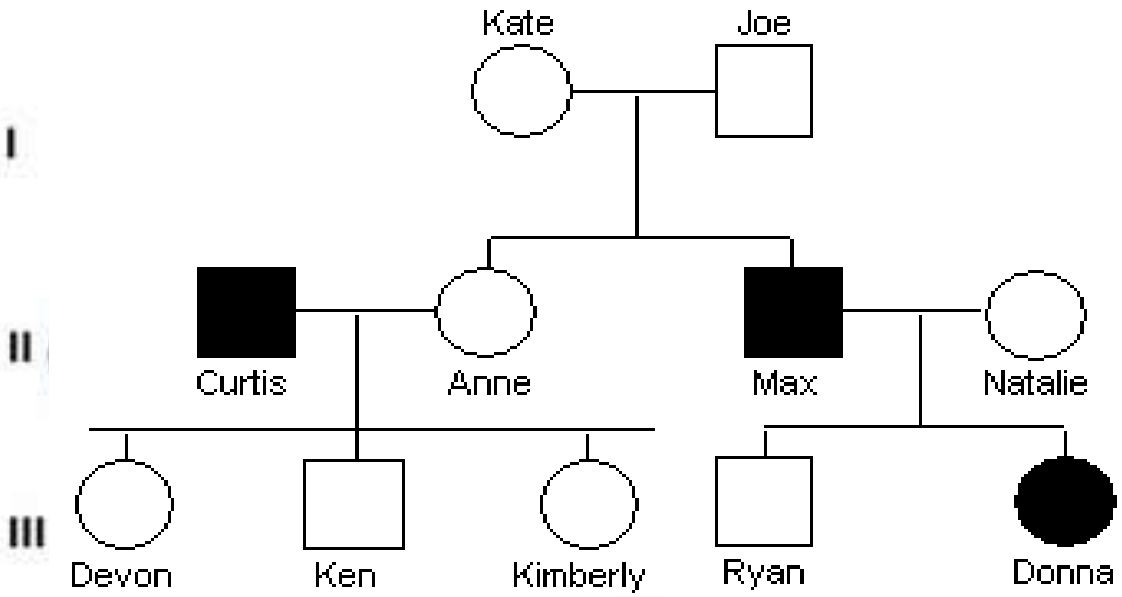
Insert
into sheep milk gene in sheep embryos

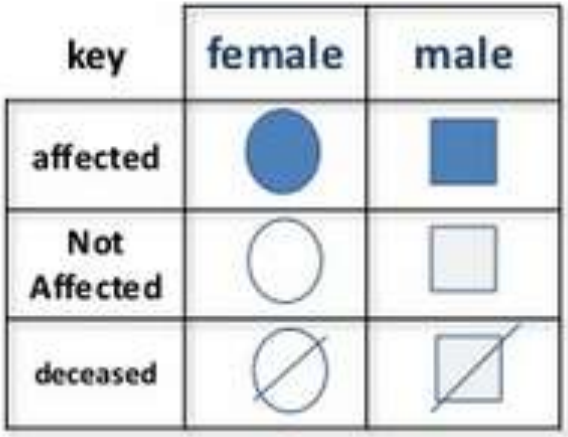
Extract
clotting factor from sheep milk

Purify
and produce injections for patients

3.4.17 Analysis of pedigree charts to deduce the pattern of inheritance of genetic diseases

Pedigree charts can be used to trace family histories and deduce genotypes and risk in the case of inherited gene-related disorders. Here is a pedigree chart for this family history.





The basics of Pedigrees:

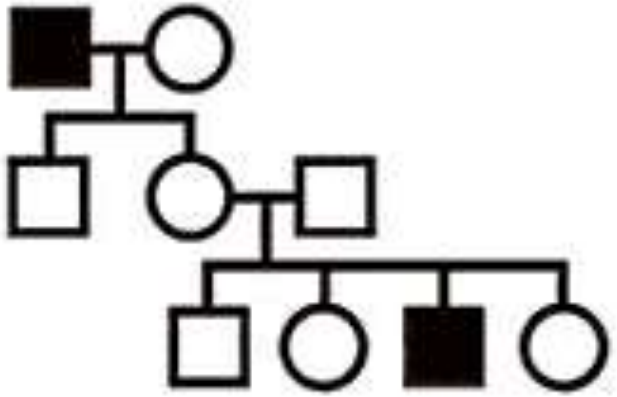
- Sex of Individual:
  - Male = Square
  - Female = Circle
- Presence of Trait:
  - Shading = Affected
  - Unshaded = Unaffected
  - Half-shade = Carrier
- Rows represent generations

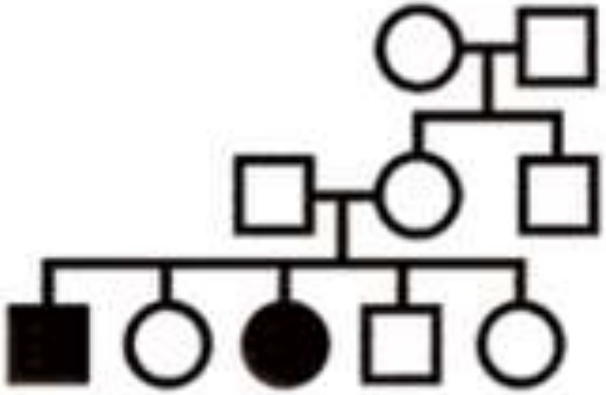
- **Autosomal Dominant or Recessive?**
  - *Recessive*
- **Genotype of Max?** (AA, Aa, or aa)
  - *aa*
- **Genotype of Ryan?** (AA, Aa, or aa)
  - *Aa*

3.4.17 Analysis of pedigree charts to deduce the pattern of inheritance of genetic diseases

Sex-Linked, Recessive:

- Trait is able to skip generations
- Males are predominantly affected



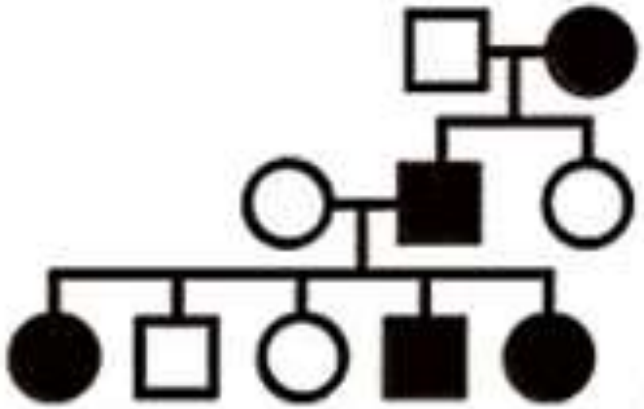


Autosomal, Recessive:

- Trait is able to skip generations
- No major sex-bias in expression

Autosomal, Dominant:

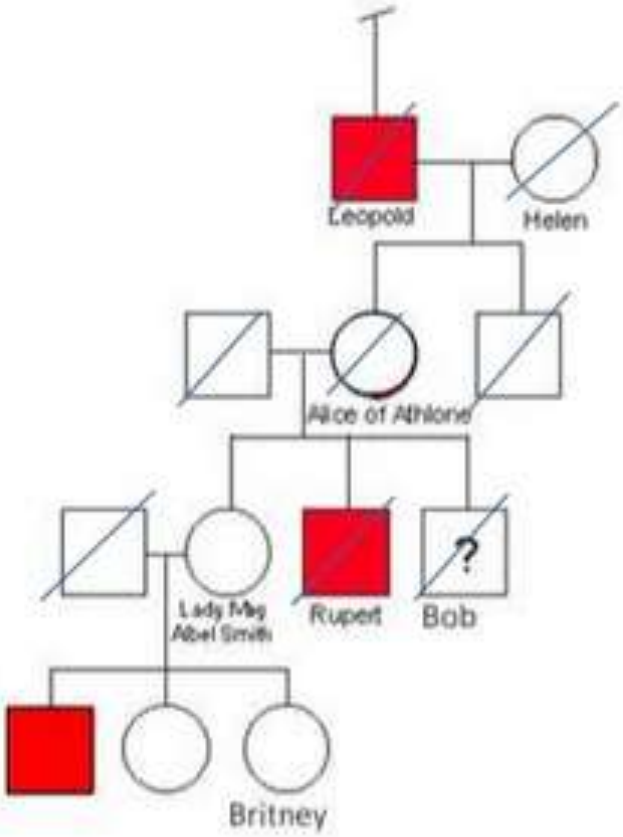
- Trait cannot skip generations
- No major sex-bias in expression



3.4.17 Analysis of pedigree charts to deduce the pattern of inheritance of genetic diseases

Hemophilia

Pedigree chart practice



State the genotypes of the following family members:

1. Leopold
2. Alice
3. Bob was killed in a tragic croquet accident before his phenotype was determined.
4. Britney

Key:	female	male
affected	●	■
Not Affected	○	□
deceased	⊘	▨

Key to alleles:

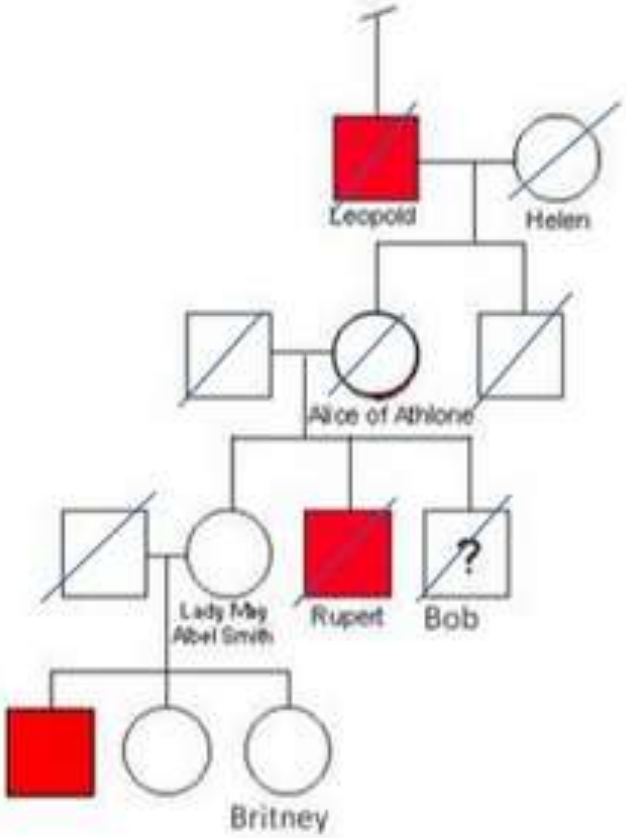
H = healthy clotting factors

h = no clotting factor

Royal Family Pedigree Chart from:

Hemophilia

Pedigree chart practice



Key to alleles:

H = healthy clotting factors

h = no clotting factor

Royal Family Pedigree Chart from:

State the genotypes of the following family members:

1. Leopold

   $X^h Y$

2. Alice

   $X^H X^h$

3. Bob was killed in a tragic croquet accident before his phenotype was determined.

   $X^H Y$ or $X^h Y$

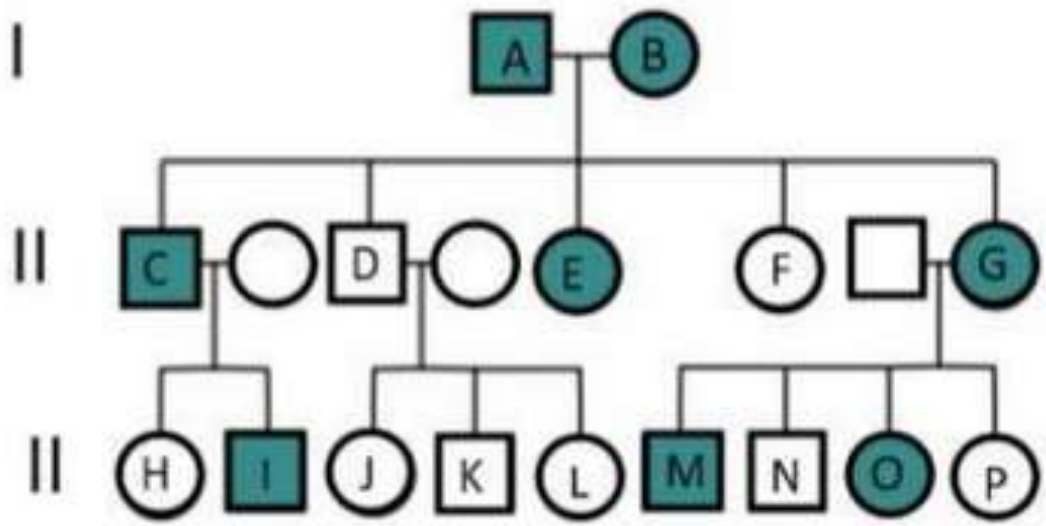
4. Britney

   $X^H X^H$ or $X^H X^h$

Key:	female	male
affected	●	■
Not Affected	○	□
deceased	⊘	⊘

3.4.17 Analysis of pedigree charts to deduce the pattern of inheritance of genetic diseases

Pedigree Chart Practice

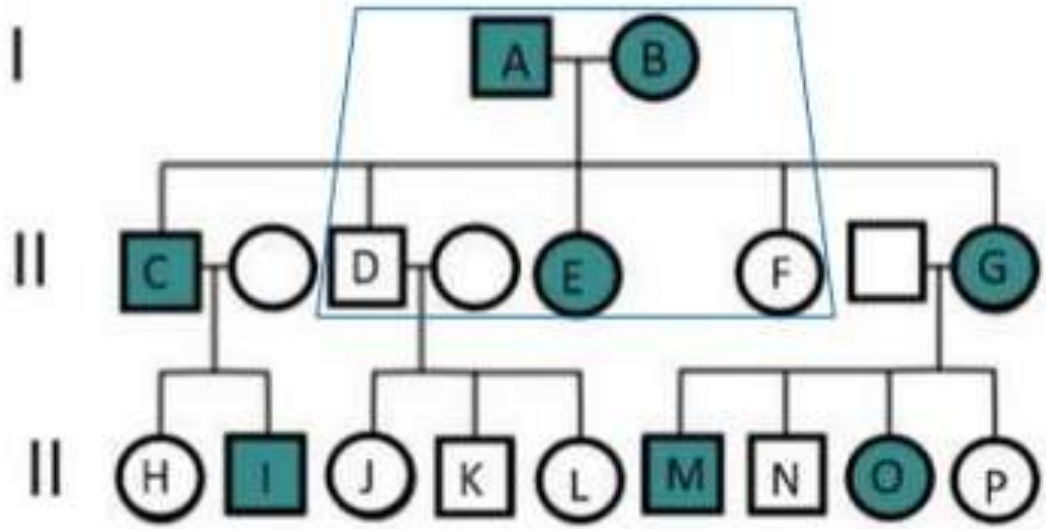


Key:	female	male
affected		
Not Affected		
deceased		

Dominant or Recessive?

Autosomal or Sex-linked?

Pedigree Chart Practice



Key:	female	male
affected		
Not Affected		
deceased		

Dominant or Recessive?

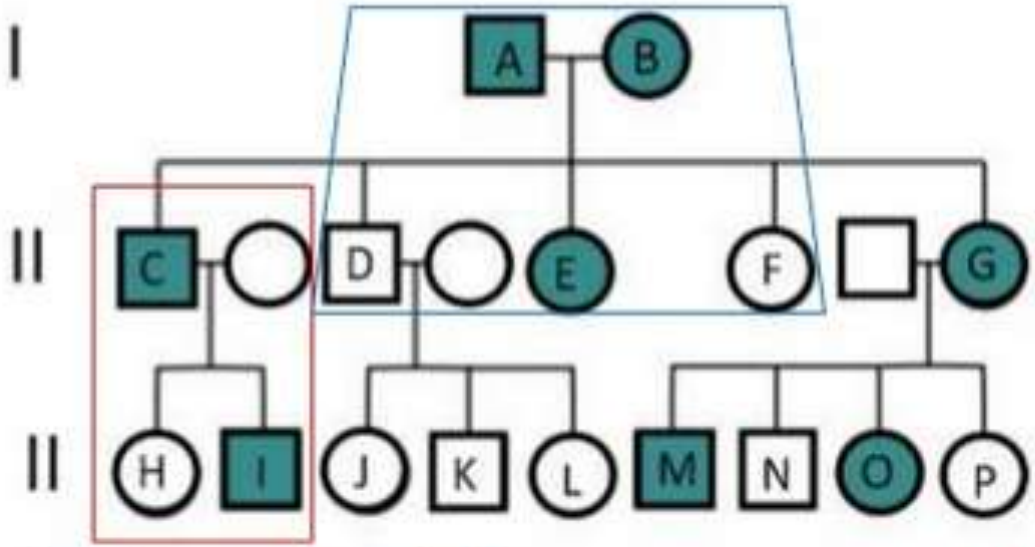
Dominant.

A and B are both affected but have produced unaffected (D & F). Therefore A and B must have been carrying recessive healthy alleles.

If it were recessive, it would need to be homozygous to be expressed in A & B – and then all offspring would be homozygous recessive.

Autosomal or Sex-linked?

Pedigree Chart Practice



Key:	female	male
affected		
Not Affected		
deceased		

Dominant or Recessive?

Dominant.

A and B are both affected but have produced unaffected (D & F). Therefore A and B must have been carrying recessive healthy alleles.

If it were recessive, it would need to be homozygous to be expressed in A & B – and then all offspring would be homozygous recessive.

Autosomal or Sex-linked?

Autosomal.

Male C can only pass on one X chromosome. If it were carried on X, daughter H would be affected by the dominant allele.

Tip: Don't get hung up on the number of individuals with each phenotype – each reproductive event is a matter of chance. Instead focus on possible and impossible genotypes. Draw out the punnet grids if needed.

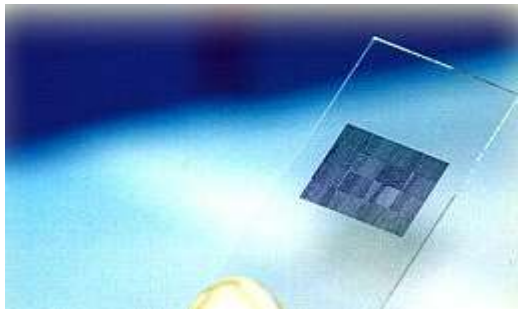
3.4.17 Analysis of pedigree charts to deduce the pattern of inheritance of genetic diseases

Medical researchers have identified more than **4,000** human genetic diseases so far.

Examples to know include *Cystic fibrosis, Huntington's disease, Sickle cell anemia,* and *Hemophilia*

Yet most people are unaffected by genetic diseases because **most are caused by very rare, recessive alleles**

Today, cheap and fast genetic tests can allow parents to determine if they carry genetic diseases before they make decisions about having children



▲ Figure 23 Alleles from two parents come together when they have a child. There is a small chance that two recessive alleles will come together and cause a genetic disease

3.4.10 Radiation and mutagenic chemicals increase the mutation rate and can cause genetic disease and cancer.

Alleles for a gene differ by just a few nitrogen base letters (SNPs). New alleles are formed by **mutation** – a random change in the base sequence of a gene

High-energy **radiation**, including Gamma rays, UV light, and X-rays, can increase mutation rate

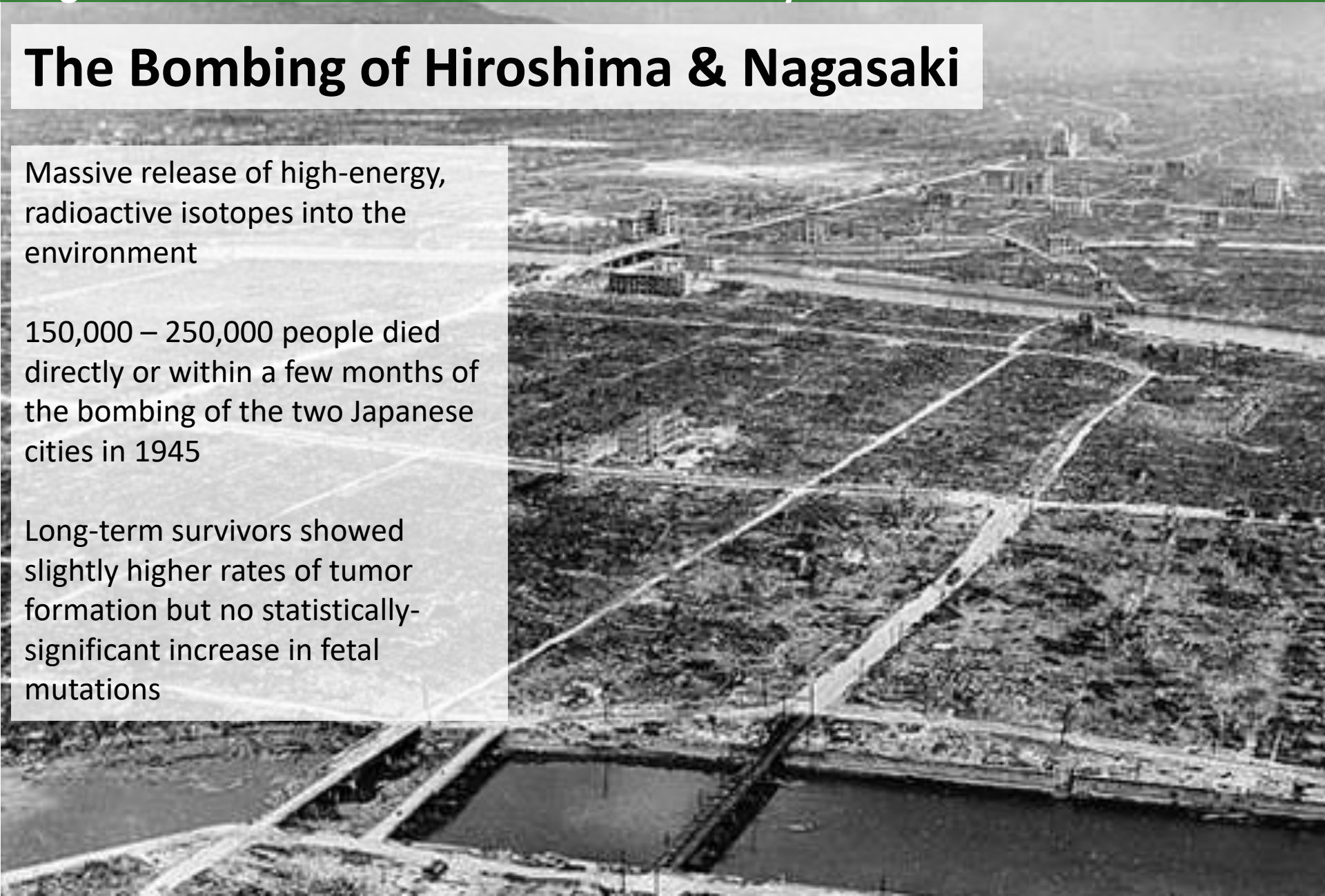
Some chemicals – called **mutagens** – can also increase mutation rate, such as mustard gas in WWI and chemicals in tobacco smoke

Mutations in ***oncogenes*** (genes that regulate the cell cycle) can lead to cancer

Mutations in genes of gametes can be passed on to children, possibly causing a genetic disease

3.4.14 Consequence of radiation after nuclear bombing of Hiroshima and Nagasaki and the nuclear accident at Chernobyl.

The Bombing of Hiroshima & Nagasaki



Massive release of high-energy, radioactive isotopes into the environment

150,000 – 250,000 people died directly or within a few months of the bombing of the two Japanese cities in 1945

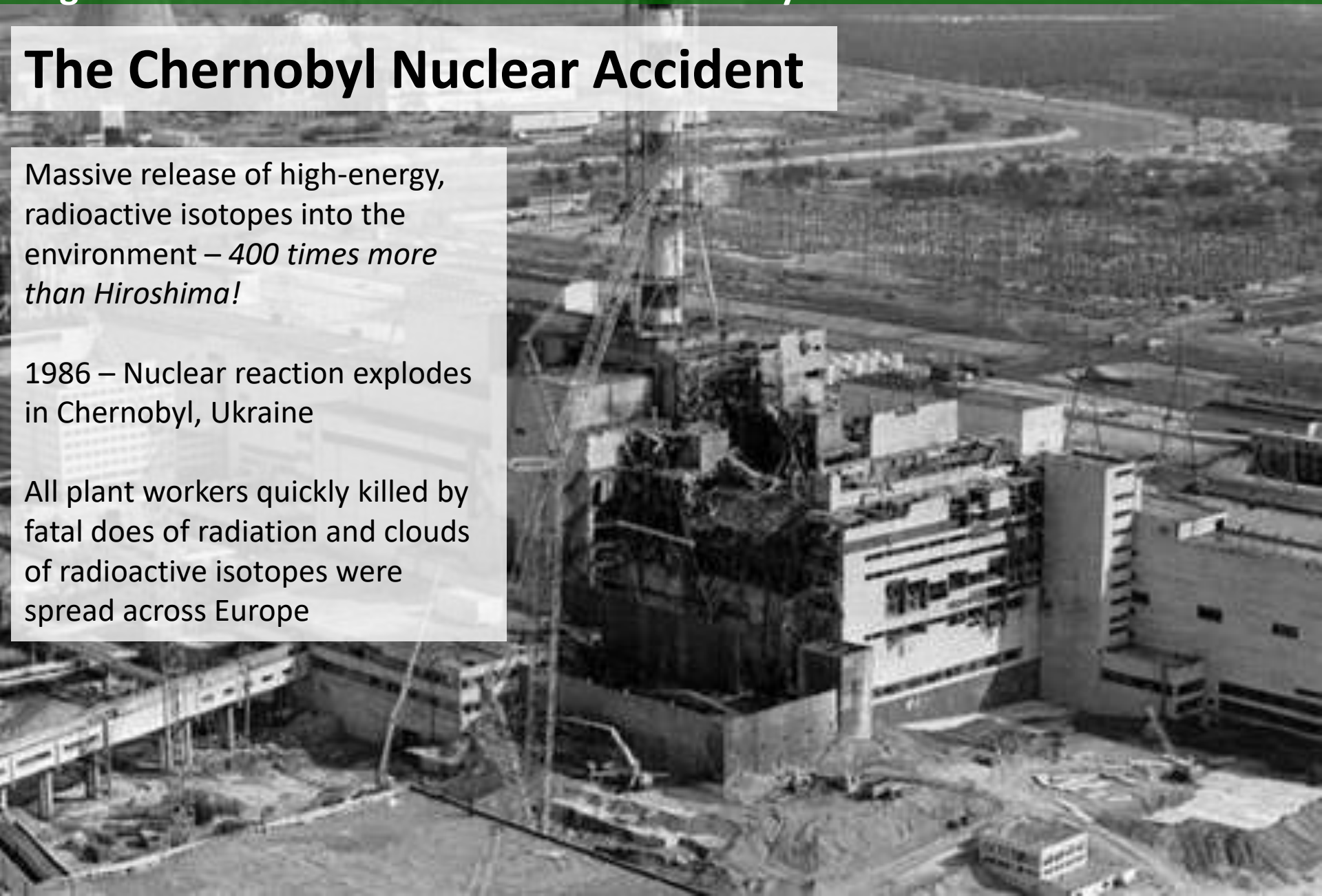
Long-term survivors showed slightly higher rates of tumor formation but no statistically-significant increase in fetal mutations

The Chernobyl Nuclear Accident

Massive release of high-energy, radioactive isotopes into the environment – *400 times more than Hiroshima!*

1986 – Nuclear reaction explodes in Chernobyl, Ukraine

All plant workers quickly killed by fatal does of radiation and clouds of radioactive isotopes were spread across Europe

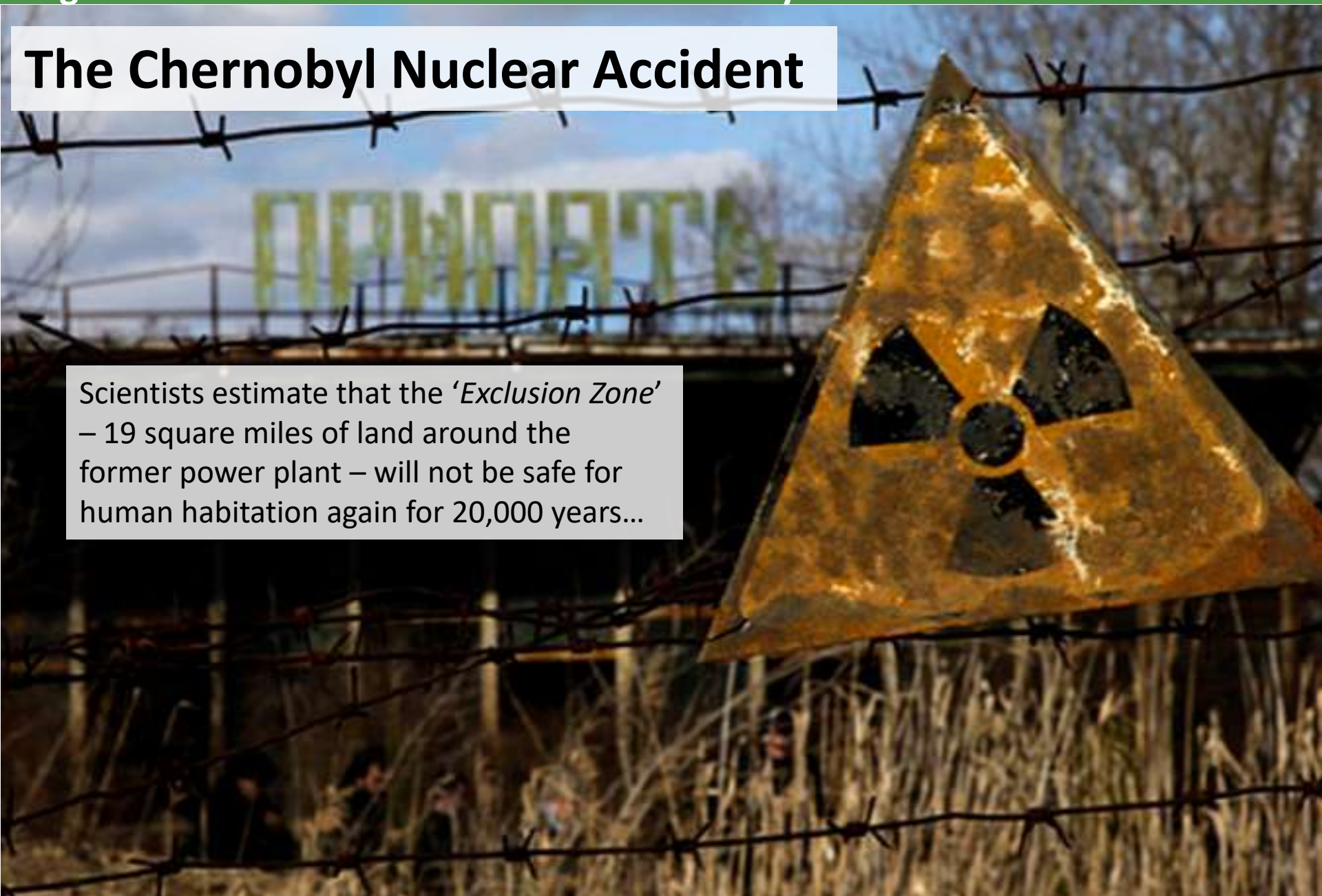


The Chernobyl Nuclear Accident

Effects of nuclear fallout:

- Miles of forest land killed, including most animals and plants
- Lynx, owls, wild boar, and other select species began to thrive in the 'exclusion zone'
- Bioaccumulation caused high levels of radioactive isotopes in fish as far away as Germany and Scandinavia
- More than 6,000 cases of thyroid cancer attributed to accident

3.4.14 Consequence of radiation after nuclear bombing of Hiroshima and Nagasaki and the nuclear accident at Chernobyl.



The Chernobyl Nuclear Accident

Scientists estimate that the '*Exclusion Zone*' – 19 square miles of land around the former power plant – will not be safe for human habitation again for 20,000 years…

Bibliography / Acknowledgments

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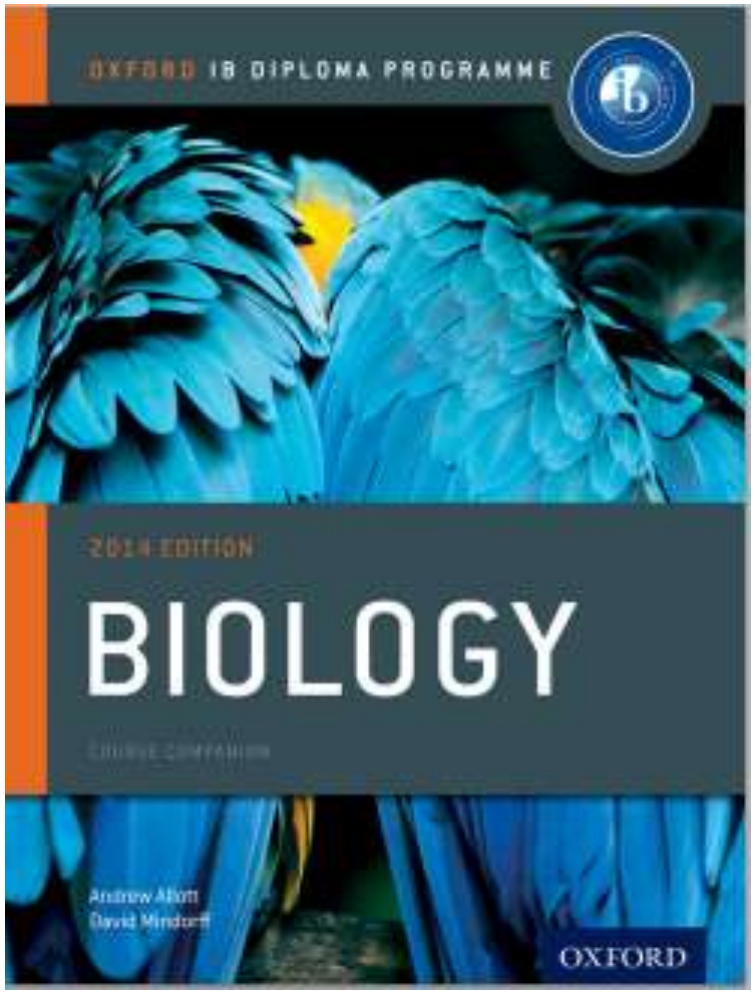

Bob Smullen