Bio Factsheet

Number 97

A Guide to Sex Linkage

This Factsheet summarises:

- **the inheritance of sex-linked genes which are carried on the X-chromosome;**
- **examples of X-linked inheritance in Drosophila, humans, birds and other animals;**
- **the inheritance of sex-linked genes which are carried on the Y-chromosome.**

Definitions

Sex-chromosomes: The pair of chromosomes in each nucleus that carry the sex-determining genes.

Autosomes: The pairs of chromosomes in each nucleus which do not carry sex-determining genes.

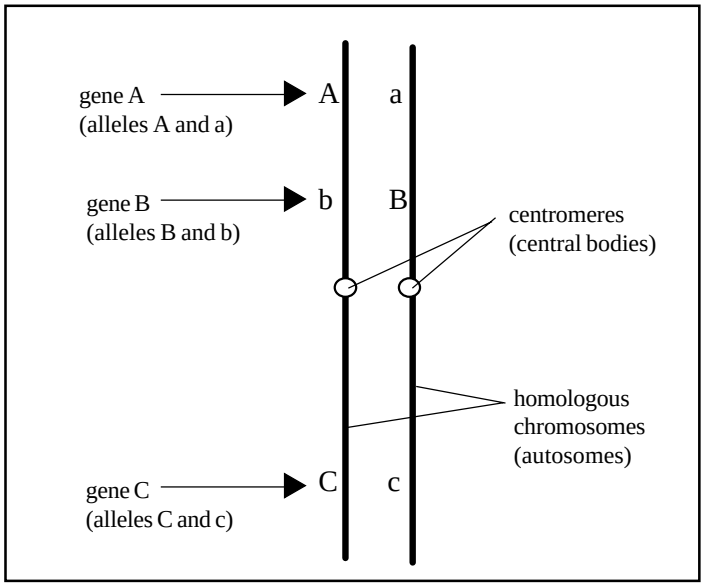
Sex linkage: Refers to genetically controlled characters (but not sex) that are only expressed in one sex (the male). Such characters are never or rarely expressed in the other sex (the female).

X-linkage: When the allele for the linked character is situated only on the X-chromosome.

Y-linkage: When the allele for the linked character is situated only on the Y-chromosome.

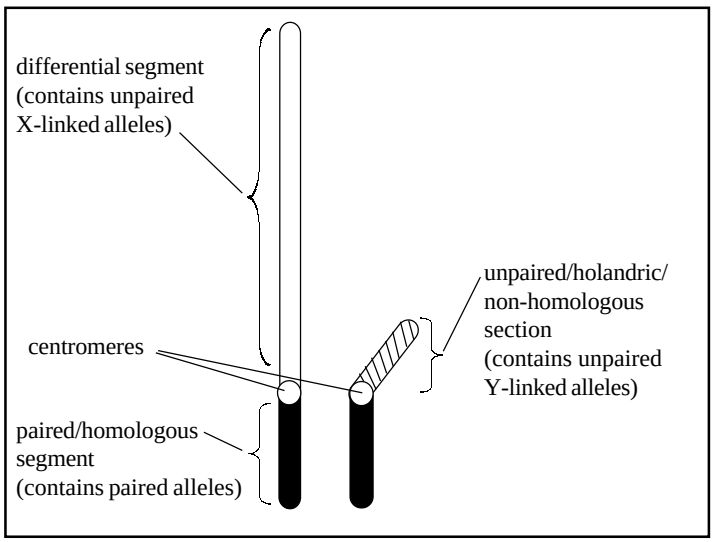
Gene locus: The specific position on a chromosome where the allele of a gene is situated. A pair of homologous chromosomes will thus contain two loci (and so two alleles) per gene. The alleles of the gene are at the same position on the homologous chromosomes (see fig 1).

Fig 1. A pair of homologous chromosomes showing some gene loci.



Remember *- human nuclei contain 23 pairs of chromosomes, 22 pairs are autosomes and the 23rd pair are sex-chromosomes. In males this pair is designated XY. In females this pair is designated XX*

Fig 2. Structure of the sex-chromosomes (male)



The human sex-chromosomes

Note that the chromosomes of an autosomal pair are structurally identical (homologous) to each other and carry identical gene loci. In contrast, the sex-chromosomes are not identical (see fig 2). Thus, although the X-chromosome and Y-chromosome do contain a short similar homologous segment, the X-chromosome is much longer than the Y-chromosome. In addition, the Y-chromosome also contains a short length which is non-homologous to the X- chromosome. This is called the holandric portion.

X-linked inheritance

The X and Y chromosomes carry the alleles responsible for the development of sex. However other non-sex related alleles are also carried on the sex-chromosomes, particularly on the differential segment of the X-chromosome. If these non-sex related alleles are recessive then the following occurs;

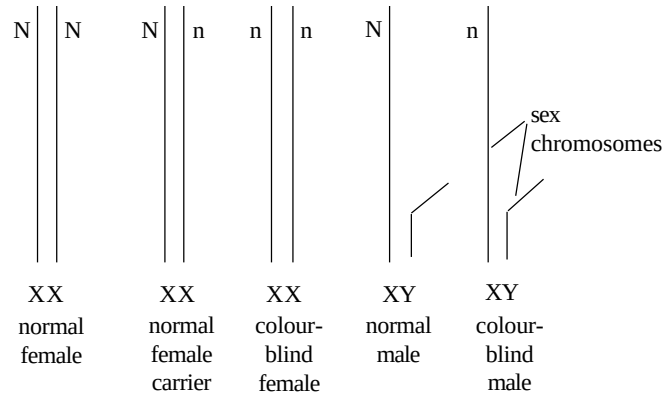
- In the male (XY) the recessive allele on the **differential segment of the X-chromosome**, (see fig 2), will be expressed because there is no second X-chromosome with a possible dominant allele present.
- In the female (XX), because two X-chromosomes are present, a recessive allele on the differential segment of the X-chromosome will usually be masked by the presence of the dominant allele on the other X-chromosome. The recessive allele will only be expressed if both X-chromosomes carry it - that is when the double recessive state is present. A female who is heterozygous for the character is called a carrier, because although she does not exhibit the recessive character she can pass it on to her offspring.

***Remember**:– the female (XX) is referred to as the **homogametic** sex because with respect to sex-chromosomes only one type of gamete (X- egg cell) is produced. The male (XY) is referred to as the **heterogametic** sex because with respect to the sex chromosomes two types of gamete are produced (X- sperm and Y-sperm)*

Fig 3 illustrates possible male and female genotypes for sex linkage.

Fig. 3. Possible male and female genotypes for sex linkage (red-green colour-blindness)

Let N be the dominant allele for normal colour vision.
Let n be the recessive allele for red-green colour-blindness.



Thus the possible genotypes and phenotypes are;

- $X^N X^N$ female with normal vision (homozygous dominant)
- $X^N X^n$ female with normal vision (heterozygous carrier of colour-blindness)
- $X^n X^n$ female with red-green colour-blindness (homozygous recessive)
- $X^N Y$ male with normal vision
- $X^n Y$ male with red-green colour-blindness

About 2.5% of men suffer from red-green colour-blindness but less than 0.1% of women have the condition. To have a chance of producing a red-green colour-blind female, a colour-blind man must have children by a carrier female. This is illustrated in the cross below.

***Exam Hint** – if you have to answer questions on sex linkage using a genetic cross, then write the cross out in the way shown below, which gives all the information. Alternatively, it is acceptable to use a punnet square diagram.*

Parental phenotypes:	carrier female		×	colour-blind male				
Parental genotypes:	$X^N X^n$			X^n Y				
Gametes:	50% X^N	50% X^n		50% X^n	50% Y			
Children:	$X^N X^n$ carrier female	$X^n X^n$ colour-blind female		X^N Y normal male	X^n Y colour-blind male			
Ratio:	1	: 1	:	1	: 1			

Other examples of X-linked inheritance

- haemophilia A and haemophilia B
- brown enamel on the teeth
- non-functional sweat glands
- absence of central incisors
- some types of deafness
- white forelocks
- juvenile glaucoma
- glucose-6-phosphate dehydrogenase (G6PD) deficiency
- juvenile muscular dystrophy
- retinitis pigmentosa
- coat colour in cats
- white eyes in Drosophila (fruit flies)
- yellow body colour in Drosophila

***Exam Hint** – data questions have been set on several of these conditions. Do not panic, just remember that the inheritance pattern for X-linked inheritance is always the same as for colour blindness.*

Haemophilia

Haemophilia is a blood disease in which the blood fails to clot adequately. Sufferers may bleed to death even from a trivial wound. Haemophilia A is most common and is due to a single recessive allele which results in a reduction in the amount of a specific clotting protein called 'anti-haemophiliac factor' (AHF) in the blood. This is the type of haemophilia which was present in Queen Victoria's family and Queen Victoria herself was a carrier of the condition. Haemophilia B is rarer and is called 'Christmas disease' after its discoverer. In this condition the recessive allele causes a reduction in the amount of the clotting protein 'plasma thromboplastin component' (PTC) in the blood. The following genetic cross shows the possible genotypes of Queen Victoria's children:

Let H be the dominant allele for normal blood clotting ability.
Let h be the recessive allele for haemophilia.

	Queen Victoria			Prince Albert				
Parental phenotypes:	carrier female		×	normal male				
Parental genotypes:	$X^H X^h$			$X^H Y$				
Gametes:	50% X^H	50% X^h		50% X^H	50% Y			
Children:	$X^H X^H$ normal female	$X^H X^h$ carrier female		X^H Y normal male	X^h Y haemophiliac male			
Ratio:	1	: 1	:	1	: 1			

Haemophiliac females can only result from interbreeding between a carrier (or haemophiliac) female and a haemophiliac male. This was impossible until recent years when clotting factors became available to curtail bleeding in haemophiliacs. Before that, haemophiliac males usually died, from haemorrhaging, in childhood.

***Remember:** – because haemophilia was normally a lethal condition that killed sufferers before they could reproduce and pass on the haemophilia allele, one would expect that the condition would rapidly become extinct. This does not happen because the normal blood clotting alleles constantly mutate into the haemophilia-causing alleles. However, the mutation rate is relatively low, for example, 1 in 20,000 live births in London (haemophilia A).*

Sex linkage was first clearly recognised in 1910 by Morgan and his co-workers using Drosophila. Morgan noticed a white-eyed male (mutant) which had suddenly appeared among his cultures of red-eyed flies. When he mated this white-eyed male with its red-eyed sisters he found that all the F_1 flies had red eyes. Thus white-eyes was recessive to red-eyes. When the F_1 flies were allowed to interbreed red-eyed and white-eyed flies appeared in a 3:1 ratio in the F_2 generation *but all the white-eyed flies were male*.

Morgan realised that the alleles controlling eye colour must be situated on the differential (unpaired) segment of the X-chromosome:

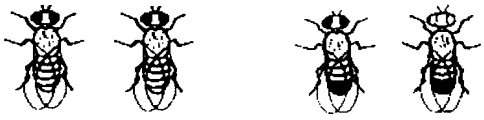
Let R be the dominant allele for red eyes.
Let r be the recessive allele for white eyes.

Parental phenotypes: red-eyed female × white-eyed male
Parental genotypes: $X^R X^R$ X^rY

Gametes: 100% X^R 50% X^r 50% Y

F_1 $X^R X^r$ × X^RY
red-eyed carrier female red-eyed male

Gametes: 50% X^R 50% X^r 50% X^R 50% Y



F_2

$X^R X^R$	$X^R X^r$	X^RY	X^rY
female	carrier female	male	male
3 red-eyed			1 white-eyed

X-linked inheritance in birds

In birds (and also in butterflies and moths) the females are the heterogametic sex (XY) and the males are the homogametic sex (XX). The same principles apply as in the examples of X-linkage above but remember that the pattern of inheritance will be reversed in the sexes, so that the females will tend to show the linked character most frequently and the males will be the carriers. Examples of X-linked inheritance characters in birds are:

- certain plumage colours in budgerigars (albino, cinnamon, lutino, opaline).
- red and white plumage colours in some breeds of poultry.
- barred plumage in chickens.

To distinguish the sex chromosomes of birds from the X –Y system the symbols Z and W are often used to identify the sex chromosomes. ZZ is male and ZW is female.

Y-linked inheritance

It is incorrect to say that the Y-chromosome is 'genetically empty' although it is true to say that the Y-chromosome contains few alleles. There are very few known examples of Y-linked conditions due to alleles carried on the holandric/non-homologous section of the Y-chromosome. Examples that are suspected to be Y-linked are:

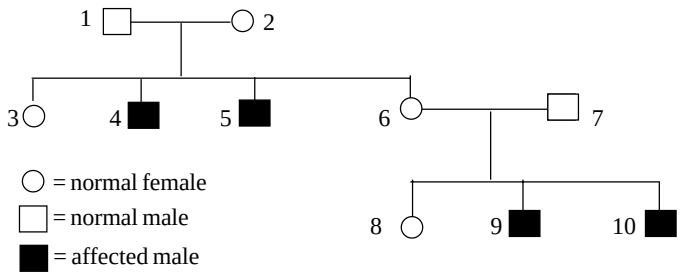
- porcupine skin
- webbed toes
- hairy external ears
- some forms of male sexual dysfunction

These conditions can only occur in men since women do not possess Y-chromosomes. They could only be passed from father to son.

Practice Questions

1. A gene for coat colour in cats has two alleles, B and b. The genotype BB gives a black coat colour, bb gives a ginger coat colour and Bb gives a tortoise-shell coat colour (mixed patches of black and ginger). Male cats never have tortoise-shell coats but can only be black or ginger.
   a) Suggest an explanation for the inheritance pattern of coat colour in cats. 5
   b) Give full genetic diagrams to illustrate,
      (i) a cross between a tortoise-shell female cat and a ginger male cat. 5
      (ii) a cross between a tortoise-shell female cat and a black male cat. 5

2. The family tree below shows the inheritance of Duchenne muscular dystrophy in a family. The disease is caused by a recessive allele of an X-linked gene.



   a) Write down the possible genotypes of individuals 1 to 10. Use D for the normal allele, d for the Duchenne allele and X and Y for the sex chromosomes. 10
   b) If individuals 6 and 7 were to have another child, what would be the probability of the child suffering from muscular dystrophy? 1
   c) Name two other X-linked diseases of humans. 2

3. In birds the female is the heterogametic sex. A budgerigar breeder found that a quarter of the eggs laid by one of his breeding pairs did not hatch. Of the young birds that did hatch, two thirds were males.
   a) Explain the meaning of the phrase 'the female is the heterogametic sex'. 2
   b) Suggest an explanation for:
      (i) the failure of some of the eggs to hatch. 2
      (ii) two thirds of the offspring being males. Include a genetic diagram in your answer. 8

4. a) Barred plumage in chickens is a dominant X-linked trait. Using B for the barred plumage allele, b for the normal plumage allele and X and Y for the sex chromosomes, write down the possible genotypes of:
      (i) a male with normal plumage,
      (ii) a male with barred plumage,
      (iii) a female with barred plumage,
      (iv) a female with normal plumage. 4
   b) Write down a full genetic diagram to show the possible results of a cross between a male who is heterozygous for barred plumage and a female who has normal plumage. 5

Answers

1. a) alleles B and b must be codominant;
must be carried on X-chromosome/X-linked;
carried on/locus on unpaired/differential segment (of X-chromosome);
thus males cannot be tortoiseshell because a male can only carry B or b but not Bb;
because male are XY and Y does not carry the colour allele; 5

b) (i)

Parental phenotypes: tortoise-shell female × ginger male
Parental genotypes: $X^B X^b$ $X^b Y$;

Gametes: 50% X^B 50% X^b 50% X^b 50% Y;

Offspring: $X^B X^b$ tortoise-shell female; $X^b X^b$ ginger female; $X^B Y$ black male; $X^b Y$ ginger male;
Ratio: 1 : 1 : 1 : 1 ; 5

(ii)

Parental phenotypes: tortoise-shell female × black male
Parental genotypes: $X^B X^b$ $X^B Y$;

Gametes: 50% X^B 50% X^b 50% X^B 50% Y ;

Offspring: $X^B X^b$ tortoise-shell female; $X^B X^B$ black female; $X^B Y$ black male; $X^b Y$ ginger male ;
Ratio: 1 : 1 : 1 : 1 ; 5

2. a) 1. $X^D Y$; 2. $X^D X^d$; 3. $X^D X^D$ or $X^D X^d$; 4. $X^d Y$; 5. $X^d Y$; 6. $X^D X^d$; 7. $X^D Y$; 8. $X^D X^D$ or $X^D X^d$; 9. $X^d Y$; 10. $X^d Y$; 10

b) 1 in 4 chance of having an affected male child; 1

c) haemophilia; red-green colour blindness;
(allow other correct examples) 2

3. a) the female is the sex with differing sex chromosomes;
females are XY/ZW and males are XX/ZZ; 2

b) (i) presence of a lethal allele/an allele that prevents hatching;
probably formed by gene mutation; 2

(ii) mutant allele carried on the X-chromosome/X-linked; (allow Z)
must be a recessive allele;
ref to the male being the carrier;

(Let H = normal allele an h = recessive lethal allele)

Parental phenotypes: carrier male × normal female
Parental genotypes: $X^H X^h$ $X^H Y$;

Gametes: 50% X^H 50% X^h 50% X^H 50% Y ;

Offspring: $X^H X^H$ normal male; $X^H X^h$ carrier male; $X^H Y$ normal female; $X^h Y$; female does not hatch;
Ratio: 1 : 1 : 1 : 0 ; 8

4. a) (i) $X^b X^b$; (ii) $X^B X^B$ and $X^B X^b$; (iii) $X^B Y$; (iv) $X^b Y$; 4

b)

Parental phenotypes: barred (carrier)male × normal female
Parental genotypes: $X^B X^b$ $X^b Y$;

Gametes: 50% X^B 50% X^b 50% X^b 50% Y ;

Offspring: $X^B X^b$ barred (carrier) male; $X^b X^h$ normal male; $X^B Y$ barred female; $X^b Y$ normal female;
Ratio: 1 : 1 : 1 : 1 ; 5

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