

FIGURE 14.1 A scanning electron micrograph of some double-stranded chromosomes (dyads). The DNA in these chromosomes has been replicated; this means that the chromosomes are composed of two sister chromatids. The inset shows TH Morgan, an American geneticist, whose experiments in 1910 with the fruit fly (*Drosophila melanogaster*) revealed that chromosomes are the carriers of the genes.

KEY KNOWLEDGE

This chapter is designed to enable students to:

- develop knowledge and understanding that chromosomes are packages of DNA containing the genetic material of organisms
- distinguish between autosomes and sex chromosomes
- recognise that chromosomes occur as homologous pairs that, in the case of the autosomes, carry the same gene loci
- identify the abnormalities that underpin human chromosomal disorders including Down syndrome
- gain understanding that the chromosomes of an organism can be shown as various presentations.



ODD FACT

Autumn crocus is not a crocus. It can be distinguished from true crocuses by the presence of 6 stamens. True crocuses have just three stamens.



FIGURE 14.2 Autumn crocus flowers, also known as naked ladies and meadow saffron. The flowers appear some time after the leaves have died off — hence the common name ‘naked ladies’.

Chromosomes: how many?

A small plant (*Colchicum autumnale*) that grows across southern Europe has the common names meadow saffron, autumn crocus and naked lady. The name ‘naked lady’ is due to the fact that after the leaves of the plant appear in spring they die off, and the flowers appear in autumn on their own (see figure 14.2).

This simple but beautiful plant is poisonous. Deaths have occurred, often after a person has mistaken the plant for wild garlic and eaten its bulb-like corm. The poison in the autumn crocus is an alkaloid, known as **colchicine**. This poison was to play an important role in establishing the correct count of the human chromosomes in somatic cells, that is, discovering that the diploid number ($2n$) of chromosomes is 46.

Treatment of plant and animal cells with colchicine stops mitosis. Colchicine acts by interfering with spindle formation by binding to and disrupting the microtubules that form the structural elements of the mitotic spindle. If the spindle is faulty, the migration of chromosomes at anaphase cannot occur. Instead, the chromosomes are left at metaphase of mitosis. So, dividing cells treated with colchicine will stop their progress through the cell cycle at metaphase.

Two techniques were critical in establishing that the normal number of chromosomes in a human somatic cell was 46 ($2n = 46$). These techniques were (1) the use of **hypotonic shock treatment** of dividing cells, which causes the contents of the nucleus including the chromosomes to spread, and (2) the use of colchicine to arrest the dividing cells at metaphase, which causes the chromosomes to contract and thicken. As a result, the cell sample contains a higher proportion of cells at metaphase than normal. The combination of hypotonic shock and colchicine treatment produces so-called **metaphase spreads**, in which the chromosomes can be viewed, each clearly distinguishable and nonoverlapping. Figure 14.3 shows a typical metaphase spread of human chromosomes arrested at metaphase by virtue of a pretty little flowering plant: the autumn crocus.

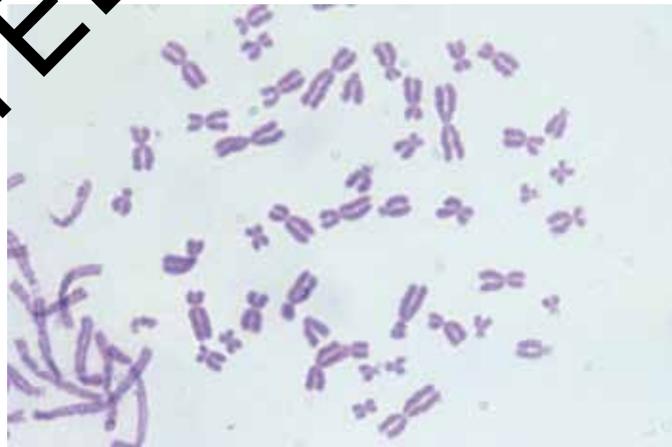


FIGURE 14.3 A metaphase spread of human chromosomes. Note that the chromosomes are spread out and do not overlap. As a result of colchicine treatment of dividing cells the proportion of cells at metaphase was increased. (Why? Because they cannot proceed further!) The chromosomes in the lower left-hand corner are from another cell and they are at late prophase.

In 1956, two scientists, Tjio and Levan, published a scientific paper that correctly reported the diploid number of human chromosomes as 46 (JH Tjio and A Levan, ‘The chromosome number of man,’ *Hereditas*, vol. 42, no. 1-2, 1956). This number was based on clear images of chromosomes made using hypotonic shock and colchicine treatment techniques. For decades before 1956 the

ODD FACT

In the early years of the twentieth century published counts of diploid human chromosomes ranged from as low as eight to as high as 50. A paper published in 1921 identified the number as 48 and that was the accepted figure until the Tjio and Levan paper of 1956.

FIGURE 14.4 Drawing of human chromosomes from a textbook published in 1934. The chromosome number is identified here as 48.

(Source: LC Dunn, *Heredity and Variation*, The University Society, New York, p. 46, 1934.)

accepted diploid number of human chromosomes was 48, based on images in a scientific paper published in 1921.

Contrast the clarity of the chromosomes in figure 14.3 with those in figure 14.4, which shows drawings of human chromosomes from a textbook published in 1934 and identifies the diploid number as 48. This crowded image of overlapping chromosomes was the best that could be obtained at this time—very different from the clear images obtained by Tjio and Levan in 1956.



The diploid number of chromosomes in human somatic cells is $2n = 46$ and the haploid number of chromosomes present in mature human gametes (eggs and sperm) is $n = 23$.

Other species of plants and animals have their characteristic diploid and haploid chromosome numbers. Table 14.1 identifies the diploid number of chromosomes in several animal and plant species.

TABLE 14.1 Diploid numbers of chromosomes in somatic cells of various species. What number would be expected in the sperm and egg cells of a rabbit?

Species	Diploid number ($2n$)
Animal	
chicken (<i>Gallus gallus</i>)	78
butterfly (<i>Lysandra nivescens</i>)	190
cat (<i>Felis catus</i>)	38
dog (<i>Canis familiaris</i>)	78
bilby (<i>Macrotis lagotis</i>)	19 (male) 18 (female)
garden snail (<i>Helix aspersa</i>)	54
honeybee (<i>Apis mellifera</i>)	32
housefly (<i>Musca domestica</i>)	12
leopard seal (<i>Hydrurga leptonyx</i>)	34
platypus (<i>Ornithorhynchus anatinus</i>)	52
rabbit (<i>Oryctolagus cuniculus</i>)	44
Eastern tiger snake (<i>Notechis scutatus</i>)	34
fruit fly (<i>Drosophila melanogaster</i>)	8
ant (<i>Myrmecia pilosula</i>)	2

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TABLE 14.1 (continued)

Species	Diploid number (2n)
Plant	
crimson bottlebrush (<i>Callistemon citrinus</i>)	22
drooping she oak (<i>Casuarina stricta</i>)	26
edible pea (<i>Pisum sativum</i>)	14
ginkgo (<i>Ginkgo biloba</i>)	24
Iceland poppy (<i>Papaver nudicaule</i>)	14
kangaroo paw (<i>Anigozanthos flavidus</i>)	12
Ovens wattle (<i>Acacia pravissima</i>)	20
pineapple (<i>Ananas comosus</i>)	50
river red gum (<i>Eucalyptus cameldulensis</i>)	20
silky oak (<i>Grevillea robusta</i>)	20
silver wattle (<i>Acacia dealbata</i>)	26
Sydney blue gum (<i>Eucalyptus saligna</i>)	22
tomato (<i>Lycopersicon esculentum</i>)	24
corn (<i>Zea mays</i>)	20

Organising chromosomes

A metaphase spread of human chromosomes is viewed through a microscope and the chromosomes are seen to be arranged randomly. In another metaphase spread the chromosomes would have different random arrangements. Contrast the two different arrangements of the same diploid set of chromosomes in figure 14.5. In figure 14.5a, the chromosomes are arranged randomly as a metaphase spread. In figure 14.5b, the chromosomes are organised by size and centromere position into matching or homologous pairs in an arrangement known as a **karyotype**.

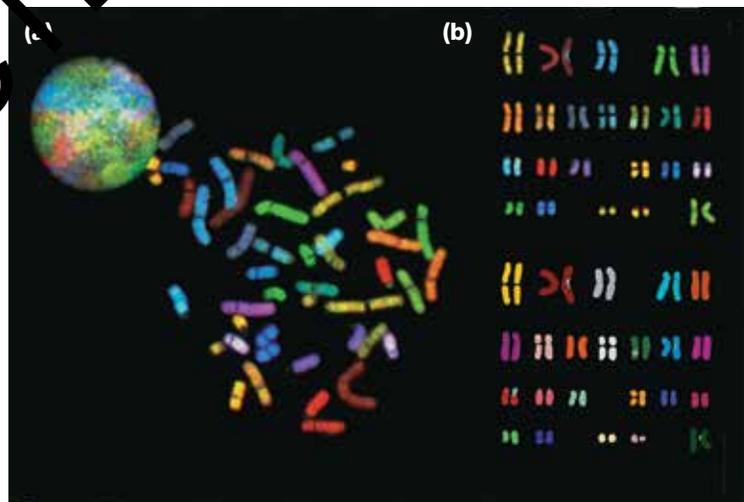


FIGURE 14.5 Spectral karyotyping of human chromosomes (a) Metaphase plate showing random arrangement of chromosomes after the simultaneous hybridisation of 24 differentially labelled chromosome painting probes (b) Organisation of the chromosomes into an arrangement called a karyotype. The image was acquired using spectral imaging through a custom-designed filter cube from Chroma Technology. (SKY™ is a registered trademark of Applied Spectral Imaging.) (Image courtesy of Evelin Schröck, Stan du Manoir, Thomas Ried and Chroma Technology)

Karyotypes are used to assist in the analysis of the chromosomes that are present in cells. In a karyotype, the chromosome images are organised in a pattern according to an international convention. Such an arrangement enables any abnormality in either number or structure of the chromosomes to be quickly identified (see figure 14.6).

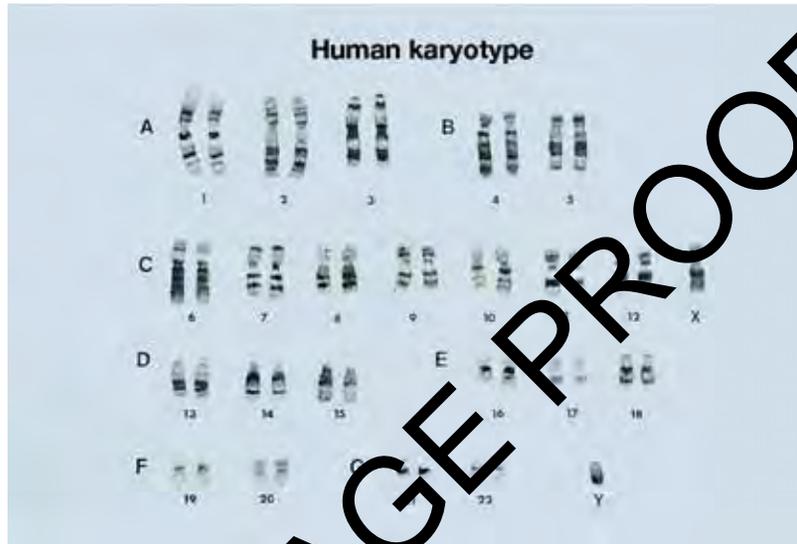


FIGURE 14.6 Chromosomes of a normal human male arranged into a karyotype. These chromosomes have been treated with a particular staining technique that results in a distinctive pattern of light and dark bands on each chromosome. How might this assist identification of matching (homologous) pairs of chromosome?

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As well as using conventional stains, chromosomes can also be stained using a range of probes with fluorescent labels that bind to specific segments of DNA on the different human chromosomes. Figure 14.7 shows a karyotype with these fluorescent labels. Each chromosome has a distinctive colour.

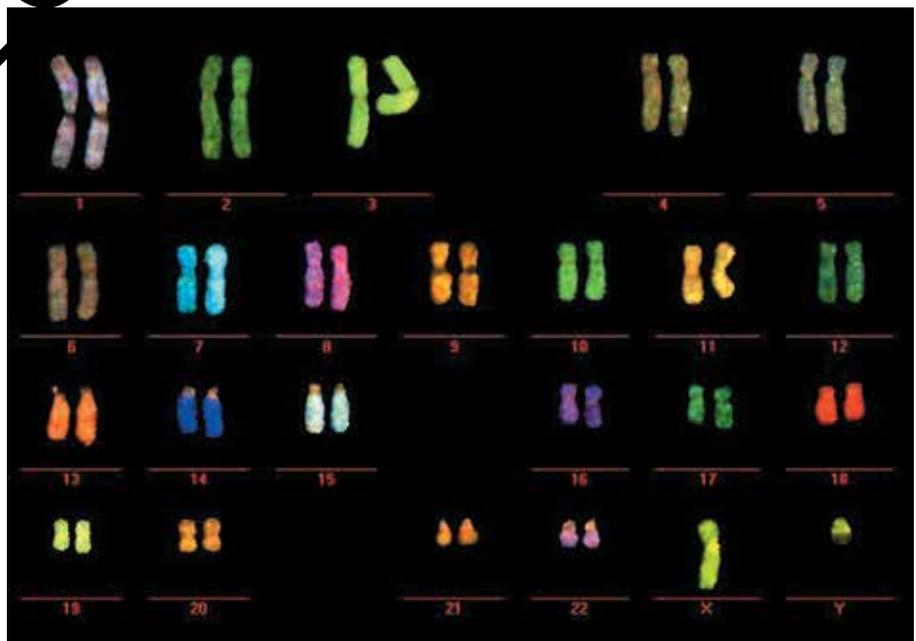


FIGURE 14.7 A spectral karyotype showing the distinctive colours of each human chromosome. Each homologous pair of chromosomes fluoresces with a distinctive colour as determined by the colour of specific fluorescent probes that bind to specific sequences in the DNA of each particular chromosome.

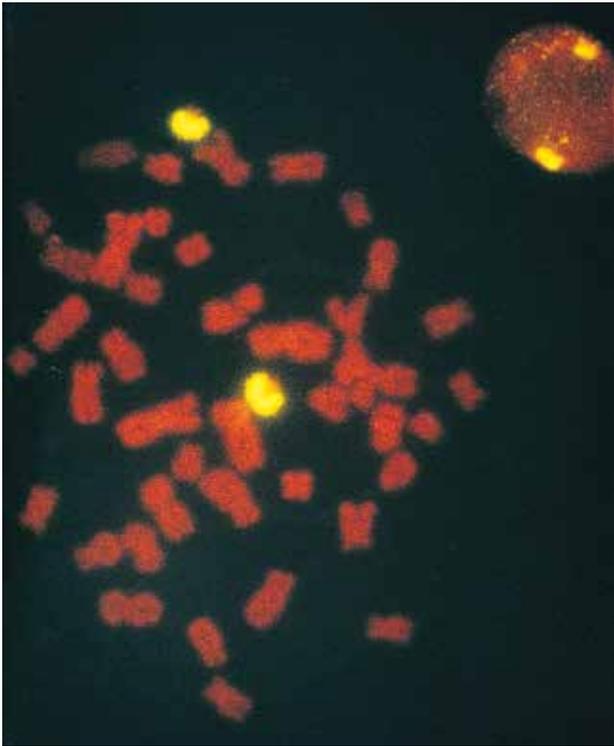


FIGURE 14.8 A fluorescent probe that appears bright yellow has been mixed with chromosomes. The probe is specific for the Y chromosome. At how many sites has the Y-specific probe become bound? The second cell (upper right) is at metaphase of mitosis.

A type of fluorescent staining called **FISH** (fluorescent in-situ hybridisation) can be used to identify specific chromosomes or short segments of specific chromosomes. Figure 14.8 shows the fluorescent labelling of the human Y chromosome where a labelled probe specific to a segment of DNA on the Y chromosome has been used to distinguish it from the other human chromosomes.

Another representation of human chromosomes is called an **ideogram**. Ideograms are schematic representations of chromosomes that show their relative sizes and the distinctive banding pattern of each chromosome (see figure 14.9). These banding patterns are produced using a specific staining.

The 46 human chromosomes from a normal human male can be arranged into 23 pairs of chromosomes, consisting of 22 matched pairs and one 'odd' pair that is made up of one larger X chromosome and a smaller Y chromosome. In a normal female, a similar arrangement is seen, except that there are two X chromosomes and no Y chromosome. The pair of chromosomes that differs between the sexes makes up the **sex chromosomes**. A shorthand way of denoting the pairs of chromosomes for each sex is as follows — normal human male: 46, XY, and normal female: 46, XX. (Note that the number indicates the total number of chromosomes including the sex chromosomes and the letters denote the sex chromosomes.) A similar pattern is seen in other mammals where the female typically has two X chromosomes and the male has one X and one Y chromosome. This is not the case in other animal groups.

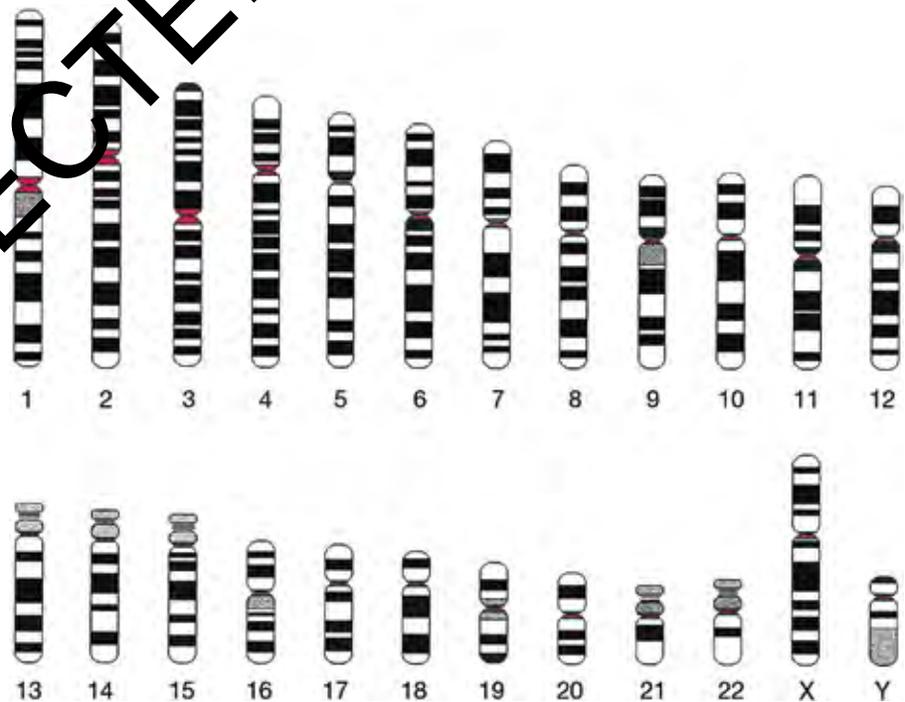


FIGURE 14.9 An ideogram of human chromosomes showing the stylised representation of the chromosomes

The 22 matched pairs of chromosomes present in both males and females are termed **autosomes**. These different autosomes can be distinguished by:

- their relative size
- the position of the **centromere**, which appears as a constriction along the chromosome. In some cases, the centromere is near the middle (e.g. the number-2 chromosome in figure 14.6), while in others it is close to one end (e.g. the number-13 chromosome in figure 14.6).
- patterns of light and dark bands that result from special staining techniques.

Autosomes are identified by the numbers 1 to 22 in order of decreasing size; the number-1 chromosomes are the longest, and the number-21 and number-22 chromosomes are the smallest. The larger the chromosome, the more DNA it contains and usually the greater the number of genes that it carries.

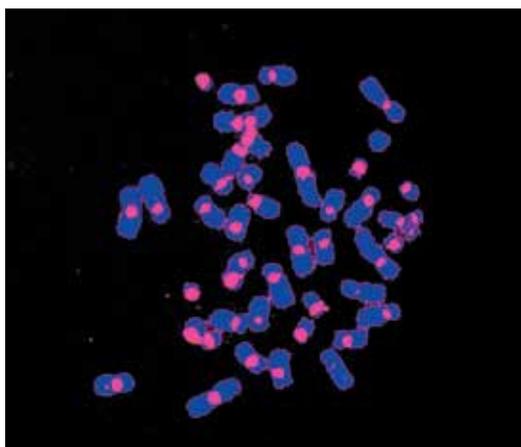


FIGURE 14.10 Human chromosomes with their centromeres made visible with a probe labelled with a pink fluorescent dye that binds to the centromeric DNA of all chromosomes. The remainder of the chromosomes have been stained with a blue fluorescent dye. Can you identify a chromosome with a centromere near the end of the chromosome?

The members of each matching pair of chromosomes, such as the two number-5 chromosomes, are said to be **homologous**. Nonmatching chromosomes, such as a number-5 chromosome and a number-14 chromosome are said to be **nonhomologous**.

At a particular location along its length, each chromosome has a constriction that is known as a **centromere**. In human chromosomes, the DNA at the centromere contains about one million base pairs and much consists of repeated sequences of bases. Figure 14.10 shows the chromosomes from a dividing white blood cell where the chromosomes have been hybridised with a pink fluorescent probe that binds to the DNA of the centromere. The centromere is surrounded by a structure, known as the **kinetochore**, that is made of protein. The kinetochore forms the attachment point for the spindle fibres that are necessary for the orderly movement of chromosomes during both cell division (mitosis) and

gamete formation (meiosis). This orderly movement of chromosomes ensures that each daughter cell formed by mitosis has a double (diploid) set of chromosomes and that gametes formed by meiosis contain a single (haploid) set of chromosomes.

Human chromosomes, like the chromosomes of other eukaryotes, have distinctive ends. Chromosome ends are known as **telomeres** and they consist of DNA made up of many thousands of repeats of short sequences of base pairs. In your chromosomes, the repeated sequence is TTAGGG. Telomeres prevent chromosomes sticking together and they enable complete replication of chromosomes to occur. To review telomeres, refer to figure 9.20 on page 405.

Analysing karyotypes

Mistakes in chromosome numbers or abnormalities of single chromosomes can produce congenital disorders. In addition, specific chromosome abnormalities are associated with various cancers and these chromosome changes can indicate the likelihood of remission. Scientists who specialise in the study of human karyotypes are known as **cytogeneticists**.

Today, in hospital cytogenetic laboratories, images of chromosome sets from cells are captured by a camera attached to a microscope (see figure 14.11). The images are then transferred to a computer where a scientist uses special software, such as CytoVision[®], that analyses the chromosomes from cells and automatically generates a karyotype (see figure 14.11). The chromosomes in a minimum of 15 cells must be examined before a karyotype can be decided. This computer-based automation has increased the capacity of hospital laboratories to prepare the karyotypes that are important in diagnosis of conditions such as Down syndrome, where an extra number-21 chromosome is present, or Prader-Willi syndrome, in which a small deletion of the number-15 chromosome occurs.

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FIGURE 14.11 A scientist in a cytogenetic laboratory analyses a patient's chromosomes under a microscope and studies the display on a computer screen.

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Abnormalities in chromosome number

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Wrong numbers and other errors

Various changes can occur involving chromosomes, including:

- changes in the total number of chromosomes
- changes involving part of one chromosome
- changed arrangements of chromosomes.

Changes in total number

Some newborn babies have an abnormal number of chromosomes in their cells. A baby may have an additional chromosome, giving a total of 47 instead of the normal 46. **One additional chromosome or one missing chromosome typically has deleterious effects** on development and, for most chromosomes, death occurs during early development and the pregnancy never proceeds to term.

A pregnancy may still be carried to term if the chromosomal changes involve a few particular chromosomes (see table 14.2). The most common chromosomal anomaly seen in human populations is **Down syndrome (DS)**, in which there is an additional copy of the number-21 chromosome. When three copies of a chromosome occur, instead of the typical pair of chromosomes, a cell or an organism is said to be **trisomic** for that chromosome. When one member of the typical pair of chromosomes is missing, the condition is termed **monosomy**. Monosomy causes embryonic death, except for a monosomy involving the sex chromosomes.

Using the shorthand mentioned on page 526 to show the karyotype, for example, 46, XX, a missing sex chromosome is usually indicated with the symbol 'O'. If an extra entire autosome is present, this is shown by the chromosome number with a plus sign in front of it, for example, +21. A plus or a minus sign after the chromosome number indicates that only part of a chromosome is either present (+) or missing (-), and either a 'p' (short) or a 'q' (long) symbol is used to denote which arm of the chromosome is involved. Table 14.2 gives some examples of shorthand notations of a karyotype.

TABLE 14.2 Some examples of chromosome changes and approximate incidence rates. Which syndrome is an example of a trisomy? A monosomy? The XYY condition does not have a clinical name.

Chromosome change	Resulting syndrome	Approximate incidence rate
<i>Addition: whole chromosome</i>		
extra number-21 (47, +21)	Down syndrome	1/700 live births
extra number-18 (47, +18)	Edwards syndrome	1/3000 live births
extra number-13 (47, +13)	Patau syndrome	1/5000 live births
extra sex chromosome (47, XXY)	Klinefelter syndrome	1/1000 male births
extra Y chromosome (47, XYY)	n/a	1/1000 male births
<i>Deletion: whole chromosome</i>		
missing sex chromosome (46, XO)	Turner syndrome	1/5000 female births
<i>Deletion: part chromosome</i>		
missing part of short arm of number-4 (46, 4p-)	Wolf-Hirschhorn syndrome	1/50 000 live births
missing part of short arm of number-5 (46, 5p-)	cri-du-chat syndrome	1/25 000 live births

Changes to parts of chromosomes

Changes can occur that involve part of a chromosome, such as:

- **duplication**, in which part of a chromosome is duplicated (see figure 14.12a)
- **deletion**, in which part of a chromosome is missing (see figure 14.12b), as in cri-du-chat syndrome, for example, so named because affected babies have a cat-like cry (see table 14.2).

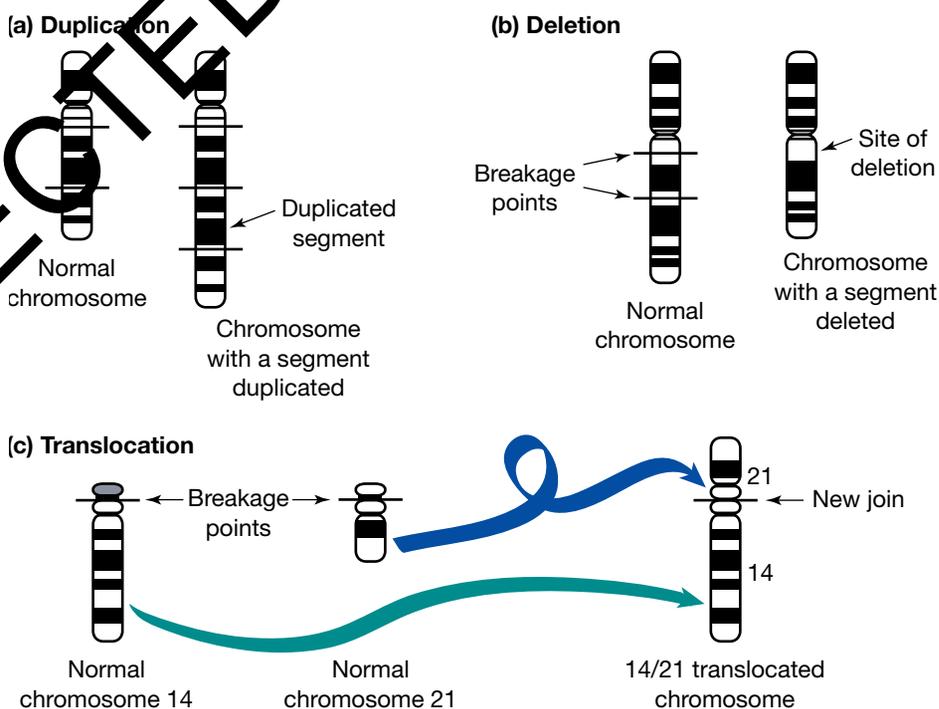


FIGURE 14.12 (a) Normal chromosome and the same chromosome showing a duplication (b) Normal chromosome and the same chromosome showing a deletion (c) An example of a 14/21 translocation

Re-arrangements of chromosomes

Structural changes may occur in which the **location of a chromosome segment is altered** so that it becomes relocated to a new region within the karyotype. Such a change is known as a **translocation**. One example is related to a special case of Down syndrome when part of the number-21 chromosome becomes physically attached to a number-14 chromosome (see figure 14.12c). **The parental origin of the chromosomes is also important.** Normally a child inherits one member of each chromosome pair from each of its parents. If both copies of a particular chromosome are inherited from one parent, instead of the usual one from each parent, abnormalities of development result. For example, **Angelman syndrome**, characterised by poor motor coordination and mental retardation, can result if an **embryo** inherits both of its number-15 chromosomes from its mother and none from its father.

A case of Down syndrome

Michael (see figure 14.13a) is a young boy who has 47 chromosomes in his body cells, instead of the normal 46. His karyotype shows the presence of an extra number-21 chromosome, which is typical of the condition Down syndrome. This karyotype can be denoted as 47,XY,+21 (where '47' denotes the total number of chromosomes, 'XY' denotes the sex chromosomes present, and '+21' denotes the identity of the extra chromosome).

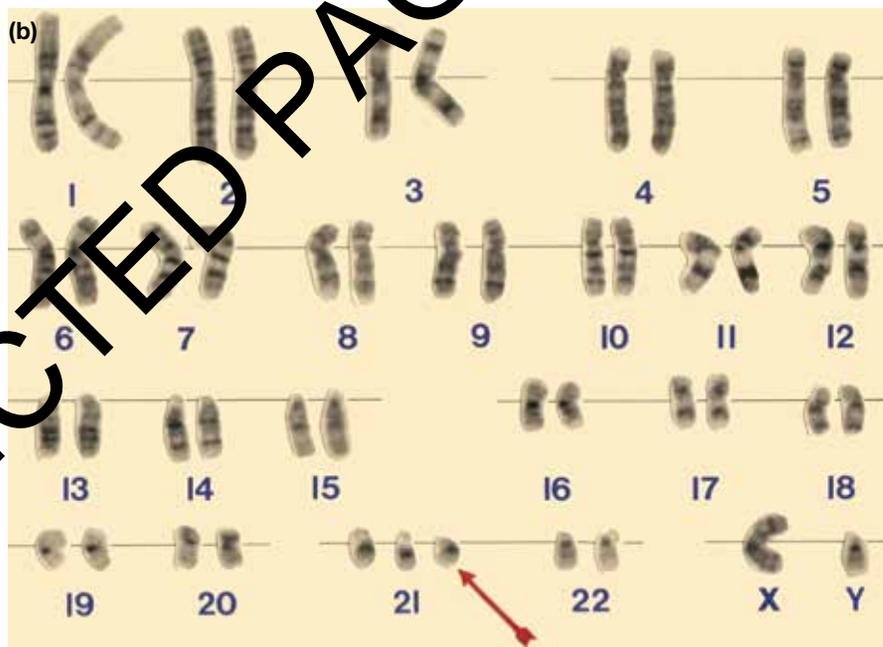
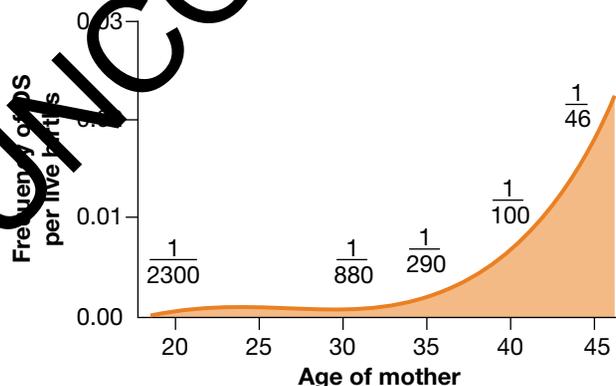


FIGURE 14.13 (a) Michael, pictured aged 11, is a DS boy who enjoys using a computer, which is one of his many interests. (b) A typical karyotype from a DS male like Michael. Which chromosome is present as a trisomy?



About one in 700 babies born in Australia has an extra number-21 chromosome, but the rate differs according to the age of the mother (see figure 14.14). The risk of having a DS baby increases with maternal age; the risk for mothers aged 20 is about 1/2300, while the risk for mothers aged 40 is about 1/100.

FIGURE 14.14 Incidence of DS births for mothers of different ages. How does the risk of a DS baby for a 40-year-old woman compare with that for a 20-year-old? Increased father's age also increases the risk, but to a lesser extent.

The presence of an extra number-21 chromosome produces various symptoms including a fold on the inner margin of the upper eyelid, a smaller than normal mouth cavity and distinctive creases on the palms of the hands and the soles of the feet. The trisomy condition in which three separate copies of the number-21 chromosome are present in the karyotype is the most common form of DS. In most cases, the extra number-21 chromosome is transmitted via an abnormal egg with 24 chromosomes, including two number-21 chromosomes. If this egg is fertilised by a normal sperm (with 23 chromosomes including one number-21 chromosome), a DS embryo will result (see figure 14.15).

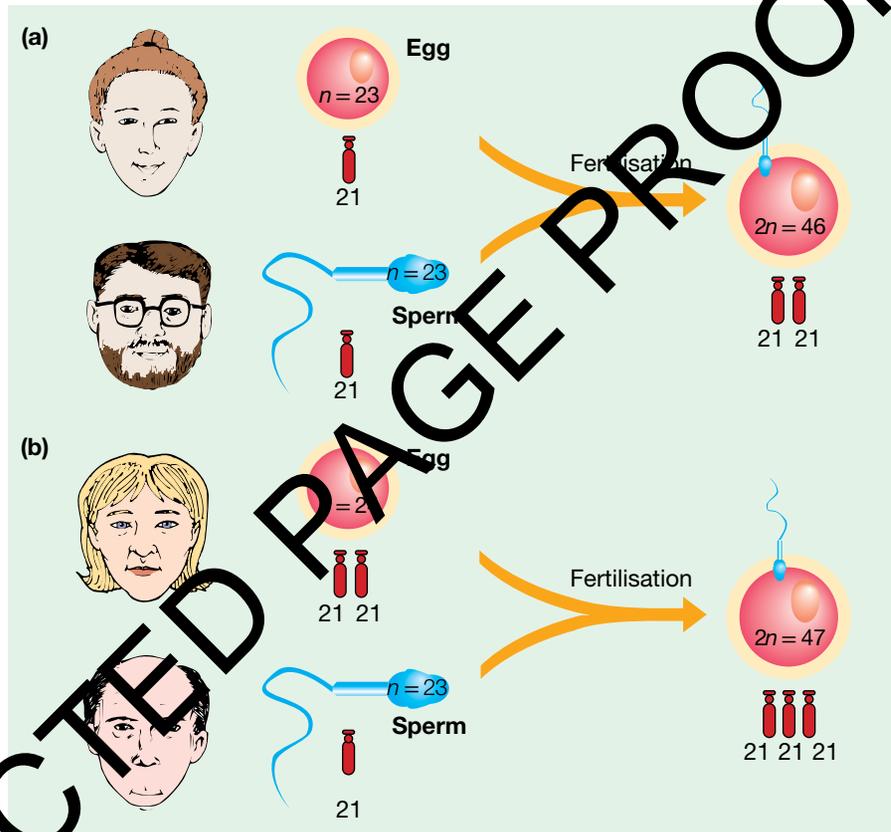


FIGURE 14.15 (a) Fertilisation of normal gametes (b) Possible gametes involved in fertilisation to produce a DS zygote (In both (a) and (b), the number-21 chromosomes are shown separately.)

An abnormal egg results when, during the process of egg formation by meiosis in the ovary, **the normal separation of the two copies of chromosome 21 to opposite poles of the spindle does not occur. This type of error is known as a nondisjunction** and is unpredictable. For parents who have a DS child who is a result of nondisjunction during egg formation in the mother (or during sperm production in the father), the risk of a second child with DS is low and is determined by the mother's age. When a child with DS is born, new challenges arise for the family concerned. Read the box on page 535, about Jane, a young woman with DS, as told by her mother.

Another form of DS: translocation

Each year in Australia, a few babies are born who show all the clinical signs of DS. Their karyotype, however, shows just 46 chromosomes, instead of the 47 expected in DS. So, what has happened?

In these cases, a third number-21 chromosome is present, but it is not a separate chromosome. Instead, the extra number-21 is joined to another chromosome, for example, the number-14 chromosome, through a translocation (see figure 14.16). As a result, the total number of chromosomes in somatic cells of this rarer form of DS is 46.

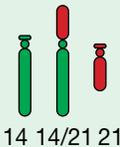
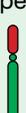
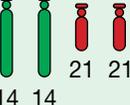
Leanne's parents	Total number of chromosomes	View of number-14 and number-21 chromosomes	Possible gametes			
	45	 14 14/21 21	Type A 	Type B 	Type C 	Type D 
	46	 14 14 21 21	 14 21			

FIGURE 14.16 A translocation form of Down syndrome in which the condition is inherited. Note that the mother can produce four kinds of egg in terms of their chromosomal make-up. Baby Leanne resulted from the fertilisation of an egg of type C with a normal sperm. What would result when an egg of type B was fertilised? A fertilised type-D egg would die. Why?

Baby Leanne has DS. Examination of her chromosomes showed a total of 46 chromosomes. The third copy of the number-21 chromosome is attached to one of her number-14 chromosomes. This type of DS is called translocation DS, because the extra number-21 chromosome has been transferred to an unusual location on another chromosome.

When a translocation DS baby is detected, the chromosomes of its parents are also investigated because many cases of translocation DS are inherited. When this is the case, one of the parents is found to have 45 instead of the expected 46 chromosomes (see figure 14.16) because this parent has one of the number-21 chromosomes translocated to another chromosome. In these cases, the chance that the next child will be affected is theoretically about one in three but in reality is about one in 10.

Errors in sex chromosomes

During gamete formation by meiosis, critical events include the orderly disjunction of homologous chromosomes to opposite poles of the spindle. In some cases, nondisjunction of homologous chromosomes may occur, for example, at anaphase 2 of meiosis, such that a gamete may have two copies of one chromosome instead of the normal single copy, or a gamete may be lacking a copy of one chromosome (see figure 14.17). The failure of homologous chromosomes to separate to opposite poles of their spindle at anaphase, or nondisjunction, during meiosis creates some gametes with an extra chromosome and some with a missing chromosome.

If nondisjunction events such as these involve one of the sex chromosomes, the fertilisation of an abnormal gamete by a normal gamete will produce a zygote with an imbalance in its sex chromosomes. Table 14.3 shows some possible abnormal outcomes, as well as the normal XX female and the normal XY male outcomes. Remember that the 'O' does not denote a chromosome, it denotes that a chromosome is missing. Gametes that are the result of a nondisjunction at anaphase 2 of meiosis are shown in red.

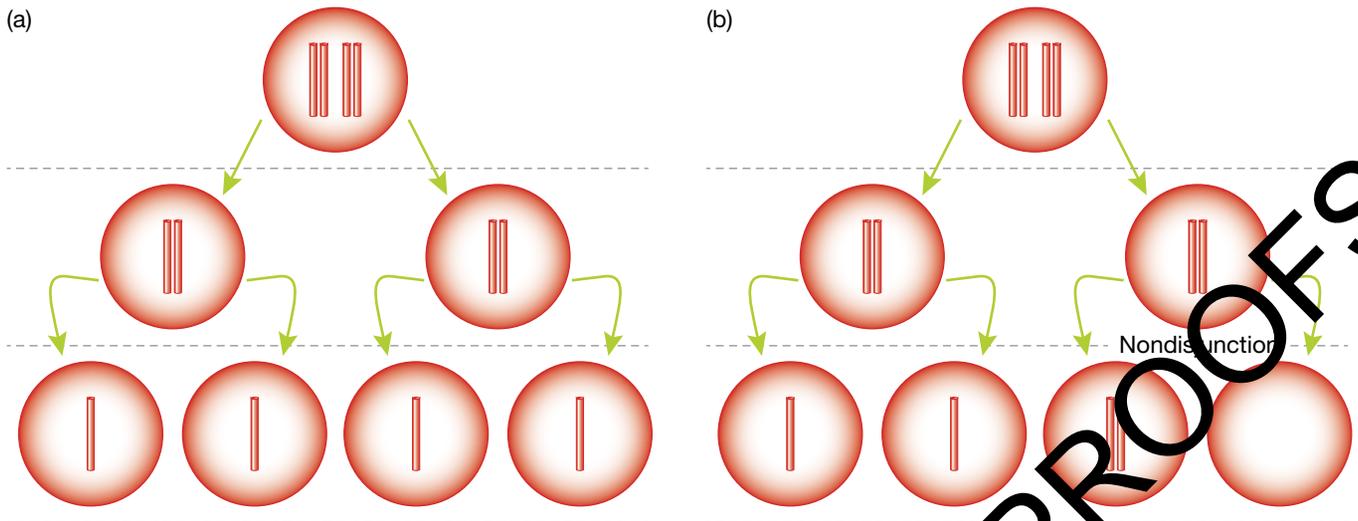


FIGURE 14.17 (a) The disjunction of a chromosome pair during an error-free meiosis. The duplicated pair of homologous chromosomes in the cell in the top of the diagram undergoes two anaphase separations to produce four gametes, each with a single copy of the chromosome. (b) The result of a nondisjunction of homologous chromosomes in anaphase 2 of meiosis

TABLE 14.3 Possible outcomes, in terms of sex chromosomes of fertilisation of an egg by a sperm, where in some cases one gamete is abnormal because of a nondisjunction of the sex chromosomes at anaphase 2 of meiosis

Egg of female parent	Sperm of male parent	Resulting zygote
X	X	XX, normal female
X	Y	XY, normal male
XX	X	XXX, triple X female
XX	Y	XXY, Klinefelter syndrome
X	XY	XXY, Klinefelter syndrome
O	X	XO, Turner syndrome
X	O	XO, Turner syndrome
O	Y	OY, nonviable
X	YY	XYY, double Y male

Of the possible outcomes, two result in a person with clinical abnormalities: Turner syndrome (45, XO) and Klinefelter syndrome (47, XXY). Persons with Turner syndrome are female and display clinical signs including sterility because of the absence of a uterus. Persons with Klinefelter syndrome are male and display clinical signs that include sterility and often female-type breast development. In contrast, females who are 47, XXX and males who are 47, XXY show no clinical signs, are fertile and typically would be unaware of their less usual chromosomal status.

If we compare the situation between the autosomes and the sex chromosomes, it becomes apparent that changes to the numbers of autosomes are far more drastic in their effects than changes to the numbers of sex chromosomes.

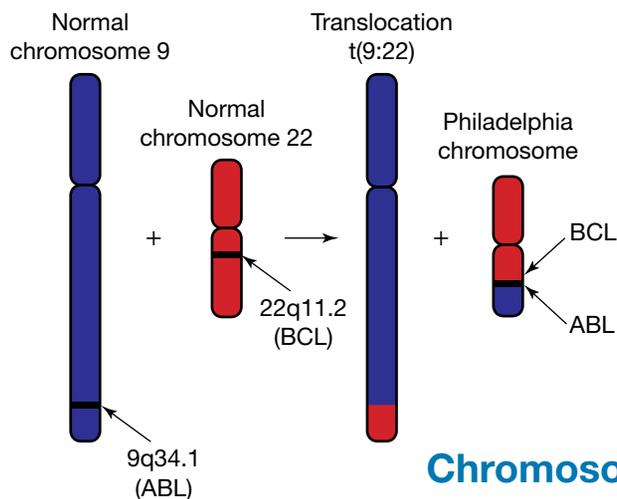


FIGURE 14.18 Diagram showing the reciprocal exchange that occurs between chromosome 9 and chromosome 22 in chronic myeloid leukaemia. The relocation of the **ABL** and the **BCR** genes into close proximity on the Philadelphia chromosome has been shown to be the cause of chronic myeloid leukaemia.

All cases of monosomy of an autosome are nonviable resulting in embryonic death, but the monosomy XO (Turner syndrome) is viable. This indicates that two copies of each autosome are essential for prenatal development. In contrast, even with only one X chromosome, prenatal development proceeds and the affected female survives into adulthood. However, the absence of both X chromosomes creates a nonviable situation.

Only a few cases of trisomy of an autosome are viable, and of these only trisomy 21 (Down syndrome) normally survives into adulthood. In contrast, a person with XXX trisomy shows no clinical signs. (We will see in chapter 15 why this is the case — it is called X inactivation.)

Chromosomal changes in cancer

In cancerous tissues multiple changes occur in the chromosomes of cells, such as where part of one chromosome becomes attached to a nonhomologous chromosome, or extra copies of chromosomes are present or chromosomes are missing.

For example, more than 90 per cent of patients with chronic myeloid leukaemia have a chromosomal change that produces a so-called Philadelphia (Ph) chromosome. The Ph chromosome is seen in bone marrow cells and it consists of the bulk of the number-22 chromosome to which part of the number-9 chromosome is attached. Likewise, the number-9 chromosome carries the missing part of the number-22 chromosome (see figure 14.18). This chromosomal change where an exchange of segments occurs between two nonhomologous chromosomes is termed a **reciprocal translocation**, in this case denoted t(9;22). Karyotypes using the FISH staining restricted to just two chromosomes can assist in identifying these changes, such as the reciprocal translocations in chronic myeloid leukaemia (see figure 14.19).

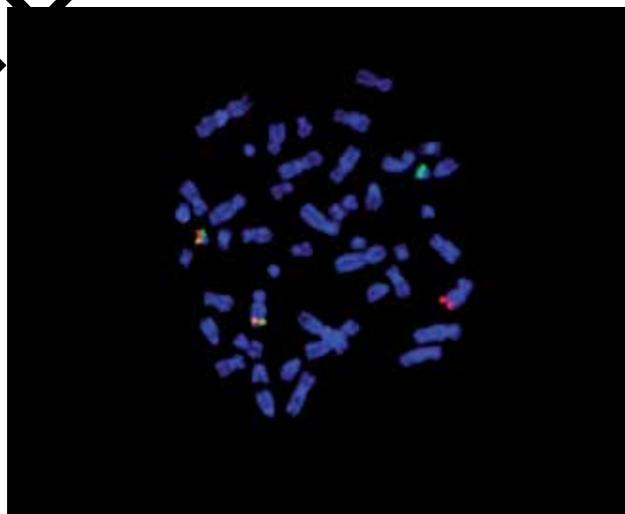


FIGURE 14.19 FISH staining of the metaphase chromosomes using fluorescent probes that bind specifically to the **ABL** gene (red) on chromosome 9 and the **BCR** gene (green) on chromosome 22, in a cell from a person with chronic myeloid leukaemia. Can you pick the Ph chromosome? Note the mixture of coloured probes on the small chromosome at the left — this is the Ph chromosome that consists of most of chromosome 22 with a small segment of chromosome 9 attached.

JANE'S STORY, AS TOLD BY HER MOTHER

'Jane is the third of four children born into our family. When she was born, little did we realise the extent to which our ideas about disability and life chances would change. We were shocked, saddened and confused about what it might mean to have a child with Down syndrome. We didn't know very much about it; however, we were fortunate to have doctors who provided us with as much information as possible and urged us to treat her just like any other baby. Jane received the same attention, the same love and the same opportunities for learning and socialising that her brothers experienced.

Jane's early development proceeded through the same stages as for other children, but more slowly. She sat up at 10 months, crawled at 15 months, walked when she was 26 months old and talked by the time she was three and a half. We came to believe that Jane could learn to do most things that other children learn, but that the learning process would take longer. She was happy to watch others but wouldn't necessarily initiate action as much as other children do, so we ensured that Jane was actively involved in as many play experiences as possible.

When Jane was three and a half, she attended a Day Training Centre for the Intellectually Handicapped, as such centres were called then. She became involved in music, painting, solving jigsaws and so on. However, she was still doing much the same things two years later and her opportunities for academic learning were very limited. We believed that Jane was capable of learning much more than was expected of her at the centre. When Jane was five, she had the opportunity of attending the local kindergarten for two days a week where she socialised with children with a much broader range of abilities. At six, Jane began to learn how to read. Having been a primary teacher, I taught Jane at home and was delighted to find that she learned with relative ease. From then on, we never assumed what Jane may or may not be capable of learning, but provided opportunities for her to learn. At this time the integration debate began, and it reinforced my conviction that Jane should attend her local school with her brothers and neighbourhood peers. So when Jane was seven, she was admitted at our local school and had her needs met in the same way as students. Although Jane was two years older than most of the other children, she was very small and was at their level developmentally, so her placement was appropriate.

In looking for secondary school options for Jane, we were delighted when she was accepted into a small Catholic girls' school that catered for individual differences in an inclusive way. Jane attended secondary school for five years, after which time the

work was becoming too complex and difficult for her, so a job placement seemed to be a more appropriate option. Her integration into the mainstream of education broadened Jane's options for integration into the workforce. Since leaving school she has been employed in fast-food businesses and in retail stores. For nearly 15 years she has been employed in a Target store under a productivity-based pay scheme whereby she is paid according to her level of productivity, as measured against the average worker. Under this scheme, she receives a disability pension reduced according to her wages, she now needs less support and has even had some long-service leave.

Jane knows that she has Down syndrome and has a simple understanding of what that means genetically, but she doesn't see herself as disabled. Indeed, she continues to learn and has reached a level of independence that we would not have believed possible.

She has had piano lessons and is interested in TV, books, music and dancing. She is capable of travelling to and from work, shopping by herself, operating quite complex video, DVD and internet technology, arranging social outings with her friends and making appointments for herself. Jane has had lessons in cooking and budgeting to enable her to achieve greater independence. Although Jane received her 'L' plates ready for driving lessons, she didn't in fact take them. The important thing is that she had the opportunity to learn.



FIGURE 14.20 Jane in 2012

KEY IDEAS

- Each species has a characteristic number of chromosomes, known as the diploid number, typically present in body (somatic) cells.
- Human chromosomes in body cells exist in pairs, normally 23 pairs.
- The 23 pairs of human chromosomes include 22 pairs of autosomes, present in both sexes, and one pair of sex chromosomes, XX in the female and XY in the male.
- Chromosome sets can be organised into karyotypes.
- An ideogram is a stylised diagrammatic representation of chromosomes.
- Additional or missing entire chromosomes or parts of chromosomes are readily identified from an analysis of karyotypes.
- Certain syndromes result from chromosomal changes.
- Cancers are associated with chromosomal changes.

QUICK CHECK

- 1 Identify a key difference between the members of the following pairs.
 - a Ideogram and karyotype
 - b Autosome and sex chromosome
 - c Haploid and diploid
 - d Centromere and kinetochore
 - e Monosomy and trisomy
 - f Deletion and duplication of a chromosome
- 2 Identify whether each of the following statements is true or false.
 - a Colchicine is a poison that arrests dividing cells at metaphase.
 - b The two number-3 chromosomes constitute a nonhomologous pair.
 - c Prader-Willi syndrome involves a small deletion of chromosome 15.
 - d Two forms of Down syndrome occur, a trisomy form and a translocation form.
- 3 Briefly explain why the chromosomal make-up of a person is more easily analysed using a karyotype than a metaphase spread.
- 4 What is the Philadelphia chromosome?

FIGURE 14.21 Pea flowers vary in colour and petal shape. If independent assortment occurs, red flowers would be expected to show erect petals just as commonly as hooded, and likewise for purple flowers. What result did Bateson and Punnett observe?



Chromosomes: genes carriers

Mendel (see chapter 13) postulated that his factors were separate particles, behaving independently of each other. However, experiments by W Bateson (1851–1926) and RC Punnett (1875–1967) in England in the early 1900s showed that in some crosses with peas a particular variation (red flower colour) tended to be inherited with another specific variation (erect petal shape). The factors concerned behaved as if they were physically coupled. Yet, in other crosses with peas the same variants were very rarely inherited together, as if they repelled each other and ‘refused to enter the same gamete’. These crosses produced red flowered offspring that nearly always had hooded petals and only rarely had erect petals (see figure 14.21).



FIGURE 14.22 This idea was first postulated by Sutton (1902) and Boveri (1903), but the first experimental evidence came only in 1910 from TH Morgan's laboratory.

Bateson and Punnett's observations that some of Mendel's factors did not behave independently when moving into gametes provided an early clue that these factors were not free-floating particles in cells but were organised into larger structures. These structures were soon to be identified as chromosomes. In 1902, in the United States, Walter Sutton (1876–1916) recognised that the thread-like structures seen in cells and known as chromosomes (*chroma* = coloured; *soma* = body) provided a mechanism for the operation of Mendel's laws. Based on the parallels that he observed in the behaviours of **Mendel's factors** and of chromosomes, Sutton came to the conclusion that Mendel's factors were located on the chromosomes (see figures 14.22 and 14.23). Just as a map can be drawn showing the location of towns along a road, a **chromosome map** can be drawn showing the location of genes along its length. These 'maps' show how genes form **linkage groups**.

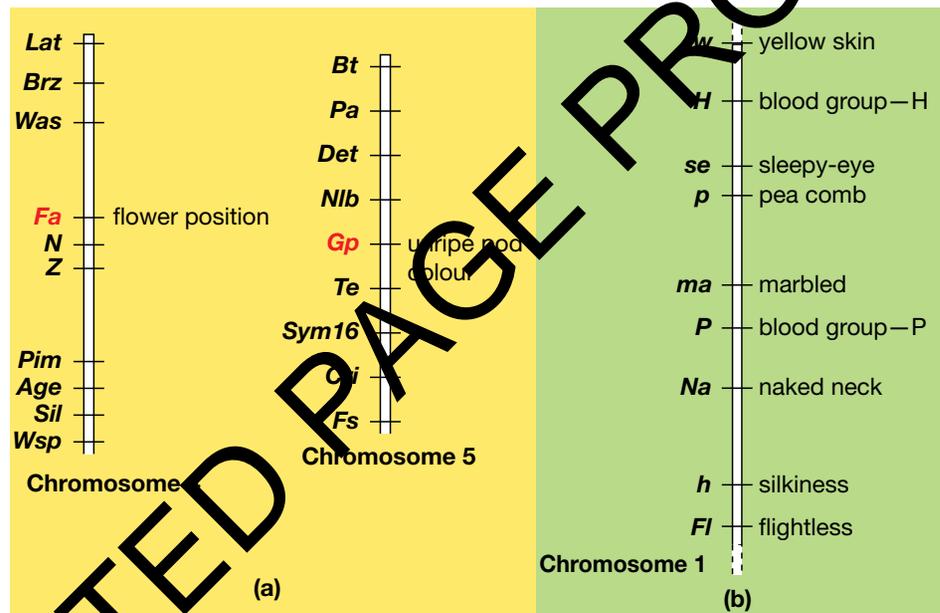


FIGURE 14.23 Genes are located on chromosomes. (a) Linked group of genes on chromosomes 4 and 5 of the edible pea (*Pisum sativum*). The genes highlighted in red are two of the seven genes that Mendel used in his crosses (refer to figure 13.27). (b) One of the linkage groups in the domestic fowl (*Gallus domesticus*)

Sutton did not carry out any experimental crosses — instead he synthesised the results of other scientists, recognised patterns and made the key link between the chromosomes studied by cytologists and the genes studied by geneticists (see table 14.4).

TABLE 14.4 Parallels between the behaviour of genes and the behaviour of chromosomes, expressed in modern terminology

Genetic behaviour	Chromosomal behaviour
segregation of the members of each pair of alleles into different gametes	separation (disjunction) of the members of each pair of matching chromosomes into different gametes (see figure 14.24)
random assortment of the alleles of different genes into gametes	random orientation of different pairs of chromosomes across the cell equator prior to their separation during gamete formation (see figure 14.25)

Figures 14.24 and 14.25 show **the parallel relationship between the behaviour of genes and chromosomes during meiosis**.

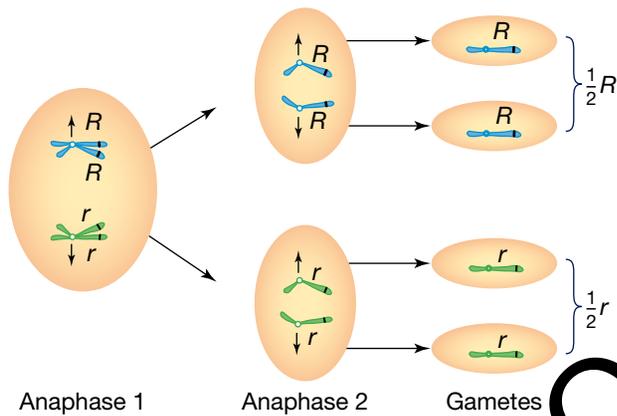


FIGURE 14.24 Disjunction of matching chromosomes into different gametes results in segregation of alleles.

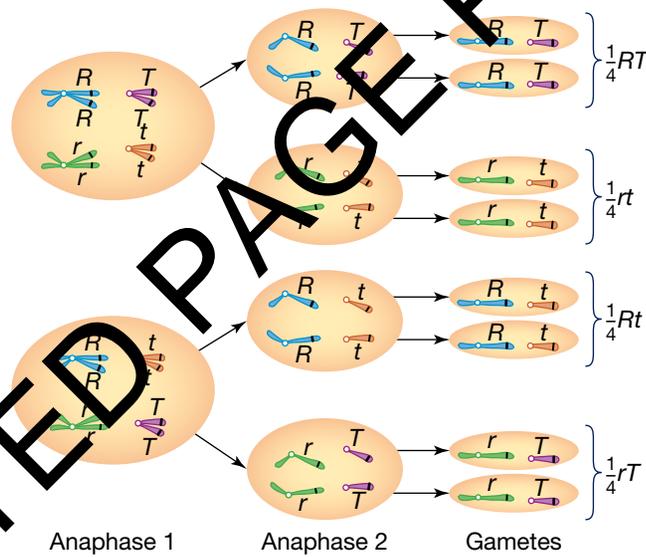
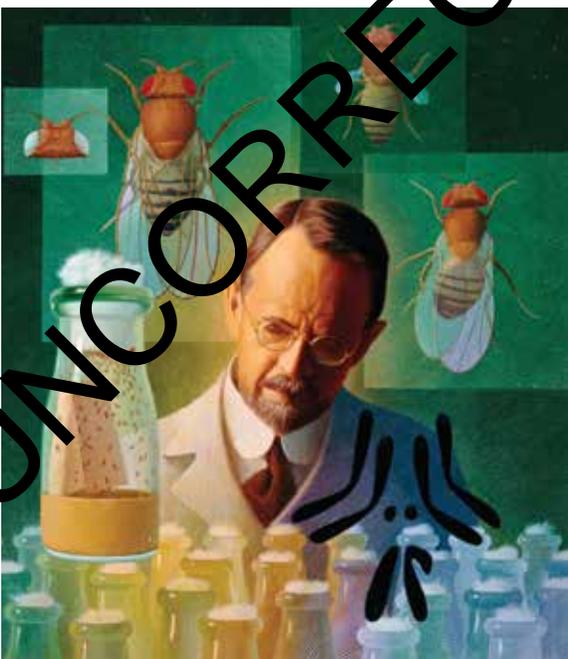


FIGURE 14.25 Random orientations of nonmatching chromosomes lead to independent assortment of genes into different gametes.



The parallel behaviour of chromosomes and genes provided strong evidence for Sutton's conclusion that genes were located on chromosomes. However, it was not until 1910 that the first specific gene was demonstrated to be located on a specific chromosome. This was done by TH Morgan (1866–1945) (see figure 14.26). Morgan and his co-workers at Columbia University (United States) confirmed Sutton's conclusion. They showed that factors (genes) were not free particles like peas in soup, but were organised into larger structures: chromosomes. They showed that when genes were located close together on homologous chromosomes specific alleles of these linked genes tended to be inherited together. Morgan's findings explained the strange observation of Bateson and Punnett. Clearly, the genes controlling pea flower shape (hooded and erect) and pea flower colour (red and blue) were located close together on the same chromosome.

FIGURE 14.26 Thomas Hunt Morgan with fly drawings. Morgan used fruit flies (*Drosophila melanogaster*) in his experiments that showed that genes were located on chromosomes. In 1933, Morgan was awarded a Nobel Prize for his contribution to genetics.

Table 14.5 provides data on the human chromosomes in terms of their length in base pairs (bp) and the approximate number of genes that each carries.

TABLE 14.5 The human chromosomes as revealed by DNA sequencing

Chromosome	Length (bp)	Number of genes (bp)
1	248 956 422	2000
2	242 193 529	1300
3	198 295 559	1000
4	190 214 555	1000
5	181 538 259	900
6	170 805 979	1000
7	159 345 973	900
8	145 138 536	700
9	138 397 417	800
10	133 757 422	700
11	135 086 622	1300
12	133 275 309	1100
13	114 364 328	300
14	107 043 718	800
15	101 991 189	600
16	90 338 345	800
17	83 257 441	1200
18	80 373 285	200
19	58 617 616	1500
20	64 444 167	500
21	46 709 983	200
22	50 818 468	500
X (sex chromosome)	156 040 895	800
Y (sex chromosome)	57 227 415	50

Chromosome and sex determination

The wife of King Farouk of Egypt had given birth to three healthy daughters. In 1948, Farouk divorced his wife because she had not produced a male heir. Was this reasonable?

In mammals, birds and some reptiles, the sex chromosomes are important in determining sex. This is because they carry certain genes that are critical in sex determination, such as the **SRY** gene on the mammalian Y chromosome, which controls testis formation. This mode is known as **genetic sex determination (GSD)** (see table 14.6).

TABLE 14.6 Genetic sex determination involving sex chromosomes

Animal group	Chromosome system
mammals and some reptiles	XX female; XY male
birds and some reptiles	WZ female; ZZ male
some insects	XX female; XO male

Mammals: the XX/XY system

The sex of a human fetus can be predicted before birth on the basis of the sex chromosomes present — **two X chromosomes indicate a female, while one X and one Y chromosome indicate a male**. A similar XX/XY situation applies with a few rare exceptions to other mammals. All the normal eggs produced by a human female during meiosis contain one X chromosome as well as 22 nonhomologous autosomes. In contrast, male mammals produce two kinds of sperm. All normal human sperm have 22 nonhomologous autosomes but some carry one X chromosome and others carry one Y chromosome (see figure 14.27).

ODD FACT

The platypus has 10 sex chromosomes: five Xs and five Ys.

ODD FACT

As expected, female swamp wallabies (*Wallabia bicolor*) are XX but normal males are exceptional in that they have one X chromosome and two Y chromosomes — one smaller one (denoted Y1) and one larger one (Y2).

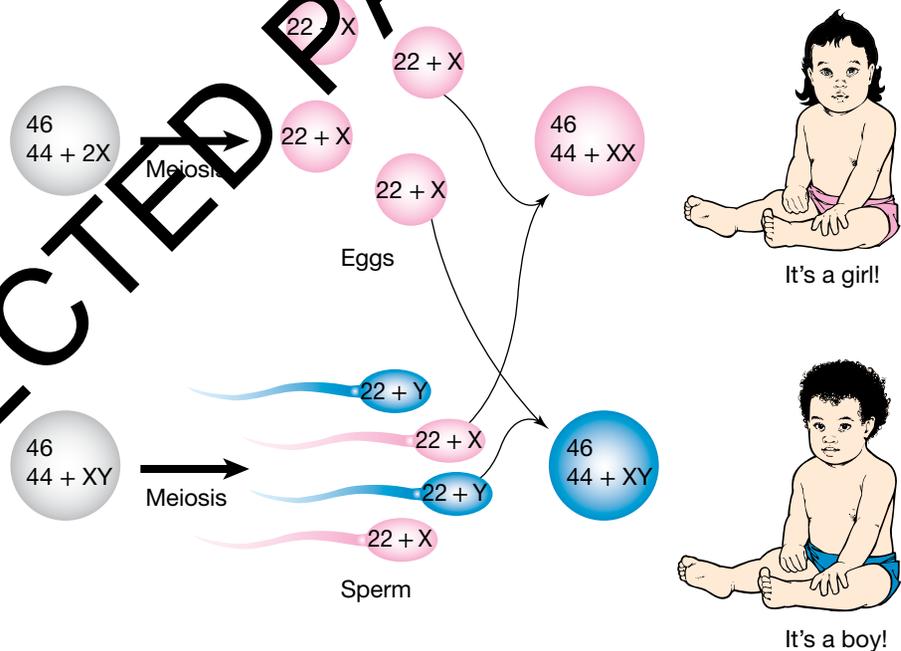


FIGURE 14.27 Which parent determines the sex of a baby? Was King Farouk reasonable in divorcing his wife?

The WZ/ZZ system

Sex chromosome differences also occur in birds but the arrangement is different from mammals. Male birds have two similar sex chromosomes that are known as Z chromosomes. In contrast, the pair of sex chromosomes in female birds comprises one W and one Z chromosome, and so it is the female parent



FIGURE 14.28 Green turtle hatchlings emerge from a nest in the sand of a northern Queensland beach. Crocodiles also have ESD.

ODD FACT

We tend to think of sex as determined for life, but individual fish of several species have the ability to change sex during their lifetimes.

in these groups that determines the sex of the offspring. This WZ/ZZ genetic system of sex determination is also seen in some reptiles, such as snakes and monitor lizards (e.g. goannas), and in amphibians, such as some frog species. Tiger snakes (*Notechis* spp.), for example, have a total of 34 chromosomes with males having two Z chromosomes and females having one Z and one W chromosome.

Reptiles – other means

It was discovered that **in some reptiles the sex of offspring depends on the incubation temperature of the eggs**. This is an example of **environmental sex determination** (ESD), and is seen in green turtles (*Chelonia mydas*) (see figure 14.28). Female turtles lay an average of 110 eggs and bury them in the sandy beaches along Australia's tropical coastline. After laying, the female turtles return to the sea. Male turtle hatchlings result from eggs that are incubated at high temperatures (above 31 °C), female hatchlings are produced when the incubation temperature is lower (27 °C and below), while at intermediate temperatures (around 29 °C) about equal numbers of both sexes are produced.

KEY IDEAS

- Genes are located on chromosomes.
 - The first suggestion that genes were located on chromosomes was made by Sutton in 1902.
 - Evidence for the location of genes on chromosomes came from observations by Sutton in 1902 on the parallels between the behaviours of genes and those of chromosomes.
 - In 1910, Morgan and his co-workers carried out the first experiments that demonstrated that genes were located on chromosomes.
 - Genes that are located on the same chromosome are said to be linked and form a linkage group.
- Various mechanisms of sex determination exist in Kingdom Animalia.

QUICK CHECK

- 5 What behaviour of chromosomes in meiosis gives rise to the segregation of alleles of one gene into different gametes?
- 6 Who was the first scientist to provide experimental evidence that genes are located on chromosomes?
- 7 Identify whether each of the following statements is true or false.
 - a Sex determination in mammals is typically an XX/XY system.
 - b A female bird would be expected to have a WZ sex chromosome pair.
 - c The sex of a mammal is determined by the genetic contribution of its male parent.

Lisette Curnow – genetic counsellor



FIGURE 14.29
Lisette Curnow

When I completed my degree in biological science, I knew that, while I enjoyed laboratory work and had a real interest in science, especially genetics, I couldn't see myself in the lab long term. Having heard about genetic counselling as an emerging profession, I liked the idea of combining my genetic interest with dealing with people in a clinical setting. The role of a genetic counsellor is to provide accurate information and options, together with counselling and support to individuals or families whose lives are impacted in some way by a genetic condition in themselves, their children or their extended family. It is a particularly important field given the dramatic advances that are being made in genetics, and complex information needs to be imparted to the public in a clear and concise way.

The convenor of the Postgraduate Diploma in Genetic Counselling (run through Melbourne University) recommended that I try to develop some counselling skills to see if that was something I would like to do. I volunteered at Lifeline, a telephone counselling service that puts volunteers through a fairly comprehensive training program, an experience that I found to be invaluable in determining whether I was interested in counselling and had any skills in the area. I subsequently completed the Graduate Diploma in genetic counselling, then travelled for 12 months, combining backpacking with six months of work experience at the Hospital for Sick Children in Toronto. On my return to Melbourne, I took up some volunteer work before embarking on my Master of Health Sciences (Genetic Counselling) degree. This gave me a real interest in research and I developed skills I have been able to use in my job.

While completing my masters, I worked part time in cancer genetics at Peter MacCallum Cancer Institute. This work involved meeting with individuals with a very strong family history of cancer to assess whether they may carry an inherited mutation in one of the cancer-predisposing genes. While testing for cancer predisposition is still limited, it may be available for families who meet 'high risk' criteria for breast cancer and some forms of bowel cancer. Assessment of people to see if they meet these criteria is done by genetic counsellors and other relevant clinicians (such as geneticists, oncologists, gastroenterologists and breast surgeons) through the various cancer genetics services.

I later worked in developing cancer services at the Royal Children's Hospital before moving into the role as genetic counsellor to the Royal Children's Hospital. This was a job with a paediatric focus where part of my role involved dealing with abnormal cystic fibrosis results from newborn screening (the heel-prick test that is carried out on every baby born in Victoria a couple of days after birth). I also attended the weekly paediatric clinic where I saw a range of patients, such as families who may have a child with a new diagnosis of a genetic condition, or a family member who is concerned about their risk of being a carrier of a condition that is present in the family. I now work primarily in adult neurogenetics and coordinate the predictive testing program for Huntington's disease (HD) in Victoria. This is a program that enables individuals at risk of HD (a debilitating adult-onset neurodegenerative disease) to find out whether they will develop the condition. This role allows me to meet people who constantly amaze me with their resilience.

I am also fortunate to be involved in coordinating the genetics component of the Master of Genetic Counselling course, as well as frequently giving lectures to various groups. Finally, I squeeze as much research as possible into my schedule as I am perfectly positioned to access valuable information regarding the impact of today's genetic technology on the public.

Our genetic knowledge is constantly evolving and, as genetics does not discriminate, the families we meet are necessarily varied and multifaceted. This ensures that there is rarely a dull moment in my day-to-day work, and we regularly encounter difficult ethical dilemmas that prompt stimulating discussions among my colleagues as we try to resolve the best way forward for our clients. The interpretation of complex genetics and technology for the people it affects every day is an extremely challenging yet rewarding field in which to work.

BIOCHALLENGE

Use the **Human Genome Resources** weblink in your eBookPLUS.

The small diagram of the human chromosomes at the upper left-hand corner allows you to click on a chromosome and see the detailed genetic information that is carried on each chromosome. **eBookplus**

- 1 Click on chromosome 21. The new screen display (see figure 14.30) will show you an ideogram of chromosome 21 and will indicate the positions of 20 of the 726 genes located on this chromosome.

Note how the genes are designated by capital letters (and, in some cases, number(s)). Don't be overwhelmed at the amount of information! This exercise is simply to show you the remarkable detail that now exists about the human genome.

- 2 Now click on the 9 at the top of the screen display to see an ideogram of the human chromosome 9.

One of the 20 genes shown on this ideogram is the **ABO** gene. Click on the ABO link and see the information that is available about this gene. Scan this information and answer the following questions:

- a What type of gene is the **ABO** gene?
- b What protein does this gene encode?

- 3 a Now return to the starting page in the weblink and use the Find A Gene box, located in the left-hand column, to find the chromosome on which the **HTT** gene is located.

controls production of the protein huntingtin is located on chromosome 4. Once you have the chromosomal location, click on the gene name for further information about the gene, and identify an inherited disorder caused by an altered form (allele) of the gene. Record your data in table 14.7.

TABLE 14.7

Gene symbol	Chromosomal location	Inherited disease
HTT		
CFTR		
DMD		
HBB		

- b Repeat the procedure in part (a) for the following genes.
 - i The **CFTR** gene that encodes the cystic fibrosis transmembrane conductance regulator (refer to chapter 1, pp. 36–7)
 - ii The **DMD** gene that controls production of the muscle protein dystrophin, which if abnormal results in Duchenne muscular dystrophy
 - iii The **HBB** gene that controls production of the beta polypeptide chains of the adult haemoglobin A molecule

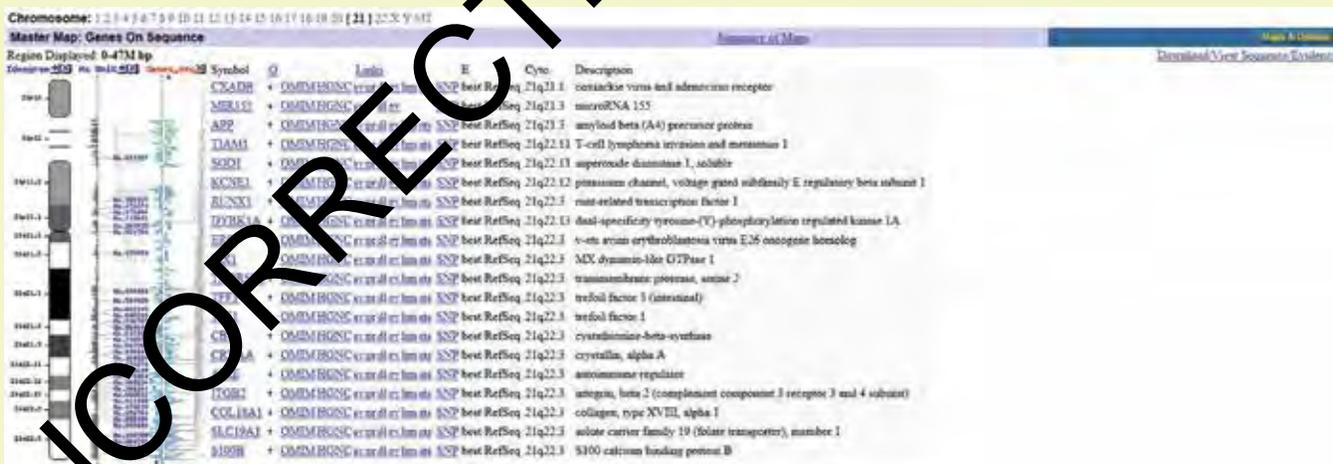


FIGURE 14.30 Screenshot from the National Center for Biotechnology Information (NCBI) website



Chapter review

Key words

- Angelman syndrome
- autosome
- centromere
- chromosome map
- colchicine
- cytogeneticist
- deletion
- Down syndrome (DS)
- duplication
- embryo
- environmental sex determination
- FISH staining
- genetic sex determination (GSD)
- homologous

- hypotonic shock treatment
- ideogram
- karyotype
- kinetochore
- linkage groups
- Mendel's factors
- metaphase spread

- monosomy
- nondisjunction
- nonhomologous
- reciprocal translocation
- sex chromosomes
- telomere
- translocation
- trisomic

Questions

- 1 **Making connections** → Use at least eight of the chapter key words to draw a concept map relating to chromosomes. You may use other words in drawing your map.
- 2 **Demonstrating knowledge** → Where would you locate each of the following?
 - a Human cells undergoing meiosis
 - b Haploid cells in a cat
 - c Cells containing 20 unpaired chromosomes in a mouse
 - d The genetic instruction for your ABO blood type
- 3 **Demonstrating your understanding** → Use words and/or diagrams to identify the differences, if any, between the items in each of the following pairs.
 - a Haploid and diploid
 - b Autosome and sex chromosome
 - c Somatic cell and germline cell
 - d Gene and allele
- 4 **Recognising patterns** → A newborn baby showed facial abnormalities and other signs including deformed kidneys and nails, and an unusual way of clenching its fist. Its karyotype was prepared (see figure 14.31). Examine this karyotype.

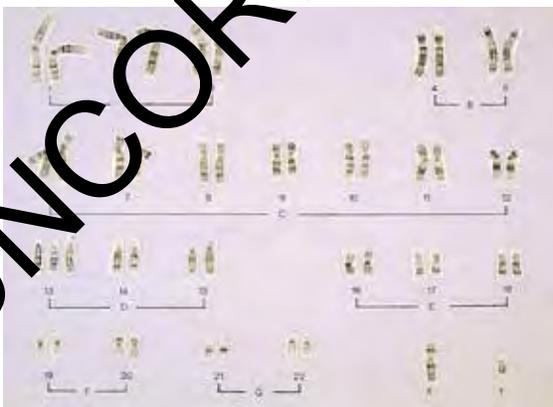


FIGURE 14.31

- a What is the total number of chromosomes?
 - b What is the sex of the baby?
 - c What abnormality is visible in the karyotype?
 - d What name is given to this condition?
- 5 Match the processes in column A to the outcome in column B.

Column A	Column B
meiosis	exchange of segments occurs between homologous chromosomes
crossing over	haploid gametes produced from a diploid cell
disjunction of homologous chromosomes	diploid number of chromosomes restored, one set from each parent
independent disjoining of nonhomologous chromosomes	alleles of one gene segregate from each other
fusion of gametes at fertilisation	random combinations of different genes produced in gametes

- 6 **Demonstrating knowledge and understanding** → Some chromosomes, when present as a trisomy in a human, produce obvious signs or clinical conditions in the affected person and are typically diagnosed soon after birth.
 - a Which chromosomes are these?
 - b How would these conditions be diagnosed?
 - c Briefly explain how a trisomy can be produced.
 - d A student stated: 'Strange how the number-1 and the number-2 chromosomes are not examples of clinically recognised trisomies. It must be that they are never involved in a nondisjunction. It looks like only a few chromosomes are subject to that kind of error.'

Carefully consider this statement and indicate whether or not you agree with this student and give a reason for your decision.

7 Applying understanding → Write the shorthand form of the karyotype of each the following.

- a Normal male
- b Female with Turner syndrome
- c Male with an extra Y chromosome
- d Female with Down syndrome
- e Male with Klinefelter syndrome
- f XXX female

8 Demonstrating knowledge → Figure 14.32 shows some 'maps' for three human chromosomes. On these chromosomal maps, the symbols 'p' and 'q' are used to denote the short and the long arm of a chromosome. (The 'p' comes from the French *petit* meaning short. Why 'q'? It's the next letter in the alphabet.)

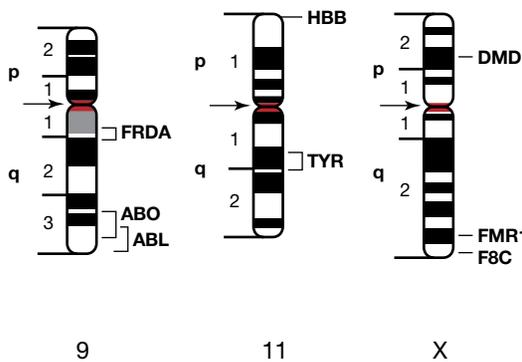


FIGURE 14.32

- a What representation of the chromosomes is shown in this figure?
- b What is the chromosomal location of the following genes?
 - i The gene that controls your ABO blood type
 - ii The gene that controls production of the beta chain of your haemoglobin
 - iii One of the genes that is translocated to become part of the Philadelphia chromosome
 - iv The gene that controls the production of the protein dystrophin in your muscles

9 Making predictions → The short arm of a chromosome is denoted by the symbol 'p'. A particular chromosomal disorder can be shown by the symbol 46, XY, 5p-.

- a Predict the meaning of this notation.
- b Check the chapter text and give a name to this human chromosomal disorder.
- c Would you predict that the condition 45, XX, 5- would have a name to refer to clinical signs seen in an affected person? Briefly explain your decision.

10 Exploring the web → Use the **Genes and disease** weblink in your eBookPLUS. From this website you can access any human chromosome and see the

ideograms that show the locations of the genes for major human diseases and disorders that are located on that chromosome. By clicking on the symbol of the gene you can gain some information about the disease associated with that disease.

eBook plus

- a Go to chromosome 4 and check out the disease that results from an altered form of the **HD** gene. Write three sentences that summarise some key features of this disease.
- b Go to the X chromosome and check out the **DMD** gene. Write three sentences that summarise some key features of this disease.
- c Check out five other chromosomes and record the symbol of one gene and its associated disease in the following table.

Chromosome no.	Gene symbol	Disease

11 Applying understanding in a new context →

Karyotypes can be prepared from cells of other organisms. Figure 14.33 overleaf shows the karyotype of an Amur tiger, called TaeGuek, whose genome was the first of that species to be sequenced.

Examine this karyotype and answer the following questions.

- a What is the sex of this tiger?
- b What is the diploid number of the tiger?
- c Show this karyotype in shorthand form.
- d Is there any evidence of an error in chromosome number? Explain your decision.
- e How many chromosomes would you expect to see in normal gametes from this tiger?
- f What reasonable prediction (it may not be correct, but that does not matter) would you make about the karyotype of a domestic cat? Briefly explain the reasoning behind your prediction.

12 Discussion question → In the past, the only test for the presence of chromosomal abnormalities in a fetus was through the use of a procedure known as amniocentesis. Amniocentesis is an invasive screening test that involves obtaining a sample of the amniotic fluid that surrounds the fetus by passing a needle into the uterus. Because this procedure has a one-in-one-hundred risk

of causing a miscarriage about 40 per cent of women offered amniocentesis decline to have amniocentesis as they risk losing a healthy fetus.

More recently, a non-invasive screening test has become available that can detect chromosomal and some other abnormalities. This test detects fetal cells in a sample of the mother's blood. This test has a 99 per cent accuracy rate.

Data from the Department of Health in the United Kingdom show that the availability of this non-invasive test has led to a 34 per cent increase in pregnancy terminations in the 3-year period from 2011 to 2014.

Some findings:

- The highest proportion of terminations (693) were due to the detection of Down syndrome.
- A small number of terminations (10) were due to the detection of cleft palate, a treatable condition.
- At least one woman had a termination after a false positive test for a chromosomal abnormality.

Hayley Goleniowska, the mother of an 8-year-old daughter with Down syndrome has commented: 'In quieter moments I weep to think of what we could lose . . . It's not the test that worries me, it's how it is implemented.'

Dr Bryan Beattie, a fetal medicine consultant, has commented: 'The real issue next, in around two or three years' time, will be an ethical one — where do you stop? Do you screen for breast cancer genes, for Huntington's — or taking a step further, test for eye and hair colour?'

Source: J MacFarlane, 'New blood test blamed as women choosing to abort babies with Down's syndrome and other serious disabilities soar 34% in three years,' *Mail on Sunday*, 14 June 2015.

Discuss these comments with a group of your classmates.

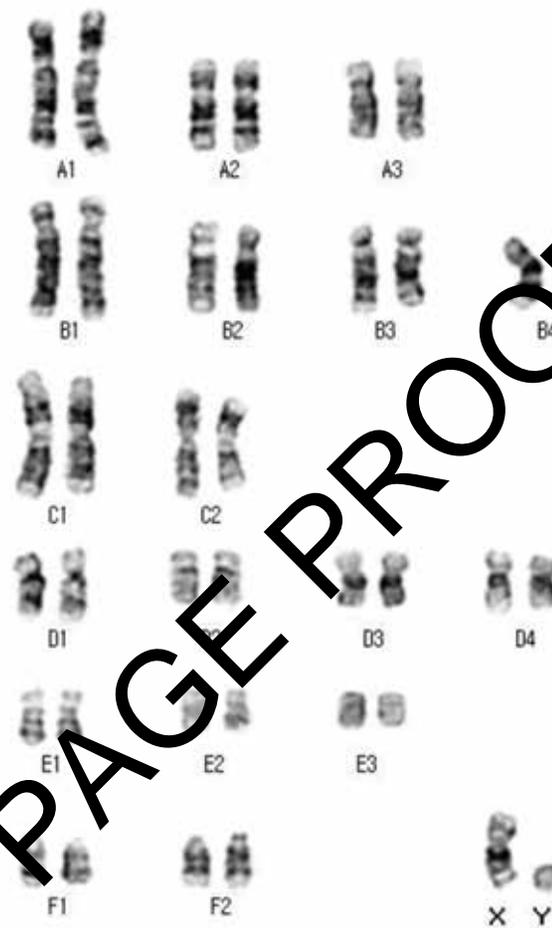


FIGURE 14.33 Karyotype of TaeGuek, an Amur tiger