UNIT 5 DEVELOPMENTAL BASIS OF SEX

Structure

5.1 INTRODUCTION

The existence of two different sexes (mating types) is necessary to carry out sexual reproduction, which provides genetic variability. This is achieved in hermaphrodite plants by ensuring cross-fertilisation and in most animals by having two separate sexes. What determines the sex of an individual, must have been clear to you from your study of Units 3 and 4.

For human, it can be said' that apart from the differences societies have created between the sexes, there is a basic biological difference between them which is undeniable. This difference is in the reproductive system and its functions. Most people are either 'normal' females or males, and they never question how or why they developed as they did.

Let us look into the genetic basis of development with respect to the differentiation of sexes. We will confine ourselves to the sexual differentiation in man to get a clear understanding of the phenomenon. The egg from female unites with the sperm from male to result in zygote or the first cell of the embryo, whose sexual development is predetermined by sex chromosome (X or Y) contributed by the sperm.

Since the role of genetic information in early development and formation of gametes is basically similar in most plant and animal species, thereby the general concepts can be applied to most of them. Information regarding intersexes and other ambiguous sex anomalies have been included in this unit. Some interesting facts about the sex ratio, factors affecting it and sex selection of offspring are also presented in this unit.

It would be useful to revise Units 3 and 4 as well as brush up your knowledge of reproductive system in man before beginning a study of this unit. You may refer to Unit 8, entitled Reproductibn, of the course LSE-05 (Physiology).

Objectives

After studying this unit you would be able to:

- distinguish between sex determination and sexual differentiation (Section 5.2);
- evaluate the role of sex chromosomes in the differentiation of gonads (Section 5.2);
- a describe the events, in chronological order, that lead to the differentiation and development of the male and the female gonads (Sub-sections 5.2.1 and 5.2.2);
- describe the causes of development of intersexes (Sub-section 5.3.1);
- contrast between true-, and pseudo-hermaphroditism (Sub-sections 5.3.2, 5.3.3 and 5.3.4);
- define free martins and explain their origin (Sub-section 5.3.5);
- contrast between hermaphrodites and mosaics (Section 5.4);
- describe the importance of sex reversal phenomenon in birds and animals (Section *5.5);*
- define sex ratio and differentiate between primary, secondary and tertiary sex ratio (Section 5.6);
- describe the different post-, and pre-fertilisation techniques of sex selection of offspring (Section 5.7).

5.2 GONAD FORMATION

Early in development both XX and XY embryos form undifferentiated or all purpose gonads called ovotestes (Fig. 5.1 a). They are bipotential and can develop into either testes (Fig. 5.1 b) or ovaries (Fig. 5.1 c). Direction in which differentiation occurs depends on whether the X-, or Y-bearing sperm has fertilised the ovum. The Y-chromosome is required for production of testes determining factor (TDF), which stimulates the 'neutral' gonads to develop in the 6th week of pregnancy, at that time certain events occur that determine which sex the individual will be.

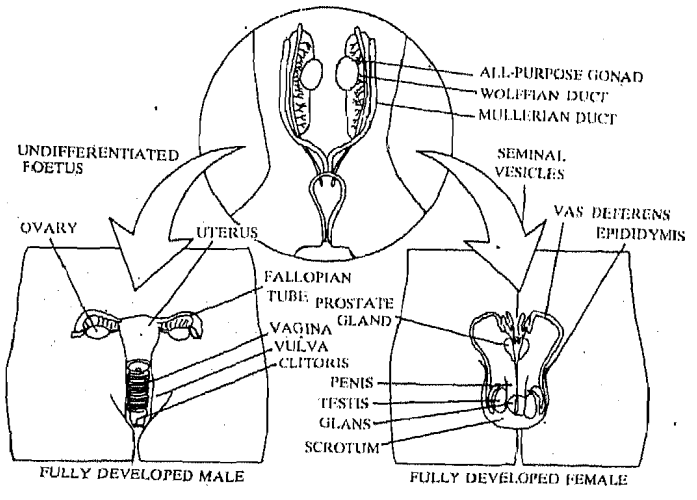

Fig. 5.1: In normal sexual differentiation, an all purpose gonad develops as either an ovary or a testis depending on the combination of chromosomes presenl. With an X chromosome from both the male and female, it develops as an ovary; with an X from the female and a Y from the male, it develops as testis. In males, the testes produce hormones, or androgens that convert certain embryonic structures into the appropriate male parts. Without the influence of these androgens, the same structures normally develop into the female counterparts.

The TDF gene located on Y chromosome is a master switch, that when turned on, activates an entire series of genes whose function is sex differentiation. No particular female-inducing substance is known. So in general it can be said that the gonadal

development proceeds towards femaleness unless switched towards maleness via TDF (Fig. 5.2).

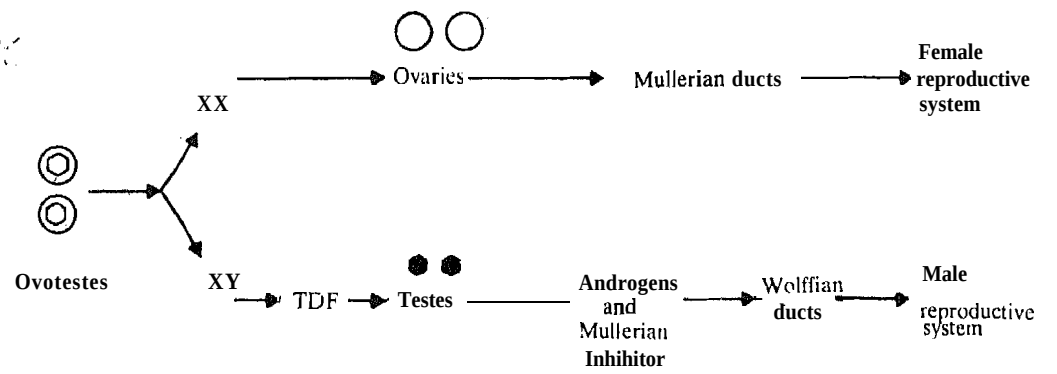

Fig. 5.2: Switch mechanisms that determine expression of human sex phenotype. Development proceeds towards maleness in two steps. First is the production of TDF under control of the Y chromosome. Second is the production of Müllerian inhibitor to inhibit the Müllerian ducts. Without TDF ovaries and Miillerian ducts develop, producing female structures.

5.2.1 Role of Hormones

In the eighth week of gestation, the testes formed earlier, begin to produce the hormone **testosterone,** some of which is converted to closely related substance dihydrotestosterone, or DHT. Such hormones are called androgens. The DHT goes on to convert the all purpose embryonic structures into glans penis, penis shaft, and scrotum. These structures would otherwise develop into their female equivalents: the clitoris, labia minora, and labia. majora.

Embryos also start out with two sets of ducts, known as the Müllerian ducts and the Wölffian ducts. In the absence of testes, the Wolffian ducts degenerate, while the Müllerian ducts grow into uterus, fallopian tubes, and the inner part of the vagina. With testes present the opposite happens: androgens produced-by the testes stimulate the Wölffian ducts lo grow into seminal vesicles, vas deferens and cpididymis. At the same time a testicular protein called **Müllerian** inhibiting factor does what its name implies: it prevents the Müllerian ducts from developing into the internal female organs (see also Fig. 5.2).

Thus, the genetic information on sex chromosomes is responsible for the *primary sex determination events.* So, sex is determined at the time when the baby is conceived (fertilisation) and no amount of listening to military marches or looking at pictures of athletes will alter its sex.

Under normal conditions once the gonads develop, further differentiation occurs under the influence of male or female hormones. Sex hormones play an important role in the *development* of *secondary sexual characteristics.* These include growth of beard, change of voice in males and breast development in females. The actual phenotypic differences between males and females are mediated by hormones, which in turn are produced according to genetic information programmed in the genome. The ability of the cells to respond to sex hormones is also under genetic control and it largely depends on their binding with specific receptors.

Hope now you can distinguish between the phenomena of sex determination, and sex differentiation.

SAQ 1

At what stage of differentiation is testosterone produced? Comment on its role in the development ot a particular sex.

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5.2.2 Role of Genes

Several genes and their products are involved in the process of sexual differentiation. Some of these have been well investigated and the knowledge thus obtained has enabled the geneticists to form a coherent picture of the process of sex differentiation and development of gonads.

H-Y Antigen: It has been known for a long time that sex determination in mammals is effected through the Y-chromosome which carries a factor that initiates male sexual developmcnt.

Gene for H-Y antigen is one of those genes which is considered to be important in sex differentiation. It was discovered in 1955 as a transplantation antigen in mice, and is found to occur in all mammalian species. The gene coding for the H-Y antigen is male specific (holandric). It is located on the short arm of the Y chromosome. The evidence for this is provided by the dose-related studies. If anti-H-Y antibodies are added to white blood cells, the H-Y antigen on the surface of the cell will bind to the antibody. And the XYY and XXYY individuals produce twice as much antigen.

The H-Y antigen *serves as an initial signal fur primary sexual differentiation.* It is essential for the development of testis in mammals. It is believed that the H-Y antigen has long been involved in sex determination during evolution.

You may recall (from Unit 3) that in amphibians and birds, the female is the heterogametic sex. In such organisms, the female – not the male, expresses the H-Y antigen. It seems that the antigen has been preserved throughout evolution and just like in the mammals, it signals the primary sexual determination.

***Sxr* Gene:** Direct evidence for sex-determining genes on the Y chromosome has come from the studies of inheritance of a dominant sex-reversal *(Sxr) gene* in *mice. Sxr* causes zygotes with two X-chromosomes to develop as males with testes, but spermatogenesis is absent. Such males exhibit X-inactivation and are mosaic for X-linked genes. The use of recent techniques'for DNA manipulation have suggested that when the *Sxr* containing segment of the Y-chromosomes is transferred to the X-chromosome during meiosis, the XX individuals formed develop as males with testes. But the adult XX *Sxr* males are sterile.

Based on the research works involving the *Sxr* trait in mice, it was concluded that whatever be the male-sex determining genes carried on the Y-chromosome, they arc essential for instructing the undifferentiated embryonic gonad to develop as a testis, the first step in the male development pathway. In the absence of testis inducing functions, the undifferentiated gonad develops as an ovary.

Tfm Gene: As indicated earlier, secondary sex developmcnt is a consequence of the sexual nature of the gonad that develops under the control of the sex chromosomal constitution. The developing testes secrete testosterone, a hormonal signal that induces male development. In the absence of this signal, female development occurs. Male development is controlled by a X-linked gene (Tfm^+) specifying a testosterone-binding protein that is present in the cytoplasm of all cells of male and female. This protein is a regulatory protein, activated by binding of testosterone (an effector molecule) (Fig. 5.3). The protein testosterone complex then enters the nucleus and activates the genes required for normal male differentiation. Mutations of the *Tfm* gene are known in several species including humans causing a syndrome called testicular feminisation (you would study about it in subsection 5.3.2). Cells of mutant *Tfm/Y* embryos are completely insensitive to the masculinising effect of testosterone; consequently the foetus develops all the external sexual characteristics of a female rather than those of a male. However, internally, testes dcvclop rather than ovaries, and the testes suppress the development of fallopian tubes and uterus by secreting another male hormone known as factor chi χ , resulting in blind vagina.

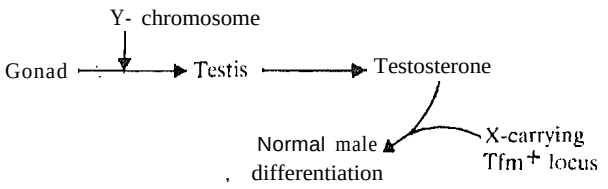

Fig. 5.3: Role of *Tfm*$^+$ locus in normal male development.

Thus a coherent picture of mammalian sexual development has emerged. The *Sxr* and *Tfm* mutations have helped to establish a framework for understanding the general features of the process of gonadal differentiation.

SAQ 2

Comment on the existence of XX males in mice.

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5.3 INTERSEXES

This section particularly the subsection 5.3.1, is closely linked to the earlier section. 5.2. In order to form a complete picture of what is happening at the time of normal as well as abnormal sexual differentiation, we suggest that yo11 read these sections at a stretch.

5.3.1 Sex Chromosomes and Intersexuality

In humans, provided all developmental processes work correctly, the Y-chromosome confers maleness on the developing embryo and the lack of chromosome Y results in a female: Thus from the very beginning, each cell receives one type of non-reversible, sex labelling through the **sex chromosomes.** And as far as the sex chromosomes arc concerned, there is no possibility of reversal. In females, the second X chromosome is required for the production of normal ovary, and some of *the genes on* X *chromosome are also essential for the production of normal testes in man.*

In Section 5.2, you have already learnt that the development of gonads of both the sexes begins from common, undifferentiated structures – the ovotcstes. Gonadal sex differentiation begins earlier in the cells carrying the male XY sex chromosomes. The ovarian changes in a female occur later on in the developmental sequence.

If the male induction process does riot begin according to schedule – early in embryonic development – abnormalities can be expected in gonadal genitalia at birth. If no induction occurs, the embryo will continue towards female development. The *correct sex chromosome complement and precise timing* are both necessary for induction processes of male dcvclopment. **Any** disturbance in this process can create varying degrees of abnormal anatomical sexual development. Such errors or accidents in development can lead to the incomplete development of one sex or the, partial display of both sexes – **intersex** in persons with normal sex chromosomes.

5.3.2 Male Pseudohermaphroditism

The most common cause of male Pseudohermaphroditism is **testicular feminisation,** which is an inherited sexual disorder. Those affected, display a normal feminine appearance and behaviour, though genetically they are male - XY. Such individuals develop female secondary sexual characters but are sterile. The vagina ends in a blind pouch and testes do not descend to their normal location in the scrotum but are located in the abdominal area. The testes produce female hormones – estrogens responsible for the secondary sexual characteristics. It is believed that a *defective gene alters the ability of Y chromosome to confer maleness on the embryo.* Some male Pscudohermaphroditcs produce testosterone, but lack cytoptasmic testostcrone receptors necessary for normal male masculinisation. Other male Pseudohermaphrodites have normal receptors but fail to produce testosterone. The gene for producing the testosterone receptor is located on the X chromosome.

In some cases of male Pseudohermaphroditism, an opening is present beneath the penis that simulates a vagina. The scrotum or scrotal sac is usually small and does not contain the (undescended) testes. Many'of these individuals have normal-appearing female genitals, and may cvcn undergo feminisation at puberty although they do not menstruate.

The male psciidohermaphrodites arc sex chromatin negative. They do not show a Barr body and have the normal male sex complement of XY not XX.

5.3.3 Female Pseudohermaphroditism

This is a rccessivcly inherited form of pseudohermaphroditism. The female pseudohermaphrodite has the normal-XX sex chromosome complement, but her genitalia display various degrees of phallic development. Female pseudohermaphroditism commonly results due to the **Congenital Androgenital Syndrome.** These females appear as intcrsexcs because there is overproduction of testosterone due to hyperactive adrenal glands. Excessive tcstostcrone inhibits the complete differentiation of the female duct system and stimulates the development of male sex organs and secondary sexual characters. There is variable expression of genital duct development. That is, the time when the male or female ducts depart from the normal depends on the levels of the hormones present.

If this recessive gene is prcscnt in an XY embryo then a precocious **male** develops, i.e., adult male characters appear at a very early age in the child. Cortisone, which inhibits testosterone activity, provides effective treatment in these conditions if administered early in embryogeny.

5.3.4 True Hermaphroditism

A true hermaphrodite possesses functional male and female reproductive systems or retains the bipotcntiality of the embryonic gonad. This condition, however, is rare in humans. Such individuals show varying dcgrccs of *intersexual development of genitals.* In many hermaphrodites, the chromosomal abnormalities in the form of XX/XY mosaicism are evident. You would study the sex mosaics in the following section.

5.3.5 Free Martins

Besides humans, sexual differentiation anomalies too occur in animals resulting in intersexes. In cattle, sheep, pigs and goats sometimes sterile intersex animals are born. This condition may occur when male and fcmale foetuses are developing in the uterus simultaneously (i.e., twins) and there is a fusion of the placenta1 membranes permitting mixing of foetal blood. As a result testosterone from the male induces male characteristics in the female twin. This kind of animals are called free martins. Free martins have XX-chromosome constitution, female internal genitalia; but male external genitalia and secondary sexual characters.

SAQ 3

If the diagnosis is testicular feminisation, what will be the genotype and phenotype of that individual?

SAQ 4

A human XX baby has both male and female characters. How could such an error in sexual development occur?

5.4 SEX MOSAICS

In many species, some individuals are made up of several cell lines, each with different chromosome number. These individuals are referred to as *mosaics* or *chimeras*. Such conditions are the result of certain mishaps that take place at various stages of embryological development, and these affect the daughter cells. Three causes have been known that result in mosaics.

Nondisjunction is the failure of chromosomes to properly separate into their respective nuclei during nuclear division.

i) The first one is *mitotic nondisjunction of sex chromosomes* (Fig. 5.4). *It* happens in a manner similar to that found in meiosis. In a male zygote (XY), there are two possibilities (Fig. 5.4 a&b). One, there may be nondisjunction of X chromosome resulting in one cell line having XXY and other having YO chromosome (Fig. 5.4a).

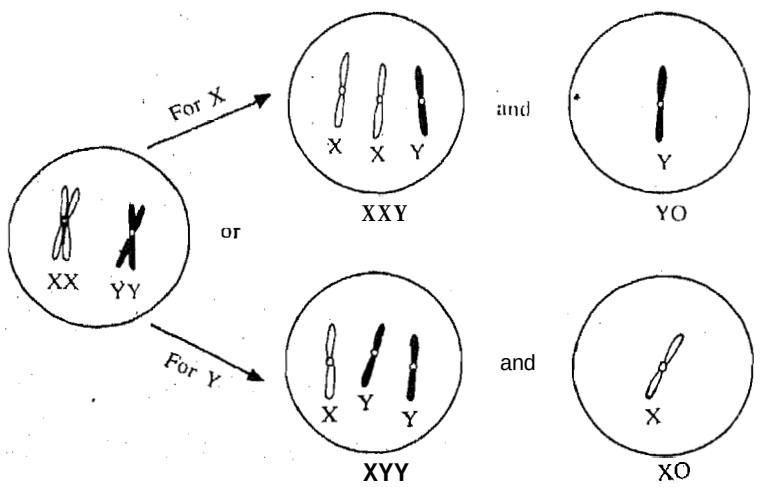

Fig. 5.4: Mosaicism due to nondisjunction of sex chromosomes in d zygote. (a) the disjoining of X chromosome results in XXY and YO cell lines, (b) and the nondisjunction of the Y chromosome leads to the formation of XXY end XO cell lines.

The latter one is inviable. In the second possibility there is nondisjunction of Y chromosome resulting in cell lines: XYY and XO (Fig. 5.4 b). In a female zygote nondisjunction would result in XXX and XO cell lines (Fig. 5.5).

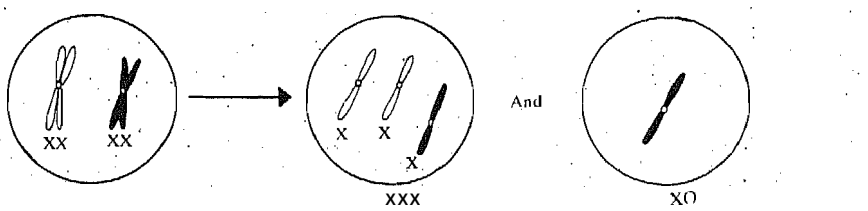

Fig. 5.5: Mosaicism due to nondisjunction of sex chromosomes in ♀ zygote leading to the formation of XXX and XO cell lines.

ii) The second cause is **chromosomal lagging.** The X chromosome may lag and fail to reach the pole at anaphase to be incorporated in the daughter nucleus (Fig. 5.6). It is left out in the cytoplasm where it disintegrates. As a result daughter cells of chromosomal complement AAXX and AAXO are formed. You may remember that in *Drosophila* AAXX results in females and AAXO in males. Therefore, the developing embryo having a mixture of AAXX - (female's) and AAXO - (male's) genotypes, have some parts that are like males and others like females. Flies with such chromosomal complement are seen in actual and are known as **gynandromorphs** or **gynanders** and also **sex mosaics.**

If the mishap, i.e., chromosomal lagging occurs at the one-called stage (Fig. 5.6) then **bilateral gynandromorphs** (Fig. 5.7.) are formed. If it occurs at a later stage of development then small patches of male tissue will be present among the female background.

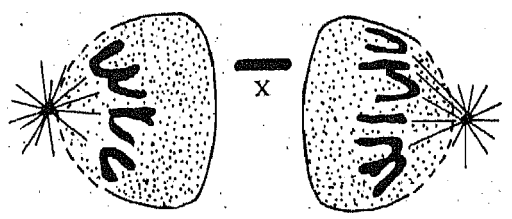

Fig. 5.6: *Drosophila melanogaster.* A lagging X chromosome in the first cleavage nf zygote, illustrating the origin of bilateral gynandromorphs.

Sex chromosome mosaics are also known'in humans. The karyotype of some of these mosaics are XX/X, XY/X, XX/XY, and XXX/X. In the case of XX/X persons, one line of cells have only one X chromosome whereas the other has two Xs. Similarly, in XXX/X individuals, one cell line has three Xs and the other has one X.

iii) The third cause of development of mosaics is by **dispermic fertilisation. A** known case of XX/XY chimera was formed by the above manner. In this two sperms, one X-bearing, and the other Y-bearing, unite with the nucleus of egg and one of the polar bodies respectively. The 'zygotes' thus 'formed, fuse and develop into one individual.

Because mosaicism can occur at any time producing a highly variable range of affected phenotypes, it is plausible that there would be many persons in the population that are mosaics to some degree. Such persons, although phenotypically normal, may have a reproductive risk. **A** portion of their gonadal cells could be chromosomally abnormal.

It must be noted that these *mosaic persons are not gynandromorphs.* No discrete patches of definite male or definite female tissues are seen in any kind of human mosaic. The mosaics may show a range of abnormal phenotypes, but hormonal activity in mammals will not allow the development in any one of them into two distinct classes of cells, i.e., those with typical female features intermingled with those that are obviously male.

Departures from normal number of chromosomes because of nondisjunction and other mishaps can affect autosomes as well as sex chromosomes. Any chromosome

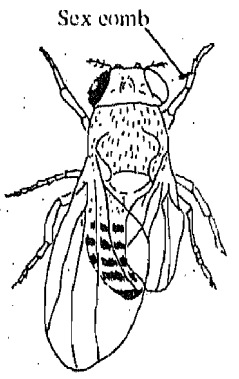

Fig. 5.7: *Drosophila*, gyrandromorph. Left side is wild type XX female. Right side is XO male, hemizygous for while eye and miniature wings.

may become altered in structure. These and other chromosomal anomalies would be discussed in detail in Units 9 and 10.

5.5 SEX REVERSAL

In the female birds normally only one gonad develops while the other side is suppressed. If ovariectomy is performed, the undifferentiated gonad develops into testis. In such a case, secondary sexual characters also appear and the resultant male can even father an offspring (i.e., it is fertile). A complete sex reversal can be seen in birds (unlike man) if hormones are injected in the embryo early in development.

In mammals early removal of gonads (castration, ovariectomy) or their destruction by disease results in an intersex appearance as it leads to partial or complete reversal of secondary sexual characters. Boys castrated before puberty (eunuchs) were employed in Middle East, North Africa and China as harem chamberlains. In Italy they were part of operatic stages and church choirs as the male hoarse voice does not develop in them.

From the above discussion it is evident that the potential hermaphrodite state can be more easily activated in birds than in mammals. In animal husbandry, castration is used to increase fat content and improve quality of meat by avoiding undesirable odours from meat, a characteristic of meat from adult males. It also contributes to docility of animals like oxen which are used for carrying loads.

A human intersex may opt for a sex reversal irrespective of the genetic constitution. Plastic surgery and hormonal treatment are given depending upon internal and external genitalia present. Such individuals, however, remain sterile.

5.6 SEX RATIO

Because sex is determined by the Y chromosomes, and because males produce X-, and Y-bearing gametes in approximately equal numbers, Mendel's law of Segregation predicts that the sexes should occur in equal proportions, or as commonly expressed in a male : female ratio of 1:1. In most species most of the time, the number of males and females is about equal, but this is not the case always. In humans, for example, different sex ratios occur for different age groups.

5.6.1 Primary Sex Ratio

It is the proportion of males and females conceived in a population. It is deduced from the male and female frequency in abortions, miscarriages and still-births, in addition to the live birth records. Although a 1:1 ratio is expected, as there is equal chance of the X-, and Y-bearing sperms to fertilise the egg, in actuality a deviation has been noted, which is more than 1.6 males : 1 female. This may be caused by one or more than one of the following three factors:

1) There may be selective fertilisation of the egg with a Y-bearing sperm due to its greater motility than the X-bearing sperm. The Y-bearing sperms may bc more motile because of their lower chromosomal mass.

2) The environment of the female ducts may be morc favourable for the survival of the Y-bearing than the X-bearing sperm.

3) The egg may react more preferentially to the approach of Y-bearicg than to the X-bearing sperm.

5.6.2 Secondary Sex Ratio

It reflects the proportion of males to females at birth. It is easy to determine, but has disadvantage of not accounting for disproportionate embryonic or foetal mortality. World-wide data of secondary sex ratio indicates a value slightly different from the expected 1:1 and is about 1.06 males : 1 female. This unequal sex ratio at birth

appears to be an established phenomenon for which no clearly defined biological mechanism has been identified.

5.6.3 Tertiary Sex Ratio

The sex ratio at any particular time after birth is known as tertiary sex ratio. It has been found that in the age group around twenty years, the number of males exceed females. This trend gradually gets reversed and female population is higher after fifty years onwards due to increased male death rate in every age category (Table 5.1).

Table 5.1: Approximate sex ratios for the human species.

Time	Male:Female
Primary ratio (conception)	> 106:100
Secondary ratio (birth)	106:100
Tertiary ratio (post-natal)	
Second to fourth decades	100:100
Fifth decade	90:100
Sixth decade	70:100
Eighth decade	50:100
Tenth decade	20:100

Thus the excess of males at conception and birth progressively diminishes throughout life and the males get outnumbered more and more by females with time. The biological weakness of males resulting in higher mortality is partly understandable as they have only single X-chromosome. If this X-chromosome carries recessive alleles resulting in lower viability, sublethality or lethality, then a male carrying it would be affected. On the other hand, a female would escape the deleterious effects of these alleles as her other X-chromosome may carry a normal allele which compensates for the defective one. Interestingly a perfect sex ratio (1:1) is ensured during the prime reproductive years, irrespective of the primary and secondary sex ratios. This appears to be an evolutionary adaptation to facilitate mating and get the process of sexual reproduction going.

SAQ 5

What is the genetic basis of the approximately 1:1 sex ratio in majority of animals?

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SAQ 6

In a population of 1440 individuals born, the number of males was 741 and of females 699. What is the sex ratio? How would you explain the excess of births of one sex as compared to the other?

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SAQ 7

In a small town the number of males under 21 years of age exceeded the number of females. From 22 years, the trend gradually reversed and the sex ratio was 100 males : 146 females for persons over 65 years. Account for this reversal.'

5.7 SEX SELECTION OF THE OFFSPRING

It has been man's desire to choose and control the sex of his offspring, Early efforts in selecting sex of newborn involved changes in physical environment or in human behaviour around thr time of conception. These methods were scientifically unsound. Currently three main approaches are employed for the selection of sex:

i) selective abortion of the foetus of unwanted sex;

ii) timing of fertilisation relative to ovulation;

iii) separation of sperm *in vitro* followed by artificial insemination. Of these three approaches the first is post-fertilisation selection, while the other two are known as pre-fcrtilisation techniques.

5.7.1 Prenatal Sex Dc termination

It has also been human curiosity to know the sex of the child before birth. In recent years, the technique of amniocentesis coupled with cell culture methods has opened the way to prenatal diagnosis of many genetic defects and the determination of sex. Amniocentesis involves withdrawing a sample of amniotic fluid surrounding the foetus, around 16 weeks of gestation. The foetal cells thus collected are stained and examined. They enable a highly accurate prediction of the sex of the foetus. Such a' predetermination of sex is useful in case of families having a history of X-linked discascs. Similarly, chorionic villi can now be sampled much earlier in pregnancy (4 to 8 weeks of gestation) and cultured for prenatal detection of genetic defects and sex of the growing embryo. This early detection gives option to terminate the pregnancy, if the foetus is of the undesired sex or has any abnormality.

In a country like India, where we face the population explosion problem, predetermination of sex has been pleaded as a help in family planning. Many couples have large families for want of a child belonging to a particular sex, thereby increasing the population. Predetermination of sex with one of these techniques could be offered to such couples so that they are able to have a child of their choice. But preference of males in our society would lead to a very large number of females being aborted. It is difficult to predict the extent to which normal sex ratio would be disrupted, if people could choose the sex of their offspring. However, judging from past records (where male births have been favoured in most countries including India) human intervention is expected to alter the balance of nature. The result of this change is more likely to create new problems for society. Hence this approach cannot be recommended as a family planning method till the time the attitude towards both sexes becomes the same in our society.

5.7.2 Timing of Fertilisation

Earlier reports suggested that male conceptions are more likely to occur if fertilisation is around the time of ovulation and females from fertilisation after ovulation time. The reason for this may be the difference in maternal hormone levels during the fertile period. This hypothesis is likely to form the basis for manipulation of sex ratio in man as well as other species where artificial insemination can be carried out.

5.7.3 Separation of X and Y Chromosome Bearing Sperms

The slight difference in size, shape, weight and density between X and Y populations of spermatozoa have been taken into consideration for the physical separation of these two types.

Separation by Ultra-centrifugation: The X and Y-bearing sperms can be separated by ultra-centrifugation where the heavier X-bearing sperms settle down and the lighter Y-carrying ones float. This difference in weight of the two types of sperms is due to the extra chromatin of X-chromosomes as compared to the Y.

Electrophoretic Separation: This method is based on the assumption that X and Y-bearing sperms differ in their electric charge and can therefore be separated in an electric field.

Separation Based on Differential Motility: columns of different types are used to separate the sperms on the basis of their differential motility. The semen is layered over albumin or sephadex columns. The sperms are then allowed to sediment or swim upwards in the columns, the Y-sperms being more motile move faster thereby getting separated from the X-sperms. So far this appears to be the most economic and extensively used method.

The control and manipulation of sex ratio in cattle is important in dairy cattle. Cows are needed in large numbers because of their milking ability and one bull is sufficient to mate with many cows. Therefore it is desirable to have more cows than bulls. This can be achieved by artificial insemination, using X-bearing sperms.

SAQ 8

When cows have twin calves of unlike sex (fraternal twins), the female twin is usually sterile and has masculinised reproductive organs. What is the calf in such a situation known as? Discuss how such an individual comes to exist?

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5.8 SUMMARY

In this unit you have learnt that:

- In mammals including man, sexual development proceeds from a stage where sex is not specified, as the embryological gonad is bipotential having the ability to develop into either sex.
- The genetic information on the sex chromosomes is responsible for the primary sex determination events.

  Y-chromosome plays a crucial role in sexual development of mammalian embryos as the presence of Y, determines male development and in its absence female development proceeds. Y-chromosomes carries genes for testis determining factor (TDF) which promotes testes (male gonad) development. There is no particular

substance which induces femaleness and so it can be deduced that in the absence of TDF, ovaries develop. In mammalian embryos the testes produces testosterone' (male hormone) and Müllerian inhibitor. These help in the formation of male reproductive tract. In the absence of Mullerian inhibitor the female reproductive tract develops. Sex hormones are essential for normal male and female sexual development.

- Sex chromosomes are not the sole determinants of human sexual identity as there are males with an XX genotype. Clearly, there are genes on the autosomes that go into shaping the final sex phenotype of an individual. When these interrelated factors malfunction, human and animal intersexes may develop. Both male and female pseudohermaphrodites and the true hermaphrodites (contain both male and female reproductive organs) have been found

  Mosaic individuals contain cell lines with different genetic constitution. Such a condition may result due to mitotic nondisjunction, chromosome lag, or dispermic fusion.

- Sex ratio is the proportion of males to females in a population. Depending on when the sex ratio is assessed it is known as primary, secondary or tertiary.

  Man has always been curious to learn about the sex of unborn children,' this is now possible by the techniques of amniocentesis and chorionic villi culture.

- It has been man's desire to produce sex of his choice and this is within his reach now as X and Y bearing sperms can be separated by various techniques.

- Since interference of man may disrupt the sex ratio and hence the natural balance, one should be very careful employing any of these techniques.

5.9 TERMINAL QUESTIONS

1) A sex-linked dominant mutation in the mouse, testicular feminisation (*Tfm*), eliminates the normal response to the testicular hormone – testosterone during sexual differentiation. An XY animal bearing the *Tfm* allele on the X chromosome develops testes, but no further male differentiation occurs. The external genitalia of such an animal are like female. From this information, what might you conclude about the role of the sex chromosomes in sex determination and differentiation in mammals?

2) a) In mice as in all mammals, the male is a heterogametic sex. Assume that sex-linkcd lethal gene is presenl in a strain of animals and that this causes the death of the embryo. How would this affect the sex ratio?

   b) Answer the same question if sex-linked lethal genes wcrc present in a strain of chickens.

3) For humans, give the genetic sex of (a) true hermaphrotlites, (b) masculinising male pseudohermaphroditcs, and (c) feminising male pseudohermaphrodites, and (d) Female pseudohermaphrodites?

4) Name the ways in which mosaicism can occur in *Drosophila*.

5) a) What is sex differentiation? Describe the role played by testis determining factor (TDF) in this.

   b) Distinguish between: (i) Hermaphrodite and Intersex; (ii) Androgenital syndrome and free martins; (iii) Primary and Secondary sex ratio.

   c) What are the advantages and disadvantages of prenatal sex detection? What social problems d o you foresee if the secondary sex ratio is imbalanced?

6) Match the following:

i) Testosterone	a) Y-linked
ii) ***Tfm***	b) Intersex
iii) Free martin	c) Sex mosaic
iv) Sxr	d) Produced by Testis
v) Gynandromorph	e) X-linked

7) Fill in the blanks:
   i) The genotype is ..... and phenotype is ..... in an individual who is suffering from testicular feminisation syndrome.
   ii) Primary sex ratio shows an increased number of ..... as compared to ..... at conception.
   iii) The two techniques primarily involved in early prenatal sex determination are .....and .....
   iv) X and Y-bearing sperms can be separated on the basis of their difference in ..... and ..... by ultra-centrifugation and electrophoresis.
   v) To suppress the development of female reproductive tract the factor responsible is .....

5.10 ANSWERS

Self-assessment Questions

1) Once the testis is formed due to the presence of Y-chromosome it produces testosterone which stimulates the development of rest of the male reproductive system and suppresses the female development.

2) When a male has a XX genotype it can be assumed that one of the two X-chrotnosomes present carries the *Sxr* gene. This sex modifying gene is responsible for spermatogenesis and may have been transferred from the Y-chromosome to the X-chromosome. Presence of the *Sxr* gene modifies the sex to male in spite of the presence of two X-chromosomes.

3) The genotype of the individual is XY and Lhe phenotype is that of a female in spite of the testis being present. The development of normal, functional male reproductive tract is prevented as the tissues arc unable to respond to the male hormone testosterone. Since female development occurs in the absence of male differentiation, female genitalia and secondary sexual characters are present.

4) This may be a case of androgenital syndrome where because of the XX-chromosome constitution the individual is expected to develop into a female, while the excessive hormone adrcnalin produced by the adrenal gland leads to masculinisation. The resultant individual has both male and female secondary sexual characters.

5) In majority of animals one of the two sexes is heterogametic (usually the male) and produces equal number of gametes of each type. These after fertilisation with gametes of the homogametic sex (the female) result in same proportion of males and females.

6) The ratio for males $741/1440 = 0.52$ and for females is $690/1440 = 0.48$. The sex ratio is slightly altered from the expected ratio, which is 1:1, with an excess of male births. The reason for this may be: (1) selective fertilisation of egg with Y-bearing sperms due Lo their faster motility; (2) the environment of the fcmalc reproductive tract may be more favourable for the survival of Y-bearing sperm; (3) the egg may react more preferentially to the approach of Y-sperm as compared to the X-sperm.

7) Excess of malcs at conception and birth progressively diminishes throughout life and the males get outnumbered by females gradually. This is due Lo the prescncc of a single X-chromosome in males unlike females. If this single X-chromosome carries deleterious gene, it can express itself in a single dose (hemizygosity) leading to differential mortality.

8) The male hormones of the male twin are produced earlier than the female hormones of the female twin. As a result, sexual differentiation in the female is abnormal because of the common placenta. The calf in such a situation is known as free martin.

Terminal Questions

1) The Y chromosome is essential for initial differentiation of testicular tissue. However, hormones subsequently produced by the testes are responsible for differentiation of the remainder of the male reproductive tract.

2) a) The females carrying the lethal gene would produce only half the expected number of male offspring since no male could be born with the allele. The 1:1 sex ratio would become distorted to 2:1 in favour of females.

   b) The males carrying the lethal gene would produce only half the expected number of female offspring: No hen would carry the allele. The sex ratio of 1:1 would change in favour of males to 2:1.

3) a) XX/XY
   b) XY
   c) XY
   d) XX

4) Mitotic nondisjunction and chromosome lag.

5) a) The differentiation and development of sex organs of either sex by the combined action of several genes. For the second part of the question refer to Section 5.2.

   b) i) See Section 5.3
   Hint: True hermaphrodites possess both male and female reproductive systems developed to various degrees. Intersexes have one sex or display some feature of both the sexes.

   ii) See Sub-sections 5.3.3 and 5.3.5.
   iii) See Sub-sections 5.6.1 and 5.6.2.

   c) Write your viewpoint on the issue.

6) i) d
   ii) e
   iii) b
   ivj a
   3) c

7) i) XY, female
   ii) males, females
   iii) amniocentesis, chrionic villi sampling
   iv) weight, clcctric charge
   v) mullerian inhibitor