# infertility management and assisted reproduction

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## The male reproductive system

#### Introduction

The anatomy and function of the male genital organs fulfil certain roles during the reproductive process; copies of the man's genetic make up are packaged in spermatozoa which are produced in the testes. These gametes are then conducted along the male genital tract. Ejaculation results in their deposition in the vagina if intravaginal intercourse takes place. A simplified physiological anatomy of the male genital tract will be presented in this chapter.

## The male sex organs

The male sex organs consist of the testes, excretory ducts, accessory glands and the penis (Table 1.1 and Figure 1.1). The testes (singular: testis) are two oval structures that normally lie in the scrotum (Figure 1.2). Each testis measures 4–6 cm in length and has a volume of about 25 ml. The testes produce spermatozoa (singular: spermatozoon) and testosterone (the male hormone). A mature spermatozoon is shown in Figure 1.3. It is a highly specialized cell that is designed for movement. The sole function of the spermatozoon is to carry a copy of the man's genetic make up, in the form of chromosomes, from the site of production in the testis, through the male and female genital tracts, to the egg that it fertilizes. The spermatozoon carries this genetic material in the head piece. The rest of the spermatozoon is made up of the mid-piece, which supplies the energy, and the tail which propels the sperm forward.

Production of spermatozoa commences at puberty and takes place inside highly coiled tubes that are found in the testes called seminiferous tubules (Figure 1.4). Following their production, spermatozoa are wafted along the seminiferous tubules, by a fluid current, and enter the excretory ducts. The epididymis is a highly coiled tube measuring 5–6 m if unwound fully. It connects the tubules of the testis to the vas deferens. The vas deferens is 35–45 cm long. From its point of origin in the scrotum the course of the vas deferens is upwards to the groin. It then enters

Table 1.1. The male reproductive organs

Components	Number
Testis	2
Excretory ducts	
epididymis	2
vas deferens	2
Accessory sex glands	
seminal vesicle	2
prostate	1
bulbo-urethral gland	2
Ejaculatory duct	2
Urethra	1
Penis	1

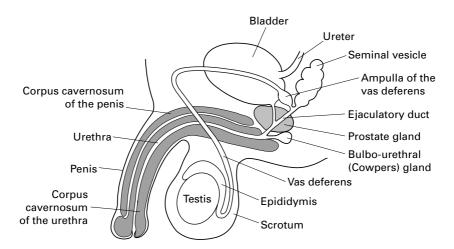


Figure 1.1 The male sex organs: side view.

the body cavity through a tunnel (called the inguinal canal) where it joins the duct of the seminal vesicle on that side to form the ejaculatory duct. Spermatozoa reaching the ejaculatory duct from the vas deferens of each side are ejected from the penis, which is the copulation organ, together with secretions from the accessory sex glands (seminal vesicles, prostate gland and bulbo-urethral glands) at the time of ejaculation. The urethra also conducts urine from the bladder to the exterior during urination. The prostate is the largest accessory sex gland. It weighs 20 g and is 3–4 cm in diameter.

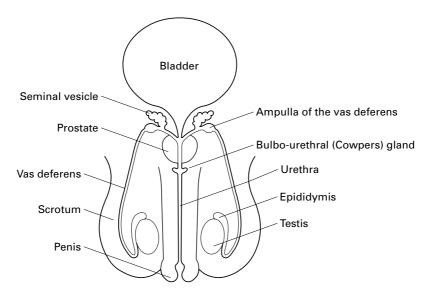


Figure 1.2 The male sex organs: front view showing paired components.

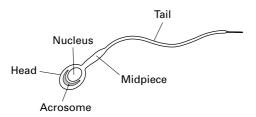
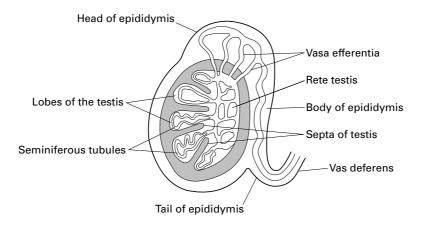
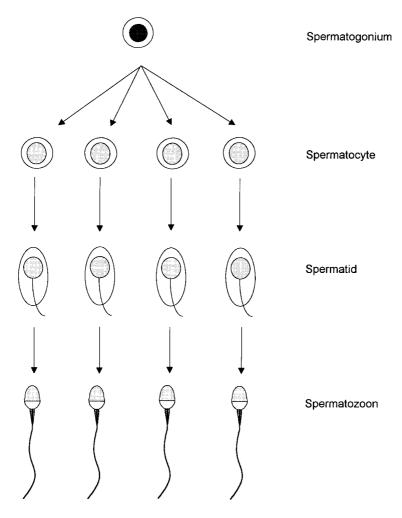


Figure 1.3 A mature spermatozoon.



**Figure 1.4** Section through the testis showing the organization of the various systems of tubules.



**Figure 1.5** Major stages during production of spermatozoa in the testes.

## **Production of spermatozoa**

The testes hang well out of the body cavity in the scrotum; this is necessary to keep the testes cooler than the rest of the body which is at 37 °C. The temperature of the testes while in the scrotum can be up to 4–7 °C lower than that of the body. The lower temperature is required for optimal production of spermatozoa. Spermatozoa develop from spermatogonia which are cells that line the inside of the seminiferous tubules. The spermatogonia do not just change into spermatozoa. They divide repeatedly and the resulting cells go through a complex series of changes before becoming fully formed spermatozoa (Figures 1.5 and 1.6). These processes take about 64 days to be complete in the testes. It then takes another

#### 7 Development of the testis

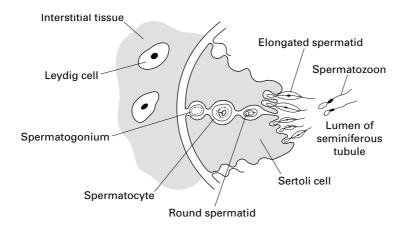
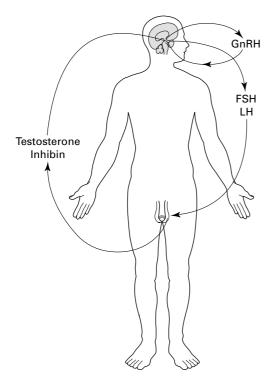


Figure 1.6 Transverse section through a seminiferous tubule and adjoining interstitial tissue.

10–14 days for these spermatozoa to pass through the epididymis and vas deferens. Although fully formed in the testes, spermatozoa are not completely mature and do not usually move. Their transit through the seminiferous tubules and into the epididymis is as a result of movement of the fluid in which they are suspended. The fluid current is set up by Sertoli cells which continuously secrete fluid into the seminiferous tubules. Sertoli cells are one of the groups of cells found within the seminiferous tubules. The spermatozoa may begin to move when they enter the epididymis but the movement tends to be in circles. Full motility is however achieved by the time they leave the epididymis. The epididymis acts as a storage organ for spermatozoa. The vas deferens also acts as a storage organ but the number of spermatozoa it contains at any point in time is usually just enough for one ejaculation. The transport of spermatozoa through the epididymis and vas deferens is by means of contraction of muscles found within the walls of these hollow tubular structures.

## **Development of the testis**

The testes originally lie in the abdomen of the developing male fetus but descend into the scrotum during the later part of pregnancy. Cells that will eventually produce spermatozoa (called primordial germ cells) are deposited in the testes in the early stage of testicular development. These primordial germ cells arise in the yolk sac of the embryo and migrate, between the fourth and sixth week of pregnancy, to the genital ridge that eventually forms the testes. The primordial germ cells develop into spermatogonia and lie dormant until the boy reaches puberty when the spermatogonia resume cell division and further development. The testes



**Figure 1.7** An adult male and the distance separating the hypothalamus and pituitary gland from the male sex organs.

do not become depleted of spermatogonia unlike the situation in the female, as will be seen in Chapter 2.

## Hormones that control the function of the adult male sex organs

The hypothalamus and pituitary gland are located in the brain and influence the function of the male sex organs, although they themselves are not sex organs. Both glands secrete hormones (Figure 1.7). Gonadotrophin releasing hormone (GnRH) is one of the hormones secreted by the hypothalamus. GnRH enters blood vessels in the brain to reach the pituitary gland which it stimulates to produce two other hormones. One is the follicle stimulating hormone (FSH) while the other is the luteinizing hormone (LH). Both FSH and LH are secreted into the blood stream through which they reach the sex organs. Inhibin, another hormone, is produced by Sertoli cells, while testosterone is produced by cells that lie outside the seminiferous tubules – the Leydig cells. FSH stimulates the production of spermatozoa within the seminiferous tubules while LH stimulates Leydig cells to produce testosterone. FSH also contributes to the stimulation of Leydig cells to produce testosterone (Figure 1.8).

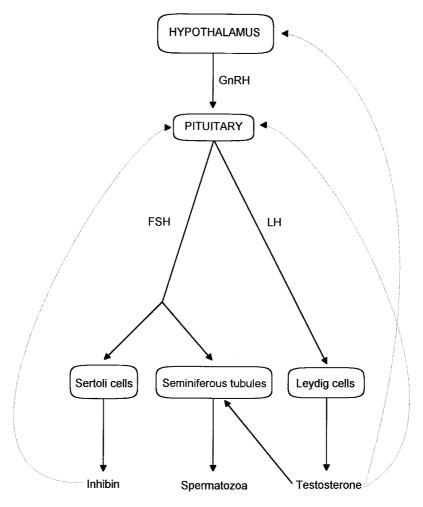


Figure 1.8 Hormonal control of testicular function.

In the adult, testosterone maintains the size and function of the various sex organs and is important for the production of spermatozoa. Feedback control mechanisms are present in various organs of the body and help to keep the production of compounds and materials at a constant level. In relation to the male reproductive organs, testosterone controls the production of LH; when the concentration of testosterone in blood decreases, the release of LH is increased and vice versa. Part of the feedback control of testosterone on LH production is through its effect on the production of GnRH by the hypothalamus. When the production of spermatozoa drops, the production of inhibin by the Sertoli cells also drops. The pituitary senses the low level of inhibin and increases the production of FSH. FSH then stimulates production of more inhibin and spermatozoa (Figure 1.8).

Table 1.2. Constituents of semen

Cells	Chemical compounds
Spermatozoa	Water
White blood cells	Hormones
Epithelial cells	Proteins
(Red blood cells)	Carbohydrates
(Bacteria)	Steroids
(Viruses)	Lipids
	Other compounds

#### **Erection and ejaculation**

Sexual arousal and excitement in men result from input of the various senses (sight, touch, sound, smell and taste). Erection of the penis is usually one of the earliest manifestations of sexual arousal. There is also erection of the nipples, increase in the heart rate and blood pressure. The excitement is maintained and even increased by sexual intercourse or masturbation. At the height of sexual excitement the smooth muscles in the walls of the epididymides and vasa deferentia (plural of vas deferens) contract and expel spermatozoa into the urethra. The muscles in and around the prostate and seminal vesicles also contract and these glands discharge their secretions into the urethra. This is also the time during which the man begins to orgasm; there is a release of sexual tension and arousal and the man has an intense feeling of pleasure. The muscles at the neck of the bladder contract and this prevents spermatozoa and the secretions from flowing back and into the bladder. Within a very short period after the emission of spermatozoa and the accessory sex gland secretions, there is repeated contraction of the muscles of the pelvis, lower extremities and the trunk. The smooth muscles of the urethra contract along with other muscles in the penis. This has the effect of expelling semen from the urethra to the outside which if the man is having vaginal sexual intercourse at that time, will be expelled into the vagina.

#### **Composition of semen**

Semen is the fluid that is ejected from the penis at the time of orgasm. It should not be confused with pre-ejaculatory fluid which is produced by the bulbo-urethral glands during sexual excitement and before ejaculation. Pre-ejaculatory fluid is thin and clear and serves to flush the urethra and neutralise any acidic remnants of urine. The constituents of semen are shown in Table 1.2. The volume of semen produced during ejaculation is usually between 2 and 6 ml. The seminal vesicles

contribute about two-thirds of the fluid while the prostate contributes one-third. The contribution to this volume by fluid from the testes, via the epididymides and vasa deferentia, is negligible. The most apparent contribution of the testes to semen are spermatozoa. Normally, both live and dead spermatozoa are found in semen together with a small number of white blood cells. These white blood cells serve the function of guarding the genital tract from infection just as in other parts of the body where they are found. They tend to engulf any micro-organism (such as bacteria) they find but they also engulf dead cells, including dead spermatozoa. When the number of white blood cells found in semen is high it may mean that there is an infection in the male genital tract. However, even after extensive investigation no source of infection will be found in a large proportion of cases. Epithelial cells can also be found in semen. These are cells that cover the surface of the genital tract and it is normal to find some in semen. Debris are found in semen and represent fragments of broken down cells and other material. Occasionally red blood cells or bacteria can be found in semen. This finding is not normal and all attempts should be made to find out the exact cause of the problem and provide appropriate treatment. It is now being realized that viruses can also be found in semen and may have a role in the causation of infertility in some couples. Semen contains numerous chemical compounds produced by the accessory sex glands. These compounds have different functions including protection and nourishment of spermatozoa. The fluid also helps to transport the spermatozoa along parts of the male genital tract. Following ejaculation the fluid protects spermatozoa from the acidic conditions of the vagina long enough for some of them to escape into the upper parts of the female genital tract. Initially after ejaculation semen forms a clot due to the action of a coagulation enzyme produced by the seminal vesicles. However, the clot begins to liquefy after a few minutes due to the liquefactive activity of seminine, an enzyme produced by the prostate gland; the process is complete usually within 30 minutes.

#### Semen parameters

As will be seen in Chapter 6, semen is analysed during the evaluation of couples who have difficulty in achieving pregnancies. The aim of this analysis is to determine if the various constituents of semen are present and in the right proportions. Attempts have been made to define normal semen parameters. Although these attempts are continuing, the following parameters are accepted as normal for the time being. Semen should liquefy within 30–60 minutes of ejaculation. Liquefied semen is not viscous. It should have a greyish-white appearance. At times it may appear a little yellowish but this is also accepted as normal. Semen should not be clear like water, it should have a translucent appearance. It should not be acidic or

too alkaline. This can be measured easily in the laboratory. The pH of semen should be 7.2 or more (i.e. neutral to slightly alkaline). The odour of semen has been described as being 'fresh'. Semen should not have an offensive odour. The volume of semen collected from one ejaculation is usually above 2 ml.

The concentration of spermatozoa in the semen sample should normally exceed 20 million spermatozoa in 1 ml of the sample. What this means is that one ejaculate may contain a total of 40 million spermatozoa if the concentration is 20 million/ml and the volume of semen is 2 ml. For an ejaculate of 6 ml with a concentration of 20 million/ml, the total number of spermatozoa will then be 120 million. Semen samples with a higher concentration will have a greater number of spermatozoa in the ejaculate. It is quite possible for a total count of 600 million spermatozoa to be found in an ejaculate. Higher values have also been recorded. At least 50% of the spermatozoa should be moving. The proportion of live spermatozoa in the sample is normally 75% or greater. A large proportion of spermatozoa are abnormal in appearance even if they are alive and moving. No one knows why this is so but this finding is universal; all men produce semen containing abnormal looking spermatozoa. However, at least 15–30% of spermatozoa in a sample should look normal. Further discussions on semen parameters can be found in Chapters 4 and 6.

## **Applied concepts**

- It is recommended that a man should not ejaculate for a period of 2–5 days before producing a semen sample for analysis. This is an attempt to ensure that every patient coming for semen analysis has the same period of abstinence. In so doing it becomes easier to interpret the results of the analysis and compare results from different patients.
- The concentration of spermatozoa in semen and some of the other parameters do not remain constant in all semen samples produced by the same individual. The concentration, for example, varies from sample to sample. That is why it is necessary to repeat semen analysis on the same man at least three times over a period of a few months to gain a full impression of how much the concentration varies from sample to sample. This is even more important if a poor result is obtained when semen analysis is performed on a man for the first time. Having said this, a man who, for example, produces a sample that has a sperm concentration of 100 million/ml is not likely to produce a sample that has a concentration of 5 million/ml. Of course he needs to abstain from ejaculation for the standard period of time and should not have any illness or ingest any drug that will decrease the production of spermatozoa during the interval between tests.

- It takes about 74–78 days for spermatozoa to be produced and appear in the ejaculate. This means that it will take that length of time, at a minimum, to find out if a bout of illness or ingestion of toxic substances or drugs affects the production of spermatozoa. It will also take that length of time to find out if treatment has had any beneficial effect on the production and quality of spermatozoa.
- Production of semen for analysis is usually by masturbation into a special sterile
  plastic container supplied by the laboratory. The container is labelled with the
  man's name, date of birth, hospital number, date and time of production of the
  sample, and other identifying information. The container is closed properly after
  collection of semen and taken to the laboratory.
- Many laboratories ask for semen samples to be produced on site. This is to enable analysis of the sample to be commenced within a short time (about 30 minutes) of its production. The longer a sample is left before analysis the harder it is to exclude the long interval as a cause of abnormal results, particularly for the assessment of motility of the spermatozoa and the percentage that are alive. Producing the sample at the laboratory also avoids the semen being exposed to extremes of temperature conditions during transport to the laboratory.
- Special rooms are set aside at the laboratory or hospital for the production of semen samples. The room is located in a quiet part of the unit and a 'do not disturb' sign is usually hung on the door. Visual aids in the form of magazines and video tapes are provided by most establishments for men who require them.
- Men who find it difficult masturbating at the laboratory or hospital are allowed to produce the sample at home by masturbation. They are usually asked to bring in the sample to the laboratory as soon as possible, within 30 minutes and not more than one hour from the time of production.
- No lubricants are allowed to be used during masturbation. This is because most lubricants are toxic to spermatozoa and may adversely affect the results of the semen analysis if they come in contact with the semen.
- Some men may find it impossible to masturbate. They are provided with special condoms to use during normal sexual intercourse. These condoms are unlike all other condoms because they are made of materials, for example medical grade silicone rubber, that are non-toxic to spermatozoa. The normal contraceptive condoms contain chemicals that kill spermatozoa, for example, nonoxynol-9 and nonoxynol-11. Following ejaculation the condom is removed and the semen emptied into a sterile plastic container before being sent to the laboratory.
- The production of spermatozoa by the testes, hence fertility, decreases with age.
  However, this may not be pronounced in many men and men have fathered children well into their old age. The effect of age on fertility is more evident in females.

- When a man does not ejaculate for some time the accumulated spermatozoa in the vas deferens dribble into the urethra where they are washed away by urine. This serves to prevent a build up of pressure in the testis, epididymis and vas deferens. It however does not mean that all accumulated spermatozoa will be discharged into the urethra this way. Some will still remain in the genital tract and eventually die.
- Avoiding ejaculation for a few days may increase the number of spermatozoa in the ejaculate. Abstinence for long periods of time, however, will not lead to any more improvement of the semen quality. Instead, the number of dead sperm will increase and this may impair the overall quality of the semen sample. Abstinence for more than 3–5 days is not likely to improve the semen quality further.

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