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Male infertility and thermoregulation during physical activity.

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Abstract

The objective of this study tends to highlight the defense mechanisms that the testicles manifest in order to enesis. Indeed, the maintenance of this temperature range results from two thermoregulatory systems which act in synergy: on the one hand, the scrotal system which increases its surface for exchange and sweat in order to cool the venous blood; and on the other hand, the vascular system of the pampiniform plexus where heat exchanges take place accordimaintain their temperature between 33°C and 34°C and thus ensure the smooth running of spermatogng to its concentration gradient, from arterial blood which is warmer to venous blood which is colder.

In this perspective, the persistence of physical exercise creates a drift in muscular but also cutaneous blood flow which competes with testicular blood flow. There is also hypovolemia which will decrease testicular venous return, which causes an increase in scrotal temperature and impairs spermatogenesis.

Introduction

Most of the body's systems work non-stop to maintain homeostasis, with the exception of the reproductive system which seems to "sleep" until puberty. This genital system, also called the gonad, is: the testicles in men and the ovaries in women.

Through these organs, sex cells or gametes are produced and secrete various steroid hormones, generally called sex hormones; The other structures that contribute to reproduction (duct; glands and external genitalia) are called the accessory genitalia.

The male genital system plays a primordial role in the events that lead to fertilization and the fusion of two sexual cells called gametes: a male gamete or sperm, from the father and a female gamete or egg from the mother.

The efficiency of sperm production is expressed by the number of sperm produced per day per gram of testicle. This production in men is lower than that of other species (5 million/d/g for testicles weighing 40 g, the number of spermatozoa is 200 million/ejaculation (Gayard, 2018, pp126-127). Every day, 100 to 200 million spermatozoa are produced through the maturation process, which lasts 65 to 70 days (Guénard, 2001, 475)

In men, sperm must be produced at a temperature slightly colder and lower than that of the body (homeothermal at 37 °C), approximately 33-34 °C testicular temperature (Desvaux, 2022), that of the scrotum (measured simultaneously) between 32.6 and 33.4°C (Mieusset&al, 1992, 32). This condition will allow better spermatogenesis, which is why the testicles are suspended outside the body and positioned in bursae (scrotum). Thus, all energetic reactions of the organism are accompanied by the release of a certain quantity of heat which cannot be stored, because it must be exchanged with its environment.

The proportion of infertile men presenting with scrotal hyperthermia is approximately 45%. (Mieusset & al, 1992, 35). With regard to testicular histological changes, in the context of scrotal hyperthermia, studies have mainly shown an arrest of spermatogenesis at the primary spermatocytic stage in numerous seminiferous ducts, associated with vasculitis-type lesions in the context of testicular oscillations. (Mieusset & al, 1992, 36).

Among the many factors that can be responsible for male infertility, two are closely related to testicular temperature: cryptorchidism and varicocele. (Mieusset & al, 1992, 32)

Indeed, some studies have demonstrated a close relationship between increased scrotal temperature and disruption of spermatogenesis (decrease in the quantity and quality of sperm produced.

As a result, during physical exercise, body temperature increases and causes vasodilation. This vasodilation distributes a large mass of blood to the skin to dissipate the heat overload.

The temperature at the inguinal level increases and thus causes an increase in the scrotal temperature where the testicles are located. Consequently, the temperature of the testicles remains slightly lower than that of the body thanks to their extra-abdominal location. This condition is in fact essential for the formation of viable sperm.

The testicles therefore find themselves in a delicate situation in that they must defend themselves against this thermal attack, in other words adapt to the hyperthermia generated by physical activity.

Hypothesis:

The testicles mobilize defense mechanisms to dissipate heat overload and ensure an optimal temperature for spermatogenesis.

1. **General objective of the study:**

The objective of the present research tends to highlight the process and the defense mechanism faced with the increase in body temperature, in the normal state then with physical effort.

2. **Procedural definition of research concepts:**

2.1. Infertility:

According to Larousse, infertility consists of the inability to procreate, both in men and women.

2.2. La thermoregulation:

It refers to the regulation of inputs and outputs so as to maintain a zero heat balance. (Guénar, 2003, 548). Thermoregulation is ensured by the hypothalamus which constitutes the center of thermolysis and thermogenesis.

2.3. Physical activity:

The World Health Organization defines physical activity as any physical movement produced by skeletal muscles and requiring the expenditure of energy. Physical activity refers to all the movements we make, especially during leisure time, at work or when we move from one place to another. Moderate or vigorous physical activity has health benefits. (WHO, 2022)

3. Adaptation mechanism:

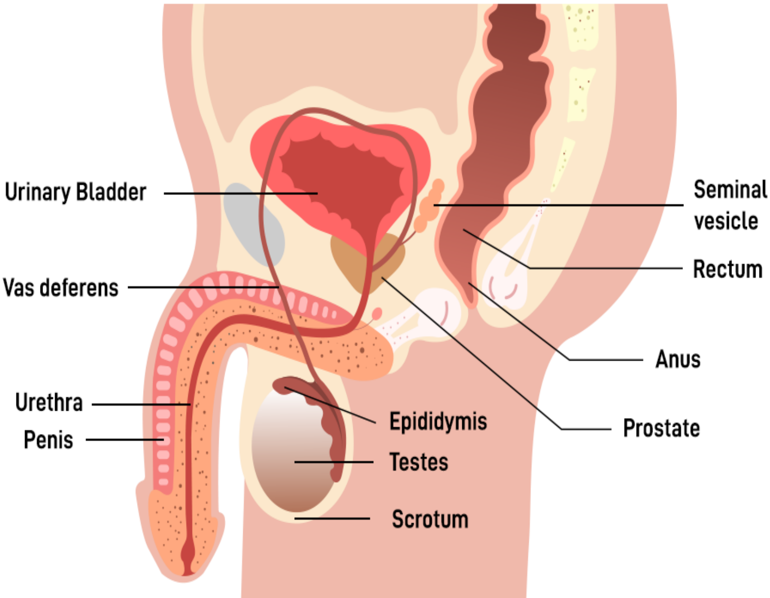
3.1. The male genital system:

The anatomy of the male reproductive system includes two categories of organs: the external genital organs represented by the scrotum (bursa) and the penis, as for the internal genital organs, they are composed of gonads or testicles located in the scrotum (which produce hormones and sperm), accessory glands (like the prostate) which secrete fluids and substances to promote the movement of sperm and finally the ducts to ensure transportation.

To exit the body, the sperm leave the testicles and follow a network of ducts which includes, in order: the epididymis (storage of sperm, coming from the testicle), the vas deferens, the ejaculatory duct and finally the urethra, which opens to the outside at the end of the penis.

The accessory sexual glands which discharge their secretions into these ducts during ejaculation are the seminal vesicles (in the abdominal cavity where they store and dilute the spermatozoa in the seminal fluid), the prostate (secretes a clear liquid which further dilutes the spermatozoa) and the bulbourethral glands. (Kamina, 2002, 361).

Fig 1: the male reproductive system



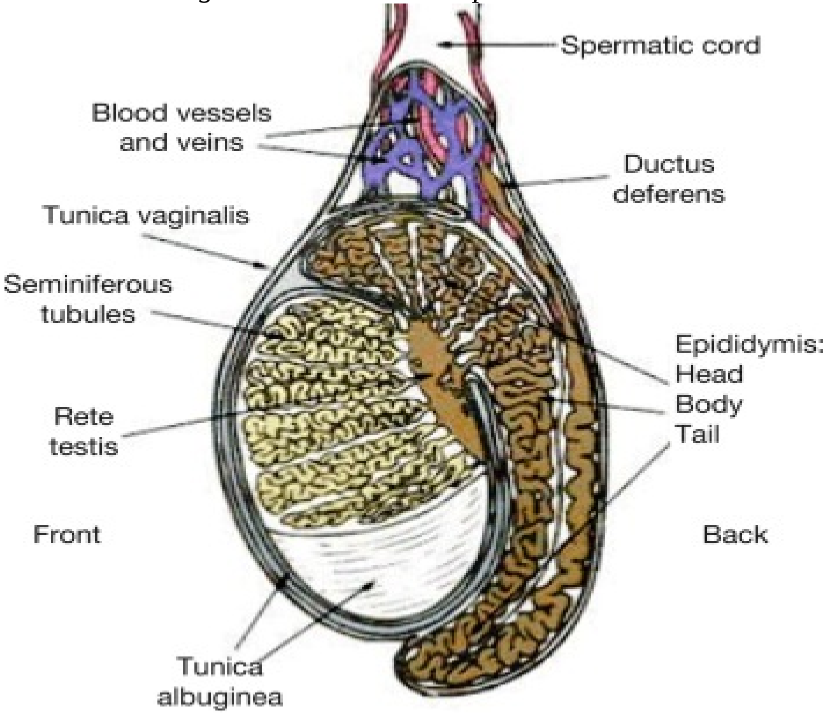
Source: https://www.geeksforgeeks.org/diagram-of-male-reproductive-system/

3.1.1. Structure of testicle:

The testicles are enclosed in a double-layered outer sac called the scrotum (bursa). The scrotum is the protective skin sac that contains the testicles. It is located in the groin, outside the abdominal cavity. Each testicle is covered by a layer of tough fibrous tissue called the tunic. The outer layer is called the tunica vaginalis and the inner layer is called the tunica albuginea.

The protruding part of the tunica albuginea forms the divisions of the testis, dividing it into 250 conical compartments called lobules. Each lobule contains tiny U-shaped tubes called seminiferous tubules. There are approximately 800 tightly coiled seminiferous ducts in the testes. The seminiferous tubules lead into a series of expanded, interconnected tubes called rete testis. A duct or tube connects the rete testis to a tightly coiled tube called the epididymis. The epididymis joins into a long, wide canal called the vas deferens.

Figure 2: The testis and spermatic ducts.



Source : https://www.sciencedirect.com/topics/medicine-and-dentistry/testis-function

Each testicle is held in the scrotum by the spermatic cord, which is made up of strong connective tissue and muscle (the cremaster muscle). Each spermatic cord contains the vas deferens, blood vessels, lymphatic vessels and nerves.

3.1.2. Functions of the testicles:

The testicles perform a dual function; exocrine and endocrine.

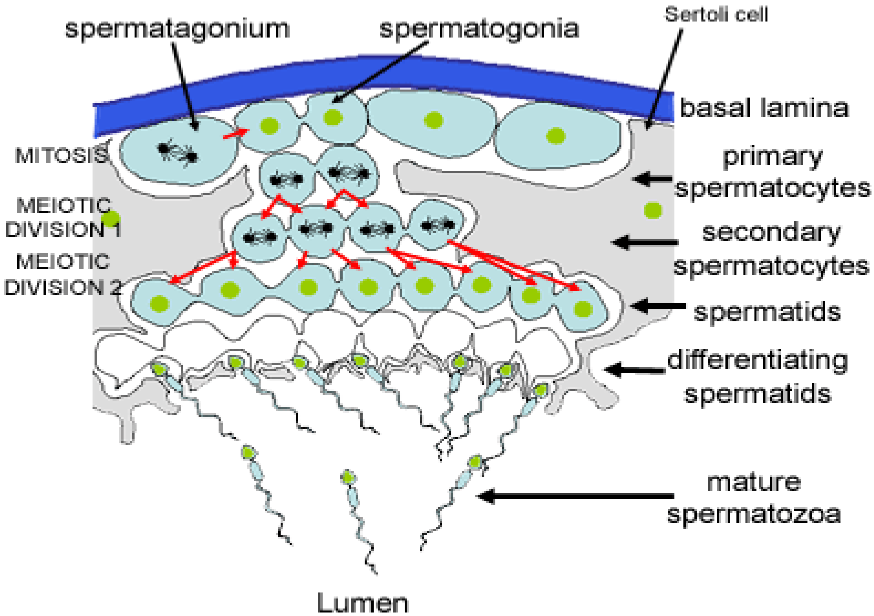
3.1.2.1. Exocrine function:

Spermatogenesis is the formation of sperm and spermatic fluid from germ cells. It takes place in humans within the seminiferous tubules and is a continuous phenomenon in adults.

The testicles can be divided into two chambers: the tubular chamber where spermatogenesis occurs and the interstitial chamber located between the seminiferous ducts. In the interstitial compartment: we find the Leydig cells which secrete testosterone and we also find the blood capillaries. In the tubular compartment, there are 2 large types of cells called Sertoli and germinal cells. Sertoli cells acquire differentiated characteristics during puberty; they are not only Sertoli cells but also trophoblasts for spermatogenesis, particularly due to the amount of growth factors secreted and the physical contact with the germ cells.

As for germ cells, they are made up of three main types of cells corresponding to the stages of spermatogenesis. The division phase involves the spermatogonia and allows the continuity of adult spermatogenesis. Meiotic stages involve spermatocytes and allow the generation of haploid cells as well as genetic mixing. Finally, during the differentiation stage, the sperm will undergo the main differentiation process, resulting in the production of sperm.

Figure 3: Spermatogenesis in the seminiferous tubule.



Source : https://www.histology.leeds.ac.uk/male/spermatogenesis.php

3.1.2.2. Endocrine function: production of testosterone

The conductor of testicular function is the hypothalamic-pituitary axis. The hypothalamus secretes the hormone GnRH which directly stimulates the pituitary gland. (Costanzo, 2018, 467). This small gland then secretes two hormones FSH and LH into the blood. (Douterloux, 2015, 133). LH stimulates the secretion of testosterone by Leydig cells, while FSH acts directly on certain cells of the seminiferous tubules and activates spermatogenesis. (Guénard, 2001, 449). Adult testes produce several hundred sperm per day. (Ramé & Thérond, 2009, 263)

The testosterone constantly secreted by the testicles into the blood also acts at the level of the hopothalamo-pituitary complex. The more the blood concentration of testosterone increases, the less the pituitary gland secretes FSH and LH. This phenomenon is called negative feedback exerted by the testes on the hypothalamic-pituitary complex. It allows the testosterone concentration to be maintained at a constant level. It is of the order of 5-10mg/24h from puberty and decreases from the age of 40 (Malméjac, 1976, 715)

3.2. Physiological responses to hyperthermia at rest:

Body temperature is the result of the balance between heat production (thermogenesis) and heat loss (pyrolysis) from all stationary tissues, including the liver, heart, brain, and inactive skeletal muscles (20–30 %). It is between 36.1 and 37.8°C regardless of the outside temperature or the amount of heat generated by the body. If the body temperature is above 41°C, there is a risk of convulsions; if it touches 43°C, it will be the absolute limit for survival. Whenever body temperature is higher than normal temperature; the hypothalamic center of thermogenesis is inhibited and the hypothalamic center of thermolysis is activated. The core temperature is relatively stable while the skin temperature can fluctuate very significantly between 20 and 40°C.

If the body temperature is above 37°C or above the external temperature, warm blood flows into the capillaries of the skin due to increased vasodilation. Thermolysis thus occurs in order to conduct and dissipate heat from the interior of the body (the core) and its surface (the periphery).

The physical mechanisms that govern the exchange of heat between our skin and the external environment are identical to those that regulate the transfer of heat between inanimate objects. Heat moves along its concentration gradient (from warmer regions to colder regions).

3.2.1. Radiation:

It is the loss of heat in the form of electromagnetic waves, its propagation does not require material support but a transparent medium (Guénard. 2003, 532) according to the gradient, from the hottest to the coldest. In normal conditions, it represents 50% of heat loss.

The simplified Stephan-Boltzman law in air shows the heat exchanges by W_R radiation as follows:

$$W_R\ (\text{Watt/m}^2\text{/s}) = 5.\ (T°\text{wall} - T°\text{skin})(°C)$$

3.2.2. Convection:

Convection is the transfer of heat between two different temperature environments with movement of one relative to the other. In the case of humans, it is the cooling of the skin by wind (fan) or water. As warm air tends to rise, the warmed air surrounding the body is continually replaced by colder air molecules.

Heat loss depends greatly on the surface-to-volume ratio of the body. The greater its relative surface area, the greater the heat loss to the environment. (Weineck, 1992, 685). The heat exchanges by W_{Cv} convection are presented as follows:

$$W_{Cv}\ (\text{Watt/m}^2\text{/s}) = 5\ .\ (T°\text{ambient} - T°\text{skin})(°C)$$

3.2.3. Conduction:

Conduction is the transfer of heat between two environments of different temperatures without moving relative to each other. In the case of humans, it is the transfer of heat between the skin and the external environment, whether it is the floor, the seat, the clothes or the air that they trap.

Le sang représente un excellent conducteur. (Weineck, 1992, 685). Plus le sang coule dans les vaisseaux cutanés plus la conduction de chaleur vers l'extérieur est grande.

Blood is an excellent conductor. (Weineck, 1992, 685). The more blood flows through the skin vessels, the greater the heat conduction towards the outside.

Conduction from the core to the bark and from the inner layers to the superficial layer of the skin is very weak because of the low value of physiological conductance of living tissues. (Guénard. 2003, 534). The heat exchanges by WCd conduction are presented as follows:

$$W_{Cd}\ (\text{Watt/m}^2\text{/s}) = \text{Hcd}\ .\ (T°\text{contact} - T°\text{skin})(°C)$$

Of which the Hcd is the exchange coefficient by conduction, which varies from one body to another. It is higher in water than in air, in solids of mineral origin (marble, iron, etc.) than in solids of biological origin (wood, groin, etc.). (Guénard, 2003, p533). These circumstances explain the high loss in the water and on the marbled soil.

3.2.4. Evaporation

Water evaporates because its molecules absorb the heat released from the skin thanks to the vasodilation of the skin vessels. The evaporation of water from the surface of the body that is in contact removes a lot of body heat because it absorbs a lot of heat before evaporating. During exercise, sweat provides additional water evaporation, a person can produce 1 to 2L/h of sweat, which evaporates and thus releases heat. (Wilmore, 2006, 270). If the air is full of water vapor, sweat will not evaporate. This explains why heat in a dry environment is much better tolerated than in a humid environment.

3.3. Physiological responses to hyperthermia during physical exercise:

Heat production linked to exercise is an advantage to the cold. It is not the same in the heat. The energy needed for muscle contraction comes from the breakdown of the ATP molecule. In fact, 20 to 25% of this energy is used for mechanical work, the rest is dissipated in the form of heat. The body uses the usual mechanisms to dissipate this heat by: convection, conduction, irradiation or evaporation. However, this heat will be more accentuated than the rest of the thermoregulatory mechanisms. Humans have around 2 million sweat glands. (Weineck, 1992, 687).

Table 01: Estimated caloric losses at rest and during prolonged exercise (room temperature).

Mechanisms of heat loss	Rest		Exercise	
	%	Kcal/min	%	Kcal/min
Conduction and convection	20	0.3	15	2.2
radiation	60	0.9	5	0.8
Evaporation	20	0.3	80	12
total	100	1.5	100	15.0

Source: (Wilmore, 2006, 265)

Indeed, it is necessary to increase simultaneously: muscle blood flow to perform the exercise and skin blood flow to facilitate heat loss. This induces a strong drift in blood mass towards active skin and muscle areas.

3.3.1. the cardiovascular function :

Physical exercise uses the cardiovascular system. The body is in a state of thermoregulation. In fact, blood carries heat from the muscles to the skin to dissipate it. The blood flow then drifts strongly towards the skin area. Blood flow to the muscles and internal organs (intestine, liver, kidneys and testicles) decreases during exercise.

The cardiovascular system must adapt in order to maintain cardiac output, despite the drift of blood towards the cutaneous territories. This redistribution of blood decreases: in fact, the venous return to the heart and the end-diastolic volume. As a result, stroke volume (SEV) is reduced. Despite everything, cardiac output remains relatively constant during 30 min of exercise performed in a moderate environment (20°C, 68°F). (Wilmore, 2006, p268). A constant decrease in VES is accompanied by an increase in heart rate. This is called cardiovascular drift. However, heart rate can only compensate for the reduction in VES within certain limits. In addition, cardiac output becomes insufficient to properly irrigate the skin and muscles at the same time, which creates an increased risk of hyperthermia and possible impact on testicular flow.

3.3.2. Energy production:

During physical activity, redox reactions increase in order to create energy that allows work to be carried out: mechanical, then thermal, electrical and chemical. (Poortmans & Boisseau, 2003, 9). Therefore the consumption of substrates increases energy such as the increase in muscle glycogen which also increases the intramuscular temperature. This hyperthermia leads to an increase in the concentration of adrenaline secreted which, in turn, increases the use of carbohydrates. (Wilmore, 2006, 269).

3.3.3. Sweating:

During physical exercise, the sweat flow will be abundant, preventing the reabsorption of mineral salts (Na+ and Cl-) and the passage of the filtrate will be accelerated, which reduces blood volume. Note that the volume of available blood is in competition between the muscles and the skin. In long-distance runners, sweat losses can reach 6% to 10% of body weight. Such dehydration will limit sweating itself, which can ultimately lead to the risk of hyperthermia. (Wilmore, 2006, 270)

A cascade of reactions follows one another: the increase in body temperature generated by physical exercise leads to an increase in sweating which causes dehydration which causes hypovolemia and subsequently reduces venous return, the stroke volume decreases which is directly related to cardiac output.

3.4. Thermoregulation in the testicles:

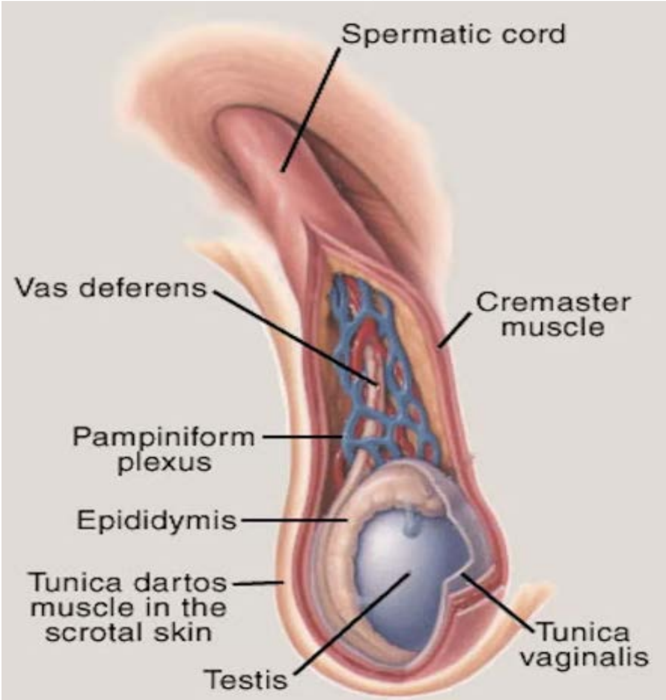
Humans have known for many years that there is a thermal gradient between the body and the testes (Badenoch, 1945, 602). The value of this gradient is affected by posture, clothing and ambient temperature (Bridley, 1982, p51; Hsiung&al, 1991a, 174), as well as hyperthermia generated by physical activity and heat dissipation by neighboring compartments.

Vasodilation allows blood to be directed to the cortex of the body to the detriment of the core. Relaxing the testicles allows the same mechanism to follow. When it's hot, the testicles move away from the body to cool down. The scrotum relaxes following the relaxation of the two muscles dartos and cremaster, it thus moves the testicles away from the body so that they release their temperature. This yoyo movement helps maintain the latter at a constant temperature, an essential condition for spermatogenesis. (Neonmag, 2022). In men, normal spermatogenesis requires physiological or relative hypothermia (euthermia) of the testes. This physiological hypothermia must be between 33 and 34°C, which allows optimal functioning. This euthermia is maintained thanks to two systems that work in synergy: the particular vascular system and the scrotal system.

3.4.1. The particular vascular system:

The thermoregulatory system is ensured at the level of the spermatic cord by a vascular system of counter-current heat exchange. This heat transfer takes place at the level of the pampiniform plexus. This pampiniform plexus is formed by the anastomoses of the branches whose origin is the testicular veins during their ascending course around the homologous artery (Académie-Medecine, 2022), and enclose it by conveying venous blood cooled by evaporation. thanks to the sweat glands. These thermal exchanges will result in the cooling of the arterial blood which enters the testicular parenchyma and the warming of the venous blood which leaves the pampiniform plexus.

Figure 4: The vascular system of the testis.

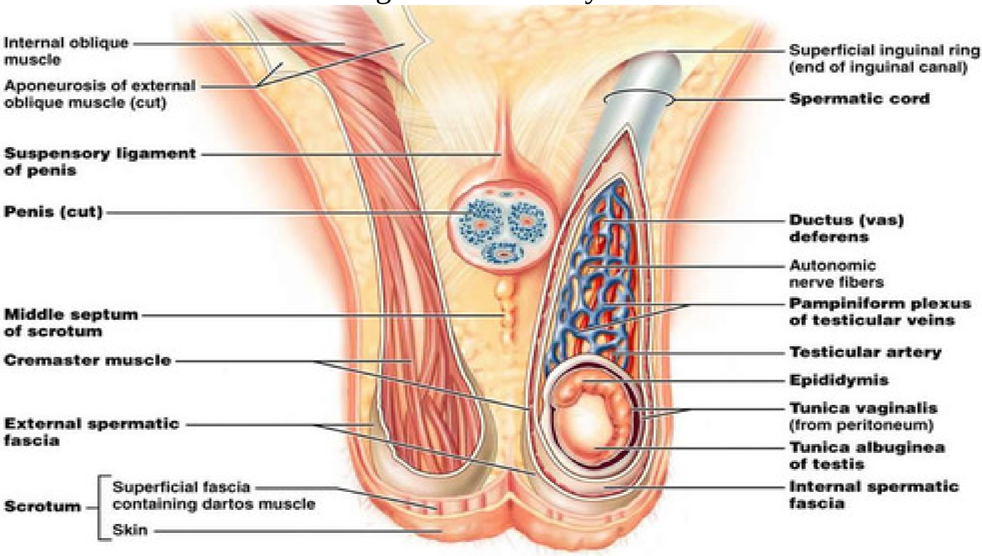


Source: https://onoluroloji.com/en/testis-torsion/

3.4.2 Scrotal system:

The scrotum ensures the low temperature of the venous blood which leaves the testicles by transferring their heat to external environments. The datos muscle is a muscle that inserts deep into the skin of the scrotum and is present on most of its outer surface. It is also present in the membrane layer that extends the spermatic cord, the spermatic fascia. The Dartos muscle regulates the balance of testicular temperature by exchanging with the external environment to ensure the survival of sperm. (Sante.journaldes femmes, 2022).

Figure 5: Scrotal system



Source: https://quizlet.com/206851621/male-reproductive-system-anatomy-final-flash-cards/

3.4.3. Regulation of scrotal hyperthermia at rest:

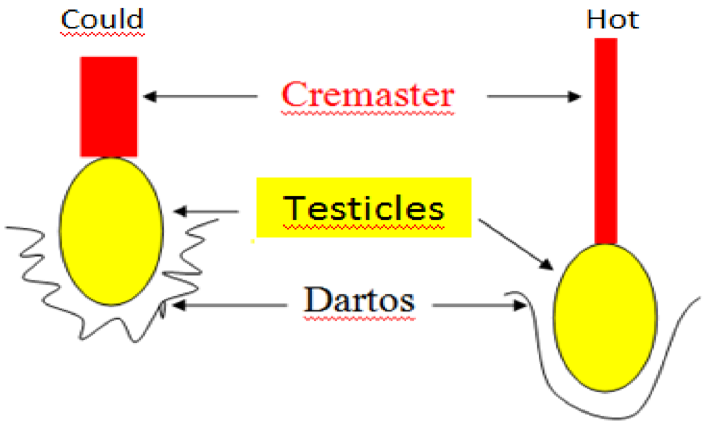
The peripheral thermoreceptors detect the rise in heat so their sensitivity increases, the nerve impulse must be conveyed to the regulatory center the set-point which is the hypothalamus. (Welmore, 2006, 266), the latter will process and analyze this information and sends an executive nerve impulse to the dartos and cremaster muscles (fascia formed of smooth muscle tissue, elastic fibers and collagen) to relax causing the relaxation of the scrotal skin by increasing its surface area and decreasing its thickness. (Vetopsy, 2022). This is to increase the cooling surface (sweating), increase scrotal blood flow and allow the testicles to move away from the body.

At the level of the pampiniform plexus, a countercurrent heat exchange occurs. As a result, the temperature of arterial blood decreases and the temperature of venous blood increases. (Dalth & Herrick, 1959, 701)

The results of this regulation are:

- Elimination of heat overload.
- Decrease in scrotal temperature.
- Decrease in testicular temperature.

Figure 6: Explanatory figure of the ascent and descent of the scrotum.



Source: Figure drawn by the author

3.4.4. Regulation of scrotal hyperthermia during physical activity:

During physical exercise, body temperature increases. The cardiovascular system must adapt to dissipate this heat through cutaneous vasodilation. The latter competes with blood redistribution in order to irrigate the active muscles. As a result, the skin at the inguinal angles increases and induces scrotal hyperthermia. The heat thermoreceptors are stimulated and conduct a nerve impulse to the hypothalamus, the skin of the scrotum relaxes in order to increase the cooling surface (sweating) and the scrotal blood flow increases in order to eliminate heat overload. which enters into itself with the skin and muscle drift.

So, when exercise continues over time, the core temperature continues to rise and causes more sweating, in other words hypovolemia. This hypovolemia makes the flow of blood difficult, particularly at the level of the pampiniform plexus, because the latter will find difficulties in thermal exchange with the arterial blood. In addition, the scrotal temperature will not find a way to dissipate and reduce the temperature of the testicles because the surrounding skin releases the excess heat.

The consequences of this hyperthermia on the body are: heat-related cramps, heat-related exhaustion, heat stroke (Wilmore, 2006, 272-273). Hyperthermia induced on the testicle results in a quantitative and qualitative decrease in the spermatozoa found during the ejaculate, resulting in a decrease in the concentration of sperm mobility as well as an increase in the rate of morphologically abnormal gametes. (Mieusset&al, 1992, p32). Note also the appearance of varicocele where the blood is less well drained and the testicles heat up (Faix, 2022).

The main studies reported in the literature indicate that scrotal hyperthermia is present in a third of infertile men (Hsiung & Clavert, 1991b, p242; Mieusset, 1987, 1007; Zorgniotti & Sealfon, 1988, 564). This intrinsic scrotal hyperthermia is associated with a quantitative and qualitative decrease in the spermatozoa produced (Mieusset, 1987, 1008; Zorgniotti & Sealfon, 1988, 564).

Conclusion:

La prévention reste le meilleur moyen, lorsque l'on :

Core temperature rises with exercise. This can alter cellular functioning and sometimes pose a risk to the individual's health. The endocrine and exocrine testes are optimally functional at a lower temperature of approximately 33-34°C. The mechanisms for maintaining this euthermia are the vascular system of the pampiniform plexus and the scrotal system.

Prevention remains the best way, when we:

- First avoid prolonged exercise
- Avoid exercising in a hot environment, and instead seek a cool environment and increase convection (fan) and reduce the external temperature (air conditioner)
- Wear loose, light-colored clothing, which reflects radiant energy and reduces heat gain.
- Avoid situations that cause an increase in scrotal temperature such as hot baths and wearing tight underwear made of synthetic fabrics.
- Cools the scrotum with a local shower of cold water or by applying dry ice to the scrotum.

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