Testicular Heat Stress and Sperm Quality

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Introduction

In the male, exposure to heat has a deleterious effect on fertility and is considered a significant risk factor for male infertility [1]. Testicular temperatures should ideally be hypothermic compared to the core body temperature of 36.9 °C. This is essential for maintaining normal spermatogenesis and ideal sperm characteristics. A crucial feature that contributes towards this is the anatomical position of the human testes, which is located outside the body. Homeothermic animals have the ability to maintain a stable core body temperature despite fluctuating environmental temperatures. This is achieved by regulating heat production and loss by means of adjusting the body's metabolism.

In most homeothermic birds and mammals, including humans, testicular function depends on temperature. Temperatures that either fall below or above the physiological range required for optimal testicular function could potentially disrupt spermatogenesis. Certain land mammals (such as elephants and rhinoceroses) and aquatic mammals (such as whales and dolphins) have intra-abdominal testes throughout their lifespan. The abdomen is metabolically active and it therefore generates a lot of heat. However, spermatogenesis functions optimally in these mammals despite the proximity of their testes to the abdomen.

Humans, on the other hand, have intra-scrotal testes that develop within the abdomen and, towards the end of the gestation period, begins its descent through the inguinal canals into the scrotum. In humans, normal testicular function is temperature dependent and the extra-abdominal testes are maintained at temperatures below that of core body temperature [2]. Under normal healthy environmental conditions, testicular thermoregulation maintains scrotal hypothermy to ensure optimal testicular function [1].

Testicular Thermoregulation

The normal physiological temperature of the human testis ranges between 32 and 35 °C [3]. Thermoregulation in the testis occurs via two mechanisms: the physiological properties of the scrotum and the counter-current mechanism.

The scrotum is a loose sac-like structure that houses each testicle. The main function of the scrotum in most mammals is to prevent heat from reaching at the testis by means of adjusting to heat stress [4]. The scrotum has features that allow free dissipation of heat through passive

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convection and radiation. These include a large total skin surface area that changes according to the surrounding temperature, a large number of sweat glands, minimal subcutaneous fat, and sparse hair. When external temperatures rise and cause the scrotal temperature to increase beyond a threshold value, cutaneous receptors on the scrotal skin are activated, initiating secretions of the scrotal sweat glands and active heat loss occurs through the evaporation of sweat [4, 5]. Vasodilation of the scrotal vessels, the very thin scrotal skin and the near-absence of surface hair further contribute to heat dissipation.

The spermatic cord is made up of the testicular artery, veins, cremaster muscle, and vas deferens. The testicular artery is greatly coiled while the veins have thin walls and poor muscularization. The bulk of the spermatic cord is composed of numerous testicular veins that anastomose and drain into the convoluted pampiniform plexus [6]. The testicular arterial and venous blood vessels are intimately associated with each other, facilitating the transfer of heat between the inflowing arterial blood to the outflowing venous blood in the spermatic cord. Thus, the arterial blood arriving at the testis is effectively cooled while the venous blood disperses this heat through the scrotal skin [7]. In a normal individual, this counter-current heat exchange regulates the temperature of the arterial blood supply to the testis and epididymis at 2–4 °C below rectal temperature [7].

Thermoregulation of the testis is further aided by two muscles: the cremasteric and dartos muscles. The cremaster muscle is skeletal-type muscle that is associated with the spermatic cord and testis. A reflex contraction of the cremasteric muscle can be produced by gently stroking the skin on the medial side of the thigh (cremasteric reflex). The dartos muscle is a layer of smooth muscle fibers that surround the testis subcutaneously. When the ambient temperature falls, both the cremaster and the dartos muscles contract involuntarily, raising the testes and bringing them closer to the warmer body. The scrotal skin wrinkles with the contraction of these muscles, reducing the exposed surface area to avoid further heat loss. Conversely, when ambient temperatures increase, the dartos and cremasteric muscles relax causing the testes to lower away from the body and the scrotal skin to become looser around the testes, aiding heat loss.

Mechanism of Heat Stress: Testicular and Germ Cell Changes

Germ cells have high mitotic activity, which makes them more susceptible to heat stress [8]. The type of germ cells that is most sensitive to heat is the pachytene and diplotene spermatocytes and early round spermatids in both the rat [9, 10] and in humans [11]. In fact, the spermatogenic process, particularly the differentiation and maturation of spermatocytes and spermatids, is temperature dependent and occurs ideally at a temperature of at least 1–2 °C below core body temperature [1, 10]. As such, raising the scrotal temperature causes testicular germinal epithelial atrophy and spermatogenic arrest [12], leading to lower sperm counts. The supportive role of Sertoli [13] and Leydig [14] cells towards germ cell development are also impacted by heat stress. Levels of a biochemical marker of spermatogenesis, inhibin B [15], decrease along with sperm concentration when scrotal temperatures are high [16]. Irreversible testicular weight loss follows shortly after heat exposure [17]. Histopathological changes in the testis following heat exposure include degeneration of the mitochondria, dilatation of the smooth endoplasmic reticulum, and wider intercellular spaces in both Sertoli and spermatid cells [18].

The fundamental mechanism by which loss of germ cells occurs in response to heat stress is due to apoptosis [9, 19]. The intensity of heat stress and duration of heat exposure influence germ cell apoptosis. For example, 2 days after a single exposure to heat (43 °C for 15 min), late pachytene and early spermatids degenerate [20]. However, shorter heat exposure of the rat testes (43 °C for 10 min) does not result in apoptotic germ cells whereas a longer heat exposure (43 °C for 30 min) intensifies germ cell apoptosis [21].

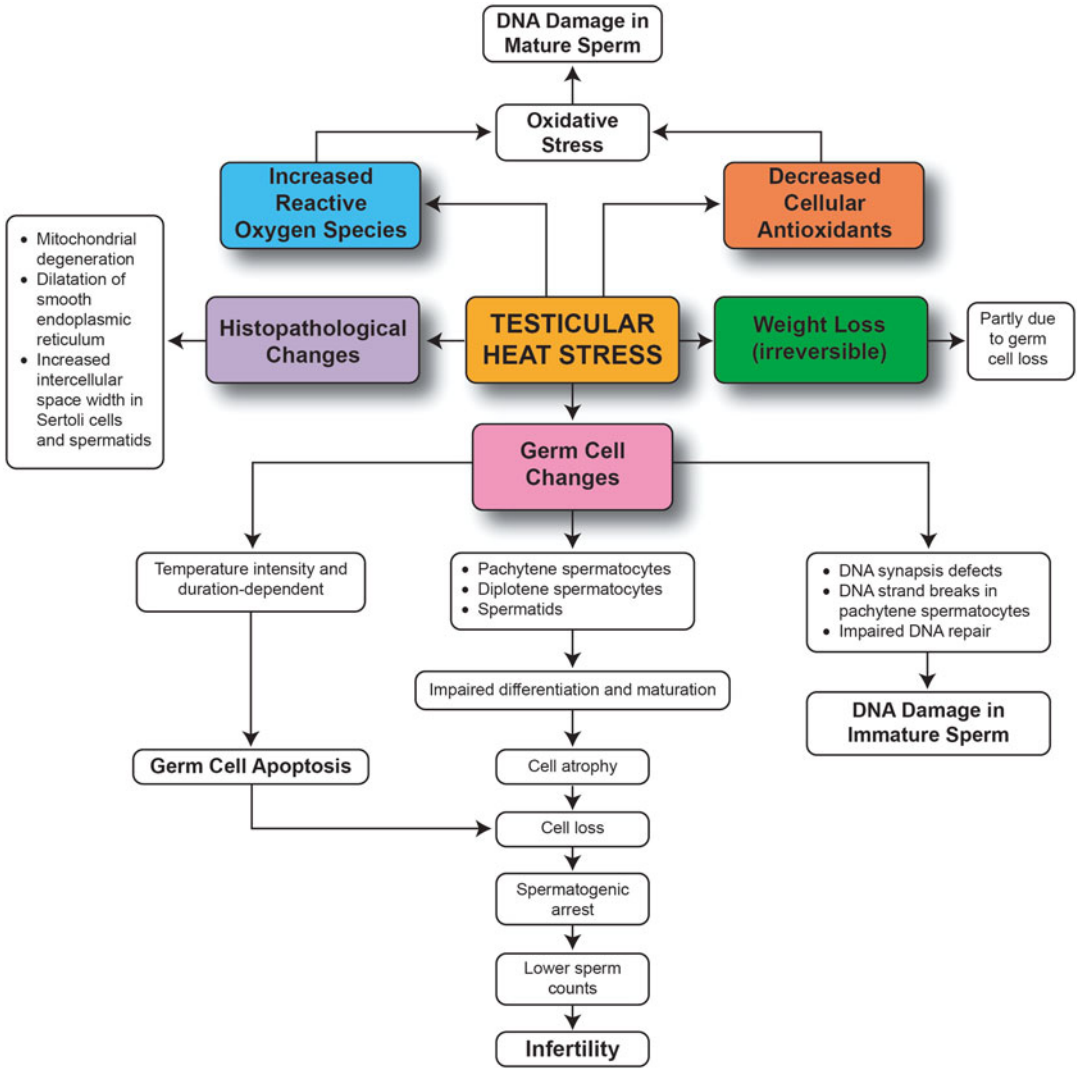

Fig. 8.1 Schematic highlighting various mechanisms by which testicular heat stress causes germ cell apoptosis, DNA damage in mature and immature sperm and male infertility

Similarly, higher heat exposure (45 °C for 15 min) causes generalized, nonspecific damage to many different germ cell types in adult rats.

Besides apoptosis, heat stress also causes defects in DNA synapsis and DNA strand breaks in pachytene spermatocytes and induces DNA damage in mature spermatozoa [20]. Sperm DNA damage that occurs in the heat-stressed testis is likely due to excessive generation of reactive oxygen species (which causes the sperm cell to be in a state of oxidative stress) as well impaired DNA repair in the germ cells [20, 22]. In experimentally cryptorchid rats, heat stress (due to increased scrotal temperatures) increases generation of reactive oxygen species leading to oxidative stress [23, 24]. Moreover, in adult rats, the effects of scrotal hyperthermia (43 °C for 30 min once daily for 6 consecutive days) include decreased levels of glutathione, superoxide dismutase, and glutathione peroxidase and increased lipid peroxidation in the testes [18]. Further, gene expression for DNA repair and cellular antioxidants are suppressed during testicular heat stress [25] (Fig. 8.1).

In summary, heat-induced changes due to increased scrotal temperatures in the testes lead to apoptosis of germ cells and sperm DNA damage, which subsequently suppresses spermatogenesis [18, 20].

Impact of Failed Thermoregulation on Semen Parameters

Semen analysis is carried out as a routine laboratory assessment of the infertile male. Fundamental sperm parameters evaluated during a standard semen analysis include sperm concentration, motility, and morphology [26]. The total count and concentration of sperm reflect semen quality and the male reproductive potential whereas sperm concentration and motility are best able to predict fertility [27]. Repeated testicular exposure to elevated levels of heat could lead to chronic thermo-dysregulation, which in time could lead to significant changes in sperm characteristics [1, 28].

Mean scrotal temperature is higher in infertile men than in fertile ones [29], and the higher the scrotal temperature, the more sperm quality is altered [29]. Men (mean age 31.8 years) who were infertile for at least 2 years (without female factor infertility) were found to have lower sperm count, percentage of motile sperm and testicular volume in both testes and higher mean scrotal temperatures compared to fertile men [29]. However, testicular hyperthermia causes modification of sperm characteristics in both the fertile and infertile male [29]. Physiological increases in scrotal temperature are associated with substantially reduced sperm concentration that results in poor semen quality [30]. An increase of 1 °C above baseline values suppresses spermatogenesis by 14 %, decreasing sperm production [31].

Elevated testicular and epididymal temperatures decrease the synthesis of sperm membrane coating protein, resulting in higher amounts of morphologically abnormal sperm [31]. Within 6–8 months of exposure to elevated temperatures, the mean value of sperm with abnormal morphology was found to double [31]. Sperm motility is also suppressed in the hyperthermic testis [32]. Exposure to high temperature causes deterioration in sperm morphology and impairs motility as well as sperm production, all of which have a deleterious effect on male fertility [33, 34].

Pathological Failure of Thermoregulation

Increased testicular temperatures due to either endogenous or exogenous stimuli decrease sperm concentration, motility, and the number of morphologically normal sperm [11, 35]. Pathophysiological abnormalities such as varicocele and cryptorchidism cause testicular hyperthermia, which could lead to male infertility [36]. Thus, any disruption (either acute or chronic) to the thermoregulation of the testis would have severe adverse effects on the spermatogenic process.

Febrile Episodes

When the hypothalamic thermoregulation of the core body temperature is compromised with the onset of fever, thermoregulation at the level of the testes is also impacted. In a case study of a fertile patient with influenza who was febrile (39.9 °C) for 1 day, semen samples analyzed 18–66 days post fever showed underlying effects on sperm chromatin structure and a temporary release of abnormal sperm [37]. In another study, the incidence of fever was reported to have a significant effect on spermatogenesis, and the more days of fever (between 1 and 11 days); the more increasingly adverse were its effects on sperm concentration, percentage of normal and immotile sperm [11]. Certain stages of spermatogenesis were found to be more predisposed to the effects of higher temperatures caused by a fever than others: sperm concentration was affected when fever occurred during meiosis (33–56 days before ejaculation) and spermiogenesis (post-meiotic phase, 9–32 days before ejaculation) while sperm morphology and motility were affected when fever occurred during spermiogenesis [11].

Varicocele

Varicocele is the most common and treatable cause of male infertility and it affects 15 % of the male population. It is implicated in 40 % of men with primary infertility and in 80 % of men with secondary infertility [38, 39]. A varicocele is the abnormal tortuosity and dilatation of the testicular veins in the pampiniform plexus causing retrograde blood flow in the internal spermatic veins and venous stasis. Consequently, the cooling of the testicular arterial blood via the counter current heat exchange becomes ineffective and testicular temperature increases towards that of the core body [40]. Increased scrotal temperature found in infertile men is most commonly caused by varicocele [29, 41]. Both Mieusset et al. [29] and Goldstein and Eid [42] reported that infertile men with varicocele have higher mean scrotal temperatures on (1) the affected testis compared to the unaffected side and (2) both testes compared to that in fertile men. Intra-testicular temperatures in the affected testis were 2.43–2.72 °C higher than that of a normal testis [42]. The underlying mechanism of varicocele-related infertility is not clear but is attributable to factors such as increased scrotal temperature, oxidative stress, and hormonal imbalance [43]. Varicocele patients have increased apoptosis (programmed cell death) [44], and the increase in scrotal temperature (but not varicocele grade) is associated with oxidative stress-induced apoptosis [43]. Chan et al. [45] found that heat shock proteins 70 and 90 were significantly upregulated in varicocele patients. Heat shock proteins are produced in response to various stress inducers including heat, and their increased expression suggest that they play a role in the mechanism of varicocele-related infertility [45].

Cryptorchidism

Cryptorchidism is among the most common congenital defects in newborns and occurs in 2–4 % of full-term male births [46]. About 50 % of these cases resolve spontaneously within the first year of birth and those that do not resolve naturally require surgical intervention. Failure of the testis to descend leads to infertility and increased risk of testicular cancer. The severity of infertility in human cryptorchidism depends on the position of the testis, whether one or both of the testis is maldescended, how soon it is surgically corrected and perhaps the underlying pathology [47]. In its supra-scrotal position, the testis is hyperthermic. This causes heat-induced loss of spermatogonial differentiation and apoptosis of all germ cells (including germ stem cells) as well as an indirect effect of increased oxidative stress and abnormal energy metabolism [23, 48, 49]. In addition, the changes in Sertoli cell junctions and abnormal levels of Leydig cell hormones noted in the cryptorchid testis are linked to hyperthermia [50, 51]. Furthermore, despite sperm appearing to be morphologically normal [52], heat stress produced in conditions of cryptorchidism and varicocele induces sperm DNA fragmentation [52, 53].

Assessing Testicular Temperature

Testicular and intra-scrotal temperatures can be measured either directly or indirectly and in the form of either a single or continuous measurement (Table 8.1). Intra-scrotal skin surface temperatures reflect the temperature of the underlying testis as the testis and epididymis constitute the largest thermal mass in the hemiscrotum [36, 54]. Testicular temperature may range between 31 and 36 °C depending on the method used for the measurement of temperature and the presence of any underlying pathology [55]. Accuracy and reproducibility of the temperature are important as temperature differences in a normal (euthermic) and pathologic (hyperthermic) testis may be as small as 0.6–1.4 °C [36]. Even these small increases can hamper spermatogenesis and epididymal maturation [36].

Single or Discontinuous Measurements

In this method evolved by Zorgniotti and MacLeod [36], the subject disrobes from the waist below and lays supine for about 6 min (to equilibrate to an ambient room temperature of about 21–23 °C) [32, 36]. A mercury thermometer is pre-warmed by placing the bulb of the thermometer in contact with

Table 8.1 Methods of measuring scrotal (testicular) temperature in humans

Method	Description	Advantage	Disadvantage	Reference(s)
Single measurement or discontinuous method				
Mercury thermometer	1. Pre-warmed bulb positioned directly over the most prominent part of the anterior testis 2. Thermometer bulb held longitudinally against the scrotum 3. Loose scrotal skin drawn around the thermometer bulb using the thumb and index finger	1. Simple and inexpensive 2. Provides accurate measurements 3. Gives repeatable and standardized values	1. Clinical thermometer unsuitable as its mercury column is constricted 2. Applicable only when subject is unclothed 3. Reproducible only under static conditions (e.g., lying down for several minutes)	[32, 36, 54, 55]
Skin surface thermocouples	1. Attached to the scrotal skin overlying the anterior testis using an adhesive 2. Electrode cables secured at trouser waistband	1. Small dimensions 2. Light weigh 3. Assessment done in a clothed state	1. May be displaced from the site of contact with the testis beneath 2. Minor movements of the scrotum could alter the readings	[55, 65]
Thermal resistor (thermistor) needles	1. Placed within the scrotum or testis	1. Direct measurement	1. Invasive procedure 2. Depth of thermistor placement could contribute to differences in reading (temperature in the peripheral testis is lower than the mediastinum testis) 3. Use of anesthesia and evaporation of the antiseptic solution applied during scrotal skin preparation would alter the temperature 4. Extremes of ambient temperature, scrotal skin inflammation, and intrascrotal disease would affect the temperature	[4, 54, 55, 108]

Infrared thermometry	1. Measures heat emitted from the scrotal skin 2. A pistol-type, non-contact, digital infrared thermometer with an accuracy of ±0.1 °C was preferred 3. Replicate readings taken at the skin over the most prominent part of the testis	1. Easy way to measure temperature in different body positions 2. Permits repeated measurement on the same area	1. For better accuracy, these thermometers needs to be calibrated using a black body prior to use 2. Variations in skin's thermal radiation or emissivity could affect readings 3. Only the surface temperature is measured and not deep scrotal temperature 4. Lacks sensitivity to record small differences in temperature	[55, 109, 110]
Thermography	1. Measured heat emitted from the scrotal skin		1. Does not provide the required accuracy for research as the comparison with the grey scale can introduce inaccuracies 2. Provides relative differences but not absolute numbers 3. Unable to obtain a preferred sensitivity of ±0.1 °C	[55]
Liquid crystal thermometry	1. Measured using temperature-sensitive crystals		1. Unable to obtain a preferred sensitivity of ±0.1 °C	[55, 109]
Continuous measurement method				
Thermoport thermocouples or thermoprobes	1. Attached to skin on the anterior face of the each scrotum using transparent tape 2. Connected to a portable data recorder attached to a belt	1. Allows for a dynamic recording of temperature 2. Representative of testicular temperature during normal daily activities		[56–58]
Thermistor	1. Thermistor attached to underwear 2. Connected to a light-weight data logger			[54, 55]

a light source or immersing it in warm water, allowing the mercury column in the thermometer to expand to a temperature that is slightly higher than the estimated temperature of the testis (i.e., around 37 °C). The thermometer is then quickly positioned directly over the most prominent part of the anterior testis and the bulb is held longitudinally against the scrotum. The loose scrotal skin is drawn around the thermometer bulb using the thumb and index finger (to include the immersion mark, if present). The mercury column will begin to drop until it reaches equilibrium (usually about 8 s). The reading at that point plus 0.1 °C represents the intrascrotal temperature [36]. The process is then repeated in the contralateral testis. This method was modified from the "invagination method" by Brindley [32] and allows for repeatable and consistent values to be obtained for use in a clinical evaluation of, for example, a varicocele [56].

Continuous Measurements

During continuous measurement, two cutaneous thermocouples (thermoprobes) are attached to the skin on the anterior face of the each scrotum using transparent tape, and these are connected to a small portable data recorder attached to a belt. Temperatures are recorded at 2-min intervals. Measurements recorded in the data recorder are downloaded to a computer through a specific program [57]. The use of a portable data recorder for continuous determination of scrotal temperature allows for a dynamic recording of temperature [58]. However, scrotal skin temperatures have also been measured noninvasively for an entire day using a thermistor attached to underwear that is connected to a light-weight data logger [56].

Risk Factors for Scrotal Hyperthermia

The temperature difference between the body and scrotum can be affected by a variety of external thermogenic factors including body posture or position, clothing, obesity, lifestyle and occupational exposure, and ambient seasonal temperature changes (Fig. 8.2).

Posture

Changes in posture affect testicular temperature. Scrotal temperature is lowest when standing disrobed [36, 59]. Heat dissipation can occur unhindered from the unsupported testis when the body is unclothed and in an upright position. When comparing body positions, scrotal temperature in the supine or seated position is higher than that in the standing position [32, 36, 58, 59]. When walking (upright and moving), scrotal temperatures are 0.3–1 °C lower than those generated when sitting regardless of clothing type [32, 59]. Scrotal temperatures are highest during sleep when the body is supine and movement is minimized [32, 58, 60] compared to other body positions. When comparing sleepwear, scrotal temperatures were the lowest when sleeping in the nude compared to sleeping in pyjamas or underwear [32]. When in a supine position, the testes are resting on the thighs and are in direct contact (conduction) with the relatively higher body temperature. Additional layers of clothing trap air and conserve heat. Using an electric blanket or quilt on top of typical nightclothes while lying down in bed after a hot bath will give a cumulative effect that is likely to lead to genital heat stress. When assessing diurnal variation, Hjollund et al. [56] found that scrotal temperatures, when measured at a 5-min interval for a continuous 24 h, were higher at night by 1.2 °C compared to those during the day.

Sitting

The length of time spent in a seated position, either due to occupational nature, long commutes and sedentary leisure activities, also contributes to testicular heat stress. A predominantly sedentary (sitting) position at work has been shown to increase scrotal temperatures [30, 56, 57]. When sitting, the testes are trapped between the thighs. Moreover, the normal seated position leads to poor ventilation in the groin area, which contributes to an increase in scrotal temperature. The positioning of the legs while sitting (i.e., legs together, apart or crossed) impacts the scrotal temperature in both the disrobed [59] and clothed state [32, 57].

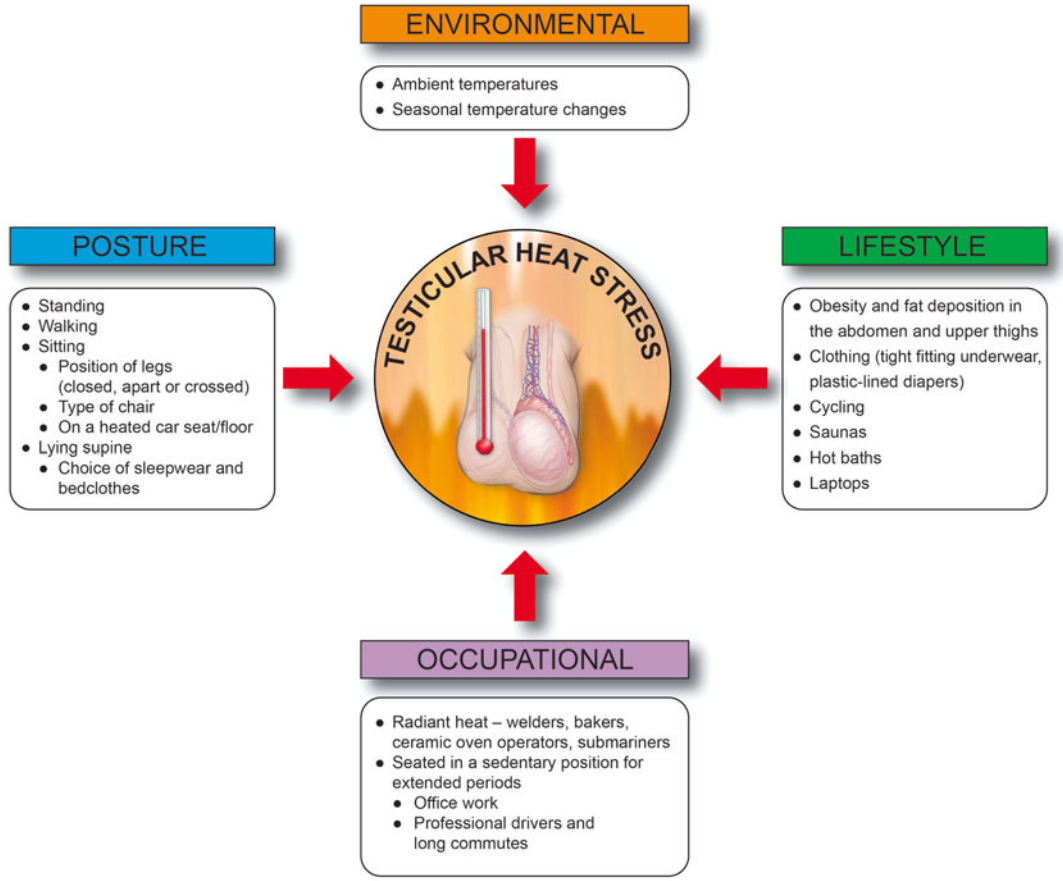

Fig. 8.2 Various lifestyle, occupational, postural, and environmental factors contributing to testicular heat stress

Paraplegic men in wheelchairs who remain seated for extended periods with closed and unmoving legs were found to have higher deep scrotal temperature and poor sperm motility than normal men who were seated freely for 20 min or more (without the position of their thighs being specified, i.e., kept close together or apart) [32]. However, when compared in a supine position, there was no significant difference in scrotal temperatures between the paraplegic and normal men [32].

The insulating effect of the seated posture is compounded by being sedentary but counteracted by physical activity. The average scrotal temperature in healthy volunteers while sitting on a conventional chair for a period longer than 35 min is 36.4 °C compared to 34.5 °C during walking [61]. Increased limb movement during physical activity increases perigenital air circulation, and this allows for better dissipation of heat, which then results in lower scrotal temperatures, compared to when being seated in a sedentary manner.

In a study comparing the increase in scrotal temperatures while seated on different types of chairs, Koskelo et al. [62] reported a 3 °C increase in scrotal temperature upon 20 min of sitting on a conventional cushioned office chair. However, they found no difference in temperature when subjects sat in a saddle chair. This is probably due to the open hip and knee angles, which allow for adequate scrotal ventilation [62]. Similarly, sitting with crossed legs causes a bigger increase in scrotal temperature than sitting with the legs apart (at an angle of about 70°) [63]. After remaining in a seated position with crossed legs for 15 min, the thermogenic effect caused by this position further persisted for a minimum of 5 min, even after standing up [63].

When sitting on surfaces with a higher temperature, the increase in scrotal temperature attributed to the seated posture is further compounded by the warmth exuding from the seated surface. In a Korean study, Song and Seo [64] investigated the effects of sitting directly on a heated floor on scrotal temperature among 6 healthy male volunteers in a controlled environmental chamber. They concluded that the floor surface temperature and the rate of metabolism while in a sedentary posture affect scrotal temperature and recommended that surface temperature of a heated floor be maintained within 23–33 °C to avoid impairment of spermatogenesis [64].

Clothing

Irrespective of the body position, wearing clothing has an insulating effect that increases scrotal temperature. In the standing and supine positions, clothing increases scrotal temperatures by 1.5–2 °C compared to the naked state [63, 65]. In men at rest who are lightly clothed, the layer of air trapped in the space between the skin and clothes is on average 3.5 °C higher than that of ambient air (at a temperature of between 21 and 32 °C) [66]. The reduction in air exchange when in a clothed state contributes to the increase in scrotal skin temperature [63]. Clothing that permits better air flow would mean that scrotal heat could be more easily dissipated, keeping temperatures closer to physiological levels. Kompanje [27] suggested that Scottish kilt-wearing possibly produced a more ideal physiological scrotal environment, especially since nearly 70 % of men chose to not wear anything underneath their kilt. In the Asian region, men often wear only a sarong when at leisure, which similarly helps in dispersing body and environmental heat to keep lower testicular temperatures.

Tight Underwear, Boxers, Jockey Shorts

It is still debated whether the type of underwear has a significant impact on testicular temperature and hence, male fertility. Studies have reported that the regular use of tight underwear over a period of time leads to a reduction in sperm motility [67, 68]. Another study found that men who wear tight underwear have decreased sperm count and sperm motility compared to those who wear loose underwear [69]. Conversely, in a study involving 97 men presenting for primary infertility (aged between 25 and 52 years), scrotal temperatures did not differ between men who wore boxer shorts and those who wore brief style underwear [12]. The authors further reasoned that brief style underwear gives a supportive effect that pushes the testes closer to the body while the boxer shorts lacks this effect. However, any additional layer of clothing that is worn over the underwear (e.g., trousers) would result in the same supportive effect on the testes [12].

Diapers

The use of disposable plastic-lined diapers is more common these days than cotton, reusable diapers. Even cotton diapers are usually used in combination with a plastic lining as a protective covering to prevent leakages. The use of plastic material reduces the skin's breathability, which would lead to a warm and moist perigenital area, thereby contributing to higher scrotal temperature. Partsch et al. [70] studied 14 neonates (term aged 0–4 weeks) and pre-term with a gestational age of 28–36 weeks (postnatal age 14–85 days), 22 infants (aged 1–12 months), and 12 toddlers (age 13–55 months) and reported that young boys wearing disposable plastic-lined nappies have increased scrotal temperatures compared to those wearing reusable cotton diapers (without protective pants). However, in another study, Grove et al. [71] found no differences in the scrotal temperature profiles of approximately 70 young boys (aged 3–25 months) wearing disposable diapers with a plastic lining compared to those wearing reusable cotton diapers covered with plastic pants. Only when the cotton diapers were used without any plastic covering were scrotal temperatures lower than those in the boys using disposable diapers [70, 71]. That being said, as cotton diapers are almost always used along with the plastic pants, it would seem that practically speaking, both the classic and modern diaper choices did not differ significantly on their effect on scrotal temperature. As to whether

diapering preferences (and the higher scrotal temperatures is generates) at a young age could contribute towards a compromised male fertility potential as an adult, Jung and Schuppe [72] reasoned that pachytene spermatocytes and round spermatids (the most temperature-sensitive testicular cells) [10] are not yet present in the age group when most children use diapers. The authors concluded that there was no convincing evidence linking genital heat stress with poor semen quality in their adulthood [72].

Lifestyle

Obesity

Obesity is a common lifestyle-related societal problem of the modern era. Many adults who are in the reproductive age group have a higher than normal body mass index (BMI, normal range: 18.0–24.9). In fact, the rate of obesity is higher in infertile men than in men with normal semen parameters [73]. A BMI ≥25 is associated with an average 25 % reduction in sperm count and motility [74]. Obesity is often associated with decreased physical activity and prolonged periods of sitting or being sedentary, which have been found to increase testicular temperatures and consequently suppress sperm production [75]. Obese males are more likely to have increased fat deposition in the abdomen and upper thighs and larger waist and hip circumferences. Additionally, scrotal lipomatosis (deposition of fat around the spermatic cord) in obese men could inhibit spermatogenesis by several means, i.e., (1) provide insulation that could disrupt the radiation of testicular heat, (2) compress blood vessels, leading to testicular congestion (venous stasis) and impaired heat exchange, (3) compress the testicular artery leading to ischemia of the testis, (4) hamper the cord's ability to reposition the testes in response to temperature changes, and (5) disrupt local thermoregulation due to excess fat in the suprapubic region [76, 77]. The compromised efficiency of testicular thermoregulation may well lead to elevated testicular temperatures. However, scrotal lipomatosis could also occur in those who are not obese [76]. In one study, removal of excess fat in the scrotal and suprapubic region helped improve sperm count, motility, and morphology in nearly 65 % of infertile patients, and nearly 20 % of these patients went on to initiate a pregnancy [77].

Sauna

Saunas are a popular method of relaxation and detoxification or cleansing in many parts of the world. Temperatures in saunas typically range between 80 and 100 °C at the level of the bather's head, with humidity ranging from 40 to 60 g of water/kg dry air [78]. Conventional saunas provide wet heat through warmed, humid air (radiation and convection) as well as warmed surfaces (radiation and conduction), while modern saunas such as infrared saunas provide dry, radiant heat.

Brown-Woodman et al. [79] examined the effect of a single sauna exposure (85 °C for 20 min) on sperm parameters at 10 weeks post-exposure compared to 3 weeks preexposure. They found that this one acute testicular heat stress episode was sufficient to cause the sperm count to reduce within a week post-exposure, only to normalize in the fifth-week post-exposure [79]. In a study that continuously (i.e., every 5 s) monitored scrotal temperature during a sauna exposure (87.6 ± 1.3 °C and <15 % humidity), scrotal temperatures were found to reach core body temperature within about 10 min of exposure to the exogenous heat [58]. Saikhun's group assessed the effects of sauna exposure on sperm parameters after a 2-week sauna exposure (at 80–90 °C for 30 min) [35]. They found that sperm movement characteristics had declined but were restored within a week after concluding the sauna exposure. They reported that sperm parameters such as semen volume, sperm count, number of motile and morphologically normal sperm as well as sperm penetration levels had remained unchanged [35]. More recently, Garolla et al. [80] investigated the effects of biweekly Finnish (dry) sauna sessions (89–90 °C for 15 min) for 3 months on ten normozoospermic men. They found that these frequent sauna exposures (that lasted long enough to cover an entire spermatogenic cycle) caused a significant reduction in sperm count and progressive motility (although

they were still within normal range) and altered mitochondrial function, DNA protamination, and chromatin condensation in the sperm [80]. However, sperm morphology and viability remained unaffected while heat shock proteins (and their regulating heat shock factors) that confer a protective effect were found to be upregulated after testicular heating [80]. These studies collectively showed that following sauna exposure, the negative impact on spermatogenesis was significant but reversible.

Hot Baths

Other lifestyle habits such as indulging in a relaxing soak in a hot tub, heated whirlpool, or a warm bath could negatively impact male fertility. Shefi et al. [81] studied the effects of wet heat exposure in a group of 11 infertile men (mean age 36.5 years) who practiced whole body immersion in either a hot tub, heated jacuzzi, or warm bath (at temperatures that were higher than that of body temperature) for more than 30 min weekly (mean weekly exposure was 149 min) for longer than 3 months. Comparison of semen parameters in samples analyzed before vs. 3 months after the discontinuation of the wet hyperthermia, showed improvements, mainly in sperm motility [81]. They concluded that in certain infertile men, refraining from these types of heat exposure could perhaps reverse the detrimental effects of hyperthermia on their semen quality.

Cycling

A regular, moderate exercise regimen bestows numerous health benefits. However, certain forms of exercise done in the pursuit of fitness, cycling, for example, may negatively affect male fertility. Scrotal temperatures during cycling may be influenced by the duration and intensity of the exercise as well as posture [82] and clothing. As a physical activity, cycling improves perigenital air circulation, which aids in the dissipation of testicular heat [82]. At the same time, cycling involves extended periods of being in a seated posture on a saddle seat for the majority of the exercise and wearing a body-fitting spandex outfit, which would contribute an insulating effect on scrotal temperatures, especially in professional cyclists [83]. However, in their study, Jung et al. [82] found that 25 healthy volunteers (median BMI of 23.2) who wore cotton wool clothing while performing moderate cycling (median speed of 25.5 km/h, power around 25 W) sitting on the saddle of a stationary cycle for 60 min had mean scrotal temperatures below 35.6 °C. Increases in scrotal temperatures did not differ significantly between the left and right scrotum and with time [82].

Laptop Usage

Sheynkin et al. [84] demonstrated among 29 healthy volunteers that using a laptop in a lap position close to the genital area (i.e., a seated position with approximated thighs) for an hour contributes to a 0.6–0.8 °C increase in scrotal temperatures compared to a 2.1 °C increase in scrotal temperatures in the same sitting position without using a working laptop. This increase in genital heat could be attributed to heat exposure from laptops that have internal operating temperatures of more than 70 °C and to the seated posture for those 60 min. Although this study did not examine changes in semen parameters, the authors suggested that since scrotal heat impairs spermatogenesis, then laptop usage also likely affects these parameters [84].

Occupation

Welders: Radiant Heat

Welders are occupationally exposed to intense radiant heat, toxic metals and their oxides, and toxic welding fumes during welding. Bonde [85] reported that 17 manual metal arc alloyed steel welders (mean age 35.9 years) with moderate exposure to radiant heat (31.1–44.8 °C) and with minimal exposure to welding fume toxicants experienced a reversible decrease in semen quality. The percentage of sperm with normal morphology decreased within 6 weeks of exposure to radiant heat but increased 4 weeks after cessation of exposure [85]. In another study, 17 welders (mean age 43.8 years) with 1–10 years or more of welding exposure possibly had some adverse effects on sperm motility, morphology and physiologic function, although they maintained a normal range of sperm concentration [86].

Bakers: Radiant Heat

Bakers are reported to take longer to initiate a pregnancy than controls, as only 14 % of bakers' partners were pregnant within 3 months (compared to 55 % of controls) and 29 % of bakers' partners were pregnant within 6 months (compared to 74 % of controls) [87]. This suggests that the bakers' occupational exposure to heat may be a contributory factor to subfertility.

Ceramic Oven Operators: Radiant Heat

Figà-Talamanca et al. [88] reported that healthy ceramics oven operators with chronic occupational exposure to high temperatures (37 °C, 8 h/day) had a higher incidence of abnormal sperm parameters compared to controls. These individuals faced difficulty in establishing a pregnancy and had a higher occurrence of not being able to father a child compared to controls [88].

Professional Drivers

Long hours of driving and remaining in a seated position have shown to have detrimental effects on male reproductive function. The negative effect of extended periods of driving on sperm parameters is attributed to an increase in scrotal temperature [57].

Sas and Szollosi [89] investigated the effects of prolonged driving on spermiogenesis in 2,984 patients, of whom 281 were occupational drivers. They found that the incidence of abnormal sperm was higher among the patients who drove professionally and more severe in those with longer occupational driving experience. Similarly, workers involved in the transport occupational group had lower sperm concentrations [90] and a higher risk of abnormal sperm motility [91] compared to other occupational groups. Figà-Talamanca et al. [92] reported that compared to control subjects, taxi drivers in the city of Rome had a higher amount of sperm with abnormal morphology and that this was more apparent in the longer-serving drivers. However, sperm concentration and motility in these drivers ($n=72$) were comparable to that of the 50 healthy control subjects, who were of similar age and had similar smoking habits. This study also suggested that prolonged driving time could compromise sperm morphology and thereby sperm quality [92]. In a study of 402 fertile couples in France, Thonneau et al. [93] found that compared to other couples, the time to pregnancy was significantly prolonged for those couples in which the male partner remained seated driving in a vehicle for longer than 3 h daily.

In addition to the effect of prolonged sitting on a car seat (which in itself causes about a 2 °C increase in scrotal temperature) [57], the use of a heated car seat for longer than 60 min was shown to cause an increase in scrotal temperature of 0.5–0.6 °C, nearing core body temperature [94]. This additional factor would likely add towards the decline in sperm quality.

Submariners

Velez de la Calle [95] and co-workers looked into the infertility risk factors in a military population from a large military naval base in Brest, France. They found that male mechanics, cooks, and submariners who were occupationally exposed to very hot working conditions while in the submarine (temperatures in the rear end of the submarine close to the motor range between 40 and 60 °C) had sought help for infertility issues.

Ambient Temperature and Seasonality

A 1 °C increase in ambient temperature induces a 0.1 °C increase in scrotal temperature [32]. In a study of semen samples taken from more than 1,000 fertile men from four European cities (Copenhagen, Denmark; Paris, France; Edinburgh, Scotland; and Turku; Finland), Jorgenson's group found a general seasonal variation in sperm concentration (summer values were 70 % of winter values) and total sperm count (summer values were 72 % of winter values), but not for sperm motility or morphology [96]. The difference of approximately 30 % in sperm count from winter (highest) to summer (lowest) could be attributed to differences in lifestyle or environmental exposures among the men [96]. Similarly, in a preliminary study of 4,435 pre-vasectomy patients, Tjoa et al. [97] reported

a circannual rhythm (biological rhythmicity approximating 1 year) in human sperm concentration and total sperm count, with a higher sperm count in winter compared to summer. Gyllenborg et al. [98] found that sperm counts among a group of unselected Danish semen donor candidates were lowest in the summer although semen volume and sperm motility remained unchanged. However, Mallidis et al. [99] did not find any effect of season in semen samples provided by normal healthy Australian men.

Mild Scrotal Heating as a Method of Contraception

Scrotal temperatures that are maintained lower than that of the core body temperature would help improve spermatogenesis and the fertility potential of men facing infertility issues. However, fertile men may find that higher scrotal temperatures could work in their favor. Commonly used methods of male contraception include hormonal approach, the use of condoms and vasectomy [100]. However, local application of heat could provide the means for a non-hormonal, noninvasive, reversible method of contraception targeting the testicular level [100]. In a preliminary study, Mieusset and Bujan [101] induced mild testicular heating (assumed as 1–2 °C) by immobilizing the testis close to the inguinal canal daily during waking hours in 9 men aged between 23 and 34 years. These methods did not affect the men's libido or sexual rhythm, and no pregnancies were reported during the study period [101]. Sperm count and motility normalized within 1–1.5 years in all the subjects involved in this study [101]. In another clinical study, Wang et al. [102] reported that hot water baths taken in combination with testosterone suppressed sperm count and motility. Thus, it would seem that mild scrotal heating could potentially serve as an alternate contraceptive method. However, the endocrine parameters involved in regulating spermatogenesis such as the hypothalamic and pituitary hormones may well be affected by the intentional increase in scrotal temperature.

Scrotal Cooling

Several studies have showed that scrotal cooling can improve sperm count, motility, and morphology [103]. Devices that have been used for testicular cooling include a curved rubber collar filled with ice cubes that was taped to both the thighs for 30 min daily for 14 consecutive days [104] and a gel ice pack that solidified upon freezing, which was wrapped in a cloth or towel and inserted in the underwear on the anterior aspect of the scrotum nightly for 2 months—the cooling effect occurred upon the thawing of the ice pack within 3–4 h [105]. Other techniques included a cotton suspensory bandage placed in close contact with the scrotum (worn for 16–22 h from 8 to 20 weeks) that released fluid (water or alcohol) to maintain a damp scrotum [106] and a device attached with a belt to the abdomen and scrotum that released a continuous air stream to achieve scrotal cooling nightly for 12 weeks [107]. In a study to assess the feasibility of a clinical trial, Osman and his group evaluated the use of a non-greasy hydrogel pad, the Babystart® FertilMate™ Scrotum Cooling Patch, in patients with mild, moderate, and severe oligoasthenospermia [103]. The pad contained 0.5 % w/w natural I-menthol and was reported to be more practical and comfortable to use than other cooling devices [103]. When the testes were cooled, spermatogenesis improved and pregnancy occurred leading to the suggestion that hyperthermia played a role in causing or aggravating male infertility [29]. The factors affecting scrotal (testicular) temperatures and their effect on sperm parameters and male infertility are summarized in Table 8.2.

Conclusion

Scrotal hyperthermia is a substantial risk factor for male infertility. Repetitive transient scrotal hyperthermia in the current modern lifestyle is likely to have a negative impact upon spermatogenesis, specifically in men who are of reproductive age and desire to have children. The normal healthy male is equipped with local

Table 8.2 Factors affecting scrotal (testicular) temperatures and their effect on sperm parameters and male fertility

Exogenous factors contributing to heat stress	Effects on scrotal/ testicular temperature	Reference(s)	Impact on sperm parameters and male fertility	Reference(s)
Posture (physical inactivity)				
1. Standing	Lower (vs. sitting or supine)	[32, 36, 58, 59]	No data	–
2. Sitting (regardless of position of legs, i.e., crossed, close together or apart)	Increased (vs. standing or supine)	[32, 36, 57–59]	Reduced motility (legs close together)	[32]
3. Sitting (legs apart)	Lower (when legs apart vs. when legs close together or crossed)	[57, 63]	No data	–
4. Sitting (on different chair types—cushioned and non-cushioned, plywood and wooden, knee-support, saddle chair)	Increased (in conventional office chair—legs narrowly apart) vs. saddle chair—legs wide apart	[62]	No data	–
5. Sitting (on heated floor, car seat)	Increased (vs. conventional floor or car seat)	[64, 94]	No data	–
6. Supine (and during night sleep)	Increased close to core body temperature (vs. standing or sitting)	[16, 30, 32, 56, 58, 60, 61, 107]	No effect on semen parameter	[16]
	Lower (when naked vs. clothed or wearing underwear)			
7. Sitting (sedentary position at work)	Increased (vs. standing or supine)	[30, 56, 57]	Not a risk factor for abnormal semen quality	[30]
	Strong correlation between scrotal temperatures and duration of sedentary work			
Posture (physical activity)				
8. Moderate walking	Lower (vs. sitting)	[16, 30, 32, 56–61, 107]	No data	–
Clothing				
1. Clothed state	Increased (vs. naked or unclothed state)	[32, 57, 63–66]	No data	–
2. Underwear (form-fitting)	Increased (vs. loose-fitting)	[32, 59, 68, 111]	No data	–
	No difference (vs. loose-fitting)	[12, 65]	No data	–

(continued)

Table 8.2 (continued)

Exogenous factors contributing to heat stress	Effects on scrotal/ testicular temperature	Reference(s)	Impact on sperm parameters and male fertility	Reference(s)
3. Diapers (disposable)	No difference (vs. reusable cloth diapers with plastic covering)	[71]	No data	–
	Higher (vs. reusable cloth diapers without plastic covering)	[70, 71]	No data	–
Lifestyle				
1. Obesity	Increased	[76, 77]	Suppressed sperm production	[75]
2. Sauna	Increased to core body temperature	[58]	Reduced sperm count within a week	[79]
	Increased to core body temperature	[35]	No change in semen volume, sperm count, morphology Reduced motility, reversible once exposure is discontinued	[35]
	Increased to core body temperature	[80]	Reduced sperm count (less efficient spermatogenesis but reversible) and lower (but reversible) progressive motility No change in sperm morphology and viability Altered DNA protamination and nuclear condensation Increased expression of genes associated with hypoxia and heat stress (up-regulation of heat shock proteins and their regulating heat shock factors)	[80]
3. Hot baths	Increased	[68, 81]	Reduced sperm motility	[81]
4. Exercise—moderate cycling	Lowered during cycling (maximum value reached is above physiological range)	[72]	Sperm density and morphology unaffected (in professional cyclists during competition year)	[83]
5. Laptop usage in lap position	Increased	[84]	No data	–
Occupational exposure				
1. Welders—radiant heat	No data	–	Adverse effects on sperm count, motility, concentration, and proportion of sperm with normal morphology reduced	[85, 86]
2. Bakers—radiant heat	No data	–	Longer time to pregnancy	[87]
3. Ceramic oven operators—radiant heat	No data	–	Longer time to pregnancy	[88]

4. Professional drivers	No data	–	Lower percentage of sperm with normal morphology, higher risk of lowered sperm motility	[89, 92, 93]
5. Submariners in a nuclear-powered submarine	No data	–	Increased infertility issues	[95]
Temperature variations				
1. Ambient temperature	Increased	[32]	No data	–
	No effect	[63]	No data	–
2. Seasonal changes	No data	–	Circannual rhythm in sperm count	[97, 98]
			Higher sperm count in winter	
	No data	–	No effect	[99]
Exogenous factors contributing to heat stress				
Pathological conditions				
1. Febrile episode	–	–	Reduced sperm concentration, sperm morphology and motility affected if fever occurs during spermiogenesis	[11, 37]
2. Varicocele	Increased	[29, 36, 58, 63]	Induces sperm DNA fragmentation	[52, 53]
3. Cryptorchidism	Increased	[3, 36, 112]	Lower sperm output	[52, 53]
			Induces sperm DNA fragmentation	
Exogenous application or removal of heat				
1. Mild scrotal heating	Increased	[29, 59, 101, 113, 114]	Reduced sperm count and percentage of motile sperm and sperm with normal morphology	[29, 101, 113, 114]
			No pregnancy established during exposure period	
2. Scrotal cooling	Decreased	[29, 104–107, 111]	Improved spermatogenesis	[29, 104–107, 111, 115]
			Improved semen quality	
			Improved sperm density and motility	

thermoregulatory mechanisms to maintain a hypothermic testis. However, posture, clothing, lifestyle factors, occupation, and environmental exposure can cause testicular heat stress. Extended hours of exposure to genital heat stress factors exacerbate their effect on semen quality and sperm parameters. Each of these factors does not occur solitarily, but many of them occur simultaneously at any given time, compounding their effect on testicular temperatures. This is especially pertinent in infertile men who already have a compromised reproductive potential.

Nevertheless, simple but significant measures can be taken by individuals to help alleviate the deleterious impact of heat stress on male fertility. These include interspersing periods of activity or movement (walking, running) between extended time spent sitting or lying down, wearing clothing that does not restrict genital airflow, maintaining a healthy weight, and making lifestyle modifications that will promote scrotal hypothermia (e.g., avoiding sauna or hot baths or using a laptop on the lap). Understandably, the occupational requirements of certain lines of work and seasonal variations, although less easily tackled, should not be a deterrent for achieving scrotal hypothermia.

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