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A Comprehensive Review of the Causes of Male Infertility

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Abstract

Male infertility is an intricate problem with important implications for men's reproductive wellness. Male reproductive capability is significantly influence able by a number of changeable, involved; genetics, infections, hormonal contraindication, abnormalities in male reproductive tissue, and varicocele. In order to infertile males, diagnostic studies like hormone examinations, imaging ultrasound tests, genetic tests, and semen fluid analysis, which includes assessments of sperm forms, sperm motility, sperm concentration and sperm deoxyribonucleic acid harm are invaluable in identifying the underlying causes of their disease.

The aim of this review research was to enhance the understanding of male infertility and to provide suggestions for researchers and medical experts for more accurate and effective treatments by carefully examining each relevant element and to provide medical personnel's and investigators at infertility and in vitro fertilization (IVF) centers installation with a useful resource to understand the complex area of male venereal health, as well as the research study conclusion explores the matters currently raised by male infertility, clarifies where it can go, and focus attention on the need for further study to fully realize to the complexity of male infertility.

Introduction

When a husbands has been demanding normally for a year and are still unable to conceive, they are classified by definition as clinically sterility **[1].** It is estimated that male factors account for 30-50% of infertility cases **[2].** Male infertility is a serious issue that has a broad impact on reproductive health. It is sometimes described as the inability to conceive even after engaging in repetitive, unprotected sexual activity **[3].** Despite the widespread belief that infertility is a problem that couples frequently face, men's health doctors are looking at reproductive issues more and more **[4].** It is crucial to understand the complexity of male infertility among fertile men, especially in view of the increasing frequency of this problem in recent years **[5].**

Both male and female, infertility affects a large number of couples around the world and it is took that 15% of couples suffer from infertility **[6].** The infertility is noteworthy that male variants contribute to infertility in 30 to 40 percent of cases, suggesting the importance of male reproductive health **[7].** Many men's and women's trying to conceive are influenced by male infertility, but its importance has historically been underestimated because it is oftentimes related with female features **[8].** It is therefore necessary to emphasize that the establishment of effective diagnostic and therapeutic procedures for male infertility involves awareness of the underlying causes and treatment options **[9].** Given the complexity of the physiology of male reproduction, it is critical to understand the variables that may affect fertility **[10].** This details, which allows medical physician, infertility and In Vitro Fertilization specialists to customize treatments for certain underlying causes, work for the basis for correct diagnosis and enhances the possibility of achieving good results **[11].** That is significant to recognize that correct discovery is ticklish in cases of male infertility because it teaches the choice of acceptable treatment choice, as well as identifying the underlying causes and located the correct treatment **[12].**

Physicians can conform treatment to the particular difficulties of each individual or couple by assessing whether infertility is caused by heredity, hormonal imbalances, structural abnormalities, or environmental causes **[13].** This personalized strategy produces better results and increases the accuracy of treatment **[14].** Furthermore, a thorough understanding of the etiology of male infertility makes it easy to create and promote new diagnostic procedures **[15].**

When used in conjunction with established causal factors, many diagnostic techniques such as seminal analysis, hormone tests, imaging investigations, and genetic testing become more relevant and specific **[16].** This integration of information enables a more accurate and rapid diagnosis, leading to complete and focused diagnostic investigations **[17].** Impact treatment possibility include a thorough understanding of both underlying sources and detections **[18].**

By changing manner of living to complex assisted reproductive techniques, treating treatment for specific causes of male infertility improves therapeutic efficacy and success rates **[19].** This personal strategy avoids unnecessary treatments, eases the mental and financial burden of couples, and increases the likelihood of a healthy pregnancy **[20].**

The objective of this review paper was to high point the prominent of male infertility as a severe reproductive health concern as well as it highlights the increased recognition of male causes in infertility, as well as the worldwide increase in male infertility ratio.

Materials and Methods

This review article systematically compiled information, sources, images, and figures from prestigious academic databases such as Google Scholar, British Journal of Nursing, Oxford University Press, PubMed, Scopus, BioMed Central, Hindawi, Wiley, and other reputable scientific journals. A comprehensive review of the literature on male factor infertility from 2018 to 2022 was conducted, with the keywords "Causes of Male Infertility" as the search method.

Anatomy and Physiology of Male Reproductive System:

1. Describe the components of the male reproductive system;

The intricate and well-coordinated network of organs and tissues that makes up the male reproductive system produces, transports, and distributes sperm for conception **[21].**

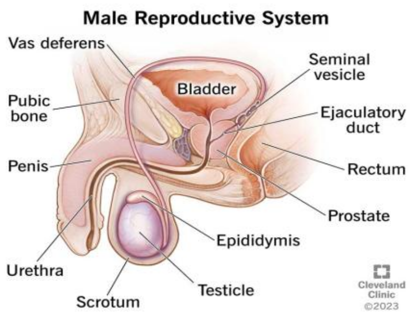

Figure 1: Male sexual intercourse and urination are made possible by the internal and exterior organs that make up the male reproductive system **[22]**.

1.1 Testes:

The testes, which are found in the scrotum, are the main reproductive organs in men **[23].** It is in charge of the spermatogenesis process, which produces sperm **[24].** The main male sex hormone, testosterone, is also secreted by the testes and is essential for the development of male reproductive tissues and secondary sexual traits **[25].**

1.2 Sperm Production (Spermatogenesis):

Spermatogenesis occurs in the seminiferous tubules of the testes. Spermatogonia (immature germ cells) divide and develop into mature sperm cells (spermatozoa) **[27].** The pituitary gland generates substances that regulate the process, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH) **[28].**

1.3 Epididymis:

After spermatogenesis, sperm go to the epididymis, a coiled tube located on the surface of each testis **[29].** In the epididymis, sperm grow, gaining motility and the ability to fertilize eggs **[30].**

1.4 Vas Deferens:

During ejaculation, mature sperm travels from the epididymis to the urethra via the vas deferens **[31].**

1.5 Seminal Vesicles, Prostate Gland, and Bulbourethral Gland:

These auxiliary sex glands produce seminal fluid, which nourishes and transports sperm **[32].** Seminal vesicles account for the bulk of the semen volume, whereas the prostate gland contributes enzymes to increase sperm motility and the bulbourethral gland produces lubricating fluid **[33].**

1.6 Urethra:

The urethra is a conduit that transports both urine and sperm out the body, although not simultaneously **[34].** During ejaculation, the bladder sphincter contracts to keep urine from mixing with sperm **[35].**

1.7 Penis:

The penis is the external organ of copulation, introducing sperm into the female reproductive canal during sexual contact **[36].**

1.8 Hormonal Regulation:

The hypothalamus, pituitary gland, and testes work together to regulate testosterone production and spermatogenesis **[37].** The hypothalamus produces gonadotropin-releasing hormone (GnRH), which encourages the pituitary gland to release FSH and LH, which control testicular activity **[38].**

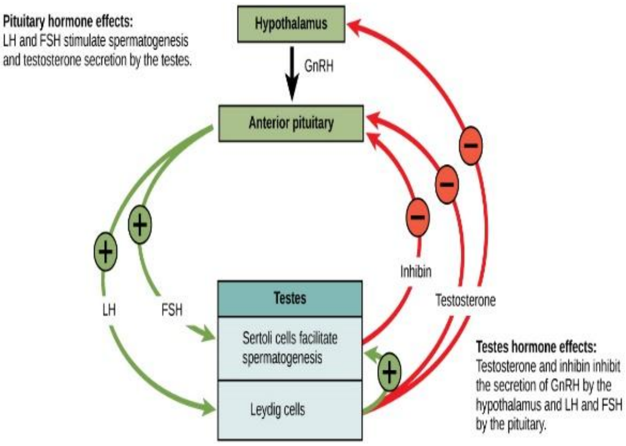

Figure 2 Sperm production is tightly controlled by a negative feedback loop including hormones. The hypothalamus, a brain area, secretes gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to create and secrete two essential horm

2. The process of spermatogenesis and sperm maturation

Spermatogenesis is the process by which immature germ cells in the testes, termed spermatogonia, divide and differentiate into mature sperm cells known as spermatozoa **[40].** This intricate process happens within the seminiferous tubules of the testes and is divided into phases **[41].** Furthermore, sperm maturation occurs in the epididymis, where sperm develop motility and the capacity to fertilize an egg **[42].**

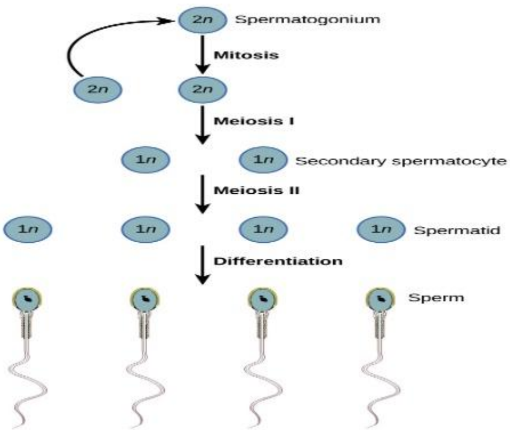

Figure 3 Spermatogenesis, the process of sperm production, entails a number of intricate cellular divisions and differentiations [43].

Spermatogenesis and sperm maturation steps includes:

2.1 Spermatogenesis

2.1.1 Spermatogonia Division

During puberty, spermatogonia, which are stem cells found in the walls of the seminiferous tubules, undergo mitotic divisions **[44].** One daughter cell stays a spermatogonium, guaranteeing a steady supply, while the other develops into a primary spermatocyte **[45].**

2.1.2 Meiosis I

Each main spermatocyte performs the first meiotic division, producing two haploid secondary spermatocytes **[46].**

2.1.3 Meiosis II

Of the secondary spermatocyte undergoes a second meiotic division, creating four haploid spermatids **[47].**

2.1.4 Spermiogenesis

Spermatids go through a process known as spermiogenesis, which involves structural changes that transform them into spermatozoa **[48].** This includes cell restructuring, the growth of a tail (flagellum), and the construction of the acrosome, which contains enzymes required for fertilization **[49].**

2.1.5 Spermiation

Spermiation is the process by which mature spermatozoa are released from the supporting Sertoli cells and into the lumen of the seminiferous tubules **[50].**

2.2 Sperm Maturation (Epididymis)

2.2.1 Transport to the Epididymis

On the surface of the testis is a coiled tube called the epididymis **[51].** The seminiferous tubules transfer newly produced sperm to the epididymis for further maturation **[52].**

2.2.2 Maturation and Storage

Sperm develop in the epididymis over a two to three week period **[53].** Sperm develop motility at this stage, which is necessary for them to migrate through the female reproductive system **[54].**

2.2.3 Functional Changes

The environment created by the epididymis enables sperm to undergo functional changes, such as enhanced swimming and the development of the capacity to enter and fertilize an egg **[55].**

2.2.4 Storage

Mature sperm are stored in the epididymis before being released during ejaculation **[56].**

3. Causes of Male Infertility

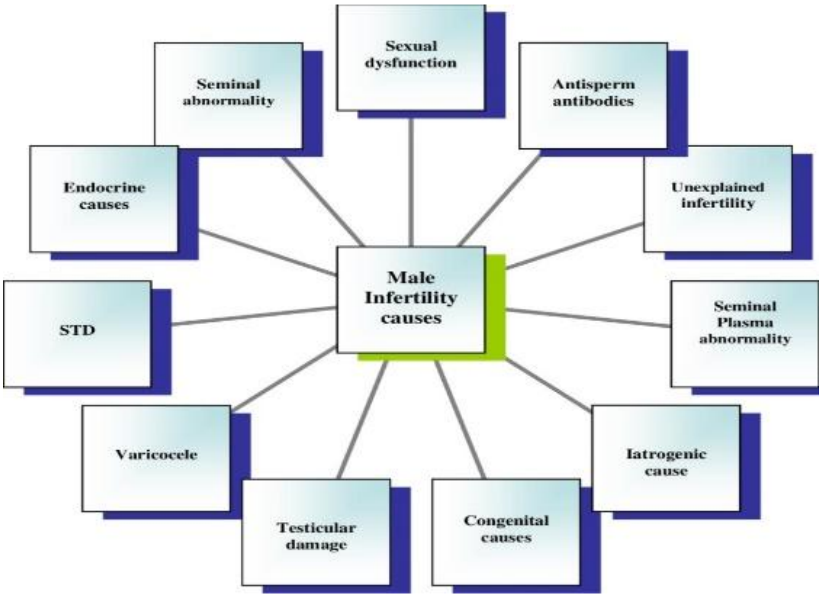

Figure 4 The World Health Organization provides diagnostic categories based on many metrics established by sperm analysis to define the causes of male infertility [57].

3.1 Genetic Factors

Male fertility is greatly influenced by genetic variables, which also have an impact on spermatogenesis, sperm function, and reproductive health **[58].** Comprehending these genetic variables is essential for precise diagnosis, guidance, and the creation of focused therapies.

3.1.1 Y-Chromosome Microdeletions

A portion of the Y chromosome, especially in the azoospermia factor (AZF) regions, can be lost in Y-chromosome microdeletions **[59].** Y-chromosome microdeletions can result in azoospermia, or the lack of sperm, or severe oligospermia, or an extremely low amount of sperm **[60].**

3.1.2 Klinefelter Syndrome

Testicular dysfunction results from the extra X chromosome (XXY) that characterizes Klinefelter syndrome **[61].** Men with Klinefelter syndrome may have poor spermatogenesis, which can lead to infertility, and they frequently have azoospermia or severe oligospermia **[62].**

3.1.3 Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Mutations

Congenital bilateral absence of the vas deferens (CBAVD), a condition caused by CFTR mutations linked to cystic fibrosis, can affect fertility **[63].** Obstructive azoospermia (CBAVD) is characterized by normal sperm production but blocked sperm transit **[64].**

3.1.4 Androgen Receptor (AR) Mutations

Androgen insensitivity syndrome, where people with XY chromosomes may have inadequate development of male reproductive organs, can be caused by mutations in the androgen receptor gene **[65].** Due to hampered testicular growth and decreased androgen sensitivity, this may result in infertility **[66].**

3.1.5 Chromosomal Abnormalities

Spermatogenesis can be influenced by structural or numerical chromosomal abnormalities such translocations or inversions **[67].** These aberrations may increase the possibility of producing sperm with chromosomal abnormalities, thus increasing the risk of miscarriage or infertility **[68].**

3.1.6 Autosomal Recessive Disorders

Autosomal recessive illnesses can have an effect on male fertility, such as congenital bilateral absence of the vas deferens (CBAVD), which is connected to cystic fibrosis **[69].** These disorders may interfere with the healthy development or function of reproductive organs and tissues **[70].**

3.1.7 Single Gene Mutations

Mutations in certain genes involved in spermatogenesis or sperm function can cause male infertility **[71].** Mutations in genes associated to cilia structure and function can alter sperm motility **[72].**

3.1.8 Mitochondrial DNA Mutations

Mutations in mitochondrial DNA that are inherited from the mother can affect sperm motility and function **[73].** These modifications may contribute to male infertility by interfering with the energy production required for sperm motility **[74].**

3.2 Hormonal Imbalances

3.2.1 Disruptions in hormonal balance and sperm production

Hormone abnormalities can have significant influence on sperm production, which can lead to male infertility. Hormones primarily control spermatogenesis, the process in the testes where new sperm cells are formed **[75].** This intricate process may be hampered by hormonal abnormalities, which might affect sperm count and quality **[76].**

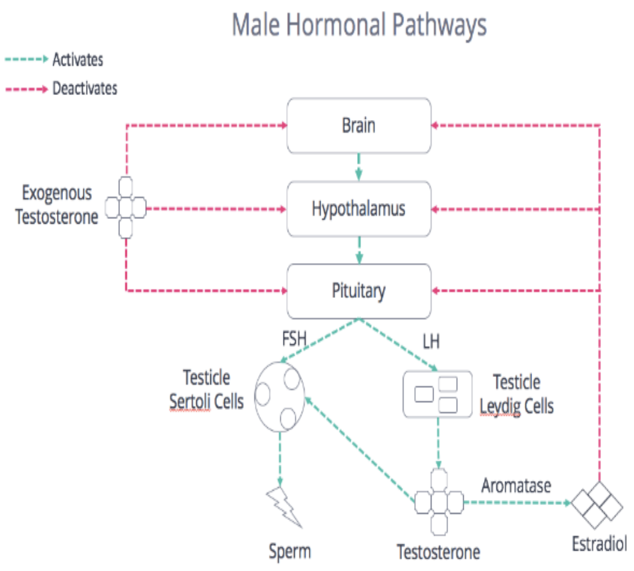

Figure 5 The hormonal management of male reproductive processes involves a complex system that coordinates sperm production and the retention of male sexual characteristics [77].

An explanation of how sperm production is affected by imbalances in hormones

3.2.1.1 Follicle-Stimulating Hormone (FSH)

FSH is a key hormone that promotes spermatogenesis by acting on Sertoli cells in the testes' seminiferous tubules **[78].** Low FSH levels may promote lower sperm cell development, resulting in fewer mature sperm ready for ejaculation **[79].**

3.2.1.2 Luteinizing Hormone (LH)

When LH stimulates the Leydig cells in the testes, they create testosterone, the primary male sex hormone [80]. Spermatogenesis requires testosterone to start and sustain **[81].** Low levels of LH or testosterone might cause decreased sperm production **[82].**

3.2.1.3 Testosterone

Male reproductive tissues, such as the testes and accessory sex organs, rely on testosterone to develop and maintain **[83].** Low testosterone levels can impair spermatogenesis, affecting sperm maturation and function **[84].**

3.2.1.4 Hypogonadism

Hypogonadism is a disease in which the testes do not produce adequate testosterone **[85].** Primary hypogonadism can result from testicular abnormalities, but secondary hypogonadism might be caused by hypothalamus or pituitary gland diseases **[86].** Hypogonadism can cause a dip in sperm production, which is typically followed by a loss in sperm motility and morphology **[87].**

3.2.1.5 Thyroid Hormones

Thyroxine (T4) and triiodothyronine (T3) are two thyroid hormones that influence metabolism, including spermatogenesis **[88].** Thyroid hormone abnormalities have the potential to disrupt the hormonal milieu required for normal sperm production **[89].**

3.2.1.6 Prolactin

Reduced gonadotropin-releasing hormone (GnRH) production can lead to reduced levels of FSH and LH when prolactin, a hormone associated with breastfeeding, is increased **[90].** This may have an impact on sperm production by reducing testosterone levels **[91].**

3.2.1.7 Cortisol and Stress Hormones

Long-term stress and elevated cortisol levels can have an influence on the hypothalamic-pituitary-gonadal (HPG) axis, resulting in aberrant reproductive hormone release **[92].** Stress-induced hormonal changes may contribute to reduced fertility and sperm quality **[93].**

3.2.1.8 Insulin and Metabolic Hormones

Insulin resistance and metabolic disorders can have an influence on reproductive hormones and sperm production **[94].** Diabetes and obesity, which are associated with insulin resistance, may be the cause of hormonal abnormalities that affect male fertility **[95].**

3.2.2 Hypogonadism and Male Infertility

The principal male sex hormone, testosterone, is produced insufficiently by the testes in a condition known as hypogonadism **[96].** Depending on where the malfunction originated, it can be categorized as primary (pituitary or hypothalamus) or secondary (testicular) **[97].**

3.2.2.1 Impact on Male Infertility

1. Spermatogenesis: Initiating and sustaining spermatogenesis requires testosterone. Insufficient testosterone levels can lead to impaired sperm production **[98].**
2. Sperm Maturation: Testosterone influences the maturation of sperm in the testes, impacting sperm quality and functionality **[99].**
3. Libido and Erectile Function: Testosterone plays a role in libido and erectile function. Low testosterone levels may contribute to reduced sexual desire and difficulties in achieving or maintaining erections **[100].**

4. Gonadotropin Levels: In primary hypogonadism, elevated levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) may be observed, indicating the testes are not responding adequately to these hormones **[101].**

3.2.2.2 Causes of Hypogonadism

1. Age-Related Decline (Late-Onset Hypogonadism): Testosterone levels naturally decline with age, and this decline may impact fertility in older men **[102].**
2. Genetic Conditions: Conditions like Klinefelter syndrome, where males have an extra X chromosome (XXY), can lead to hypogonadism and infertility **[103].**
3. Testicular Trauma or Injury: Physical damage to the testes can disrupt testosterone production **[104].**
4. Infections: Infections, such as mumps orchitis, can cause inflammation and damage to the testes **[105].**

3.2.2.3 Thyroid Disorders and Male Infertility

1. Influence on Metabolism: Thyroid hormones (thyroxine, T4, and triiodothyronine, T3) play a crucial role in metabolism, including energy production required for spermatogenesis **[106].**
2. Hormonal Balance Disruption: Thyroid hormone imbalances have the potential to upset the hormonal balance necessary for healthy sperm development **[107].**

3.2.2.4 Impact on Male Infertility

1. Sperm Quality Management: Thyroid conditions such as hyperthyroidism or hypothyroidism can impact sperm motility and morphology **[108].**
2. Erectile roles: Sexual function is affected by libido and erectile function, which are both impacted by thyroid issue **[109].**

3.2.2.5 Causes of Thyroid Disorders

1. Autoimmune Diseases: In diseases such as hyperthyroidism (Graves' disease) and hypothyroidism (Hashimoto's thyroiditis), the immune system assaults the thyroid gland **[110].**
2. Iodine Overabundance or Shortage: Iodine is essential for thyroid hormone production, and it can be caused by either too high or too less thyroid hormone **[111].**
3. Thyroid Tumors: Abnormal growths in the thyroid gland might interfere with hormone production **[112].**

3.2.2.6 Thyroid Hormones and Spermatogenesis

1. The influences on Metabolism: Thyroid hormones triiodothyronine (T3) and thyroxine (T4) are necessary for metabolism, which involves energy production associated with spermatogenesis **[113].**
2. Disruption of Hormonal Balance: The balance of hormonal required for normal sperm production can be severely disrupted by thyroid hormone abnormalities **[114].**

3.2.2.7 Impact on Male Infertility

1. An management of sperm classifications: Thyroid disorders, such as hyperthyroidism or hypothyroidism, can affect sperm motility and morphology **[115].**
2. Erectile Dysfunction: Thyroid matters can affect libido and erectile function, among other aspects of sexual function in males **[116].**

3.2.2.8 Causes of Thyroid Disorders

1. Autoimmune Diseases: The thyroid gland is attacked by the immune system in conditions such as Hashimoto's thyroiditis (hypothyroidism) and Graves' disease (hyperthyroidism) **[117].**
2. Iodine Deficiency or Excess: Iodine is essential for thyroid hormone production. Deficiency or excess can lead to thyroid dysfunction **[118].**
3. Thyroid Nodules or Tumors: Abnormal growths in the thyroid gland may disrupt hormone production **[119].**

3.3 Varicocele

Varicocele is a condition characterized by the enlargement of veins within the scrotum, specifically the pampiniform plexus, which drains blood from the testicles **[120].** It is one of the most common causes of male infertility and affects approximately 15% of the general male population and about 40% of men evaluated for infertility **[121].**

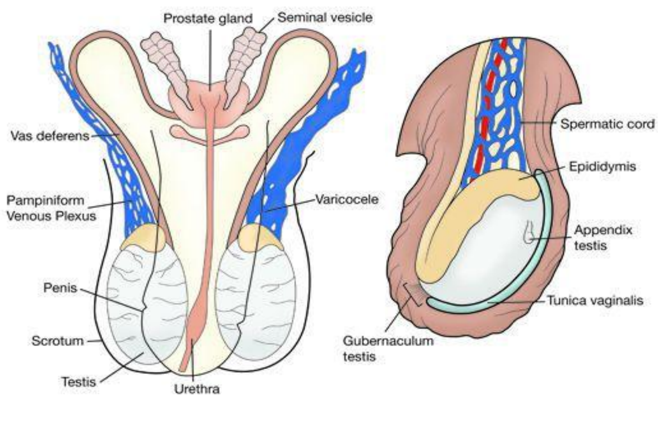

Figure 6 Varicocele is a common condition that occurs when the veins within the scrotum become enlarged and dilated [122].

3.3.1 Mechanism of Impact

The exact mechanism by which varicoceles contribute to male infertility is not fully understood, but several hypotheses have been proposed:

1. Testicular Temperature: Varicoceles may lead to an increase in testicular temperature. Elevated temperatures in the testicles can negatively impact sperm production (spermatogenesis). The testicles are normally maintained at a slightly lower temperature than the body, and varicoceles may disrupt this thermoregulation **[123].**

2. Venous Stasis and Hypoxia: The enlarged veins in varicoceles can cause venous stasis, leading to reduced blood flow and oxygen delivery to the testicles. This hypoxic environment may adversely affect spermatogenesis and the quality of developing sperm **[124].**

3. Development of harmful Metabolites: When blood in the veins stagnates, harmful metabolites may build up. The growth and functionality of sperm may be negatively impacted by these compounds **[125].**

4. Hormonal Imbalance: Varicoceles may affect the testicular hormone environment, which might change the hormone balance involved in reproduction. The maturation and generation of sperm may be impacted by this hormonal imbalance **[126].**

3.3.2 Impact on Male Infertility

1. Sperm Parameters: Varicoceles have been linked to reduced motility, morphology, and sperm count—all of which are important aspects of male fertility **[127].**

2. Enhanced Risk of Infertility: Men who have varicoceles have a higher chance of becoming infertile than men who do not. Not all men with varicoceles will experience reproductive problems, and the severity of infertility might vary **[128].**

3. Impact on Assisted Reproductive Technologies (ART): Varicoceles have been shown to lower the success rates of ART procedures including intracytoplasmic sperm injection (ICSI) and in vitro fertilization (IVF) **[129].**

3.4 Environmental Factors

Lifestyle choices have a significant impact on the quality of sperm and overall fertility in men **[130].** Male infertility has been associated with a number of habits, including drug and alcohol abuse, smoking, and alcohol drinking **[131].** For individuals and couples looking to maximize their odds of conception, it is imperative that they comprehend the influence of these lifestyle variables **[132].**

3.4.1 Smoking

1. Sperm Quality: According to research, smoking reduces sperm motility, count, and morphology **[133].**

2. DNA Damage: Tobacco smoke includes toxic chemicals that can damage sperm's DNA, which may have an impact on conception and the growth of embryos **[134].**

3. Oxidative Stress: Smoking causes oxidative stress, which throws off the reproductive system's delicate equilibrium between antioxidants and free radicals **[135].**

4. Hormonal Disruption: Smoking has been shown to affect testosterone levels, which are necessary for healthy sperm development **[136].**

3.4.2 Alcohol Consumption

1. Sperm Quality: Excessive alcohol consumption can lead to a reduction in sperm motility, count, and morphology **[137].**

2. Hormonal Imbalance: Alcohol use can lead to a hormonal imbalance that may affect testosterone levels and perhaps lead to infertility **[138].**

3. Liver Function: Consuming alcohol over an extended period of time may harm the liver, which influences the metabolism of nutrients and hormones required for the creation of sperm **[139].**

4. Testicular Atrophy: Prolonged alcohol abuse can lead to testicular atrophy, which can further reduce fertility **[140].**

3.4.3 Drug Use

1. Sperm Quality: It has been demonstrated that using drugs recreationally, such as cocaine and marijuana, lowers the motility, count, and morphology of sperm **[141].**

2. Hormonal Disruption: The endocannabinoid system may be disturbed by marijuana and other substances, which may have an effect on spermatogenesis and hormone regulation **[142].**

3. Testicular Atrophy: This disorder, which affects the reproductive system as a whole, may be caused by opioids and certain drugs **[143].**

4. Sexual Dysfunction: Some drugs may lead to sexual dysfunction, affecting sexual performance and fertility **[144].**

3.4.4 Weight and Physical Activity

1. Obesity: Obesity has been linked to lower testosterone levels, altered sperm parameters, and increased oxidative stress **[145].**

2. Underweight: Low body weight can lead to hormonal imbalances, affecting reproductive function **[146].**

3. Sedentary Lifestyle: Lack of physical activity may contribute to obesity and can also impact hormonal regulation **[147].**

3.4.5 Heat Exposure

Increased Scrotal Temperature: Prolonged exposure to high temperatures, such as from hot baths, saunas, or tight clothing, can raise scrotal temperature, negatively affecting sperm production **[148].**

3.5 Infections and Inflammation

3.5.1 The role of infections in the reproductive system and their impact on sperm quality

Infections of the male reproductive system can have a major influence on sperm quality and fertility **[149].** Infections can produce inflammation in the reproductive organs, which directly affects sperm motility, morphology, and generation **[150].**

3.5.1.1 Common Infections

1. Sexually transmitted infections (STIs): Some disorders that might impair the reproductive system and sperm quality include syphilis, gonorrhea, and chlamydia **[151].**
2. Urinary Tract Infections (UTIs): According to reference **[152],** UTIs can spread to the reproductive organs.

3.5.1.2 Impact on Sperm Quality

1. Spermatogenesis Disruption: Infections that interfere with spermatogenesis might cause a decrease in sperm count **[153].**
2. Motility and Morphology: An infection may alter the morphology and motility of sperm, limiting their ability to reach and fertilize an egg **[154].**
3. DNA damage: Inflammatory responses associated with infections may compromise sperm genetic integrity by damaging DNA **[155].**

3.5.1.3 Inflammatory Response

1. Orchitis and Epididymitis: Infections in the testes (orchitis) or the epididymis (epididymitis) can cause inflammation and reduced sperm production **[156].**
2. Prostatitis: An inflammation of the prostate gland that can change the composition of seminal fluid and cause abnormal sperm activity **[157].**

3.5.1.4 Obstruction and Scarring

1. Hydrospermia: An infection may cause an excess of fluid to accumulate in the seminal vesicles; this condition is known as hydrospermia and may affect the sperm concentration **[158].**

2. Blockages and Scarring: Ongoing infections can result in blockages and scarring of the generative ducts, which stops sperm from flowing properly **[159].**

3.5.1.5 Immune Response

1. Autoimmune Reactions: In some cases, infections can trigger an immune response that mistakenly targets sperm cells, leading to autoimmune reactions that affect sperm function **[160].**

3.5.1.6 Impact of Treatment

Antibiotics: While antibiotics are commonly used to treat infections, certain antibiotics may have adverse effects on sperm quality. It's essential to consider the potential impact of medications on fertility **[161].**

3.5.1.7 Prevention and Safe Practices

1. Safe Sex Practices: Practicing safe sex and using barrier methods can help prevent sexually transmitted infections **[162].**
2. Hygiene: Maintaining good genital hygiene can reduce the risk of infections **[163].**

3.5.1.8 Timing of Infections

1. Timing Concerns: Infections occurring during critical stages of sperm development may have more pronounced effects on sperm quality **[164].**

3.5.1.9 Chronic Infections

1. Persistent Effects: Chronic or recurrent infections may have prolonged effects on sperm quality and fertility **[165].**

3.5.2 Sexually Transmitted Infections (STIs) in Male Infertility

Sexually transmitted infections (STIs) can have significant consequences on male reproductive health, affecting various aspects of the male reproductive system and contributing to infertility **[166].** The impact of STIs on male fertility can manifest through direct damage to reproductive organs, disruption of sperm function, and the development of inflammatory conditions **[167].**

3.5.2.1 Chlamydia

Chlamydia trachomatis has the capacity to diffuse throughout the male reproductive system, resulting in diseases such orchitis, epididymitis, and prostatitis **[168],** as well as one of the significant negative effect of Chlamydia-induced epididymitis is a reduction in sperm grade.

The normal process of sperm maturation within the epididymis can be hampered by the inflammatory response associated with epididymitis, as a result of this interference, sperm motility, sperm concentration and sperm classifications might be make less, potentially causing reproductive issues **[169].**

In addition to structural effects on the epididymis, chlamydial infection can generate inflammatory processes that have a wider impact on sperm quality, and this contain reduced sperm functions, sperm DNA damage, and generation of oxidative stress **[170].**

3.5.2.2 Gonorrhea

Neisseria gonorrhea, the bacterial disease has a range of negative effects on male fertility health **[171].** Gonorrhea can create inflammatory conditions that impair sperm maturation and interact with Chlamydia trachomatis, while this underscores the widespread impact on the essential reproductive organs, including the risk of prostatitis, epididymitis, and urethritis **[172].**

3.5.2.3 Syphilis

Treponema pallidum, the bacteria that causes syphilis in males, has an important influence on the male reproductive organs, especially when the disease is advanced, and the severity of the impact on primary components of the male reproductive system, such as the development of orchitis and testicular atrophy **[173].** Syphilis and testicular infection can cause inflammation, which reduces sperm production and quality **[174].**

3.5.2.4 Human Papillomavirus (HPV)

Human papillomavirus, the Virus infection affects the male reproductive systems in a variety of roads, including the development of genital warts, furthermore, high-risk HPV strains have been associated with a variety of cancers including; prostatic cancers, penile cancer, underscoring the potentially catastrophic implications of HPV-related difficulties for reproductive male health **[175].** Although the specific effect of HPV on sperm quality is uncertain, the association between high-risk HPV strains and cancer creates an indirect concern for male fertility **[176].**

3.5.2.5 Herpes Simplex Virus (HSV)

Herpes Simplex Virus (HSV) poses distinctive effects on male reproductive organs, primarily through the development of genital herpes, characterized by recurrent outbreaks resulting in discomfort and the formation of ulcers **[177]**. In addition to the localized effects, active HSV infections may extend their influence to sperm quality. Such infections have been associated with increased levels of reactive oxygen species (ROS), introducing a potential link between HSV and oxidative stress that can impact sperm function **[178].**

3.5.2.6 Human Immunodeficiency Virus (HIV)

HIV instigates profound effects on male reproductive organs by inducing systemic immune suppression and making individuals susceptible to opportunistic infections, thereby influencing overall health **[179].** While HIV may not directly affect sperm quality, the associated immunodeficiency can lead to other infections that have the potential to compromise fertility. The indirect impact arises from the immunocompromised state, creating an environment where opportunistic infections can thrive and subsequently exert detrimental effects on sperm quality **[180].**

Conclusion

At the end, an overall rating of a complex set of variables affecting male infertility let out a complex interaction with far-reaching consequences for reproductive health. In more network includes hormonal imbalances, genetic predisposition, anatomical abnormalities, and environmental revealed, all of which contribute to male infertility. The diagnostic style was critical in order to identify the underlying causes and provide customized treatment plans. It combines traditional semen analysis with the latest genetic testing. Deciphering the complex nature of male infertility requires an understanding of the subtleties of spermatogenesis, the proper operation of the male reproductive system, and the importance of hormonal balance. It was essential to have a comprehensive strategy that addresses issues including skeletal abnormalities, hypogonadism, and the effects of sexually transmitted diseases. A multidisciplinary approach supported by contemporary research and advances in assisted reproductive technologies and lifestyle modifications underscores how important it is to diagnose and prepare for treatment effectively. Positive results increase dramatically when diseases including obstructive azoospermia, varicocele diseases, and erectile dysfunction were recognize and treated at the same time.

The multiplex interplay between disease, seminal grade, environmental pollutants and employment risk highlight the importance of a proactive proceed toward to male reproductive health and this paper review study was for technologists, medical professionals, and anyone interested in learning more about the complexities of male infertility, who expected results include get larger for understanding of these important variables, further study of the complexity of male reproductive health, and inclusive treatment scheme and diagnostic techniques.

References

[1] Vander Borght, M., & Wyns, C. (2018). Fertility and infertility: Definition and epidemiology. Clinical biochemistry, 62, 2-10.
[2] Agarwal, A., Baskaran, S., Parekh, N., Cho, C. L., Henkel, R., Vij, S., ... & Shah, R. (2021). Male infertility. The Lancet, 397(10271), 319-333.
[3] Garcia III, G. A. (2021). The Experience of Loss Among Men with Infertility (Doctoral dissertation, Northcentral University).
[4] Turner, K. A., Rambhatla, A., Schon, S., Agarwal, A., Krawetz, S. A., Dupree, J. M., & Avidor-Reiss, T. (2020). Male infertility is a women's health issue—research and clinical evaluation of male infertility is needed. Cells, 9(4), 990.
[5] Pallotti, F., Barbonetti, A., Rastrelli, G., Santi, D., Corona, G., & Lombardo, F. (2022). The impact of male factors and their correct and early diagnosis in the infertile couple's pathway: 2021 perspectives. Journal of endocrinological investigation, 45(10), 1807-1822.
[6] Jaber, D. J., Basheer, H. A., Albsoul-Younes, A. M., Elsalem, L. M., Hamadneh, J. M., Dweib, M. K., & Ahmedah, H. T. (2022). Prevalence and predictive factors for infertility-related stress among infertile couples. Saudi Medical Journal, 43(10), 1149-1156.
[7] Houston, B. J., Riera-Escamilla, A., Wyrwoll, M. J., Salas-Huetos, A., Xavier, M. J., Nagirnaja, L., ... & Oud, M. S. (2022). A systematic review of the validated monogenic causes of human male infertility: 2020 update and a discussion of emerging gene–disease relationships. Human reproduction update, 28(1), 15-29.
[8] Ward, M. C. (2019). Poor women, powerful men: America's great experiment in family planning. Routledge.
[9] Aside, M. (2022). Infertility in men: Advances towards a comprehensive and integrative strategy for precision theranostics. Cells, 11(10), 1711.
[10] Liu, B., Mo, W. J., Zhang, D., De Storme, N., & Geelen, D. (2019). Cold influences male reproductive development in plants: a hazard to fertility, but a window for evolution. Plant and Cell Physiology, 60(1), 7-18.
[11] Shlipak, M. G., Tummalapalli, S. L., Boulware, L. E., Grams, M. E., Ix, J. H., Jha, V., ... & Zomer, E. (2021). The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney international, 99(1), 34-47.
[12] Agarwal, A., Parekh, N., Selvam, M. K. P., Henkel, R., Shah, R., Homa, S. T., ... & Harlev, A. (2019). Male oxidative stress infertility (MOSI): proposed terminology and clinical practice guidelines for management of idiopathic male infertility. The world journal of men's health, 37(3), 296-312.
[13] Martín, L. P., & Marina, D. T. (2018). Multiple Pregnancy in Women of Advanced Reproductive Age. In Multiple Pregnancy-New Challenges. IntechOpen.
[14] Kent, D. M., Steyerberg, E., & van Klaveren, D. (2018). Personalized evidence based medicine: predictive approaches to heterogeneous treatment effects. Bmj, 363.
[15] de Santiago, I., & Polanski, L. (2022). Data-Driven Medicine in the Diagnosis and Treatment of Infertility. Journal of Clinical Medicine, 11(21), 6426.
[16] Cariati, F., D'Argenio, V., & Tomaiuolo, R. (2019). The evolving role of genetic tests in reproductive medicine. Journal of translational medicine, 17, 1-33.
[17] Walter, W., Haferlach, C., Nadarajah, N., Schmidts, I., Kühn, C., Kern, W., & Haferlach, T. (2021). How artificial intelligence might disrupt diagnostics in hematology in the near future. Oncogene, 40(25), 4271-4280.

[18] Eells, T. D. (Ed.). (2022). Handbook of psychotherapy case formulation. Guilford Publications.
[19] Assidi, M. (2022). Infertility in men: Advances towards a comprehensive and integrative strategy for precision theranostics. Cells, 11(10), 1711.
[20] Adamson, G. D., & Norman, R. J. (2020). Why are multiple pregnancy rates and single embryo transfer rates so different globally, and what do we do about it?. Fertility and Sterility, 114(4), 680-689.
[21] Dutta, S., Sengupta, P., Das, S., Slama, P., & Roychoudhury, S. (2022). Reactive Nitrogen Species and Male Reproduction: Physiological and Pathological Aspects. International Journal of Molecular Sciences, 23(18), 10574.
[22] Professional, C. C. M. (n.d.). Male reproductive system. Cleveland Clinic. https://my.clevelandclinic.org/health/body/9117-male-reproductive-system.
[23] Gurung, P., Yetiskul, E., & Jialal, I. (2022). Physiology, male reproductive system. In StatPearls [Internet]. Statpearls publishing.
[24] Sengupta, P., Arafa, M., & Elbardisi, H. (2019). Hormonal regulation of spermatogenesis. In Molecular signaling in spermatogenesis and male infertility (pp. 41-49). CRC Press.
[25] Nassar, G. N., & Leslie, S. W. (2018). Physiology, testosterone.
[26] Suede, S. H., Malik, A., & Sapra, A. (2020). Histology, spermatogenesis.
[27] Kubota, H., & Brinster, R. L. (2018). Spermatogonial stem cells. Biology of reproduction, 99(1), 52-74.
[28] Oduwole, O. O., Peltoketo, H., & Huhtaniemi, I. T. (2018). Role of follicle-stimulating hormone in spermatogenesis. Frontiers in endocrinology, 9, 763.
[29] Elbashir, S., Magdi, Y., Rashed, A., Henkel, R., & Agarwal, A. (2021). Epididymal contribution to male infertility: An overlooked problem. Andrologia, 53(1), e13721.
[30] James, E. R., Carrell, D. T., Aston, K. I., Jenkins, T. G., Yeste, M., & Salas-Huetos, A. (2020). The role of the epididymis and the contribution of epididymosomes to mammalian reproduction. International Journal of Molecular Sciences, 21(15), 5377.
[31] Ramírez-González, J. A., & Sansone, A. (2022). Male reproductive system. In Fertility, Pregnancy, and Wellness (pp. 23-36). Elsevier.
[32] Obukohwo, O. M., Kingsley, N. E., Rume, R. A., & Victor, E. (2021). The concept of Male reproductive anatomy. Male Reproductive anatomy.
[33] Gamblin, A. P., & Morgan-Smith, R. K. (2020). The characteristics of seminal fluid and the forensic tests available to identify it. Wiley Interdisciplinary Reviews: Forensic Science, 2(3), e1363.
[34] Svintsitskaya, N. L., Hryn, V. H., & Katsenko, A. L. (2021). Anatomy of the Urinary and Reproductive Systems. Structural Features in Childhood. Abnormalities.
[35] Cox, A., Jefferies, M., & Persad, R. (2019). Prostate Structure and Function. Blandy's Urology, 509-521.
[36] Sajjad, A., Akhtar, M. A., & Sajjad, Y. (2018). Pathologies of the Male Reproductive Tract. Clinical Reproductive Science, 159.
[37] Liu, P. Y., & Veldhuis, J. D. (2019). Hypothalamo-pituitary unit, testis, and male accessory organs. Yen and Jaffe's reproductive endocrinology, 285-300.
[38] Dwyer, A. A., & Quinton, R. (2019). Anatomy and physiology of the hypothalamic-pituitary-gonadal (HPG) axis. Advanced Practice in Endocrinology Nursing, 839-852.
[39] Molnar, C. (2015, May 14). 24.4. Hormonal Control of Human Reproduction. Pressbooks. https://opentextbc.ca/biology/chapter/24-4-hormonal-control-of-human-reproduction/
[40] Kubota, H., & Brinster, R. L. (2018). Spermatogonial stem cells. Biology of reproduction, 99(1), 52-74.
[41] Dalia, K., Ali, K., & Ghina, G. (2019). The developmental process of spermatogenesis. J Androl Gynaecol, 7(1), 3.
[42] Björkgren, I., & Sipilä, P. (2019). The impact of epididymal proteins on sperm function. Reproduction, 158(5), R155-R167.

[43] Lumen Learning. (n.d.). Gametogenesis | Biology for Majors II. https://courses.lumenlearning.com/wm-biology2/chapter/gametogenesis/
[44] Sharma, S., Wistuba, J., Pock, T., Schlatt, S., & Neuhaus, N. (2019). Spermatogonial stem cells: updates from specification to clinical relevance. Human reproduction update, 25(3), 275-297.
[45] Desai, N., Rehmer, J. M., Ludgin, J., Sharma, R., Anirudh, R. K., & Agarwal, A. (2022). Female and male gametogenesis. In Clinical reproductive medicine and surgery: A practical guide (pp. 23-54). Cham: Springer International Publishing.
[46] Chakravarty, B. N., Biswas, A., & Kalapahar, S. (2018). The Male Gamete: A Unique Cell. Practical Guide in Andrology and Embryology, 1.
[47] Suede, S. H., Malik, A., & Sapra, A. (2020). Histology, spermatogenesis.
[48] Dalia, K., Ali, K., & Ghina, G. (2019). The developmental process of spermatogenesis. J Androl Gynaecol, 7(1), 3.
[49] Wei, Y. L., & Yang, W. X. (2018). The acroframosome-acroplaxome-manchette axis may function in sperm head shaping and male fertility. Gene, 660, 28-40.
[50] Houda, A., Nyaz, S., Sobhy, B. M., Bosilah, A. H., Romeo, M., Michael, J. P., & Eid, H. M. (2021). Seminiferous tubules and spermatogenesis. Male Reproductive Anatomy.
[51] Huff, D. S., & Ruchelli, E. D. (2019). Epididymis. Color Atlas of Human Fetal and Neonatal Histology, 147-155.
[52] Sullivan, R., D'Amours, O., Caballero, J., & Belleannee, C. (2018). The sperm journey in the excurrent duct: functions of microvesicles on sperm maturation and gene expression along the epididymis. Animal Reproduction (AR), 12(1), 88-92.
[53] Roque, M., Bedoschi, G., & Esteves, S. C. (2020). Sperm physiology and assessment of spermatogenesis kinetics in vivo. Male Infertility: Contemporary Clinical Approaches, Andrology, ART and Antioxidants, 347-360.
[54] Rickard, J. P., Pool, K. R., Druart, X., & de Graaf, S. P. (2019). The fate of spermatozoa in the female reproductive tract: A comparative review. Theriogenology, 137, 104-112.
[55] Colaco, S., & Modi, D. (2019). Consequences of Y chromosome microdeletions beyond male infertility. Journal of assisted reproduction and genetics, 36, 1329-1337.
[56] James, E. R., Carrell, D. T., Aston, K. I., Jenkins, T. G., Yeste, M., & Salas-Huetos, A. (2020). The role of the epididymis and the contribution of epididymosomes to mammalian reproduction. International Journal of Molecular Sciences, 21(15), 5377.
[57] Al-Haija, R. W. M. A. (2011). Main causes of infertility among men treated at Razan Centers in West Bank: Retrospective study (Doctoral dissertation).
[58] Vanderhout, S. M., Panah, M. R., Garcia-Bailo, B., Grace-Farfaglia, P., Samsel, K., Dockray, J., ... & El-Sohemy, A. (2021). Nutrition, genetic variation and male fertility. Translational andrology and urology, 10(3), 1410.
[59] Colaco, S., & Modi, D. (2019). Consequences of Y chromosome microdeletions beyond male infertility. Journal of assisted reproduction and genetics, 36, 1329-1337.
[60] Colaco, S., & Modi, D. (2018). Genetics of the human Y chromosome and its association with male infertility. Reproductive biology and endocrinology, 16, 1-24.
[61] Kanakis, G. A., & Nieschlag, E. (2018). Klinefelter syndrome: more than hypogonadism. Metabolism, 86, 135-144.
[62] Fainberg, J., Hayden, R. P., & Schlegel, P. N. (2019). Fertility management of Klinefelter syndrome. Expert review of endocrinology & metabolism, 14(6), 369-380.
[63] Cai, Z., & Li, H. (2022). Congenital bilateral absence of the vas deferens. Frontiers in Genetics, 13, 775123.

[64] Ghieh, F., Mitchell, V., Mandon-Pepin, B., & Vialard, F. (2019). Genetic defects in human azoospermia. Basic and clinical andrology, 29(1), 1-16.

[65] Batista, R. L., Costa, E. M. F., Rodrigues, A. D. S., Gomes, N. L., Faria Jr, J. A., Nishi, M. Y., ... & Mendonca, B. B. D. (2018). Androgen insensitivity syndrome: a review. Archives of endocrinology and metabolism, 62, 227-235.

[66] Christin-Maitre, S., & Young, J. (2022, June). Androgens and spermatogenesis. In Annales d'Endocrinologie (Vol. 83, No. 3, pp. 155-158). Elsevier Masson.

[67] Khalafalla, K., Sengupta, P., Arafa, M., Majzoub, A., & Elbardisi, H. (2020). Chromosomal translocations and inversion in male infertility. Genetics of Male Infertility: A Case-Based Guide for Clinicians, 207-219.

[68] Yahaya, T. O., Oladele, E. O., Anyebe, D., Obi, C., Bunza, M. D. A., Sulaiman, R., & Liman, U. U. (2021). Chromosomal abnormalities predisposing to infertility, testing, and management: a narrative review. Bulletin of the National Research Centre, 45(1), 1-15.

[69] de Souza, D. A. S., Faucz, F. R., Pereira-Ferrari, L., Sotomaior, V. S., & Raskin, S. (2018). Congenital bilateral absence of the vas deferens as an atypical form of cystic fibrosis: reproductive implications and genetic counseling. Andrology, 6(1), 127-135.

[70] Bieth, E., Hamdi, S. M., & Mieusset, R. (2021). Genetics of the congenital absence of the vas deferens. Human Genetics, 140, 59-76.

[71] Krausz, C., & Riera-Escamilla, A. (2018). Genetics of male infertility. Nature Reviews Urology, 15(6), 369-384.

[72] Sironen, A., Shoemark, A., Patel, M., Loebinger, M. R., & Mitchison, H. M. (2020). Sperm defects in primary ciliary dyskinesia and related causes of male infertility. Cellular and Molecular Life Sciences, 77, 2029-2048.

[73] Yan, C., Duanmu, X., Zeng, L., Liu, B., & Song, Z. (2019). Mitochondrial DNA: distribution, mutations, and elimination. Cells, 8(4), 379.

[74] Al-Darawsha, T. Z., Dayioglu, N., Al-Azzawi, B. R., & Irez, T. (2023). Study a relationship between age, body mass index, and sperm parameters with sperm DNA fragmentation levels in Iraqi infertile patients. Al-Ameed Journal for Medical Research and Health Sciences, 1(2), 3.

[75] Dutta, S., Biswas, A., & Sengupta, P. (2019). Obesity, endocrine disruption and male infertility. Asian Pacific Journal of Reproduction, 8(5), 195-202.

[76] Sengupta, P., Arafa, M., & Elbardisi, H. (2019). Hormonal regulation of spermatogenesis. In Molecular signaling in spermatogenesis and male infertility (pp. 41-49). CRC Press.

[77] Testosterone, hormone imbalances, and male factor infertility. (n.d.). FertilityIQ. https://www.fertilityiq.com/fertilityiq/male-factor-infertility/testosterone-hormone-imbalances-and-male-factor-infertility

[78] Khuder, H. A. Q. (2021). Androgen Hormone and Male Infertility. International Journal for Research in Applied Sciences and Biotechnology, 8(1), 168-174.

[79] Oduwole, O. O., Peltoketo, H., & Huhtaniemi, I. T. (2018). Role of follicle-stimulating hormone in spermatogenesis. Frontiers in endocrinology, 9, 763.

[80] Muratori, M., & Baldi, E. (2018). Effects of FSH on sperm DNA fragmentation: review of clinical studies and possible mechanisms of action. Frontiers in Endocrinology, 9, 734.

[81] Oduwole, O. O., Huhtaniemi, I. T., & Misrahi, M. (2021). The roles of luteinizing hormone, follicle-stimulating hormone and testosterone in spermatogenesis and folliculogenesis revisited. International journal of molecular sciences, 22(23), 12735.

[82] Walker, W. H. (2021). Androgen Actions in the Testis and the Regulation of Spermatogenesis. Molecular Mechanisms in Spermatogenesis, 175-203.

[83] Christin-Maitre, S., & Young, J. (2022, June). Androgens and spermatogenesis. In Annales d'Endocrinologie (Vol. 83, No. 3, pp. 155-158). Elsevier Masson.
[84] Gurung, P., Yetiskul, E., & Jialal, I. (2022). Physiology, male reproductive system. In StatPearls [Internet]. Statpearls publishing.
[85] Al-Darawsha, T. Z. (2023). Testosterone Hormone; Clinical Indications, Dysregulation and Therapeutic methods. Al-Ameed Journal for Medical Research and Health Sciences, 1(2), 1.
[86] Hohl, A., & Ronsoni, M. F. (2022). Male hypogonadism. In Endocrinology and Diabetes: A Problem Oriented Approach (pp. 139-155). Cham: Springer International Publishing.
[87] Salonia, A., Rastrelli, G., Hackett, G., Seminara, S. B., Huhtaniemi, I. T., Rey, R. A., ... & Maggi, M. (2019). Paediatric and adult-onset male hypogonadism. Nature reviews Disease primers, 5(1), 38.
[88] Marcelli, M., & Mediwala, S. N. (2020). Male hypogonadism: a review. Journal of Investigative Medicine, 68(2), 335-356.
[89] Alahmar, A., Dutta, S., & Sengupta, P. (2019). Thyroid hormones in male reproduction and infertility. Asian Pacific Journal of Reproduction, 8(5), 203-210.
[90] Sabir, S., Akhtar, M. F., & Saleem, A. (2019). Endocrine disruption as an adverse effect of non-endocrine targeting pharmaceuticals. Environmental Science and Pollution Research, 26, 1277-1286.
[91] Tritos, N. A., & Klibanski, A. (2019). Prolactin and its role in human reproduction. In Yen and Jaffe's Reproductive Endocrinology (pp. 58-74). Elsevier.
[92] Wrzosek, M., Woźniak, J., & Włodarek, D. (2020). The causes of adverse changes of testosterone levels in men. Expert Review of Endocrinology & Metabolism, 15(5), 355-362.
[93] Son, Y. L., Ubuka, T., & Tsutsui, K. (2022). Regulation of stress response on the hypothalamic-pituitary-gonadal axis via gonadotropin-inhibitory hormone. Frontiers in Neuroendocrinology, 64, 100953.
[94] Shahat, A. M., Rizzoto, G., & Kastelic, J. P. (2020). Amelioration of heat stress-induced damage to testes and sperm quality. Theriogenology, 158, 84-96.
[95] Dutta, S., Biswas, A., & Sengupta, P. (2019). Obesity, endocrine disruption and male infertility. Asian Pacific Journal of Reproduction, 8(5), 195-202.
[96] Dutta, S., Biswas, A., & Sengupta, P. (2019). Obesity, endocrine disruption and male infertility. Asian Pacific Journal of Reproduction, 8(5), 195-202.
[97] Grinspon, R. P., Bergadá, I., & Rey, R. A. (2020). Male hypogonadism and disorders of sex development. Frontiers in Endocrinology, 11, 211.
[98] Salvio, G., Martino, M., Giancola, G., Arnaldi, G., & Balercia, G. (2021). Hypothalamic–pituitary diseases and erectile dysfunction. Journal of Clinical Medicine, 10(12), 2551.
[99] Christin-Maitre, S., & Young, J. (2022, June). Androgens and spermatogenesis. In Annales d'Endocrinologie (Vol. 83, No. 3, pp. 155-158). Elsevier Masson.
[100] Dutta, S., Sengupta, P., & Muhamad, S. (2019). Male reproductive hormones and semen quality. Asian Pacific Journal of Reproduction, 8(5).
[101] Galansky, L. B., Levy, J. A., & Burnett, A. L. (2022). Testosterone and male sexual function. Urologic Clinics.
[102] Oduwole, O. O., Huhtaniemi, I. T., & Misrahi, M. (2021). The roles of luteinizing hormone, follicle-stimulating hormone and testosterone in spermatogenesis and folliculogenesis revisited. International journal of molecular sciences, 22(23), 12735.
[103] Swee, D. S., & Gan, E. H. (2019). Late-onset hypogonadism as primary testicular failure. Frontiers in Endocrinology, 10, 372.
[104] Gravholt, C. H., Chang, S., Wallentin, M., Fedder, J., Moore, P., & Skakkebæk, A. (2018). Klinefelter syndrome: integrating genetics, neuropsychology, and endocrinology. Endocrine Reviews, 39(4), 389-423.

[105] Dutta, S., Sengupta, P., Slama, P., & Roychoudhury, S. (2021). Oxidative stress, testicular inflammatory pathways, and male reproduction. International journal of molecular sciences, 22(18), 10043.
[106] Henkel, R. (2020). Infection in infertility. Male Infertility: Contemporary Clinical Approaches, Andrology, ART and Antioxidants, 409-424.
[107] Sahoo, D. K., Jena, S., & Chainy, G. B. (2019). Thyroid dysfunction and testicular redox status: an intriguing association. Oxidants, Antioxidants and Impact of the Oxidative Status in Male Reproduction, 149-170.
[108] Sabir, S., Akhtar, M. F., & Saleem, A. (2019). Endocrine disruption as an adverse effect of non-endocrine targeting pharmaceuticals. Environmental Science and Pollution Research, 26, 1277-1286.
[109] Sahoo, D. K., Jena, S., & Chainy, G. B. (2019). Thyroid dysfunction and testicular redox status: an intriguing association. Oxidants, Antioxidants and Impact of the Oxidative Status in Male Reproduction, 149-170.
[110] Dick, B., Koller, C., Herzog, B., Greenberg, J., & Hellstrom, W. J. (2020). The role of hormones in male sexual function. Current Sexual Health Reports, 12, 101-112.
[111] Ralli, M., Angeletti, D., Fiore, M., D'Aguanno, V., Lambiase, A., Artico, M., ... & Greco, A. (2020). Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. Autoimmunity Reviews, 19(10), 102649.
[112] Farebrother, J., Zimmermann, M. B., & Andersson, M. (2019). Excess iodine intake: sources, assessment, and effects on thyroid function. Annals of the New York Academy of Sciences, 1446(1), 44-65.
[113] Parsa, A. A., & Gharib, H. (2018). Epidemiology of thyroid nodules. Thyroid Nodules: Diagnosis and Management, 1-11.
[114] Sahoo, D. K., Jena, S., & Chainy, G. B. (2019). Thyroid dysfunction and testicular redox status: an intriguing association. Oxidants, Antioxidants and Impact of the Oxidative Status in Male Reproduction, 149-170.
[115] Dutta, S., Biswas, A., & Sengupta, P. (2019). Obesity, endocrine disruption and male infertility. Asian Pacific Journal of Reproduction, 8(5), 195-202.
[116] Krassas, G. E., & Markou, K. B. (2019). The impact of thyroid diseases starting from birth on reproductive function. Hormones, 18(4), 365-381.
[117] Dick, B., Koller, C., Herzog, B., Greenberg, J., & Hellstrom, W. J. (2020). The role of hormones in male sexual function. Current Sexual Health Reports, 12, 101-112.
[118] Ferrari, S. M., Fallahi, P., Elia, G., Ragusa, F., Ruffilli, I., Paparo, S. R., & Antonelli, A. (2020, August). Thyroid autoimmune disorders and cancer. In Seminars in cancer biology (Vol. 64, pp. 135-146). Academic Press.
[119] Farebrother, J., Zimmermann, M. B., & Andersson, M. (2019). Excess iodine intake: sources, assessment, and effects on thyroid function. Annals of the New York Academy of Sciences, 1446(1), 44-65.
[120] Krashin, E., Piekiełko-Witkowska, A., Ellis, M., & Ashur-Fabian, O. (2019). Thyroid hormones and cancer: a comprehensive review of preclinical and clinical studies. Frontiers in endocrinology, 10, 59.
[121] Kang, C., Punjani, N., Lee, R. K., Li, P. S., & Goldstein, M. (2022, January). Effect of varicoceles on spermatogenesis. In Seminars in Cell & Developmental Biology (Vol. 121, pp. 114-124). Academic Press.
[122] Surgical treatment of varicocele. (n.d.). https://drseymur.az/en/xidmetler/surgical-treatment-of-varicocele/
[123] Hassanin, A. M., Ahmed, H. H., & Kaddah, A. N. (2018). A global view of the pathophysiology of varicocele. Andrology, 6(5), 654-661.

[124] Tadros, N. N., & Sabanegh Jr, E. (2019). Varicocele. In Oxidants, Antioxidants and Impact of the Oxidative Status in Male Reproduction (pp. 105-115). Academic Press.
[125] Yang, L., Shen, Q., Zeng, T., Li, J., Li, W., & Wang, Y. (2020). Enrichment of imidacloprid and its metabolites in lizards and its toxic effects on gonads. Environmental Pollution, 258, 113748.
[126] Fang, Y., Su, Y., Xu, J., Hu, Z., Zhao, K., Liu, C., & Zhang, H. (2021). Varicocele-mediated male infertility: from the perspective of testicular immunity and inflammation. Frontiers in Immunology, 12, 729539.
[127] Kang, C., Punjani, N., Lee, R. K., Li, P. S., & Goldstein, M. (2022, January). Effect of varicoceles on spermatogenesis. In Seminars in Cell & Developmental Biology (Vol. 121, pp. 114-124). Academic Press.
[128] Zavattaro, M., Ceruti, C., Motta, G., Allasia, S., Marinelli, L., Di Bisceglie, C., ... & Lanfranco, F. (2018). Treating varicocele in 2018: current knowledge and treatment options. Journal of endocrinological investigation, 41, 1365-1375.
[129] Li, X., Yang, X., Wang, X., Wang, L., Liu, J., Cai, F., ... & Lu, S. (2020). Comparison of outcomes in intrauterine insemination, in vitro fertilisation and intracytoplasmic sperm injection in men with and without varicocele. International Journal of Medical Sciences, 17(14), 2155.
[130] Durairajanayagam, D. (2018). Lifestyle causes of male infertility. Arab journal of urology, 16(1), 10-20.
[131] Sansone, A., Di Dato, C., de Angelis, C., Menafra, D., Pozza, C., Pivonello, R., ... & Gianfrilli, D. (2018). Smoke, alcohol and drug addiction and male fertility. Reproductive biology and endocrinology, 16(1), 1-11.
[132] Emokpae, M. A., & Brown, S. I. (2021). Effects of lifestyle factors on fertility: practical recommendations for modification. Reproduction and Fertility, 2(1), R13-R26.
[133] Kulaksiz, D., Toprak, T., Tokat, E., Yilmaz, M., Ramazanoglu, M. A., Garayev, A., ... & Verit, A. (2022). Sperm concentration and semen volume increase after smoking cessation in infertile men. International Journal of Impotence Research, 34(6), 614-619.
[134] Margiana, R. (2018). Effect of cigarettes smoking on embryo development through its effect on sperm DNA fragmentation-A systematic review. Asian Journal of Pharmaceutics (AJP), 12(03).
[135] Golbidi, S., Li, H., & Laher, I. (2018). Oxidative stress: a unifying mechanism for cell damage induced by noise,(water-pipe) smoking, and emotional stress—therapeutic strategies targeting redox imbalance. Antioxidants & redox signaling, 28(9), 741-759.
[136] Bundhun, P. K., Janoo, G., Bhurtu, A., Teeluck, A. R., Soogund, M. Z. S., Pursun, M., & Huang, F. (2019). Tobacco smoking and semen quality in infertile males: a systematic review and meta-analysis. BMC public health, 19(1), 1-11.
[137] Kazimoglu, H., Topdagi, Y. E., Solakhan, M., & Guzel, A. I. (2021). May Smoking and Alcohol Consumption Worsen the Spermiogram Results?. Gynecology Obstetrics & Reproductive Medicine, 27(1), 44-48.
[138] Durairajanayagam, D. (2018). Lifestyle causes of male infertility. Arab journal of urology, 16(1), 10-20.
[139] Finelli, R., Mottola, F., & Agarwal, A. (2021). Impact of alcohol consumption on male fertility potential: a narrative review. International Journal of Environmental Research and Public Health, 19(1), 328.
[140] Sharma, A., Minhas, S., Dhillo, W. S., & Jayasena, C. N. (2021). Male infertility due to testicular disorders. The Journal of Clinical Endocrinology & Metabolism, 106(2), e442-e459.
[141] Schifano, N., Chiappini, S., Mosca, A., Miuli, A., Santovito, M. C., Pettorruso, M., ... & Schifano, F. (2022). Recreational Drug Misuse and Its Potential Contribution to Male Fertility Levels' Decline: A Narrative Review. Brain Sciences, 12(11), 1582.

[142] Maccarrone, M., Rapino, C., Francavilla, F., & Barbonetti, A. (2021). Cannabinoid signalling and effects of cannabis on the male reproductive system. Nature Reviews Urology, 18(1), 19-32.

[143] Ajayi, A. F., & Akhigbe, R. E. (2020). The physiology of male reproduction: Impact of drugs and their abuse on male fertility. Andrologia, 52(9), e13672.

[144] Abbasihormozi, S., Babapour, V., Naslji, A. N., Afraz, K., Zolfaghary, Z., & Shahverdi, A. (2019). Stress hormone and oxidative stress biomarkers link obesity and diabetes with reduced fertility potential. Cell Journal (Yakhteh), 21(3), 307.

[145] Boutari, C., Pappas, P. D., Mintziori, G., Nigdelis, M. P., Athanasiadis, L., Goulis, D. G., & Mantzoros, C. S. (2020). The effect of underweight on female and male reproduction. Metabolism, 107, 154229.

[146] Elagizi, A., Kachur, S., Carbone, S., Lavie, C. J., & Blair, S. N. (2020). A review of obesity, physical activity, and cardiovascular disease. Current obesity reports, 9, 571-581.

[147] Aldahhan, R. A., & Stanton, P. G. (2021). Heat stress response of somatic cells in the testis. Molecular and cellular endocrinology, 527, 111216.

[148] Farsimadan, M., & Motamedifar, M. (2020). Bacterial infection of the male reproductive system causing infertility. Journal of reproductive immunology, 142, 103183.

[149] Liu, K. S., Mao, X. D., Pan, F., & An, R. F. (2021). Effect and mechanisms of reproductive tract infection on oxidative stress parameters, sperm DNA fragmentation, and semen quality in infertile males. Reproductive Biology and Endocrinology, 19(1), 1-12.

[150] Henkel, R. (2021). Long-term consequences of sexually transmitted infections on men's sexual function: A systematic review. Arab Journal of Urology, 19(3), 411-418.

[151] Oghbaei, H., Rezaei, Y. R., Nikanfar, S., Zarezadeh, R., Sadegi, M., Latifi, Z., ... & Bleisinger, N. (2020). Effects of bacteria on male fertility: Spermatogenesis and sperm function. Life Sciences, 256, 117891.

[152] Bryan, E. R., Kim, J., Beagley, K. W., & Carey, A. J. (2020). Testicular inflammation and infertility: Could chlamydial infections be contributing?. American Journal of Reproductive Immunology, 84(3), e13286.

[153] Moazenchi, M., Totonchi, M., Salman Yazdi, R., Hratian, K., Mohseni Meybodi, M. A., Ahmadi Panah, M., ... & Mohseni Meybodi, A. (2018). The impact of Chlamydia trachomatis infection on sperm parameters and male fertility: A comprehensive study. International journal of STD & AIDS, 29(5), 466-473.

[154] Eini, F., Kutenaei, M. A., Zareei, F., Dastjerdi, Z. S., Shirzeyli, M. H., & Salehi, E. (2021). Effect of bacterial infection on sperm quality and DNA fragmentation in subfertile men with Leukocytospermia. BMC Molecular and Cell Biology, 22(1), 1-10.

[155] Pleuger, C., Silva, E. J. R., Pilatz, A., Bhushan, S., & Meinhardt, A. (2020). Differential immune response to infection and acute inflammation along the epididymis. Frontiers in immunology, 11, 599594.

[156] Ricardo, L. H. J. (2018). Male accessory glands and sperm function. Spermatozoa-Facts Perspect, 101-116.

[157] Rosenfeld, C. S., Javurek, A. B., Johnson, S. A., Lei, Z., Sumner, L. W., & Hess, R. A. (2018). Seminal fluid metabolome and epididymal changes after antibiotic treatment in mice. Reproduction, 156(1), 1-10.

[158] Tamessar, C. T., Trigg, N. A., Nixon, B., Skerrett-Byrne, D. A., Sharkey, D. J., Robertson, S. A., ... & Schjenken, J. E. (2021). Roles of male reproductive tract extracellular vesicles in reproduction. American Journal of Reproductive Immunology, 85(2), e13338.

[159] Silva, A. F., Ramalho-Santos, J., & Amaral, S. (2021). The impact of antisperm antibodies on human male reproductive function: an update. Reproduction, 162(4), R55-R71.

[160] Bouchicha, A. E. B., Kalem, A., Mimoune, N., Djouadi, S., Khelef, D., & Kaidi, R. (2022). Study of antibiotics and symbiotic effects on sperm quality using the CASA system. Veterinarska stanica, 53(4), 377-388.
[161] Grubb, L. K., Alderman, E. M., Chung, R. J., Lee, J., Powers, M. E., Rahmandar, M. H., ... & Wallace, S. B. (2020). Barrier protection use by adolescents during sexual activity. Pediatrics, 146(2).
[162] Pete, P. M. N., Biguioh, R. M., Izacar, A. G. B., Adogaye, S. B. B., & Nguemo, C. (2019). Genital hygiene behaviors and practices: A cross-sectional descriptive study among antenatal care attendees. Journal of public health in Africa, 10(1).
[163] Liu, K. S., Mao, X. D., Pan, F., & An, R. F. (2021). Effect and mechanisms of reproductive tract infection on oxidative stress parameters, sperm DNA fragmentation, and semen quality in infertile males. Reproductive Biology and Endocrinology, 19(1), 1-12.
[164] Henkel, R. (2020). Infection in infertility. Male Infertility: Contemporary Clinical Approaches, Andrology, ART and Antioxidants, 409-424.
[165] Van Gerwen, O. T., Muzny, C. A., & Marrazzo, J. M. (2022). Sexually transmitted infections and female reproductive health. Nature Microbiology, 7(8), 1116-1126.
[166] Goulart, A. C. X., Farnezi, H. C. M., França, J. P. B. M., Dos Santos, A., Ramos, M. G., & Penna, M. L. F. (2020). HIV, HPV and Chlamydia trachomatis: impacts on male fertility. JBRA assisted reproduction, 24(4), 492.
[167] Hassan, J. S., Salah, R. F., & Gaidan, A. M. (2019). The Role of Chlamydial Infection in Male Infertility. Indian Journal of Public Health Research & Development, 10(2).
[168] Hsu, K. (2019). Clinical manifestations and diagnosis of Chlamydia trachomatis infections.
[169] Bryan, E. R., Kollipara, A., Trim, L. K., Armitage, C. W., Carey, A. J., Mihalas, B., ... & Beagley, K. W. (2019). Hematogenous dissemination of Chlamydia muridarum from the urethra in macrophages causes testicular infection and sperm DNA damage. Biology of reproduction, 101(4), 748-759.
[170] Quillin, S. J., & Seifert, H. S. (2018). Neisseria gonorrhoeae host adaptation and pathogenesis. Nature Reviews Microbiology, 16(4), 226-240.
[171] Whelan, J., Eeuwijk, J., Bunge, E., & Beck, E. (2021). Systematic literature review and quantitative analysis of health problems associated with sexually transmitted Neisseria gonorrhoeae infection. Infectious Diseases and Therapy, 10, 1887-1905.
[172] Oghbaei, H., Rezaei, Y. R., Nikanfar, S., Zarezadeh, R., Sadegi, M., Latifi, Z., ... & Bleisinger, N. (2020). Effects of bacteria on male fertility: Spermatogenesis and sperm function. Life Sciences, 256, 117891.
[173] Fijak, M., Pilatz, A., Hedger, M. P., Nicolas, N., Bhushan, S., Michel, V., ... & Meinhardt, A. (2018). Infectious, inflammatory and 'autoimmune'male factor infertility: how do rodent models inform clinical practice?. Human reproduction update, 24(4), 416-441.
[174] Sarier, M., Ceyhan, A. M., Sepin, N., Ozel, E., Inal, M. M., Kukul, E., & Soylu, A. (2020). HPV infection in urology practice. International Urology and Nephrology, 52(1), 1-8.
[175] Le Tortorec, A., Matusali, G., Mahé, D., Aubry, F., Mazaud-Guittot, S., Houzet, L., & Dejucq-Rainsford, N. (2020). From ancient to emerging infections: the odyssey of viruses in the male genital tract. Physiological reviews, 100(3), 1349-1414.
[176] Omarova, S., Cannon, A., Weiss, W., Bruccoleri, A., & Puccio, J. (2022). Genital Herpes Simplex Virus—An Updated Review. Advances in Pediatrics, 69(1), 149-162.
[177] Rathbun, M. M., & Szpara, M. L. (2021). A holistic perspective on herpes simplex virus (HSV) ecology and evolution. Advances in virus research, 110, 27-57.

[178] Akhigbe, R. E., Dutta, S., Hamed, M. A., Ajayi, A. F., Sengupta, P., & Ahmad, G. (2022). Viral infections and male infertility: a comprehensive review of the role of oxidative stress. Frontiers in Reproductive Health, 4, 782915.

[179] Cito, G., Coccia, M. E., Fucci, R., Picone, R., Cocci, A., Russo, G. I., ... & Natali, A. (2019). Influence of male human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection on the reproductive outcomes in serodiscordant couples: a case–control study. Andrology, 7(6), 852-858.

[180] Teixeira, T. A., Oliveira, Y. C., Bernardes, F. S., Kallas, E. G., Duarte-Neto, A. N., Esteves, S. C., ... & Hallak, J. (2021). Viral infections and implications for male reproductive health. Asian journal of andrology, 23(4), 335.