

# Etiologic classification, evaluation, and management of hematospermia

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**Abstract:** Hematospermia is defined by the presence of blood in the semen typically occurring in men younger than 40 years of age. Symptoms can occur due to a multitude of reasons, but are usually benign and self-limiting, requiring no additional treatment or evaluation. Despite this, the condition often impairs quality of life due to associated anxiety and must be taken seriously by the patient and the physician, particularly if recurrent, refractory, and painful. The etiology of hematospermia can be classified into inflammatory, infectious, lithiasis, cystic, obstructive, tumoral, vascular, traumatic, iatrogenic, and systemic origin. Alternatively, it can also be divided into subcategories based on anatomical origins such as prostate, bladder, spermatic cord, seminal vesicles, or epididymis. A complete history and physician examination, laboratory testing, and a variety of invasive and non-invasive imaging and instrumentation modalities can help to identify and treat the underlying pathology promptly.

**Keywords:** Hematospermia; hemospermia; accessory sex glands; semen; genital diseases; ejaculatory dysfunction

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## Introduction

Hematospermia (i.e., hemospermia or bloody ejaculate) is defined by the presence of blood in the semen. This medical condition has been documented for many centuries including in the writings of Hippocrates, Galen, Morgagni, etc. The etiology of hematospermia may be classified into inflammation, infection, ductal blockage, cyst formation, systemic conditions, tumors, vascular aberrations of accessory sex glands, and iatrogenic causes (1). Currently, the precise incidence of hematospermia is yet to be determined as most men do not frequently examine their semen, and there is a lack of reporting for consultation.

Though the age range of those afflicted with hematospermia is commonly between 30 and 40 years, men over 40 have been observed to also present symptoms (2). We presently explore an up-to-date classification and catalog of etiology with associating manifestation of hematospermia. We also review the clinical evaluation and management options of hematospermia.

## Anatomy of the ejaculatory apparatus

The ejaculatory apparatus is composed of the seminal vesicles, vas deferens, and ejaculatory ducts. The vas deferens rises from within the scrotal walls, crosses the

inguinal canal, and inserts into the internal inguinal ring to enter the extraperitoneal space of the pelvis. From there, it inferomedially arches toward the bladder base where it ends as a tangled mass known as the ampulla of the vas deferens. The ampulla is medial to the seminal vesicles, causing them to merge at the base of the prostate to form the ejaculatory duct. The ejaculatory duct enters the glandular portion of the prostate, forming a prostatic capsule. The prostatic capsule traverses the verumontanum and continues to meet with the muscular fibers of Denonvilliers' fascia, the structure responsible for peristalsis and sphincteric function of the ejaculatory apparatus. The ejaculatory duct is present within the central zone of the prostate and ends in the posterior urethra. The posterior urethra is lateral and proximal to the verumontanum. The seminal vesicles are glands usually exceeding 2.5 cm in length with anteroposterior dimensions between 0.7 and 1.5 cm, having the function of holding liquid to mix with sperm to form semen (3).

### Physiology of emission and ejaculation

The stages of human sexual response are a series of phases that include desire, excitation, orgasm, and resolution. Emission of seminal fluid secretions from sex glands and testes is followed by expulsion, where a mixture of spermatozoa, enzymes, lipids, sugars, and oligo-elements are secreted into the posterior urethra by phasic contractions by the glands and ducts as well as pelvic-perineal striated muscle contractions. Orgasm is a neuropsychophysiological occurrence that concludes the ejaculatory response (4). During Phase I (i.e., erection), the urethra, which is usually a wide and curved tube, becomes a straight canal for fluid. The corpus spongiosum fills with blood, which constricts the perineal musculature and increases pressure within the tube. The periurethral Littre glands also begin secretion to ease the transport of semen. Phase II is defined as the orgasm and emission phase, which occurs almost simultaneously, as spermatozoa and plasma travel from production sites into the urethra. The smooth muscle contractions are initiated in the ductuli efferentes, which then affect the Cowper's glands, prostate, ampulla, and seminal vesicles. In phase III, the pressure increases even further by the loading of semen into the posterior urethra. There is a small chamber near the distal tip of the urethra to collect semen. Then, it quickly transitions to the final stage, expulsion, where the contraction ejects the ejaculate out of the penis (5). Hematospermia often becomes an issue by creating

anxiety in the affected person, or by signaling an internal problem that must be seriously evaluated by the evaluating physician.

### Etiology

The etiology of hematospermia can be categorized into the following ten categories based on the pathophysiological mechanisms of hematospermia: (I) inflammatory; (II) infectious; (III) lithiasis; (IV) cystic; (V) obstructive; (VI) tumoral; (VII) vascular; (VIII) traumatic; (IX) iatrogenic; and (X) systemic origin (see *Table 1*). Alternatively, the etiology of hematospermia can also be subclassified based on anatomical origin, namely the prostate, bladder, spermatic cord, seminal vesicles, or epididymis.

#### Prostate

##### Prostatitis

*Enterococcus faecalis* is a very commonly associated organism with chronic bacterial prostatitis. Prostatitis-associated hematospermia can be sub-classified into chronic bacterial prostatitis, chronic nonbacterial prostatitis, asymptomatic prostatitis, and prostatodynia. Patients having hematospermia with prostatitis have been associated with a poorer quality of life compared to prostatitis patients without hematospermia (10).

##### Xanthogranulomatous prostatitis

Xanthogranulomatous prostatitis is an unusual, nonspecific, yet benign inflammatory process of the prostate gland. It is a highly rare subtype of a common granulomatous prostatitis which is characterized by its classic histological feature: the presence of granuloma (13). Although the precise pathogenesis of this rare clinical entity is not yet known, it is believed to be caused by a blockage of prostatic ducts leading to stasis of prostate gland secretions, subsequently resulting in an inflammatory response (13,14). Although hematospermia is reported as an accompanying symptom of xanthogranulomatous prostatitis, Pastore *et al.* concluded hematospermia as the presenting symptom in 40% of the cases (13). Thus, it is vital for physicians to be familiar with this rare clinical entity for a proper and timely diagnosis of the underlying condition and prompt treatment.

##### Prostate cancer

Han *et al.* found evidence that there is an increased risk of

**Table 1** Etiologic classification of hematospermia

Classification	Etiology
Inflammatory	Epididymitis (6)
	Epididymo-orchitis (7,8)
	Urethritis (9)
	Prostatitis (10,11)
	Seminal vesiculitis (12)
	Xanthogranulomatous prostatitis (13,14)
Infectious	Human immunodeficiency virus
	Cytomegalovirus (15-17)
	Genitourinary tuberculosis (18-20)
	Schistosomiasis (21-24)
	Sexually transmitted pathogens
	<i>Chlamydia trachomatis</i> (25,26)
	<i>Enterococcus faecalis</i> (25)
	<i>Herpes simplex virus</i> (27)
	<i>Ureaplasma urealyticum</i> (25,26)
	Sexually transmitted disease
	Gonorrhea (28)
Syphilis	
Hydatid disease (29)	
Zika virus (30)	
Lithiasis	Calculi of seminal vesicles, ejaculatory duct, or prostate (31-34)
	Calculi of urethra, bladder, or ureter
	Ejaculatory duct calculus (35)
	Seminal vesicle calculi (36)
Cystic	Ejaculatory duct and seminal vesicle cyst (18,19,37)
	Median raphe cyst (38)
	Midline prostatic cyst (39-41)
	Müllerian duct cyst (42,43)
	Seminal vesicle cyst (44-47)
	Utricular cyst (43,48)
Obstructive	Dilation of seminal vesicles (49)
	Diverticula of seminal vesicles
	Ejaculatory duct obstruction (50)
	Urethral stricture (51)
	Benign prostatic hyperplasia (31,52,53)

**Table 1** (continued)

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Classification		Etiology
Tumoral	Benign	Granulations
		Papillary adenoma
Tumoral	Benign	Adenomatous polyps of the Verumontanum (54)
		Prostatic urethra (55-57)
		Adenomyosis of seminal vesicle (58)
		Condylomata acuminata of urethra and meatus (59)
		Angioleiomyoma of the testicle (60)
		Tumors of spermatic cord or prostatic utricle (61)
	Malignant	Adenocarcinoma of seminal vesicles (62)
		Carcinoma of seminal vesicles (63,64)
		Intraductal carcinoma
		Melanoma (33,65)
		Prostate cancer (66,67)
		Renal cell carcinoma (68)
		Sarcoma of prostate or seminal vesicles
Vascular	Small cell carcinoma of bladder (69)	Small cell carcinoma of bladder (69)
		Testicular cancer
		Yolk sac tumor of seminal vesicles (70)
		Cloacogenic transitional cell carcinoma (71)
		Abnormal veins in prostatic urethra (e.g., posterior urethral veins)
	Vascular	Arteriovenous/vascular malformation (72,73)
		Cavernous hemangioma of spermatic cord (61)
		Hemangioma (74-76)
		Hemangioma of the posterior urethra (37)
		Hemorrhage (44,77)
Vascular	Hypertension (78,79)	
	Prothrombin deficiency (9)	
	Vaso-venous fistula	
	Prostatic varices	
	Prostatic telengectasia	

**Table 1** (continued)

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Classification		Etiology
Traumatic		Excessive sexual intercourse or masturbation (80)
		Injury (81)
Iatrogenic		Trauma to perineum/genitals/pelvis
		Aspirin (82)
		Brachytherapy (83)
		External beam radiation (84,85)
		Foley catheterization (86)
		High-frequency ultrasound (87,88)
		HIV protease inhibitors (9)
		Post-hemorrhoidal sclerotherapy
		Post-orchietomy
		Post-prostate cryosurgery
		Post-vasectomy (89)
		Vaso-venous fistula
		Prostatic injections
Systemic	Congenital	Ultrasound-guided prostate biopsy (90)
		Ureteral stents
		Agenesis of seminal vesicle (91)
		Hemophilia
		Von Willebrand disease (6,92,93)
	Acquired	Zinner's syndrome with seminal vesicle hypoplasia (94)
		Bleeding diathesis
		Amyloidosis (95-97)
		Hypertension
		Leukemia
		Lymphoma (98)
		Purpura
		Scurvy (99)
		Cirrhosis of the liver (8)
		Hyperuricemia (100)
Chronic liver disease		
Renovascular disease		

prostate cancer for people with hematospermia. However, hematospermia is exceedingly rare at an occurrence of 0.5% in patients with prostate cancer (101). In a separate study examining 302 individuals with prostate cancer, 45.3% of patients had hematospermia (66).

## Bladder

### Bladder tumor

Although rare, hematospermia has been recorded to be a symptom of a small cell bladder carcinoma. In a study, the average tumor size was 5.1 cm, rising toward the lateral bladder wall and fundus, and in some cases rising from the bladder diverticulum or urachal remnant (69).

### Seminal vesicles

#### Adenocarcinoma

Adenocarcinoma is a rare and challenging diagnosis of hematospermia, as the adenocarcinoma frequently spreads to the surrounding areas such as the prostate. Tumor cells are present with papillary and glandular masses in the mass lesion filling the seminal vesicles (62). In a case study, a patient who had advanced testicular cancer presented with a severe antineutrophil cytoplasmic antibody vasculitis when he was diagnosed with metastatic cancer of the seminal vesicles. This demonstrates the possibility of developing autoimmune vasculitis in association with adenocarcinoma of the seminal vesicles (102).

#### Amyloidosis

Amyloidosis causes thickening of the seminal vesicle wall thereby narrowing the vesicular lumen (96). Recurrent or random episodes of hematospermia are known to occur simultaneously with seminal vesicle amyloidosis (96).

### Epididymis

#### Epididymitis

Otherwise referred to as epididymo-orchitis or orchitis, inflammation of the epididymis can be caused by an infectious agent such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Dissemination of the organism of infection can spread through the bloodstream or by direct contact with a focus in the epididymis. The inflammation from epididymitis can cause hematospermia (6).

### Tumors, lesions, and masses

#### Condylomata acuminata of urethra and meatus

Condylomata acuminata of urethra and meatus, also known as genital warts, are benign proliferative lesions produced by the human papillomavirus, usually of the types 6 and 11.

About 20% of all genital warts occur in the urethra and external meatus of the urethra. Although it is not common, hematospermia can occur with condylomata (59).

Additionally, hematospermia can result due to dilation of the ejaculatory duct and seminal vesicle cysts (103,104). Transrectal ultrasonography (TRUS) can detect ejaculatory duct and seminal vesicle cysts, which may be congenital or secondary (22,23,103,104).

### **Hemangioma**

Posterior urethral hemangiomas are benign vascular tumors that are believed to originate from unipotent angioblastic cells that do not successfully develop into normal blood vessels. Urethral hemangiomas are usually present between the verumontanum and the external urethral sphincter, causing pressure in the high venous area and thereby forming hemangioma. Hemangiomas are the spaces that contain blood and thrombi. Classifications of hemangioma such as cavernous, capillary, venous, and racemose can cause hematospermia (74).

### **Median raphe cyst**

Median raphe cysts are benign lesions that are formed due to trapping of tissue during urethral fold development. These cysts are subdivided into four categories: urethral, epidermoid, glandular, and mixed. Although many patients with median raphe cysts are asymptomatic, voiding difficulties and hematospermia can result (38).

### **Melanoma**

An isolated case of metastatic melanoma in the seminal vesicles showed hematospermia as the only symptom. A magnetic resonance imaging (MRI) scan was conducted instead of TRUS because infection with HIV made the patient susceptible to infection, and hematospermia had occurred for five months. Metastatic melanoma to the seminal vesicles is a rare occurrence, and is hypothesized to be due to complete regression of the primary melanoma or by malignant transformation of ectopic nevi cells (33).

### **Papillary urethritis**

Papillary urethritis is a papillary lesion in the prostatic urethra representing proliferative reactive changes to chronic inflammation. Long-lasting hematospermia was noted in a case study of a patient that suffered from megacava associated with the circumaortic renal vein. Varicose plexus in the pelvic floor is an indicator of the presence of varicose plexuses in other areas of the lower

extremity as well as for vulvar and pudendal varicosities, hemorrhoids, and varicoceles. For this reason, urine and blood tests, prostate-specific antigen (PSA) level tests, coagulation function, and cultures of urine and semen should be conducted (72).

### **Polypoid lesions**

Polypoid lesions can develop in the prostatic urethra, which can contribute to hematospermia. In a case report, the polypoid lesions were identified as adenomatous polyps, appearing as a normal prostate, as well as intraductal carcinomas. After resection surgery, hematospermia can resolve itself, but the probability is not definite. Cystoscopy should be performed on patients that have hematospermia refractory to antibiotic therapy (55).

### **Seminal vesicle cyst**

Congenital seminal vesicle cysts are usually associated with abnormal genitourinary structures, as well as ipsilateral renal agenesis or dysgenesis. About 44–60% of the patients with autosomal dominant polycystic kidney disease have bilateral seminal vesicle cysts (44).

### **Utricular cyst**

Utricular cysts are endodermal in origin. Cystic dilation of the utricle can be a cause of the lesion for hematospermia. In these cases, seminal vesicle fluid is proven to be hemorrhagic in most patients, as the midline cyst communicates with the urethra or ejaculatory ducts. Midline cysts include the prostatic utricular, ejaculatory duct, müllerian duct, as well as prostatic and seminal vesicle cysts (48).

### **Iatrogenic**

#### **Brachytherapy**

In a 2005 cross-sectional analysis, 16 patients experienced hematospermia after brachytherapy treatment (105). In 2001, hematospermia along with orgasmalgia occurred in 26% of the patients (83).

#### **External beam radiation**

Gold markers that are 5 mm in length, 1 mm in diameter, with a 0.3-mm diameter steel core are inserted into random positions within the prostate, which serve to improve visualization on MRI when testing for the inter-fraction motion of the prostate. Five hundred mg of prophylaxis antibiotic is taken twice daily for 3 days to

prevent infection. These transrectal markers can cause complications of pain and fever, voiding difficulties, and hematospermia (84).

### **HIV protease inhibitors**

Spontaneous bleeding has been known to occur in patients who were HIV-positive hemophiliacs taking HIV protease inhibitors (106). In a select few patients, bleeding appeared in the form of hematospermia upon taking HIV protease inhibitors (9).

### **TRUS**

Although TRUS is a safe, rapid, and well-accepted procedure, the incidence of hematospermia following TRUS has been reported between 5.1% and 89%. The average time for spontaneous self-resolution was 3.5 weeks in a study by Manoharan *et al.* (107).

### **Vasectomy complication**

Vaso-venous fistula occurring after vasectomy has been associated with hematospermia. In a case study, a patient who had a vasectomy had a testicle become swollen and tender. A significant amount of blood was voided upon ejaculation. Upon cystoscopy, the patient had blood originating from the ejaculatory duct. Surgical intervention showed a left scrotal vein traversing into the vas deferens as well as abnormal vascular structures, chronic inflammation, and nerve proliferation (89).

### **High-intensity focus ultrasonography**

High-intensity focus ultrasonography causes tissue ablation by coagulative necrosis for patients undergoing benign prostatic hyperplasia treatment (52). An adverse side effect of this treatment includes hematospermia (53).

### **Systemic diseases**

#### **Cytomegalovirus**

Cytomegalovirus is a common virus throughout the world that comes from the order *Herpesvirales*. Babies who are born with congenital cytomegalovirus by transmission through breastmilk or by birth show symptoms of jaundice, purple skin rashes, pneumonia, seizures, poor functioning livers, and low birth weight. This virus can manifest into an active form later in life in those who are immunocompromised (15,16). A man can contract cytomegalovirus, leading to hematospermia in various ways (17).

### **Genitourinary tuberculosis**

Pulmonary tuberculosis mycobacterium may spread into the kidneys, bladder, or scrotum through blood. This may cause symptoms of irritated voiding, weight loss, dysuria, urgency, renal failure, flank pain, acute pyelonephritis, and fistulae. Hematospermia is reported in about 10% of the cases of genitourinary tuberculosis (18). In a case study, genitourinary tuberculosis was present 14% of the 35 cases studied (19). Genitourinary tuberculosis should be tested in patients with hematospermia by intradermal injection of tuberculin-purified protein derivatives, regardless of the absence of other genitourinary tuberculosis symptoms (20).

### **Hyperuricemia**

In 2014, Kurkar *et al.* concluded that hyperuricemia is a possible cause of hematospermia. Out of 143 patients observed, the hyperuricemic and hematospermia patients were younger by an average of 13.5 years than those who did not have hematospermia (100).

### **Hypertension**

Patients with hematospermia are known to have significantly higher blood pressures, as hematospermia is associated with hypertension. Men presenting with hematospermia should monitor their blood pressure levels to ensure no further complications develop and receive antihypertensive treatment if necessary (78).

### **Lymphoma**

A lymphoma is a group of blood cancers that affects the immune system through the lymph nodes, spleen, thymus gland, and bone marrow. The two most common types of lymphoma are Hodgkin's and non-Hodgkin's lymphoma. Solid tumors in the immune system grow, as cancer affects lymphocytes, compromising the ability of the body to fight off infection. Geoghegan and Bonavia reported a case of hematospermia as a presenting symptom of lymphoma (98).

### **Prothrombin deficiency**

Prothrombin deficiency is a bleeding disorder that is characterized by an extended amount of time for blood to clot. In severe cases, prothrombin deficiency causes heavy bleeding even after small injuries. The reason for the rarity of hematospermia with congenital bleeding disorders may be potentially due to sphincter muscles and perineal muscles having the ability to stop bleeding by compression (9).

### Schistosomiasis

*Schistosoma haematobium* eggs can be found in the prostate and seminal vesicles, causing hematospermia as well as a decreased viscosity and yellow discoloration of semen. Hematospermia was noted primarily in patients with more severe cases of schismatic infection (21). An increased resistance to praziquantel, the treatment for *S. haematobium*, may develop due to the decreased immune response caused by these worms (22). Recently, Spanish male tourists developed hematospermia; *S. intercalatum*, *S. haematobium*, and *S. mansoni* eggs were found in their urine and feces as well as in the ejaculate (23).

### Herpes simplex virus

Herpes simplex virus is widely known as one of the most common pathogens responsible for hematospermia. About 60% of patients who present with HSV-2 have abnormal variations of the disease that are usually unrecognizable. For example, patients with HSV-2 seropositivity had the virus without having genital ulcers or other symptoms, causing the patient to be unaware of their disease and corresponding hematospermia (27).

### Von Willebrand disease

Von Willebrand disease is a congenital bleeding disorder that presents as mucocutaneous bleeding with easy bruising, menorrhagia, epistaxis, and in select few cases, hematospermia. Von Willebrand disease is caused by mutations at the von Willebrand factor locus on chromosome 12. Hematospermia occurs with this disease most commonly secondary to self-instrumentation, falls, straddle injuries, or catheterization (93).

### Parasitic or bacterial infection

#### Echinococcosis

Echinococcosis, or hydatid disease, is a tapeworm infection that occurs when eggs or proglottid of *Echinococcus granulosus* or *E. multilocularis* are ingested. Although *E. multilocularis* usually affects the liver or the lung, it has been reported as a retrovesical pseudotumoral mass causing hematospermia (29).

#### Ureaplasma urealyticum

A possible pathogen responsible for hematospermia may be *Ureaplasma urealyticum*, which is a strain of bacterium causing urogenital or extragenital infections. In 2005, Golan *et al.* reported a correlation between *U. urealyticum* and hematospermia (25).

### Miscellaneous

#### Congenital or drug-induced bleeding

Najafi and Noohi reported a case of a 32-year-old man admitted due to hematospermia which turned out to be due to acetylsalicylic acid use, as the aspirin may have contributed to damaging the congested mucosa or by changing the amount of platelet produced after the penis experienced trauma post-ejaculation (82).

#### Excessive sexual intercourse or masturbation

In most cases where hematospermia occurs due to excessive masturbation, the condition self-resolves in an average of 1 to 2 months. The most common reason for blood in the ejaculate is because of a ruptured blood vessel after continuous ejaculations, as the epididymal duct can become sensitive and unable to recover to its normal function (80). Thus, it is vital for the evaluating physician to take a detailed history including current medication use and surgical history. If a patient has a history of excessive coitus, the sexual history and ejaculation frequency of the patient should also be submitted for evaluation.

#### Hemorrhage

Hemorrhage in the seminal vesicles, vas deferens, or müllerian duct is usually present in patients with hematospermia. An axial T1-weighted MRI study can show a hemorrhage. Usually, hemorrhage can be shown along with renal agenesis or abnormal urogenital structures (44). Hemorrhage can occur due to a multitude of reasons, including post-transrectal prostate needle biopsy (77).

#### Vascular malformations

Arteriovenous malformation is defined as incorrect or inefficient communication between veins and arteries. Many causes of arteriovenous malformation exist, including gunshot and other trauma as well as erroneous surgical procedures. In a case study by Avargues *et al.*, a patient had a circumaortic vein and presented a nonaneurysmal dilation of the inferior vena cava and iliac veins. The inferior vena cava experienced megacava, which caused reflux in the pelvic venous plexuses and created pelvic floor varicosities resulting in hematospermia (72).

### Evaluation

#### History

Obtaining a thorough history is instrumental in pinpointing

the etiology of hematospermia. Factors such as the amount of bleeding as well as type and duration of symptoms should also be determined. In addition to bleeding, patients may experience weight loss, fever, pain, voiding dysfunction, and sexual manifestations. Depending on etiology, hematospermia can clinically manifest as painful, painless, intermittent, and persistent. It is important to identify the treatable causes and avoid mistaking hematospermia from other conditions. Uterine or cervical carcinoma may cause bleeding following sexual intercourse and may imitate hematospermia. Urethral bleeding and melanospermia present with similar symptoms. Condom tests are recommended to distinguish the partner as a cause of hematospermia. If a patient presents with a history of dysuria, proper antibiotic treatment may be necessary if an infection is suspected. Travel history to places where the prevalence of schistosomiasis or tuberculosis is higher should also be investigated. For instance, there have been several cases reported in the literature where *S. haematobium* eggs were contained within the ejaculate in addition to hematospermia (21,108).

### Physical examination

Similar to patient history, a thorough physical examination is essential for a proper diagnosis of hematospermia. Vital signs including blood pressure and temperature should be recorded, and the abdomen should be assessed for abnormal lumps to exclude liver and spleen enlargement or pelvic masses. The groin, perineum, as well as the external genitalia including the urethral meatus, testes, and spermatic cord, should be examined for dermal lesions and presence of hypospadias. A rectal examination should be performed to eliminate the possibility of rectal, prostate, and seminal vesicle cysts and masses. If masses are not identified in any area, a transperineal ultrasound or an MRI scan should be obtained to gain images of the genital glands and the respective drainage ducts (1). A condom test may be utilized to examine blood in the ejaculate (109). *Figure 1* establishes an evaluation algorithm for hematospermia.

### Laboratory studies

Laboratory tests such as urine cytology must be conducted to exclude any bladder-related pathologies (109). Further laboratory tests including semen culture, urethral swabs, mycobacterial cultures, and viral serology should be utilized

to rule out an infectious etiology (109). Patients presenting with hematospermia and urethritis should also be tested for gonorrhea and chlamydia.

Basic metabolic panel (BMP) is a blood test that measures the amount of sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine, glucose, and calcium. BMP should be obtained to test the liver and kidney function.

PSA, a protein contained within the prostate that ensures sperm will survive when in the vagina after intercourse, should also be obtained to rule out possible prostate cancer as men with prostate cancer typically have increased PSA levels.

Furthermore, cystoscopy and seminal vesiculography should be utilized for direct visualization of an anatomical abnormality.

### Imaging studies

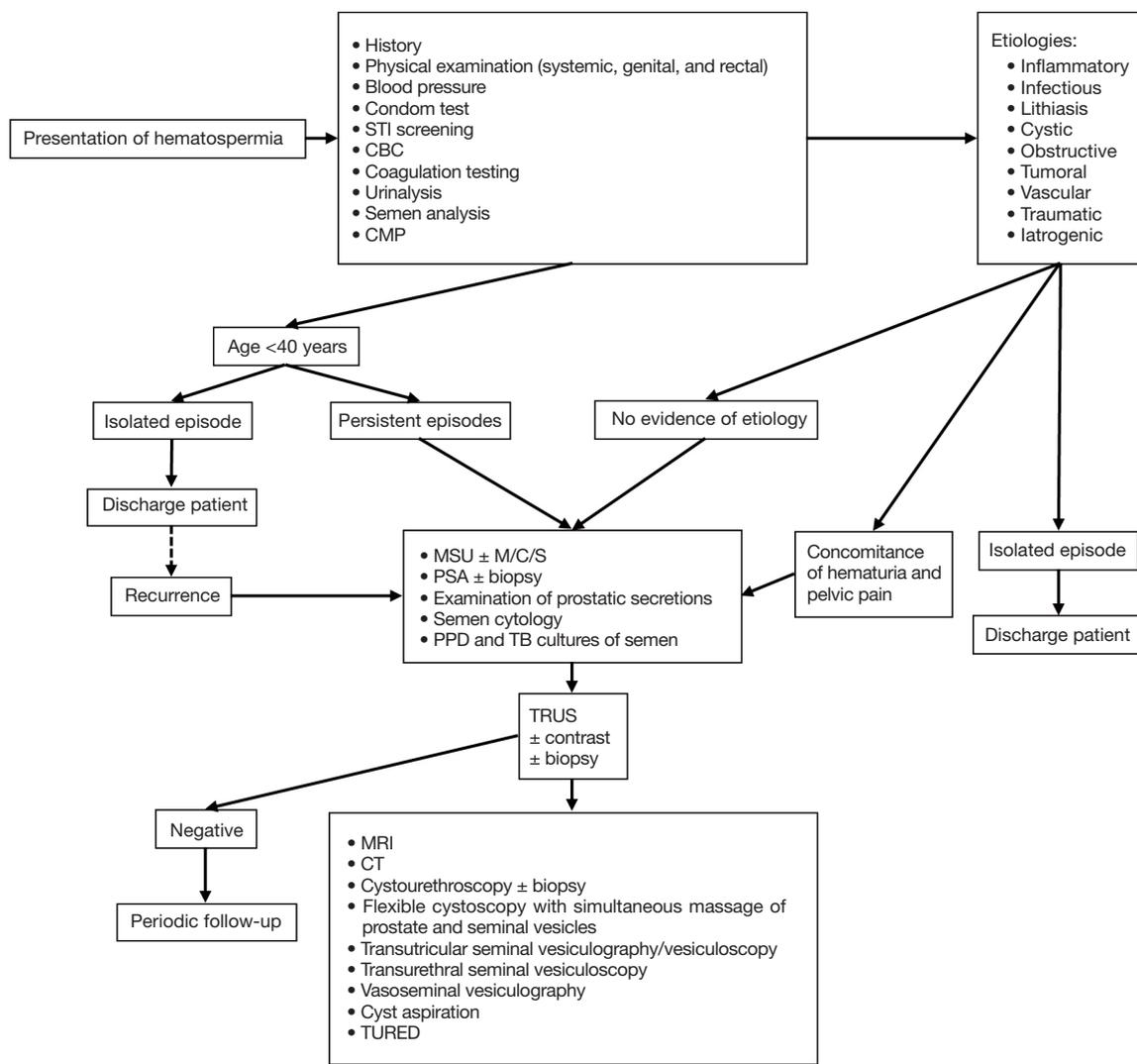
There are various imaging modalities available for examining the ejaculatory apparatus. This includes cystourethroscopy, TRUS, and computed tomography (CT). TRUS is the most widely used, as it is safe, inexpensive, and has a high rate of detection. TRUS use is recommended if hematospermia persists longer than one month (110,111). TRUS is effective in visualizing the internal structures of the seminal vesicle, vas deferens, ejaculatory duct, and prostate (112).

If positive for a suspicious lesion or nodule, an MRI scan or a flexible cystoscopy should be obtained (113). If negative, the patient should have periodic follow-ups to ensure no complications are present (113). TRUS is useful in detecting communication between a midline cyst and the urethra by the utricular orifice, as it is the only modality able to identify this communication by the use of dye and contrast medium. One of the complications of TRUS is a failure to properly aspirate the lesion (48).

Transrectal MRI of the ejaculatory apparatus can also be performed to aid in the diagnosis. Since seminal vesicle amyloidosis appears hypointensive on a T2- and T1-weighted MRI scan (96).

### Management

Hematospermia usually self-resolves in many cases, stopping in occurrence over time, especially for patients below the age of 40. In a prospective study, Furuya *et al.* concluded that in patients presenting with hematospermia without inflammation, infection, or malignancy, hematospermia



**Figure 1** Hematospermia evaluation algorithm. MRI, magnetic resonance imaging; CT, computed tomography; TRUS, transrectal ultrasonography; STI, sexually transmitted infection; CBC, complete blood count; CMP, comprehensive metabolic panel; MSU, midstream specimen of urine; M/C/S, microscopy, culture, and sensitivity; PSA, prostate specific antigen; PPD, purified protein derivative; TB, tuberculosis; TURED, transurethral resection of ejaculatory ducts.

resolved spontaneously in more than 88% of the patients with a mean disease duration of 1.5 months (114). Since hematospermia has a higher rate of persistence in patients with seminal vesical hemorrhage, midline cyst, seminal vesical dilation, and age older than 50, it is imperative that the underlying condition is properly diagnosed and treated to completely resolve hematospermia (114). Similarly, one of the most important aspects of managing hematospermia is patient reassurance. The physician must evaluate the patient, rule out life-threatening conditions such as cancer, and relieve the anxiety and stress meanwhile providing a

proper follow-up and observation (114). Surgery should be performed and proper medication should be prescribed based on the pathophysiological nature of hematospermia. The primary care physician must be able to safely manage idiopathic conditions that often presents as hematospermia. Prompt consultation with a specialist should be obtained if a patient has recurring symptoms, elevated PSA, or unusual findings during the physical examinations. Patients over the age of 40 with high-risk factors such as recurrent symptoms, hematuria, or history of prostate cancer are required to seek urologist for a detailed investigation (115). If the seminal

vesicles are dilated, and the patient has no resolution of hematospermia after conservative therapies, then the patient may opt to undergo bilateral seminal vesicle puncture and drug injection with ultrasound guidance to stop hematospermia (103).

### **Instrumentation**

Transurethral seminal vesiculoscopy is an often-performed treatment in addition to the aforementioned diagnostic approach (116). Transutricular seminal vesiculoscopy can also be conducted with newer endoscopic equipment. Such methods are usual in targeting abnormal urethral or prostatic vessels (117). Additionally, duct obstruction can be managed by transurethral incision.

### **Pharmacotherapy**

Certain drugs can also be taken to help alleviate hematospermia symptoms. For example, finasteride is used to control hematospermia due to benign prostatic hypertrophy, and even for patients with idiopathic refractory hematospermia after excluding other organic causes (118). To target bacterial infection or sexually transmitted infection-suspected cases of hematospermia, antibiotic therapy is utilized. The more frequent pathogens that cause hematospermia include chlamydia, gonorrhea, and herpes simplex. In these cases, antibiotic therapy should be considered; a course of doxycycline with 5-aminoquinolone or sulfamethoxazole may help absolve the infection (109).

### **Endoscopy**

The endoscopic treatment utilizes a holmium laser to incise the obstructed ejaculatory duct, fragment stones, and coagulate hemorrhagic mucosa to treat diseases of the ejaculatory duct and seminal vesicle, which are common causes of hematospermia (119).

### **Conclusions**

The occurrence of hematospermia can be quite alarming, especially for men who do not know the causes of blood in the ejaculate. As most causes of hematospermia are self-resolving, the physician should reassure the patient of his wellbeing and condition, and continue with follow up until hematospermia ceases. If the condition continues

or worsens, different imaging modalities are available for observation and diagnosis of further complications. Case studies of the various etiologies of hematospermia are discussed but are not limited to the ones listed in this review. The etiology can be classified into inflammatory, infectious, lithiasis, cystic, obstructive, tumoral, vascular, traumatic, iatrogenic, and systemic origin or divided into subcategories based on anatomical origins such as prostate, bladder, spermatic cord, seminal vesicles, or epididymis. Evaluating the etiology is the best approach to the initial management of hematospermia.

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### **Footnote**

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