LESSON 13

Hematospermia

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe the differential diagnosis of hematospermia, tailor the evaluation and treatment of hematospermia to individual patient scenarios, and identify which patients warrant which diagnostic testing to identify dangerous pathologies.

This AUA Update aligns with the American Board of Urology Module on Impotence, Infertility and Andrology. Additional information on this topic can be found in the AUA Core Curriculum section on Sexual Medicine and Andrology.

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KEY WORDS: hematospermia, hemospermia, bloody ejaculate

BACKGROUND

Hematospermia, or hemospermia, is defined as blood in the ejaculate or seminal fluid. This can be seen with the naked eye. The color and consistency of hematospermia ejaculate may vary, from more pink or bright red with more fresh blood, to darker brown or black sometimes with particulate debris seen with a longer duration since the original bleed. There may also be streaking of red to brown blood mixed throughout the ejaculate or only in parts of the ejaculate. Episodes may occur in isolation or may be recurrent or chronic in frequency. The incidence and prevalence can be difficult to determine; it is most commonly seen after masturbation since this is when the ejaculate fluid is easily visible. However, there is nothing inherent to the masturbation process that predisposes to hematospermia. Hematospermia may also be identified by a partner who is not sure if the blood is from them or the male partner.¹ One study has estimated that hematospermia was the cause for consultation in 1:5,000 urological visits.²

When detected, hematospermia may be alarming to patients and may prompt medical evaluation to rule out malignancy or other pathology. In many cases the cause is never determined, and recent series show that the exact etiology for hematospermia was undetermined after evaluation in >70% of cases. As diagnostic technologies advance, the root cause may be identified in a growing proportion of cases. The optimal evaluation and management algorithms are not clearly defined and are generally tailored to the individual patient history and symptoms.

ETIOLOGY

Hematospermia may result from a variety of anatomical locations (fig. 1) or etiological sources (table 1). **Of note, most identifiable causes for hematospermia are benign.** A systematic literature review found that among the 30% of patients with an identifiable etiology, the following broad causes of hematospermia were discovered: infections in 20.1%, inflammation without identified infection in 20.1%, prostatic/seminal vesicle/urethral calculi in 9.5%, systemic hypertension in 7.7% and malignancy in 5.4%.

Trauma. With a corresponding history, a common cause of hematospermia is trauma. This is commonly seen after vasectomy, orchiectomy, prostate biopsy or other prostatic manipulation. A review of complications after prostate biopsy found that visible hematospermia was the most variably reported complication after prostate biopsy, ranging from 1.1% to 92.6%.⁶ The presence of hematospermia after prostate biopsy has been shown to be inversely correlated with age, previous transurethral resection of the prostate and prostate volume.⁷ As expected, the frequency of hematospermia increases with an increasing number of cores taken (31.8%, 37.4% and 38.4% after 6-, 10- and 15-core biopsy, respectively; p<0.001).⁸ Other authors have estimated that over 80% of

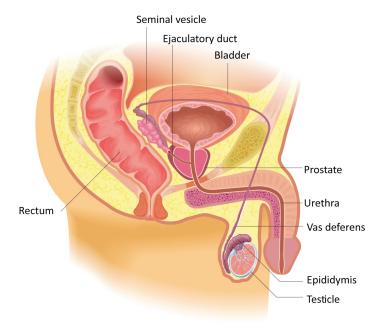


Figure 1. Male reproductive tract, with possible anatomical origins of hematospermia.

men undergoing prostate biopsy will experience hematospermia, which can last up to 1 month but typically does resolve spontaneously without the need for therapy or intervention. Biopsy oncologic results have not been found to correlate with presence or duration of bleeding. Hematospermia can also be seen after treatments for prostate cancer.

Hematospermia can be seen in up to 26% of cases after brachytherapy for prostate cancer. Likewise, hematospermia is a known possibility after high-intensity focused ultrasonography (1.4%) or focal cryosurgical ablation (0.8%) of the prostate for prostatic tissue ablation. It has also been seen in 4.4% of men undergoing prostatic artery embolization. Currently there are no reports of hematospermia after external beam radiation.

Hematospermia can also be seen after urinary instrumentation, such as cystoscopy or traumatic catheter placement. It is also common to see hematospermia after vasectomy. In addition, it can be related to some sexual practices or sexual pleasure devices, such as prostatic manipulation, urethral sounding, foreign bodies or penis rings. Finally, there have been reported cases of hematospermia after excessive masturbation secondary to ruptured blood vessel. ¹⁴ Conversely, the authors have seen hematospermia after prolonged durations of abstinence.

Infectious or inflammatory causes. Another common cause of hematospermia is infections, both sexually and nonsexually transmitted. While infections are among the most commonly identified causes, a systematic review found that urogenital infections were only diagnosed in 20.1% of men presenting with hematospermia. Infectious causes are more commonly seen in men less than 40 years of age. One study found that infections were observed in 15% of men under 40 years with hematospermia and 10% of men

ABBREVIATIONS: complete blood count (CBC), human immunodeficiency virus (HIV), magnetic resonance imaging (MRI), prostate specific antigen (PSA), transrectal ultrasound (TRUS)

over 40 years old. ¹⁵ Acute prostatitis, particularly bacterial, is the most common infectious source, although urethritis and epididymo-orchitis can also be seen. Of men with known prostatitis, 40%-55% may experience hematospermia. ^{4,16}

Sexually transmitted pathogens that may cause hematospermia include *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, herpes simplex virus, *Ureaplasma urealyticum* and human immunodeficiency virus (HIV).^{17,18} Data from a sexual health clinic found that an infectious pathogen could be identified in 75% of cases of hematospermia, including herpes simplex in 42% of cases, *C. trachomatis* in 33%, *Enterococcus faecalis* in 17% and *U. urealyticum* in 8%.¹⁷ Nonsexually transmitted pathogens that may result in hematospermia include *E. faecalis*, *Escherichia coli*, cytomegalovirus, schistosomiasis, Zika virus and other pathogens.^{17,19} These organisms can infect different organs of the male lower urinary tract, with either the infection or concurrent inflammation resulting in hematospermia.¹⁸

Prostatic, testicular or epididymal tuberculosis may also result in hematospermia in an estimated 25% of cases. 20 Xanthogranulomatous prostatitis is a rare, benign inflammatory condition of the prostate, characterized by granulomas seen on histological analysis. 21 This condition is believed to be caused by prostatic ductal blockage resulting in congestion of prostatic glandular secretions, with resultant inflammation. 21 Finally, urethral condylomata acuminata, or genital warts, typically of the urethra or meatus, can result in hematospermia. 22

Anatomical causes. Hematospermia may be the manifestation of anatomical anomalies, including vascular, calculi related and cystic. Vascular causes may include dilated prostatic urethral veins, arteriovenous malformations, vaso-venous fistulas, hemangiomas, prostatic varices or prostatic telangiectasias. In particular, posterior urethral hemangiomas are usually present between the verumontanum and external urethral sphincter and form as the result of high intraprostatic pressures. Hematospermia may be also caused by calcifications within the seminal vesicles, prostate, ejaculatory duct or urethra. 18,24

Cysts may also cause hematospermia, including intraprostatic and extraprostatic. Intraprostatic cysts can be further classified into median cysts (prostatic utricle cysts, müllerian duct cysts), paramedian cysts (ejaculatory duct cysts) and lateral cysts (prostatic retention cysts, cystic degeneration of benign prostatic hypertrophy, cysts associated with tumors, prostatic abscess). Extraprostatic cysts include cysts of the seminal vesicle, vas deferens and Cowper duct.²⁴ Hematospermia can be caused by the cyst itself or by subsequent blockage and backpressure in the seminal vesicles, ^{20,25} ejaculatory duct, prostate or urethra.²⁶

Tumors. More seriously, and more rarely, hematospermia may be associated with tumors of benign and malignant origins. It is hypothesized that friable aberrant vessels produced by tumor angiogenic stimuli contribute to this condition. Benign possible tumors include adenomatous polyps of the verumontanum²⁷ and prostatic urethra.²⁸ Malignant tumors are often what patients fear most. Possible malignancies presenting with hematospermia include prostate cancer,⁷ carcinomas of the seminal vesicles, testicles, penis, urethra or, rarely, bladder cancers.¹⁸

The complete relationship between hematospermia and prostate cancer is unclear. The 2 conditions can coexist, but whether hematospermia portends a higher risk of more severe Gleason score or worse prognosis for prostate cancer is unknown. It is

generally accepted that in recurrent cases of hematospermia in males over 40 years of age, there is a higher risk of identifying treatable pathology, including prostate cancer. In a series of 300 males with hematospermia, prostate cancer was the cause for hematospermia in 5.7% of cases. Conversely, in series of men with known prostate cancer, the incidence of hematospermia varies, with one study finding 0.5% and another reporting 45.3% of men having hematospermia. In both series, men did have risk factors for prostate cancer, including abnormal digital rectal examination or prostate specific antigen (PSA) >3 ng/dl. As discussed earlier, hematospermia can also be seen after treatments for prostate cancer.

Systemic causes. Systemic bleeding disorders may be associated with hematospermia, including those seen with bleeding diatheses, liver cirrhosis or clotting issues.²⁹ Arterial hypertension may also be associated, as well as hemophilia (von Willebrand disease).^{29,30} Regarding medications, men taking anticoagulants and protease inhibitors for HIV have higher rates of hematospermia.²⁹ Hematospermia is also associated with hypertension, and males with hematospermia are known to often have higher blood pressure.³⁰

DIAGNOSIS

History and physical examination. While the cause of most hematospermia cases remains unknown, 1,3,4 efforts should be made to identify and treat any contributing and/or causal factors. A suggested algorithm for the management of hematospermia is provided in figure 2. A systematic and complete history and physical should be the first step. Factors including the amount of bleeding, and frequency and duration of symptoms should be elicited. Patients should be asked about weight loss, fevers, voiding dysfunction, pain with urination or ejaculation, urethral discharge, systemic bleeding, antecedent traumas and family histories. It is also important to make the distinction between hematospermia and hematuria, as both may present with blood in the toilet. A detailed sexual history should be taken, including sexual practices and the frequency

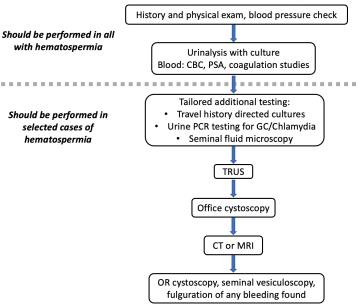


Figure 2. Suggested evaluation and treatment algorithm for hematospermia. *GC, N.* gonorrhoeae. *OR,* operating room. *PCR,* polymerase chain reaction.

of ejaculation. Travel history should be elicited, particularly to regions where schistosomiasis and tuberculosis are more common. Medications should be reviewed for anticoagulants. It is important that the patient be questioned directly as to the conditions under which hematospermia was observed. Sexual partners can be the source of blood (for example, as a product of menstruation, cervical cancer or an anorectal disorder). If there is any question, collecting the ejaculate in a condom can ensure that the blood is actually from the patient.

Physical examination should be directed toward detecting both local and systemic causes. A blood pressure and temperature check should be performed. The abdomen should be palpated for any hepatomegaly or splenomegaly or lymph node swelling. A focused genitourinary examination should be performed. This should include testicular examination for masses or tenderness, and meatus and penile examination for palpable abnormalities or open lesions. The presence of skin tears, rash or blister should prompt questions about sexual behaviors. Digital rectal examination should be performed, feeling for prostatic mass or pain, as well as assessment of seminal vesicle fullness.

Laboratory testing. The degree of laboratory testing performed should be tailored to the patient. With a complete history and physical, a young, healthy patient and an isolated hematospermia episode, often the only additional testing that is required is relatively straightforward laboratory testing. It is widely accepted that chronic, persistent hematospermia requires more extensive investigation, as does the appearance of this symptom in older males. ¹⁶

A urinalysis with microscopy and reflex to culture should be performed in all males with hematospermia.¹⁶ Sexually transmitted disease screening (testing for gonorrhea, chlamydia and syphilis) should be performed in sexually active males or those deemed to have risk factors by the treating physician. Urine cytology to identify any bladder related pathologies may be performed in at-risk males.3 A microscopic examination and culture of the ejaculate fluid may also be performed, although the clinical utility of this is debatable as false-positive results from contaminants may be seen and result in overuse of antibiotics.³¹ When concern exists, the seminal fluid may be sent for acid fast bacilli culture to evaluate for tuberculosis.²⁰ If tuberculosis is suspected, the patient should be sent for an intradermal injection of tuberculin-purified protein derivatives.³² Urethral swab and expressed prostatic secretions may also be examined when clinically indicated. 18 If any of these are positive or if the patient reports dysuria, then antibiotic therapy may be indicated.

A complete blood count (CBC) with differential and platelet count and coagulation parameters (prothrombin time, partial thromboplastin time, international normalized ratio) should be performed in males with bleeding tendencies. Males taking blood thinners with concern for supratherapeutic coagulation can either have coagulation parameters checked or be referred to the physician who is managing these medications, at the discretion of the urologist. A CBC and comprehensive metabolic panel may also be checked at the discretion of the treating urologist. It is particularly important that all males over 40 years of age or in appropriate risk categories have PSA checked.^{5,16}

Imaging. Transrectal ultrasound (TRUS) is a safe, rapid, minimally invasive means for investigating the cause of hematospermia and may also identify any concurrent

malignant pathology.³³ Despite its minimally invasive nature, this may still be a source of discomfort or anxiety for men. This may be used to identify dilated ejaculatory ducts and ejaculatory duct or seminal vesicle cysts, which may be primary or secondary.³⁴ TRUS has been recommended if hematospermia persists for greater than 1 month.³⁴ In a prospective series of males undergoing TRUS for hematospermia, abnormalities were identified in 94.8% of cases, including pathology of the seminal vesicles in 46.3%, ejaculatory ducts in 29.6%, prostate in 55.2% and bladder in 0.4%. Malignant conditions were more likely to be identified in males over 40 years of age.³⁵ When testicular pathology is suspected, scrotal and testicular ultrasound should be performed.

Endoscopy. Cystoscopy has also been recommended in patients with hematospermia refractory to antibiotic therapy, ¹⁸ and is imperative when concurrent hematuria (gross or microscopic) is present. This may identify any prominent prostatic blood vessels that may be bleeding during ejaculation. It may also identify urethral strictures or polyps or bulging ejaculatory ducts.⁴

Transurethral seminal vesiculoscopy in the operative suite may also play a role in both the diagnosis and management of hematospermia. Visualization of the seminal vesicles and ejaculatory ducts can be performed via 7Fr or 8Fr rigid ureteroscopy directly or guided over a 0.032-inch guidewire. The data supporting this modality are limited, but it may be indicated in select patients. The ejaculatory ducts and seminal vesicles can be visualized endoscopically via the verumontanum, looking for abnormal or bleeding urethral or prostatic vessels. In 1 series, the cause of hematospermia was identified in 74.5% of males undergoing transurethral seminal vesiculoscopy, with the most frequent diagnoses including ejaculatory duct stones and urethral strictures. These vessels may be cauterized, making this procedure both diagnostic and therapeutic.

In men with persistent hematospermia, computerized tomography (CT) or magnetic resonance imaging (MRI) may be used.³⁶ MRI may have the added benefit of detecting prostate cancer risk areas.⁹ On MRI an axial T1-weighted study may identify a hemorrhage in the seminal vesicles, vas deferens or müllerian ductal structures.¹⁸ The optimal imaging modality of TRUS versus MRI is presently unclear. In a recent review of 23 men with intractable hematospermia, the positive finding rates of MRI versus TRUS were 95.7% (22/23) versus 39.1% (9/23).³⁷ While these are compelling data, the imaging modality of choice should be tailored to the individual patient.

MANAGEMENT

Many cases of hematospermia will self-resolve. Once appropriate workup is complete (fig. 2), patients should be reassured that in most cases, particularly for those under 40 years of age, no serious pathology will likely be identified. For males with bright red hematospermia a trial of abstinence may be needed, and for males with darker brown hematospermia a trial of increased frequency of ejaculation may be helpful. A holiday from nonsteroidals, antiplatelets or other blood thinners may also be indicated in conjunction with the patient's other physicians. A review of patients undergoing urological hematospermia evaluation, including examination, PSA testing, ultrasound of the abdomen and scrotum, TRUS and cystoscopy, found that in 90% of cases, no specific diagnosis was made.³⁸ In a series of 189 males, hematospermia resolved spontaneously in 88.9% of

patients, with a median duration of 1.5 months. Persistence rates of hematospermia were 57.7% at 1 month, 34.2% at 3 months, 23.3% at 6 months, 12.5% at 1 year and 7.6% at 2 years. Hematospermia reoccurred in 20 (13.5%) of the 148 patients who had adequate followup.³⁹ One of the most important aspects in the management of hematospermia is patient reassurance.³⁹

Patients may ask about the impact of hematospermia on fertility, and the available data on this are limited. One study looking at 90 males with hematospermia from ejaculatory duct obstruction found that the mean semen analysis parameters even before treatment were normal, showing a mean±SD volume of 1.76±0.69 mL, sperm concentration of 62.52±58.16 million/mL and motility of 59.71%±27.32%. The volume and motility increased after ejaculatory duct resection, likely from relief of the obstruction, while the concentration remained the same.⁴⁰ Conversely, in the andrology laboratory realm, limited data have shown that red blood cells in the ejaculate may affect the fertilization potential of sperm, particularly after the freeze-thaw process.⁴¹

Whenever possible, the treatment of hematospermia should be directed at the evaluation findings (fig. 2). All of the diagnostic modalities available have both advantages and disadvantages, which should be taken into consideration when managing the individual patient (table 2). Patient age, specific risk factors and accompanying symptoms will also tailor management. All males being managed for hematospermia should have blood pressure checked at each clinic visit, with referral to primary care (or if needed, urgent care) if this is elevated. If the source is determined to be from excessive masturbation, this should resolve with abstinence for several weeks. Men over 40 years, with an elevated PSA or a family history of prostate cancer should be evaluated for prostate cancer.

If infection is suspected, but no pathogens are identified, empirical antibiotics may be justified. A systematic review found that for males with hematospermia, pyuria was identified with a negative culture in 20% of men with hematospermia.⁵ Genitourinary infections have been shown to be the most common source of hematospermia in males <40 years of age. 43 One series of 165 men with hematospermia treated with empirical fluoroquinolone antibiotics with anti-inflammatories found that in 96% of cases the hematospermia resolved.⁴⁴ Second-line antibiotics to consider include doxycycline and azithromycin, with consideration being given to covering chlamydia and gonorrhea.⁴⁵ However, antibiotics in the absence of a positive culture should not be prescribed without careful consideration, given our growing understanding of the implications of antibiotic resistance. If herpes simplex virus infection is identified, this should be treated with appropriate antivirals and patients should be followed in a genitourinary clinic for contact tracing.

Other pharmacological treatment options may be directed at minimizing prostatic bleeding, including with finasteride. 46 In 1 study of males with cause-indeterminate hematospermia treated with finasteride, 66.7% treated with finasteride had remission of the hematospermia versus 25% in the placebo group. 46

If dilated seminal vesicles are identified, transrectal aspiration may be considered.⁴⁷ If seminal vesicle tumors are seen, these can be excised laparoscopically.

If seminal vesicle or prostatic utricle calculi are identified, transurethral seminal vesiculoscopy with removal by holmium laser lithotripsy and/or basket extraction may be attempted.⁴⁸

These procedures would be done in the operative suite. In a review of 103 men with hematospermia and ejaculatory duct obstruction treated with transurethral resection, at 12 months of followup 93% of men had resolution of the hematospermia. Cautery or holmium laser may be used to manage hematospermia, by incising or unroofing obstructed ejaculatory ducts or midline prostatic cysts and coagulating hemorrhagic mucosa. If bleeding blood vessels or hemangiomas are seen, fulguration may be performed.

FUTURE DIRECTIONS

As diagnostic technologies evolve, the cause of a growing proportion of cases of hematospermia will likely be discovered. The role of MRI versus TRUS in the evaluation of hematospermia is still being determined. While data do show that MRI may provide more actionable data for some patients, the full and precise role is still being determined.³⁷ Likewise, the role of MRI and the Prostate Imaging Reporting and Data System in the diagnostic evaluation of hematospermia is still being determined.

CONCLUSIONS

Hematospermia can be alarming for patients, although in most cases is benign. In many cases no clear cause is identified, and in the majority of cases it is self-limiting. In males <40 years old infection is a common cause, and in those >40 years cancerous causes should be investigated. Infectious, inflammatory and traumatic causes are common, and a thorough history, physical examination and laboratory testing should be performed to identify these. If the condition persists, or history warrants, TRUS or other imaging should be considered. The etiology can be grouped into traumatic, infectious or inflammatory, anatomical, tumors and systemic. Management should be tailored to the diagnostic findings to identify any causes while managing limited medical resources. When no source is identified, patients can be reassured.

DID YOU KNOW?

- Hematospermia can be alarming for patients, although in most cases it is benign and self-limiting.
- In males <40 years old infection is a common cause, and in those >40 years cancerous causes should be investigated.
- Hematospermia must be differentiated from hematuria.
- Infectious, inflammatory and traumatic causes are common, and a thorough history, physical examination and laboratory testing should be performed to identify these.
- The etiology can be grouped into traumatic, infectious or inflammatory, anatomical, tumors and systemic.
- Management should be tailored to the diagnostic findings to identify any causes while managing medical resources.

 Table 1. Possible etiologies of hematospermia

Broad Category	Individual Causes	Subcauses
Traumatic	Prostatic	Prostate biopsy
		Prostate Ca treatments
		Benign prostatic hypertrophy treatments
	Cystoscopy	
	Traumatic catheter placement	
	Vasectomy	
	Sexual practices	
	Excessive or not enough ejaculation	
Infectious	Bacterial	C. trachomatis
		Gonorrhea
		Syphilis
		E. faecalis
		E. coli
		U. urealyticum
		Tuberculosis
	Viral	Herpes simplex virus
		HIV
		Cytomegalovirus
		Zika virus
	Parasitic	Schistosomiasis
		Genital warts
Anatomical	Vascular	Prostatic varices
		Arteriovenous malformations
		Hemangiomas
	Calcifications	Seminal vesicles
		Prostate
		Ejaculatory duct
		Urethra
	Cysts	Intraprostatic
		Prostatic utricle
		Müllerian duct
		Ejaculatory duct
		Prostatic retention
		Cowper duct
Tumors	Benign	Adenomatous polyps of the verumontanum or prostatic urethra
	Malignant	Prostate
		Seminal vesicle
		Testicle
		Bladder
Systematic	Bleeding disorders	Liver-related coagulopathy
		Hemophilia
	Medications	Anticoagulants
		Protease inhibitors
	Hypertension	

Table 2. Advantages and disadvantages of diagnostic modalities for hematospermia

Diagnostic Test	Advantage(s)	Disadvantage(s)
Voided urine tests	May direct antibiotic therapy	May have false-positive or false-negative results, resulting in over or under antibiotic treatment
Expressed prostatic secretion culture	May direct antibiotic therapy	May have false-positive or false-negative results, resulting in over or under antibiotic treatment May be uncomfortable for pt
Seminal fluid microscopy	May direct antibiotic therapy	May have false-positive or false-negative results, resulting in over or under antibiotic treatment
TRUS	May identify treatable pathology May identify concurrent pathology (prostate Ca)	May result in hematospermia May be uncomfortable for pt
Office cystoscopy	May identify treatable pathology May identify concurrent bladder or urethral pathology	Low chance of identifying source of hematospermia
CT scan	May identify treatable pathology May identify incidental pelvic pathology	Pt is exposed to radiation Low chance of identifying source of hematospermia
MRI	May identify treatable pathology May identify incidental pelvic pathology	Low chance of identifying source of hematospermia Insurance may not cover
Endoscopy in the operating room	May identify treatable pathology May identify incidental pelvic pathology	Low chance of identifying source of hematospermia Pt exposed to risks of surgery

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Study Questions Volume 41 Lesson 13

- 1. You are seeing a 25-year-old male with history of a single, painless episode of hematospermia. Physical examination, urinalysis, infectious screen, CBC and coagulation parameters are all normal. PSA is 0.4. What is the most likely cause?
 - a. prostate cancer
 - b. systemic clotting issue
 - c. ejaculatory duct obstruction
 - d. gonorrhea infection
- 2. Which vital sign is particularly important to note in the clinic evaluation of hematuria?
 - a. pulse
 - b. blood pressure
 - c. heart rate
 - d. respiration rate
- 3. A 70-year-old male presents with recurrent bright red hematospermia for 3 months. Physical examination is unremarkable. Urinalysis and infectious screen are both normal. What blood tests should be ordered?
 - a. CBC, liver function tests
 - b. CBC, comprehensive metabolic panel, PSA
 - c. CBC, coagulation parameters
 - d. CBC, coagulation parameters, PSA

- 4. A 72-year-old male has recurrent bright red hematospermia with every ejaculate weekly for 2 months. His urinalysis shows 10–12 red blood cells/high-powered field, urine culture is clean and PSA is 1.2. What is the best next step?
 - a. TRUS
 - b. MRI of the prostate
 - c. cystoscopy
 - d. reassurance
- 5. An 82-year-old male presents with bright red hematospermia. He notes that the hematospermia is only present during vaginal intercourse with his 78-year-old wife, not during masturbation. What is the best next step?
 - a. advise him to have intercourse with a condom
 - b. TRUS
 - c. cystoscopy
 - d. reassurance