REVIEW ARTICLE

Hematospermia—a Symptom With Many Possible Causes

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SUMMARY

Background: Hematospermia, or blood in the ejaculate, is a symptom with many possible causes that often gives rise to worry. Precise figures on its prevalence are unavailable. It is most common in men under 40, and its cause is usually benign; nonetheless, even a single episode of hematospermia calls for a basic diagnostic evaluation.

Methods: This review is based on pertinent articles retrieved by a search in PubMed with the key words "hematospermia," "hemospermia," "ejaculation," "male semen," and "transrectal ultrasound."

Results: A diagnostic algorithm for hematospermia is described. The most common cause is iatrogenic trauma, in particular transrectal ultrasound-guided prostate biopsy to rule out prostate cancer. Urogenital infections are the second most common cause. Pathological changes of the prostate should be considered along with systemic causes, e.g., arterial hypertension or various hematologic disorders. A single event in men under 40 should be evaluated by precise history-taking, a meticulous physical examination including blood-pressure measurement, and urinalysis. Repeated episodes, or hematospermia in men over 40, calls for additional evaluation with further laboratory tests, imaging studies, and, in some cases, interventional diagnostic procedures.

Conclusion: Further tests, preferably imaging studies, seem a reasonable way to detect or exclude potential causes of hematospermia, especially malignant ones. The treatment is directed at the underlying cause.

▶ **Cite this as:**
Mathers MJ, Degener S, Sperling H, Roth S: Hematospermia—a symptom with many possible causes. Dtsch Arztebl Int 2017; 114: 186–91. DOI: 10.3238/arztebl.2017.0186

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Hematospermia, also known as hemospermia, is a potentially alarming occurrence. The definition of hematospermia is presence of blood in the seminal fluid. The blood is sometimes visible to the naked eye, but the term hematospermia also covers microscopic amounts of blood in the ejaculate, as occasionally detected incidentally in a spermiogram.

The effect of blood on the color of the ejaculate may depend on how much time has elapsed since the bleeding event. Fresh blood will be light red to brownish in color, while darker, even dark brown or black clots usually mean that some time has passed since hemorrhage occurred. In most cases hematospermia is painless.

Hematospermia may occur only once, but may also be sporadic or chronic. It often goes unnoticed and is typically self-limiting, so the exact prevalence is unknown. Quantification is also difficult because most men do not often look at their ejaculate (1, 2).

Hematospermia is thought to make up about 1% of all urological symptoms (3). Its prevalence is estimated at approx. 1: 5000 urological patients (4). In a series of 26 126 men with a median age of 61 years who underwent routine prostate cancer screening, 0.5% reported hematospermia (5). Those affected are usually younger men under the age of 40, as shown in six large series each including over 500 patients (6). In a selected group of patients at a large andrological department in 2015, erythrocytes were detected by microscopy in the ejaculate of 13.8% of the men who had their semen examined—generally because of infertility (personal communication, Prof. Dr. Frank Sommer, President of the German Society for Men's Health; *Deutsche Gesellschaft für Mann und Gesundheit e. V.*). Erythrocytes are also often found when semen is harvested by rectal electrical stimulation of the accessory glands, but are then usually merely a contaminant with no pathological value.

The diagnosis of hematospermia is usually disturbing for the men or couples affected, because they are worried about sexually transmitted disease (STD) or malignancy.

Historically, hematospermia was viewed as a consequence of either prolonged sexual abstinence or excessive sexual activity. Even in recent decades, the exact etiology was unknown in over 70% of cases (1, 6, 7). As a result of advances in diagnostics, however, the etiology of hematospermia has in recent years been identified in most cases.

Recurring or chronic hematospermia, in particular, may result from a variety of etiological factors:

- Infection
- Anomalies
- Tumor
- Trauma
- Iatrogenic causes, such as prostate biopsy and other urological interventions
- Systemic disease
- Deviant sexual practices.

Deviant sexual behavior can cause bleeding by trauma, e.g., injury of the prostate by a stimulator, damage to the urethra by a tight penis ring, or the introduction of foreign bodies.

In the continued absence of guidelines for uniform investigation of these patients, this article reviews the causes and above all the diagnosis and treatment of hematospermia.

Methods

A search of the PubMed database was carried out in 2015 to find relevant publications, with no limit on publication date. The search terms were "hematospermia," "hemospermia," "ejaculation," "male semen," and "transrectal ultrasound". A total of 621 systematic reviews and original research articles were identified and linked with the content criteria. Eighty-four articles were extracted and examined in more detail, eliminating duplicate publications. All the authors of this review, acting independently, were in agreement regarding the clinical relevance of the 33 publications that were eventually included, with methodological quality as one of the criteria.

Etiology

There are many possible causes of hematospermia, most of them benign (6) *(Table 1)*. In recurrent cases and in men over 40 years of age, however, there is an association between hematospermia and treatment-necessitating disease, e.g., a malignancy, so in these groups further investigation is required (4, 5). In a large study of 26 126 men screened for prostate carcinoma, 13.9% of the probands who reported hematospermia on the initial interview, all of them over 40, were found to have prostate cancer (5). Despite exhaustive diagnostic work-up, the reason for the occurrence of hematospermia remains unknown in ca. 10 to 20% of cases (9). We will now discuss the known causes of hematospermia.

Trauma

One common cause of hematospermia is iatrogenic trauma, especially after transrectal ultrasound-guided prostate biopsy to exclude prostate cancer. In two large prospective studies, >80% of men reported hematospermia lasting for up to 4 weeks following prostate biopsy (10–12). However, there was no demonstrable association between the duration of bleeding and the biopsy result (5, 6). Hematospermia has been described in 17% of cases after brachytherapy for prostate cancer (13).

TABLE 1

Possible causes of hematospermia

Anatomic structure / type of anomaly	Cause
Prostate	Prostatitis (ca. 40%) (4) Polyps/cysts/stones Teleangiectasias/varices Carcinoma/sarcoma Malacoplakia
Urethra/bladder	Condylomas/polyps/hemangiomas Stricture Utricular cysts
Seminal vesicle	Stones/cysts/diverticulum Carcinoma
Infection	Gram-negative bacteria (often *Escherichia coli*), gonococci, *Treponema pallidum*, schistosomes, cytomegaly, *Mycobacterium tuberculosis*
Trauma/iatrogenic	Prostate biopsy/injection Sclerosing hemorrhoids Perineal or testicular trauma Autoerotic
Systemic	Arterial hypertension Hemophilia/anticoagulation/liver disease Lymphoma/leukemia
Other	Epididymo-orchitis Testicular tumor Tumor of lesser pelvis Idiopathic (ca. 30%) (20)

Modified from (6, 8)

Hematospermia can also occur after insertion of instruments (e.g., cystoscopy) or after manipulations involved in certain (e.g., autoerotic) sexual practices. Further possible causes of hematospermia include injury of the pelvis, perineum, or genitals.

Infection

The second most frequent cause of hematospermia is infection. Hematospermia in men under and over 40 years of age is not uncommonly due to infection (15% in men under 40, 10.3% in men over 40) (14). The most likely infection is prostatovesiculitis, but posterior urethritis should also be considered. The prevalence of hematospermia following these diseases is stated as 40 to 55% (6, 15). In most cases the pathogen is one of those typically responsible for urinary tract infections: among others, *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, and *Enterobacter*. Hematospermia is not, however, a typical symptom of chronic prostatitis or chronic pelvic pain syndrome.

In tuberculosis disease, hematospermia is found in 26.3% of cases of prostate involvement and in 7.1% of cases of accompanying orchidoepididymitis (16). Other specific infections include the following pathogens: *Neisseria gonorrhoeae*, *Treponema pallidum*, and *Cytomegalovirus* (8). In endemic areas, schistosomiasis is also thought to be a cause of hematospermia (8).

TABLE 2

Studies on investigation of hematospermia with the aid of transrectal prostatic sonography

Author	n	Normal findings n (%)	Prostate calcifications n (%)	Abnormalities of seminal vesicle/spermatic duct n (%)
Worischeck (25)	28	2 (8)	0	26 (92)
Yagci (24)	54	2 (5.5)	23 (42.6)	46 (90.1)
Zhao (27)	270	14 (5.2)	104 (40)	205 (75.9)
Raviv (28)	115	0	98 (58.2)	48 (41.7)

Organ-related causes

Obstruction caused by cysts of the seminal vesicles (congenital or acquired) can lead to hematospermia, as can obstruction of the müllerian duct or the ejaculatory duct. Malignant tumors of these structures or of the testicles are a possible but very rare cause of hematospermia. Polyps, condylomas and strictures of the urethra, arteriovenous fistulas, hemangiomas, and other vascular anomalies are other occasional causes (17).

Pathological changes in the prostate, such as vascular disease, polyps, or calculi, may also cause hematospermia. Rarely, the underlying cause of hematospermia is a prostate tumor. Prostate cancer was the cause in 5.7% of patients in a large prospective investigation of 300 consecutive cases of hematospermia (14). All of the men affected were over 40 years of age and had either an elevated concentration of prostate-specific antigen (PSA) (>3.0 ng/mL) or an abnormal finding on rectal palpation of the prostate. In a large prostate cancer screening study, 0.5% of the participants reported hematospermia. These men, with a median age of 61 years, had a 1.73-fold risk (adjusted for age and PSA) of developing prostate cancer (5).

Systemic causes

Various systemic diseases may be associated with hematospermia, although in no case has the link been demonstrated beyond doubt: these include refractory arterial hypertension (18) and hematological conditions such as hemophilia (8, 19) and coagulation disorders (18, 20), which may occur during anticoagulation or due to severe hepatic disease (21), e.g., liver cirrhosis. It is speculated whether elevated portal pressure causes venous reflux in the prostatic and hemorrhoidal plexuses and thus hematospermia. Patients with hyperuricemia have also been shown to be at increased risk of hematospermia (22).

Diagnosis

The goal of diagnostic investigation is to detect a clinically relevant or treatable cause of the hematospermia or to exclude malignancy (7). Detailed documentation of the patient's medical history and thorough physical examination including digital rectal examination are indispensable.

Medical history

The primary goal when investigating the patient's medical history should be early exclusion of pseudohematospermia, in which the affected person misinterprets blood in his urine (macrohematuria) or blood from his sexual partner as hematospermia.

Questioning should establish the duration and development of the symptoms, pain on erection, penetration, or ejaculation, and pain in the genital or perineal area, all of which may be relevant to the cause. Disorders of micturition such as pollakiuria, alguria, and weakening of the urinary stream may indicate lower urinary tract infection and must be excluded. Moreover, (iatrogenic) factors such as sexual practices, medical examinations, previous trauma, medication, and comorbidities may be responsible. Depending on the patient's age, these aspects should be evaluated.

Clinical examination

High blood pressure or fever may point to a systemic cause or to infection. Complete inspection and examination of the external genitals including the spermatic ducts and epididymes as far as the superficial inguinal ring together with the regional lymph nodes is obligatory, as is digital rectal examination of the prostate and the seminal vesicles.

Clinical chemistry

Whenever possible, the ejaculate should be examined macroscopically and microscopically. Microscopy can help to differentiate between true hematospermia *(Figure 1)* and discoloration caused by other factors. Ejaculate cultures are seldom productive but should be carried out particularly if tuberculosis is suspected (8). Suspicion of schistosomiasis mandates specific investigation of the ejaculate.

Examination of urethral swabs and urinary sediment seems expedient, together with cultures of urine harvested if necessary after prostatic massage, although demonstration of pathogens is often not achieved (23).

Suspicion of anemia, or an underlying infection or coagulation disorder may be confirmed by a blood count and analysis of coagulation parameters. Uric acid can be determined to exclude hyperuricemia,

and men over 40 years of age should have their PSA measured.

Imaging

Transrectal sonography (TRUS) is a safe, minimally invasive, and inexpensive way of investigating the individual structures that may have a causal role. Some studies, albeit mostly with low numbers of participants, have shown that TRUS can be helpful in investigating causes of hematospermia (24–26). Furthermore, TRUS simultaneously enables biopsy of suspect (prostate) areas.

Zhao et al. (27) confirmed the effectiveness of TRUS in a prospective study. Over 80% of 270 men with hematospermia had visible pathology. However, the authors could not demonstrate definitively that these findings were responsible for the hematospermia. In another prospective study, Raviv et al. (28) identified an anatomical correlate as causal factor in a group of over 100 men with hematospermia by means of TRUS *(Table 2)*.

There are indications that invasive transurethral vesiculoscopy may be superior to TRUS with regard to diagnosis of hematospermia. This procedure involves entering and exploring the ejaculatory ducts, which open into the central segment of the urethra at the verumontanum. Invasive transurethral vesiculoscopy is still largely experimental. In a prospective study of 106 men with persisting hematospermia, the cause was demonstrated by TRUS in 45.3% and by transurethral vesiculoscopy in 74.5% of the participants ($p<0.001$); the two procedures combined were successful in 87.7% of cases ($n = 93$; $p>0.001$). The most frequently established diagnoses were calcifications/stones, obstructions, and strictures (29). The sonographic examination should include Doppler imaging of the testicle; abdominal sonography may also be useful.

More recent studies, mostly in men with persisting hematospermia, have shown that computed tomography (CT) or magnetic resonance imaging (MRI), particularly with an endorectal coil, is indispensable (26, 30). With the aid of MRI one can not only identify and localize, for example, cysts or calcifications of the male adnexa, but also often differentiate between recent and older bleeding. Moreover, there are clear indications that MRI may be helpful in detecting prostate cancer (31).

In a retrospective analysis of 88 men with persisting hematospermia (>6 months), MRI identified a morphological correlate as cause of the bleeding (volume or signal increase of the male adnexa in the form of cysts). The diagnosis was confirmed by urethral vesiculoscopy in all cases (12).

Cystoscopy is indicated to locate the exact site of the bleeding. By this means, urethral disorders such as strictures, anomalies, e.g., polyps or stones, prostatic cysts, or vascular anomalies can be detected and, if appropriate, treated under visual control (6, 32). Parallel prostate massage may be helpful in localizing the bleeding source.

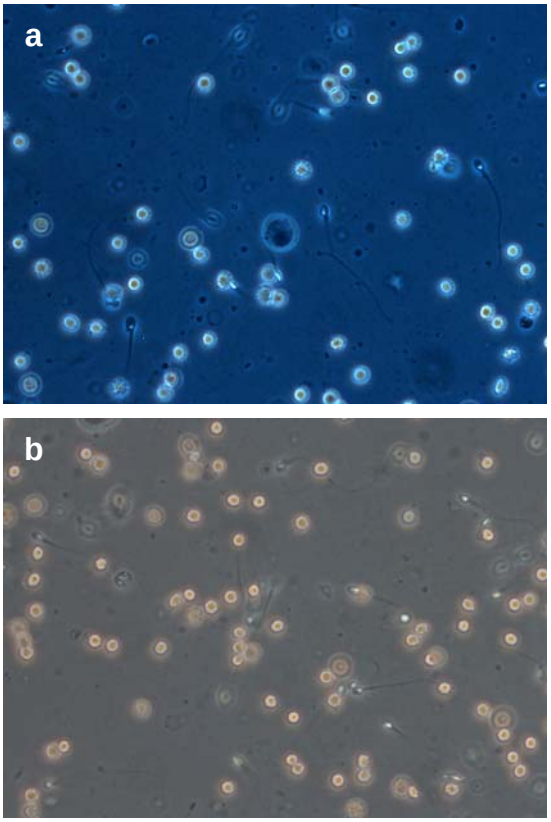


Figure 1: Microscopic images of hematospermia (400× enlargement; unenhanced). a) With filter, b) without filter; reproduced by kind permission of Dr. J. Cremers, Center for Reproductive Medicine and Andrology, University Hospital Münster

Treatment

The plan of action in a case of hematospermia is determined by the following factors:

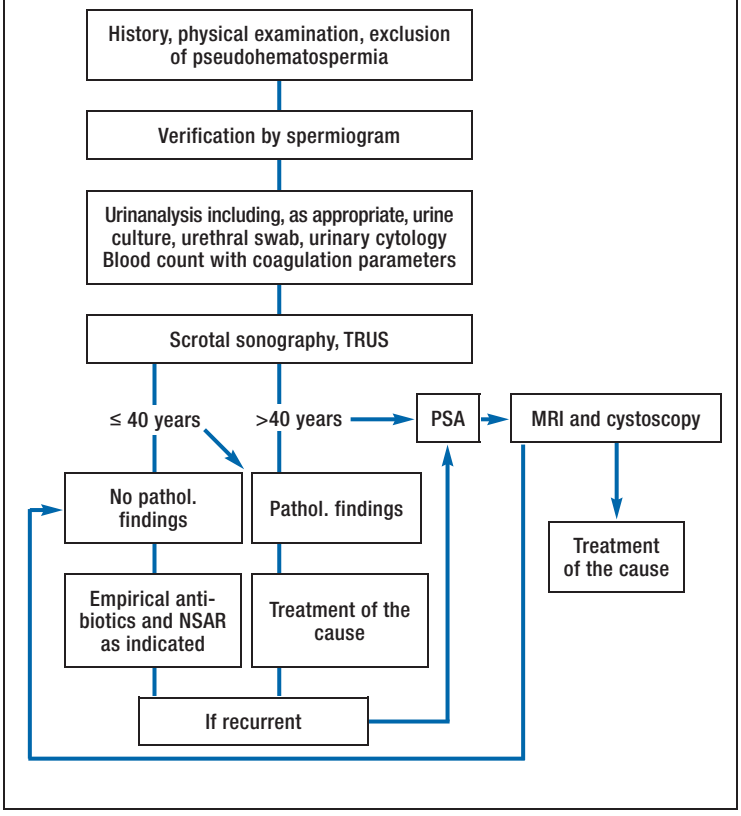
- The extent and duration of the hematospermia
- The patient's age
- The accompanying symptoms.

The patient should first be reassured that in most cases of hematospermia, particularly under 40 years of age, there is no serious underlying disease. Patients under 40 with a single instance of hematospermia can therefore be investigated by means of history taking, physical examination (external genitals and prostate), urinalysis (urinary status including bacteriology and cytology), sonography of the scrotal contents and the prostate, and routine clinical chemistry (33). Any unusual findings on physical examination should prompt an exhaustive urological work-up. The latter is also indicated in patients with risk factors, i.e., age over 40 years, repetitive or persisting hematospermia, family history of prostate cancer, elevated PSA, or hematuria *(Figure 2)*.

Even after a medical work-up the cause of hematospermia often remains unclear, precluding causal treatment.

Whenever possible, the treatment is tailored to the underlying cause. If vascular anomalies, cysts, polyps, calcifications, or other anomalies are demonstrated,

FIGURE 2



Algorithm for diagnosis of hematospermia: Step-by-step investigation of hematuria in routine practice, modified from (8)
MRI, magnetic resonance imaging; NSAR, nonsteroidal antirheumatic; pathol., pathological; PSA, prostate-specific antigen; TRUS, transrectal sonography

causal treatment, surgical if required, is indicated *(Table 1)*. Empirical treatment may be indicated if the cause of bleeding has not been found. Administration of estrogens or cortisone derivatives, previously described in the literature, lacks a rationale and is not backed up by studies (34).

If infection is suspected but no pathogens have been identified, empirical administration of antibiotics is justified in certain circumstances, provided all potential benefits and risks are considered. In one large but noncontrolled and retrospective study, 165 men with hematospermia were treated empirically with a fluoroquinolone and a nonsteroidal antirheumatic drug (9). In 96 % of cases (n = 159) the hematospermia ceased. Nevertheless, prescription of antibiotics without demonstration of a pathogen needs to be weighed up carefully. In the remaining six cases, further diagnostic investigation identified a definitively benign cause.

After exclusion of STD, an antirheumatic drug plus doxycycline, azithromycin, or a quinolone can be given (8). After identification of the pathogen or a resistogram, infections should be treated according to the test results and guideline recommendations.

Otherwise, the treatment of hematospermia is oriented on the potential causes and includes blood pressure adjustment, further investigation of coagulation, and possibly correction of existing anticoagulant treatment or initiation of uricostatic measures.

Conflict of interest statement
The authors declare that no conflict of interest exists.

Manuscript submitted on 2 June 2016, revised version accepted on 8 December 2016.

Translated from the original German by David Roseveare

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KEY MESSAGES

- The cause of hematospermia often remains unknown even after diagnostic investigation, precluding causal treatment.
- Any unusual aspects of the patient's medical history or abnormalities on clinical chemistry or physical examination should prompt an exhaustive urological work-up.
- If vascular anomalies, cysts, polyps, calcifications, or other anomalies are demonstrated, causal treatment, surgical if required, is indicated.
- If infection is suspected but no pathogens have been identified, administration of antibiotics is justified in certain circumstances, provided all potential benefits and risks are considered.

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