Review: doi: 10.37072/JCS.2022.01.04

THE MICROBIOME OF SEMINAL FLUID

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Abstract

The microbiome of semen is a field of increasing scientific interest. Compared to other body sites, the seminal microbiota has been minimally investigated.

Recent studies indicate that presence of bacteria in semen is relatively frequent, including in fertile individuals with normal sperm parameters. Semen has a unique microbiome.

The seminal microbiome encompasses a metabolically and phylogenetically diverse group of microorganisms. The host immune system may play a crucial role in the dynamics of the semen microbiota. The reproductive microbiome may have an important role in sexual conflict.

A dysbiotic microbiota composition may have an influence on sperm quality. The simple presence of bacteria in semen samples may compromise sperm quality.

The bacteria reportedly in seminal fluids include Peptoniphilis, Anaerococcus, Finegoldia, Peptostreptococcus spp., Staphylococcus, Streptococcus, Corynebacteium, Enterococcus, Lactobacillus, Gardnerella, Prevotella, and Escherichia coli.

This review discusses the microbiome of seminal fuid, the link between semen microbiome dysbiosis and male infertility.

Keywords:

microbiota, semen, microbiome, bacterial communities, male infertility, reproduction

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Infertility has become an important health issue worldwide. Microbiota have been suggested to also play a role in this context.

In particular, while several studies have been carried out focusing on the female reproductive system, less is known about male microbiota and its influence on reproduction and fertility. In particular, alterations of the seminal microbiome have been associated with some sperm features (1-4).

Nevertheless, few studies have been carried out to date to deeper investigate semen microbiome origins and functions, and its correlations with the partner's reproductive tract microbiome (5,6).

Compared to other body sites, the seminal microbiota has been minimally investigated. The host immune system may play a crucial role in the dynamics of the semen microbiota. Semen is grey opalescent fluid which consists of suspension of spermatozoa in seminal plasma.

It is made up of the secretions of all accessory glands of the male genital tract as well as testicular component. It also clarified that the seminal fluid is actually different from the sperm.

Semen quality and quantity are both measures of fertility and can be classified as asthenozoospermia, oligoasthenozoospermia, severe oligoasthenozoospermia, and azoospermia.

Male semen, being a mixture of sperm and secretions of sexual accessory glands, containing nutrients (such us lipids, proteins, glycans and inorganic ions), is an ideal environment for microbe growth. The seminal microbiota may originate from the upper genital tract.

The most recognized hypothesis is that the seminal microbiome may have a combined multiple origin from different urogenital tissues and from the gut, mouth, blood and vagina.

While in the past it was thought that the presence of bacteria in the semen was a sign of infection, the use of next generation sequencing-based approaches has revealed that the human semen is not sterile and hosts a specific microbiota.

Certain bacteria, fungi, viruses, and parasites are known to interfere with reproductive functions in both sexes, and infections of the genitourinary tract account for 15% of male infertility cases.

The male seminal microbiota has been suggested as an important factor able to influence couple's health and pregnancy outcomes, as well as offspring health. In addition, currently the origin of this microbiota is still unclear (Fig,1).

Recently, microbiota have been characterized in both female vagina and male semen with the use of culture-independent methods. Semen has been found to serve as a medium for the transmission of bacteria and viruses between men and women, contributing to the development of sexually transmitted diseases (STDs).

Moreover, certain bacteria, fungi, viruses, and parasites are known to interfere with reproductive functions in both sexes, and infections of the genitourinary tract account for 15% of male infertility cases. However, multiple statistical tests showed a significant

negative association between sperm quality and the presence of Anaerococcus.

This paper summarizes data on the male reproductive system microbiome and its changes in infertility.

The seminal liquid is produced like this: the testicles produce millions of sperms every day. Sperms mature and are stored in the epididymis. When the man ejaculates, the sperms are pushed through the seminal ducts.

Sperms are transported to the prostate and seminal vesicles. Sperms are mixed with liquid. Together, the liquid and the sperms form the seminal fluid. The seminal fluid is expelled from the penis through the urethra.

A negative association between sperm quality and the presence of seminal dysbiosis has been reported.

Infections and consequent inflammation in the male reproductive tract may compromise spermatogenesis and sperm cell function. The relationship between the presence of pathogenic microorganisms in the reproductive tract and infertility is widely documented.

To date, the functions of this resident microbiota in maintaining a healthy status in men have not been completely understood, and it seems that these men microbiota could be involved in immune system reactions (7).

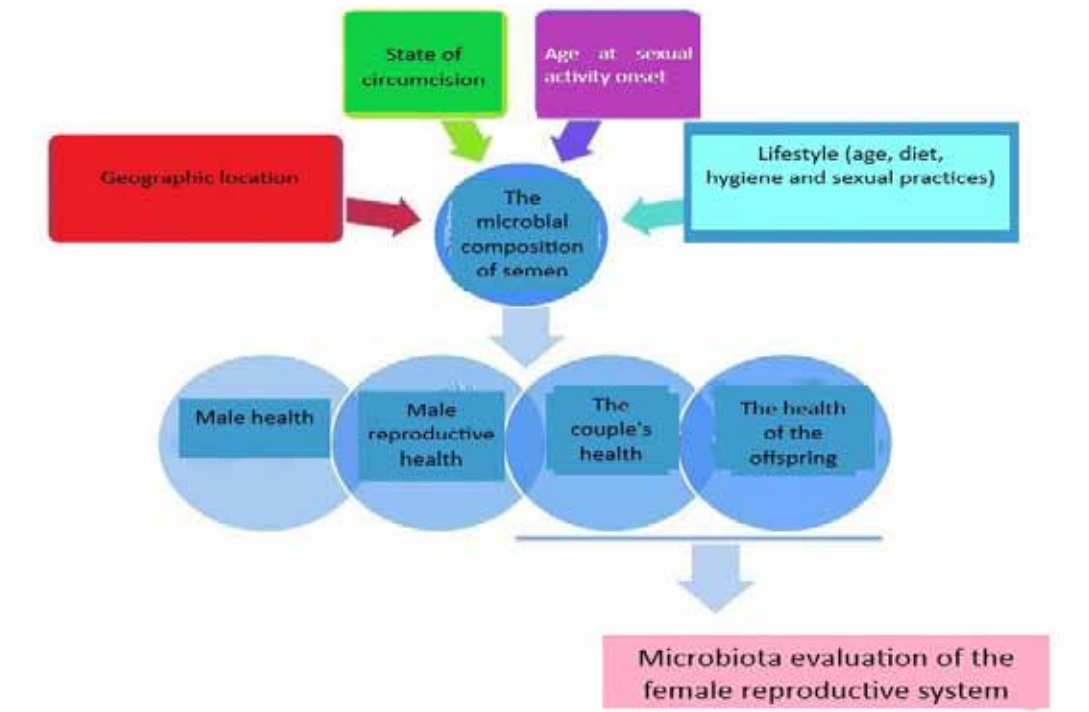

Fig. 1 Individual variability factors affecting semen microbiota composition and processes in which semen microbiota has been suggested to play a role(2)

Several kinds of microorganisms found in the male urogenital tract are associated with sperm abnormalities, especially aberrant motility, deficient mitochondrial function, and loss of DNA integrity.

Semen has been found to serve as a medium for the transmission of bacteria and viruses between men and women, moreover, certain bacteria, fungi, viruses, and parasites are known to interfere with reproductive functions in both sexes.

Recent studies have demonstrated that microbiota exist in seminal plasma. The bacterial diversity in semen samples of healthy and infertile men were characterized by pyrosequencing the V1-V2 region of 16S rRNA genes that had been amplified from total genomic DNA isolated from each sample.

The use of 16S rRNA gene sequence data in studies of bacterial diversity have been used to describe the species composition of various communities, including those in the human gastrointestinal tract, skin, and oral and urogenital tracts.

There are a variety of organisms proposed to be part of seminal microbiome (Lactobacillus, Veillonella, Streptococcus, Porphyromonas and Atopobium), which draws nutrition from seminal fluid rich in Fructose.

The seminal fluid microbiome is influential of metabolism. For example, P. acnes, Streptophyta spp, Corynebacterium spp, Pseudomonas veronii, and Acinetobacter spp. are positively associated with significant amounts of metabolic pathway changes in the seminal fluid.

Therefore, it is important to understand the bacterial species composition of seminal fluids. Other bacterial species in semen have been previously shown to be present in the urethra and the skin of the penis.

The presence of Anaerococcus might be a biomarker for low sperm quality. Prevotella relative abundance was increased in samples with defective sperm motility.

Moreover, bacteria may have a direct negative impact on spermatozoa physiology, reducing viability or motility but the true impact of bacterial infections on male fertility remains controversial.

This paper reports the state of the art regarding the male reproductive system microbiome and its alterations in infertility.

The microbiome has huge potential to influence human physiology, both in health and in disease.

The seminal microbiome has important implications for the reproductive health of men, the health of the couple and even the health of offspring, owing to transfer of microorganisms to the partner and offspring (4).

Lactobacilli have been reported in normospermic samples and are known to positively influence the vaginal ecosystem (8).

The presence of Anaerococcus might be a biomarker for low sperm quality (9).

Bacteria are present in semen samples of men and can be transmitted to their female sexual partners, but it is unclear whether these bacteria originate from colonies established in the seminal vesicles or elsewhere in the male reproductive and urinary tract systems (10).

Recent studies indicate that presence of bacteria in semen is relatively frequent, including in fertile individuals with normal sperm parameters (11).

The host immune system may play a crucial role in the dynamics of the semen microbiota, since its activation during infections is related to significant changes in the microbiota composition (12).

Given the limited number of studies, it is still unclear whether the presence of specific bacterial communities has the potential to influence sperm function.

It was also observed that samples with normal morphology were significantly enriched with Lactobacillus genus.

Although bacteriospermia was previously considered to be negatively associated with fertility, recent studies indicate that presence of bacteria in semen is relatively frequent, including in fertile individuals with normal sperm parameters

Lactobacilli have been previously reported in normospermic samples and are

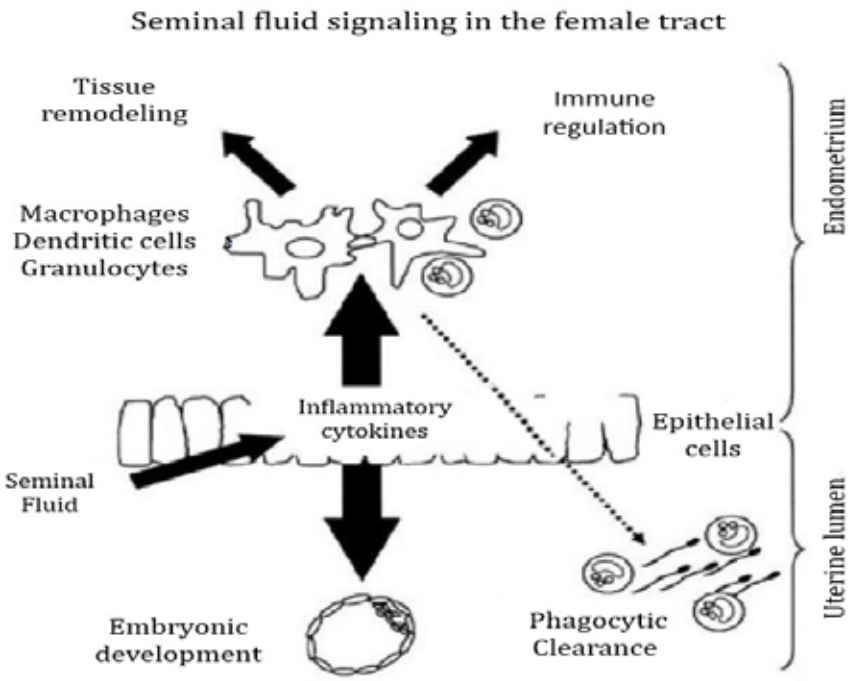

Fig. 2 Schematic diagram illustrating the actions of seminal fluid in the female reproductive tract (17)

known to positively influence the vaginal ecosystem (8).

In addition, exposure of spermatozoa to lactobacilli has been shown to have a positive effect on motility and viability (13).

These observations are in agreement with previous culture-dependent studies, in which normospermic microflora was associated with the presence of Gram-positive bacteria (lactobacilli, coagulase-negative staphylococci, streptococci) (10).

Regarding Corynebacteriaceae, it has been consistently defined as a natural component of seminal flora in humans (14. Other authors state that they are commensal bacteria that can become pathogenic when the flora unbalances or when there is a high activity of caspases (14-16), (Fig,2).

Ejaculate microbes can also influence competitive fertilisation success indirectly by triggering differential immune responses in the female reproductive tract, with sperm being collateral damage of the female immune attack on inseminated bacteria (18,19), (Fig3).

The sperm and seminal fluid are produced continuously. They don t run out. And to have a good sperm count, you need to live healthy, eat well, exercise, and drink lots of water.

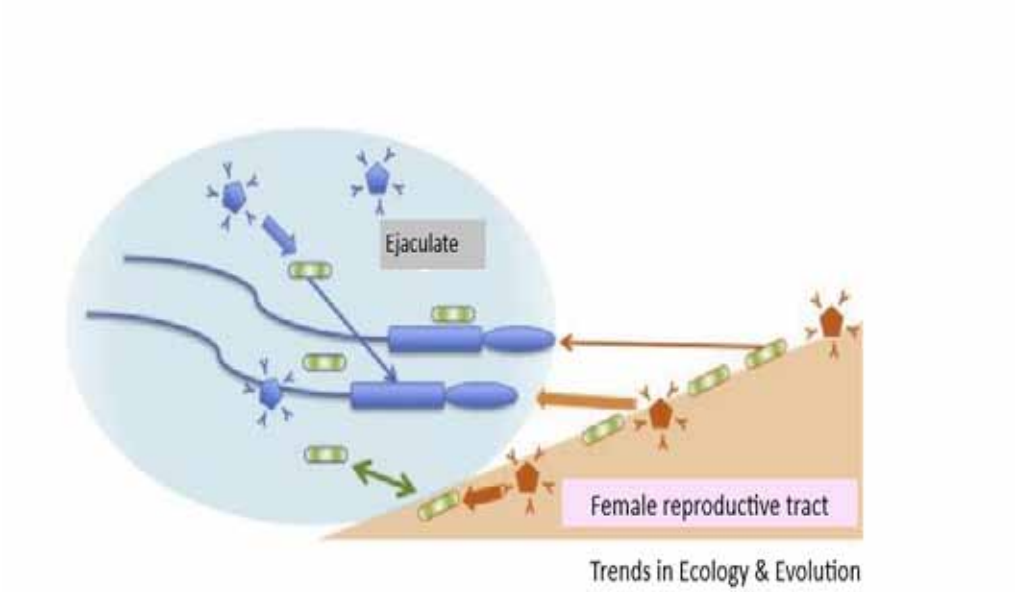

Fig. 3 Potential impact of reproductive microbes on sperm function and the dynamics of fertilisation (19)

The present study, along with several earlier studies, confirmed that there were high numbers of bacteria present in semen (9).

In humans, Valcarce et al. assessed that a 6-week supplementation with Lactobacillus and Bifidobacterium improved sperm motility and reduced the percentage of sperm DNA fragmentation in asthenozoospermic males (20).

Maretti et al. verified that the daily administration of Lactobacillus paracasei, arabinogalactan, fructo-oligosaccharides, and l-glutamine over a period of 6 months ameliorated sperm count and motility, and reduced the rate of atypical forms, in comparison to the placebo-receiving group (21).

Compared to its female counterpart (23), the microbiota of the male genital tract has not been studied extensively.

In several circumstances, male infertility has been linked to bacterial infections of the genital tract, which might cause inflammation of tissues, obstruction of genital ducts, epididymitis and orchitis among others. Moreover, bacteria may have a direct negative impact on spermatozoa physiology, reducing viability or motility (22).

It remains unclear if the microorganisms found in semen necessarily signify infection and significantly contribute to male infertility. Study of the seminal microbiome is still in its infancy, and further well-designed, large-cohort, functional studies are required.

Although they have provided important insights into the microbiology of semen, they are limited because many species of bacteria are recalcitrant to cultivation.

Further studies are required to challenge this finding and develop potential strategies to induce the formation of a healthy seminal microbiota.

Conclusion

Alterations in the bacterial composition of semen have been linked to a variety of disorders, including subinfertility and poor semen quality, prostatitis.

Male reproductive tracts are not sterile and that the male reproductive tract harbors a large number of bacteria. Thus, semen microbiome dysbiosis may lead to diseases.

A dysbiotic microbiota composition may have an influence on sperm quality.

Conflict of interest

The author declare no conflict of interest

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