INVESTIGATING THE ROLE OF GUT AND REPRODUCTIVE TRACT MICROBIOMES IN HUMAN INFERTLITY

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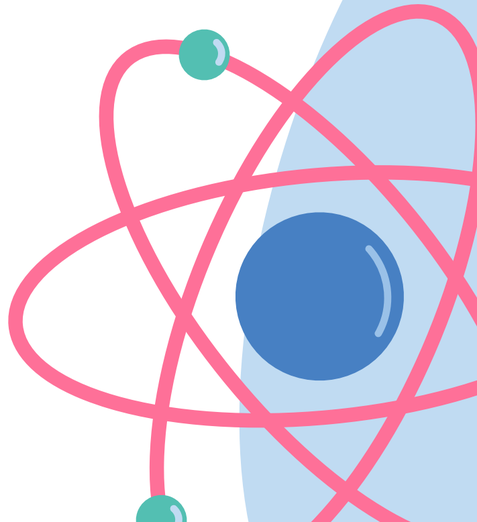
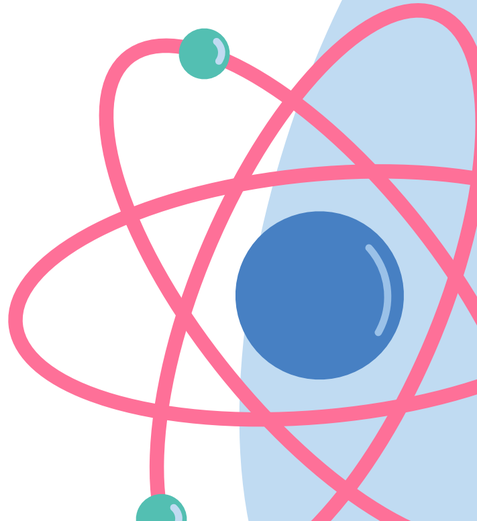


INTRODUCTION



infertility

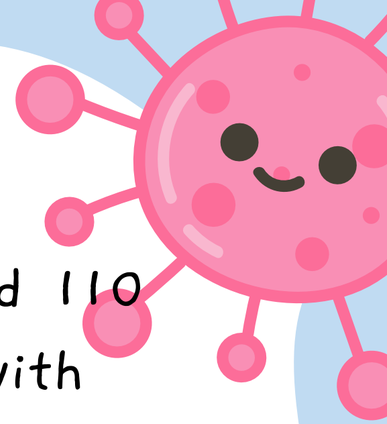
The desire for parenthood is universal, but infertility affects about 1 in 6 people worldwide, causing significant physical, mental, and social challenges. **Infertility is defined as the inability to achieve pregnancy after one year or more of regular, unprotected intercourse.**

It can be

Primary infertility: Never achieving pregnancy.

Secondary infertility: Difficulty conceiving after a previous pregnancy.

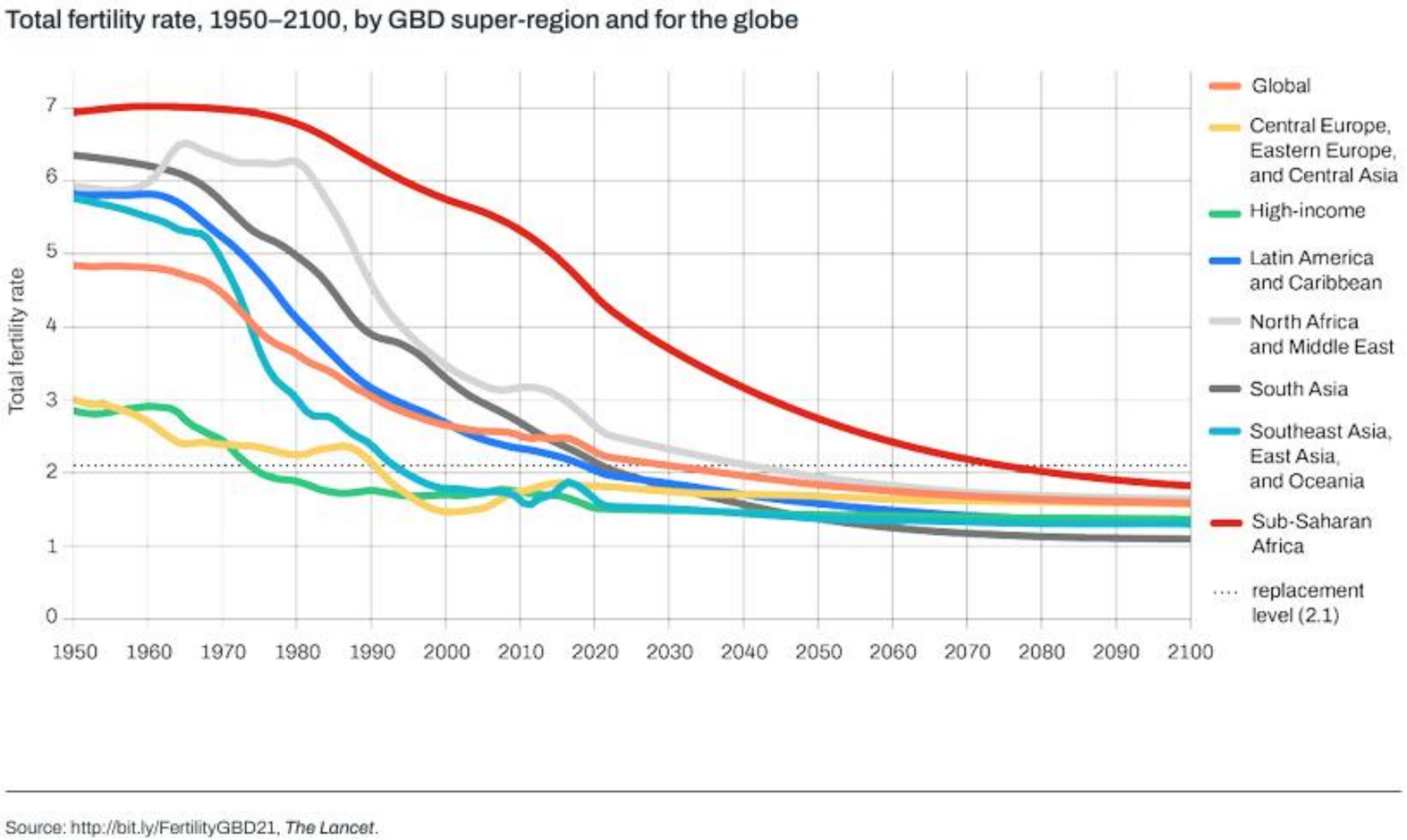
- Causes are both preventable (e.g., lifestyle habits, infections) and unpreventable (e.g., age-related decline, genetic factors).
- **Women are often affected earlier due to a fixed number of oocytes that decline in quality and quantity after age 32, with a rapid decrease after 37.**
- Female infertility is commonly linked to ovulatory disorders, endometriosis, and tubal issues.
- Male infertility is often due to testicular defects, low sperm quality, and hormonal imbalances.
- **The global prevalence of infertility has risen over recent decades, with India among the countries most affected.**
- Infertility leads to social stigma, mental health issues, and financial strain.
- Addressing infertility is crucial for upholding reproductive rights and achieving global health and gender equality goals (SDG 3 and SDG 5)



- In the year 2021, 55 million males (1.8% of the male population) and 110 million females (3.7% of the female population) globally were living with infertility.
- Global prevalence of infertility among the reproductive age group from 1990-2021 was approximately twice as high in women as compared to men. But as the infertility burden increases, male infertility will be projected to grow more rapidly than females from 2022-40.
- The highest infertile age group was 35- 39 years.
  (https://pubmed.ncbi.nlm.nih.gov/39752330/)

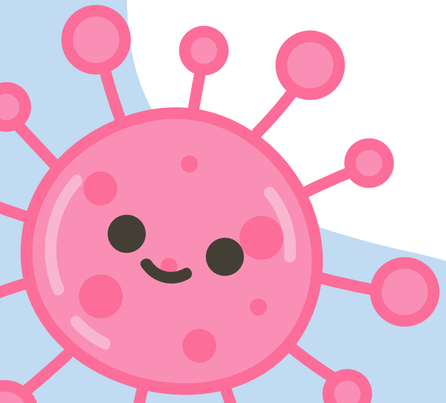
- According to IHME fertiltiy rate by 2100 expected to fall below replacement level (2.1) in 97% of countries and territories
  https://ghdx.healthdata.org/record/ihme-data/global-burden-disease-study-2021-gbd-2021-fertility-1950-2100

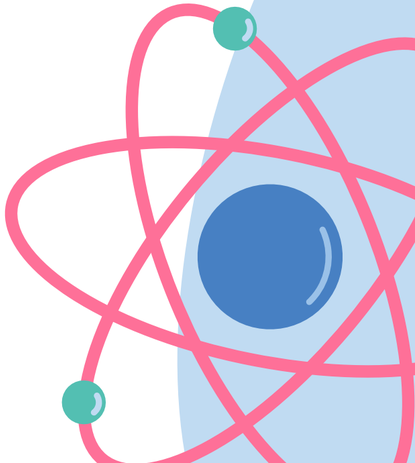
Total fertility rate, 1950–2100, by GBD super-region and for the globe (Adapted from(Highlights Most Countries Will Experience Below-Replacement * Levels of Fertility by Mid-Century, n.d.)

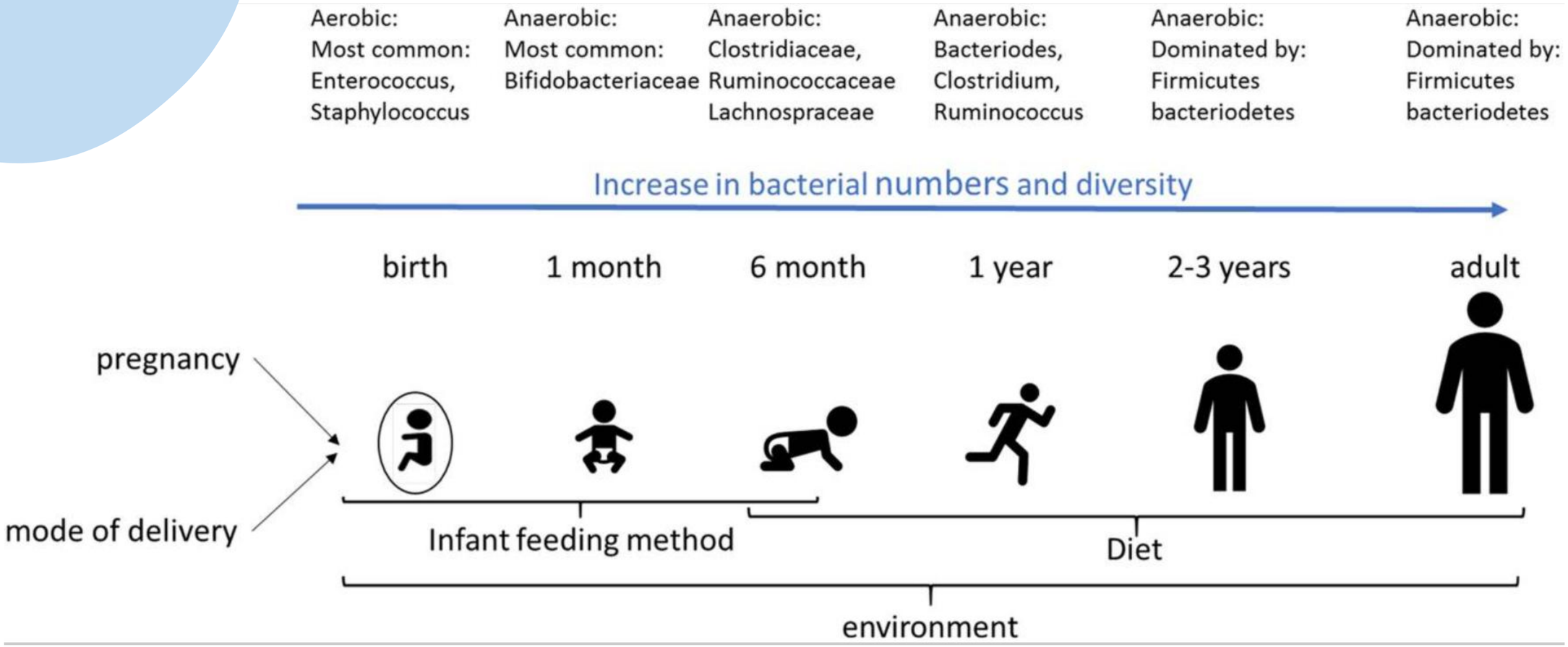


Human Microbiome

- The human microbiome comprises bacteria, viruses, fungi, and protozoa.
- Present in the gut, skin, respiratory, and reproductive tracts and various body sites
- Play essential roles in maintaining health and preventing disease through immune regulation, metabolism, and physiological balance.
- The gut hosts the largest and most diverse microbiome
- Dysbiosis ia an imbalance in microbial composition—can lead to serious conditions such as inflammatory, neurological, autoimmune, cardiovascular, etc diseases
- Microbiome composition varies with age, sex, hormones, and lifestyle factors, and its disruption is linked to multiple health problems

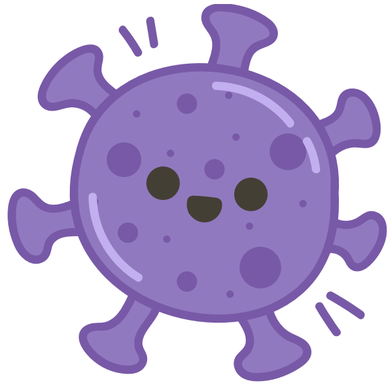






Infant gut microbiome development and its influencing factors. (Adapted from Mohajeri et al., 2018)

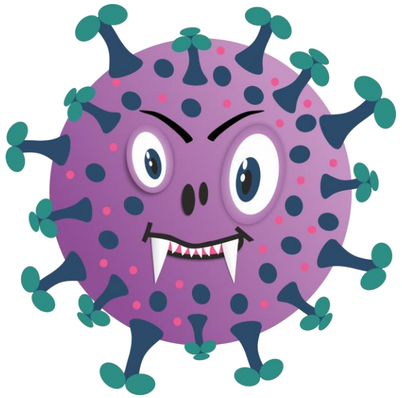
Beneficial gut bacteria



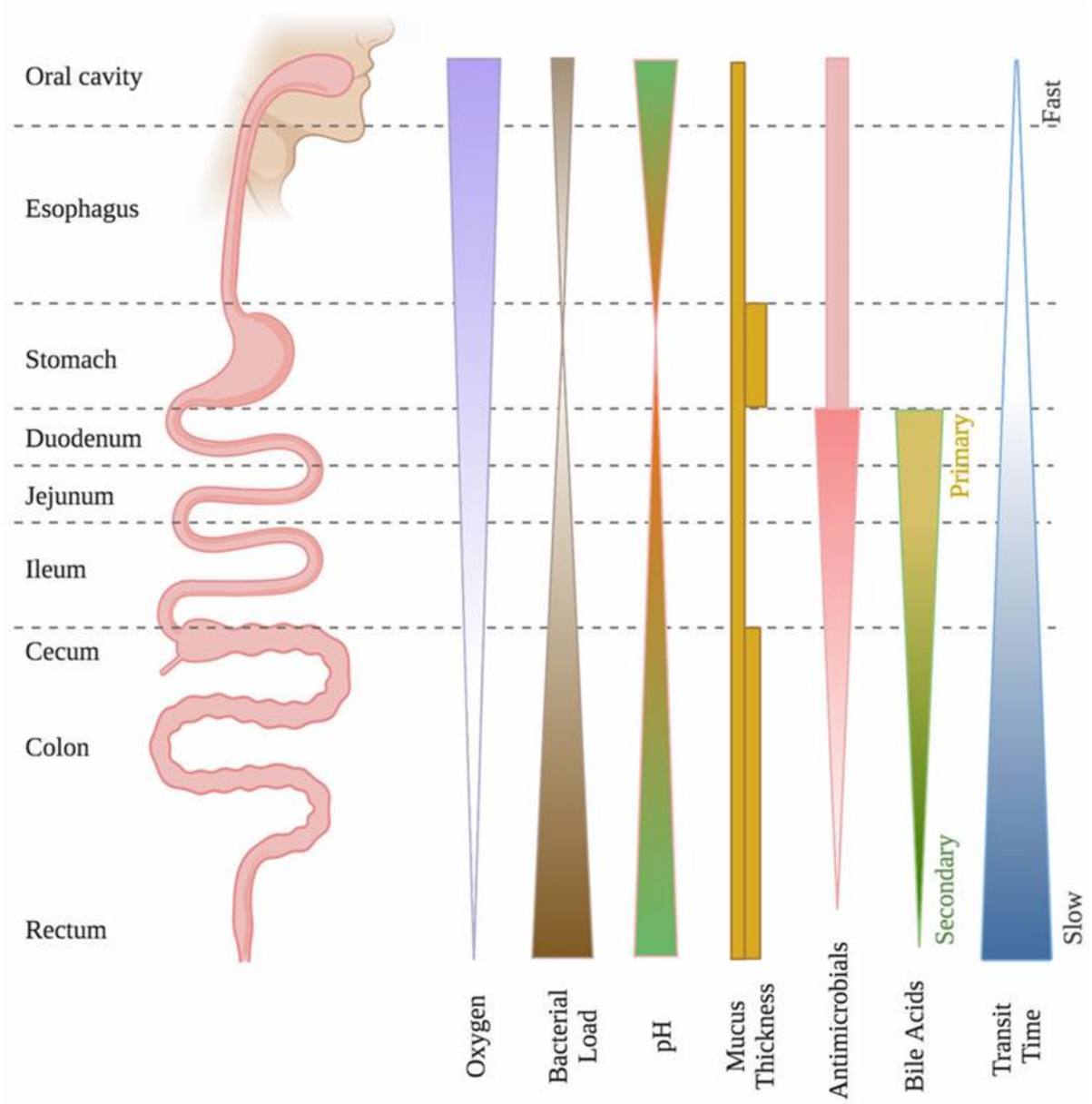
- Bacteroidetes
- Prevotella
- Lactobacillus
- Roseburia
- Eubacterium rectale
- Bifidobacterium
- Enterococcus

vs

Harmful gut bacteria



- Firmicutes
- Proteobacteria
- Mollicutes
- Bacteroides
- Alistipes
- Bilophila
- Enterobacteriacea
- Escherichia
- Klebsiells
- Shigella



Gut loads from Proximal to Distal

These change along the gut

create different environments

that determine

which microbes can live in each section.

(Adapted from Kennedy & Chang, 2020)

Sex selective differences in Gut Microbiome

(Adapted from Ashonibare et al., 2024)

Anaerotruncus

Alistipes

Bacteroides

Bifidobacteriaceae

Clostridia

Collinsella

Desulfobibrio

Lactobacillaceae

Methanobrevibacter

Phascolarctobacterium

Desulfovibrio

Faecalibacterium

Holdemania

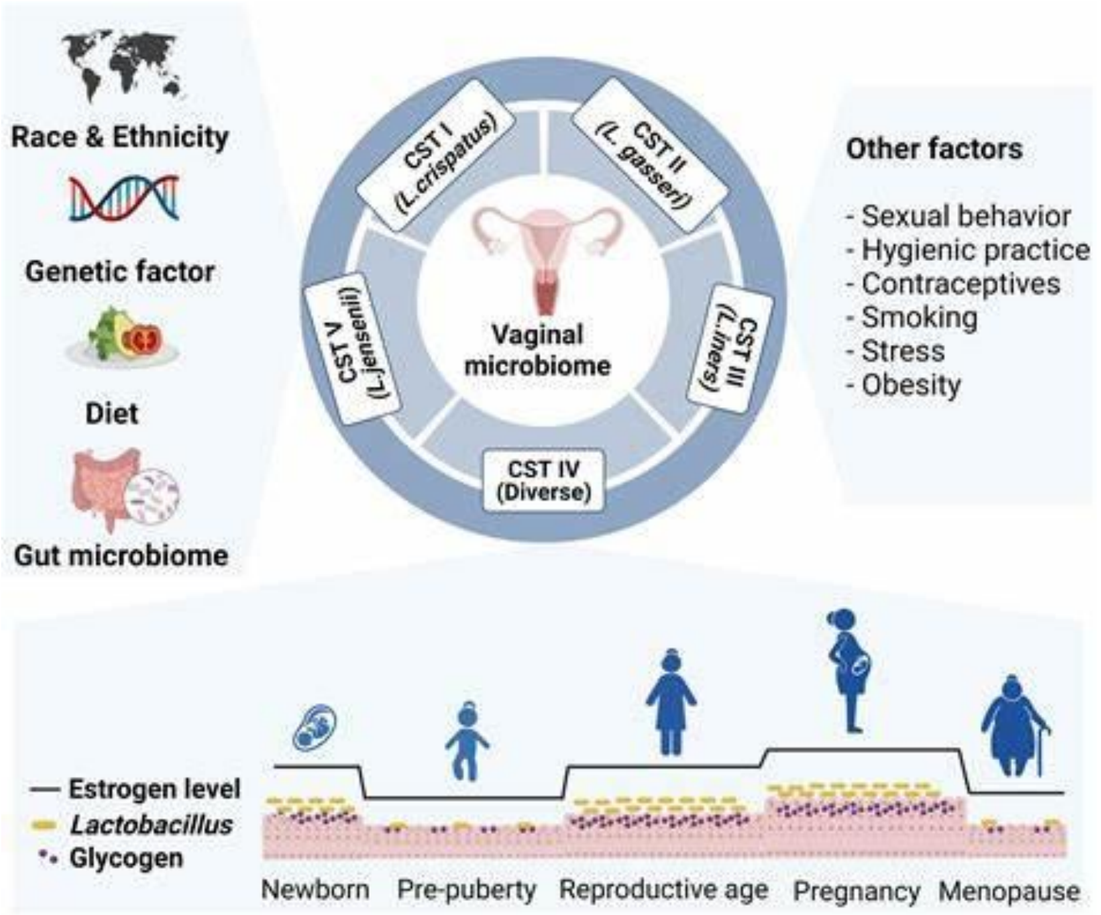
Prevotella

Rikenellaceae

Roseburia

Ruminococcaceae

Vaginal Microbiome

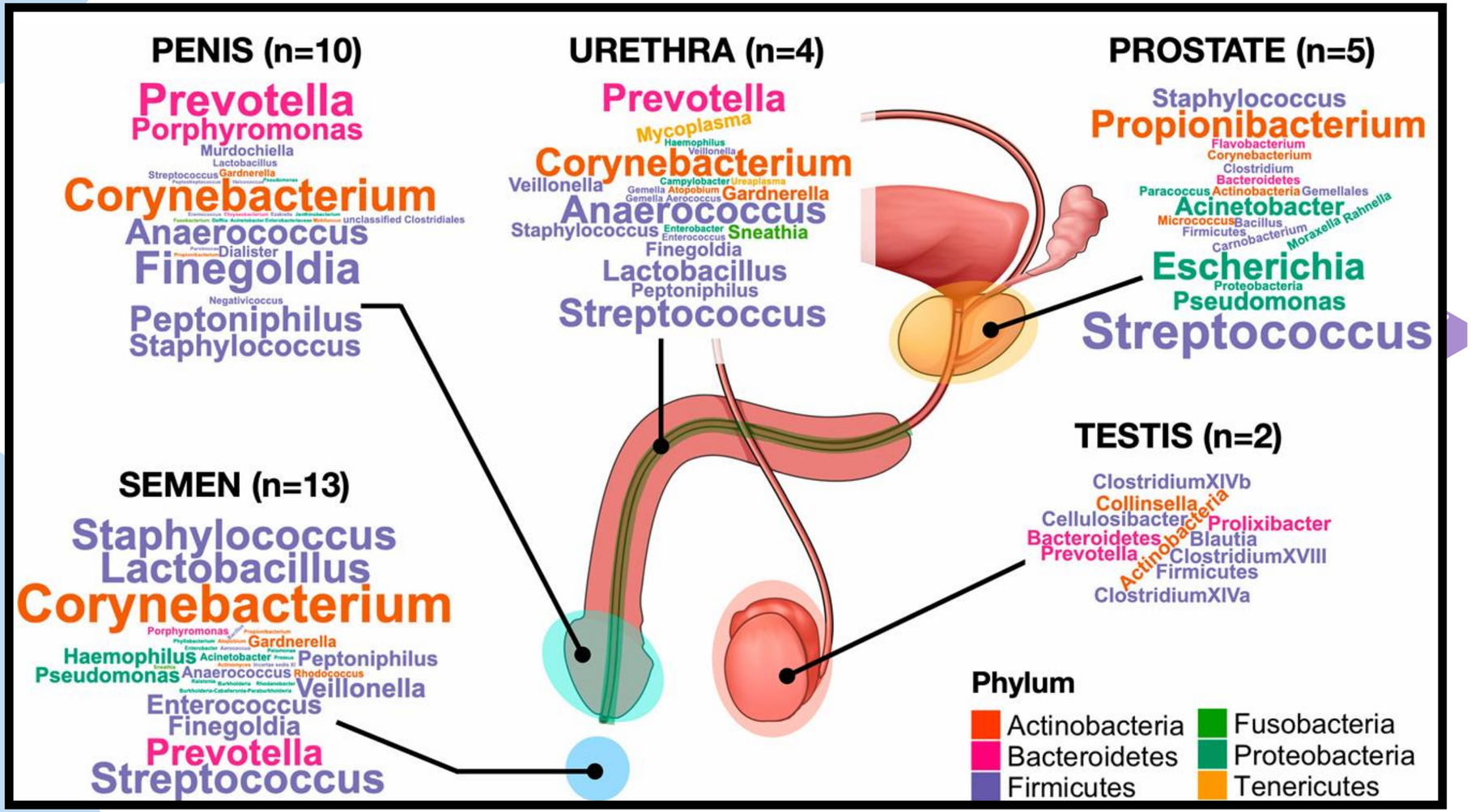


Vaginal Microbiome and factors affecting them, and level of oestrogen, lactobacillus and glycogen with age (adapted from Kwon & Lee, 2022)

Impact of Hormonal and Glycogen Changes on Vaginal Microbiome Composition Across Life Stages and Pregnancy

Life Stage / Pregnancy Stage	Hormonal/Glycogen Status	Vaginal Microbiome Composition / Changes
Newborns (early days)	High maternal oestrogen, high glycogen	Adult-like glycogen; Lactobacillus not yet dominant
Prepubertal Girls	Low oestrogen and glycogen	Dominated by Staphylococcus epidermidis, E. coli, Peptococcus
Reproductive Age Women	High oestrogen and glycogen	Dominated by Lactobacillus species (healthy CSTs)
Postmenopausal Women	Decreased oestrogen and glycogen	Low Lactobacillus abundance, high microbial diversity (often CST-IVA)
First Trimester (Pregnancy)	Rising oestrogen, progesterone	Similar to non-pregnant women
Second Trimester (Pregnancy)	High oestrogen and progesterone	Increased Proteobacteria, Actinobacteria; decreased diversity
Third Trimester (Pregnancy)	Low oestrogen and progesterone	Gradual return to pre-pregnancy microbiota

Male microbiome



Microbiome of the male reproductive tract (Adapted from Zuber et al., 2023)

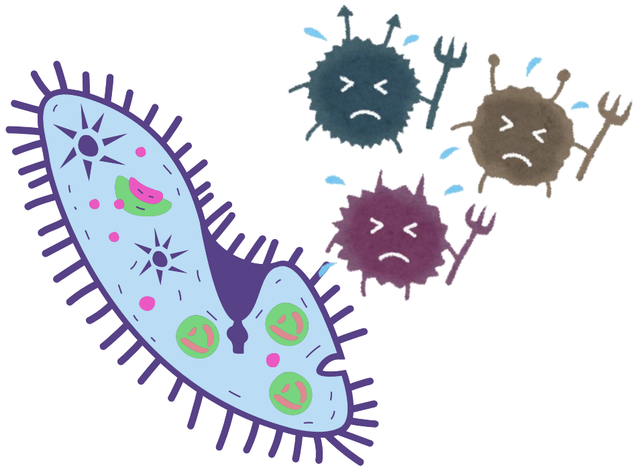
Functions of Gut microbiomes

Metabolic function

SCFA synthesis, Productin of vitamins and polyamines, Enhance mineral absoption, Processing of bile acid, breakdown polyphenols, metabolism of xenobiotic, and Degradation of amino acid and cholins

Defensive function

Competet with pathogens for nutrition and attachment sites, secretion of antimicrobial compounds, stimulation of IgA production, Induction of antimicrobial protein synthesis



Trophic Function

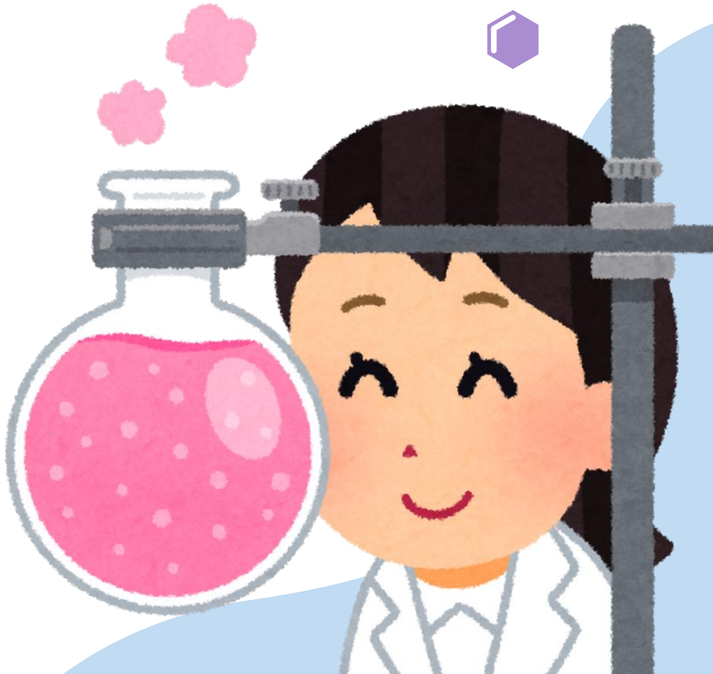
Effects on distant organs such as CNS, liver, stimualtion of peristasis, regulating the development of intestinal epithelium and immune system and its functions, maintenance of intestinal epithelium integrit

16S rRNA

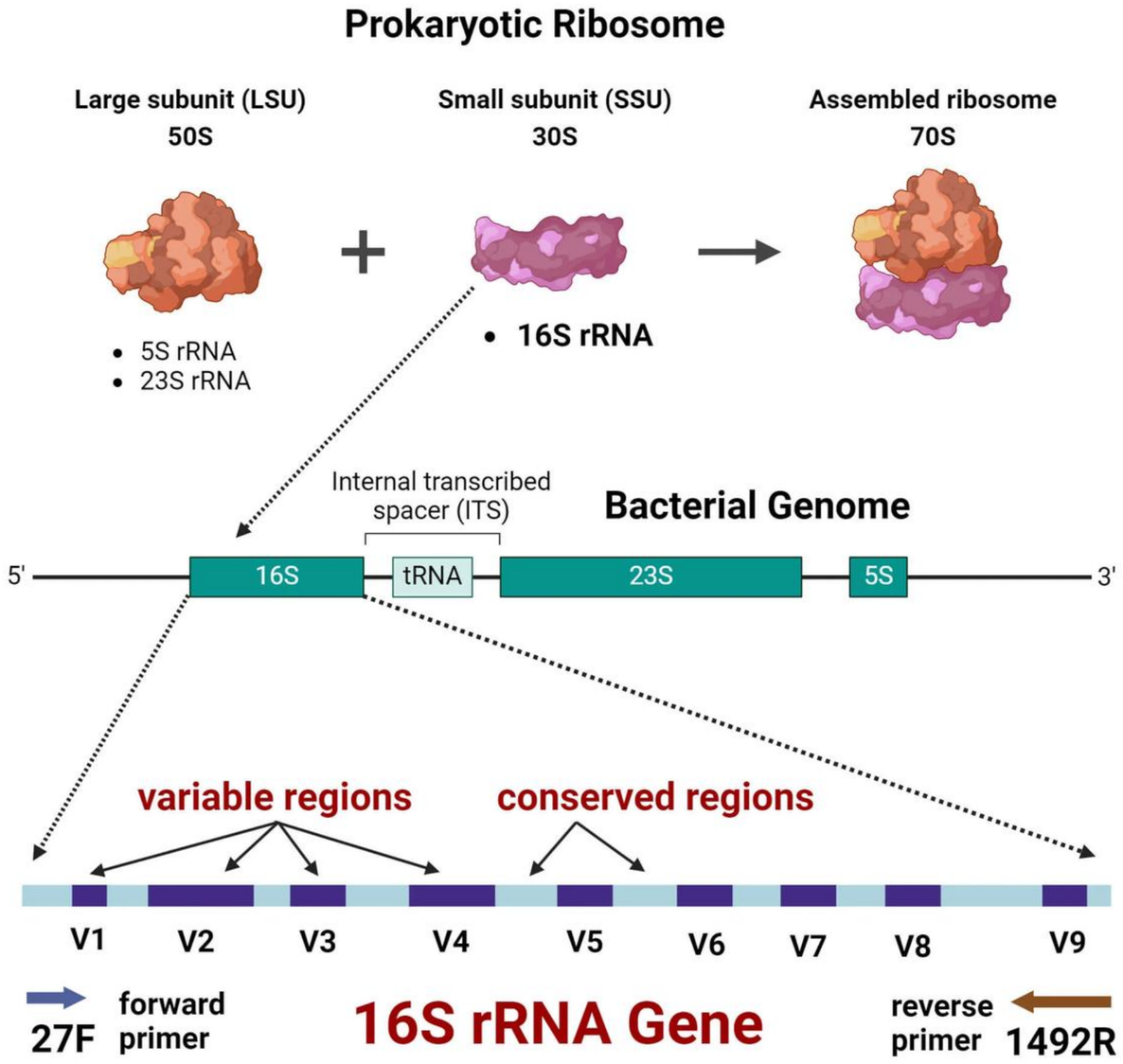
16S rRNA gene sequencing is the most common and an amplicon-based sequencing (amplicon is a piece of DNA or RNA that is the source and/or product of amplification or replication events) method that is used to identify and classify bacteria present in bulk and complex biological sample

16S rRNA is a rapid and most efficient study for the identification of bulk samples, it also identifies the next generation of species.

Ribosomes are biological structures involved in protein synthesis that contain two subunits made up of proteins and ribosomal RNA (rRNA). rRNA translates the information in mRNA (messenger RNA) into the proteins



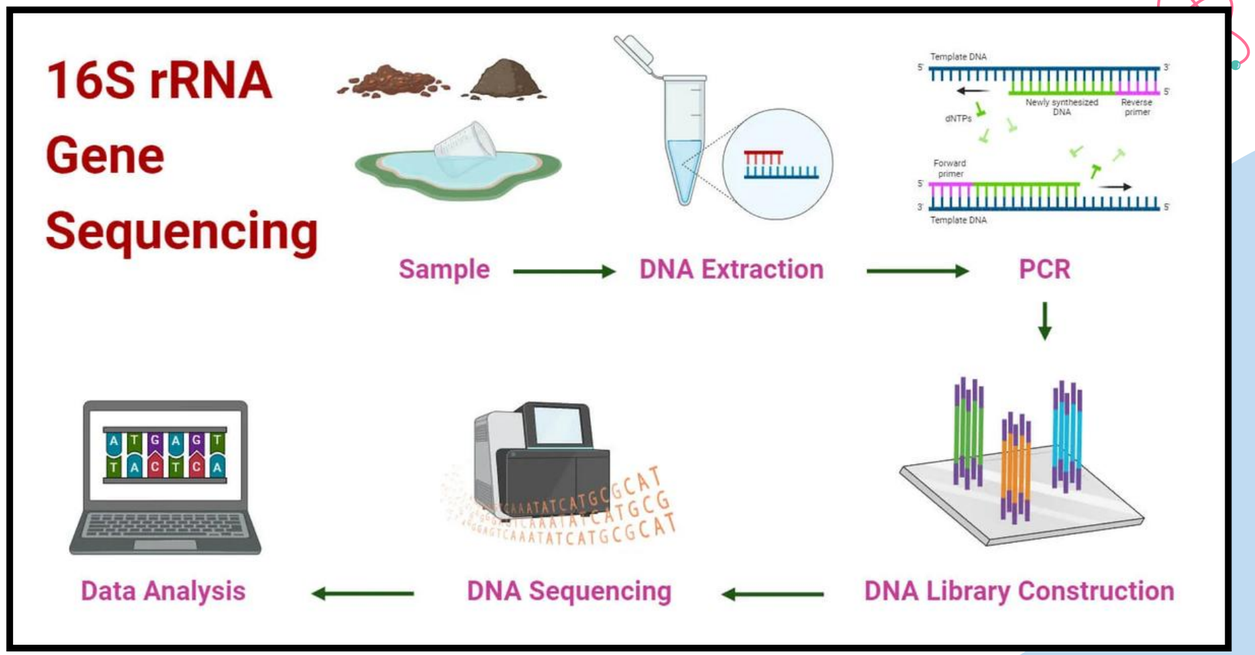
What is 16S rRNA gene?



ribosomes are composed of a 30S subunit and a 50S subunit, which form a complete 70S ribosome. The 30S subunit contains **16S rRNA** and 21 proteins.

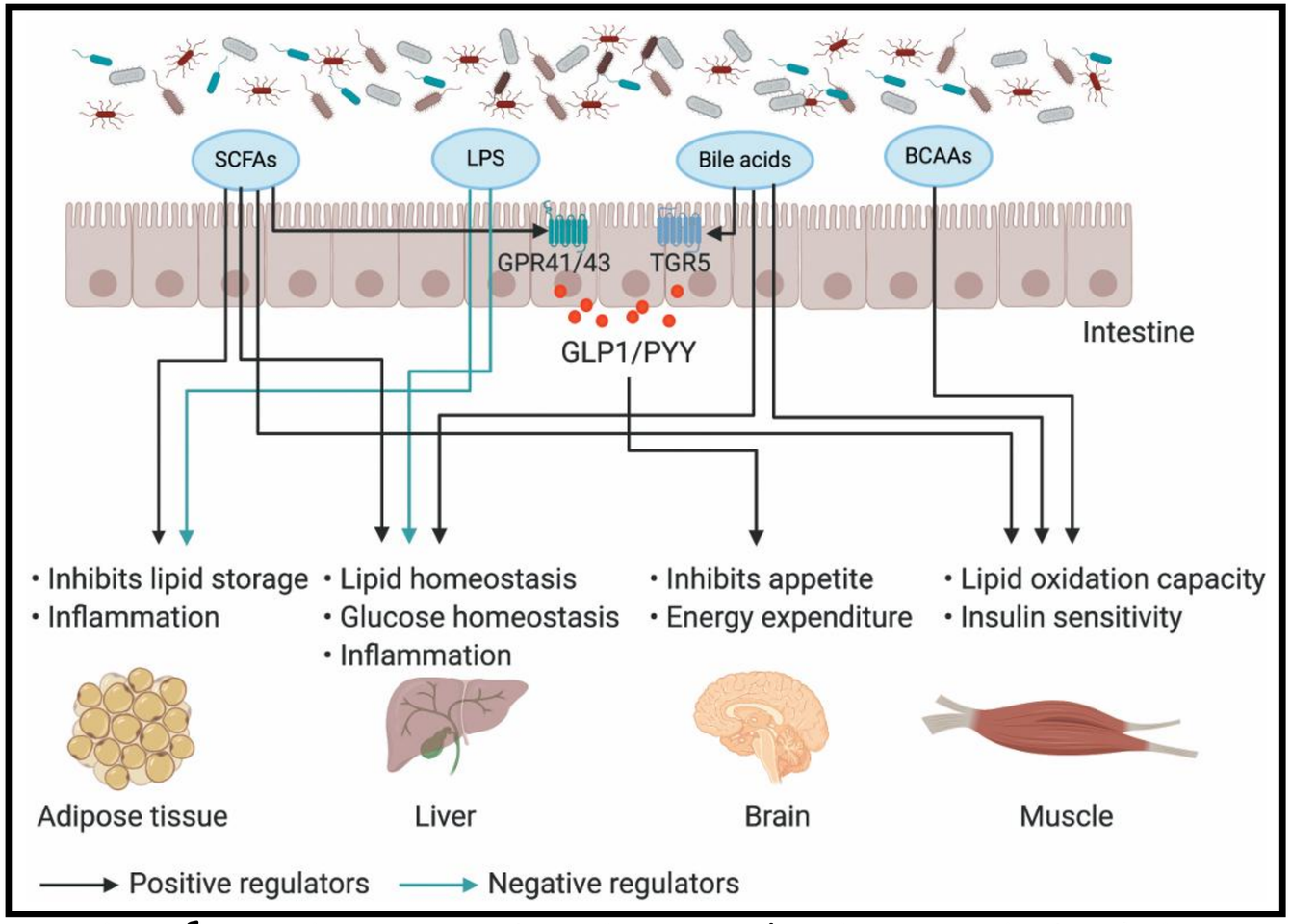
The 16S rRNA gene is about 1500 base pairs (bp) long and contains variable regions scattered between conserved regions.

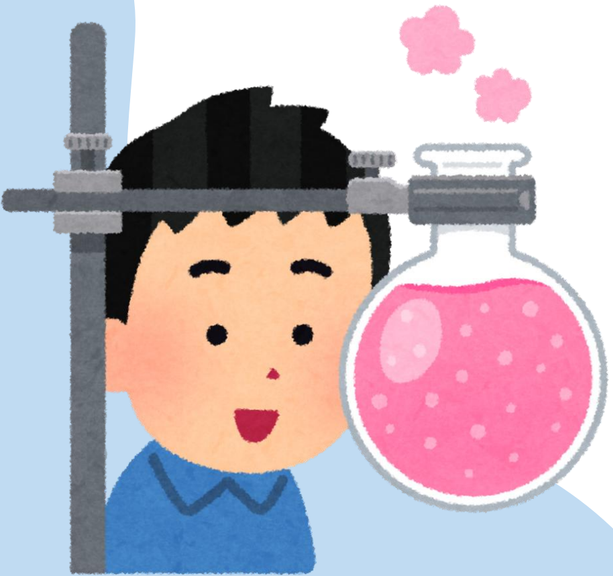
conserved parts are similar in all bacteria; The variable parts are different from one bacterium to another



Adapted from https://microbenotes.com/16s-rrna-gene-sequencing/

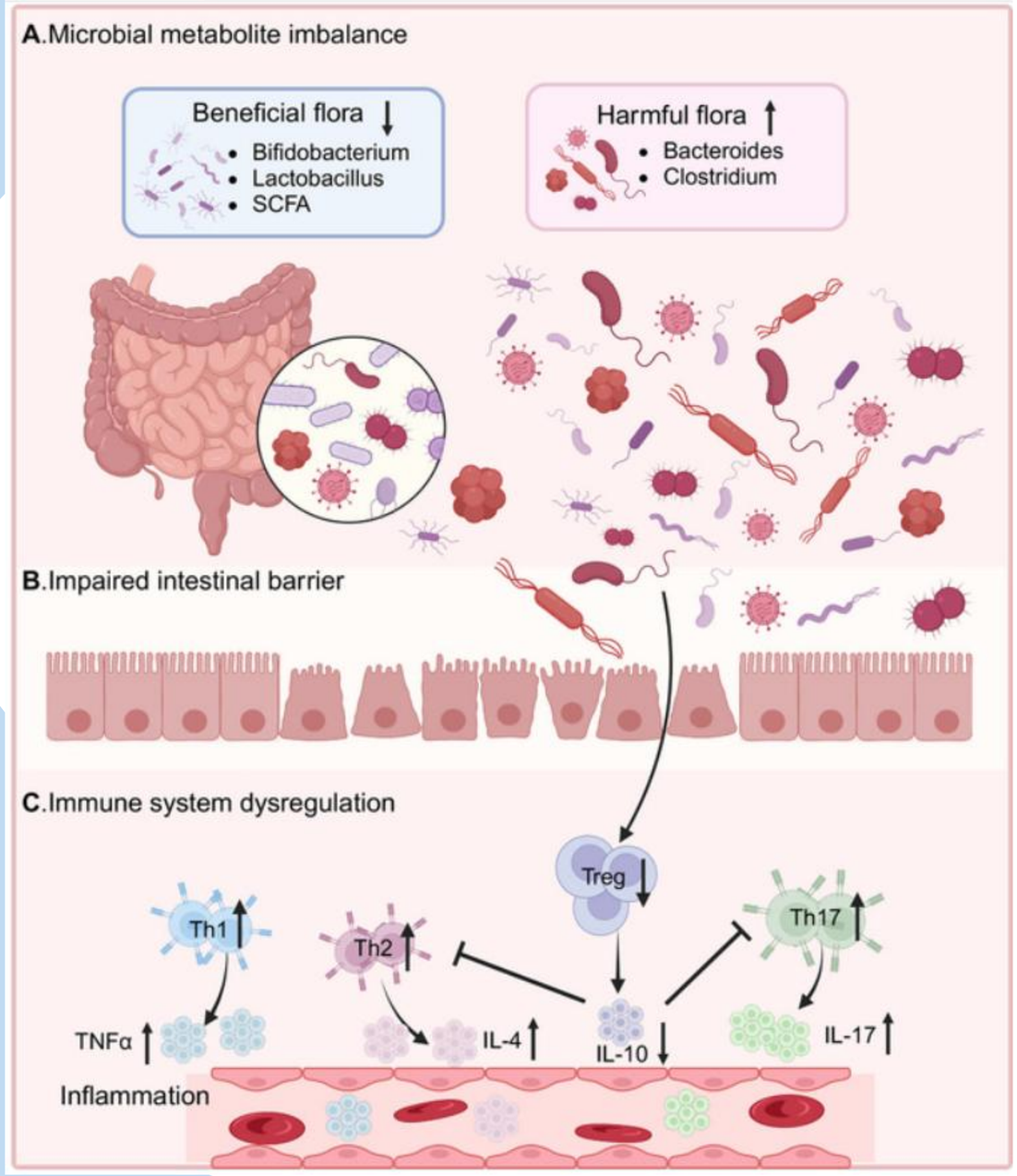
Microbial Metabolites





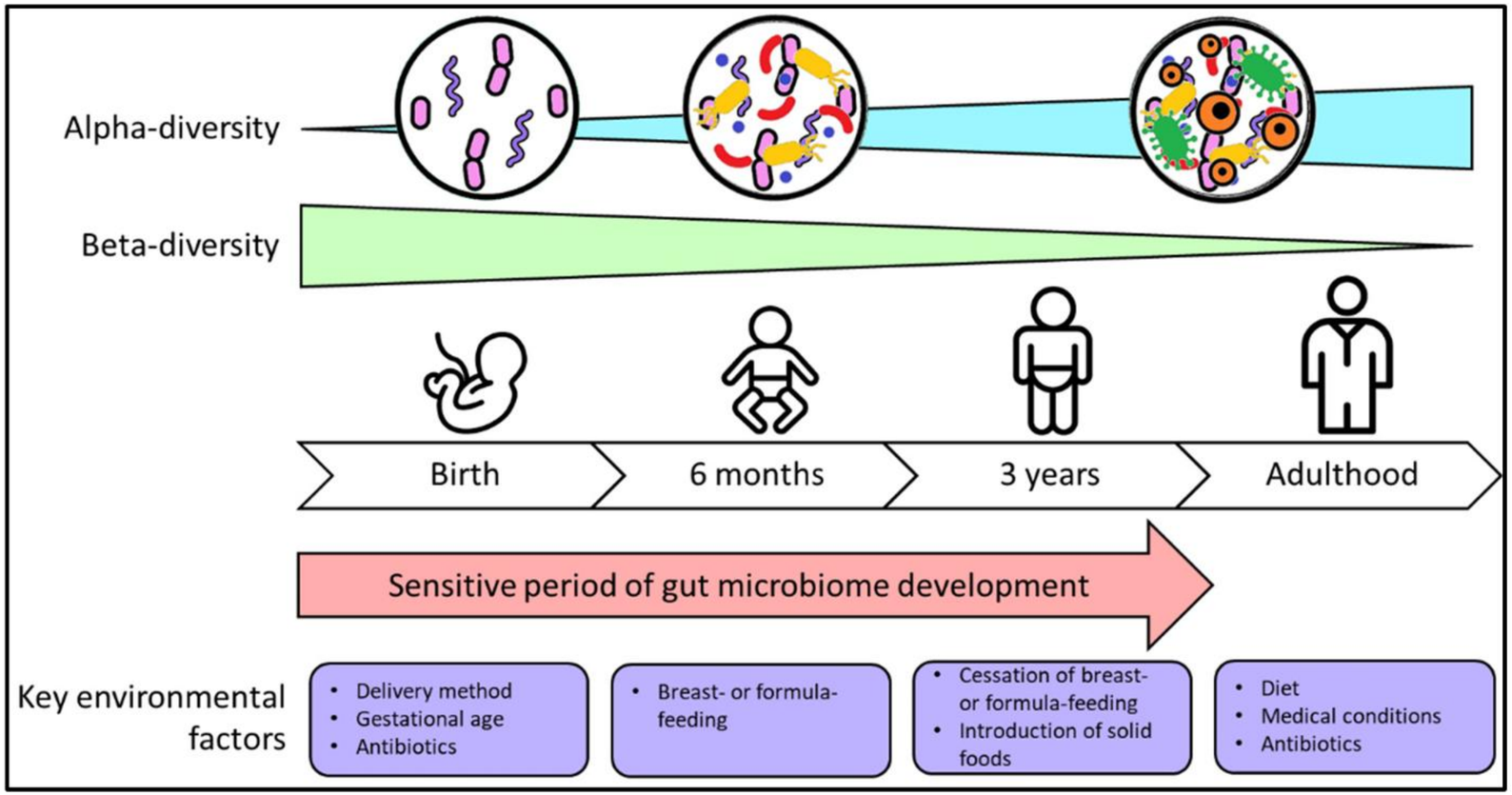
The impact of gut microbiota and its metabolites on organ

Mechanism of Dysbiosis



Gut Microbiome dysbiosis leads to the onset and progression of disease (Adapted from Shen et al., 2025)

Factors causing dysbiosis



- Mode of delivery- (vaginal or caesarean C-section)
- Population differences
- exposure to pets
- Diet
- Lifestyle
- Antibiotic use
- Inflammation
- Genetics

Factors causing dysbiosis from birth to adulthood (Adapted from (Parkin et al., 2021)

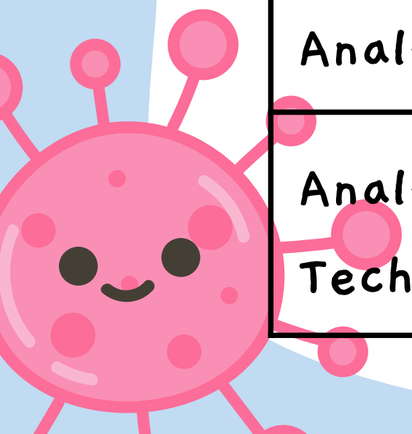
Rationale OF STUDY

Infertility is an escalating public health challenge in India, impacting an estimated 27.5 million couples, according to the ICMR. Despite various diagnostic and therapeutic advancements, there is a large burden of infertility cases. This literature review **aims to critically examine the role of gut and reproductive microbiome impact on infertility.** This review will give new insights that will help in preventing infertility by managing microbes. This not only enhances treatment outcomes but also supports many couples to achieve parenthood and governments to achieve Sustainable Development Goal 3 by 2030, which includes targets as universal access to reproductive healthcare and well-being.

Study objective

To investigate the role of gut and reproductive tract microbiomes in the development, progression, and management of human infertility, with a focus on understanding microbial influence on reproductive health in both males and females.

Study Type	Literature review
Study design	Qualitative, narrative, comparative review
data sources	peer reviewd articles, clinical studies, meta analyses
Inclusion criteria	Studies on microbiome composition, dysbiosis, reproductive outcomes, molecular methods
Exlusion criteria	Non-clinical, non-molecular, non-peer-reviewed, non-English, irrelevant studies
Analysis	Qualitative analysis, Comparative tables, narrative integration
Analytical Techniques	16S rRNA sequencing, meta analysis, systematic review

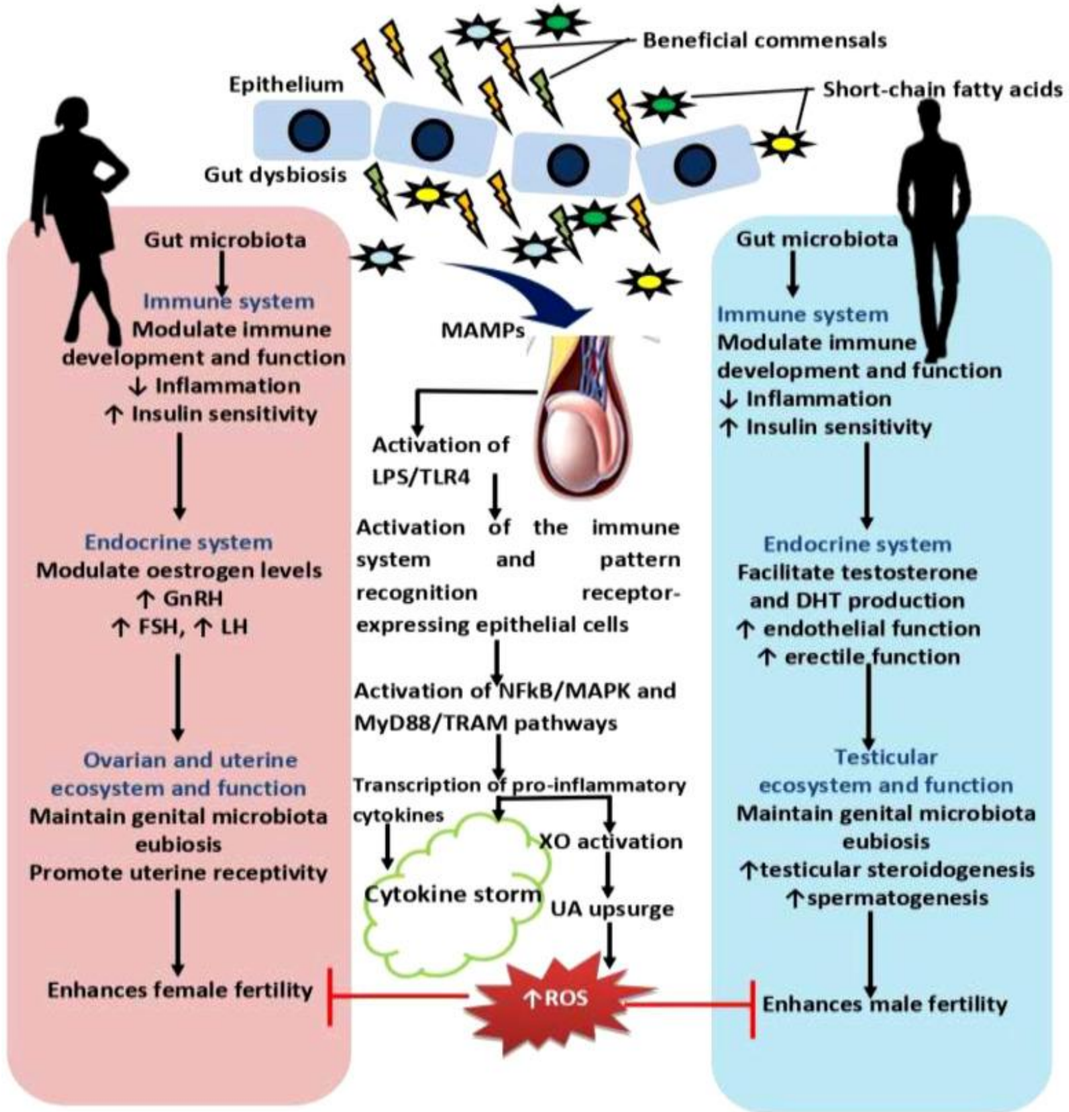


Gut microbiome vs Reproductive microbiome

Location	Gastrointestinal tract	Male and female reproductive tract
Diversity	Very high — hundreds to thousands of species	Lower mainly dominated by Lactobacillus species
Dominant phy;a/ Genera	Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Clostridium, Bacteroides, Prevotella, Akkermansia	Lactobacillus (primary), Gardnerella, Prevotella, Streptococcus, Pseudomonas
Functions	Digestive, immune modulation, metabolic, hormonal regulation	Local defense, pH maintenance, sperm maturation, conception, fertility

Stability	Relatively stable unless dysbiosis occurs	Dynamic — varies with cycle, hormones, pregnancy, sexual activity
Gender Differences	Minimal	Significant — testicular microbiome in males, Lactobacillus dominance in females
Factors Influencing	Diet, age, genetics, antibiotics, environment	pH, hormones, antibiotics, pregnancy, menstruation, sexual activity, infections
Dysbiosis Consequences	Linked to metabolic disorders (obesity, diabetes, cancer) and impacts fertility	Directly causes PCOS, endometriosis, prostatitis, poor sperm quality, preterm birth
Clinical Relevance	Systemic impact; affects overall health and hormonal balance	Local reproductive health, fertility outcomes
Microbiome Interaction	Influences reproductive tract via the gut-reproductive axis	Receives signals from gut microbiota

GUT MICROBIOME RELATIONS WITH INFERTILITY



Effect of gut microbiome and dysbiosis on male and female reproductive function

1. Dysbiosis (Gut Microbial Imbalance)]
2. Weakening of Intestinal Lining
3. Leakage of MAMPs (LPS, Peptidoglycans, Lipoproteins) into the Bloodstream]
4. Entry via Lymphatic System & Hepatic Portal Vein
5. Activation of Immune System
6. Hyperimmune Response in Ovaries & Testes
7. Inflammation & Tissue Damage in Ovaries and Testes
8. Activation of Xanthine Oxidase Enzyme
9. Increased Uric Acid Production
10. Oxidative Stress
11. Impaired Fertility (Ovarian & Testicular Injury)]

GUT MICROBIOME RELATIONS WITH INFERTILITY

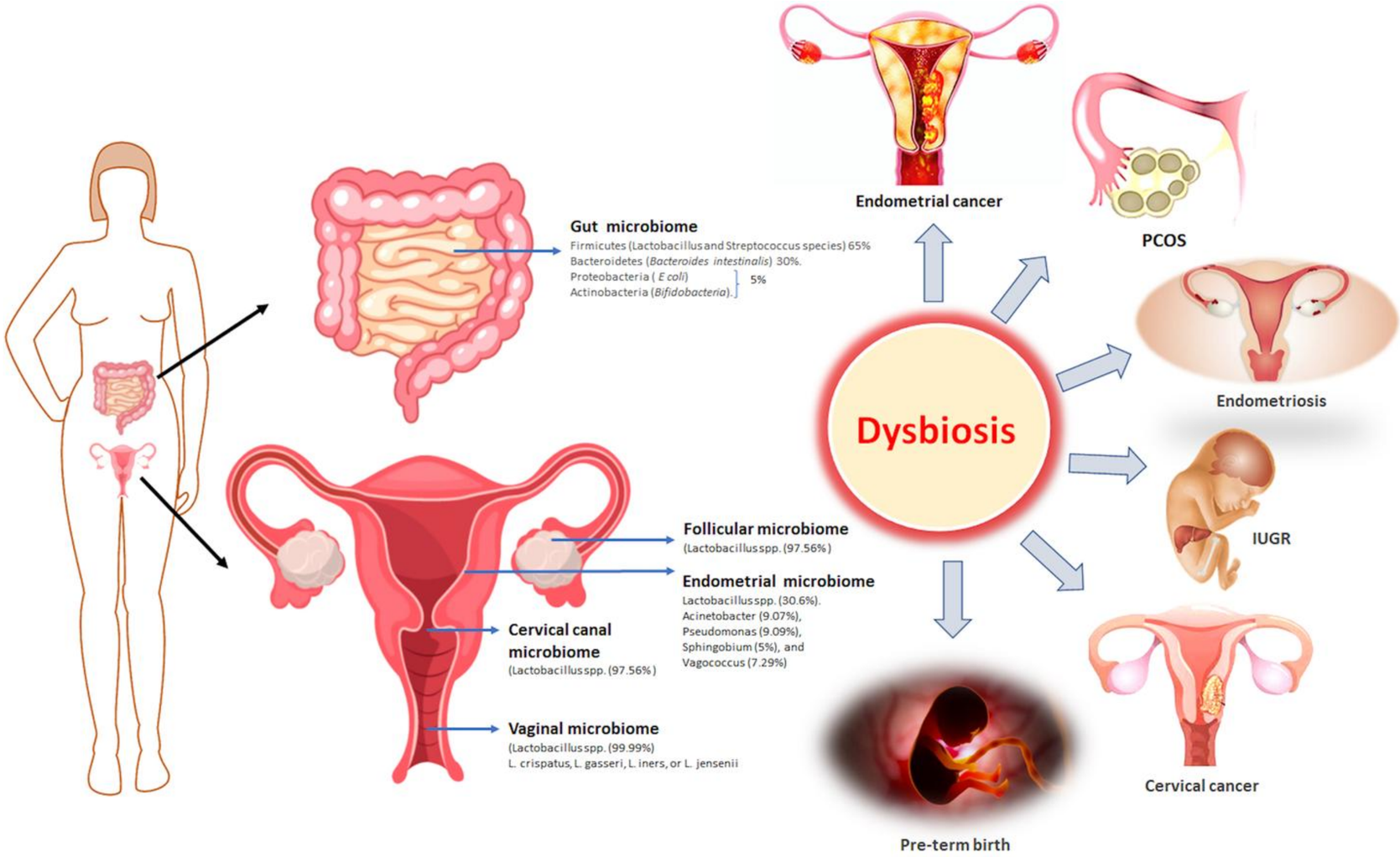
16S rRNA technique used to identify the relationship in gut microbiome and reproductive microbiomes dysbiosis leads changes in fertility various evidences are attached to identify the relarionship between gut microbiome and infertili

SAMPLE/ METHOD	MAIN FINDINGS	MICROBIAL CHANGES	KEY MICROBES	REFERENCES
36 women total: 18 infertile and 18 age-matched fertile controls. Faecal samples analysed via 16S rRNA (V3–V4 regions) sequencing,12 infertile women received ART + PHGG Intervention	Gut microbiota composition was significantly different in infertile women. Higher abundance of Verrucomicrobia,58.3% pregnancy rate (7/12) with PHGG + ART	Infertile women had altered β diversity. PHGG may help restore microbial balance, Positive trends in microbial profile linked to pregnancy success	Increase in Infertile Women: Verrucomicrobia, Phascolarctobacterium, unclassified Barnesiellaceae Decreased: Roseburia, Streptococcus, Stenotrophomonas Associated with Pregnancy Success: Higher Bifidobacterium, Lower Paraprevotella & Blautia	(Kamiya et al., 2020)
Bidirectional two-sample Mendelian Randomization (MR) analysis, GWAS data from MiBioGen consortium (gut microbiota), GWAS data on male infertility and abnormal spermatozoa, Methods used: IVW, MR-Egger, weighted median, Steiger filtering	Causal links found between specific gut microbes and male infertility and abnormal spermatozoa, no evidence of pleiotropy, indicating robust causal inference	Increased risk: Eubacterium oxidoreducens group (infertility), Streptococcaceae family (abnormal spermatozoa) - Decreased risk: Bacteroidaceae, Porphyromonadaceae families	Risk Factors: Eubacterium oxidoreducens group, Streptococcaceae family - Protective Factors: Bacteroidaceae, Porphyromonadaceae families	(Han et al., 2024)

SAMPLE/ METHOD	MAIN FINDINGS	MICROBIAL CHANGES	KEY MICROBES	REFERENCES
Two-sample Mendelian Randomization (MR) study, Data from MiBioGen consortium (18,340 individuals), Methods: IVW, MR-Egger, MR-RAPS, MR-PRESSO	Certain gut microbes are causally linked to infertility, some microbes show protective effects while others increase infertility risk	Protective: Family XIII AD3011 group, Ruminococcaceae NK4A214 group, Bacteroidaceae, Bacteroides -Risk factors: Betaproteobacteria, Burkholderiales, etc.	Protective: - Ruminococcaceae NK4A214 group - Bacteroidaceae - Bacteroides - Family XIII AD3011 group Risk-associated: - Betaproteobacteria - Burkholderiales - Candidatus Soleaferrea - Lentisphaerae - Anaerotruncus	(Zhang et al., 2023)
- Animal Study: Male mice fed high-fat diet (HFD) or normal diet (ND) - FMT: Transplantation of gut microbes from HFD-fed mice to ND-fed mice - Assessments: Sperm analysis, RNA sequencing of testes, cytokine profiling, and inflammation markers - Human Study: Stool, blood, and semen analysis from human subjects	- HFD-induced gut dysbiosis caused reduced sperm count and motility - Increased inflammatory responses in the epididymis - Downregulation of genes involved in spermatogenesis and mitochondrial function - In humans, poor sperm motility was associated with higher levels of gut-derived endotoxins	- Increased abundance of pro-inflammatory gut bacteria - Shift in microbial composition leading to systemic inflammation and testicular dysfunction	Bacteroides - Prevotella - Notably, Prevotella copri linked to poor sperm quality and increased endotoxemia	(Ding et al., 2020a)

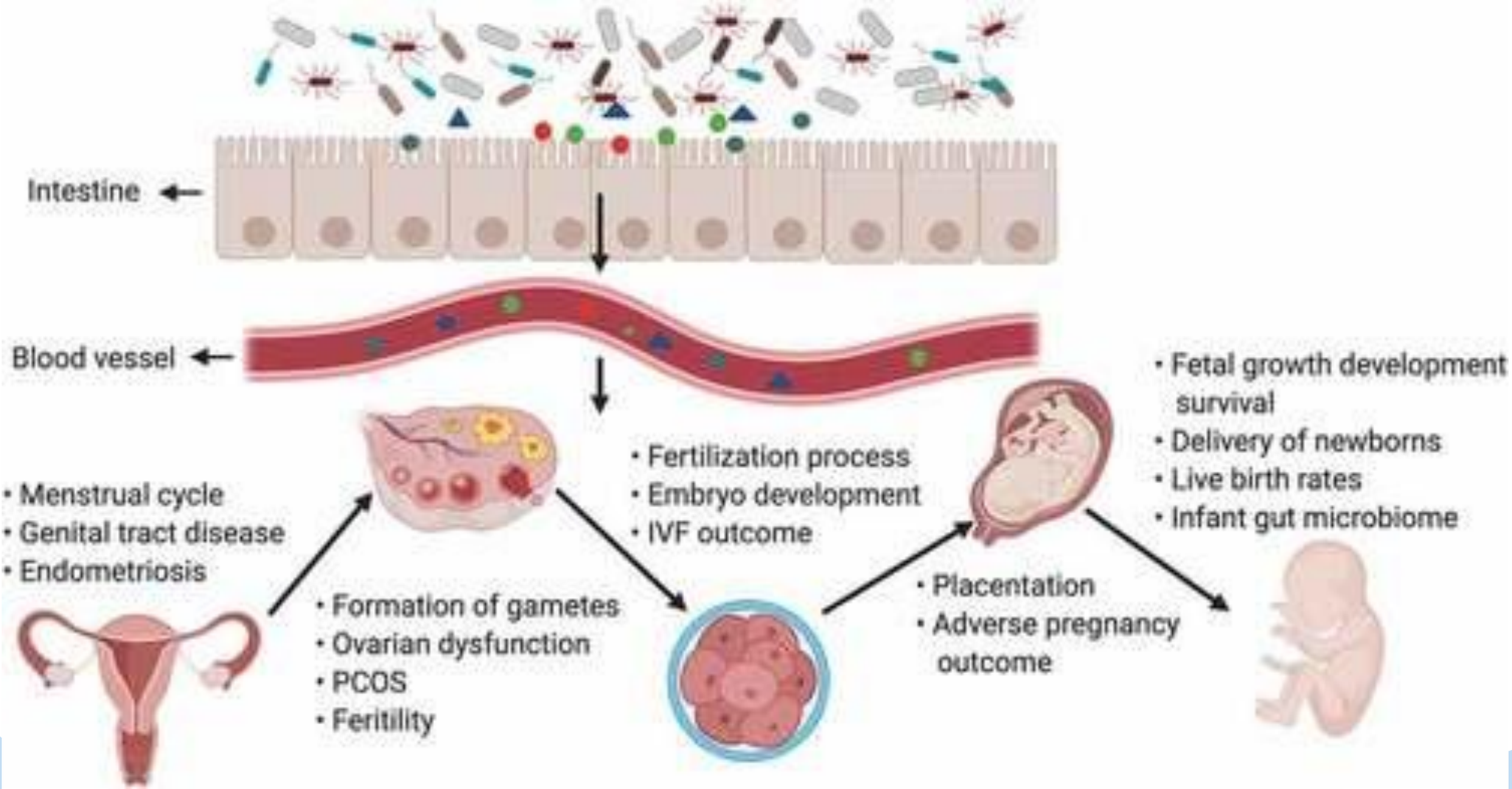
SAMPLE/ METHOD	MAIN FINDINGS	MICROBIAL CHANGES	KEY MICROBES	REFERENCES
36 infertile couples undergoing IVF Samples: Seminal fluid and vaginal swabs, Technique: 16S rRNA gene sequencing (V4 region, Illumina MiSeq)	Semen: Lower bacterial concentration, higher diversity - Azoospermic men had more Mycoplasma and Ureaplasma - Lactobacillus dominant in both sexes	Semen (Positive IVF): ↑ L. jensenii, Faecalibacterium Semen (Negative IVF): ↑ Proteobacteria, Prevotella, Bacteroides Vagina (Positive IVF): ↑ L. gasseri Vagina (Negative IVF): ↑ L. iners, Bacteroides	Positive IVF: Lactobacillus jensenii, Faecalibacterium, Lactobacillus gasseri Negative IVF: Proteobacteria, Prevotella, Bacteroides, L. iners	(Okwelogu et al., 2021)
Semen 16S RNA sequencing pooled (89 mens with infertility conditions and 29 healthy controls)	Seminal viscosity associated with distinct microbiota, OAT cases show increased pathogens and reduced beneficial bacteria, infertile men' s having reduced number of microbial diversity and increased inflammation risk	Increased proteobacteria, gram negative bacteria and pathogens Decreased lactobacillus and diversity	Increased pseudomonas klebsiella, Neisseria and prevotella Decreased lactobacillus	(Monteiro et al., 2018)
Human clinical study of infertile men and fertile controls - Biological samples: gut (stool), urine, and semen - Microbial analysis using 16S rRNA gene sequencing and shotgun metagenomics	Infertile men exhibited significant dysbiosis across all three microbiomes - Functional changes linked to oxidative stress, immune disruption, and poor sperm quality - Strong associations with reduced sperm motility, concentration, and increased DNA fragmentation	Loss of beneficial commensals and overrepresentation of pathogenic/pro-inflammatory microbes - Altered pathways: LPS biosynthesis, bacterial secretion, oxidative phosphorylation	Decreased: Lactobacillus, Bifidobacterium, Faecal bacterium - Increased: Prevotella, Escherichia-Shigella, Gardnerella, and altered Firmicutes/Bacteroidetes ratio	(Lundy et al., 2021)

Gut microbiome relations with underlying female reproductive disorders



Reproductive microbiome composition and associated diseases (adapted from (Chadchan et al., 2022a)

The gut microbiota and its impact on the female reproductive tract, embryo development, and pregnancy. (Adapted from Qi et al., 2021a)

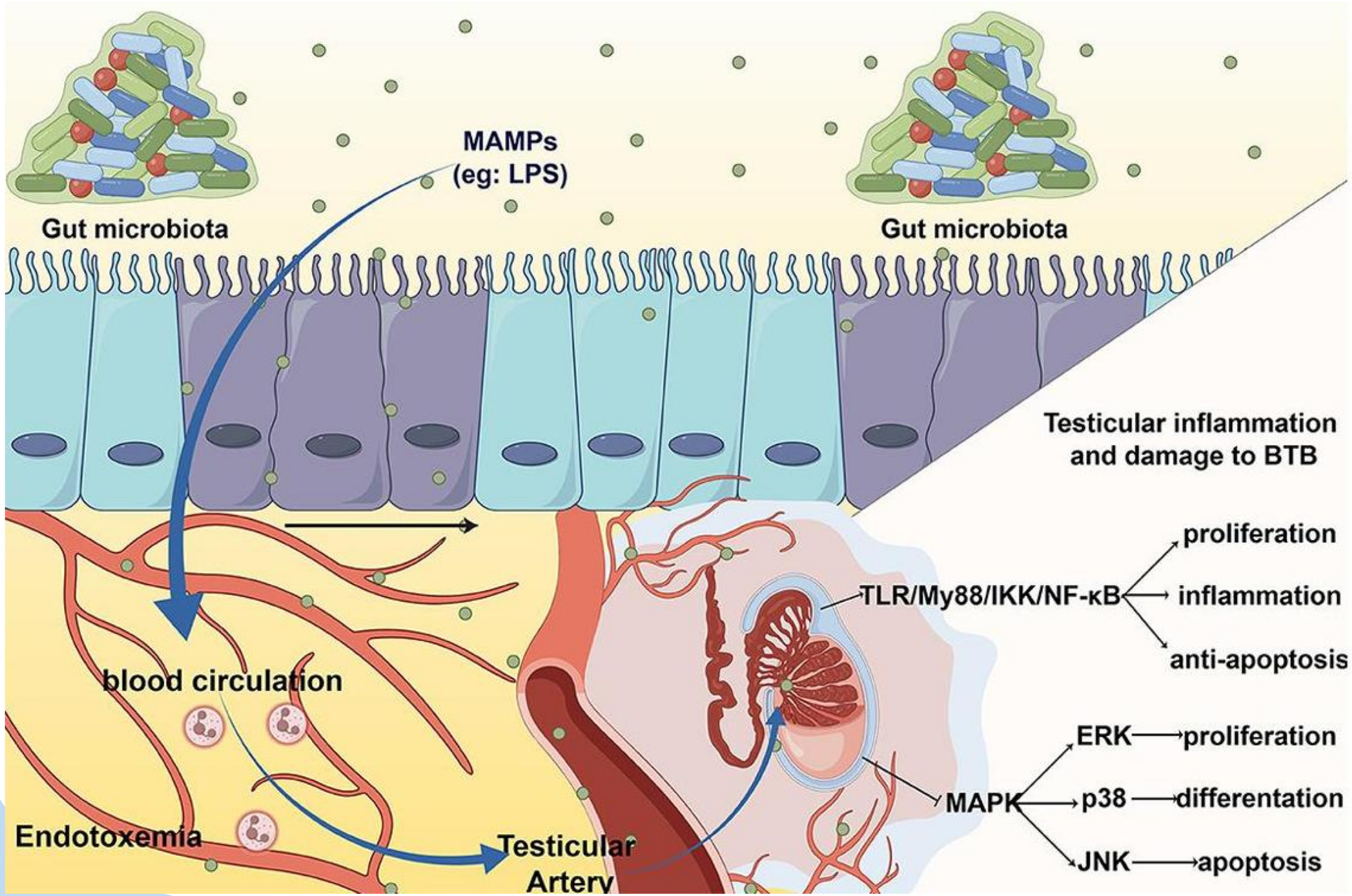


This table links various evidence of female infertility to gut and genital tract dysbiosis and associated microbial alteration with various female reproductive tract disorders

Disease name	Clinical Finding	Hormonal Change	Microbial Change	Key Microbes (↑/↓)	Reference
PCOS	Hirsutism, acne	↑ Androgens (testosterone)	↓ Alpha diversity, ↑ LPS-producers	↑ Bacteroides, Escherichia/Shigella, ↓ Akkermansia, Ruminococcaceae	(Sun et al., 2023b) (R. Liu et al., 2017)17a)
PCOS	Infertility, hyperandrogenism, oligo/amenorrhea, polycystic ovaries	↑ Androgens, ↑ LH/FSH ratio, insulin resistance	↓ Diversity, ↑ Firmicutes/Bacteroidetes ratio, ↑ Gram-negative bacteria	↑ Bacteroides, ↑ Escherichia/Shigella, ↑ Streptococcus, ↓ Lactobacillus, ↓ Akkermansia, ↓ Ruminococcaceae	(Chadchan et al., 2022b)
Endometriosis	Chronic pelvic pain, infertility	↑ Oestrogen (oestradiol), ↑ Erβ	↓ Lactobacillus, ↑ β-glucuronidase producers	↑ Escherichia/Shigella, Bacteroides, Clostridia, Ruminococcaceae, Blautia, Dorea, ↓ Lactobacillus	(Ata et al., 2019; Chantalat et al., 2020; Guo & Zhang, 2024; Uzuner et al., 2023)
Endometriosis	Cyclic bleeding of lesions	↑ Circulating oestrogen via the oestrobolome	↑ β-glucuronidase activity, ↑ oestrogen reabsorption	↑ β-glucuronidase (from Bacteroides, Clostridia, Escherichia)	(Guo & Zhang, 2024; Uzuner et al., 2023)
Endometrial cancer	Abnormal uterine bleeding, postmenopausal bleeding	↑ Oestrogen (unopposed), altered oestrogen metabolism	↑ β-glucuronidase-producing bacteria, dysbiosis, ↑ Pro-inflammatory bacteria	↑ Clostridium, ↑ Bacteroides, ↑ Escherichia, Atopobium, ↑ Porphyromonas, ↓ Lactobacillus	(Chadchan et al., 2022b)

Disease name	Clinical Finding	Hormonal Change	Microbial Change	Key Microbes (↑/↓)	Reference
Pregnancy Complications	Preeclampsia, gestational diabetes, preterm birth	Altered progesterone, oestrogen, and insulin	↓ Diversity, ↑ Pathobionts, altered SCFA producers	↑ Prevotella, ↑ Streptococcus, ↑ Escherichia, ↓ Lactobacillus, ↓	(Chadchan et al., 2022b)
Recurrent Vaginal Infections	Vaginal discharge, irritation, lebsiella infection risk	Decreased oestrogen, altered vaginal pH	↓ Lactobacillus dominance, ↑ Anaerobes	↓ Lactobacillus, ↑ Gardnerella, ↑ Atopobium, ↑ Mobiluncus	(Chadchan et al., 2022b)
Female genital tract disease	Bacterial vaginosis	Often linked to menstrual/hormonal fluctuations (↓ oestradiol, ↑ pH)	↓ Lactobacillus, ↑ diversity, ↑ anaerobes	↑ Gardnerella, Atopobium, Mobiluncus, Prevotella, Bacteroides, Sneathia, Leptotrichia, Clostridia; ↓	(Bv, n.d.; Prof. Ina Schuppe Koistinen, 2025; Song et al., 2020; Vinerbi et al., 2025)
Female genital tract disease	Pelvic inflammatory disease	Not mentioned	↑ pathogenic bacteria	↑ Gardnerella, Atopobium, Mobiluncus, Prevotella, Bacteroides, Sneathia, Leptotrichia, Clostridia, ↓	(Bv, n.d.)
Female genital tract disease	Tubal factor infertility, early abortion	Not mentioned	↑ BV-associated bacteria	↑ Gardnerella, Atopobium, Mobiluncus, Prevotella, Bacteroides, Sneathia, Leptotrichia, Clostridia; ↓	-
Female genital tract disease	Increased STI risk	Not mentioned	↓ Lactobacillus, ↑ pathogens	↑ Gardnerella, Atopobium, Mobiluncus, Prevotella, Bacteroides, Sneathia, Leptotrichia, Clostridia; ↓	(Bv, n.d.)

Gut microbiome relations with underlying male reproductive disorders



Entry of Lipopolysaccharides into blood circulation leads to BTB damage (Adapted from Lv et al., 2024) .

This table links various evidence of male infertility to gut dysbiosis and associated microbial alteration with various male reproductive disorders

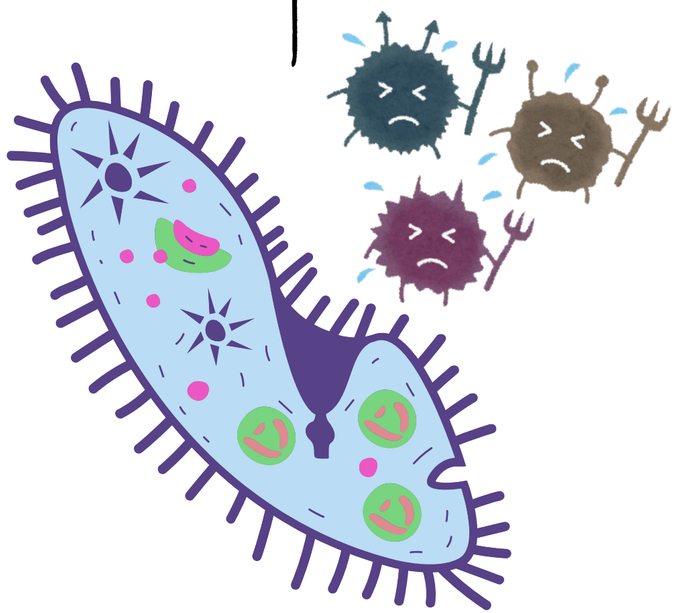
Disease name	Clinical Finding	Hormonal Change	Microbial Change	Key Microbes (↑/↓)	Reference
Erectile dysfunction	Reduced erectile function, vascular klebsiellas, and endothelial injury	↓ Testosterone (due to low Alistipes), ↑ TNF-α	↑ Clostridium XVIII, ↓ Alistipes	↑ Clostridium XVIII, ↓ Alistipes	(Hsu et al., 2015)
Insulin Resistance & testicular damage	Impaired spermatogenesis, testicular damage, metabolic syndrome, hyperinsulinemia	↓ LH/FSH, ↓ Testosterone, ↑ Insulin (disrupts SHBG and free testosterone balance)	↓ Diversity, ↑ LPS-producing bacteria, ↑ pro-inflammatory taxa	↑ Bacteroides, ↑ Prevotella, ↓ Lactobacillus, ↓ Bifidobacterium	(Ding et al., 2020b) (Pedersen et al., 2016)
nonobstructive azoospermia	Idiopathic infertility, impaired BTB development, delayed spermatogenesis	↓ Testosterone (Leydig cell dysfunction)	↓ Diversity in testicular microbiota, ↓ Bacteroides/Proteobacteria	↓ Bacteroides, ↓ Proteobacteria, ↑ Actinobacteria, ↑ Firmicutes	(Alfano et al., 2018; Molina et al., 2021)
Spermatogenesis Impairment	Reduced sperm motility, DNA fragmentation, oxidative stress	↓ Testosterone, ↑ ROS (oxidative stress)	Altered gut-testis axis, ↑ LPS, ↓ SCFA producers	↓ Lactobacillus, ↓ Bifidobacterium, ↑ Escherichia/Shigella, ↑ Streptococcus	(Valcarce et al., 2017) (Ding et al., 2020b)
Gut-Testis Axis Inflammation	Chronic testicular inflammation, Blood testis barrier leakage, Leydig/Sertoli cell damage	↓ Anti-inflammatory factors (e.g., IL-10), ↑ Pro-inflammatory cytokines (TNF-α, IL-6)	↑ LPS-producing bacteria, ↑ TLR4/NF-KB signalling	↑ Clostridium, ↑ Bacteroides, ↑ Prevotella, ↓ Lactobacillus	(Ding et al., 2020b)
Male Infertility (linked to impaired spermatogenesis and reduced sperm motility)	Reduced sperm count and motility , Epididymal klebsiellas (↑ T cells, macrophages) - ↑ Blood endotoxin levels (endotoxemia)	No significant systemic sex hormone changes reported; local testicular dysfunction via altered gene expression	Gut dysbiosis due to high-fat diet (HFD) - ↑ Bacteroides, ↑ Prevotella - Microbial profile linked to inflammation and endotoxin	↑ Bacteroides ↑ Prevotella ↓ (Implied loss of beneficial microbial diversity)	(Ding et al., 2020a)
Male Infertility	Men with infertility showed significant alterations in the gut, urine, and semen klebsiellas compared to fertile controls. - Presence of sperm DNA fragmentation and	Not mentioned in the study	Reduced microbial diversity in gut, urine, and semen samples of infertile men. - Increased pro-inflammatory bacteria and decreased beneficial commensals	↑ Bacteroides, ↑ Streptococcus, ↑ Prevotella - ↓ Lactobacillus, ↓ Faecal bacterium, ↓ Ruminococcaceae	(Lundy et al., 2021)

Management of infertility through Gut microbiome improvement

Dietary Interventions

Prebiotics & Probiotocs

Lifestyle Modifications



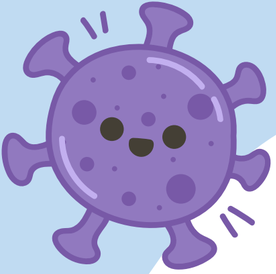
Omega 3 fatty acids

Adavnace therapies

Strategy	Benefits/ Details
Dietary Changes	High-fiber fruits, vegetables, and plant-based diets enhance gut flora and reduce inflam
Wholegrainsetabolism .	Oats, quinoa, brown rice, etc. improve microbial diversity and glucose m
Gluten-Free Wholegrains	Quinoa, millet, buckwheat benefit gut integrity and reduce inflammation in sensitive individuals.
Plant-Based Proteins	Beans, tofu, soy, nuts enhance hormone balance, SCFA production, and gut barrier function.
Animal-Based Proteins	Especially chicken improves Lactobacillus, Akkermansia, and reduces inflammation. Bifidobacterium.
Dairy Products	Yogurt, kefir, chaach increase probiotic bacteria like Lactobacillus and

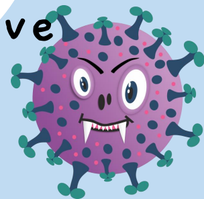
Strategy	Benefits/ Details
Probiotics	Found in fermented foods; restore gut flora and support hormonal regulation.
Prebiotics	Garlic, onions, bananas feed good bacteria and improve microbial balance.
Synbiotics	Combination of probiotics + prebiotics; synergistically improve gut health and fertility.
Omega-3 Fatty Acids	Found in fish, flaxseed, chia seeds; reduce inflammation, regulate hormones, improve egg quality

Strategy	Benefits/ Details
Physical Activity	Regular aerobic + resistance training boosts SCFA, beneficial microbes, and reproductive function.
Stress management	yoga, meditation, music reduce cortisol, restore gut-brain axis balance, and reduce infertility risk.
Avoid Harmful Factors	Limit alcohol, tobacco, fast food, preservatives, stress, and antibiotics to prevent gut dysbiosis.
Faecal Microbiota Transplantation	Used for severe dysbiosis; restores healthy gut flora especially post recurrent infections or antibiotics.



Conclusion

- Gut microbiota significantly influences hormonal regulation, immunity, and metabolism, producing SCFAs, vitamins, and neurotransmitters that affect reproductive health.
- Despite the high infertility burden in India (27.5 million couples), microbiome-based approaches are underutilized in public health.
- Gut dysbiosis contributes to systemic inflammation, hormonal imbalances, and impaired immune functions, all of which negatively impact fertility.
- The gut is rich in microbial diversity, while the reproductive tract (especially female) is dominated by Lactobacillus, crucial for maintaining pH and preventing infections.
- Dysbiosis is mechanistically linked to: PCOS, endometriosis, implantation failure in females. Poor sperm quality, motility, and testicular inflammation in males.
- Therapeutic strategies such as dietary changes, probiotics, prebiotics, exercise, and emerging interventions like FMT have shown positive effects on restoring microbial balance and improving fertility.
- The study strongly advocates for integrating microbiome research into reproductive healthcare, aligning with SDG 3 (good health and well-being by 2030).
- Policy and clinical frameworks should prioritize microbiome modulation as a non-invasive and cost-effective infertility management strategy.



Limitations

- **No Primary Data** – Study based only on secondary literature; lacks clinical or sequencing data from Indian population.
- **Limited Indian Context** – Most studies are from Western countries; results may not reflect Indian population due to regional differences.
- **Study Design Variability** – Diverse methodologies (sample sizes, sequencing tools) hinder direct comparison.
- **Evolving Science** – Microbiome research is still in early stages; many interactions are not fully understood.
- **Lack of Standard Protocols** – No universal definition of a "healthy" reproductive microbiome.
- **Preliminary Intervention Evidence** – Insufficient clinical trials to support microbiome-based infertility treatments.

Recommendations

- **Microbiome Screening in Fertility Clinics** – Include gut and reproductive microbiome profiling in infertility workups.
- **Public Awareness Campaigns** – Educate public and professionals on gut-reproductive health link.
- **Integration with National Health Programs** – Incorporate microbiome research into Ayushman Bharat and RCH initiatives.
- **India-Specific Clinical Research** – Conduct local trials to validate the gut-infertility link and design targeted treatments.
- **Microbiome-Based Treatments** – Promote development of probiotics, prebiotics, FMT, and other microbiome therapies.
- **Multidisciplinary Collaboration** – Encourage teamwork among health professionals for holistic infertility care.
- **Diet and Lifestyle Counselling** – Include personalized lifestyle advice in fertility programs to restore microbial balance.
- **Policy and Funding Support** – Advocate for investment and policy backing to advance microbiome innovations aligned with SDG-3.

References

1. Ahmad, F., Ahmed, S. H., Choucair, F., Chouliaras, S., Awwad, J., & Terranegra, A. (2025). A disturbed communication between hypothalamic-pituitary-ovary axis and gut microbiota in female infertility: is diet to blame? Journal of Translational Medicine, 23(1), 92. https://doi.org/10.1186/s12967-025-06117-x

2. Alagiakrishnan, K., Morgadinho, J., & Halverson, T. (2024). Approach to the diagnosis and management of dysbiosis. In Frontiers in Nutrition (Vol. 11). Frontiers Media SA. https://doi.org/10.3389/fnut.2024.1330903

3. Alfano, M., Ferrarese, R., Locatelli, I., Ventimiglia, E., Ippolito, S., Gallina, P., Cesana, D., Canducci, F., Pagliardini, L., ViganÒ, P., Clementi, M., Nebuloni, M., Montorsi, F., & Salonia, A. (2018). Testicular microbiome in azoospermic men—first evidence of the impact of an altered microenvironment. Human Reproduction, 33(7), 1212–1217. https://doi.org/10.1093/humrep/dey116

4. Amy Owen; Karen Carlson; Paul B. Sparzak. (2024). Age-Related Fertility Decline .

5. Ashonibare, V. J., Akorede, B. A., Ashonibare, P. J., Akhigbe, T. M., & Akhigbe, R. E. (2024). Gut microbiota-gonadal axis: the impact of gut microbiota on reproductive functions. In Frontiers in Immunology (Vol. 15). Frontiers Media SA. https://doi.org/10.3389/fimmu.2024.1346035

6. Aslam, H., Marx, W., Rocks, T., Loughman, A., Chandrasekaran, V., Ruusunen, A., Dawson, S. L., West, M., Mullarkey, E., Pasco, J. A., & Jacka, F. N. (2020). The effects of dairy and dairy derivatives on the gut microbiota: a systematic literature review. Gut Microbes, 12(1), 1799533. https://doi.org/10.1080/19490976.2020.1799533

7. Ata, B., Yildiz, S., Turkgeldi, E., Brocal, V. P., Dinleyici, E. C., Moya, A., & Urman, B. (2019). The Endobiota Study: Comparison of Vaginal, Cervical and Gut Microbiota Between Women with Stage 3/4 Endometriosis and Healthy Controls. Scientific Reports, 9(1). https://doi.org/10.1038/s41598-019-39700-6

8. Baker, J. M., Al-Nakkash, L., & Herbst-Kralovetz, M. M. (2017). Estrogen–gut microbiome axis: Physiological and clinical implications. Maturitas, 103, 45–53. https://doi.org/10.1016/j.maturitas.2017.06.025

9. Banfi, D., Moro, E., Bosi, A., Bistoletti, M., Cerantola, S., Crema, F., Maggi, F., Giron, M. C., Giaroni, C., & Baj, A. (2021). Impact of Microbial Metabolites on Microbiota–Gut–Brain Axis in Inflammatory Bowel Disease. International Journal of Molecular Sciences, 22(4), 1623. https://doi.org/10.3390/ijms22041623

10. Beam, A., Clinger, E., & Hao, L. (2021). Effect of Diet and Dietary Components on the Composition of the Gut Microbiota. Nutrients, 13(8), 2795. https://doi.org/10.3390/nu13082795

1. bv. (n.d.).
2. Caio, G., Lungaro, L., Segata, N., Guarino, M., Zoli, G., Volta, U., & De Giorgio, R. (2020). Effect of Gluten-Free Diet on Gut Microbiota Composition in Patients with Celiac Disease and Non-Celiac Gluten/Wheat Sensitivity. Nutrients, 12(6). https://doi.org/10.3390/nu12061832
3. Chadchan, S. B., Singh, V., & Kommagani, R. (2022a). Female reproductive dysfunctions and the gut microbiota. In Journal of Molecular Endocrinology (Vol. 69, Issue 3, pp. R81–R94). BioScientifica Ltd. https://doi.org/10.1530/JME-21-0238
4. Chadchan, S. B., Singh, V., & Kommagani, R. (2022b). Female reproductive dysfunctions and the gut microbiota. In Journal of Molecular Endocrinology (Vol. 69, Issue 3, pp. R81–R94). BioScientifica Ltd. https://doi.org/10.1530/JME-21-0238
5. Chakravorty, S., Helb, D., Burday, M., Connell, N., & Alland, D. (2007). A detailed analysis of 16S ribosomal RNA gene segments for the diagnosis of pathogenic bacteria. Journal of Microbiological Methods, 69(2), 330–339. https://doi.org/10.1016/j.mimet.2007.02.005
6. Chantalat, E., Valera, M. C., Vaysse, C., Noirrit, E., Rusidze, M., Weyl, A., Vergriete, K., Buscail, E., Lluel, P., Fontaine, C., Arnal, J. F., & Lenfant, F. (2020). Estrogen receptors and endometriosis. In International Journal of Molecular Sciences (Vol. 21, Issue 8). MDPI AG. https://doi.org/10.3390/ijms21082815
7. Cleveland Clinic. (2023, August 5). Male Reproductive System. Cleveland Clinic.
8. Corrie, L., Awasthi, A., Kaur, J., Vishwas, S., Gulati, M., Kaur, I. P., Gupta, G., Kommineni, N., Dua, K., & Singh, S. K. (2023). Interplay of Gut Microbiota in Polycystic Ovarian Syndrome: Role of Gut Microbiota, Mechanistic Pathways and Potential Treatment Strategies. Pharmaceuticals, 16(2), 197. https://doi.org/10.3390/ph16020197
9. D' Argenio, V., & Salvatore, F. (2015). The role of the gut microbiome in the healthy adult status. Clinica Chimica Acta, 451, 97–102. https://doi.org/10.1016/j.cca.2015.01.003
10. Dasriya, V. L., Samtiya, M., Ranveer, S., Dhillon, H. S., Devi, N., Sharma, V., Nikam, P., Puniya, M., Chaudhary, P., Chaudhary, V., Behare, P. V, Dhewa, T., Vemuri, R., Raposo, A., Puniya, D. V., Khedkar, G. D., Vishweswaraiah, R. H., Vij, S., Alarifi, S. N., ... Puniya, A. K. (2024). Modulation of gut-microbiota through probiotics and dietary interventions to improve host health. Journal of the Science of Food and Agriculture, 104(11), 6359–6375. https://doi.org/10.1002/jsfa.13370

1. De Filippis, F., Valentino, V., Sequino, G., Borriello, G., Riccardi, M. G., Pierri, B., Cerino, P., Pizzolante, A., Pasolli, E., Esposito, M., Limone, A., & Ercolini, D. (2024). Exposure to environmental pollutants selects for xenobiotic-degrading functions in the human gut microbiome. Nature Communications, 15(1). https://doi.org/10.1038/s41467-024-48739-7
2. den Besten, G., van Eunen, K., Groen, A. K., Venema, K., Reijngoud, D.-J., & Bakker, B. M. (2013). The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. Journal of Lipid Research, 54(9), 2325–2340. https://doi.org/10.1194/jlr.R036012
3. Di Vincenzo, F., Del Gaudio, A., Petito, V., Lopetuso, L. R., & Scaldaferri, F. (2024). Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. In Internal and Emergency Medicine (Vol. 19, Issue 2, pp. 275–293). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s11739-023-03374-w
4. Ding, N., Zhang, X., Zhang, X. Di, Jing, J., Liu, S. S., Mu, Y. P., Peng, L. L., Yan, Y. J., Xiao, G. M., Bi, X. Y., Chen, H., Li, F. H., Yao, B., & Zhao, A. Z. (2020a). Impairment of spermatogenesis and sperm motility by the high-fat diet-induced dysbiosis of gut microbes. Gut, 69(9), 1608–1619. https://doi.org/10.1136/gutjnl-2019-319127
5. Ding, N., Zhang, X., Zhang, X. Di, Jing, J., Liu, S. S., Mu, Y. P., Peng, L. L., Yan, Y. J., Xiao, G. M., Bi, X. Y., Chen, H., Li, F. H., Yao, B., & Zhao, A. Z. (2020b). Impairment of spermatogenesis and sperm motility by the high-fat diet-induced dysbiosis of gut microbes. Gut, 69(9), 1608–1619. https://doi.org/10.1136/gutjnl-2019-319127
6. Dr Alena Pribyl. (2023, January 2). Important functions of the gut microbiome. MICROBA.
7. Filardo, S., Di Pietro, M., Protano, C., Antonucci, A., Vitali, M., & Sessa, R. (2022). Impact of Air Pollution on the Composition and Diversity of Human Gut Microbiota in General and Vulnerable Populations: A Systematic Review. In Toxics (Vol. 10, Issue 10). MDPI. https://doi.org/10.3390/toxics10100579
8. Francino, M. P. (2016). Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. Frontiers in Microbiology, 6. https://doi.org/10.3389/fmicb.2015.01543
9. Fu, Y., Wang, Y., Gao, H., Li, D., Jiang, R., Ge, L., Tong, C., & Xu, K. (2021). Associations among Dietary Omega-3 Polyunsaturated Fatty Acids, the Gut Microbiota, and Intestinal Immunity. Mediators of Inflammation, 2021, 1–11. https://doi.org/10.1155/2021/8879227
10. Gaskins, A. J., Chiu, Y.-H., Williams, P. L., Keller, M. G., Toth, T. L., Hauser, R., & Chavarro, J. E. (2016). Maternal whole grain intake and outcomes of in vitro fertilization. Fertility and Sterility, 105(6), 1503-1510.e4. https://doi.org/10.1016/j.fertnstert.2016.02.015
11. Gilbert, J. A., Blaser, M. J., Caporaso, J. G., Jansson, J. K., Lynch, S. V, & Knight, R. (2018). Current understanding of the human microbiome. Nature Medicine, 24(4), 392–400. https://doi.org/10.1038/nm.4517
12. Glasier, A., Gülmezoglu, M., Schmid, G. P., Moreno, C. G., Fa, P., Look, V., & Lothian, N. (2006). Sexual and Reproductive Health 1 Sexual and reproductive health: a matter of life and death. Www.Thelancet.Com, 368, 1595–1607. https://doi.org/10.1016/S0140
13. Goodrich, J. K., Waters, J. L., Poole, A. C., Sutter, J. L., Koren, O., Blekhman, R., Beaumont, M., Van Treuren, W., Knight, R., Bell, J. T., Spector, T. D., Clark, A. G., & Ley, R. E. (2014). Human Genetics Shape the Gut Microbiome. Cell, 159(4), 789–799. https://doi.org/10.1016/j.cell.2014.09.053
14. Guo, C., & Zhang, C. (2024). Role of the gut microbiota in the pathogenesis of endometriosis: a review. In Frontiers in Microbiology (Vol. 15). Frontiers Media SA. https://doi.org/10.3389/fmicb.2024.1363455
15. Han, X., Tian, H., Yang, L., & Ji, Y. (2024). Bidirectional Mendelian randomization to explore the causal relationships between the gut microbiota and male reproductive diseases. Scientific Reports, 14(1). https://doi.org/10.1038/s41598-024-69179-9
16. Highlights Most countries will experience below-replacement * levels of fertility by mid-century. (n.d.). http://bit.ly/FertilityGBD21,
17. Hill, C., Guarner, F., Reid, G., Gibson, G. R., Merenstein, D. J., Pot, B., Morelli, L., Canani, R. B., Flint, H. J., Salminen, S., Calder, P. C., & Sanders, M. E. (2014). The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology, 11(8), 506–514. https://doi.org/10.1038/nrgastro.2014.66
18. Hrncir, T. (2022). Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic Options. Microorganisms, 10(3). https://doi.org/10.3390/microorganisms10030578
19. Hsu, C.-Y., Lin, C.-L., & Kao, C.-H. (2015). Irritable bowel syndrome is associated not only with organic but also psychogenic erectile dysfunction. International Journal of Impotence Research, 27(6), 233–238. https://doi.org/10.1038/ijir.2015.25
20. Infertility prevalence estimates. (n.d.-a).
21. Infertility prevalence estimates. (n.d.-b).

1.
2. Janda, J. M., & Abbott, S. L. (2007). 16S rRNA gene sequencing for bacterial identification in the diagnostic laboratory: Pluses, perils, and pitfalls. In Journal of Clinical Microbiology (Vol. 45, Issue 9, pp. 2761–2764). https://doi.org/10.1128/JCM.01228-07
3. Janićijević, A., Pavlović, V. P., Kovačević, D., Perić, M., Vlahović, B., Pavlović, V. B., & Filipović, S. (2022). Structural Characterization of Nanocellulose/Fe3O4 Hybrid Nanomaterials. Polymers, 14(9), 1819. https://doi.org/10.3390/polym14091819
4. Johnson, J. S., Spakowicz, D. J., Hong, B. Y., Petersen, L. M., Demkowicz, P., Chen, L., Leopold, S. R., Hanson, B. M., Agresta, H. O., Gerstein, M., Sodergren, E., & Weinstock, G. M. (2019). Evaluation of 16S rRNA gene sequencing for species and strain-level microbiome analysis. Nature Communications, 10(1). https://doi.org/10.1038/s41467-019-13036-1
5. Kennedy, M. S., & Chang, E. B. (2020). The microbiome: Composition and locations. In Progress in Molecular Biology and Translational Science (Vol. 176, pp. 1–42). Elsevier B.V. https://doi.org/10.1016/bs.pmbts.2020.08.013
6. Kish, L., Hotte, N., Kaplan, G. G., Vincent, R., Tso, R., Gänzle, M., Rioux, K. P., Thiesen, A., Barkema, H. W., Wine, E., & Madsen, K. L. (2013). Environmental Particulate Matter Induces Murine Intestinal Inflammatory Responses and Alters the Gut Microbiome. PLoS ONE, 8(4). https://doi.org/10.1371/journal.pone.0062220
7. Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016a). From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. Cell, 165(6), 1332–1345. https://doi.org/10.1016/j.cell.2016.05.041
8. Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016b). From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. Cell, 165(6), 1332–1345. https://doi.org/10.1016/j.cell.2016.05.041
9. Komiya, S., Naito, Y., Okada, H., Matsuo, Y., Hirota, K., Takagi, T., Mizushima, K., Inoue, R., Abe, A., & Morimoto, Y. (2020). Characterizing the gut microbiota in females with infertility and preliminary results of a waterrsoluble dietary fiber intervention study. J. Clin. Biochem. Nutr, 67(1), 105–111. https://doi.org/10.3164/jcbn.20053
10. Kumari, N., Kumari, R., Dua, A., Singh, M., Kumar, R., Singh, P., Duyar-Ayerdi, S., Pradeep, S., Ojesina, A. I., & Kumar, R. (2024). From Gut to Hormones: Unraveling the Role of Gut Microbiota in (Phyto)Estrogen Modulation in Health and Disease. Molecular Nutrition & Food Research, 68(6). https://doi.org/10.1002/mnfr.202300688
11. Kwon, M. S., & Lee, H. K. (2022). Host and Microbiome Interplay Shapes the Vaginal Microenvironment. In Frontiers in Immunology (Vol. 13). Frontiers Media S.A. https://doi.org/10.3389/fimmu.2022.919728
12. Lee, C., Lee, J., Eor, J. Y., Kwak, M. J., Huh, C. S., & Kim, Y. (2023). Effect of Consumption of Animal Products on the Gut Microbiome Composition and Gut Health. Food Science of Animal Resources, 43(5), 723–750. https://doi.org/10.5851/kosfa.2023.e44
13. Li, M., Chang, Q., Luo, Y., Pan, J., Hu, Y., Liu, B., Ma, M., Wang, Q., Guo, Y., & Wang, Q. (2024). The gut microbial composition in polycystic ovary syndrome with hyperandrogenemia and its association with steroid hormones. Frontiers in Cell and Developmental Biology, 12. https://doi.org/10.3389/fcell.2024.1384233
14. Li, T., Shao, W., Wang, Y., Zhou, R., Yun, Z., He, Y., & Wu, Y. (2023). A two-sample mendelian randomization analysis investigates associations between gut microbiota and infertility. Scientific Reports, 13(1). https://doi.org/10.1038/s41598-023-38624-6
15. Liang, Y., Huang, J., Zhao, Q., Mo, H., Su, Z., Feng, S., Li, S., & Ruan, X. (2025a). Global, regional, and national prevalence and trends of infertility among individuals of reproductive age (15–49 years) from 1990 to 2021, with projections to 2040. Human Reproduction (Oxford, England). https://doi.org/10.1093/humrep/deae292
16. Liang, Y., Huang, J., Zhao, Q., Mo, H., Su, Z., Feng, S., Li, S., & Ruan, X. (2025b). Global, regional, and national prevalence and trends of infertility among individuals of reproductive age (15–49 years) from 1990 to 2021, with projections to 2040. Human Reproduction, 40(3), 529–544. https://doi.org/10.1093/humrep/deae292
17. Liu, R., Zhang, C., Shi, Y., Zhang, F., Li, L., Wang, X., Ling, Y., Fu, H., Dong, W., Shen, J., Reeves, A., Greenberg, A. S., Zhao, L., Peng, Y., & Ding, X. (2017). Dysbiosis of Gut Microbiota Associated with Clinical Parameters in Polycystic Ovary Syndrome. Frontiers in Microbiology, 8. https://doi.org/10.3389/fmicb.2017.00324
18. Liu, T., Chen, X., Xu, Y., Wu, W., Tang, W., Chen, Z., Ji, G., Peng, J., Jiang, Q., Xiao, J., Li, X., Zeng, W., Xu, X., Hu, J., Guo, Y., Zou, F., Du, Q., Zhou, H., He, Y., & Ma, W. (2019). Gut microbiota partially mediates the effects of fine particulate matter on type 2 diabetes: Evidence from a population-based epidemiological study. Environment International, 130, 104882. https://doi.org/10.1016/j.envint.2019.05.076
19. Loh, J. S., Mak, W. Q., Tan, L. K. S., Ng, C. X., Chan, H. H., Yeow, S. H., Foo, J. B., Ong, Y. S., How, C. W., & Khaw, K. Y. (2024). Microbiota–gut–brain axis and its therapeutic applications in neurodegenerative diseases. In Signal Transduction and Targeted Therapy (Vol. 9, Issue 1). Springer Nature. https://doi.org/10.1038/s41392-024-01743-1
20. Lu, N., Li, M., Lei, H., Jiang, X., Tu, W., Lu, Y., & Xia, D. (2017). Butyric acid regulates progesterone and estradiol secretion via cAMP signaling pathway in porcine granulosa cells. The Journal of Steroid Biochemistry and Molecular Biology, 172, 89–97. https://doi.org/10.1016/j.jsbmb.2017.06.004

1.
2. Lundy, S. D., Sangwan, N., Parekh, N. V., Selvam, M. K. P., Gupta, S., McCaffrey, P., Bessoff, K., Vala, A., Agarwal, A., Sabanegh, E. S., Vij, S. C., & Eng, C. (2021). Functional and Taxonomic Dysbiosis of the Gut, Urine, and Semen Microbiomes in Male Infertility[Formula presented]. European Urology, 79(6), 826–836. https://doi.org/10.1016/j.eururo.2021.01.014
3. Lv, S., Huang, J., Luo, Y., Wen, Y., Chen, B., Qiu, H., Chen, H., Yue, T., He, L., Feng, B., Yu, Z., Zhao, M., Yang, Q., He, M., Xiao, W., Zou, X., Gu, C., & Lu, R. (2024). Gut microbiota is involved in male reproductive function: a review. In Frontiers in Microbiology (Vol. 15). Frontiers Media SA. https://doi.org/10.3389/fmicb.2024.1371667
4. Magill, R. G., & MacDonald, S. M. (2023). Male infertility and the human microbiome. Frontiers in Reproductive Health, 5. https://doi.org/10.3389/frph.2023.1166201
5. Manco, M., Putignani, L., & Bottazzo, G. F. (2010). Gut Microbiota, Lipopolysaccharides, and Innate Immunity in the Pathogenesis of Obesity and Cardiovascular Risk. Endocrine Reviews, 31(6), 817–844. https://doi.org/10.1210/er.2009-0030
6. Martínez, I., Lattimer, J. M., Hubach, K. L., Case, J. A., Yang, J., Weber, C. G., Louk, J. A., Rose, D. J., Kyureghian, G., Peterson, D. A., Haub, M. D., & Walter, J. (2013). Gut microbiome composition is linked to whole grain-induced immunological improvements. ISME Journal, 7(2), 269–280. https://doi.org/10.1038/ismej.2012.104
7. Matthew H. Walker; Kyle J. Tobler. (2022). Female Infertility . StatPearls Publishing.
8. Mohajeri, M. H., Brummer, R. J. M., Rastall, R. A., Weersma, R. K., Harmsen, H. J. M., Faas, M., & Eggersdorfer, M. (2018). The role of the microbiome for human health: from basic science to clinical applications. European Journal of Nutrition, 57(S1), 1–14. https://doi.org/10.1007/s00394-018-1703-4
MÖhler, H. (2012). The GABA system in anxiety and depression and its therapeutic potential. Neuropharmacology, 62(1), 42–53. https://doi.org/10.1016/j.neuropharm.2011.08.040

122 References were used during this study

Thank You