Chapter 15

Microbiome and Gender Differences

Introduction

Sex differences in the human microbiome are increasingly recognized and reflect the influence of sex hormones on microbial composition and function. These interactions, termed the "microgenderome," affect metabolism, immunity, and disease risk across life stages. Hormonal transitions — puberty, PCOS, and menopause — significantly shape the microbiome, while the microbiome modulates sex hormone availability, particularly estrogens.

15.1 Hormonal Transitions and the Microbiome

Puberty:

- Gonadal steroid surges during puberty create sexual dimorphism in gut microbiota.
- Females show enrichment of pathways for carbohydrate and lipid metabolism; males exhibit distinct microbial patterns influenced by testosterone.
- Animal studies confirm sex hormones causally shape microbiota. [1,2]

PCOS:

- Hyperandrogenism in PCOS is linked to gut dysbiosis, including reduced *Lactobacilli* and *Bifidobacteria*, altered *Prevotellaceae* abundance, and decreased α-diversity.
- Dysbiosis may contribute to insulin resistance, inflammation, and hormonal imbalances. [3,4]

Menopause:

- Decline in ovarian hormones leads to reduced microbial diversity and altered Firmicutes/Bacteroidetes ratio.
- These changes can impair the estrobolome, affecting estrogen reabsorption and contributing to metabolic and systemic disease risk. [5,6]

Estrogen–Microbiome Interaction

- Gut microbes express enzymes (β-glucuronidase, hydroxysteroid dehydrogenases) that deconjugate estrogens, enabling enterohepatic recycling.
- Microbiome composition influences circulating estrogen levels, while estrogens shape microbial diversity and abundance.
- Dysbiosis may impair estrogen metabolism, potentially affecting bone, metabolic, and cardiovascular health. [7,8]

Clinical Implications

- Sex hormone–microbiome interactions contribute to metabolic, reproductive, and systemic disease risk.
- Understanding these dynamics can inform interventions in PCOS, menopause, and other hormone-related conditions.
- Microbiome-targeted therapies (probiotics, diet, prebiotics) hold potential but require further study. [2,4,7]

Here's a **concise reference table** summarizing key hormones, life stages, and microbiome effects:

Life Stage/ Condition	**Key Hormones**	**Microbiome Changes**	**Notes / Clinical Implications**
Pre-puberty	Low sex steroids	Similar microbiome between sexes	Baseline microbial composition before hormonal influence
Puberty	↑ Estrogen (females), ↑ Testosterone (males)	Sexual dimorphism emerges; females: ↑carbohydrate/lipid metabolism pathways; males: distinct microbial composition	Hormones drive gut microbiome differences that may influence metabolism
PCOS	↑ Androgens, altered estrogen	↓ Lactobacilli, Bifidobacteria; altered Prevotellaceae; ↓α-diversity	Dysbiosis may contribute to insulin resistance, inflammation, and hormonal imbalance
Reproductiv	Cyclic	Fluctuating	Microbiome

e-age women	estrogen & progestero ne	microbiome diversity with menstrualcycle; enriched estrobolome function	can metabolize estrogens, modulating systemic hormone levels
Pregnancy	↑ Estrogen, ↑ Progester one	↑Proteobacteria& Actinobacteria; ↓ diversity in late pregnancy	Microbiome supports metabolic adaptation and immune tolerance
Perimenopa use / Menopause	↓ Estrogen, ↓ Progester one	↓ Diversity; ↑ Firmicutes/Bacteroi detes ratio; altered estrobolome	May contributetometabolic syndrome, bone loss, and systemic inflammatio n
Postmenopa use	Lowsex steroids	Persistentlyaltered microbiome; impaired estrogen metabolism	Increased risk for metabolic, cardiovascu lar, and bone-related disorders

Notes:

- "Estrobolome" refers to gut microbial genes capable of metabolizing estrogens.
- Microbiome–hormone interactions are bidirectional: hormones shape microbiota, microbiota modulate hormone availability.
- Clinical relevance: dysbiosis at these stages may contribute to disease risk and could be targeted via diet, probiotics, or other interventions.

Conclusion

Hormonal transitions across life stages drive sex-specific microbiome changes, while the microbiome reciprocally regulates sex hormone availability. The bidirectional interplay between hormones and microbes underlies health and disease susceptibility in a sex-dependent manner, highlighting the microgenderome as a promising focus for personalized medicine.

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