

# MICR BIOTALK

by Biocodex Microbiota Institute

2024 World AMR Awareness Week

# **Antimicrobial resistance**

## **The microbiota at the core of a silent pandemic**

**Educate:** Human, environment & animal resistome



## Pr. Etienne RUPPE

→ **Professor of Bacteriology**  
at the University of Paris and **clinical bacteriologist**  
at the Bichat-Claude Bernard Hospital.

→ He is also **deputy director of the IAME Research Unit** and **head of a research team**.  
His research focuses on antibiotic resistance in the  
intestinal microbiota.



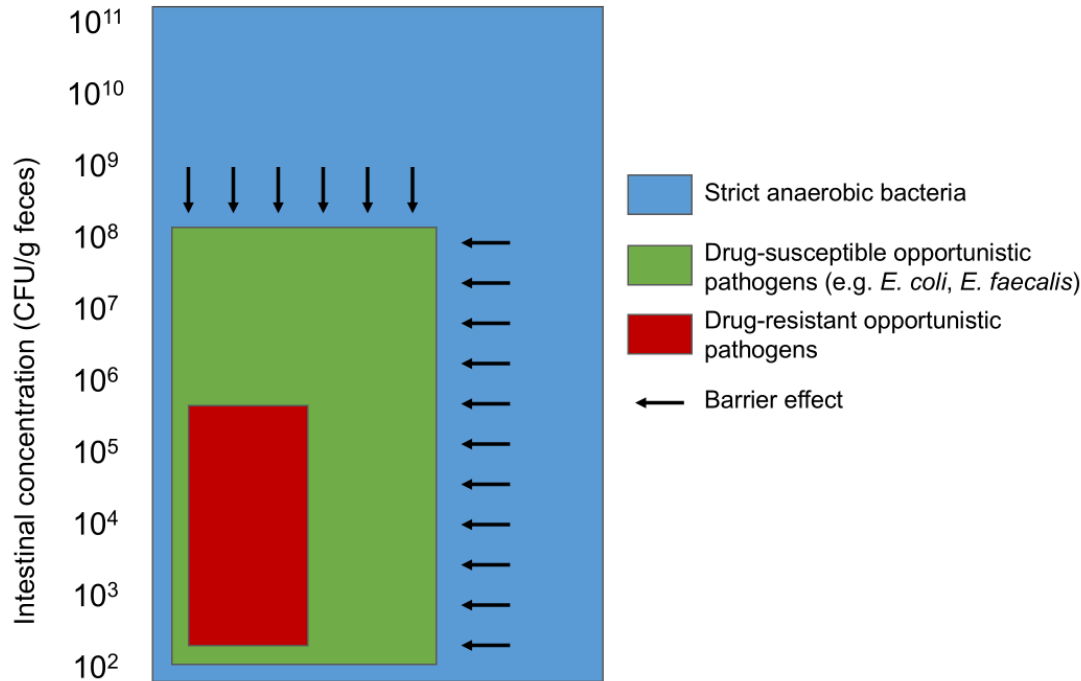


The intestinal microbiota  
and antibiotic resistance

Etienne Ruppé

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AP-HP, Hôpital Bichat, Laboratoire de Bactériologie

# Quantitative representation of the intestinal microbiota



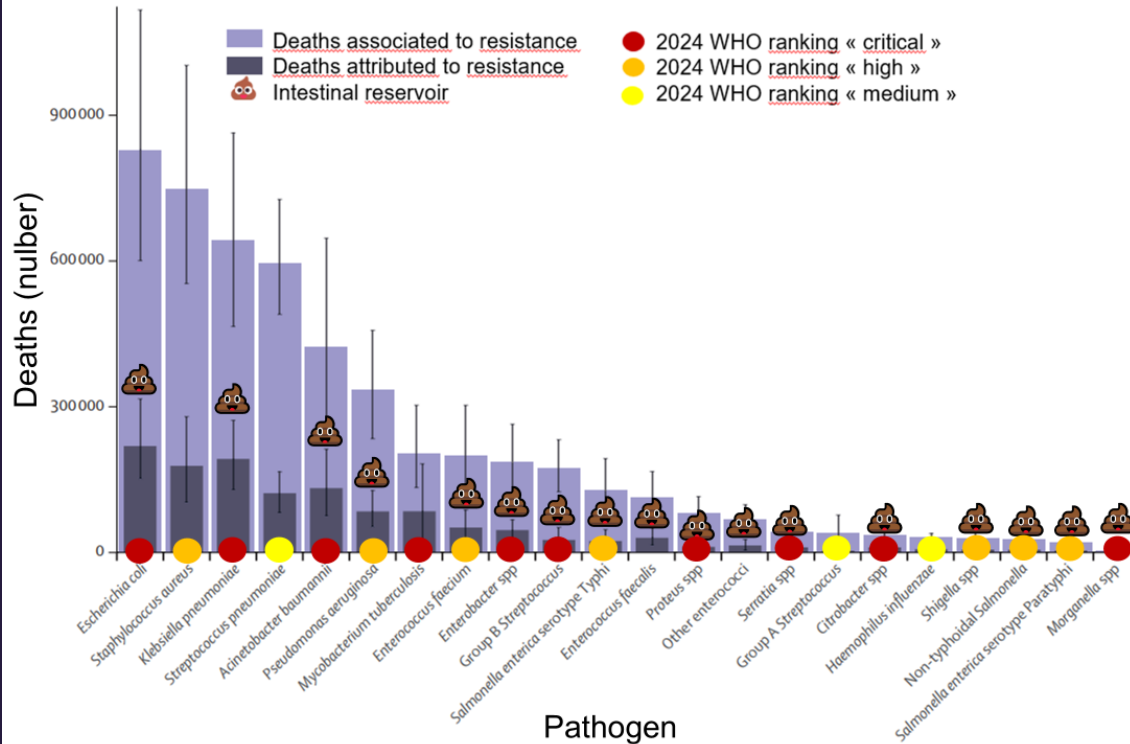
- **High number of bacteria nombre** ( $3 \times 10^{13}$ )<sup>1</sup>
- **High diversity** (hundreds of species), mainly anaerobic bacteria
- Most bacteria are hardly culturable
- The microbiota opposes to the sustained colonisation by exogenous bacteria: barrier effect (=colonisation resistance)

From Grall N et Ruppé E. EMC Biologie, 2017. CFU: colony-forming unit



2

# The threat of antibiotic resistance lies in the gut



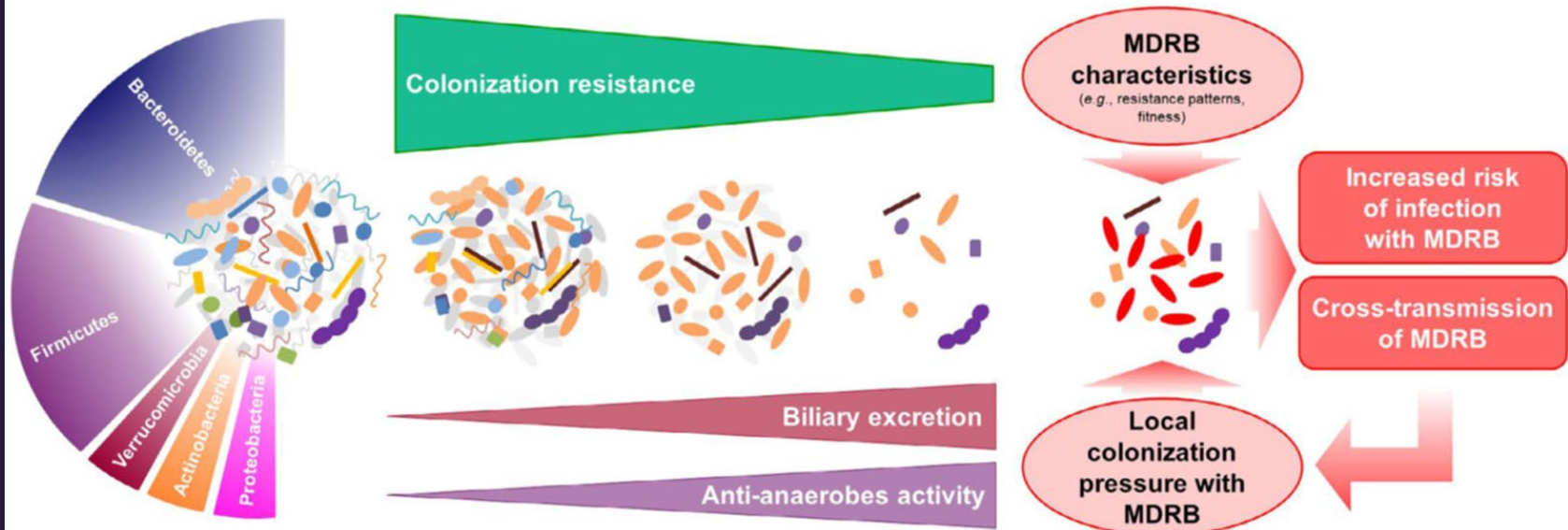
- **1.1M deaths** attributed to antibiotic resistance in 2021.
- Cumulative 39M deaths by 2050
- 0.6M: Enterobacterales, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (Proteobacteria)
- Majority of bacteria **present in the gut** microbiota before causing infections

Adapted from Antimicrobial Resistance Collaborators. et al. *The Lancet* 399, 629–655 (2022).



3

# Impact of antibiotics on the intestinal microbiota



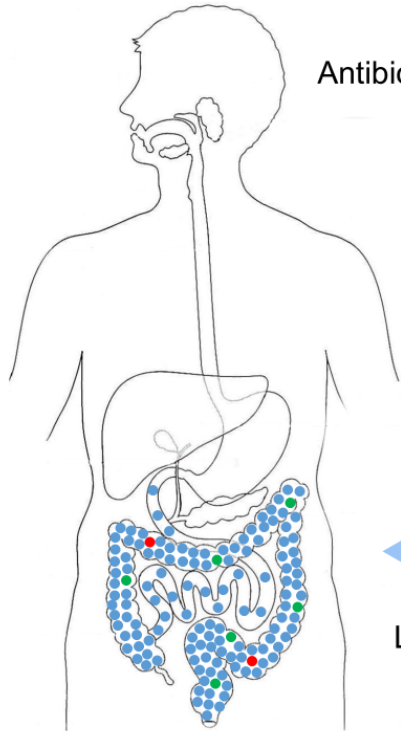
MDRB: multidrug-resistant bacteria

Adapted from **Woerther, P.-L.** et al. *International Journal of Antimicrobial Agents* **52**, 762–770 (2018).



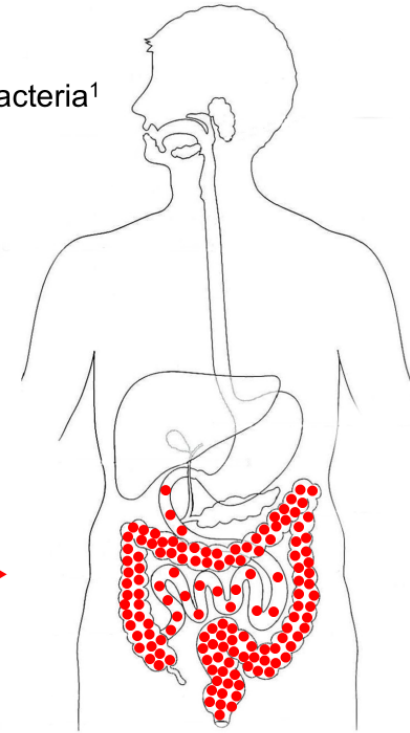
# High intestinal concentrations of resistant bacteria have consequences

Antibiotics increase the intestinal concentrations of drug-resistant bacteria<sup>1</sup>



Low risk

Urinary-tract infection<sup>1</sup>  
Bacterial translocation<sup>2</sup>  
Spread in the environment<sup>3</sup>  
Long-term carriage<sup>4</sup>  
Ventilator-associated pneumonia<sup>5</sup>



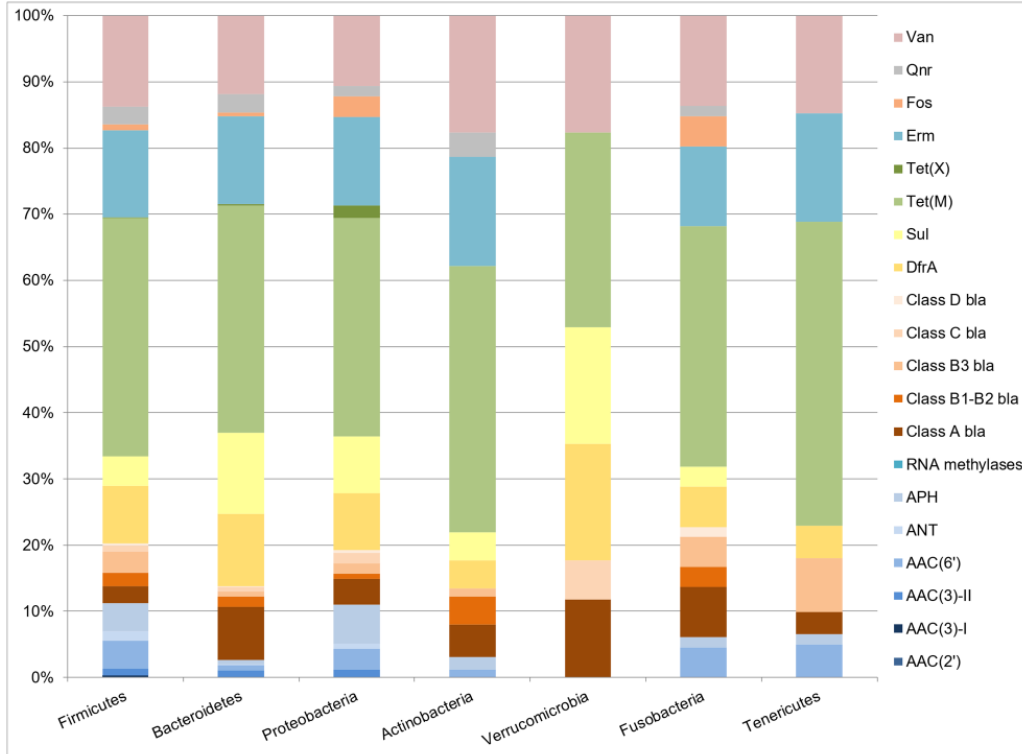
High risk

1. Ruppé, E. et al. Antimicrob. Agents Chemother; 2. Taur, Y. et al. Clin. Infect. Dis. 55, 905–914 (2012); 57, 4512–4517 (2013); 3. Donskey, C. J. et al. N. Engl. J. Med. 343, 1925–1932 (2000); 4. Ruppé, E. et al. Clin. Infect. Dis. 61, 593–600 (2015); 5. Andremont, O. et al. Intensive Care Medicine 46, 1232–1242 (2020).





# Intestinal bacteria harbor a vast diversity of antibiotic resistance genes (ARG)



- N=6095 ARG predicted (0.2% of 3,9 million gene catalogue)
- Average 1377 ARG per subject (min. 258, max. 2367)
- Low identity with known ARG (mean 29,8% amino-acid identity)
- Present in the main gut phyla
- Mostly chromosomal
- Transferability to pathogens?

Ruppé, Ghoulane, Tap et al. *Nat Microbiol* 4, 112–123 (2019).



6

The intestinal microbiota is mainly made of **anaerobic bacteria**, opportunistic pathogens are subdominant

Majority of WHO priority pathogens have an **intestinal reservoir**

Antibiotics **affect** the intestinal microbiota and promote the expansion of resistant bacteria

Anaerobic bacteria harbor a vast diversity of **antibiotic resistance genes**, yet they are different from those carried by resistant pathogens

# Thank you!

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