



# The Human Microbiome

Department of Medical Microbiology

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used some slides from the presentation Strauss Lecture Series October 19, 2016



# Traditional Clinical Microbiology

- Microbes as agents of disease: pathogenic “terrorists”
- Detected by microscopy and culture
- Characterized by growth on specific media, sensitivity to antibiotics...

...but 99% of all bacteria are unculturable, hence

-taxonomy is based on DNA sequencing

- characterized by genetic expression



# Human microbiome

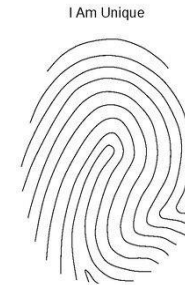
- The totality of microbes, their genomes and environmental interactions in & on the human organism

Composition of the microbiota (collective microorganisms) varies with each individual

Most species fairly stable

Some species transient

Each individual has a unique microbial “fingerprint”





# The normal microbiota

Humans are like mobile warm-blooded coral reefs, home to vast numbers of microbial ecosystems that are rich in biodiversity.

The vast majority of microbes are harmless or beneficial.



Robert Rountree, MD  
Strauss Lecture Series



“It is reasonable to propose that the composition of the microbiome and its activities are involved in most, if not all, of the biological processes that constitute human health and disease”

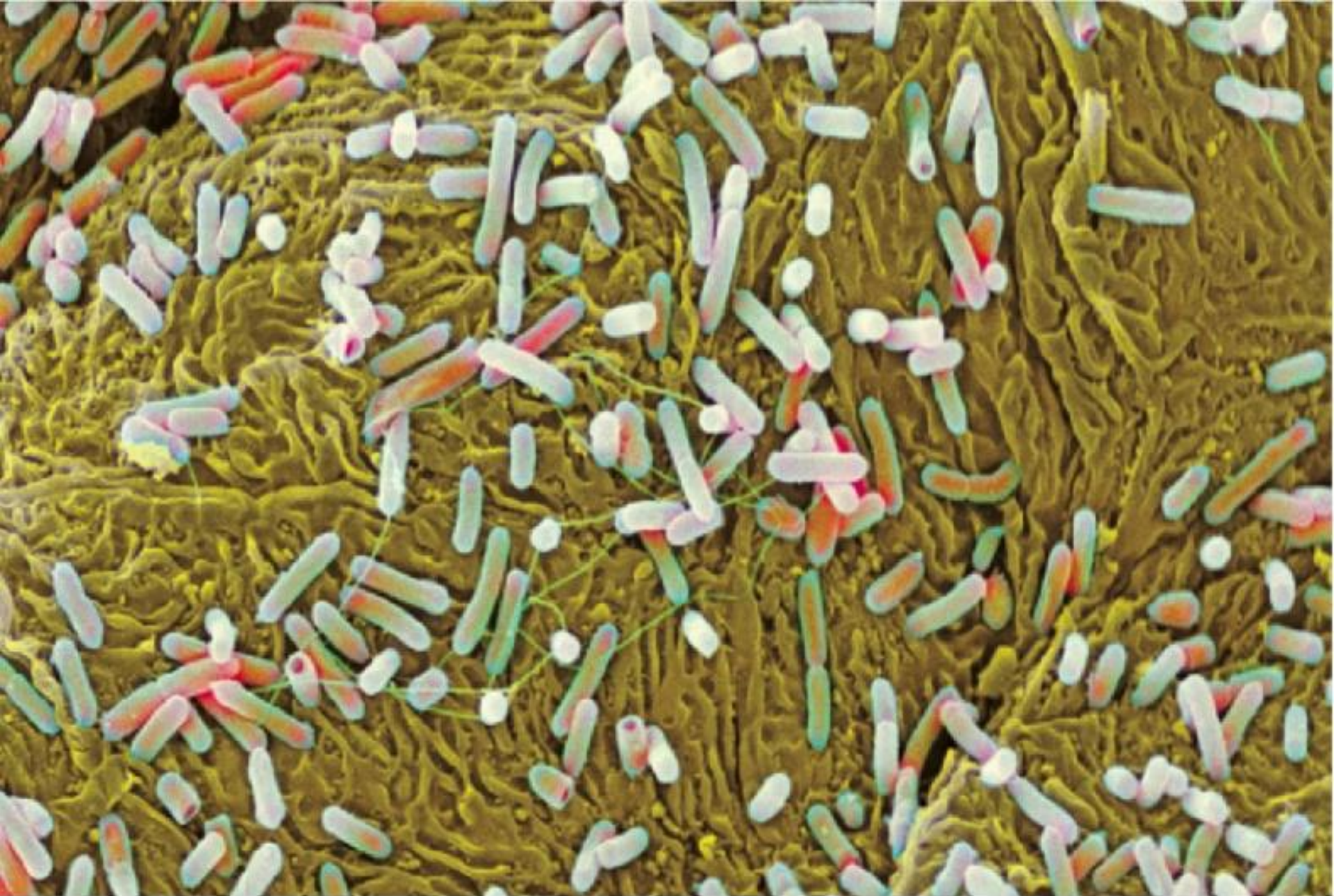
Martin J Blaser, MD

J Clin Invest. 2014;124(10):4162-4165



# Types of Human Microbiota

- Viruses (acellular, “nonliving”)
- Prokaryotes (without a nucleus):
  - Archaea (strict anaerobes)
  - Bacteria (aerobes and anaerobes)
- Eukaryotes (possess nucleus + organelles)
  - Microfungi (mycobiome)
  - Protozoa
  - Helminths (parasitic worms)



Bacteria colonizing the gut mucosa



# The Microbiome: Comparative Mass

## Meet your microbiome

The bacteria that call you home

### NOSE

Mass of microbes **10g**

Typical resident *Streptococcus*

### MOUTH

Mass of microbes **20g**

Typical resident  
*Streptococcus* (cheek),  
*Neisseria* (teeth)

### VAGINA

Mass of microbes **20g**

Typical resident *Lactobacillus*

### SKIN

Mass of microbes **200g**

Typical resident  
*Staphylococcus* (oily areas),  
*Corynebacteria* (moist areas)

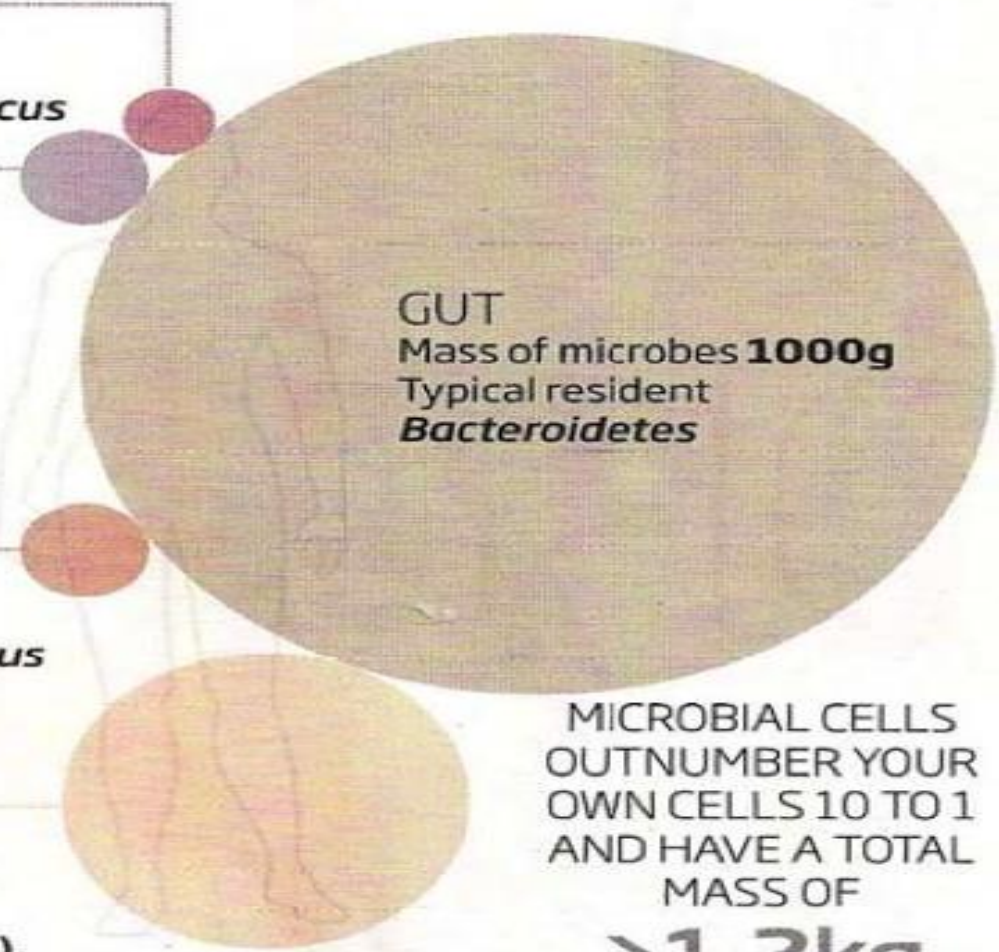
### GUT

Mass of microbes **1000g**


Typical resident  
*Bacteroidetes*

MICROBIAL CELLS  
OUTNUMBER YOUR  
OWN CELLS 10 TO 1  
AND HAVE A TOTAL  
MASS OF

**> 1.2kg**







6-10 billion bacteria  
archaea  
protozoa  
fungi  
viruses

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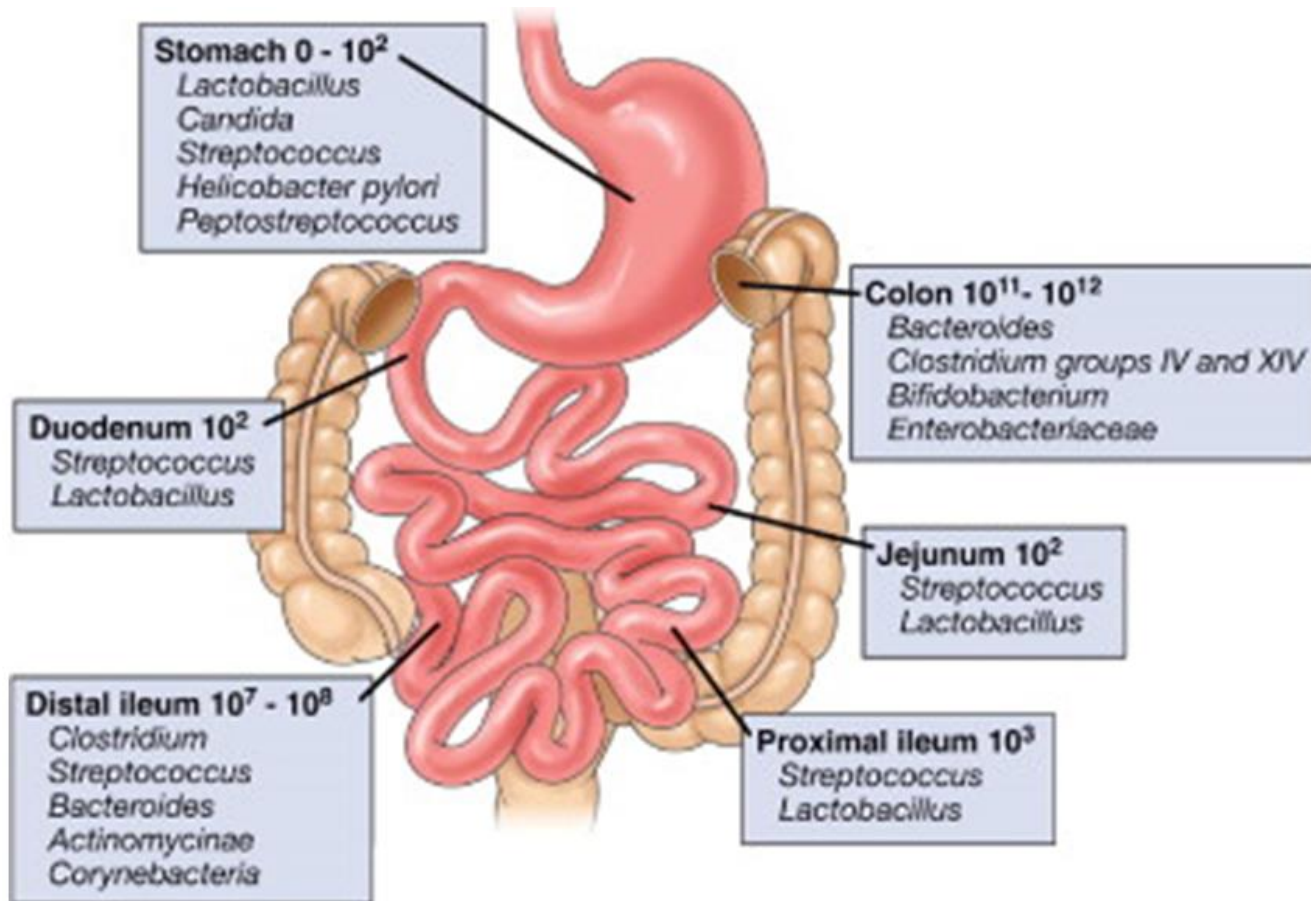
# Shaping the oral microbiota through intimate kissing

- Kissing for 10 seconds transfers an average of 80 million bacteria
- Couples who reported they kissed more often ended up having more similar microbiota than less-frequent kissers
- Similarity most pronounced for tongue surface





# Composition and luminal concentrations of dominant microbial species in various regions of the gastrointestinal tract





# Intestinal microbiota

- $>10^{14}$  microorganisms in GIT making us 90% bugs and 10% “us”!
- “Dysbiosis”= dysregulated (abnormal) microbiota. Common to many diseases including diabetes, colon cancer, and IBD
- Site specific microbiota in GIT



# Functions of the Gut Metagenome

- Digestion/metabolism: energy and nutrient extraction
- Production of vitamins & metabolites
- Protection against infection
- Maintenance of gut barrier
- Immune modulation
- Influences on mood & behavior



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# Major Influences on Individual Microbiomes

- Host genotype
- Type of birth (vaginal vs C-section)
- Excessive hygiene
- Diet (macronutrients, fiber, phytochemicals, alcohol)
- Stress (social, emotional)



Exposures during human evolution	Situation in modern urban centre
<b>Helminths</b> Gut and non-gut (blood)	LOST
<b>Ectoparasites</b> Fleas, lice, mites, ticks	MOSTLY LOST
<b>Carrier states</b> Salmonella, hepatitis A virus, <i>H. pylori</i> , TB, toxoplasma	MOSTLY LOST
<b>Microbiota</b> of other humans: skin, gut, airway, oropharyngeal, genitourinary	DIMINISHED diversity
<b>Microbiota</b> of natural environment: animals, soil, air, plants (rhizosphere, phyllosphere)	VARIABLE loss



# Richness of human gut microbiome correlates with metabolic markers

Nature 2013, Vol 500: 541-549

- Individuals with a low bacterial richness (23% of the population) are characterized by more marked overall adiposity, insulin resistance and dyslipidemia and a more pronounced inflammatory phenotype when compared with high bacterial richness individuals
- The obese individuals among the lower bacterial richness group also gain more weight over time





# Antibiotic overuse: Stop the killing of beneficial bacteria

Blaser; Nature, 2011, Vol 476: 393-394

- Evidence is accumulating that our welcome residents do not recover completely from antibiotics or are replaced in the long term by resistant organisms
- Overuse of antibiotics could be fueling the dramatic increase in conditions such as obesity, type 1 diabetes, inflammatory bowel disease, allergies and asthma, which have more than doubled in many populations



David J. Phillip / Getty Images

Stop the killing of  
beneficial bacteria

Concerns about antibiotics focus on bacterial resistance — but permanent changes to our protective flora could have more serious consequences, says **Martin Blaser**.



## Increased Risk of Childhood Asthma From Antibiotic Use in Early Life\*

Anita L. Kozyrskyj, PhD; Pierre Ernst, MD; and Allan B. Becker, MD

*Background:* To address the major methodological issues of reverse causation and selection bias in epidemiologic studies of antibiotic use in early life and the development of asthma, we undertook a cohort study of this association in a complete population of children.

*Methods:* Using the health-care and prescription databases of Manitoba, Canada, this longitudinal

“Independent of well-known asthma risk factors, asthma was significantly more likely to develop at age 7 years in children who had received antibiotics in the first year of life.”

1.14 to 1.88), especially among rural children, and in the absence of maternal asthma or a dog in the birth year. Broad-spectrum (BS) cephalosporin use was more common in these subpopulations of children.

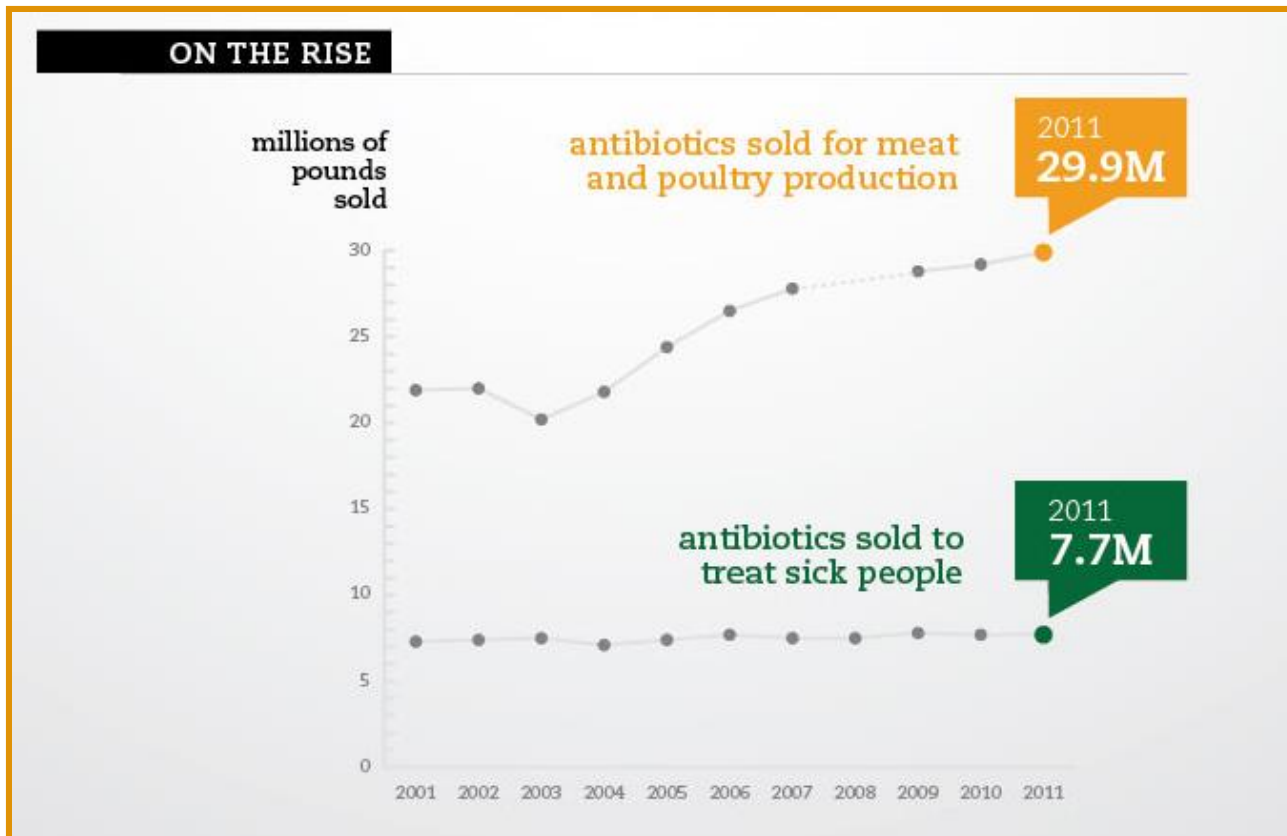
*Conclusions:* Antibiotic use in early life was associated with the development of childhood asthma, a risk that may be reduced by avoiding the use of BS cephalosporins.

(CHEST 2007; 131:1753–1759)



40% of all adults and 70% of all children in the U.S. take one or more courses of antibiotics every year (CDC)

80% of antibiotics in U.S. are given to animals for non-therapeutic purposes





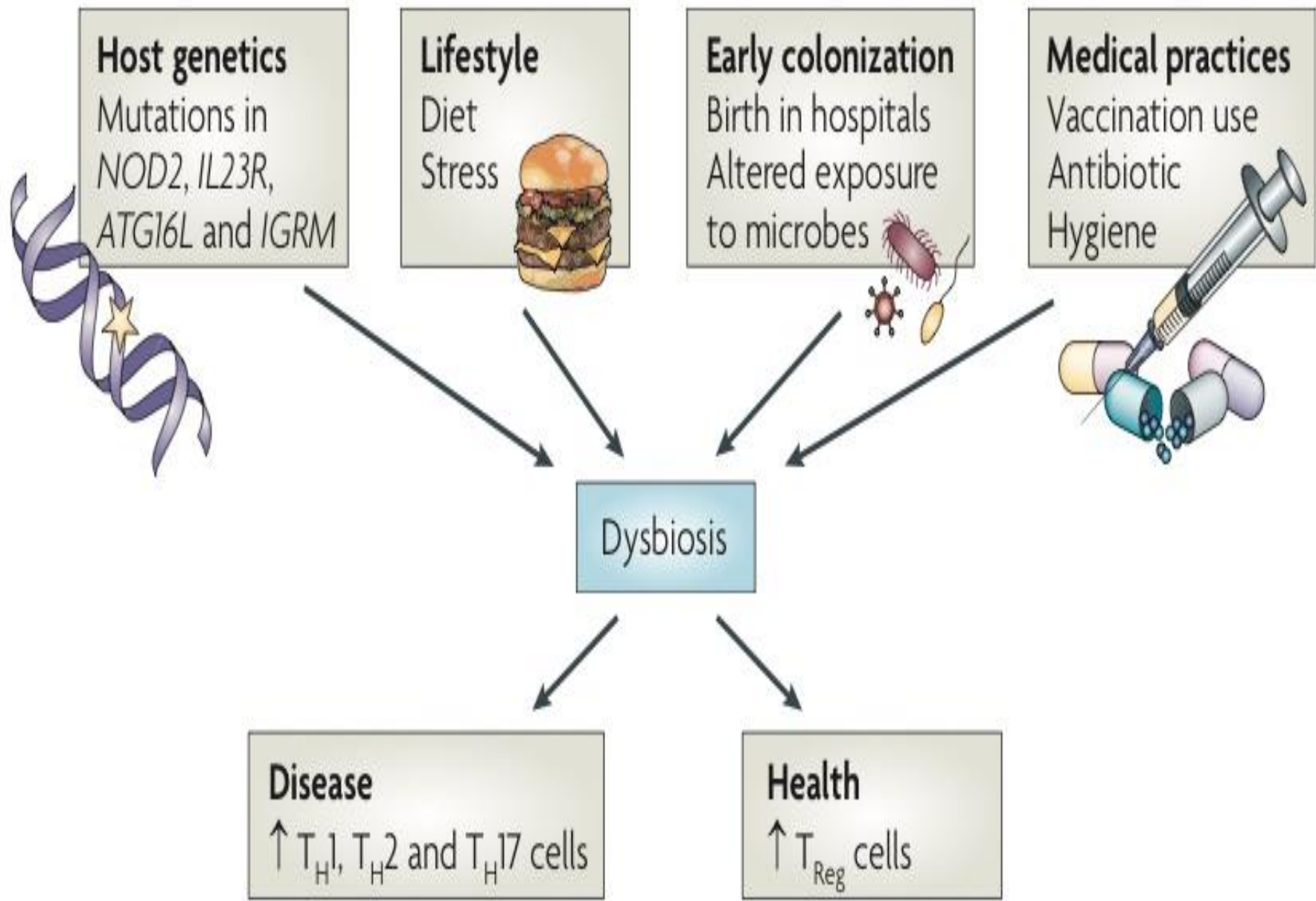
# Dysbiosis

- Microbial imbalance, most commonly in the gastrointestinal tract
- Associated with chronic intestinal symptoms: gas, bloating, diarrhea, constipation
- May predispose to a chronic diseases
- Contributes to “leaky gut” syndrome (hyperpermeable tight junctions)



# Membership and Behavior of Ultra-Low-Diversity Pathogen Communities Present in the Gut of Humans during Prolonged Critical Illness

- Prolonged stays in ICU leads to “complete ecological collapse” with the emergence of ultra-low (1–4 taxa) multi-drug resistant pathogenic bacteria communities in 30% of patients;
- ~75% of cases *C albicans* & *C glabrata* overgrowth
- These limited communities keep each other in check until triggered by acute stressful events (opioids) which can lead to life-threatening sepsis





# Dysbiotic Events in Gut Microbiota: Impact on Human Health

Nutrients 2014, 6, 5786-5805

Dybiosis (gut microbial imbalance) has been linked with important human diseases, including autoimmune and/or autoinflammatory disorders, such as IBD, metabolic disorders, such as, obesity, type 2 diabetes, allergies, and neurological disorders



# Supporting The Microbiome

- **Consume prebiotic fibers:**
  - pectin, inulin, fructo-oligosaccharides, hydrolyzed guar, larch arabinogalactan, gum arabic, beta glucans, boabab, chicory root, asparagus, dandelion greens, garlic, onions, leeks, wheat bran, bananas
- Eat fermented foods: fresh sauerkraut, kimchi
- Take probiotics
  - Yogurt (homemade)
  - Lactobacilli (multiple species)
  - Bifidobacteria (multiple species)
  - *Saccharomyces boulardii*





# Conclusions I

- Research into the microbiome using DNA sequencing has redefined what it means to be human
- Humans are superorganisms that represent a blend of genetic traits from human & microbial cells
- Our microbiomes have a major impact on our digestion, metabolism, neurology & immunology



# Conclusions II

- The vast majority of our interactions with bacteria are either neutral or mutually beneficial: maintaining tolerance is essential to health
- Alteration of the microbiome by our modern lifestyle (diet, stress, excessive hygiene and antibiotics) may be responsible for many chronic diseases
- Dietary changes, prebiotics and probiotics may help to maintain a healthy microbiome