تأثير المضادات الحيوية ومتبقياتها على صحه وسلامه الانسان

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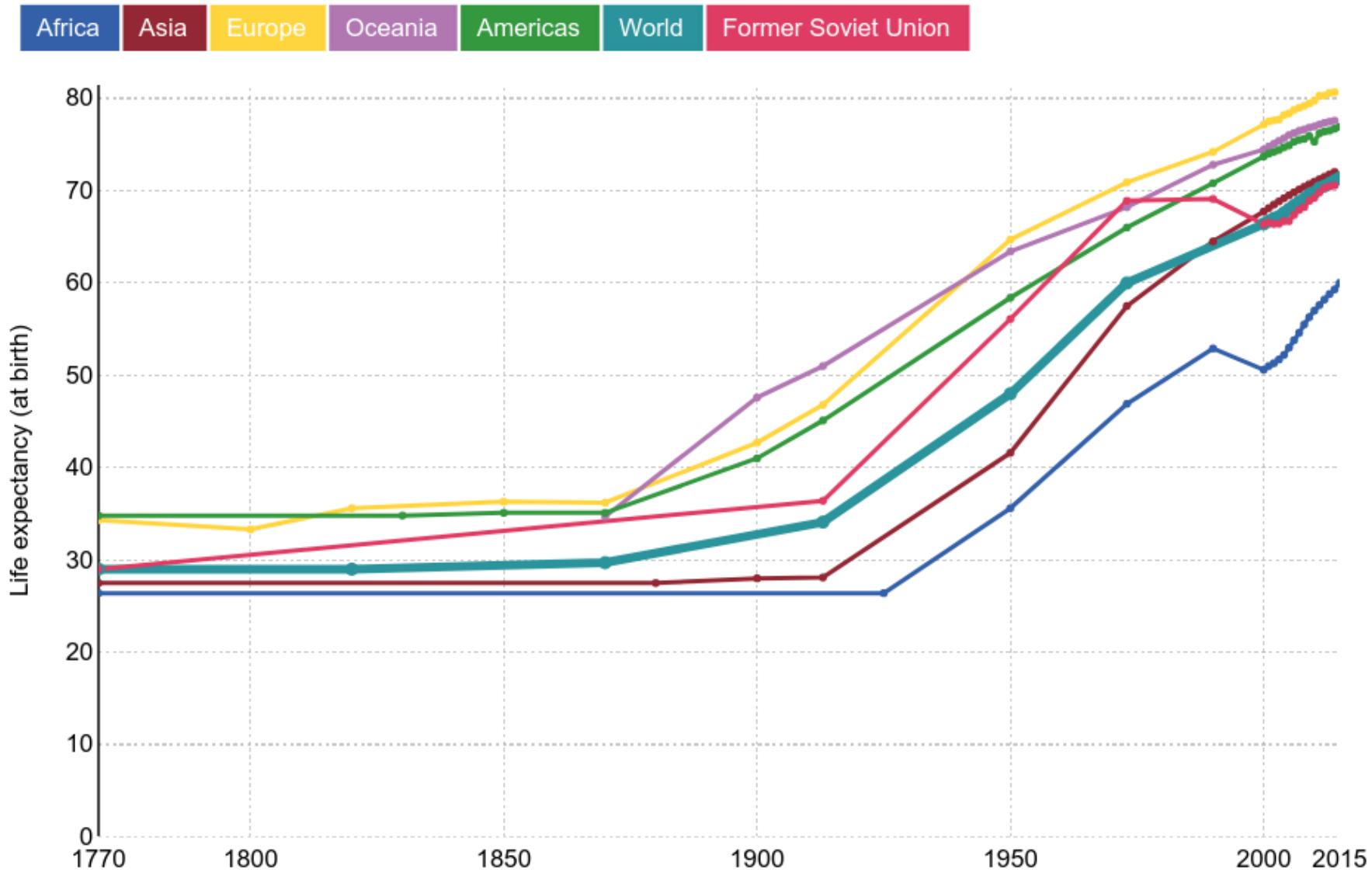
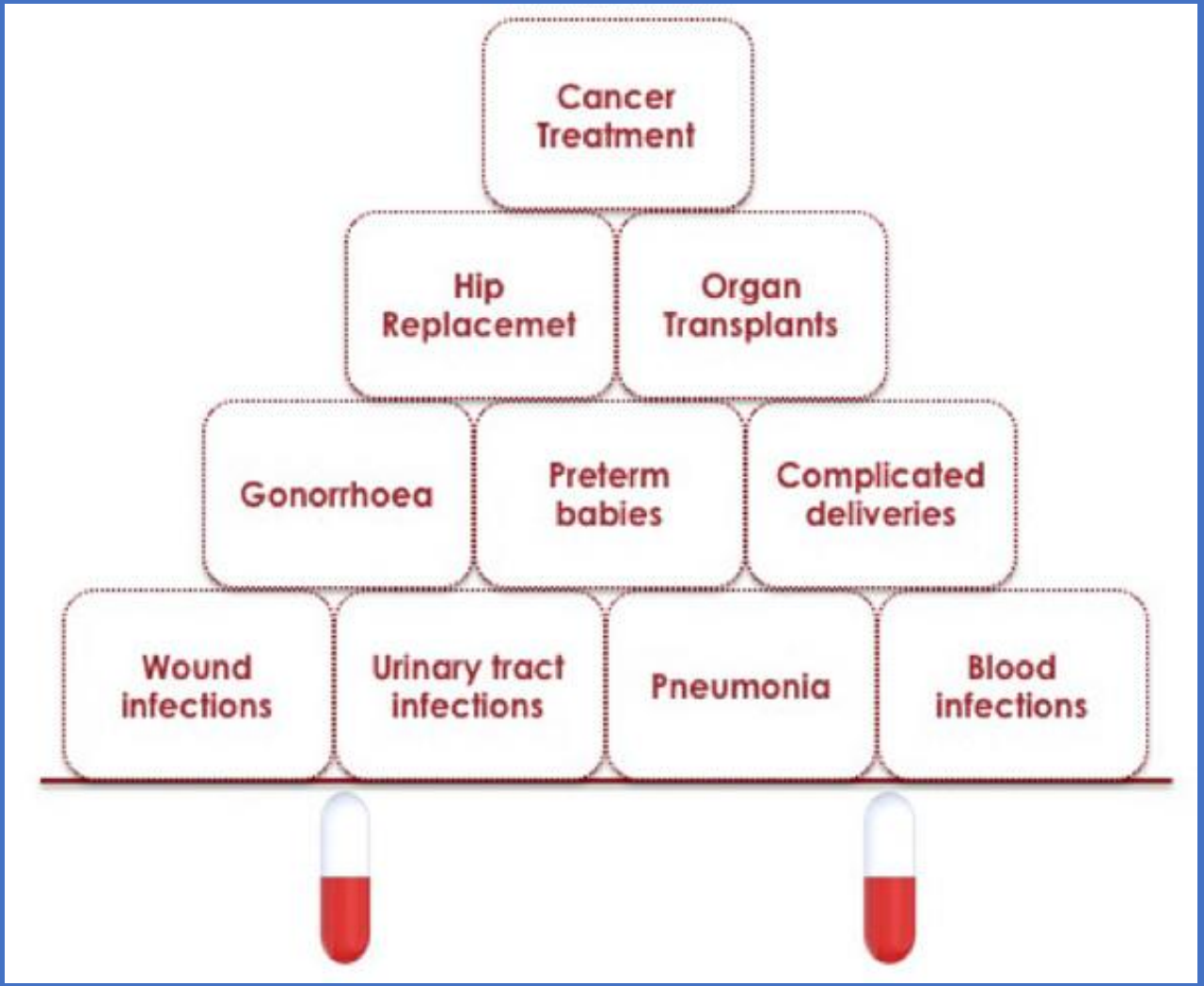
جامعه النجاح الوطنية

Life expectancy globally and by world regions since 1770



Source: Life expectancy – James Riley for data 1990 and earlier; WHO and World Bank for later data (by Max Roser) OurWorldInData.org/life-expectancy/ • CC BY-SA

Antibiotics changed the world



Without antibiotics 1 in every 6 would die.

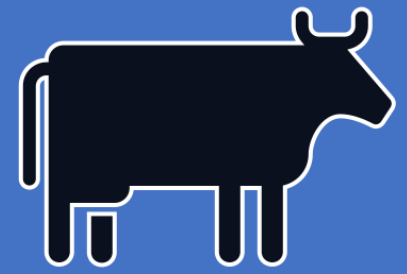
However…

Discovery	Resistance	
Penicillin 1943	• 1945	2 years
Vancomycin 1972	• 1988	16 years
Daptomycin 2003	• 2004	1 year

Overuse of antibiotics- the facts

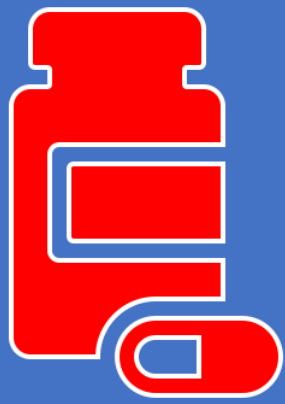
- The unpleasant truth is that our use and misuse of antibiotics has eroded their efficiency and fueled the spread of antibiotic resistance
- All antibiotic use, whether appropriate or not, contributes to the development and spread of resistant bacteria.
- Worldwide, antibiotics are used in massive amounts within the health care, veterinary and agricultural sectors.
- Antibiotic consumption for human health increased by 36% globally between 2000 and 2010, and the demand for antibiotics keeps increasing.

- Antibiotics used in production of food animals was estimated at >63,000 tons in 2010.

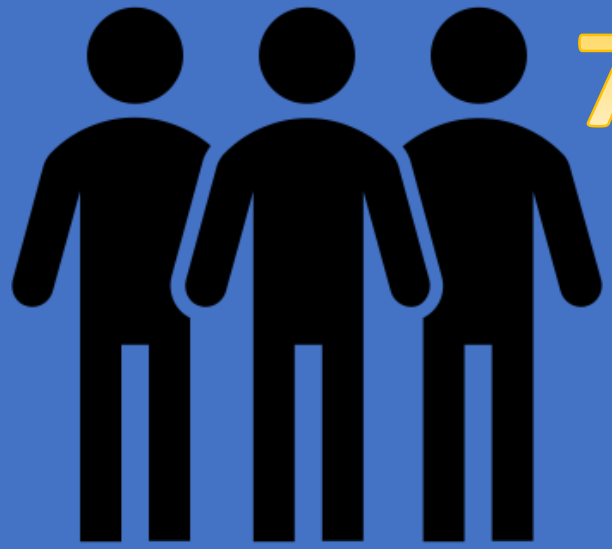


- Without major policy changes, consumption in the livestock sector is projected to rise by more than 60% by 2030.
- In the USA 60-80% antibiotics are given to healthy animals.

- Studies show that up to 75% of patients with colds are inappropriately given antibiotics. Antibiotics have no effect at all on colds.



Antibiotic resistance…



700,000 d… ye…

1 million human

…,000 death

…due to sepsis

Due to:

- Reduced **ability to cure common infectious diseases** such as pneumonia, tuberculosis and gonorrhea.
- **Undermine major medical advances** such as surgeries, treatment of cancer patients and care of preterm babies.
- Reduced **ability to reach global health goals** such as reduction of child mortality and improvement of maternal health.

Economic burden data of antibiotic resistance

- There is a lack of data on the economic burden of antibiotic resistance
- It was estimated:

The United States: Up to 20 billion US Dollars direct, and up to 35 billion indirect

European union: ~1.5 billion Euros

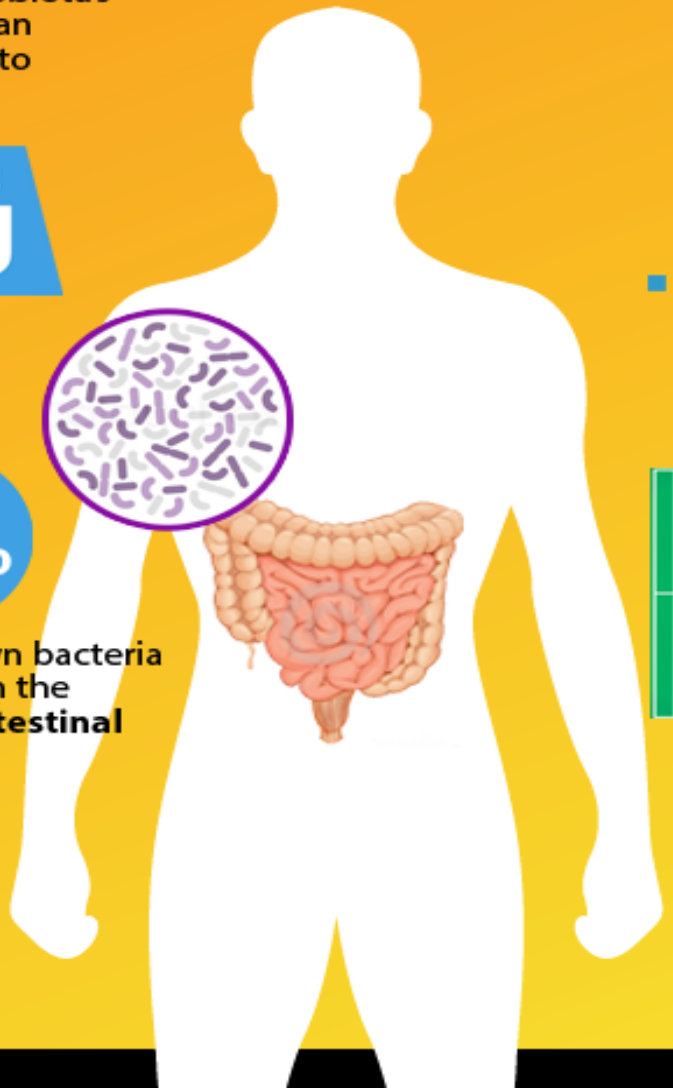
The most important effect of antibiotics residues in our food is:

They damage our own microbiota

Getting to know your gut microbiota

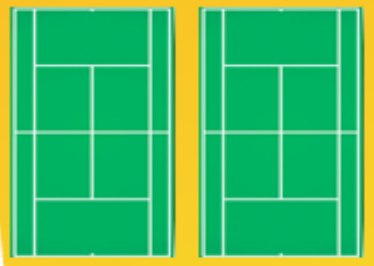
A huge quantity (hundreds of trillions) of bacteria and other microorganisms inhabit your intestines fulfilling key functions for your health and wellbeing

- Gut microbiota's **weight** can reach up to

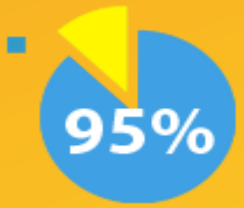


- Bacteria are **10 to 50** times smaller than human cells

- The **GI tract** surface is as big as 2 tennis courts **400m²**



- In our body **microbes outnumber** human cells by **10 :1**

- 

of our own bacteria located in the **gastrointestinal (GI) tract**

- Laid end to end, our body's bacteria would **circle the earth** **2,5 times**

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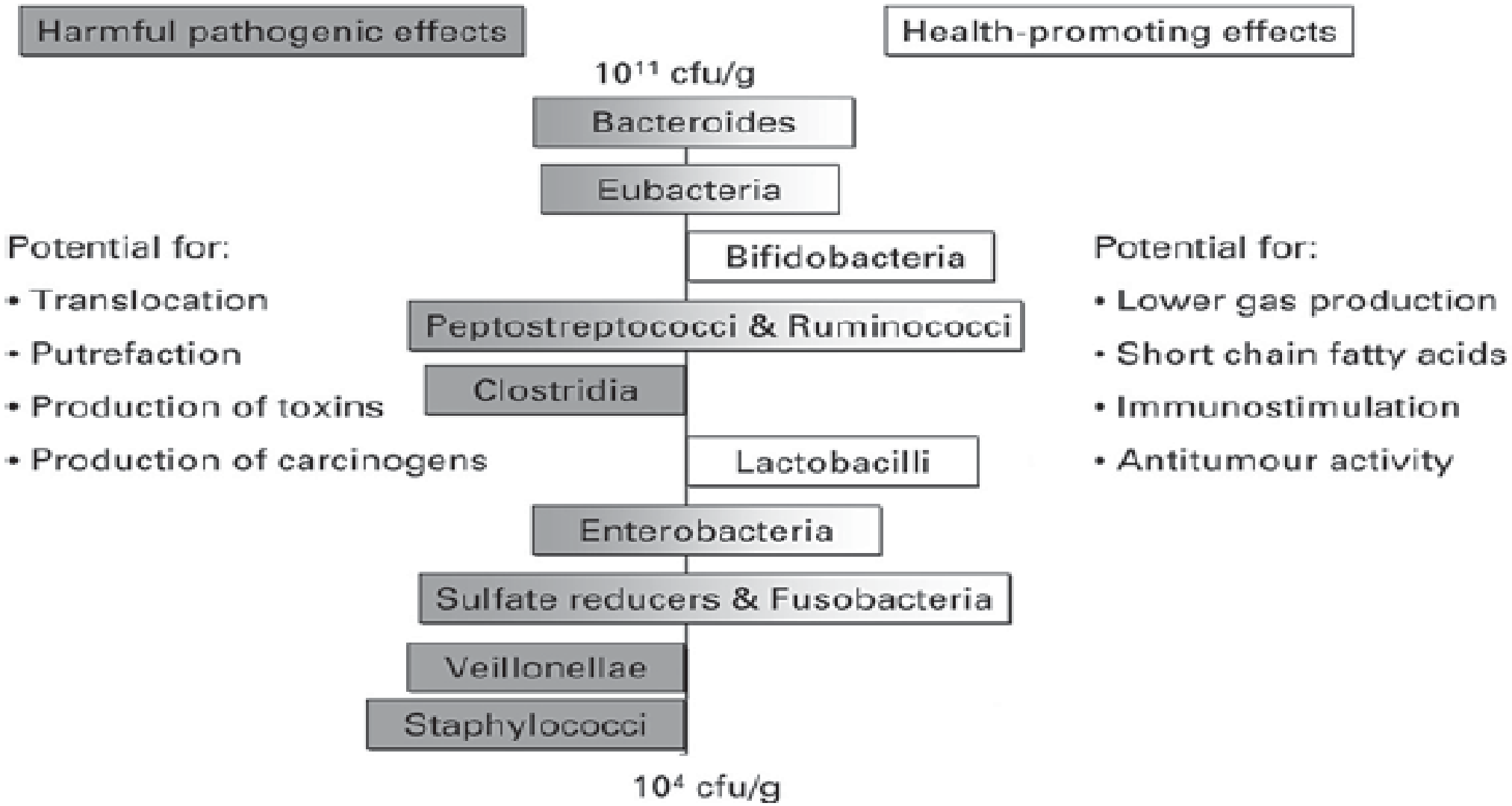
- Microbes live in a commensal way in the gut, they either:

1. Beneficial bacteria such as Befidobacteria, Lactobacillus spp.
2. Harmful bacteria such as Clostridia spp. (not always)
3. Neutral (not identified yet)

- A healthy person will have a balanced microbiota with minimum level of the harmful ones.
- **Dysbiosis**: when harmful bacteria take over in the system


Harmful pathogenic effects
Health-promoting effects
10^{11} cfu/g
Bacteroides
Eubacteria
Bifidobacteria
Peptostreptococci & Ruminococci
Clostridia
Lactobacilli
Enterobacteria
Sulfate reducers & Fusobacteria
Veillonellae
Staphylococci
10^{4} cfu/g
Potential for:
• Translocation
• Putrefaction
• Production of toxins
• Production of carcinogens
Potential for:
• Lower gas production
• Short chain fatty acids
• Immunostimulation
• Antitumour activity

What is the role of Gut Microbiota?

- Can convert dietary fibre to energy
- Produce some vitamins
- Protect against pathogens
- Reinforce gut barrier
- Boost the immune system
- Enhance liver, kidneys, brain, pancreas and skin functions
- Modulate hormones
- Affect lipids circulation
- And more

We can manipulate the gut microbiota by:

1. Food

2. Life style

3. Antibiotics

Some evidence

Cell Mol Life Sci. 2016 Jan;73(1):147-62. doi: 10.1007/s00018-015-2061-5. Epub 2015 Oct 12.

Gut microbiota and obesity.

Gérard P[1,2].

Author information

Abstract

The human intestine harbors a complex bacterial community called the gut microbiota. This microbiota is specific to each individual despite the existence of several bacterial species shared by the majority of adults. The influence of the gut microbiota in human health and disease has been revealed in the recent years. Particularly, the use of germ-free animals and microbiota transplant showed that the gut microbiota may play a causal role in the development of obesity and associated metabolic disorders, and lead to identification of several mechanisms. In humans, differences in microbiota composition, functional genes and metabolic activities are observed between obese and lean individuals suggesting a contribution of the gut microbiota to these phenotypes. Finally, the evidence linking gut bacteria to host metabolism could allow the development of new therapeutic strategies based on gut microbiota modulation to treat or prevent obesity.

KEYWORDS: Antibiotics; Fecal transplant; Gnotobiotic models; Intestinal permeability; Metabolic syndrome; Microbiome; Prebiotics; Probiotics

The gut microbiota, obesity and insulin resistance.

Shen J[1], Obin MS, Zhao L.

Author information

Abstract

The human gut is densely populated by commensal and symbiotic microbes (the "gut microbiota"), with the majority of the constituent microorganisms being bacteria. Accumulating evidence indicates that the gut microbiota plays a significant role in the development of obesity, obesity-associated inflammation and insulin resistance. In this review we discuss molecular and cell biological mechanisms by which the microbiota participate in host functions that impact the development and maintenance of the obese state, including host ingestive behavior, energy harvest, energy expenditure and fat storage. We additionally explore the diverse signaling pathways that regulate gut permeability and bacterial translocation to the host and how these are altered in the obese state to promote the systemic inflammation ("metabolic endotoxemia") that is a hallmark of obesity and its complications. Fundamental to our discussions is the concept of "crosstalk", i.e., the biochemical exchange between host and microbiota that maintains the metabolic health of the superorganism and whose dysregulation is a hallmark of the obese state. Differences in community composition, functional genes and metabolic activities of the gut microbiota appear to distinguish lean vs obese individuals, suggesting that gut 'dysbiosis' contributes to the development of obesity and/or its complications. The current challenge is to determine the relative importance of obesity-associated compositional and functional changes in the microbiota and to identify the relevant taxa and functional gene modules that promote leanness and metabolic health. As diet appears to play a predominant role in shaping the microbiota and promoting obesity-associated dysbiosis, parallel initiatives are required to elucidate dietary patterns and diet components (e.g., prebiotics, probiotics) that promote healthy gut microbiota. How the microbiota promotes human health and disease is a rich area of investigation that is likely to generate fundamental discoveries in energy metabolism, molecular endocrinology and immunobiology and may lead to new strategies for prevention of obesity and its complications.

Genome Med. 2016 Apr 20;8(1):42. doi: 10.1186/s13073-016-0303-2.

Impact of the gut microbiota on inflammation, obesity, and metabolic disease.

Boulangé CL[1], Neves AL[2], Chilloux J[2], Nicholson JK[3,4], Dumas ME[5].

Author information

Abstract

The human gut harbors more than 100 trillion microbial cells, which have an essential role in human metabolic regulation via their symbiotic interactions with the host. Altered gut microbial ecosystems have been associated with increased metabolic and immune disorders in animals and humans. Molecular interactions linking the gut microbiota with host energy metabolism, lipid accumulation, and immunity have also been identified. However, the exact mechanisms that link specific variations in the composition of the gut microbiota with the development of obesity and metabolic diseases in humans remain obscure owing to the complex etiology of these pathologies. In this review, we discuss current knowledge about the mechanistic interactions between the gut microbiota, host energy metabolism, and the host immune system in the context of obesity and metabolic disease, with a focus on the importance of the axis that links gut microbes and host metabolic inflammation. Finally, we discuss therapeutic approaches aimed at reshaping the gut microbial ecosystem to regulate obesity and related pathologies, as well as the challenges that remain in this area.

PMID: 27098727 PMCID: PMC4839080 DOI: 10.1186/s13073-016-0303-2

Circ Res. 2017 Mar 31;120(7):1183-1196. doi: 10.1161/CIRCRESAHA.117.309715.

Gut Microbiota in Cardiovascular Health and Disease.

Tang WH[1], Kitai T[2], Hazen SL[2].

Author information

Abstract

Significant interest in recent years has focused on gut microbiota-host interaction because accumulating evidence has revealed that intestinal microbiota play an important role in human health and disease, including cardiovascular diseases. Changes in the composition of gut microbiota associated with disease, referred to as dysbiosis, have been linked to pathologies such as atherosclerosis, hypertension, heart failure, chronic kidney disease, obesity, and type 2 diabetes mellitus. In addition to alterations in gut microbiota composition, the metabolic potential of gut microbiota has been identified as a contributing factor in the development of diseases. Recent studies revealed that gut microbiota can elicit a variety of effects on the host. Indeed, the gut microbiome functions like an endocrine organ, generating bioactive metabolites, that can impact host physiology. Microbiota interact with the host through many pathways, including the trimethylamine/trimethylamine *N*-oxide pathway, short-chain fatty acids pathway, and primary and secondary bile acids pathways. In addition to these metabolism-dependent pathways, metabolism-independent processes are suggested to also potentially contribute to cardiovascular disease pathogenesis. For example, heart failure-associated splanchnic circulation congestion, bowel wall edema, and impaired intestinal barrier function are thought to result in bacterial translocation, the presence of bacterial products in the systemic circulation and heightened inflammatory state. These are thought to also contribute to further progression of heart failure and atherosclerosis. The purpose of the current review is to highlight the complex interplay between microbiota, their metabolites, and the development and progression of cardiovascular diseases. We will also discuss the roles of gut microbiota in normal physiology and the potential of modulating intestinal microbial inhabitants as novel therapeutic targets.

J Alzheimers Dis. 2017;58(1):1-15. doi: 10.3233/JAD-161141.

The Gut Microbiota and Alzheimer's Disease.

Jiang C[1], Li G[2], Huang P[1], Liu Z[1], Zhao B[1].

Author information

Abstract

The gut microbiota comprises a complex community of microorganism species that resides in our gastrointestinal ecosystem and whose alterations influence not only various gut disorders but also central nervous system disorders such as Alzheimer's disease (AD). AD, the most common form of dementia, is a neurodegenerative disorder associated with impaired cognition and cerebral accumulation of amyloid-β peptides (Aβ). Most notably, the microbiota-gut-brain axis is a bidirectional communication system that is not fully understood, but includes neural, immune, endocrine, and metabolic pathways. Studies in germ-free animals and in animals exposed to pathogenic microbial infections, antibiotics, probiotics, or fecal microbiota transplantation suggest a role for the gut microbiota in host cognition or AD-related pathogenesis. The increased permeability of the gut and blood-brain barrier induced by microbiota dysbiosis may mediate or affect AD pathogenesis and other neurodegenerative disorders, especially those associated with aging. In addition, bacteria populating the gut microbiota can secrete large amounts of amyloids and lipopolysaccharides, which might contribute to the modulation of signaling pathways and the production of proinflammatory cytokines associated with the pathogenesis of AD. Moreover, imbalances in the gut microbiota can induce inflammation that is associated with the pathogenesis of obesity, type 2 diabetes mellitus, and AD. The purpose of this review is to summarize and discuss the current findings that may elucidate the role of the gut microbiota in the development of AD. Understanding the underlying mechanisms may provide new insights into novel therapeutic strategies for AD.

KEYWORDS: Aging; Alzheimer’s disease; amyloid; amyloid beta-peptides; blood-brain barrier; dysbiosis; gut microbiota; lipopolysaccharides; obesity; type 2 diabetes mellitus

Nat Rev Gastroenterol Hepatol. 2017 Oct;14(10):573-584. doi: 10.1038/nrgastro.2017.88. Epub 2017 Jul 19.

Gut microbiota and IBD: causation or correlation?

Ni J[1], Wu GD[1], Albenberg L[2], Tomov VT[1].

Author information

Abstract

A general consensus exists that IBD is associated with compositional and metabolic changes in the intestinal microbiota (dysbiosis). However, a direct causal relationship between dysbiosis and IBD has not been definitively established in humans. Findings from animal models have revealed diverse and context-specific roles of the gut microbiota in health and disease, ranging from protective to pro-inflammatory actions. Moreover, evidence from these experimental models suggest that although gut bacteria often drive immune activation, chronic inflammation in turn shapes the gut microbiota and contributes to dysbiosis. The purpose of this Review is to summarize current associations between IBD and dysbiosis, describe the role of the gut microbiota in the context of specific animal models of colitis, and discuss the potential role of microbiota-focused interventions in the treatment of human IBD. Ultimately, more studies will be needed to define host-microbial relationships relevant to human disease and amenable to therapeutic interventions.

PMID: 28743984 PMCID: PMC5880536 DOI: 10.1038/nrgastro.2017.88

ANTIBIOTICS ALTER THE BALANCE OF COMMUNITY AND FUNCTION OF INTESTINAL MICROBIOTA

- Studies on the effect of exposure to antibiotics immediately after birth show that the abundance and diversity of intestinal microbiota change regardless of the kind of antibiotic
- In particular, the abundance and diversity of the intestinal microbiota decreases rapidly with exposure to meropenem, cefotaxime, and ticarcillin-clavulanate.
- In particular, ticarcillin-clavulanate and ampicillin are associated with a marked increase in *Klebsiella pneumoniae*
- Clindamycin is known to have the greatest effect on the function of intestinal microbiota that shows resistance to the pathogenic bacteria *C. difficile.*

- Studies of the effects of clarithromycin, metronidazole, and omeprazole on the composition of the pharyngeal and fecal bacterial taxa show that these antibiotics may affect 30% or more of the microbiota composition, and although the microbiota may partially recover, the effects can persist for at least 4 years after exposure.
- Ciprofloxacin was prescribed for 5 days to patients who had not taken the antibiotic previously, showed that bacterial taxa decreased by approximately one-third, and the taxonomic abundance, diversity, and uniformity of the intestinal microbiota decreased.
- Some changes persist after 6 months
- re-exposure to the same amount of ciprofloxacin 6 months later showed similar effects on the structure of intestinal microbiota, with less efficiency for recovery.

How can we help our microbiota.

- Increase probiotics, prebiotics and synbiotics in the diet
- Increase dietary fibre
- No antibiotic unless it is really needed. Also NSAID.
- Increase fruits and vegetables (coloured fruits and veges)
- Nuts
- Olive oil more than seeds oil
- Lean meat and to minimum level
- Moderate tea and coffee consumption
- Exercise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