Microbe of the month

Breaking The Chain of Infection

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Newsletter

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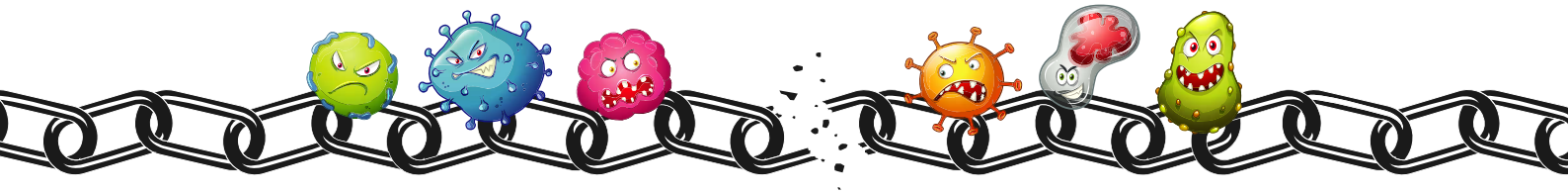


Featured this month:

The human microbiome and the immune system

A mystery we are only just beginning to understand

We share our bodies with more than a ***hundred trillion*** microbes, and they outnumber our human cells by ten to one. The majority live in our gut – especially the large intestine – and their wellbeing and diversity are key factors for good health, playing an important role in our predisposition to chronic diseases and infection.

Throughout the history of microbiology, most human studies have focused on disease-causing (pathogenic) organisms found in or on people; very few have examined the benefits of ***commensal*** microbes. In the past decade, research into this poorly-understood subject has become one of the most exciting fields in science.

What is the microbiome?

The microbiome comprises the genetic material of all the bacteria, fungi and viruses that live on and inside the human body. This genetic material is 200 times the number of genes in the human genome, and the microbiome is estimated to weigh as much as five pounds (2.25kg)!

The gastrointestinal tract has the largest and most complex population of microorganisms, as well as the largest mass of ***lymphoid tissue*** , the first line of defence of the intestinal mucosa.

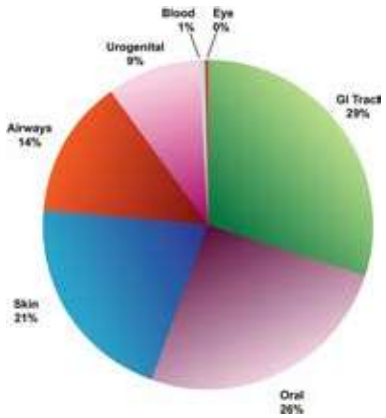
The ***microbiota*** present at different body sites affects numerous biological functions important for maintaining health, whereas disruption of the composition and function of gut flora (referred to as ***dysbiosis***) can contribute to disease development.

The International Human Microbiome Consortium(IHMC) and the Human Microbiome Project (HMP)

The IHMC was constituted in 2005 in order to understand how microbes influence human health and disease.

In 2008, the National Human Genome Research Institute (part of the U.S. National Institutes of Health (NIH) joined this effort as an extension of the Human Genome Project, studying the normal microbial composition of 4 body sites – the gastrointestinal tract, the mouth, the vagina and the skin.

The discovery of previously-uncharted microbial species and genes serves as a roadmap for discovering the role of the microbiome in health, nutrition, immunity and disease.



Bacterial distribution by body site

Why is this relevant to clinical practice?

The bacteria living in and on us are not invaders, but beneficial ***colonisers***.
They help to digest our food, regulate our immune response, protect against other pathogenic bacteria, and produce several vitamins, which include vitamin B12, thiamine and riboflavin, and vitamin K which is required for clotting.

In microbiology, there are many examples of microbial cooperation:

- ***Mutualism*** is a relationship in which both species benefit.
- ***Commensalism*** is a relationship between microbial species in which one benefits and the other is unaffected.
- ***Symbiotic*** relationships are usually long-term and have a strong impact on the fitness of one or both organisms.

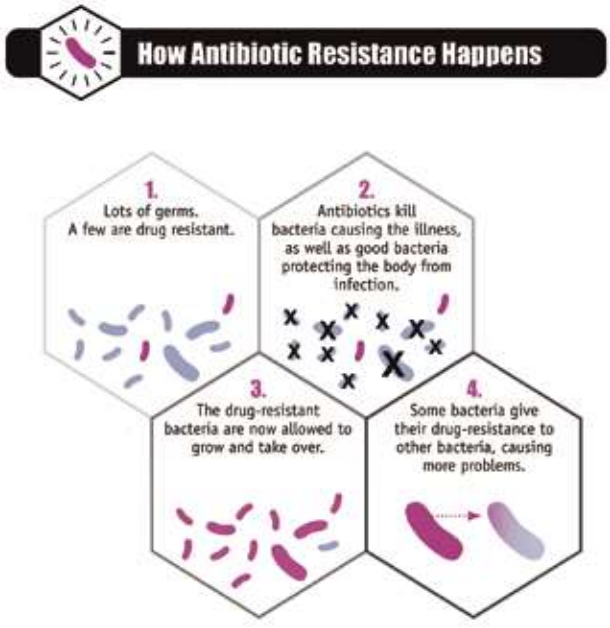
In chronic and non-healing wounds, it is important to understand that many of the bacterial species - and even fungi – colonizing the wound, or even causing wound infection, will also be representative of the species present on the patient's skin and in their intestine. Combinations of certain bacterial species are also known to trigger inflammatory symptoms and delay healing.

If you take a superficial swab of the wound bed for microbiological analysis, multiple species of microorganisms will be present – most of them harmless colonizers – whilst pathogens may be missed entirely! Therefore, always use the correct technique for obtaining specimens, and provide some background for the laboratory technologist Eg. patient risk factors, any underlying chronic conditions, recent antibiotic consumption and most importantly, ***the site*** from which the wound specimen was taken.

Mutualistic microbes interact with many physiological processes and participate in the regulation of immune and metabolic ***homeostasis***. Studies in mice have demonstrated that some combinations of microbes even determine the bioavailability and metabolism of drugs. A more complete understanding of the diversity of microbes in the human microbiome could lead to new therapies – for example, treating a bacterial infection caused by a species or combination of pathogenic bacteria by increasing the numbers of 'good' or beneficial bacteria.

BE ANTIBIOTICS AWARE
SMART USE, BEST CARE

The effects of antibiotics on the gut microbiota

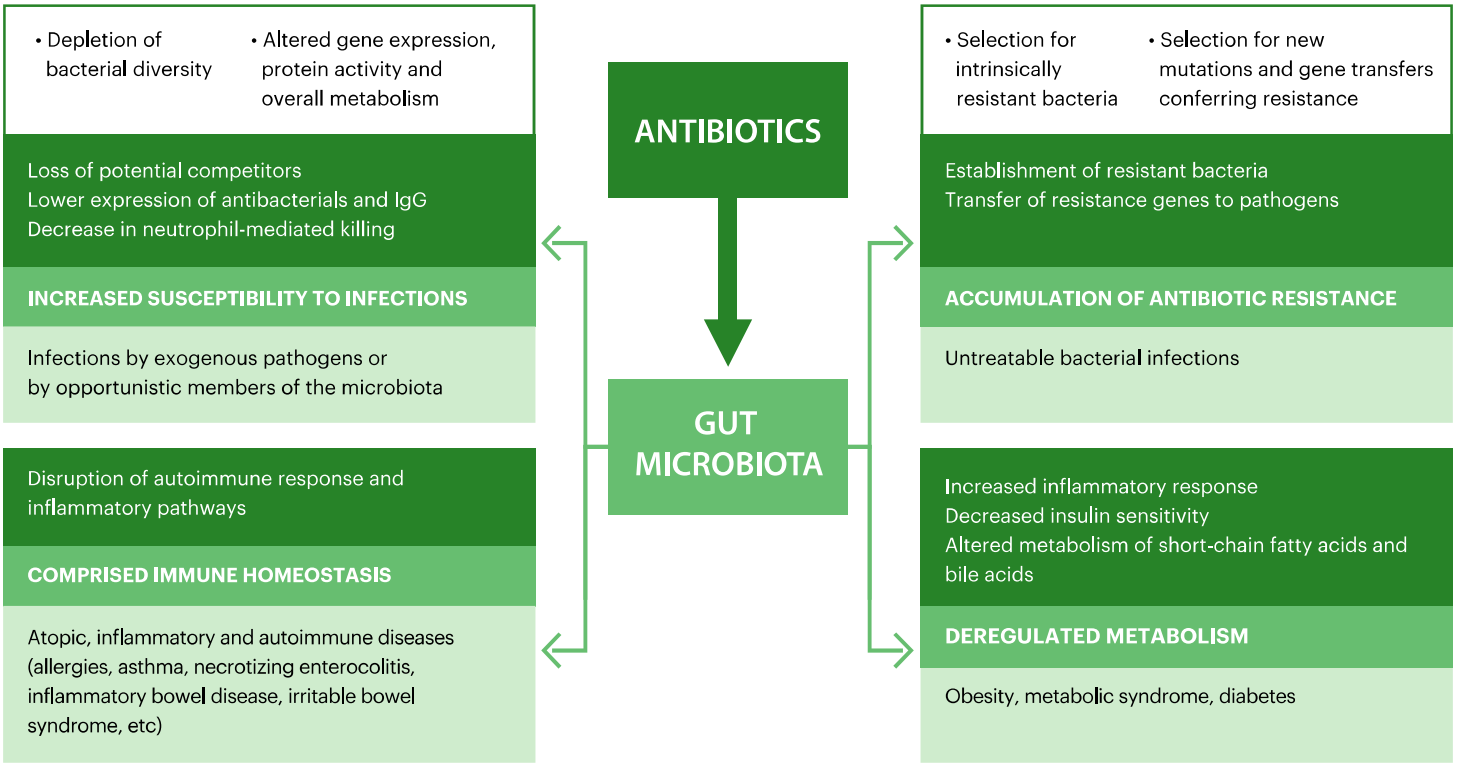


Source: Melissa Brower, CDC

The human microbiome is overly-exposed to antibiotics given their use in medicine, and also in farm animals and crops. Composition of the human microbiome is rapidly altered by exposure to antibiotics, with potentially immediate effects on health – for example, through the selection of ***resistant opportunistic pathogens***. Thus, the human gut has long been established as a significant ***reservoir of antibiotic resistance***.

Antibiotic-induced imbalances in the gut microbiome may also impact on the types of microbial species in a chronic wound – the fungus *Candida albicans* and carbapenem resistant strains of the bacteria *Pseudomonas aeruginosa or E. coli* (referred to as 'CRE') are common examples.

Broad spectrum antibiotic therapy can affect 30% of the gut community, causing a rapid and significant drop in species diversity. Once antibiotic treatment has stopped, the microbiota may demonstrate a degree of resilience. This may see it returning to a composition similar to the original one, but the initial state is often not completely recovered. In fact, antibiotic-induced dysbiosis can persist for long periods of time, spanning months or even years. The use of probiotic bacteria aimed at impeding dysbiosis or at re-establishing the gut microbiota after antibiotic treatment is a promising approach.[3]



Antibiotic effects on the gut microbiota and associated health problems

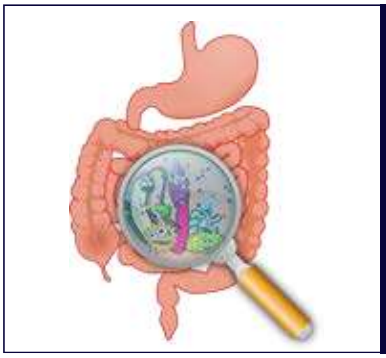
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4709861/

The effects of antibiotic-induced dysbiosis on immune and metabolic health

Intestinal microbes consume non-digestible carbohydrates to produce short-chain fatty acids (SCFAs) which are used locally by the protective epithelial cells of the colon, or are transported across the gut epithelium into the bloodstream. SCFAs are major players in the maintenance of gut physiology and integrity, promoting immune and metabolic homeostasis and having important anti-inflammatory and anti-tumour effects.
One of the greatest threats from alterations in the gut microbiota is the increased susceptibility to intestinal infections, which can stem from newly-acquired pathogens or from the sudden overgrowth and pathogenic behaviour of opportunistic organisms already present.

In particular, antibiotic-associated diarrhoeas (AAD) due to nosocomial pathogens are a frequent occurrence. These are often associated with organisms such as *Klebsiella pneumoniae, Staphylococcus aureus* and, of most concern, *Clostridium difficile*, which can cause intractable, long-term recurrent infections, and even a potentially lethal pseudomembranous colitis. In premature infants who are heavily treated with broad-spectrum antibiotics, disruption of gut microbiota composition has been linked to numerous disorders involving processes of inflammation and autoimmunity, dramatically increasing the risk of necrotizing enterocolitis (NEC).

Bloodstream infection in immunocompromised individuals is a life-threatening condition that increases in risk due to antibiotic treatment. In the clinical setting, intestinal domination by vancomycin-resistant *Enterococcus* has been shown to precede bloodstream infection by this pathogen. Crohn's disease (CD), another inflammatory bowel disease, increases in incidence in those children who receive antibiotics before 5 years of age.[3]



Faecal microbiota transplantation (FMT) is a clinical procedure that replaces and restores healthy bacteria in the colon by introducing stool via enema or colonoscopy from a healthy human donor. Potentially fatal *Clostridium difficile* (C. diff) infections have been cured within days using FMT.

The diabetes connection

Bacteria living in the digestive tract have also been linked to obesity and inflammation – both contributors to type 2 diabetes.

Antibiotics have also recently been implicated in an increased risk of type 1 diabetes, an autoimmune disease whose incidence has been increasing steadily in industrialized countries.

Abnormal sugar metabolism has been seen in patients treated with β-lactam antibiotics (e.g., penicillin derivatives, cephalosporins, monobactams, and carbapenems), macrolides (e.g., erythromycin) and quinolones (e.g., ciprofloxacin) similar to that observed in obese individuals. Gestational diabetes and obesity during pregnancy may impact the maternal microbiome and the type of bacteria mothers pass on to their children during birth and breast feeding, potentially contributing to obesity in their offspring later in life.[3]

Did you know ...

The gut microbiome is different between obese and lean twins.

It has been found that obese twins have a lower diversity of gut bacteria and higher levels of digestive enzymes, which seems to indicate that obese twins are more efficient at digesting food and harvesting calories. Obesity has also been associated with a poor combination of microbes in the gut.

Genetic studies measuring the relative abundance of different species in the human microbiome have linked combinations of microbial species to certain human health conditions:

- Type 2 diabetes mellitus
- Rheumatoid arthritis
- Muscular dystrophy
- Multiple sclerosis
- Crohn's disease
- Irritable bowel syndrome
- Cardiovascular disorders
- Obesity
- Ankylosing spondylitis
- Colorectal tumours
- Abnormal stress response
- Reduced resistance of the eye to infection
- Neurodegenerative disorders, e.g., dementia

References:

1. Curry, A. (2015). *Forecast Diabetes Magazine* Nov-Dec 2015 (Note: journal reference is always in italics). Understanding the Microbiome. http://www.diabetesforecast.org/2015/nov-dec/understanding-the-microbiome.html?print=t **2.** Hair, M., Sharpe, J. (2014) University of Washington: Center for Ecogenetics and Environmental Health. Fast Facts About the Human Microbiome. **3.** Francino, M.P. (2016). Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. *Frontiers in Microbiology* January 2016; *Vol 6*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4709861/ **4.** Rivera-Amill, V. (2014) Editorial. The Human Microbiome and the Immune System: An Ever-Evolving Understanding. *Jnl. of Clinical Cell Immunology Vol 5;* (6) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4831629/ **5.** The NIH HMP Working Group (2009). The NIH Human Microbiome Project. *Genome Research.* https://genome.cshlp.org/content/19/12/2317.full