Mr Ben Harris

Medical Laboratory Scientist

Honorary Lecturer, University of Otago

Saturday, August 13, 2016

(Room 7)

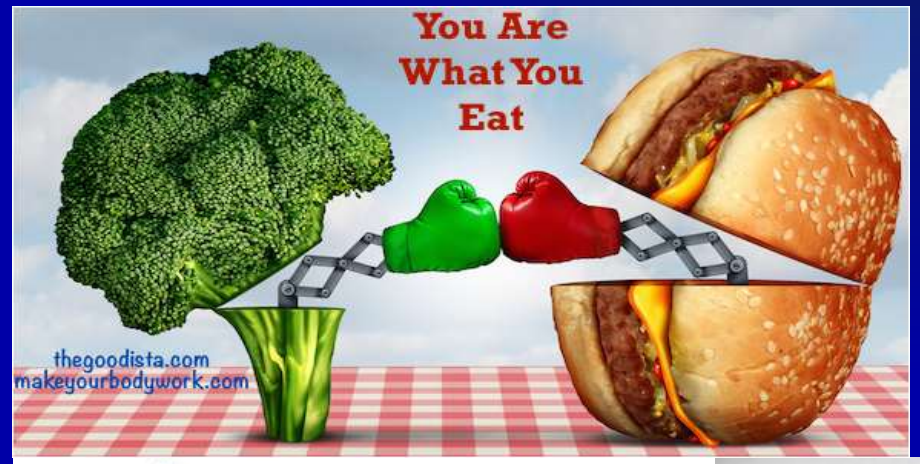
14:00 - 14:55 WS #111: Understanding Our Microbiome

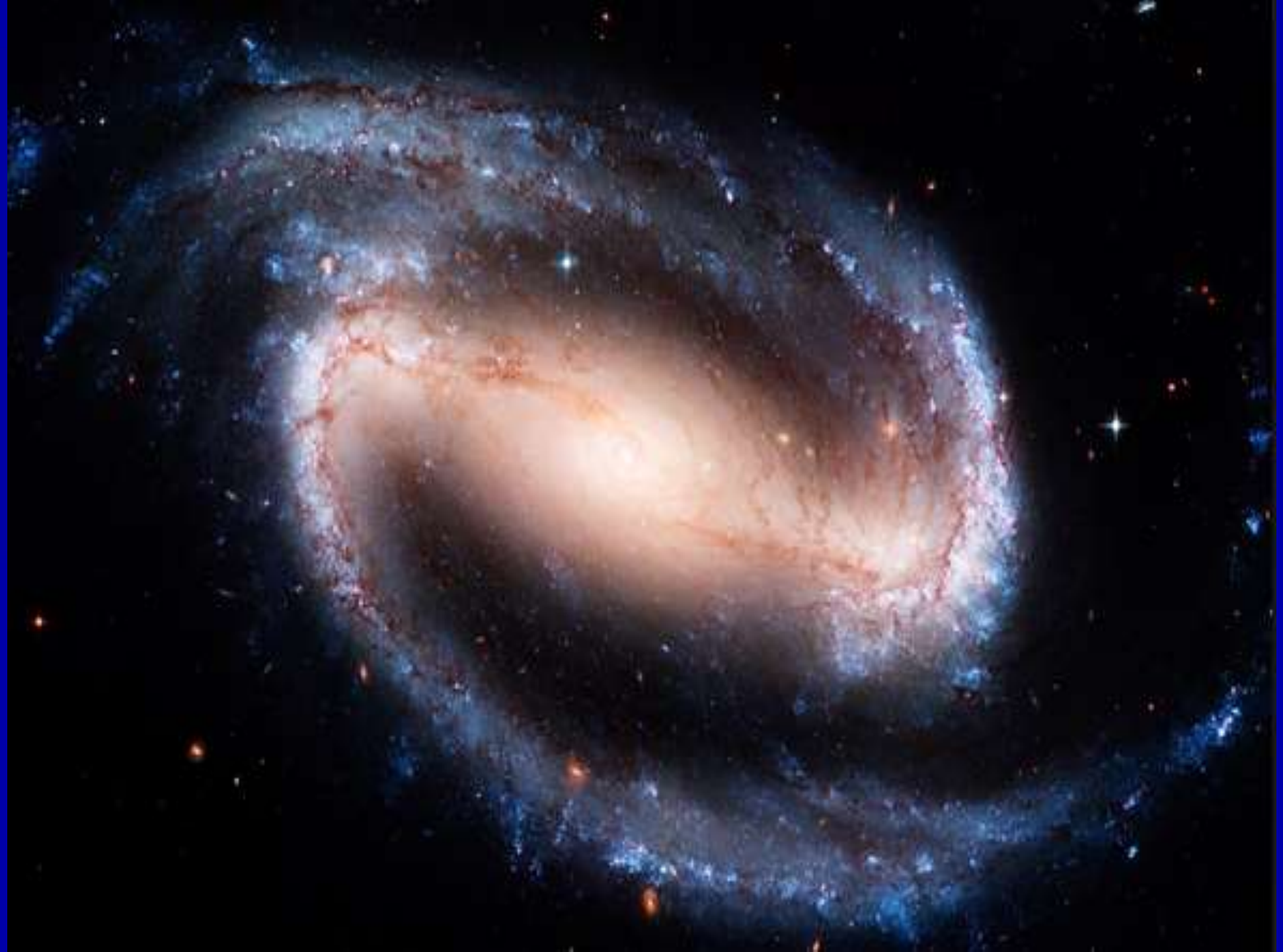
15:05 - 16:00 WS #122: Understanding Our Microbiome (Repeated)

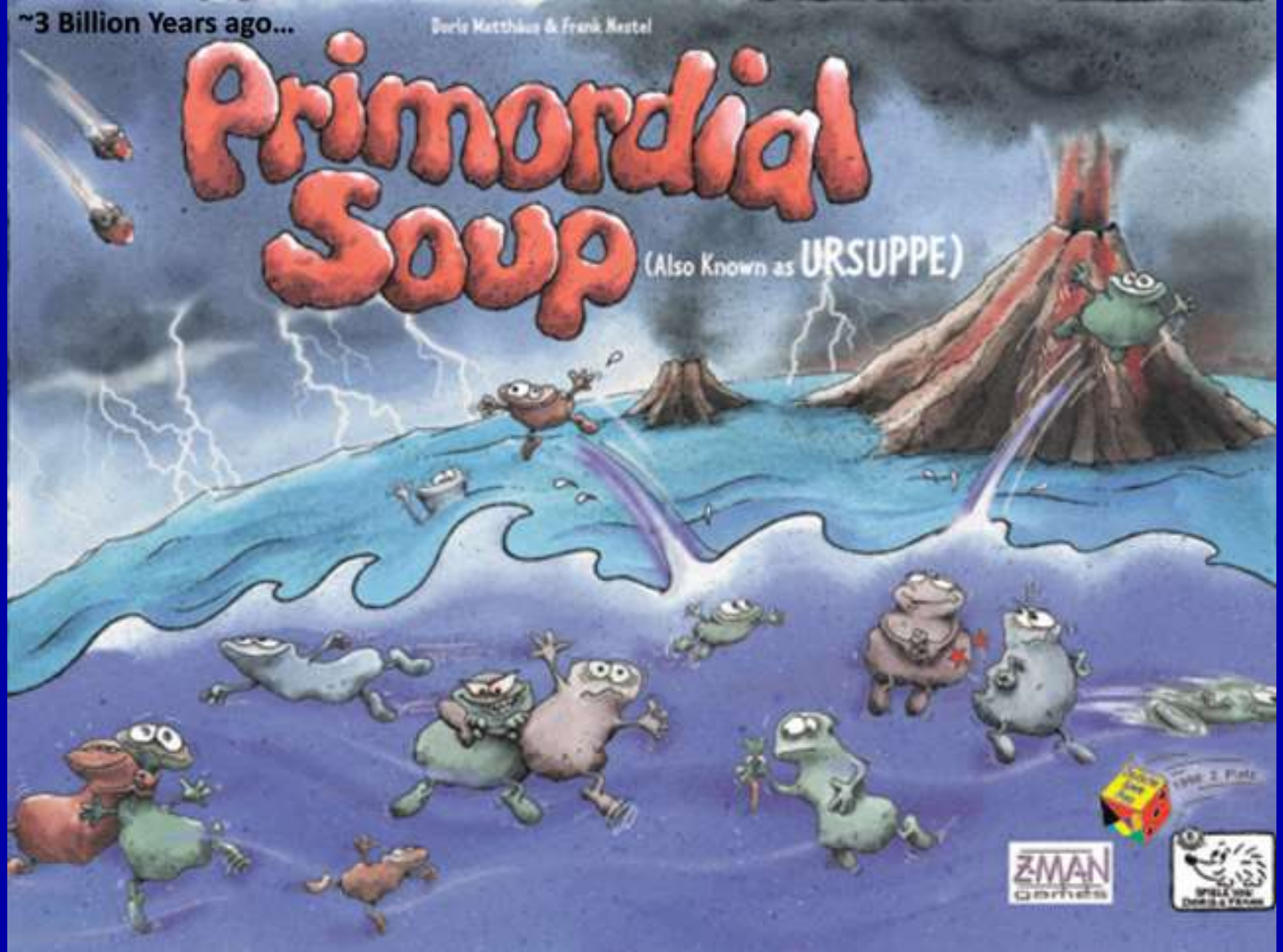
Our Microbiome

Linking Microbes, Health & Disease

Ben Harris Med Lab Scientist Infection Prevention & Control

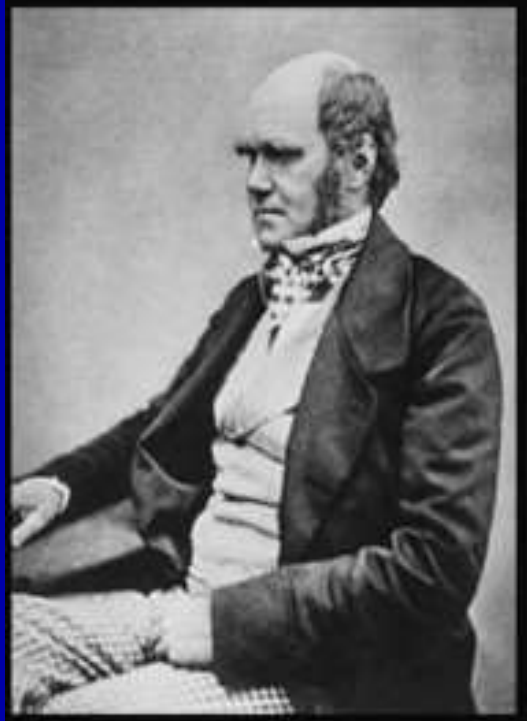





~3 Billion Years ago...
Primordial Soup
(Also Known as URSUPPE)
Z-MAN games

Important Dates

Years Ago	
• 4.5 Billion	Origin of the Earth
• 3.5 Billion	Prokaryote Bacteria
• 2.5 Billion	Oxygen in Atmosphere
• 1.5 Billion	Eukaryote cells with nucleus
• 0.5 Billion	Cambrian explosion multicelleular Eukaryote organisms, plants & animals



In the struggle for survival, the fittest win out at the expense of their rivals because they succeed in adapting themselves best to their environment.

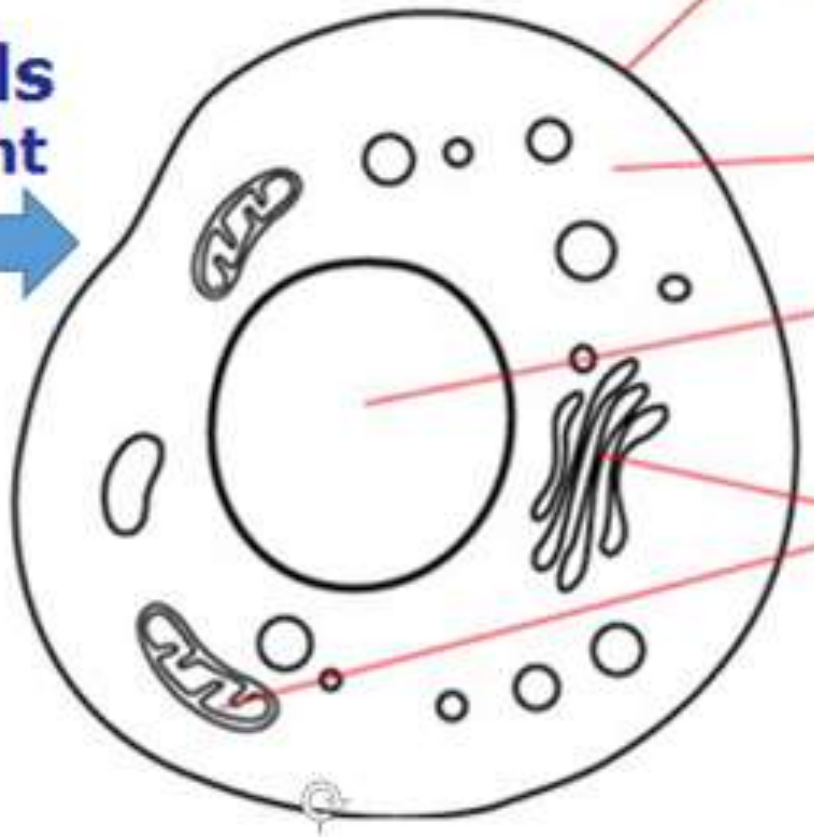
(Charles Darwin)

Cell membrane

Cytoplasm

Prokaryote Cells
e.g. bacteria

Eukaryote Cells
e.g. animal, plant

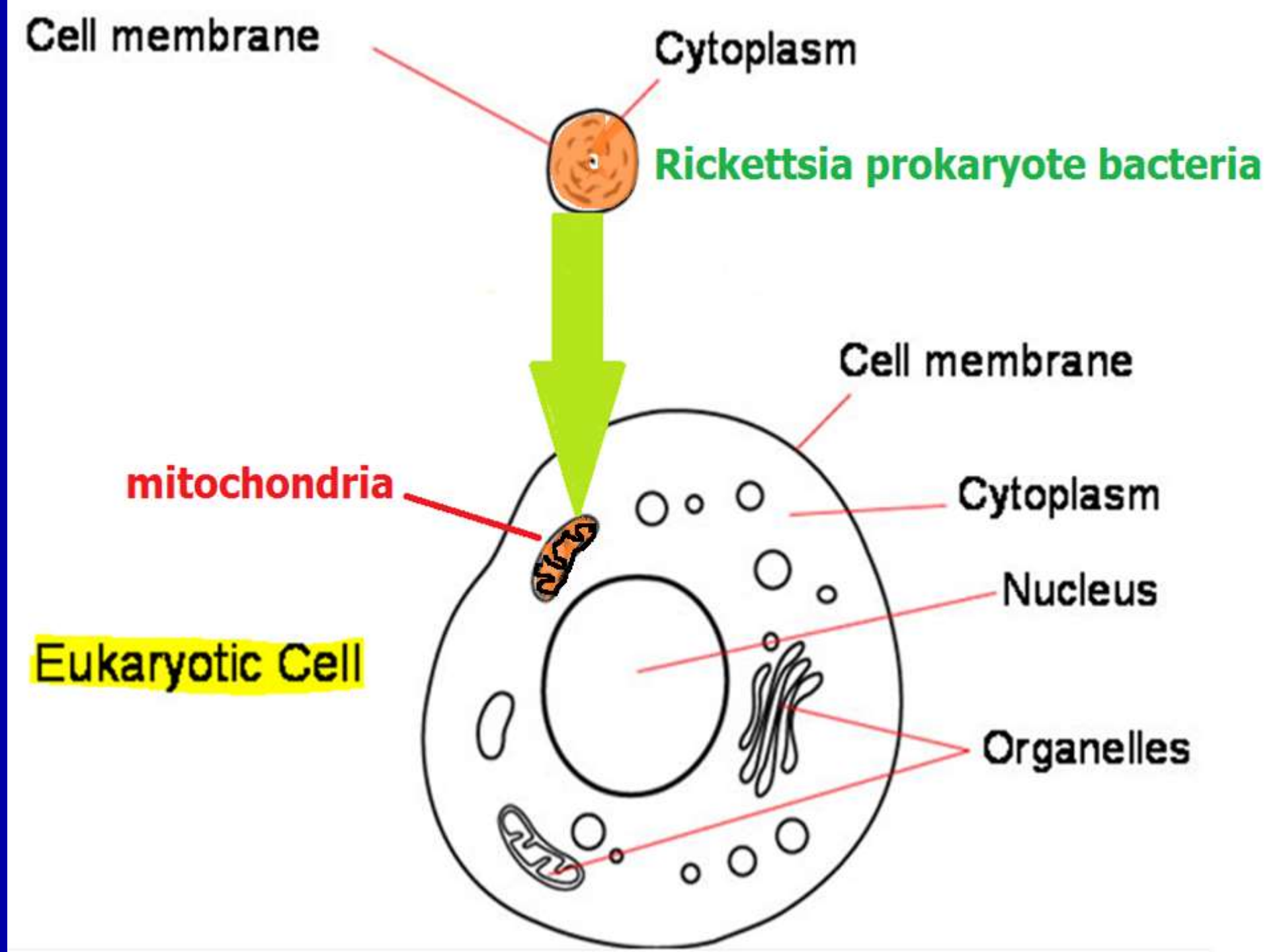


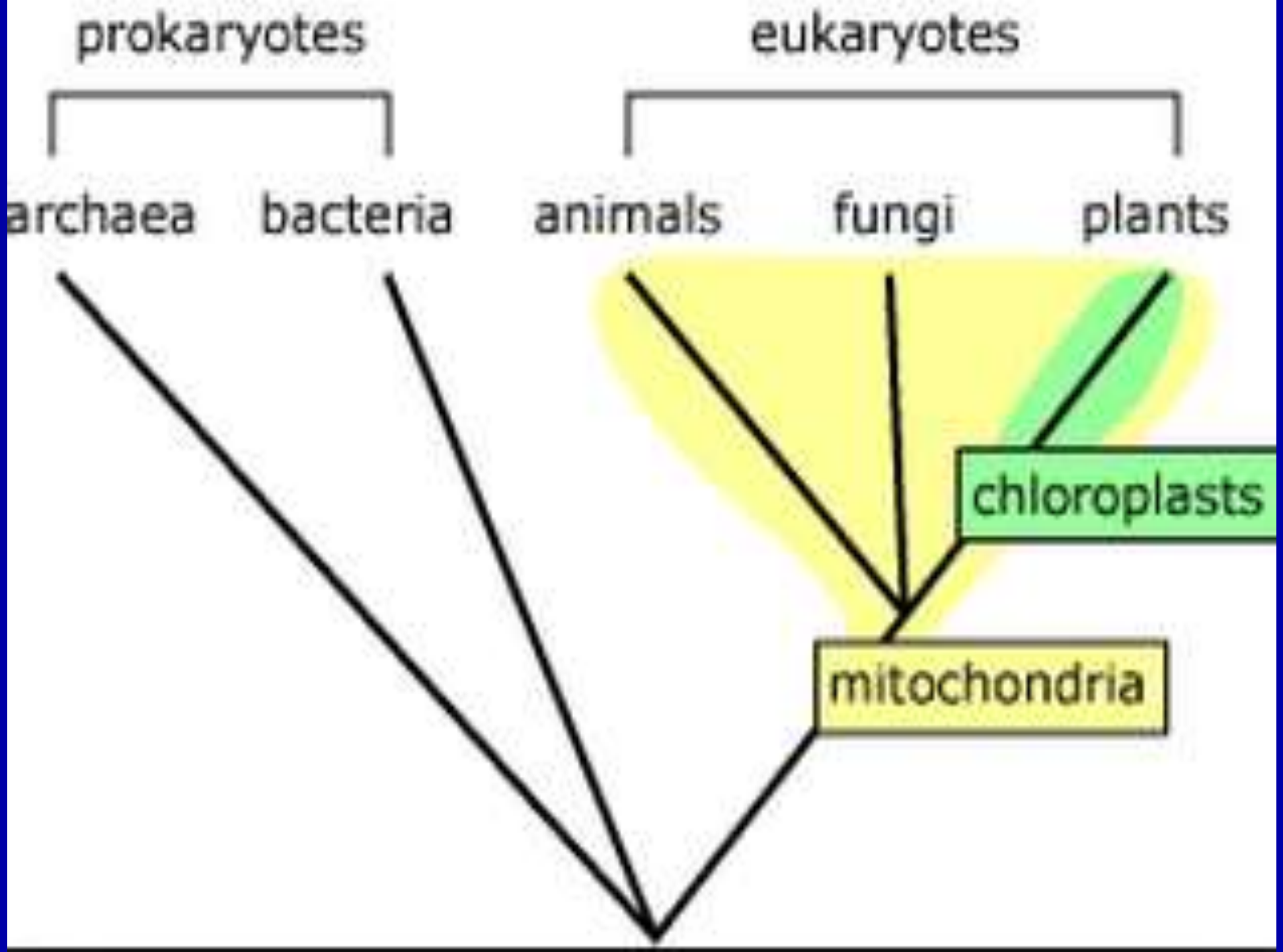
Cell membrane

Cytoplasm

Nucleus

Organelles


Cell membrane
Cytoplasm
Rickettsia prokaryote bacteria
Cell membrane
mitochondria
Cytoplasm
Nucleus
Eukaryotic Cell
Organelles

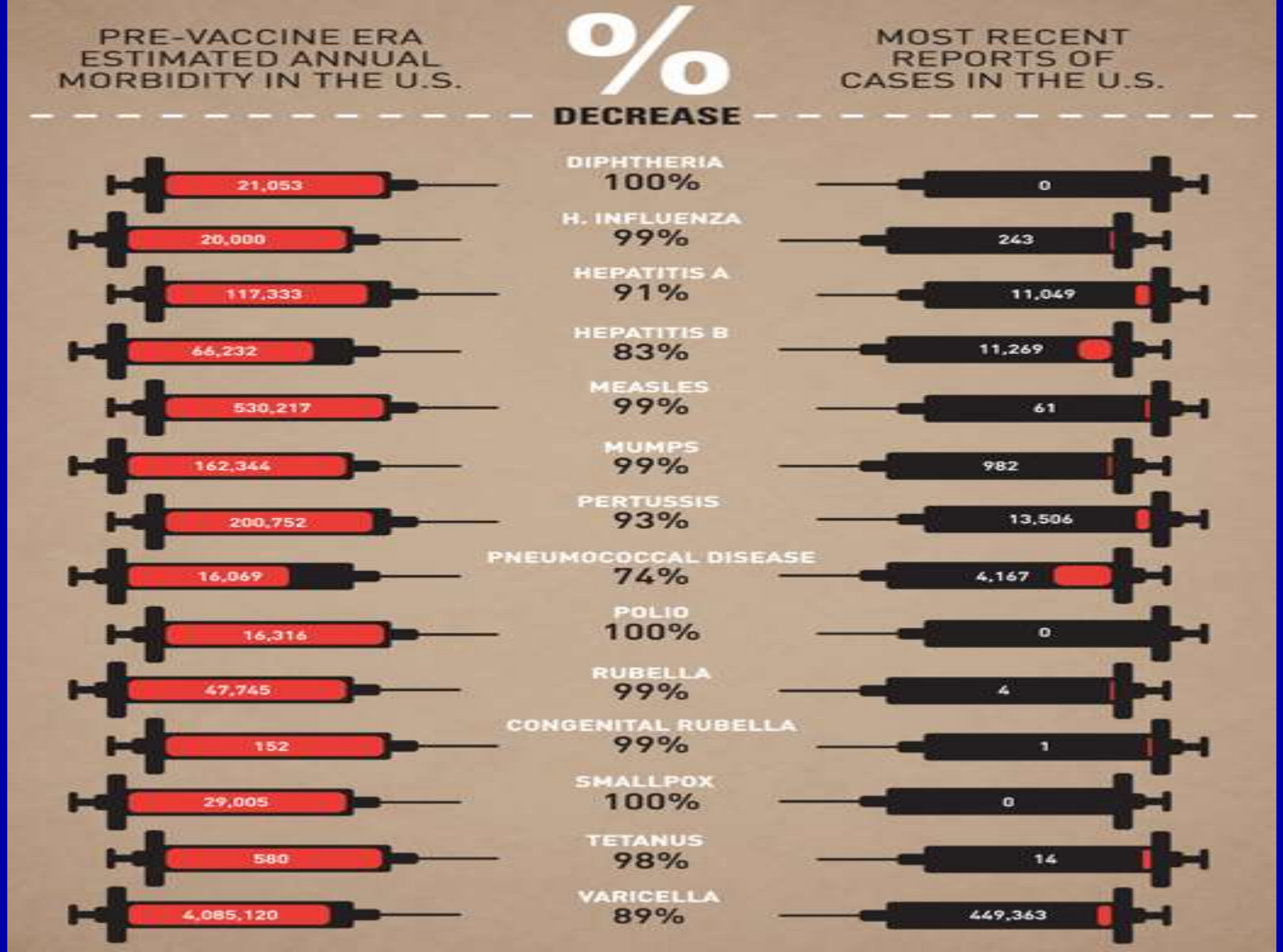

prokaryotes
eukaryotes
archaea
bacteria
animals
fungi
plants
chloroplasts
mitochondria

Paleo Diet

Warning 'All Bugs are Bad

Deadliest pandemics including:

- 14th-century Black Death 75 to 200 million plague deaths in Europe
- 1492 Post Colombus South America
  ? 37 million population was reduced by 90%
- 1900-1977 smallpox deaths 300-500 million
- 1918–1919 Spanish influenza pandemic at least 50 to 100 million deaths
- ongoing HIV/AIDS pandemic, more than 35 million deaths


PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY IN THE U.S.
%
DECREASE
MOST RECENT REPORTS OF CASES IN THE U.S.
DIPHTHERIA
100%
21,053
0
H. INFLUENZA
99%
20,000
243
HEPATITIS A
91%
117,333
11,049
HEPATITIS B
83%
66,232
11,269
MEASLES
99%
530,217
61
MUMPS
99%
162,344
982
PERTUSSIS
93%
200,752
13,506
PNEUMOCOCCAL DISEASE
74%
16,069
4,167
POLIO
100%
16,316
0
RUBELLA
99%
47,745
4
CONGENITAL RUBELLA
99%
152
1
SMALLPOX
100%
29,005
0
TETANUS
98%
580
14
VARICELLA
89%
4,085,120
449,363

Human Infections (1)

Used to be mainly epidemics:

Smallpox, plague, cholera, diphtheria, TB, syphilis, influenza, measles, etc

i.e. exogenous source *'all bugs are bad'*

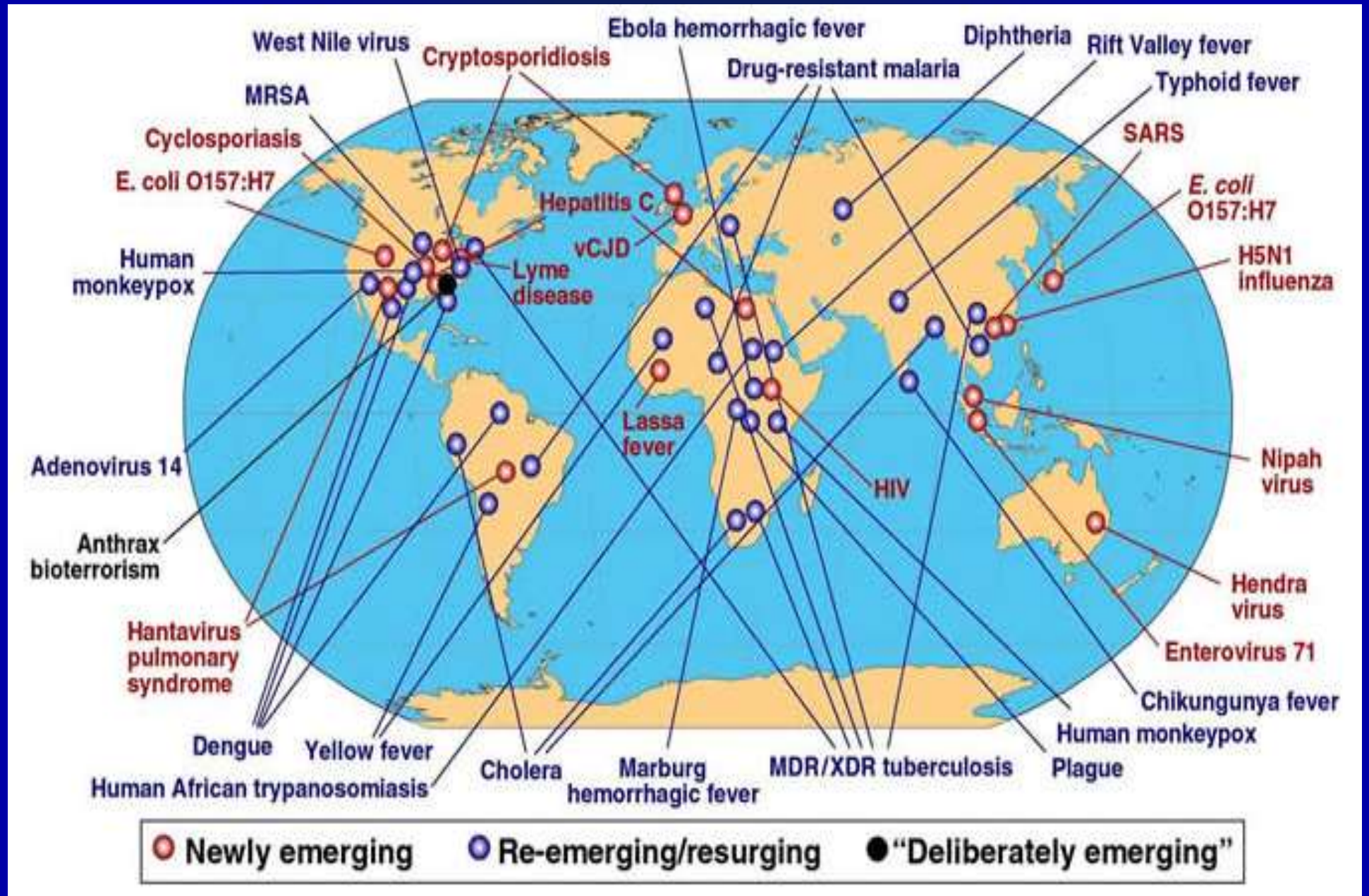
Public Health, Sanitation, Vaccinations
have largely contained or eliminated these

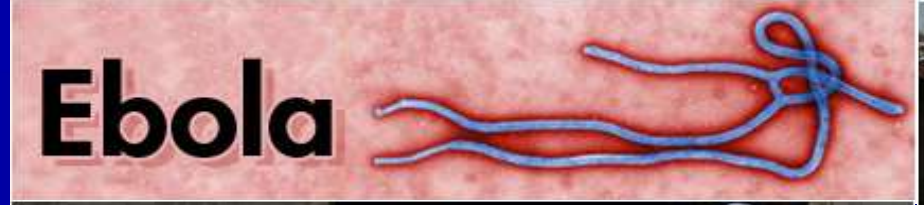
Emerging Infectious Diseases

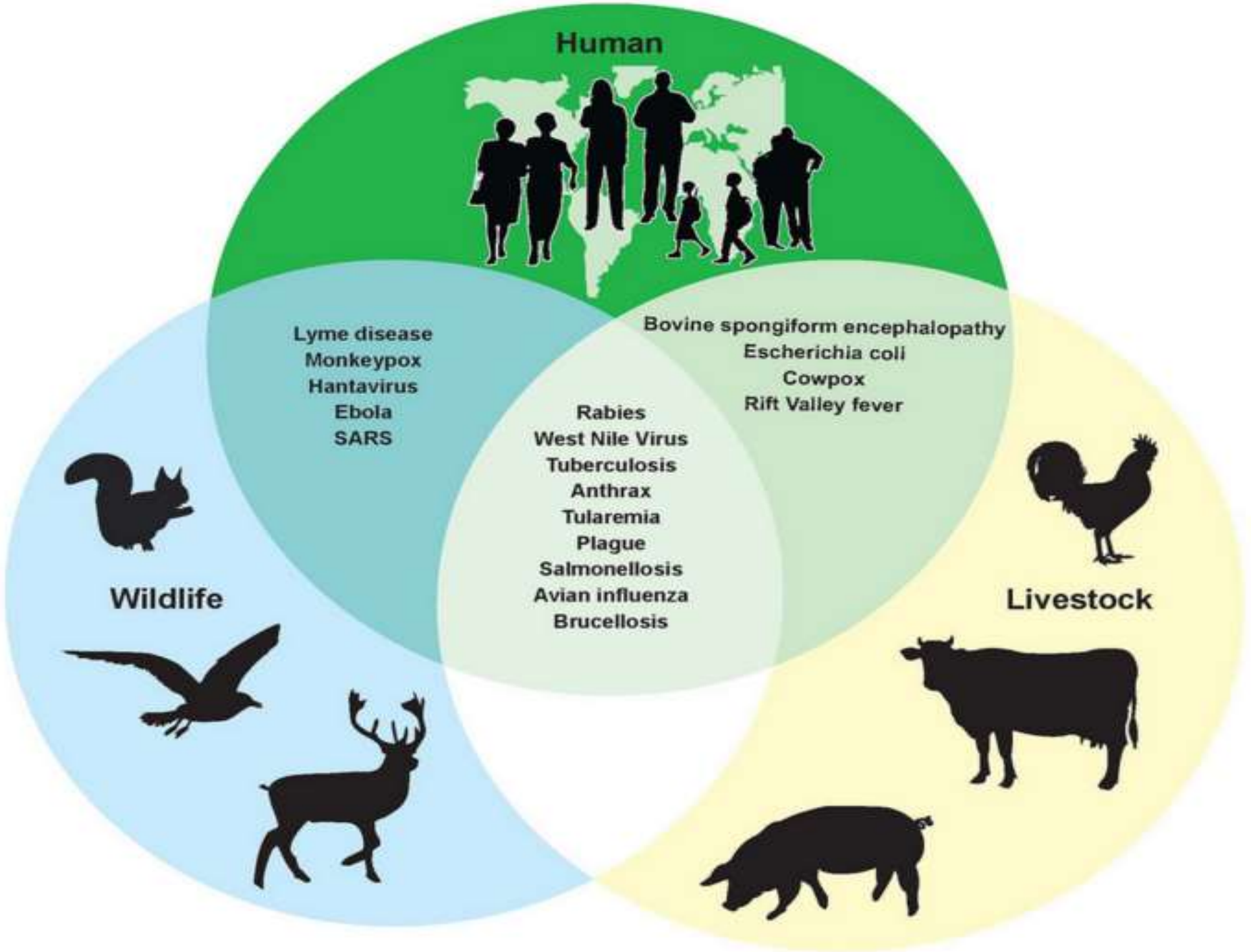
335 infectious diseases emerged globally in humans
between 1940 and 2004
nearly two-thirds originated in wildlife

Infectious Diseases cause nearly 1 in 5 deaths worldwide

Recent Emerging Diseases




Ebola


Human
Lyme disease
Monkeypox
Hantavirus
Ebola
SARS
Bovine spongiform encephalopathy
Escherichia coli
Cowpox
Rift Valley fever
Rabies
West Nile Virus
Tuberculosis
Anthrax
Tularemia
Plague
Salmonellosis
Avian influenza
Brucellosis
Wildlife
Livestock

Human Infections (2)

Now mainly

Emerge from our own microbio me

i.e. endogenous source

Infections

⬆Endogenous vs ⬇⬇Exogenous

Endogenous

- *Staph aureus*
- *E.coli, Klebsiella*
  Proteus, etc
- *Strep*
- Anaerobes

i.e. Most non viral infections

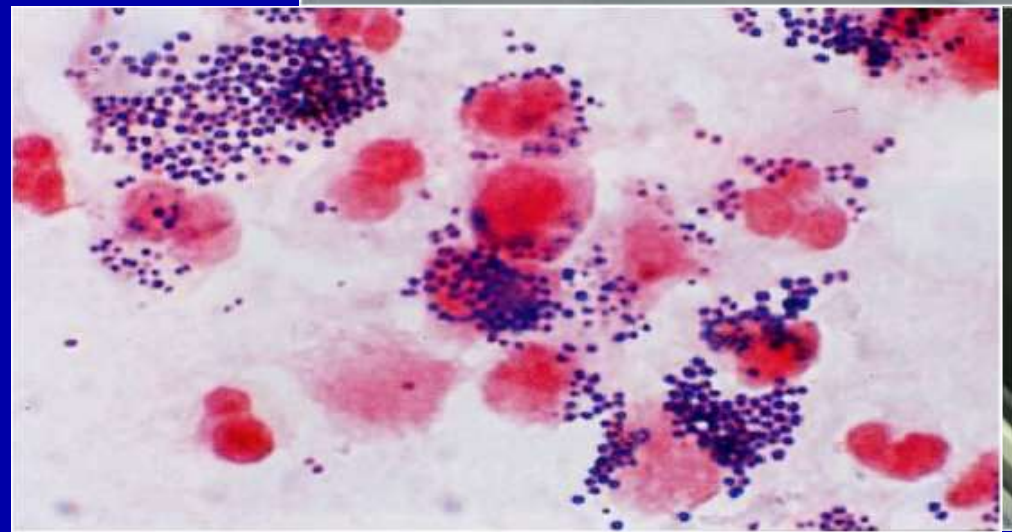
Exogenous

- HIV/AIDS
- *Influenza*
- *Hepatitis*
- *Mumps, Measles, Rubella*

- TB
- *Campylobacter*
- *Salmonella, Shigella*
- *Pasteurella* (cat/dog bites)
- *Brucella* (unpasteurized milk cheese, endemic countries)

Staph aureus infection

single species ‘microbes are bad’ eliminate them



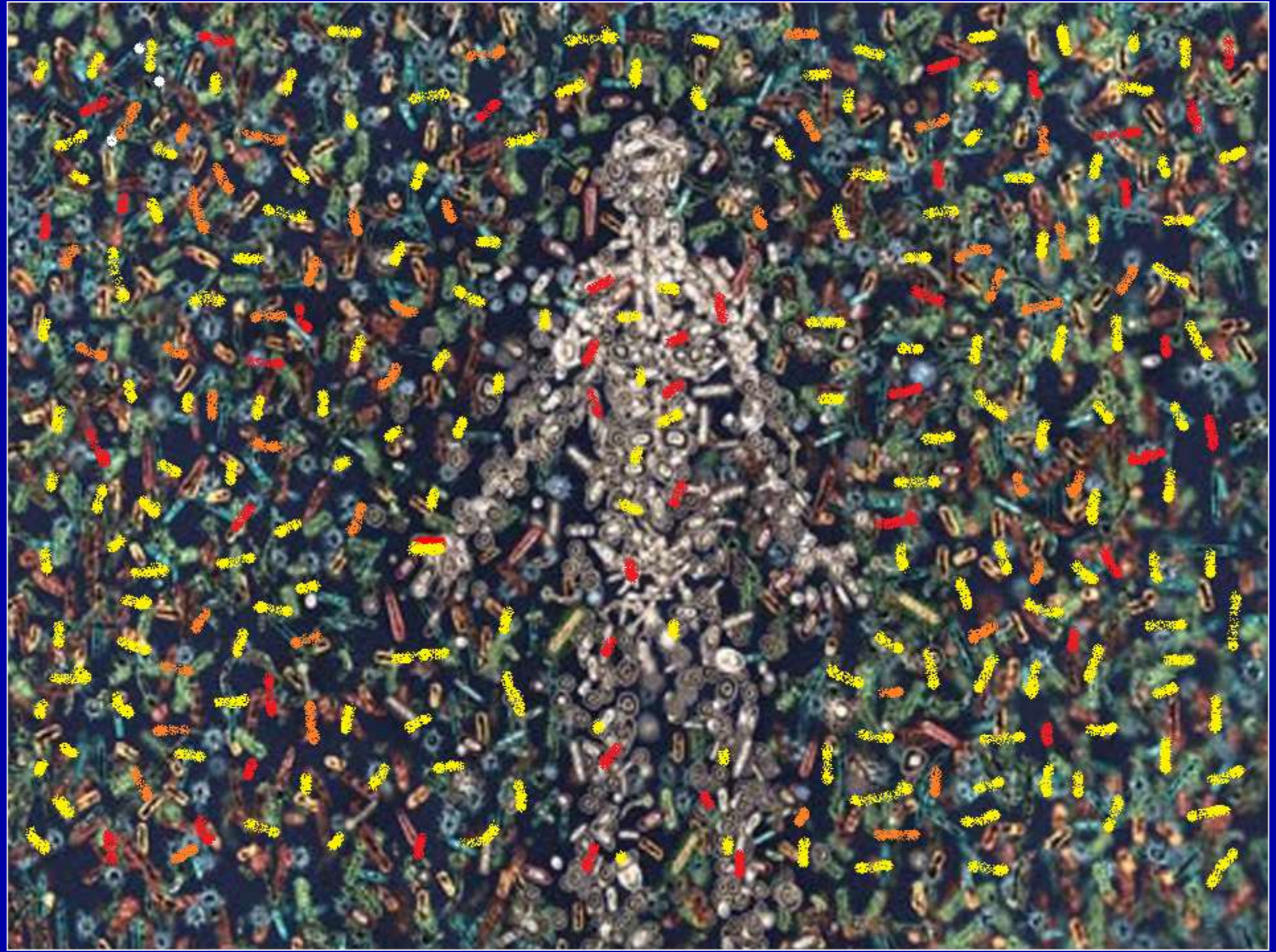
World Infection Trends

New forms of old diseases - endogenous

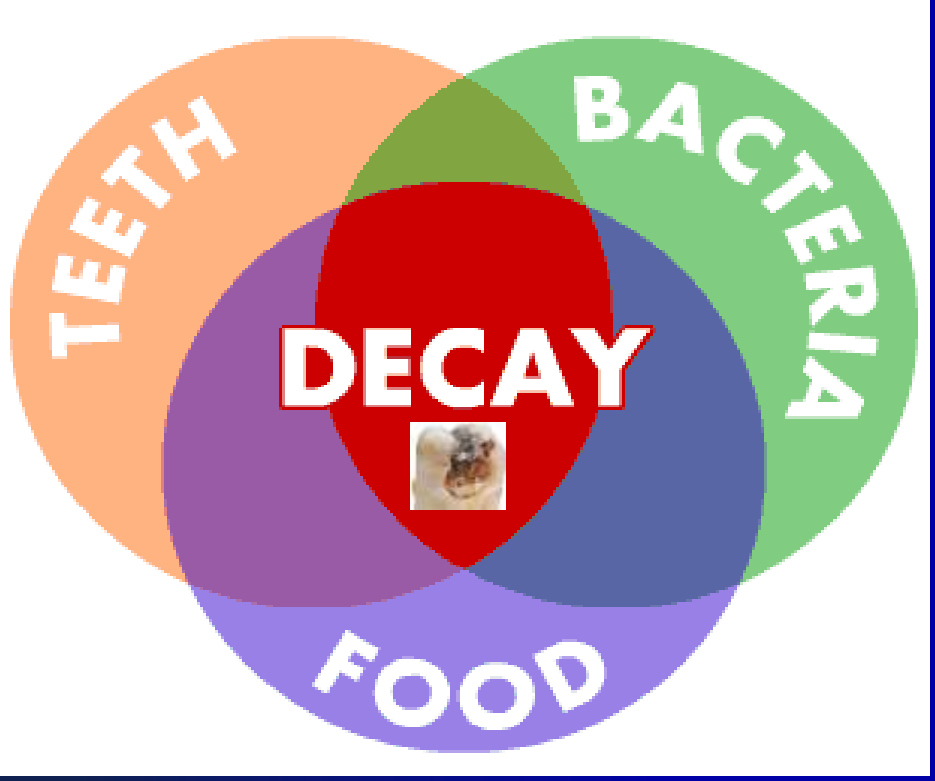
including **MDRO's**

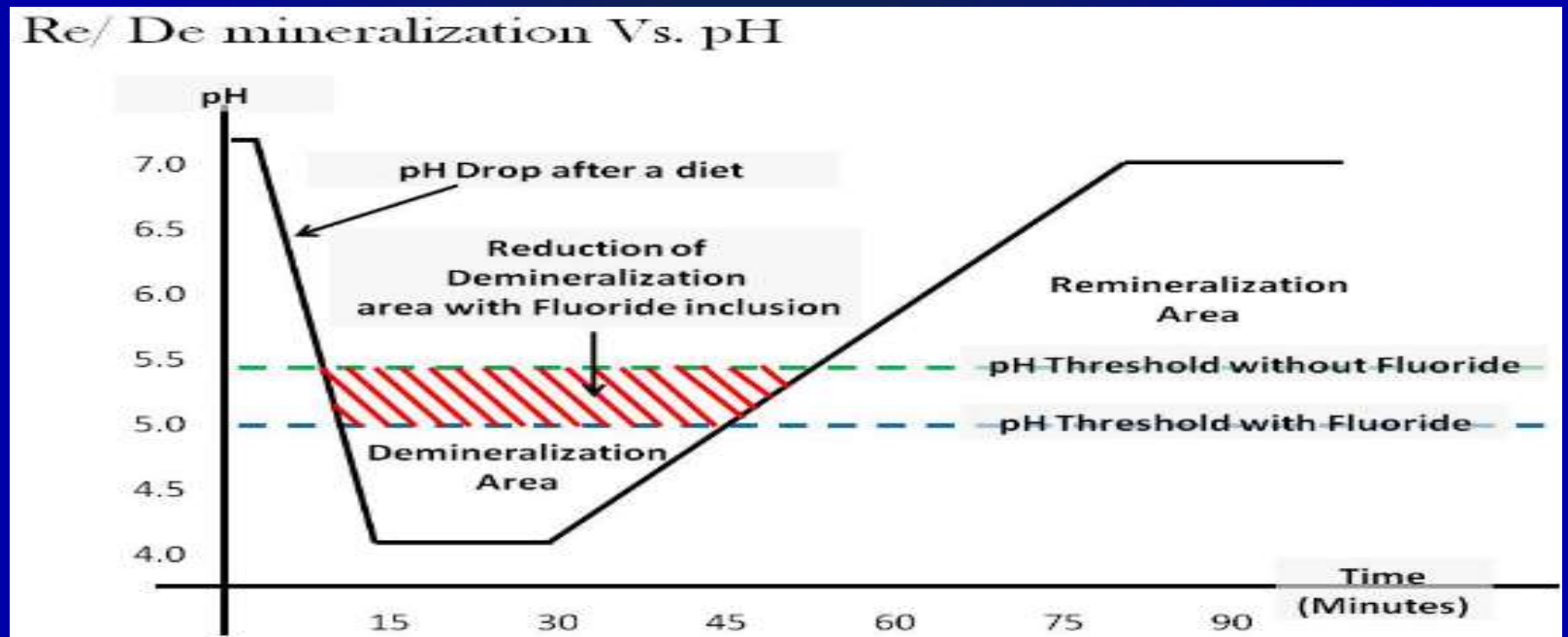
- MRSA
- ESBL
- VRE
- *C. difficile*
- CRE carbapenemases

From our own shared microbiome

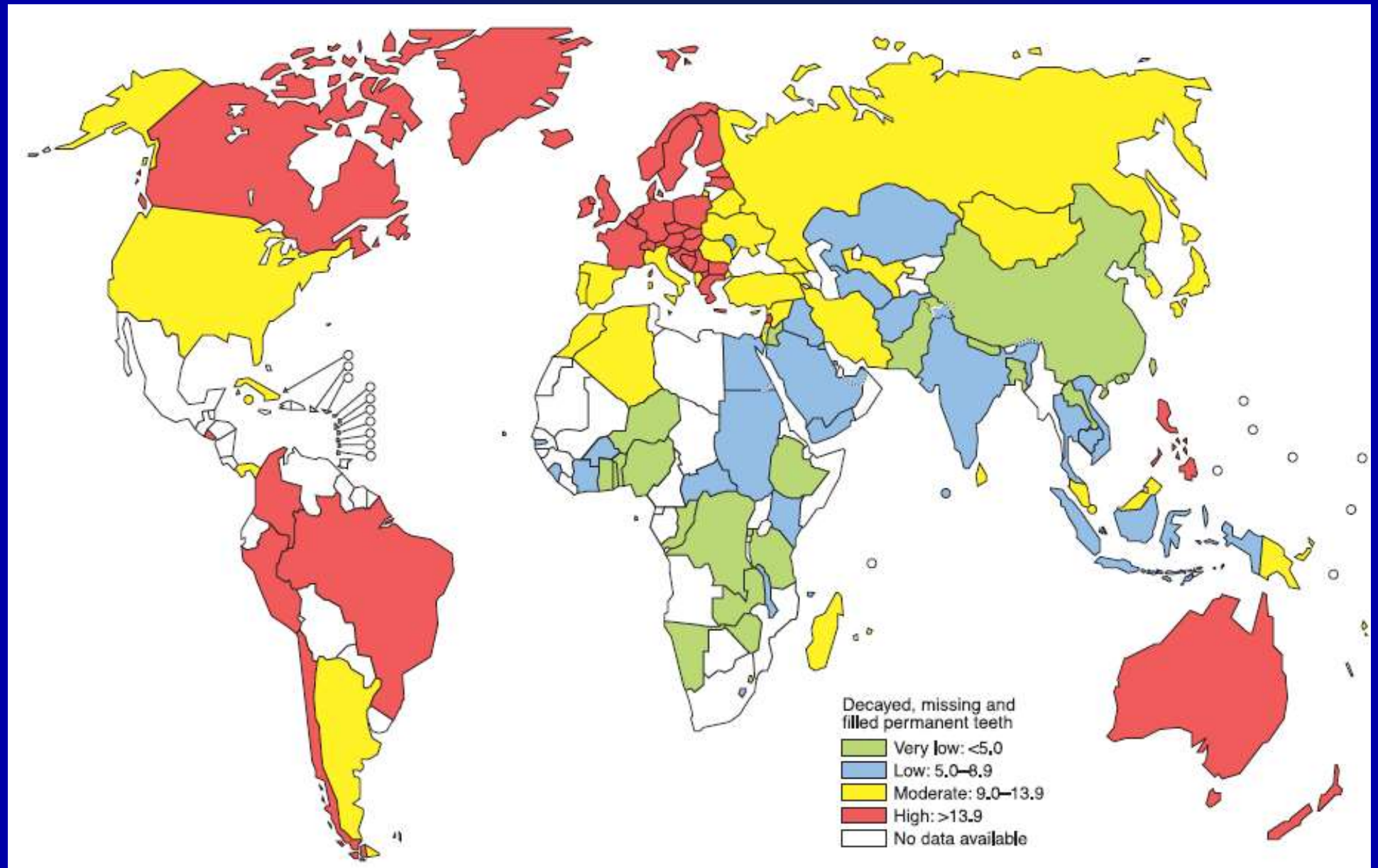


Sweet Tooth Diet Emerged

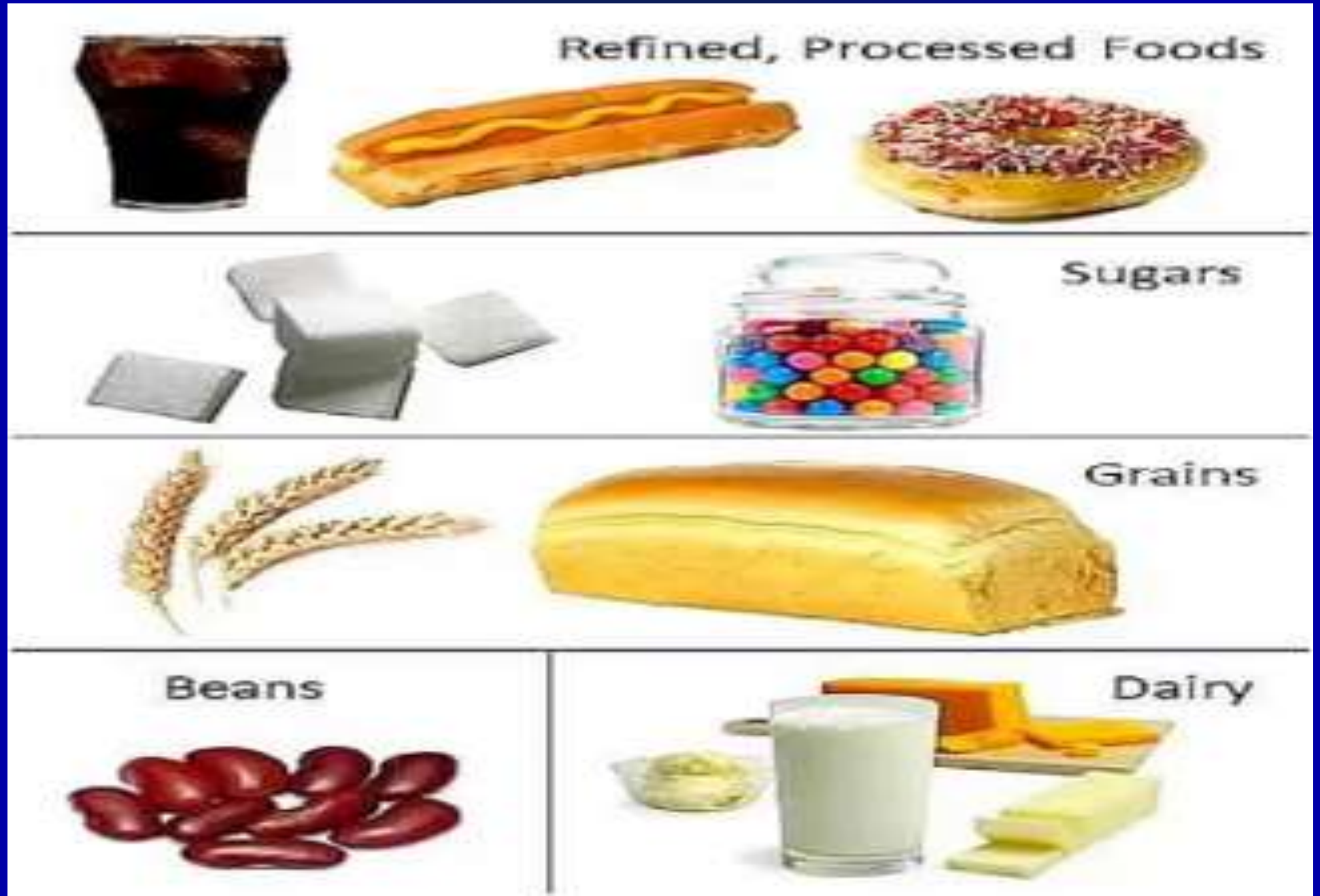

TEETH
BACTERIA
FOOD
DECAY


Re/ De mineralization Vs. pH
pH
7.0
6.5
6.0
5.5
5.0
4.5
4.0
pH Drop after a diet
Reduction of
Demineralization
area with Fluoride inclusion
Demineralization
Area
Remineralization
Area
pH Threshold without Fluoride
pH Threshold with Fluoride
Time
(Minutes)
15
30
45
60
75
90

Dental Caries

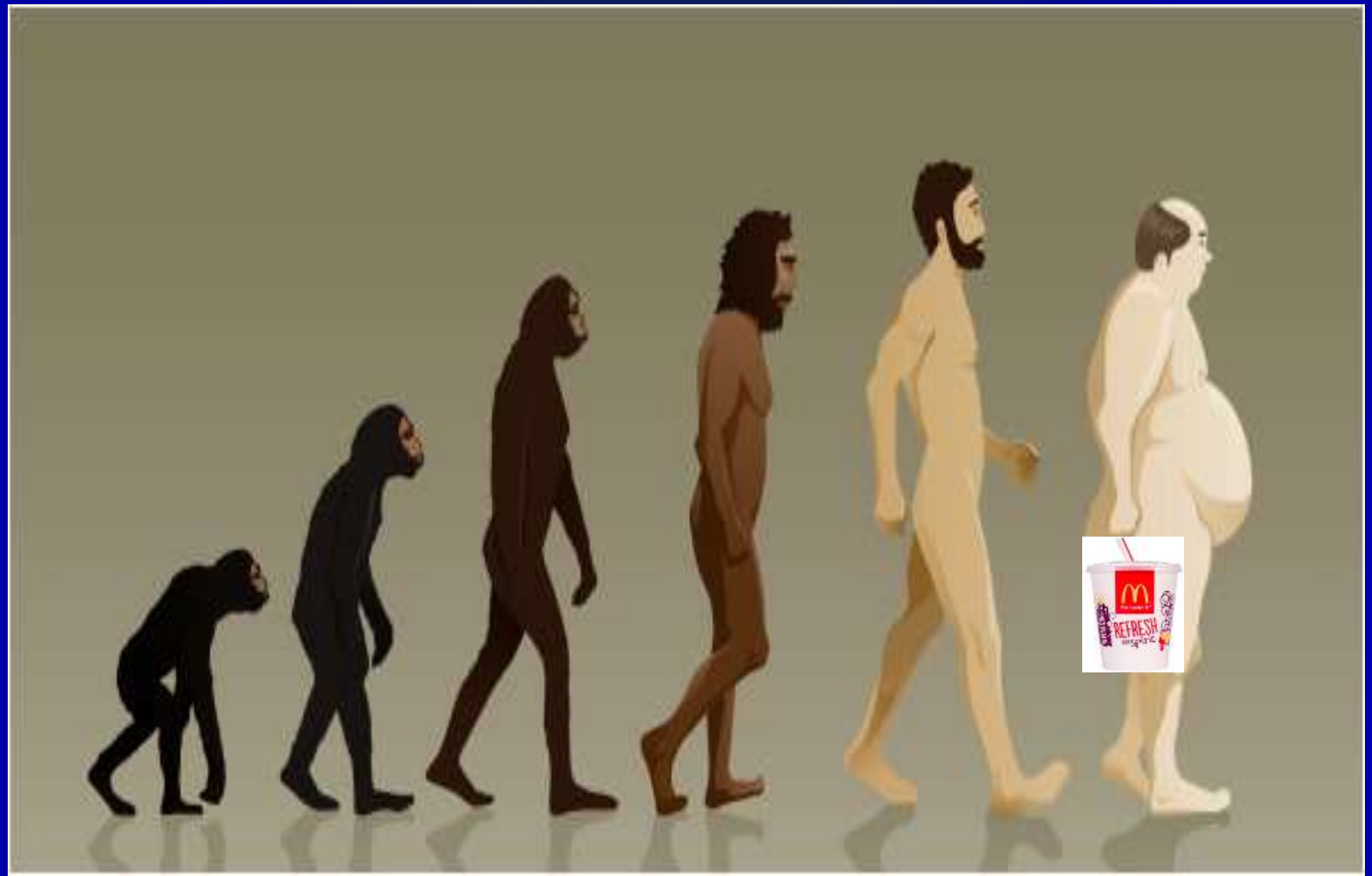


Non Paleo Diet



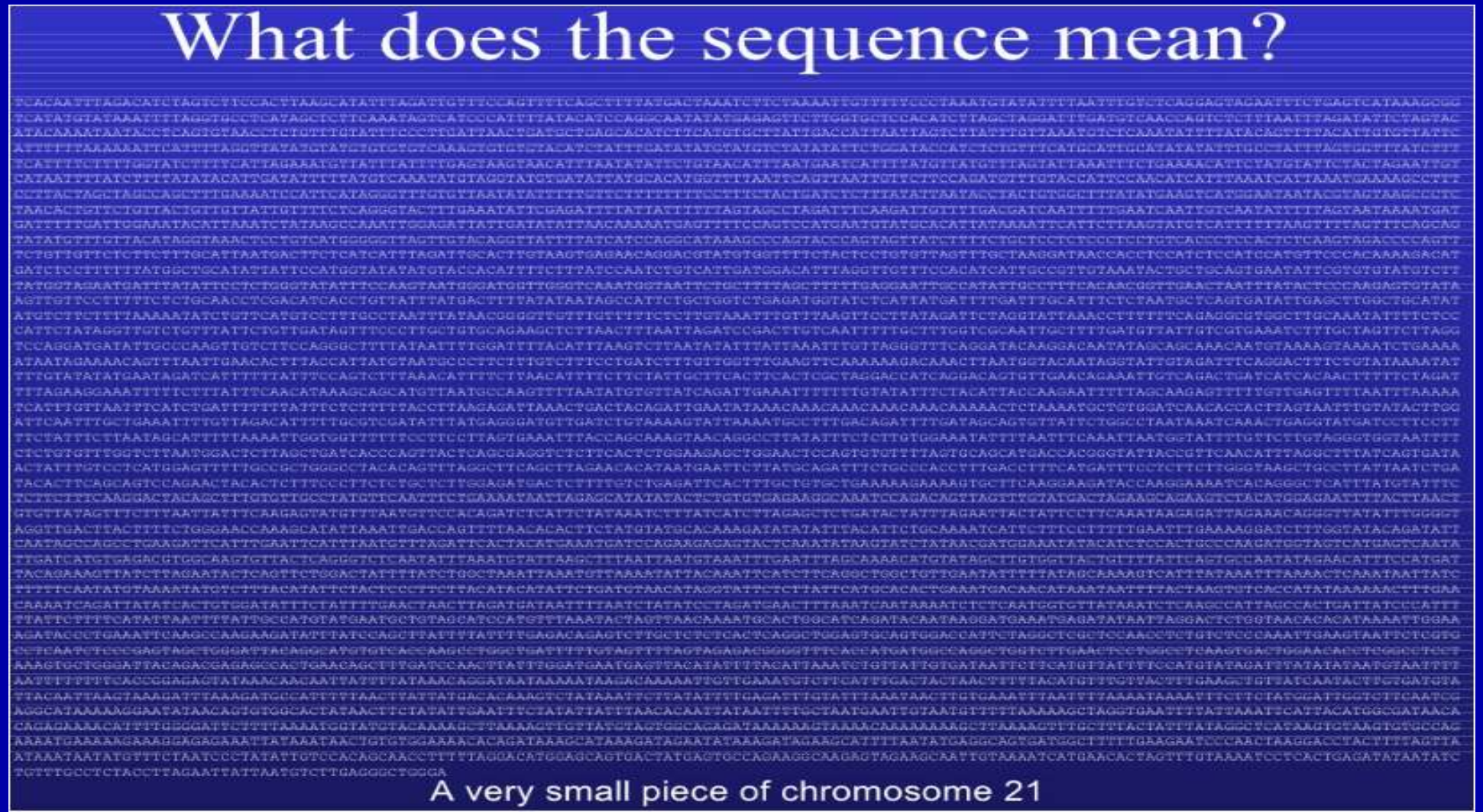

BISCUIT with egg
McCafé
iced
mocha
cappuccino
McCafé
mocha
McCafé

Dietary Change Consequences



Human Genome Project

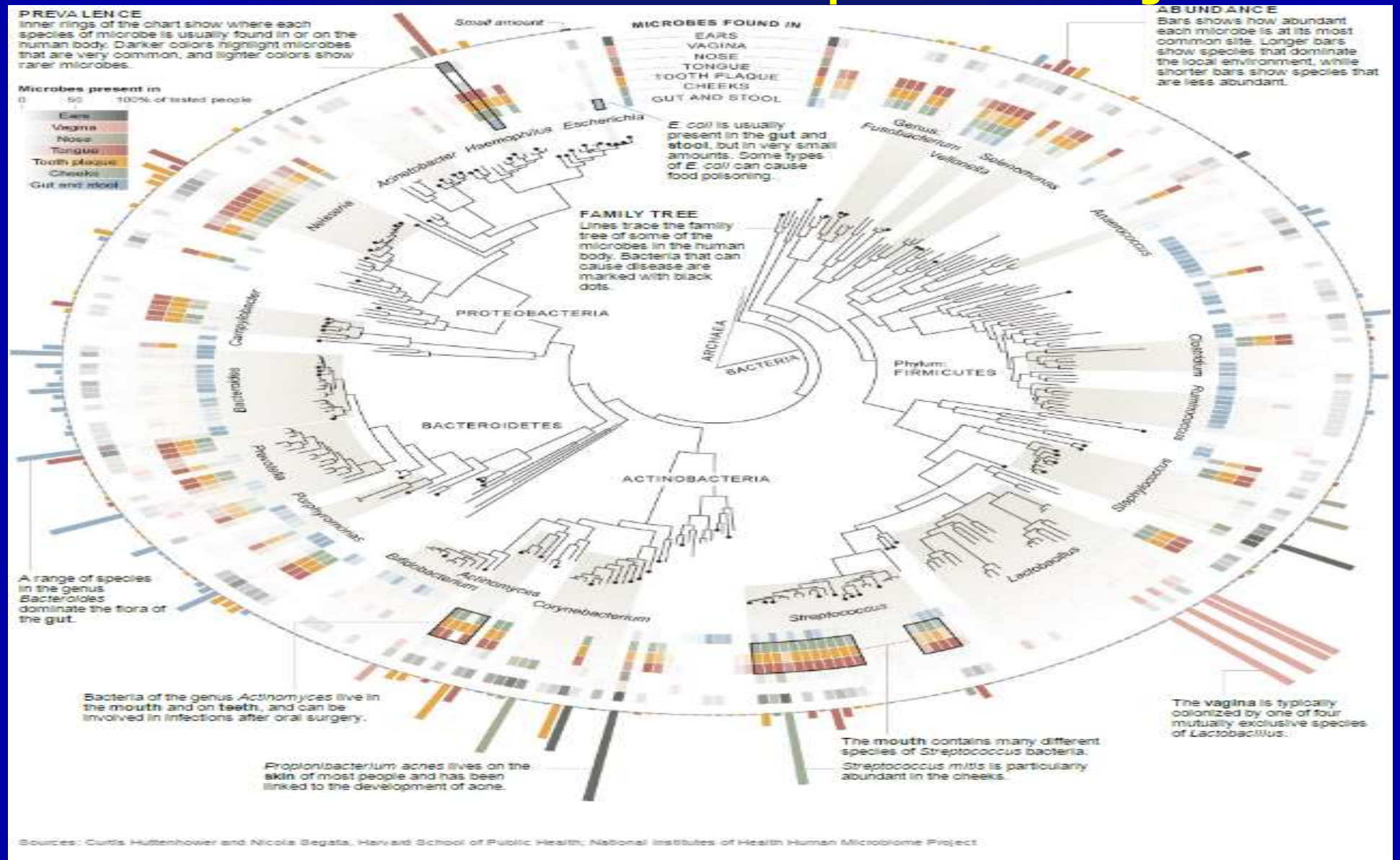
3 billion base pairs
20,000+ genes
98% 'junk DNA'

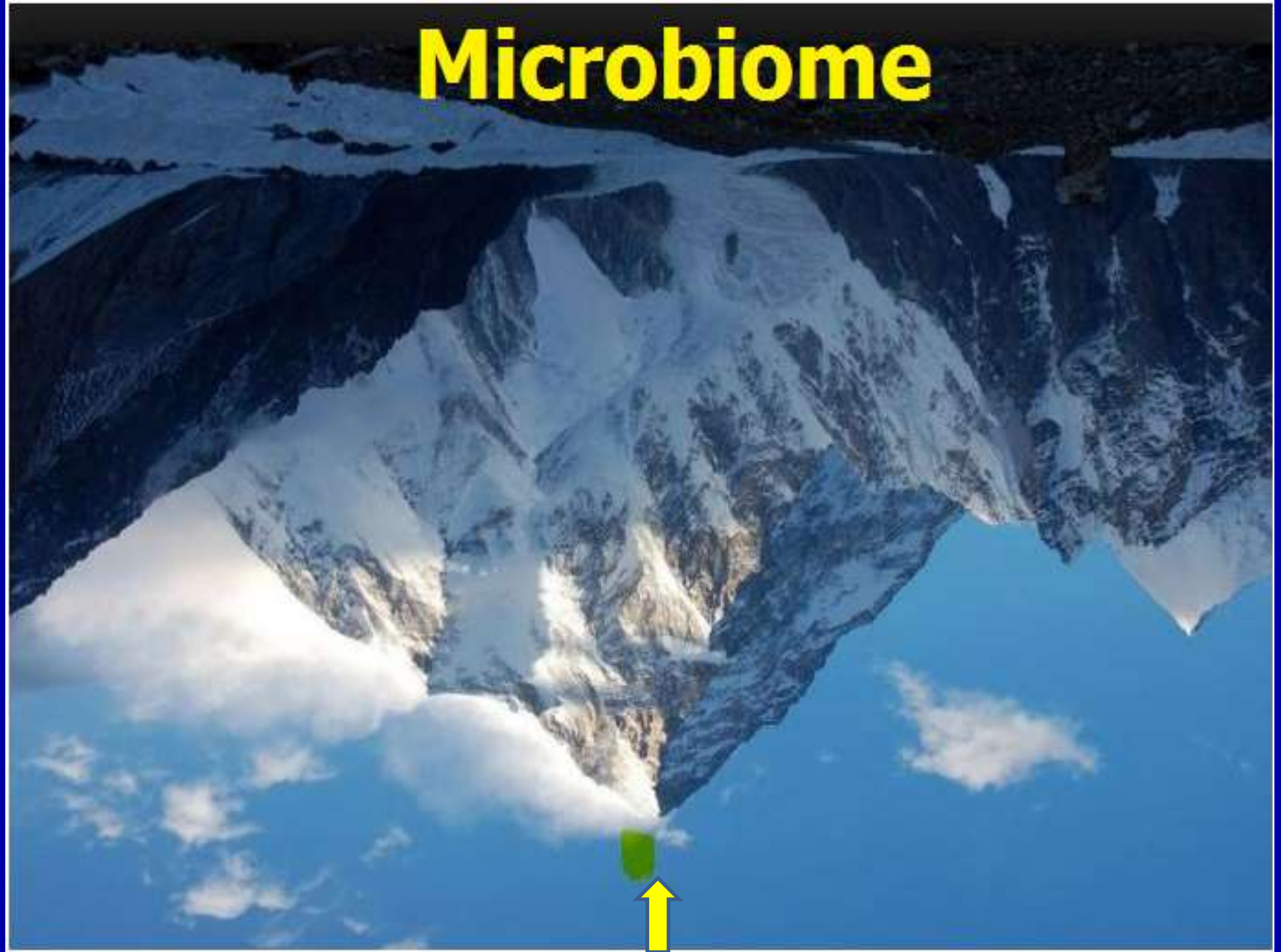


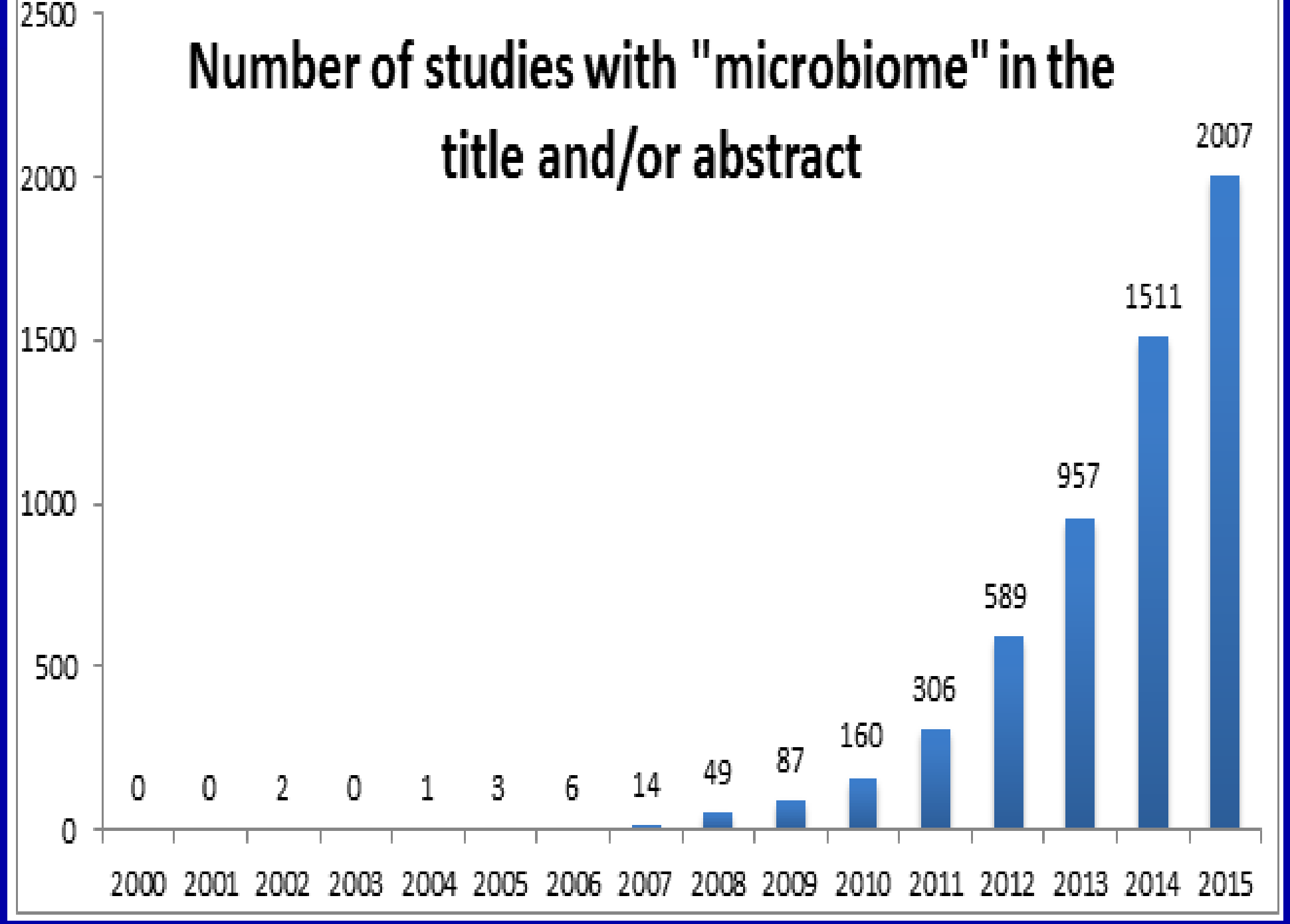
Human Microbiome Project

E. coli **alone approx 4 million base pairs, 3,000 genes**

Our microbiome has ≥ 500 -1000 species = n x10^6 genes




Microbiome

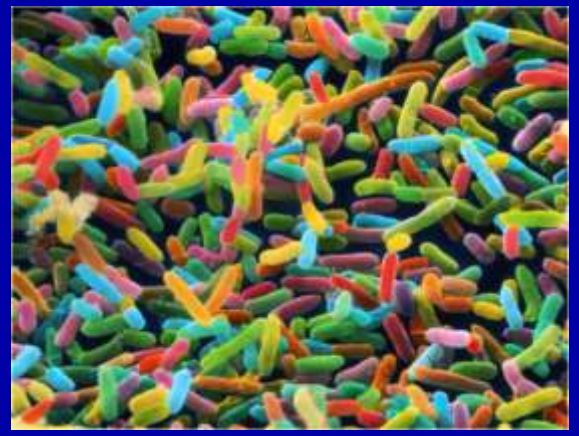

Number of studies with "microbiome" in the title and/or abstract
2500
2000
1500
1000
500
0
0
0
2
0
1
3
6
14
49
87
160
306
589
957
1511
2007
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015


What's the
Microbiome?

Our ‘Microbiome’

- Mass of Bacteria, Fungi, Viruses - unique to each of us
- Daily activities impact this e.g. bathing, diet, hygiene
- Dynamic over our lifetime – numbers and proportions
- Small composition changes can have major effects

Susceptible to major disturbances from antibiotics



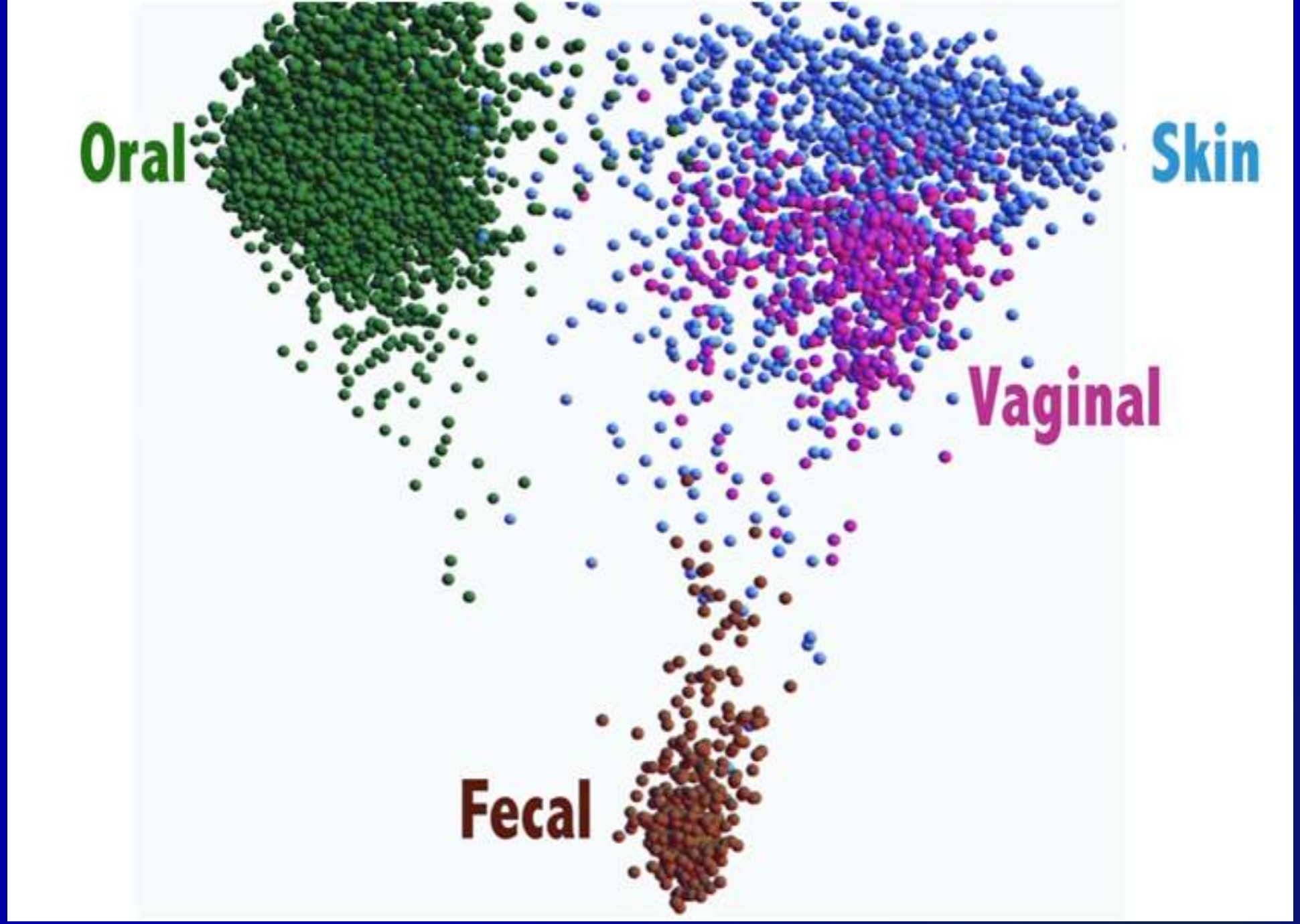
Our Microbial Garden

Emerging realisation of importance of resident microbes to our health and well-being

particularly with respect to roles played in:

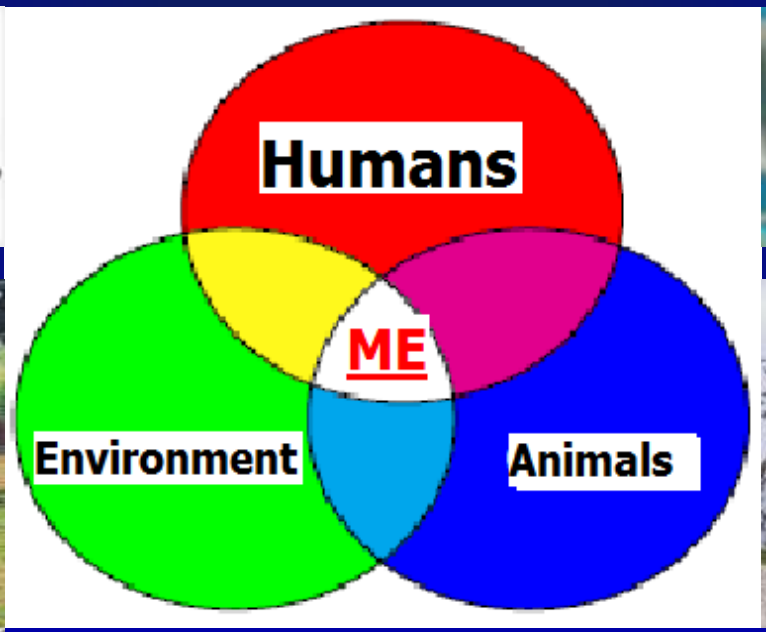
- our immune system
- contributing to food digestion
- acting as first line of defense against ‘pathogens’

Many diseases are the result of disturbed microbiomes - ‘dysbiosis’



Prof Rob Knight Ted Talks https://www.ted.com/talks/rob_knight_how_our_microbes_make_us_who_we_are?language=en#t-231745

Sharing my microbiome



This vast microbiome is routinely shared with others + animals and environment

Microbiome Sequencing
3 Key Questions

1. What organisms are present?

2. What do they do, health and disease?

3. How do they do it?

More Questions

- Which organism(s) responsible for which functions?
- How do microbiomes change over time?
- What are the drivers of those changes? The environment? Diet? Health status?
- How does the prevalence of certain species affect other species in that community?

Microbiome Lifetime Dynamics

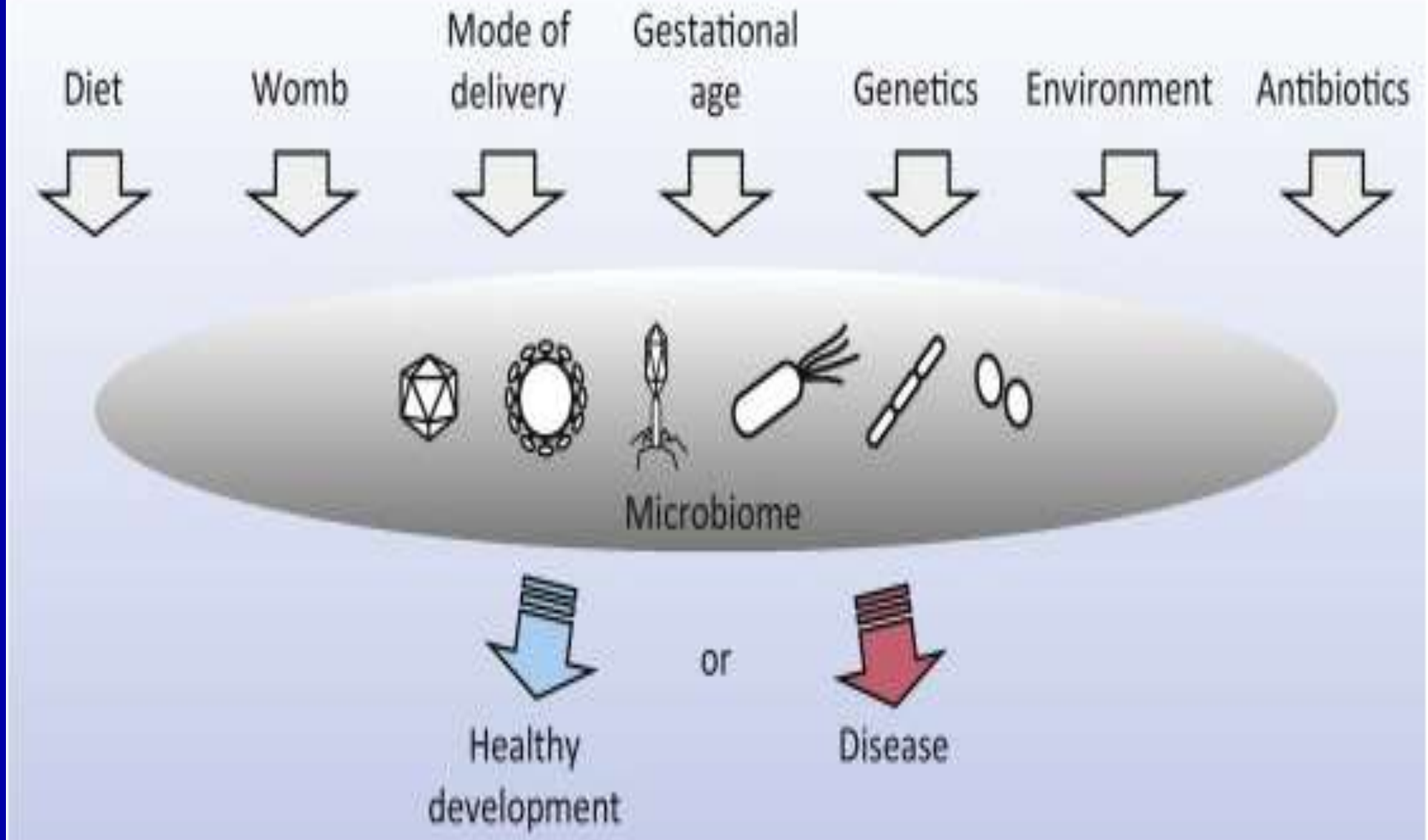
Caesarian vs Vaginal Delivery

Associated Childhood Diseases

Josef Neu et al Clin Perinatol. 2011 Jun; 38(2): 321–331

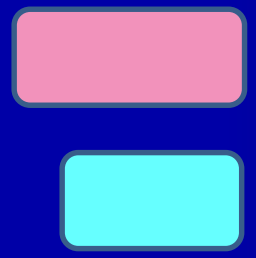
Caesarian Delivery	Odds Ratio 95% CI versus vaginal delivery	
Allergic Rhinitis		
All Caesarians	**1.37**	(1.14 – 1.63)
Repeat Caesarians only no Rupt.Mem	**1.78**	(1.34 - 2.37)
Asthma		
All Caesarians	**1.24**	(1.01 – 1.53)
Female	**1.53**	(1.10 – 2.10)
Female & Repeat Caesarians no RM	**1.83**	(1.13 – 2.97)
Coeliac Disease	**1.8**	(1.13 – 2.88)
Diabetes Mellitus (Type 1)	**1.19**	(1.04 – 1.36)
Gastroenteritis requiring hospitalisation	**1.31**	(1.24 – 1.38)
Gastroenteritis AND Asthma	**1.74**	(1.36 – 2.23)

Influences on microbiome during infant development



Efrem S. Lim et al
http://www.cell.com/trends/microbiology/fulltext/S0966-842X(16)30064-6 Trends in Microbiology

Major Bacterial Class Grouping



Firmicutes *e.g. Lactobacillus, Clostridium* (Gram +)

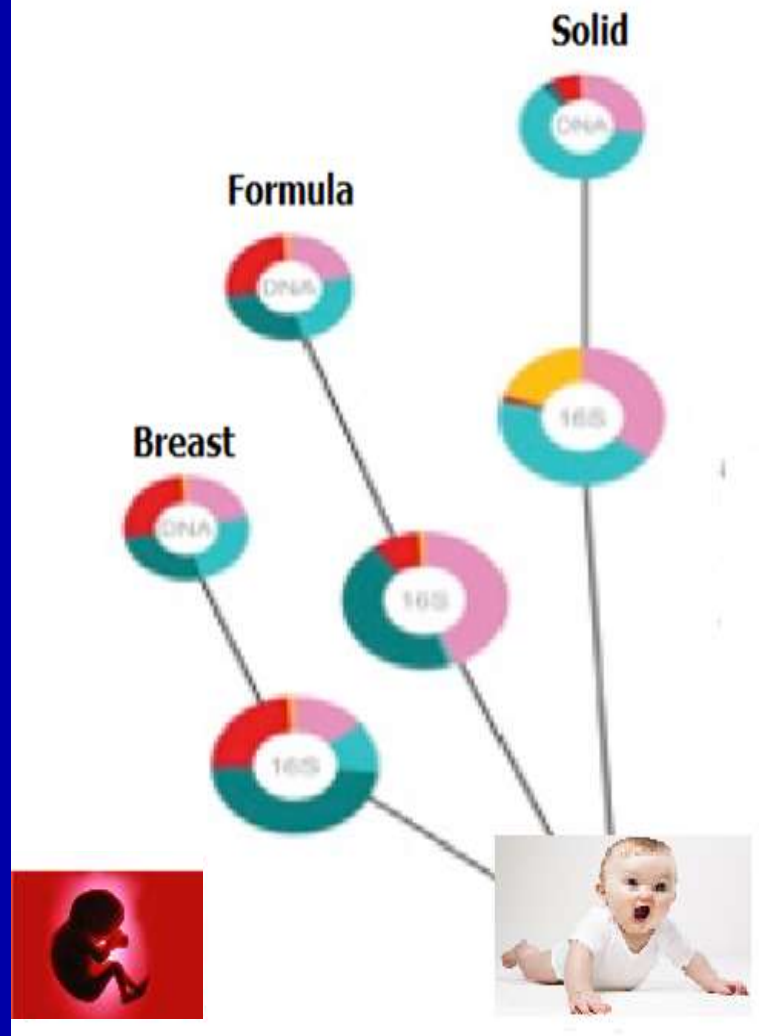
Bacteroidetes *e.g. Bacteroides, Prevotella* (Gram -)

Actinobacteria *e.g. Bifidobacteria, Actinomyces*

Proteobacteria *e.g. E. coli, Helicobacter*

Others

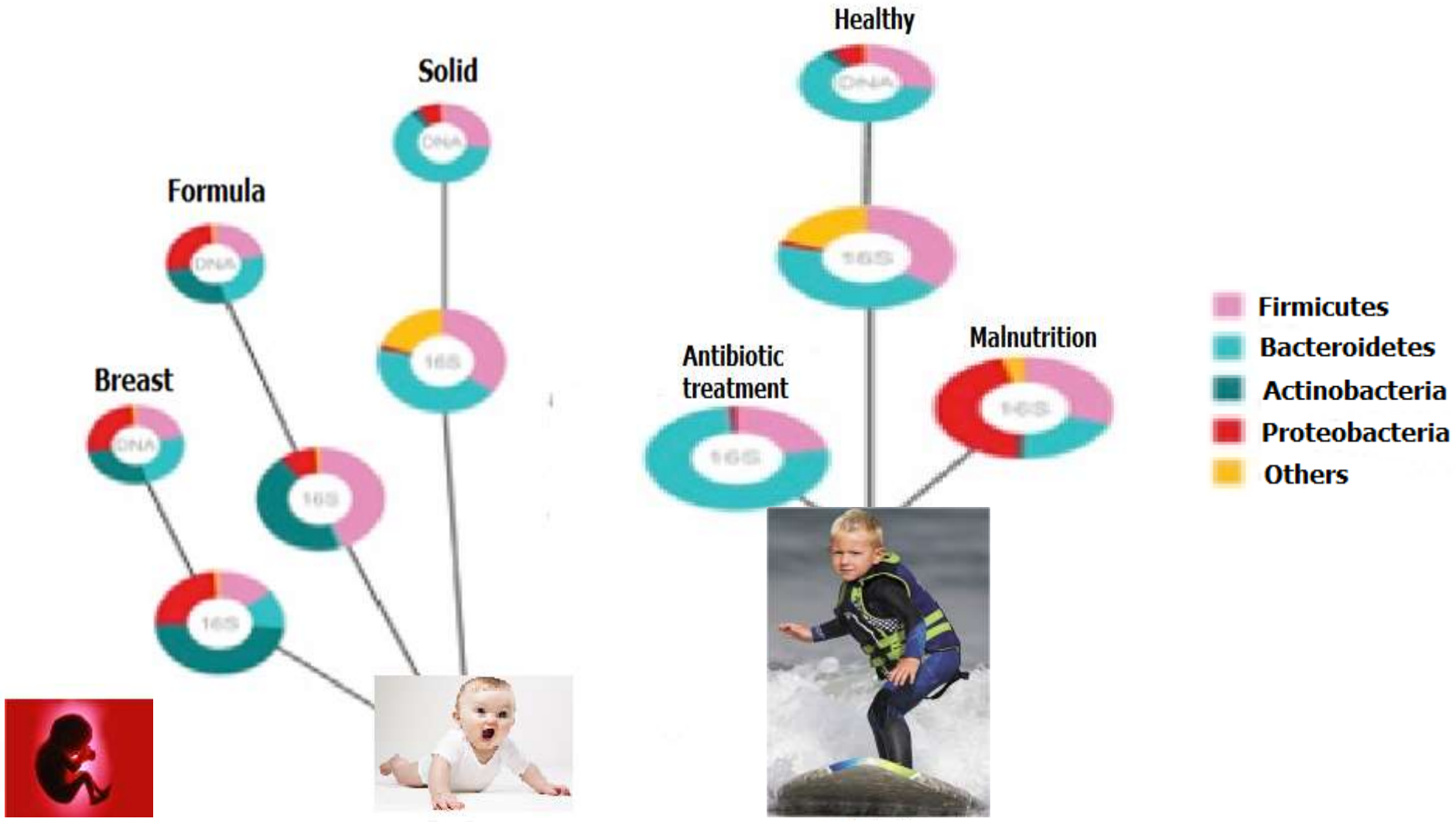
Microbiome Lifetime Dynamics



- Firmicutes
- Bacteroidetes
- Actinobacteria
- Proteobacteria
- Others

Cell. Inf. Microbio. 2:104. doi: 10.3389/fcimb.2012.00104

Microbiome Lifetime Dynamics



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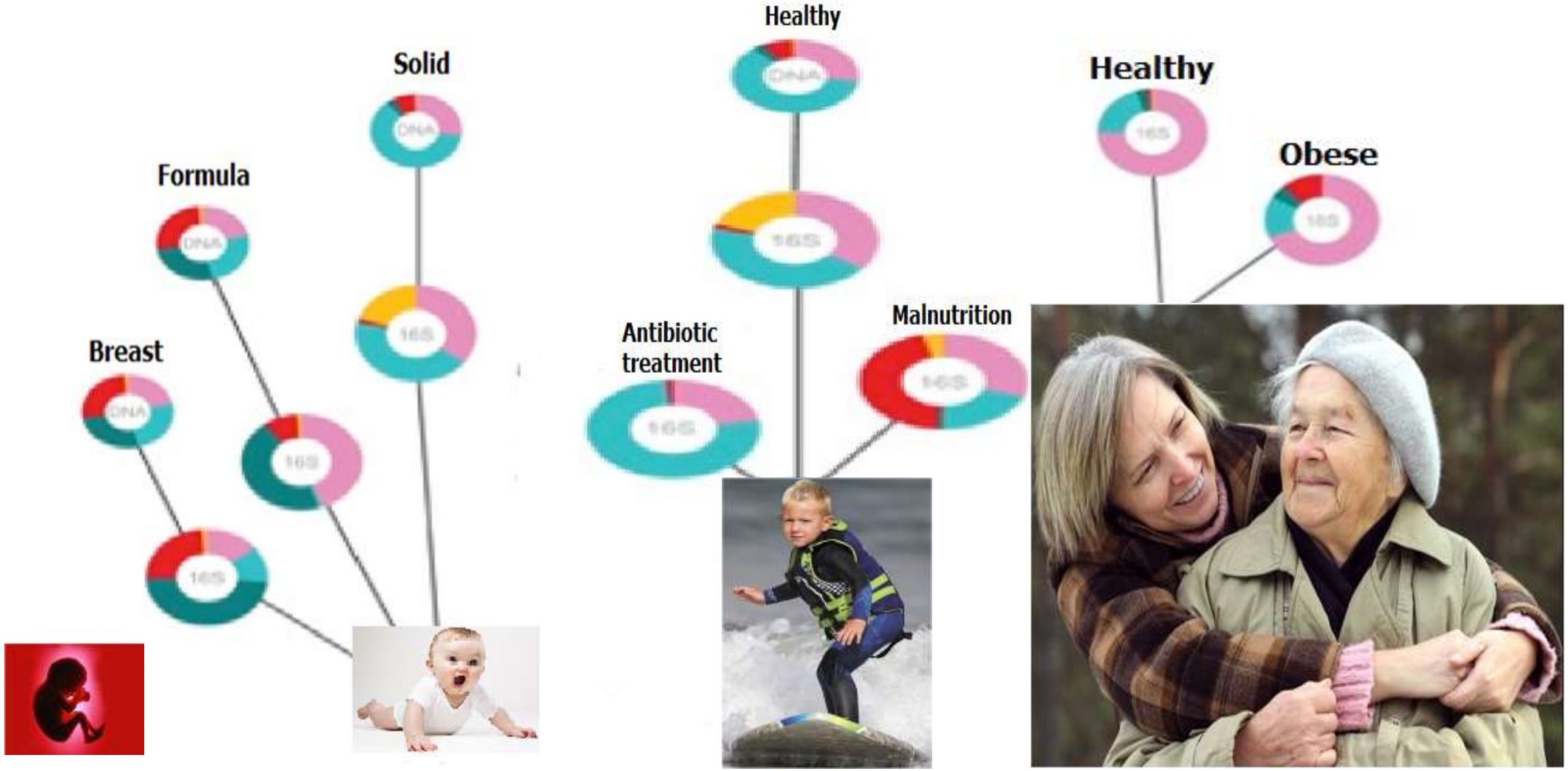
Microbiome Lifetime Dynamics



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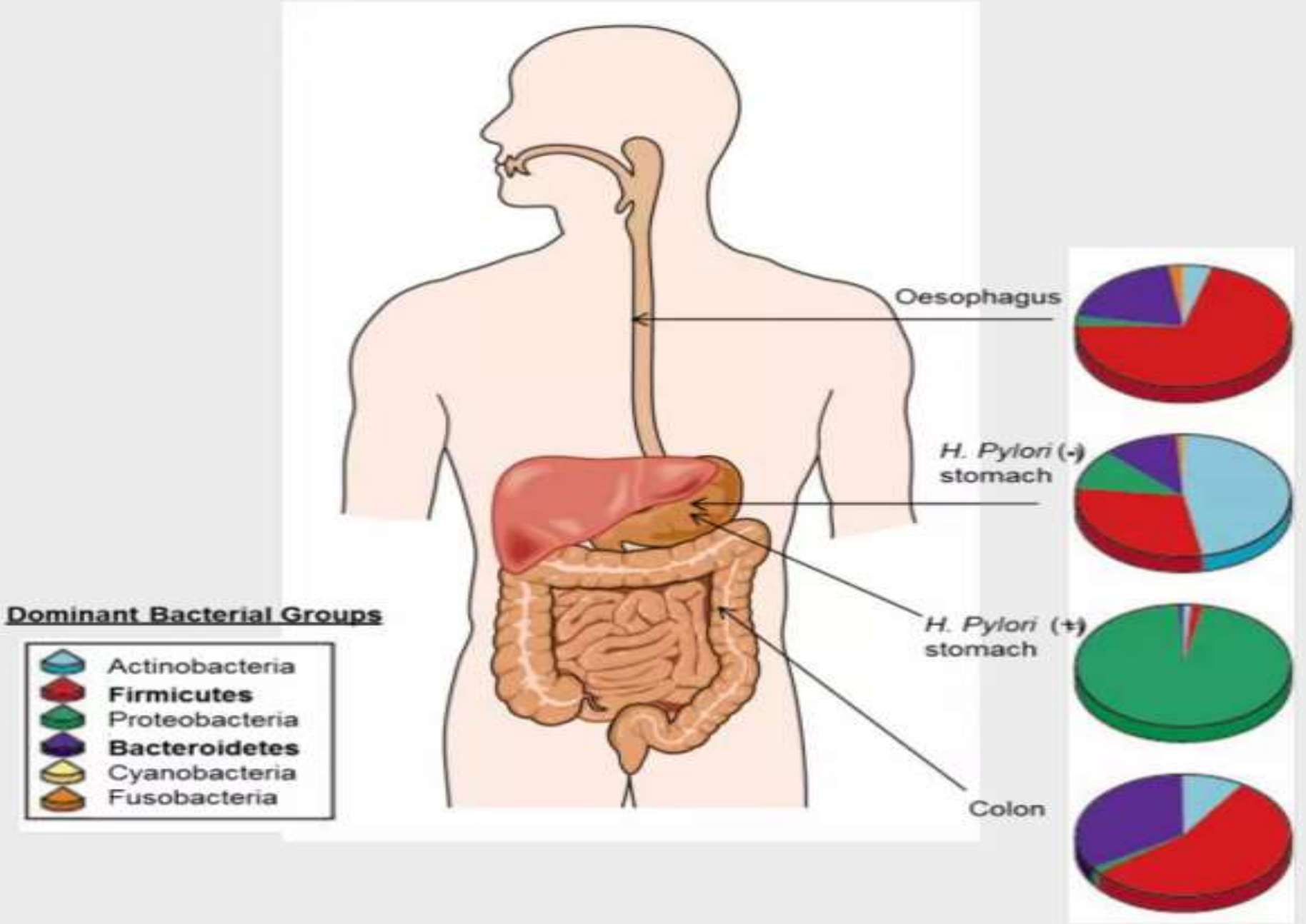
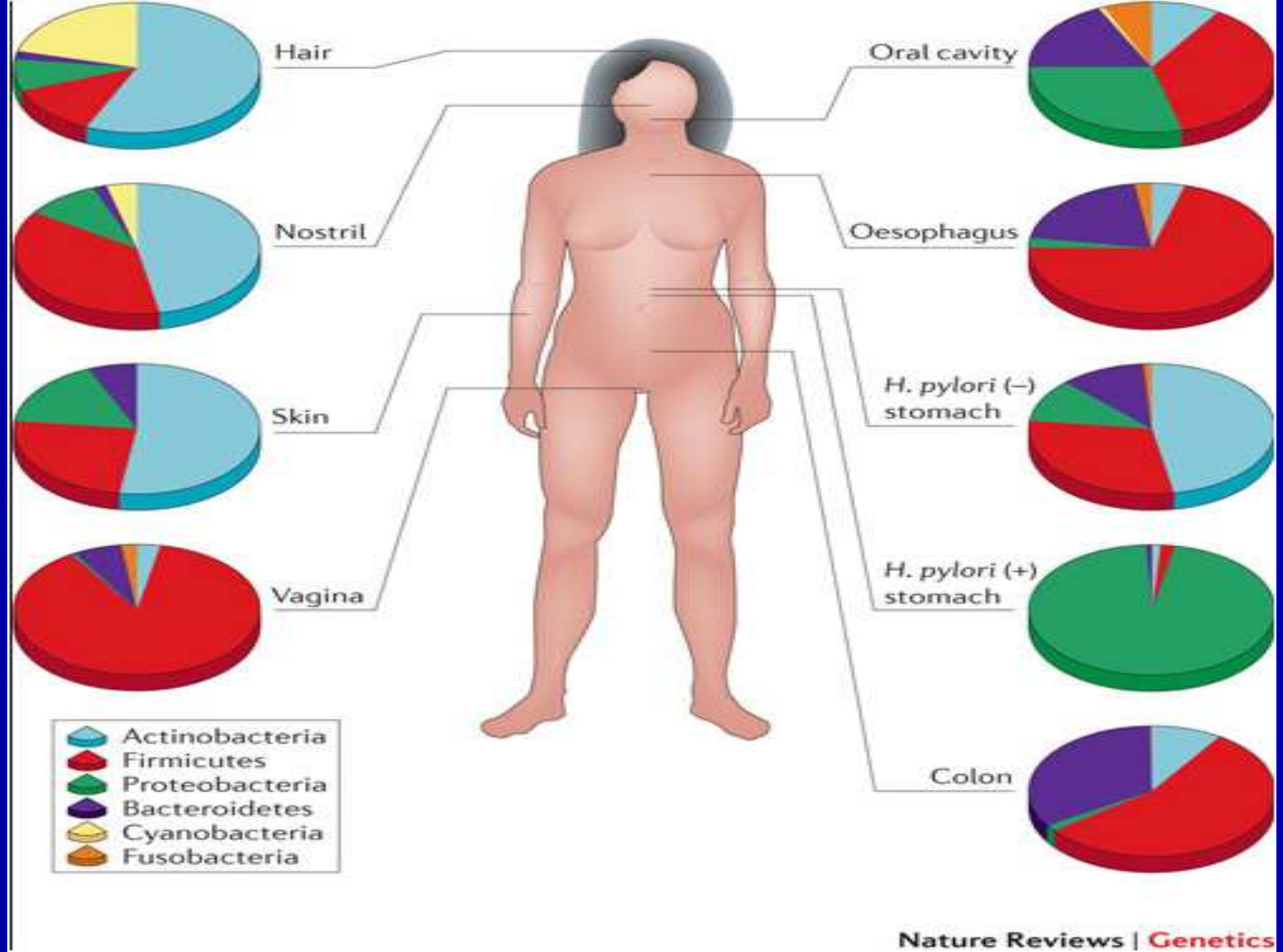
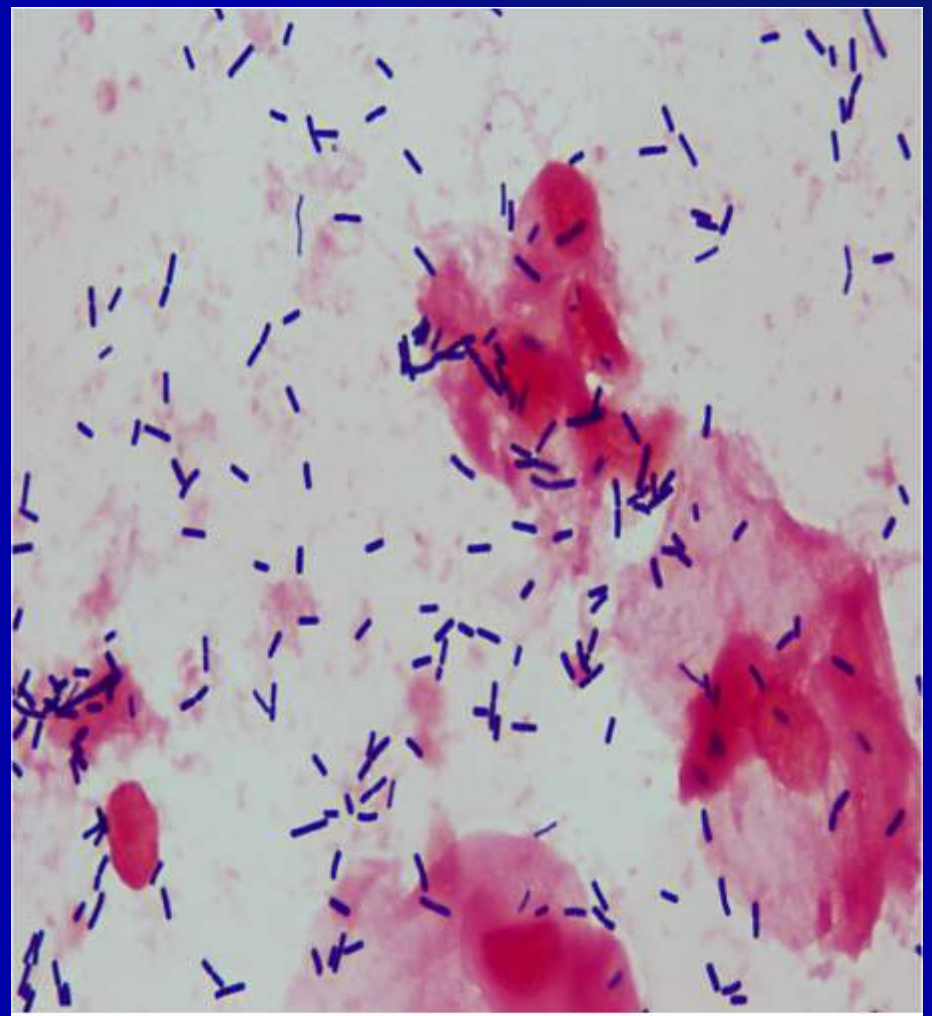


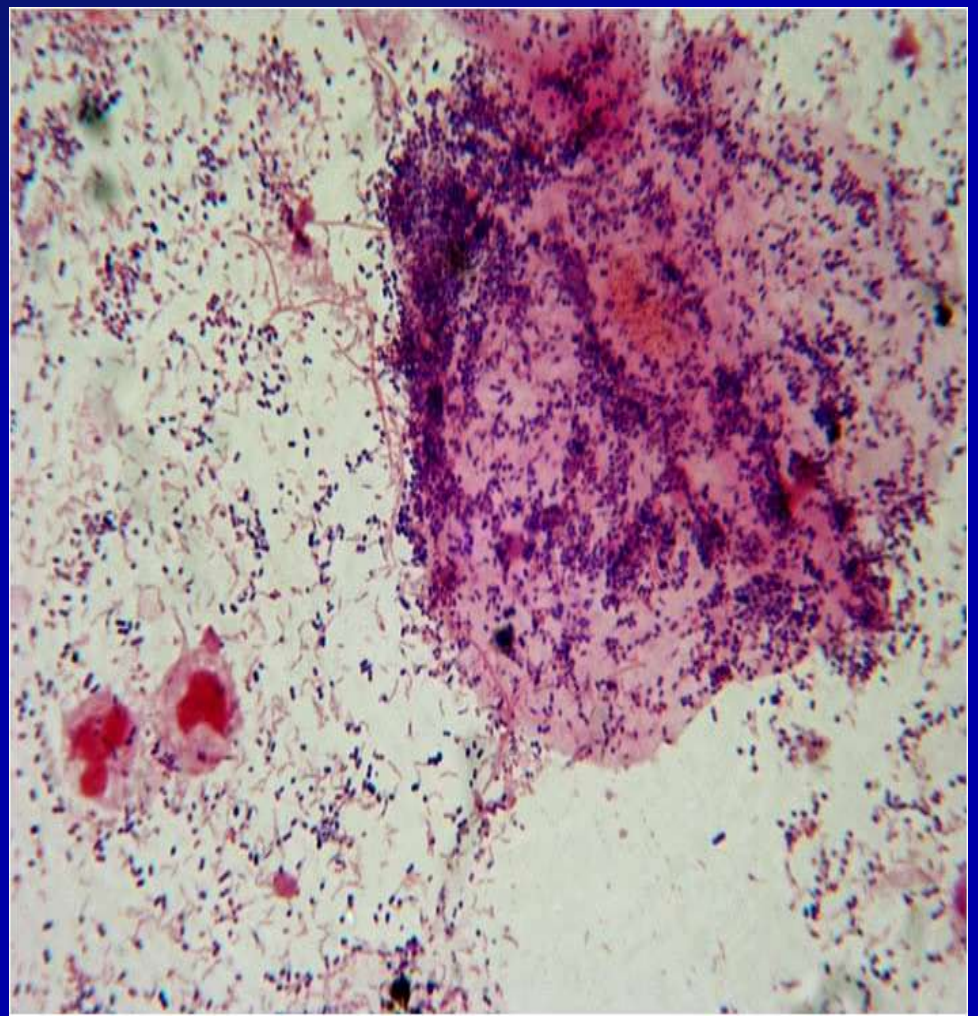
Bacterial composition of the adult gut. Bacteroidetes bacteria and Firmicutes bacteria (in bold) are the most dominant bacterial groups. Modified from Cho I, Blaser MJ. (2012).The human microbiome: at the interface of health and disease. Nat Rev Gen. 13(4), 260-270.


Hair
Nostril
Skin
Vagina
Oral cavity
Oesophagus
H. pylori (–) stomach
H. pylori (+) stomach
Colon
Actinobacteria
Firmicutes
Proteobacteria
Bacteroidetes
Cyanobacteria
Fusobacteria

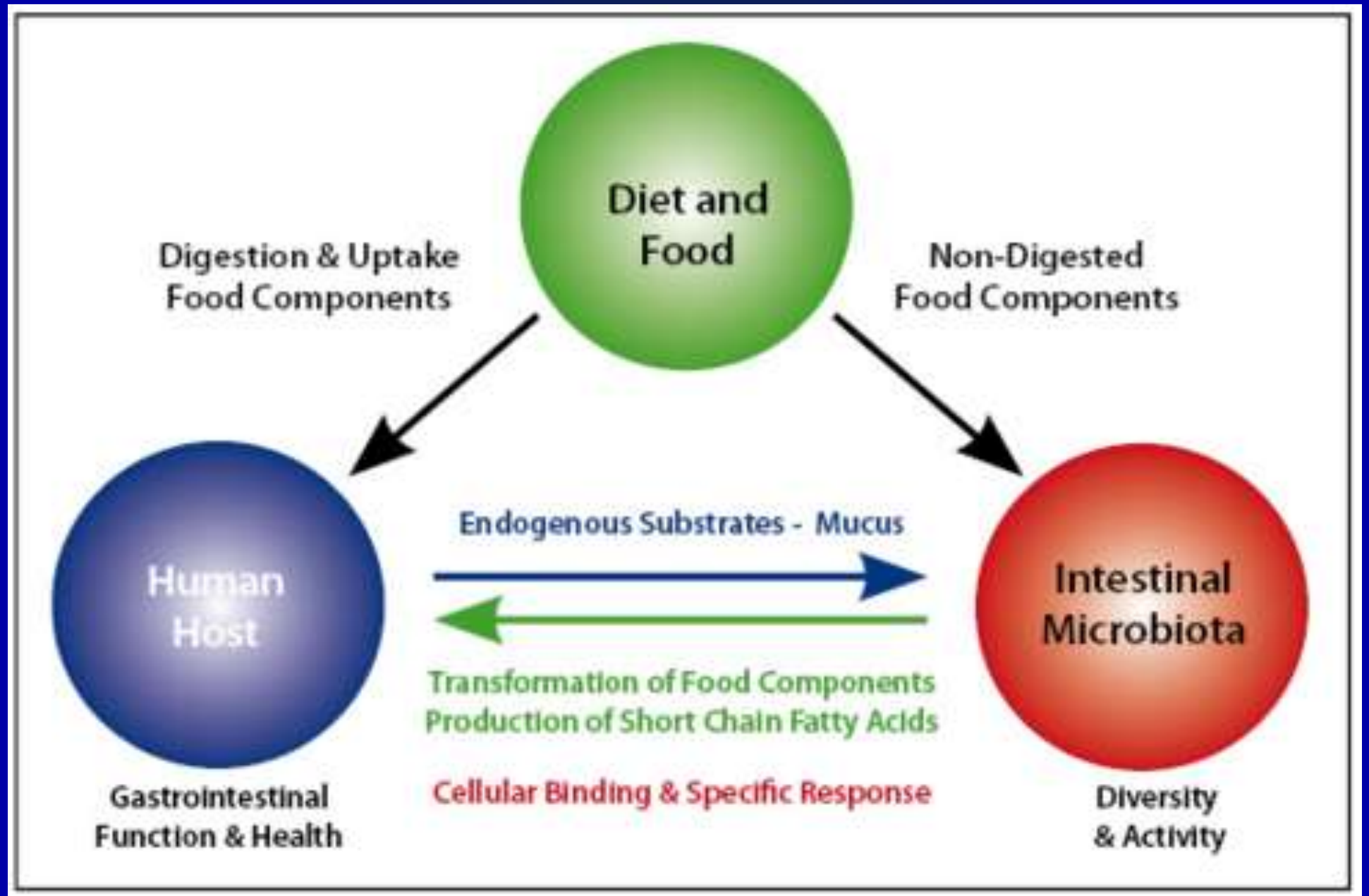
Vaginal Gram Stain

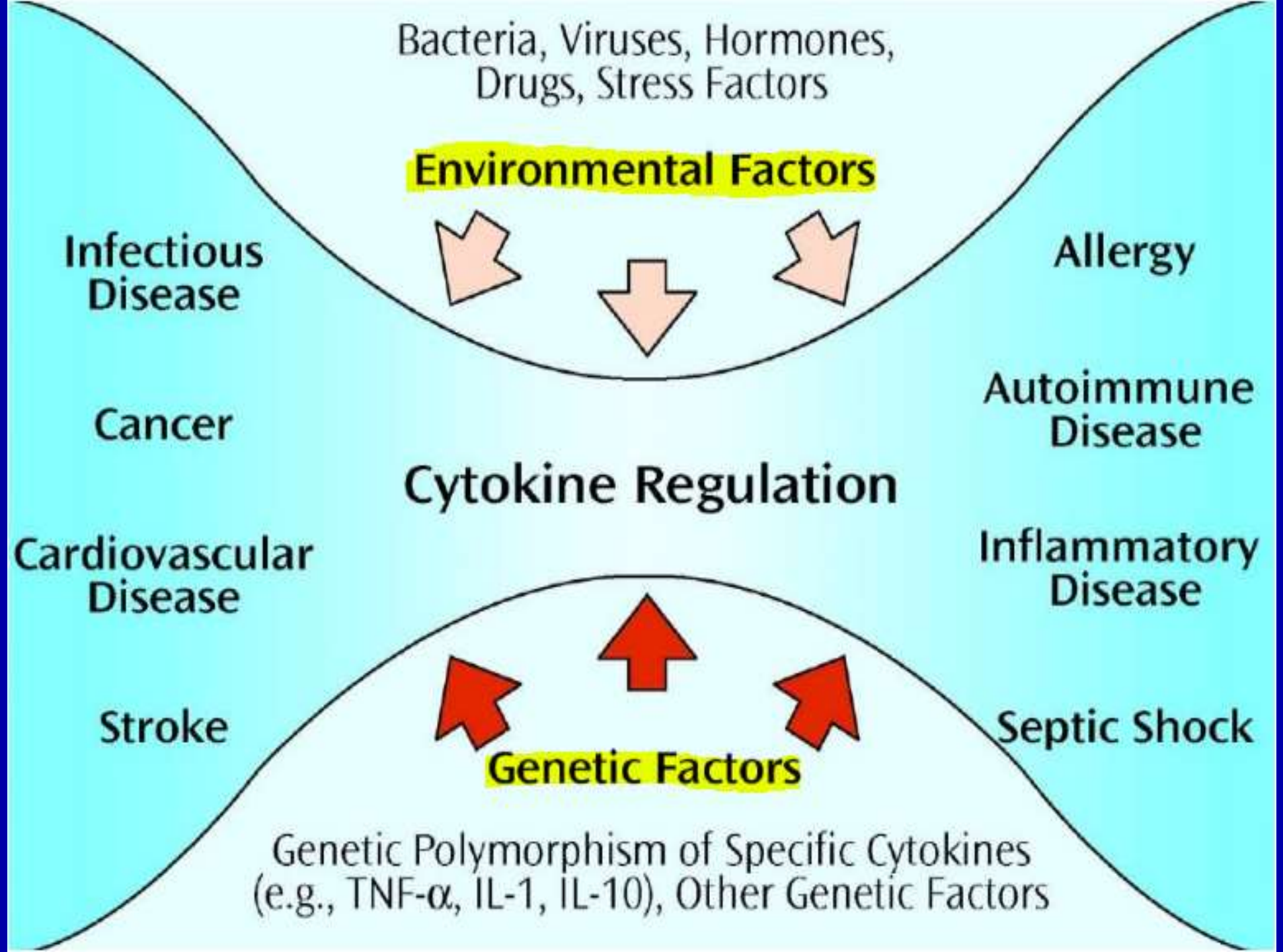
Normal ⇨ Bacterial Vaginosis





Intestinal Interactions




Bacteria, Viruses, Hormones,
Drugs, Stress Factors
Environmental Factors
Infectious Disease
Allergy
Cancer
Autoimmune Disease
Cytokine Regulation
Cardiovascular Disease
Inflammatory Disease
Stroke
Septic Shock
Genetic Factors
Genetic Polymorphism of Specific Cytokines
(e.g., TNF-α, IL-1, IL-10), Other Genetic Factors

Microbiome

Causal Health Links

or

Associations only ???

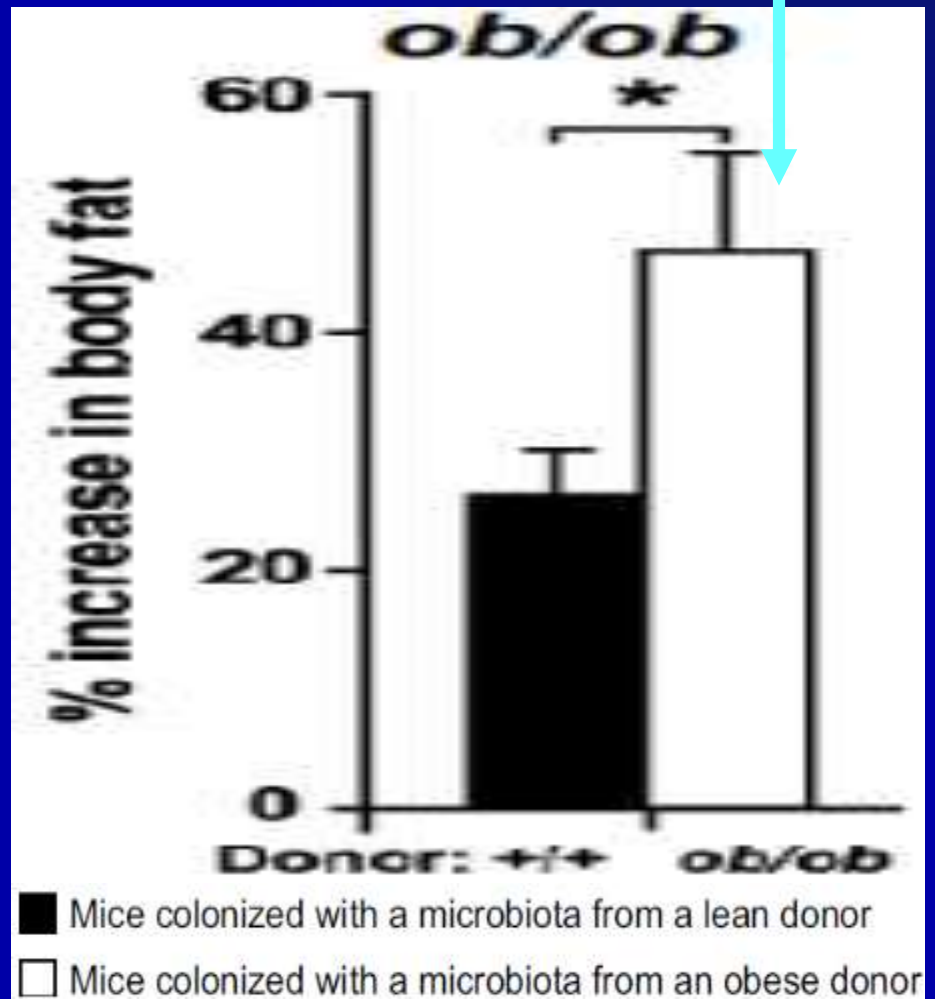
Gut Microbiome

connecting genes, environment & immune system

Fat Gain Differences

Germ Free Mice
Faecal transplant with

Genetically Obese
faecal donor ob/ob

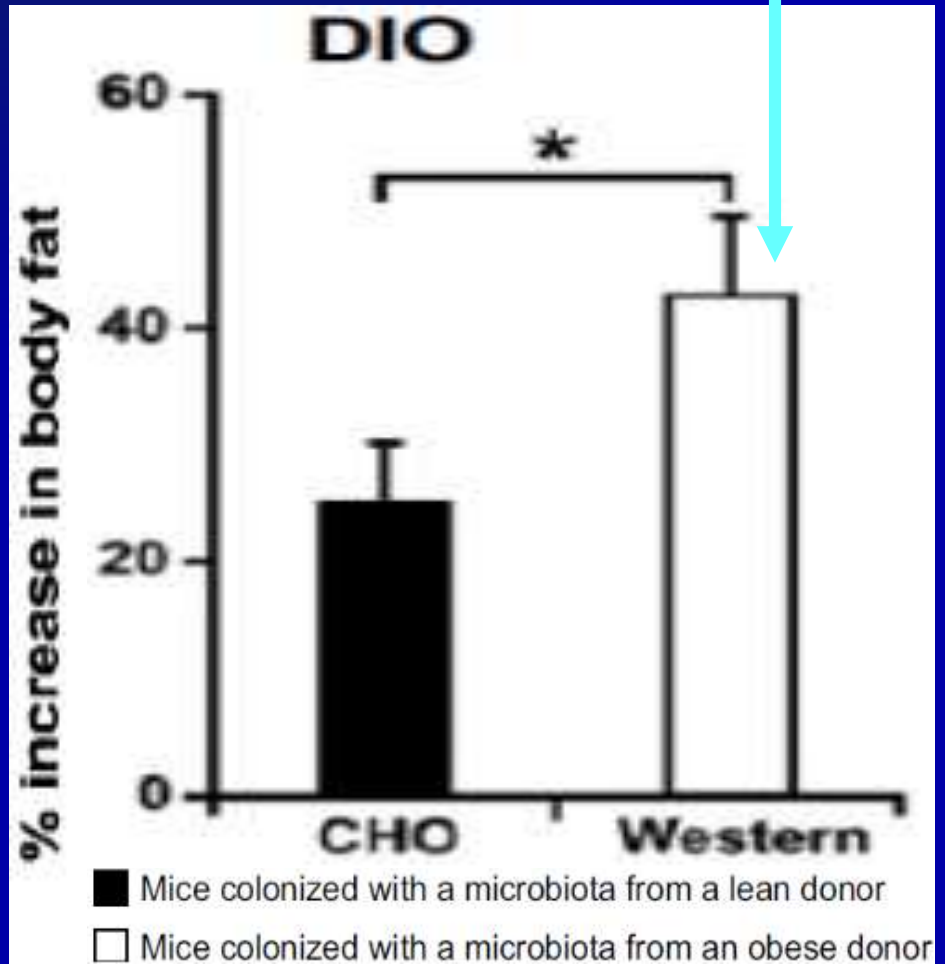


SOURCE: Turnbaugh et al., 2006, 2008

Fat Gain Differences

Germ Free Mice
Faecal transplanted

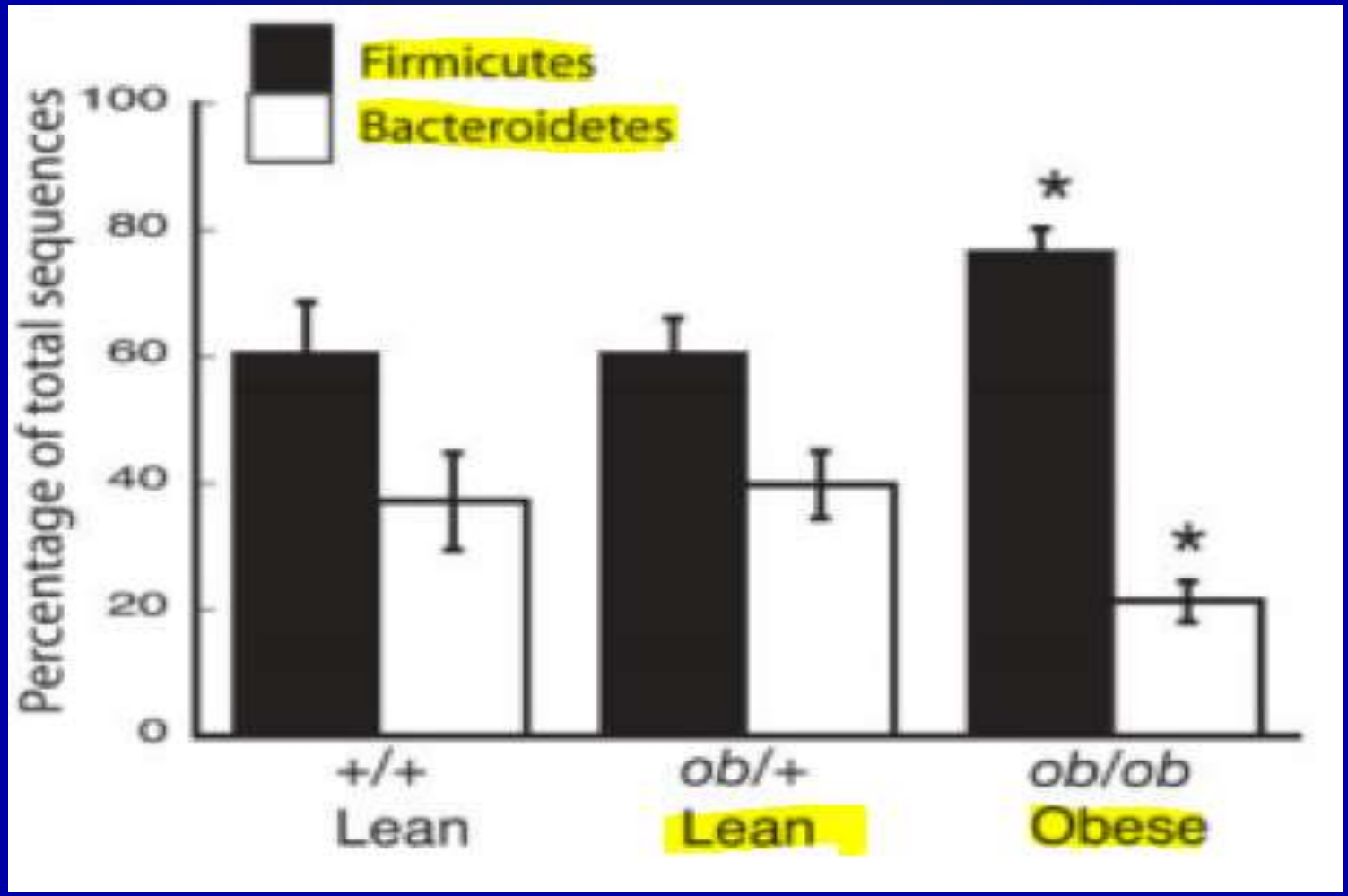
Diet Induced Obese (DIO)
faecal donor



SOURCE: Turnbaugh et al., 2006, 2008.

Firmicutes and *Bacteroidetes* Ratio lean vs obese mice

Small Ratio Differences ⇨ Large Weight Differences



Ley, R.E., Bäckhed, F., Turnbaugh, P., Lozupone, C.A., Knight, R.D. and Gordon, J.I. "Obesity alters gut microbial ecology." Proc. Natl Acad. Sci. USA, 2005

Fat, Firmicutes, Bacteroidetes

Germ Free Mouse

↓Fat

↓*Firmicutes*

↑*Bacteroidetes*

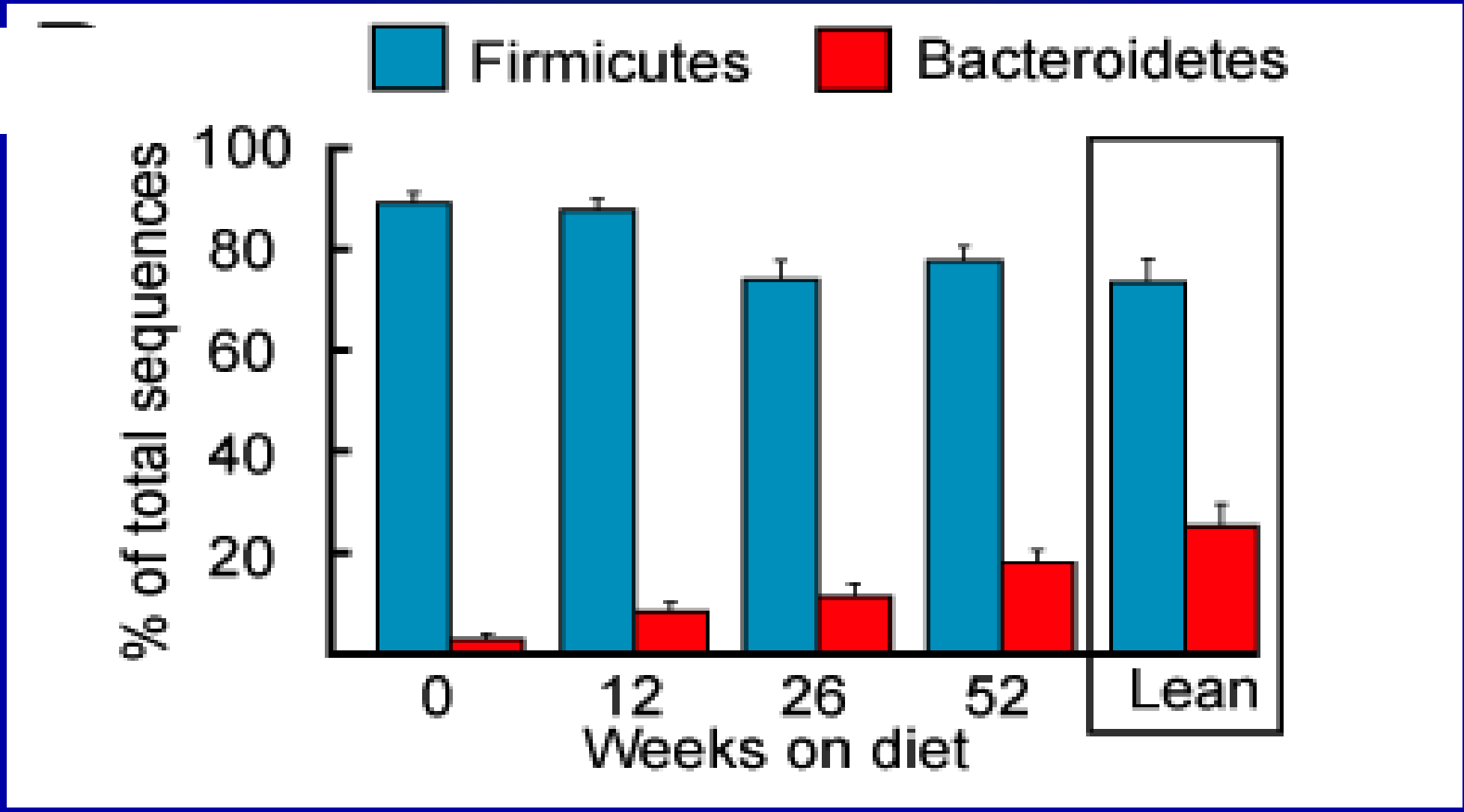
Conventional Mouse

↑Fat

↑*Firmicutes*

↓*Bacteroidetes*

Microbiome Effects of Dieting - humans



Ley *et al*. Nature 444: 1022 (2006)

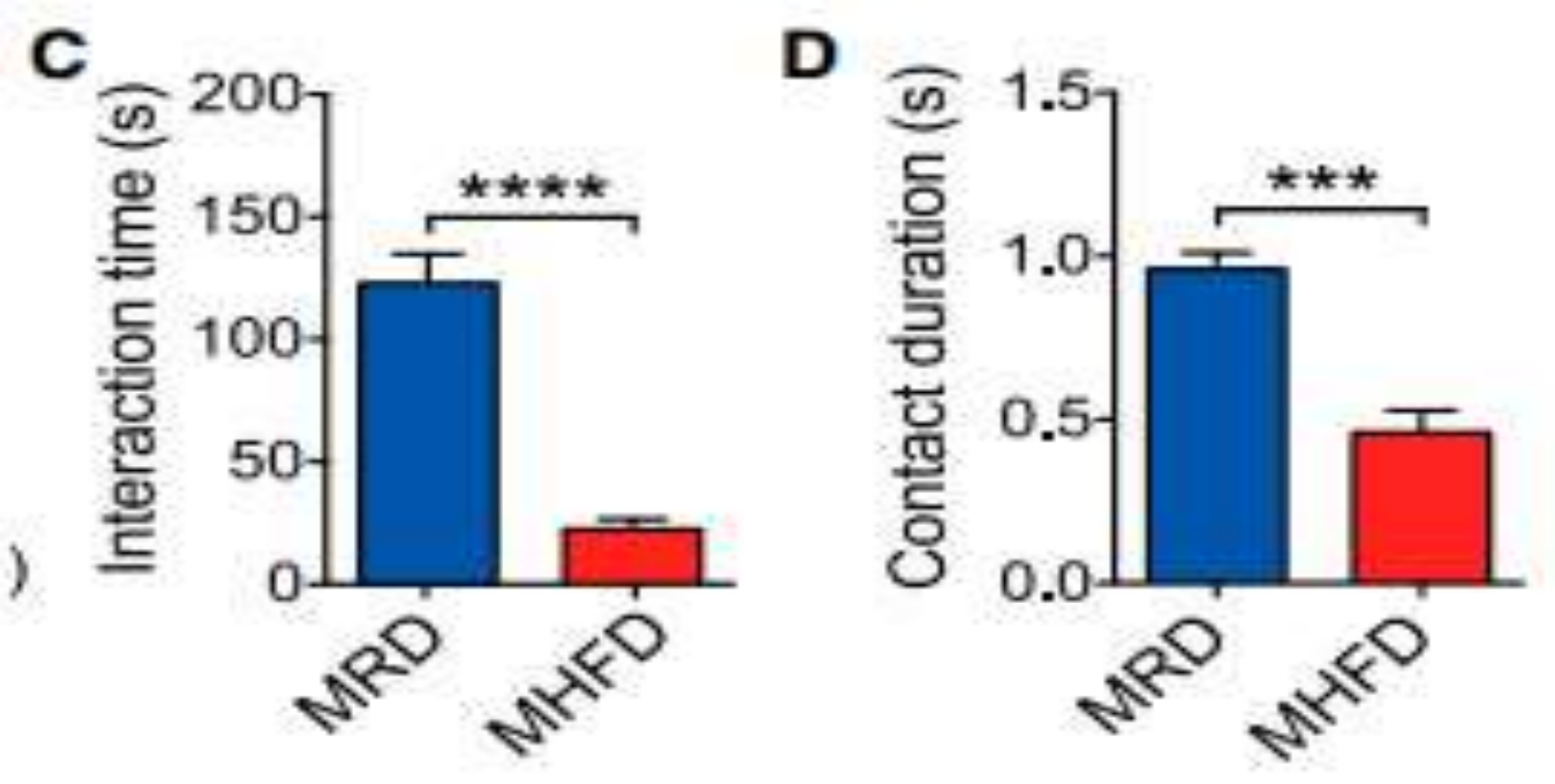
Diet Behaviour Link Mice

RD = Regular Diet
HFD = High Fat Diet

Cell, Vol 165, #7, p1762–1775, 16 June 2016 S Buffington et al
Microbial Reconstitution Reverses Maternal Diet-Induced Social and Synaptic Deficits in Offspring

Sociability Effects

Effect on Interaction time & Contact time



Cell, Vol 165, #7, p1762–1775, 16 June 2016 S Buffington et al
Microbial Reconstitution Reverses Maternal Diet-Induced Social and Synaptic Deficits in Offspring

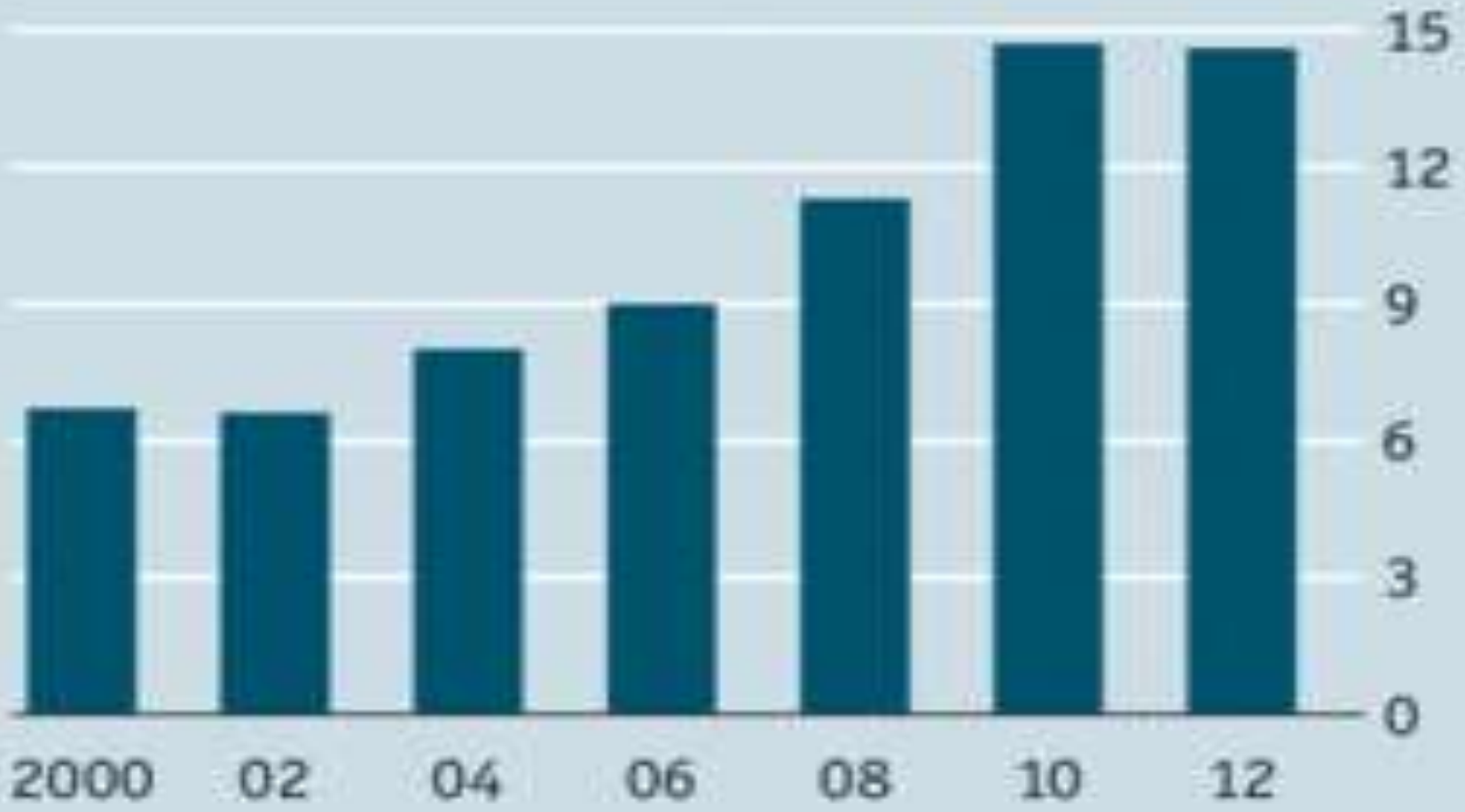
Study Highlights

- Maternal high-fat diet (MHFD) induced behaviour changes in offspring
- MHFD caused alterations in gut microbial ecology in offspring
- MHFD offspring had deficient oxytocin levels
- *Lactobacillus reuteri* treatment restored oxytocin levels, and social behaviour

A change of condition

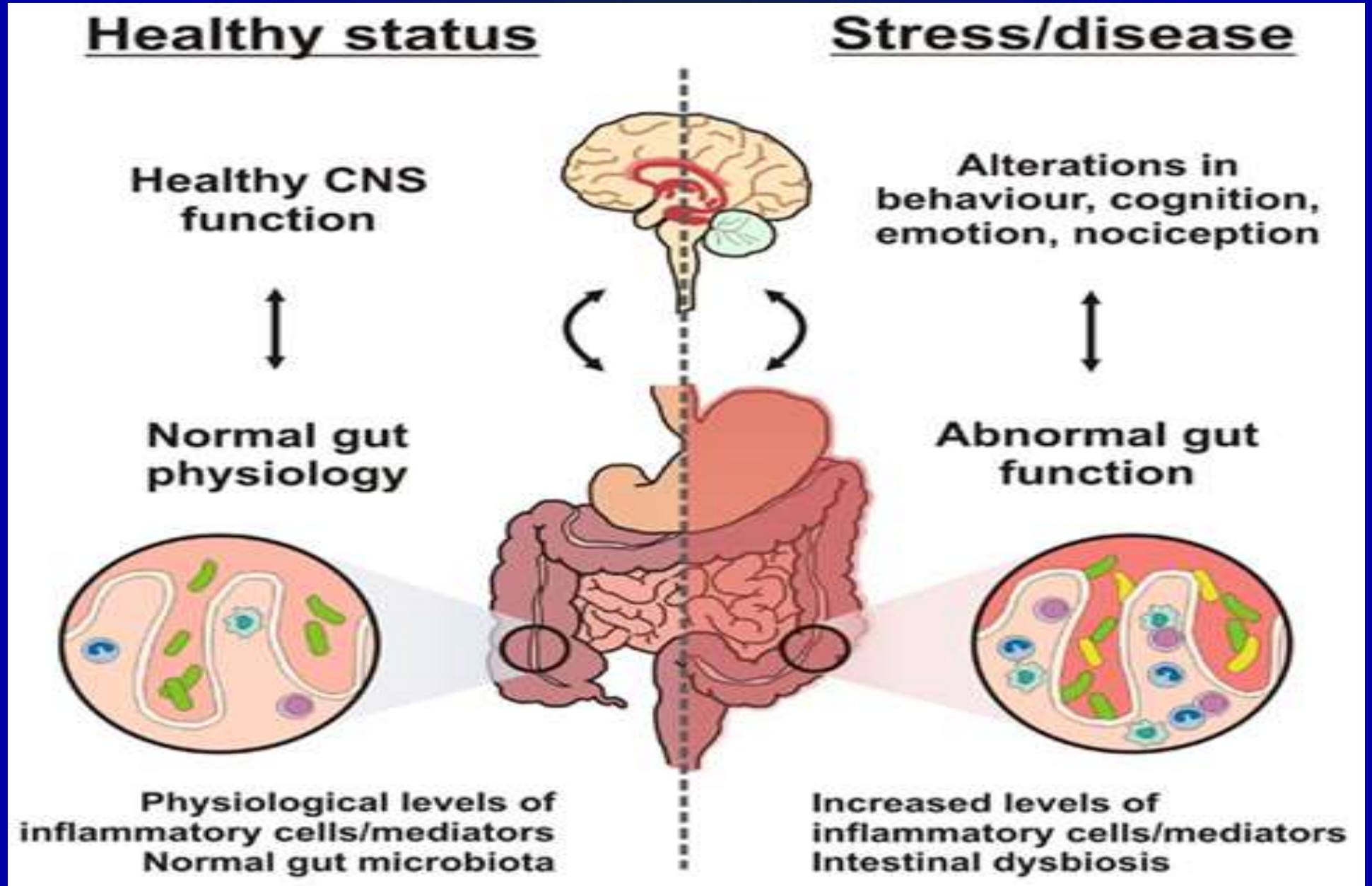
Number of eight-year-olds in America with autism

Per 1,000 of age group

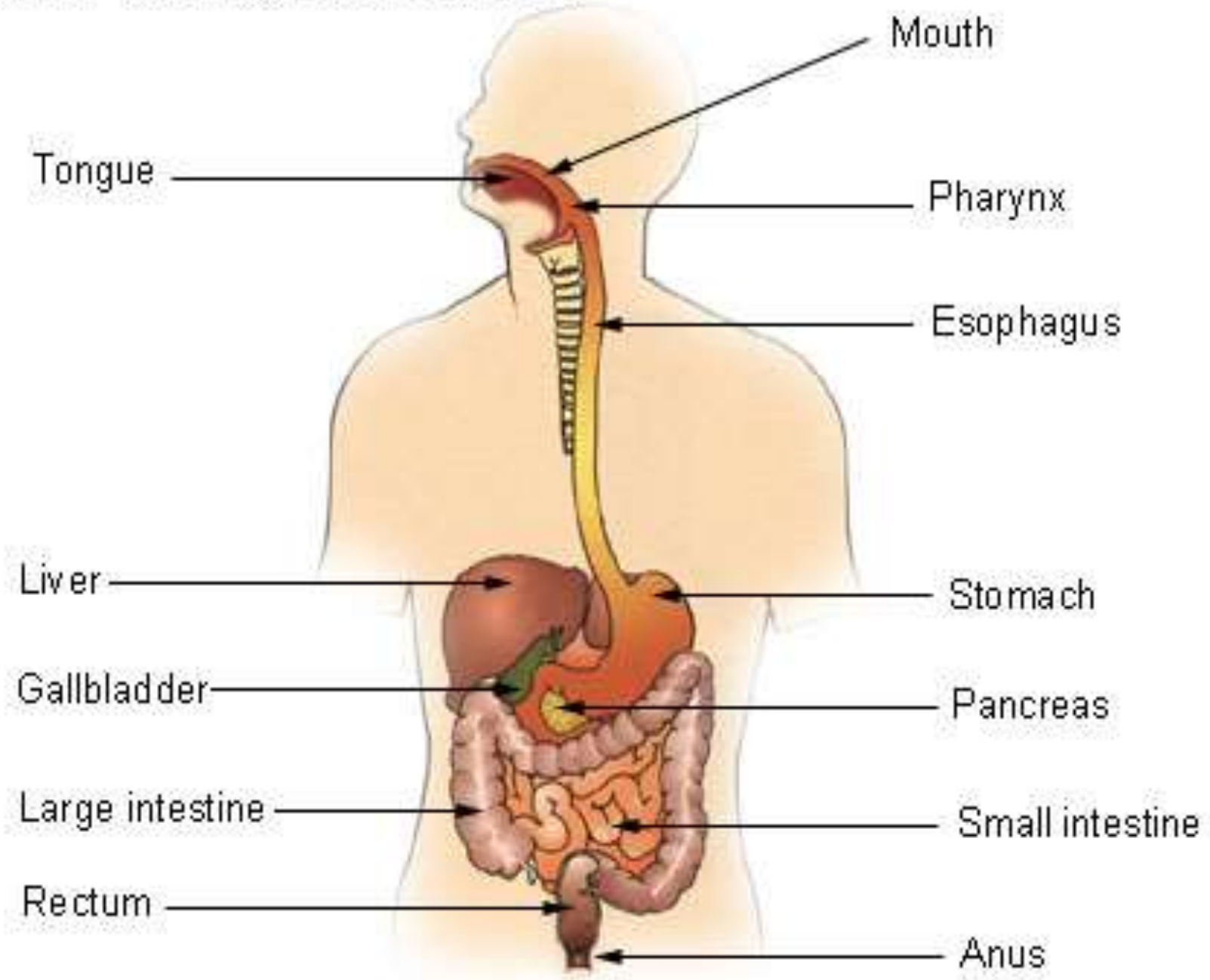


Source: US Centres for Disease Control and Prevention

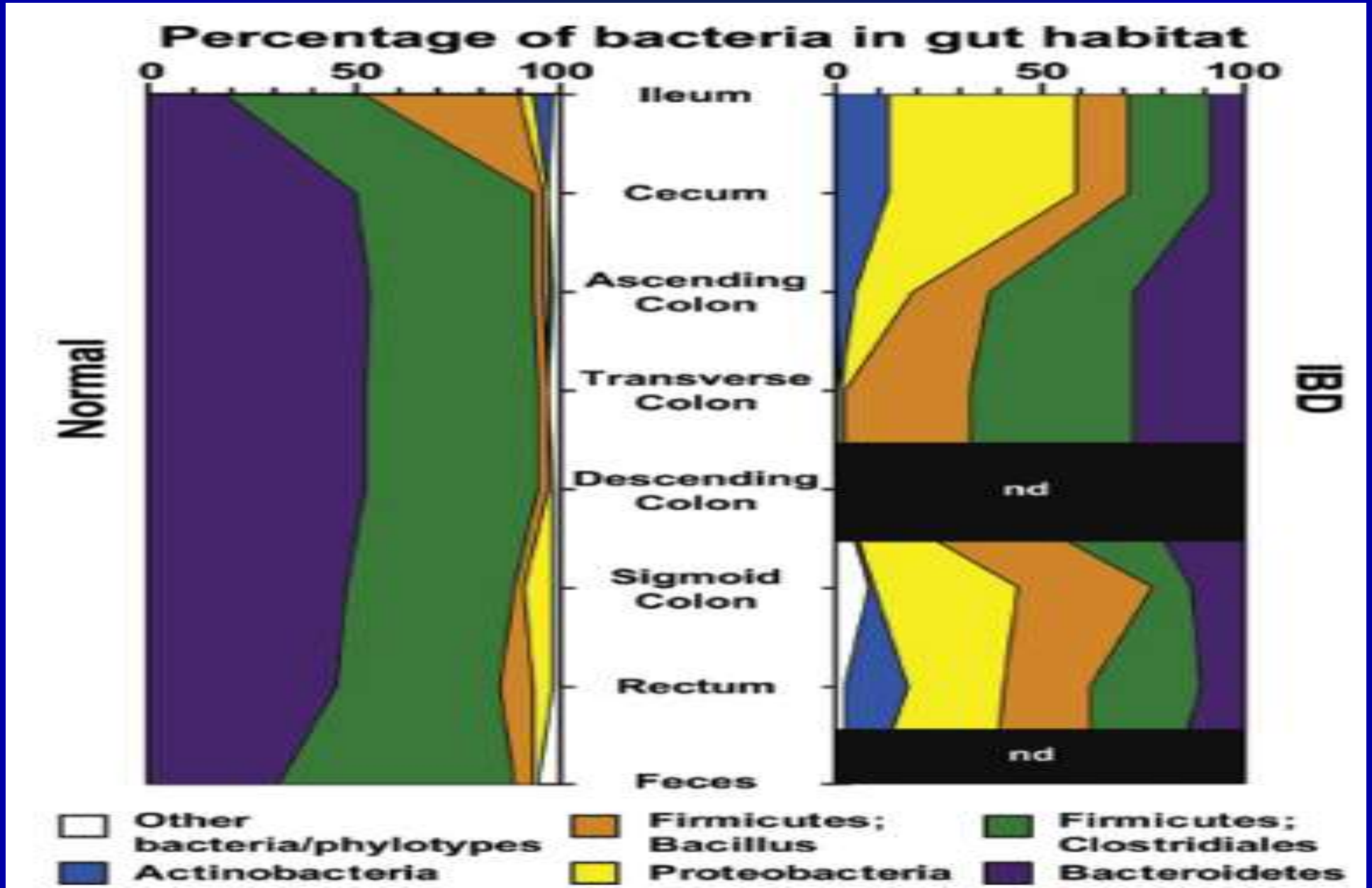
'Dysbiosis' and CNS Interaction



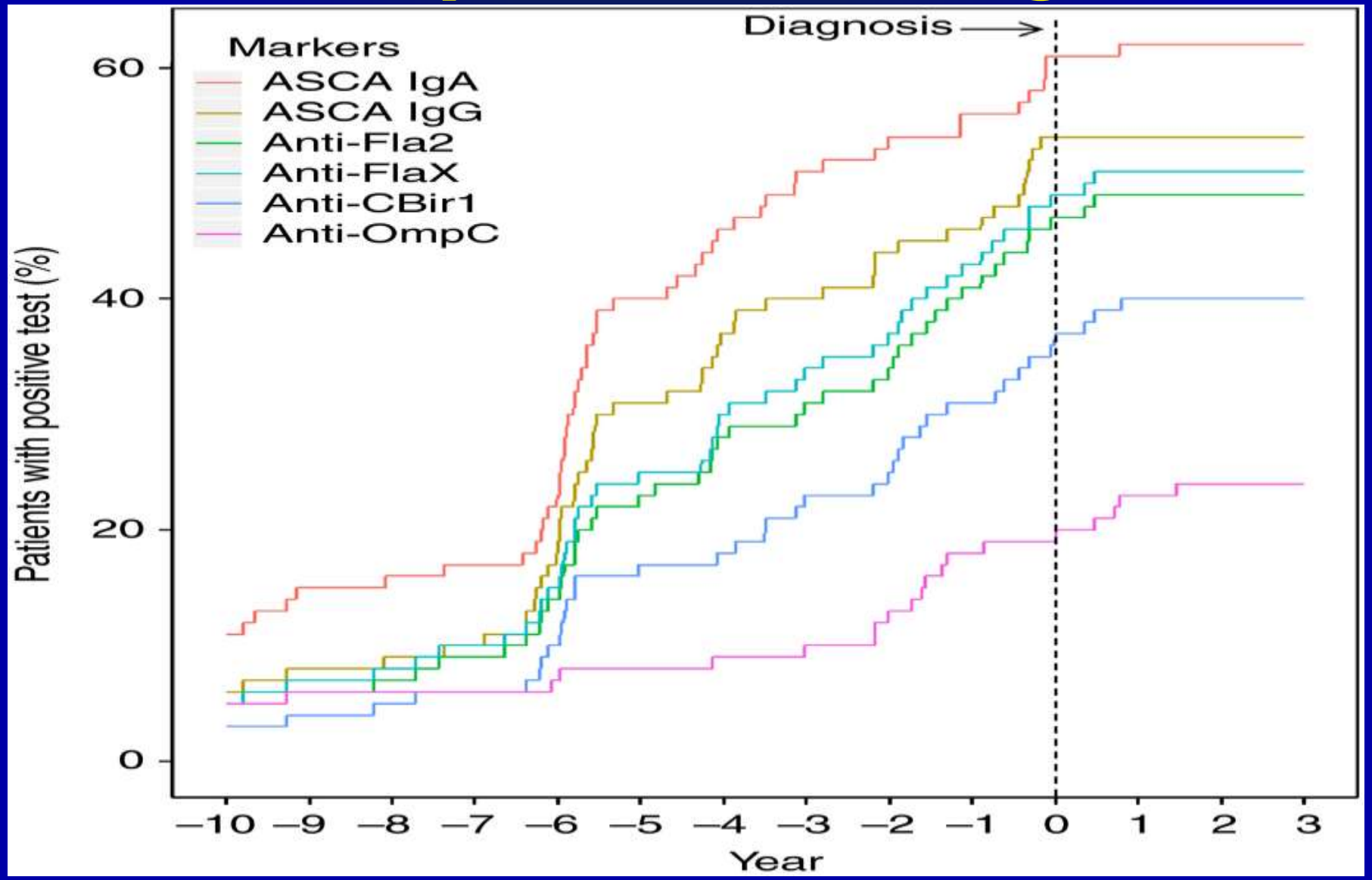
Organs of the Digestive System



Biota Differences Normal vs IBD



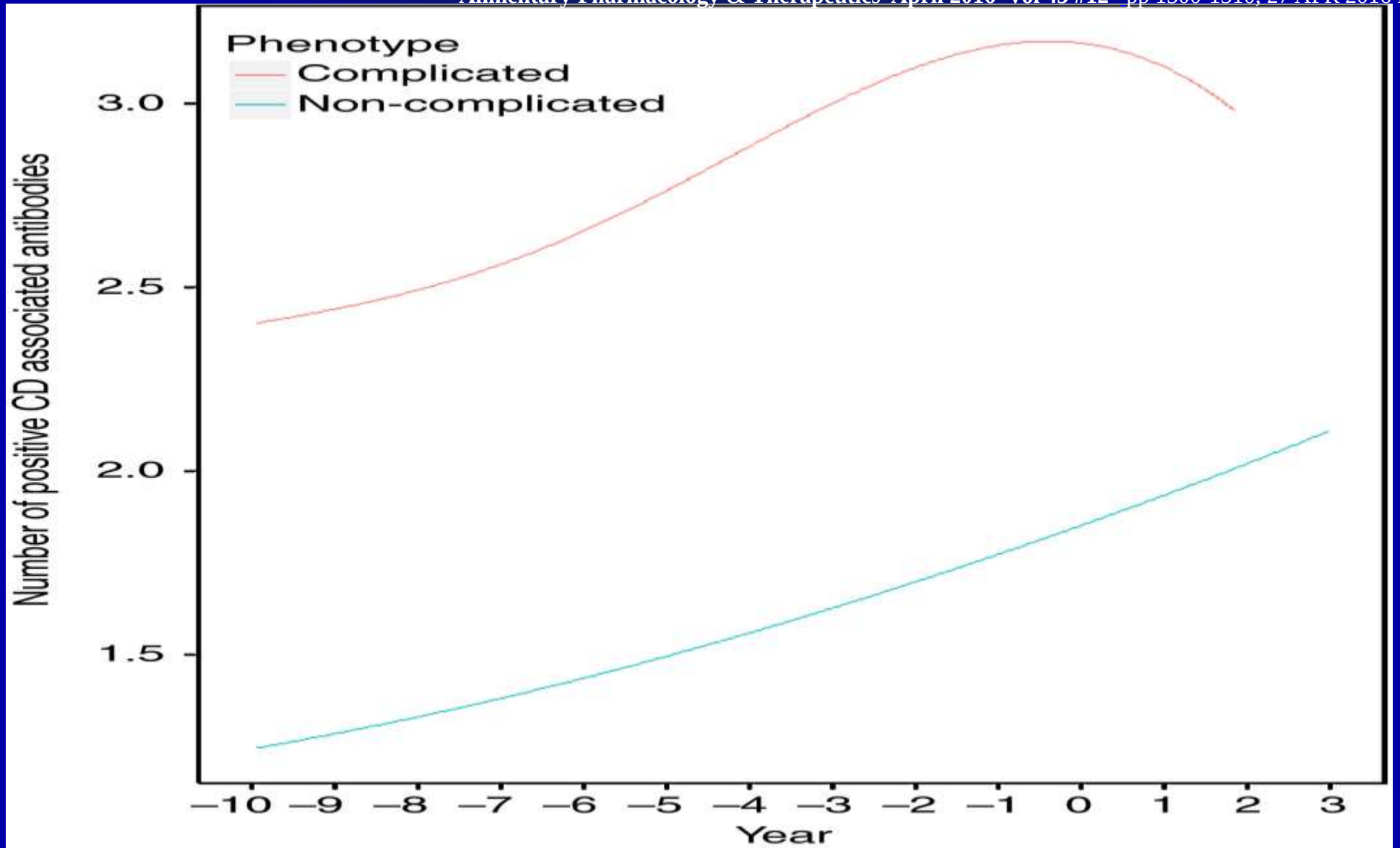
Serologic markers predict Crohn's years before diagnosis



Alimentary Pharmacology & Therapeutics April 2016 Vol 43 #12 pp 1300-1310, 27 APR 2016 DOI: 10.1111/apt.13641

Serologic markers predict Crohn's years before diagnosis

Alimentary Pharmacology & Therapeutics April 2016 Vol 43 #12 pp 1300-1310, 27 APR 2016 DOI: 10.1111/



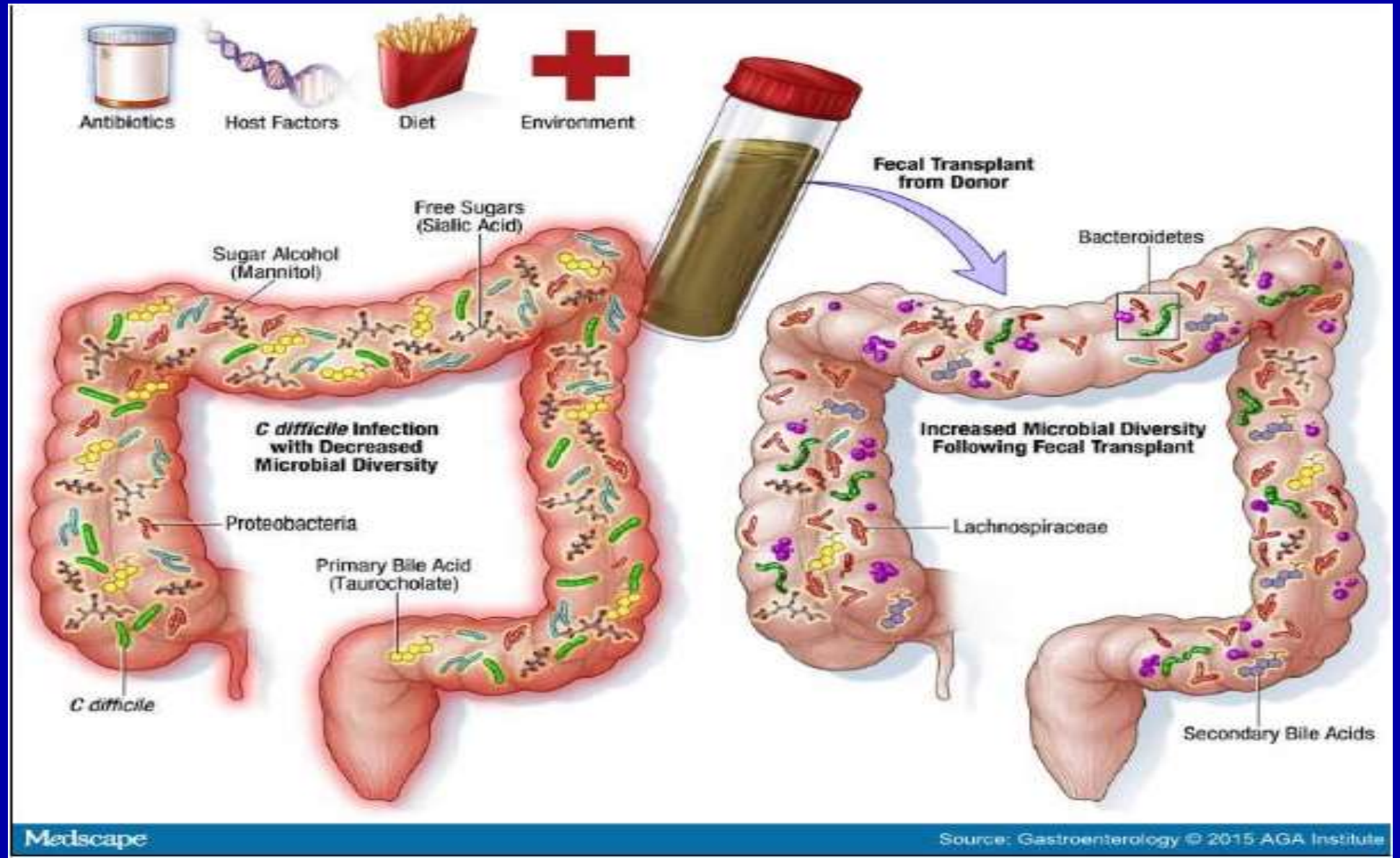
Reference intervals of CD-associated antibodies determined by

- 722 serum samples from 200 healthy controls
- 522 patients with non-IBD gastrointestinal disease

522 patients with non IBD GI disease

- 193 had IBS
- 158 GERD
- 51 hepatitis
- 48 diverticular disease
- 40 coeliac disease
- 18 chronic diarrhoea
- 6 microscopic colitis
- 8 other diseases

Faecal Transplant for Clostridium difficile

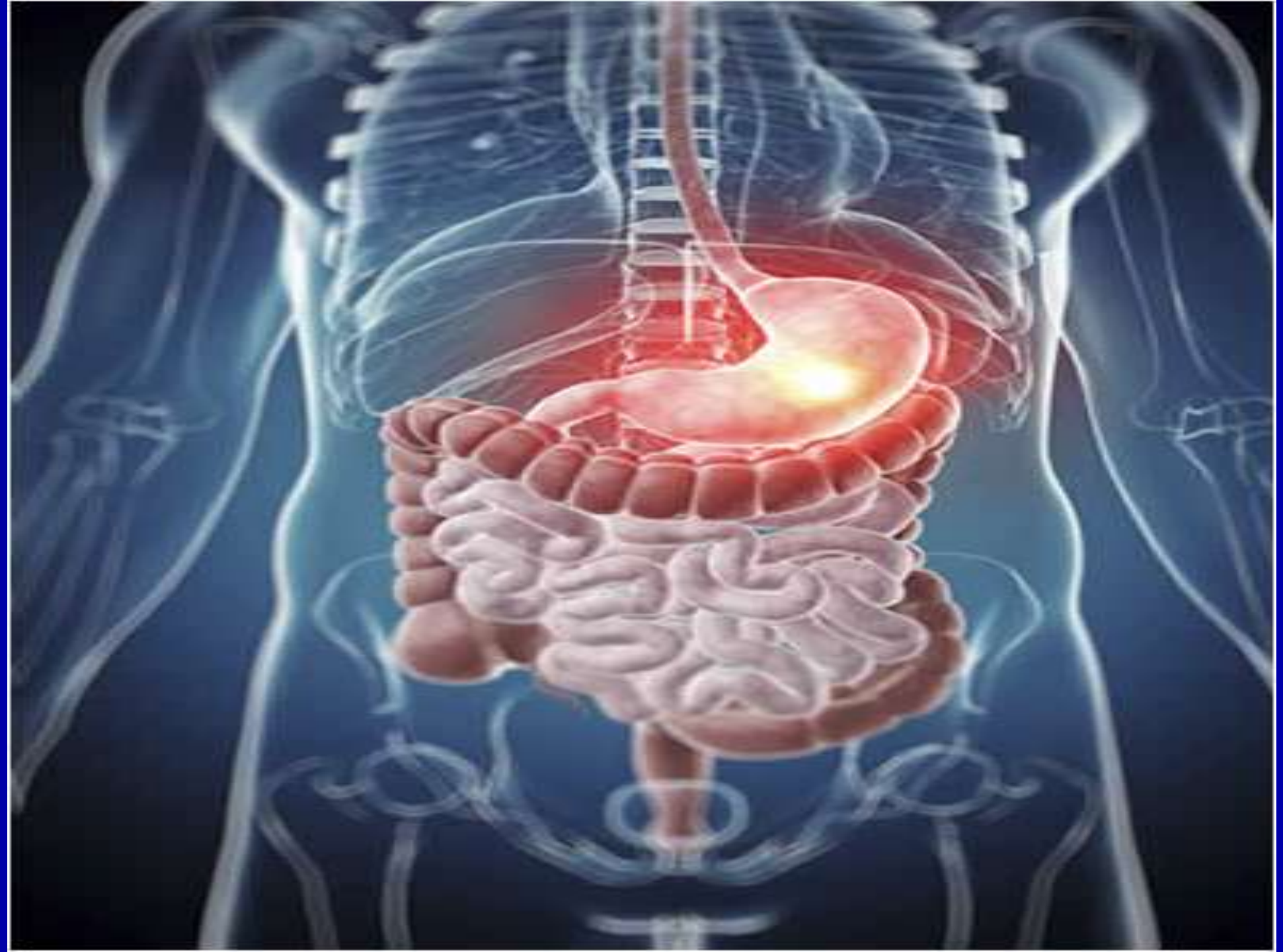


INTESTINAL MICROFLORA

10^{14} micro-organisms, >500 differentes species

	Stomach	10^2 to 10^3
Lactobacilli	Duodenum	$<10^{4-5}$
Streptococci Lactobacilli	Jejunum	
Enterobacteria Enterococcus Faecalis Bacteroides Bifidobacteria Peptococcus Peptostreptococc Ruminococcus Clostridia Lactobacilli	Ileum	10^3 to 10^7
and....	Colon with appendix	10^9 to 10^{12}

https://microbewiki.kenyon.edu/index.php/File:Intestinal_bacteria.jpg



Probiotics

- Live bacteria culture
- May survive acid and enzyme digestion to help seed gut flora in small numbers

e.g. yoghurt, sauerkraut, kimchi, miso

Probiotics
Live Microbes

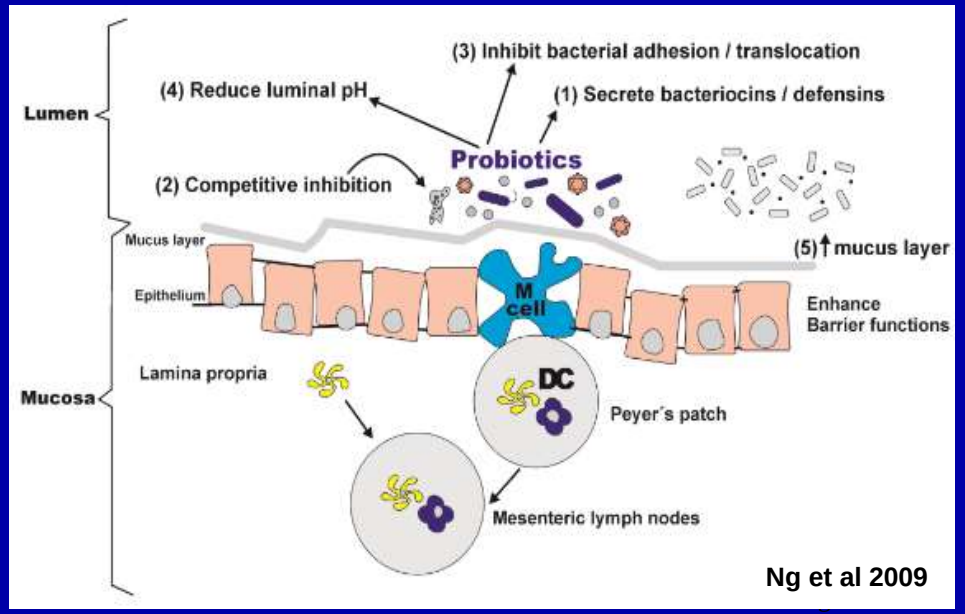
Same species have different strains and even these can all have different metabolic activities

- ***Lactobacillus*** **genus currently contains over 180 species**

- ***Lactobacillus, Bifidobacterium, Bacillus Enterococcus, E coli,*** **Lactococcus, *Streptococcus*, *Pediococcus*, yeast species and mixed cultures**

Ng et al 2009

Probiotic mechanisms on immune system are not completely clear. However, probiotics have immune-modulating effects



Ng et al 2009

Are Probiotics Always Safe?

EDITORIAL

Probiotics and obesity: a link?

Didier Raoult cautions that the use of probiotics as growth promoters in the farming industry means that further studies should be carried out before they are regarded as safe for use in humans.

Recent studies on the human gut microbiota have shown that obesity is associated with a reduction in Gram-negative bacteria, specifically members of the Bacteroidetes, and an increase in Gram-positive Firmicutes[1]. Additionally, it has been shown that the gut microbiota of obese individuals is less diverse than that of non-obese individuals[2]. The manipulation of the gut microbiota — through the administration of probiotics and antibiotics — has been used for

Functional foods, including fermented dairy products containing probiotics, are gaining popularity in many countries, among children in particular, but little research has been carried out on the connection between these products and weight gain. These food products are often sold under the guise of having positive effects on children's health, but there are little conclusive data to support these claims. Surprisingly, the

Didier Raoult Nature Reviews Microbiology 7, 616 (September 2009)

Prebiotics

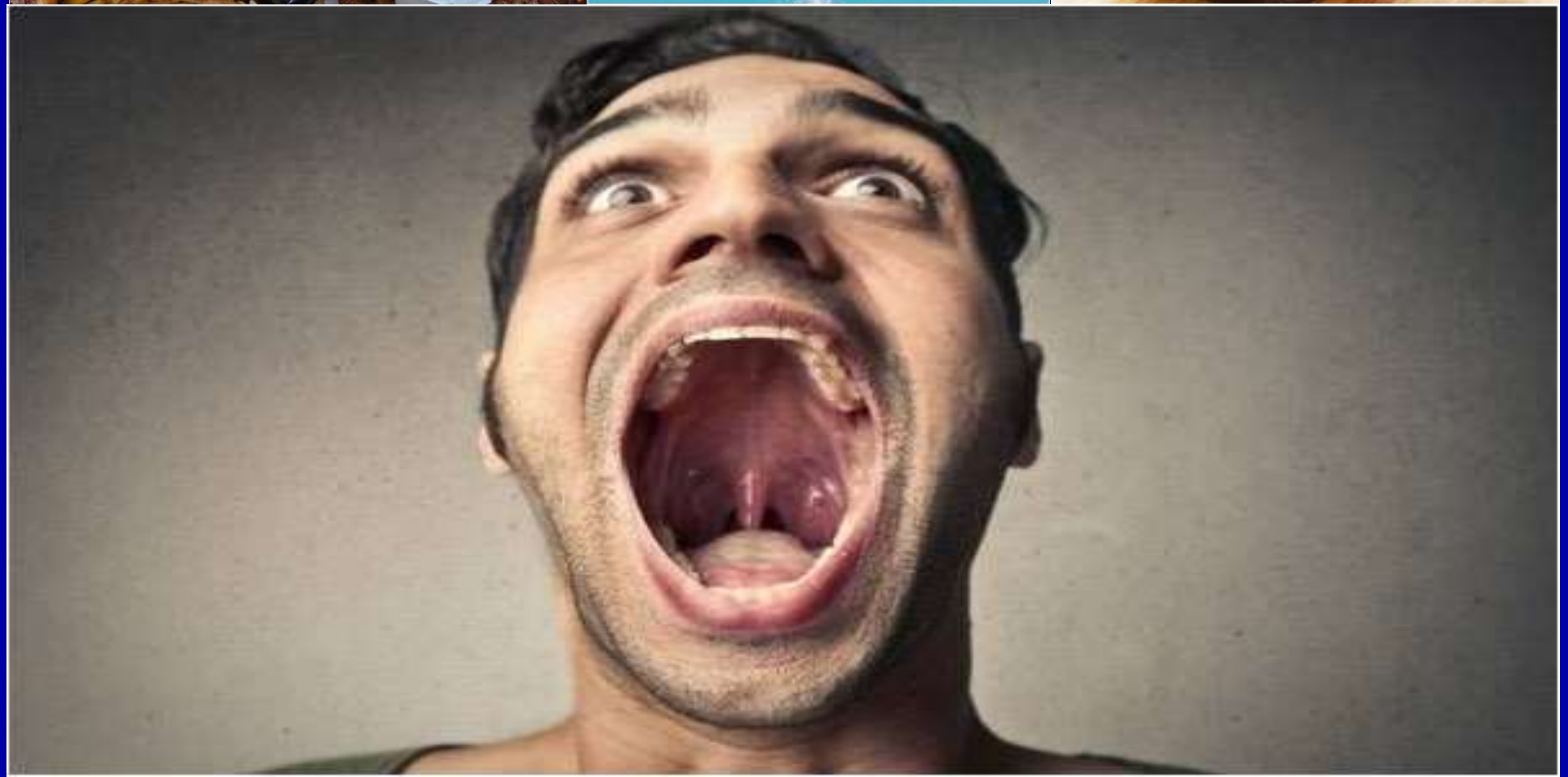
- Non living food for Gut Bacteria
- Substances that can only be metabolised by gut bacteria

not by acid, enzymes, etc

e.g. vegetables, fruit, grains, fibre
complex polysachharides

Classification	Origin/manufacturing procedure
Disaccharides	
Lactulose	Lactose synthetic
Lactitol	Lactose synthetic
Oligosaccharides	
Fructo-oligosaccharides	Legumes, vegetables, extracts/ hydrolysis of cereals
Soybean oligosaccharides	Extraction/hydrolysis of soy bean
Xylo-oligosaccharides	Plant sources
Trans galacto-oligosaccharides	Lactose synthetic
Polysaccharides	
Inulin	Extracts obtained from legumes, vegetables, and cereals
Resistant starches	Extracts obtained from legumes, vegetables, and cereals

Prebiotics



Making Foie Gras

Foie Gras Modern

Approach to probiotics by food and drug regulators:

GRAS

FOIE

G	Generally
R	Regarded
A	As
S	Safe

Changes Affecting Our Microbiota

Change	⇨	Consequence
• ↑ Clean water	⇨	↓ faecal transmission
• ↑ Caesarian sections	⇨	↓ vaginal transmission
• ↑ preterm antibiotic	⇨	↓ vaginal transmission
• ↓ breastfeeding	⇨	↓ skin transmission + altered immunology

Changes Affecting Our Microbiota

Change	⇨	Consequence
• ↓ family size	⇨	↓ Baby early life transmission
• ↑ antibiotic use	⇨	Changes our microbe composition
• ↑ bathing, shower antibacterial soaps	⇨	Changes our microbe composition

Ice Man

Disease		? Microbiome Mechanism
• Obesity	↔	↓ ratio Bacteroidetes to Firmicutes
• Childhood onset asthma	↔	Absence gastric *H. pylori*
• IBD	↔	↓ microbial diversity, antibiotics, modern diet

Disease

? Microbiome Mechanism

- Colorectal carcinoma ↔ Larger populations Fusobacterium sp
- Allergic disorders ↔ ↓ microbial diversity
- CVD ↔ *Gut- microbiota-dependent metabolism of phophatidylcholine*

Diseases with potential links to the gut microbiome
Khanna S,Tosh P (2014), Mayo Clin Proc 89(1), 107-114
CHO I, Blasér MJ (2012) Nat Rev Gen 13(4), 260-270

SCIENCE AND SOCIETY

Farm living: effects on childhood asthma and allergy

Erika von Mutius and Donata Vercelli

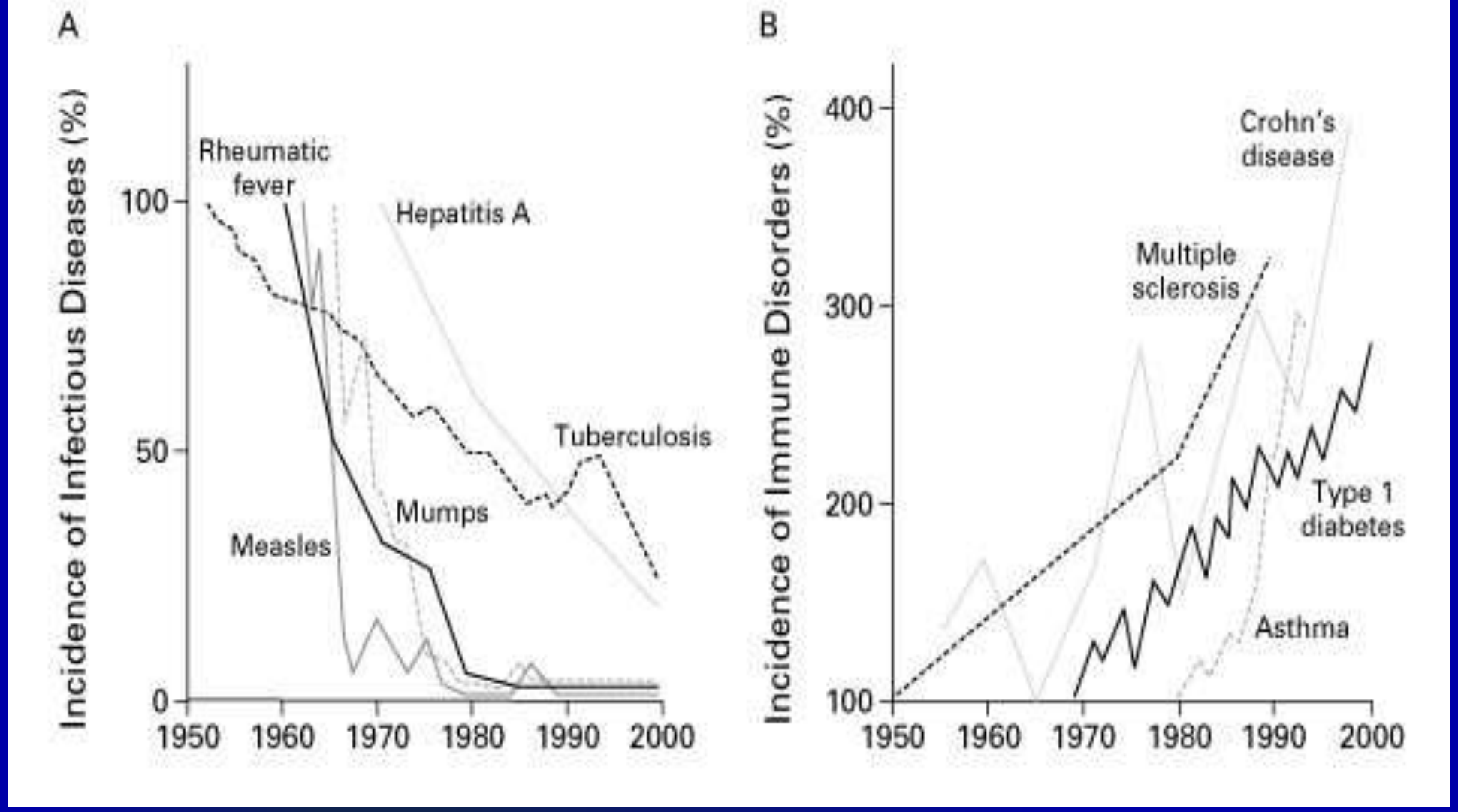
Abstract | Numerous epidemiological studies have shown that children who grow up on traditional farms are protected from asthma, hay fever and allergic sensitization. Early-life contact with livestock and their fodder, and consumption of unprocessed cow's milk have been identified as the most effective protective exposures. Studies of the immunobiology of farm living point to activation and modulation of innate and adaptive immune responses by intense microbial exposures and possibly xenogeneic signals delivered before or soon after birth.

Allergy-protective farm exposures

Several studies have identified some of the exposures associated with a farming lifestyle that contribute to the reduced risk of asthma and allergies in farm children, namely contact with livestock, mostly cattle, pigs and poultry; contact with animal feed such as hay, grain, straw and silage; and the consumption of unprocessed cow's milk[4,6–9]. These exposures had an independent protective farm effect, which indicates that inhalation and ingestion are the two main routes of exposure. Other differences in lifestyle, such as duration of breast feeding, family and sibship size, day care, pet ownership, other dietary habits, parental education and a family history of asthma and allergies, did not account for the pro-

Nature Reviews Immunology 10, 861-868 (December 2010) | doi:10.1038/nri287

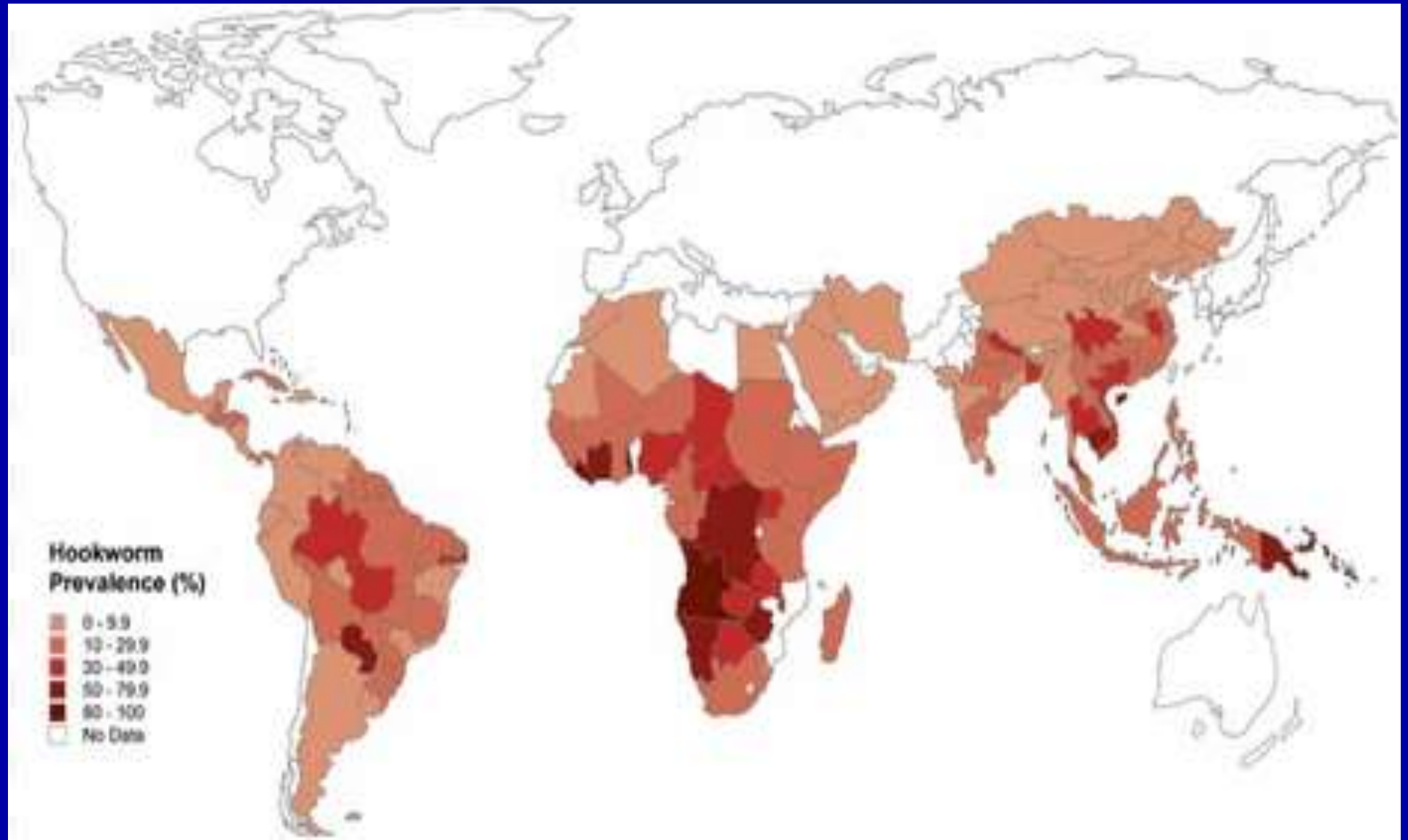
Inverse Relation Incidence (1950-2000)
Infectious Diseases ⬇ and Immune Disorders ⬆



Bach J. N Engl J Med 2002;347:911-920.

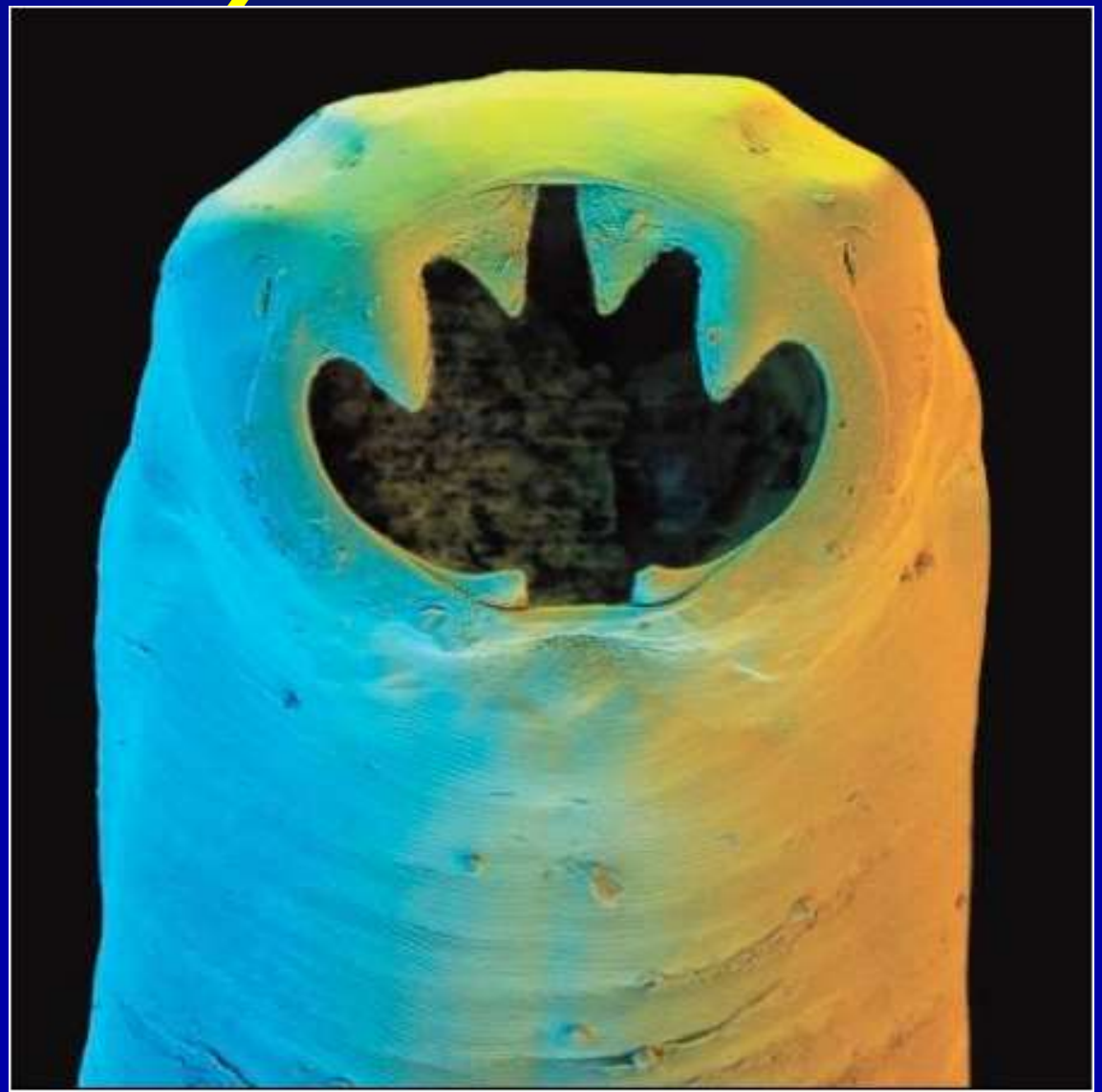
The NEW ENGLAND JOURNAL of MEDICINE

Hookworm Prevalence



Hookworm

'A Face Only a Mother Could Love' ?!



IBD & Number Antibiotic courses in children correlation

Gut 60, 49-54 :2011 A Hviid et al

Nature 25 August 2011 vol 76, p393

P. DUREUIL/PHOTOALTO/ALAMY

Dosed up: could excessive prescription of antibiotics be hampering children's ability to fight disease?

Stop the killing of beneficial bacteria

Imagine a World Without Antibiotics

- You know how you are FEELING better than anyone else
- Your medical practitioner knows what the CAUSE is, bacterial, viral or other and what to treat you with better than anyone else.

Listen, do not ask for or demand antibiotics – they may well cause you and others significant harm

Illness	Usual Cause		Antibiotic Needed
	Viruses	Bacteria	
Cold/Runny Nose	✓		NO
Bronchitis/Chest Cold (in otherwise healthy children and adults)	✓		NO
Whooping Cough		✓	Yes
Flu	✓		NO
Strep Throat		✓	Yes
Sore Throat (except strep)	✓		NO
Fluid in the Middle Ear (otitis media with effusion)	✓		NO
Urinary Tract Infection		✓	Yes

http://www.cdc.gov/getsmart/community/for-patients/common-illnesses/

NZ Antibiotic Use 2012

Assoc Prof Mark Thomas, University of Auckland

Annually:

- **180 AB courses per 100 children <5y !!!!**
- **60 AB courses per 100 25-29yrs old**

the lowest prescribing rate age group! !

Antibiotics

‘the biggest impact on post industrial medicine’

Public Health

sanitation, sewage, clean water, vaccinations

Antibiotics

the biggest impact on post industrial medicine

Public Health sanitation, sewage, water
vaccinations

⬇ ⬇

Our Microbiome

diet, environment, pre/probiotics
genes, immunity, metabolism

⬆ ⬆ ⬆

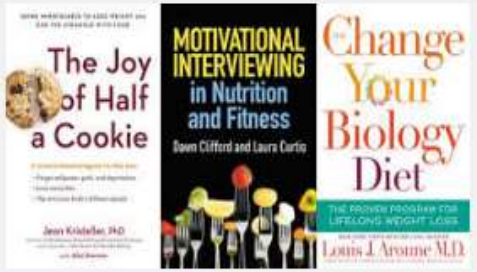
Antibiotics

the biggest impact on post
industrial medicine

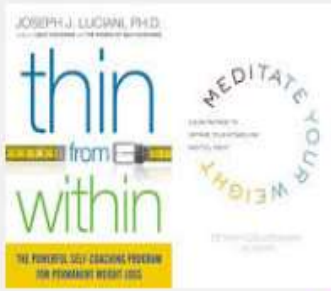

Deliciously Ella
LEAN IN 15
JOE WICKS


Burn off the winter carbs
FROM £4.99
SKINNY SOUPS
LEAN IN 15
JOE WICKS
SIMPLICIOUS
SARAH WILSON
SHOP NOW ›


Always Hungry?
David Ludwig, MD, PhD
First Bite
DR. JOSH AXE
eat dirt

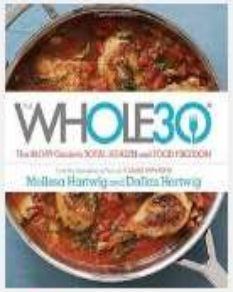

The Joy of Half a Cookie
MOTIVATIONAL INTERVIEWING in Nutrition and Fitness
Dawn Clifford and Laura Curtis
Change Your Biology Diet
THE PROVEN PROGRAM FOR LIFELONG WEIGHT LOSS
Louis J. Aronne M.D.

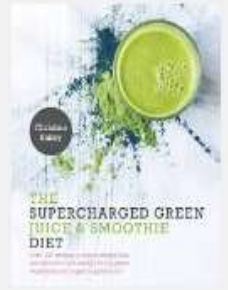

Bulletproof Diet
nom nom paleo
FOOD FOR HUMANS
DASH DIET Action Plan
WHOLE30

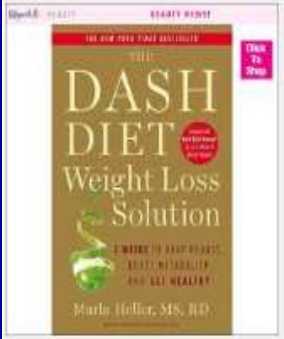

JOSEPH J. LUCIANI, PH.D.
thin from within
THE POWERFUL SELF-COACHING PROGRAM FOR PERMANENT WEIGHT LOSS

MEDITATE YOUR WEIGHT


HOW BAD DO YOU WANT IT?
MIND OVER MUNCH
MATT FITZGERALD

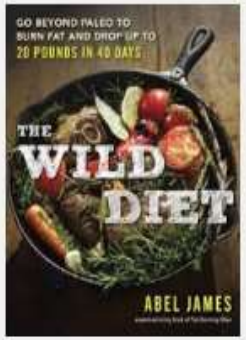

WHOLE30
Melissa Hartwig and Dallas Hartwig

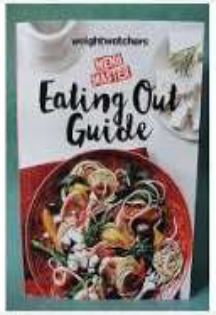

THE SUPERCHARGED GREEN JUICE & SMOOTHIE DIET

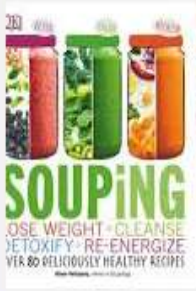

DASH DIET
Weight Loss Solution
Marla Heller, MS, RD


The TACO CLEANSE
THE TORTILLA-BASED DIET PROVEN TO CHANGE YOUR LIFE
WITH OVER 75 VEGAN RECIPES


FULLY RAW DIET


GO BEYOND PALEO TO BURN FAT AND DROP UP TO 20 POUNDS IN 40 DAYS
THE WILD DIET
ABEL JAMES


weightwatchers
Eating Out Guide


SOUPiNG
LOSE WEIGHT • CLEANSE
DETOXIFY • RE-ENERGIZE
OVER 80 DELICIOUSLY HEALTHY RECIPES


THE SOUP CLEANSE
SOUPELINA'S SOUP CLEANSE


Always Hungry?
David Ludwig, MD, PhD


The KetoDiet Cookbook


RECIPES FOR ALL THE FOOD YOU WANT TO EAT
Cravings


PALEOBETIC DIET
DEFEAT


LOSE WEIGHT AND LIVE LONGER
THE 8-WEEK


#1 New York Times Bestselling Author

Merde

Excursions into Scientific, Cultural and Socio-Historical Coprology

RALPH A. LEWIN

MORE ON MERDE

BY RALPH A LEWIN published 1999

"Think of yourself as a sausage machine"

merde

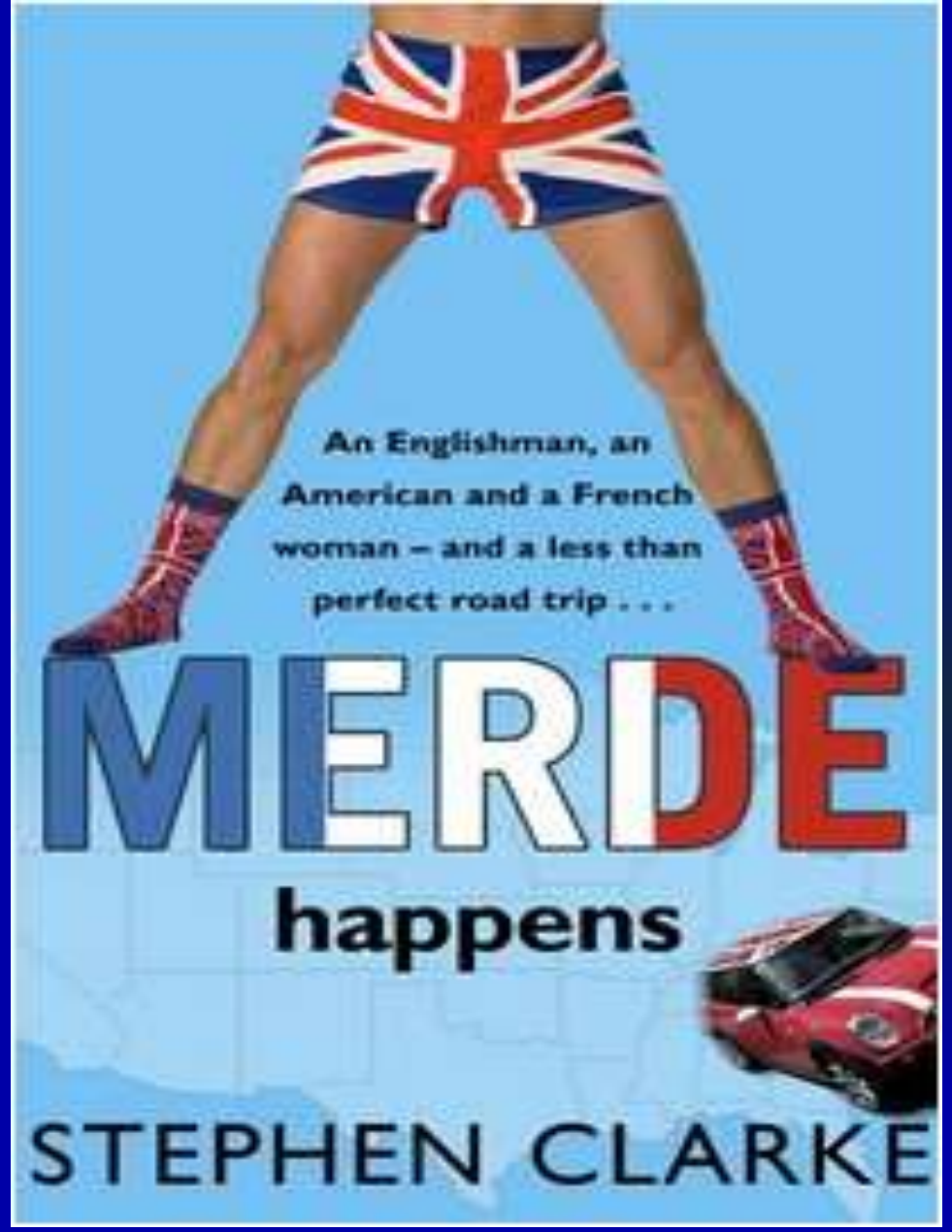
/mɛ:d,French mɛʀd/

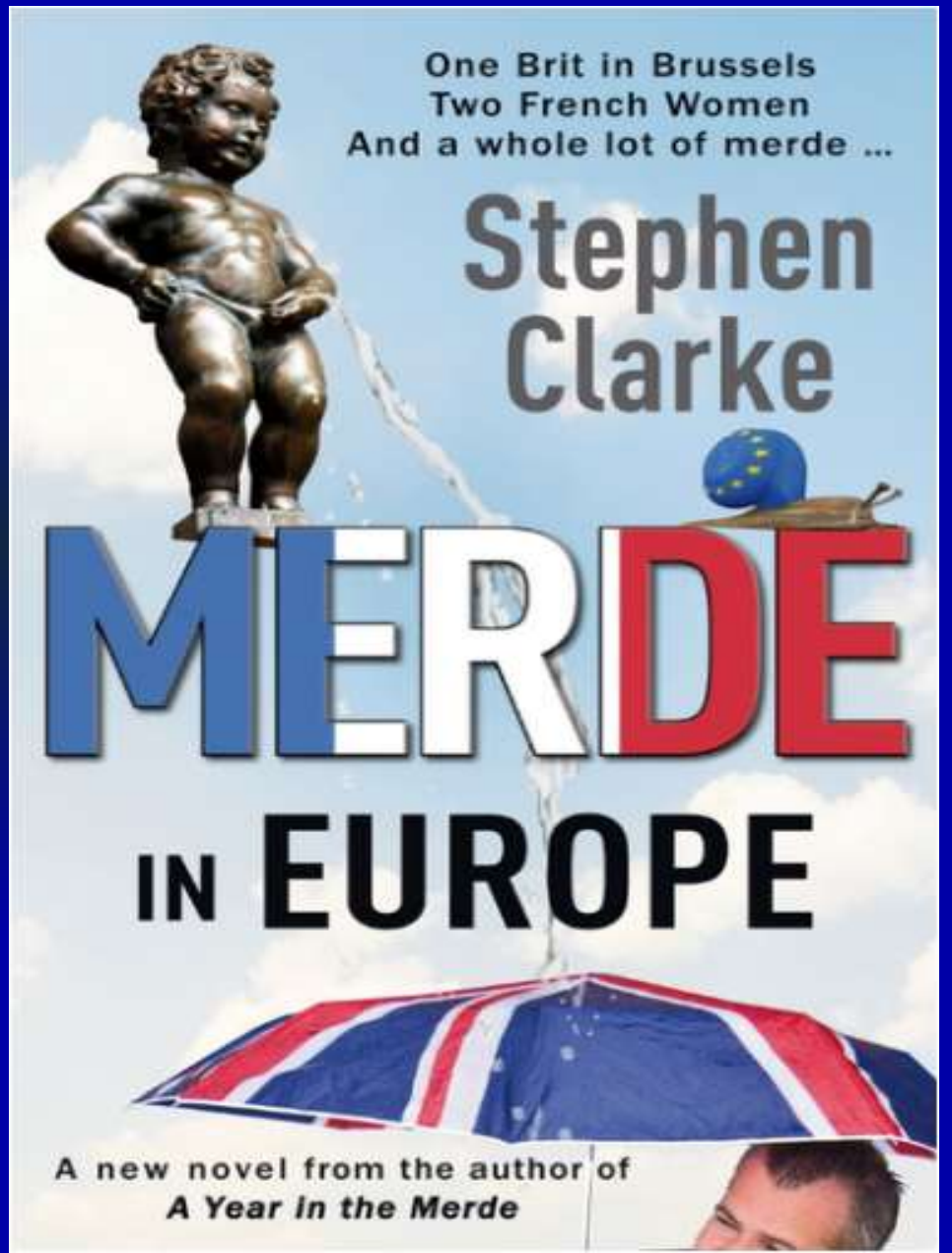
exclamation

used as a mild, generally humorous substitute for 'shit'
"Merde! What had she done!"

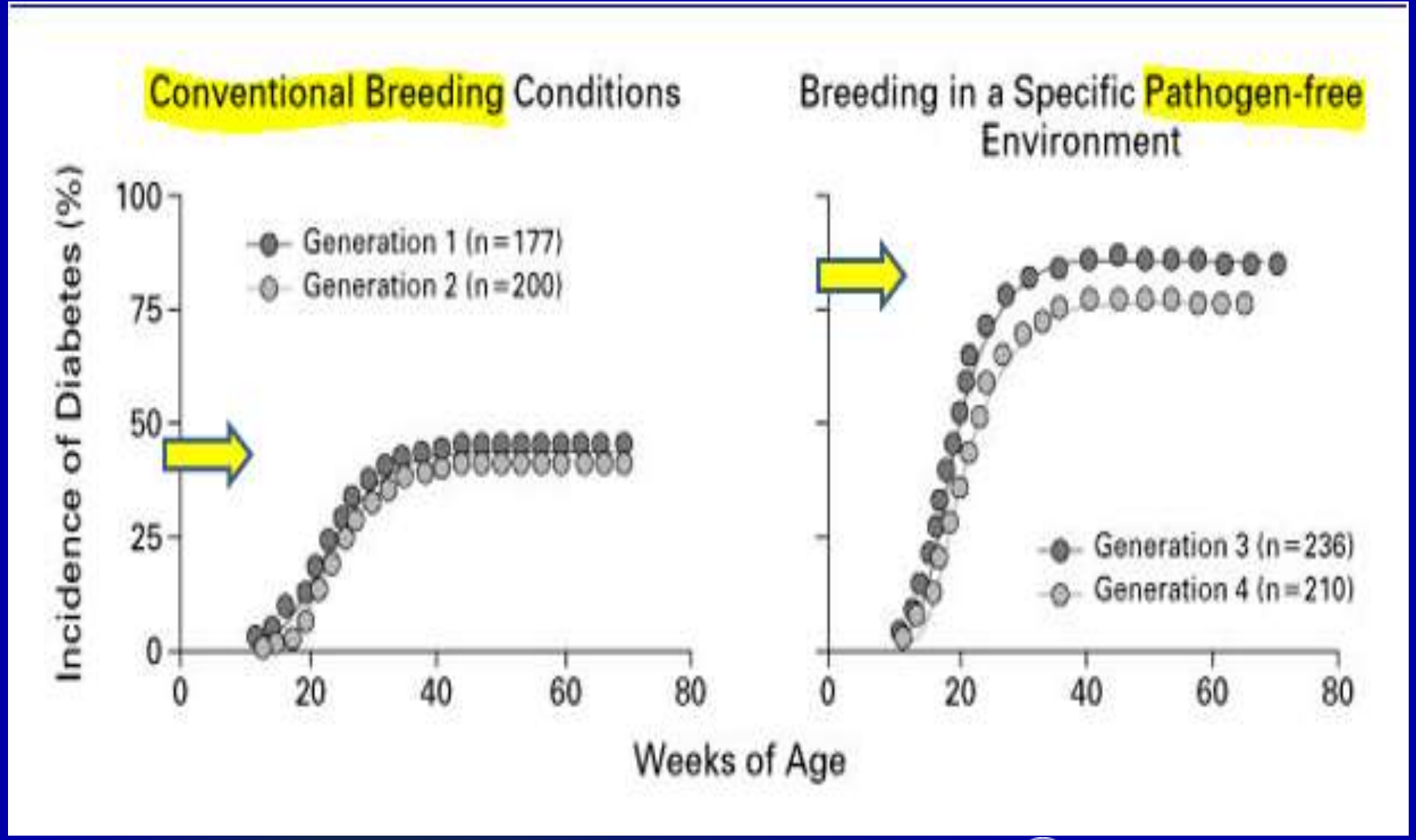
Origin and Etymology of MERDE

French, from Old French, from Latin *merda;* perhaps akin to Lithuanian *smirdėti* to stink


An Englishman, an American and a French woman – and a less than perfect road trip . . .
MERDE
happens
STEPHEN CLARKE


One Brit in Brussels
Two French Women
And a whole lot of merde ...
Stephen Clarke
MERDE
IN EUROPE
A new novel from the author of
A Year in the Merde

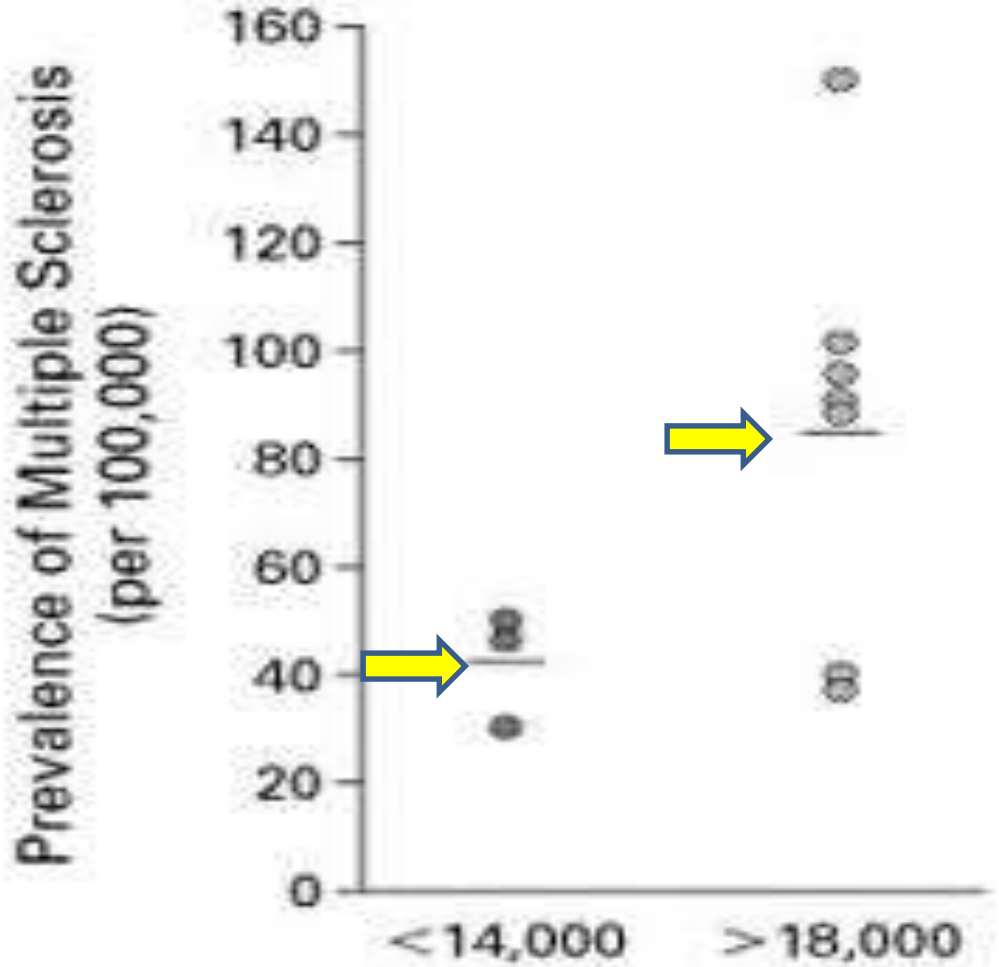
Infections Effect on Diabetes in Mice
Conventional vs Pathogen Free Breeding



Bach J. N Engl J Med 2002;347:911-920.

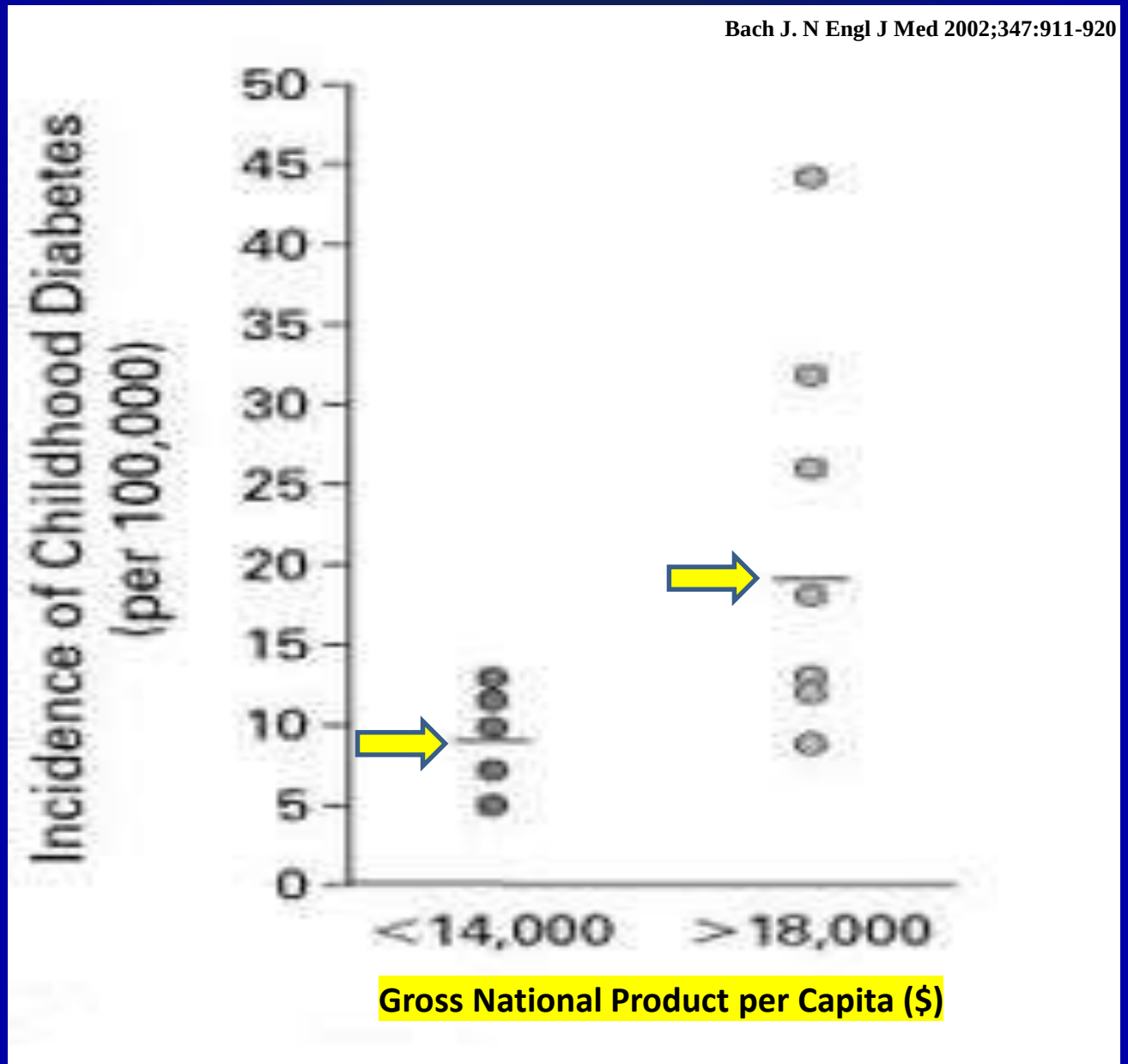
Multiple Sclerosis Frequency
12 EU Countries and GNP per Capita

Bach J. N Engl J Med 2002;347:911-920

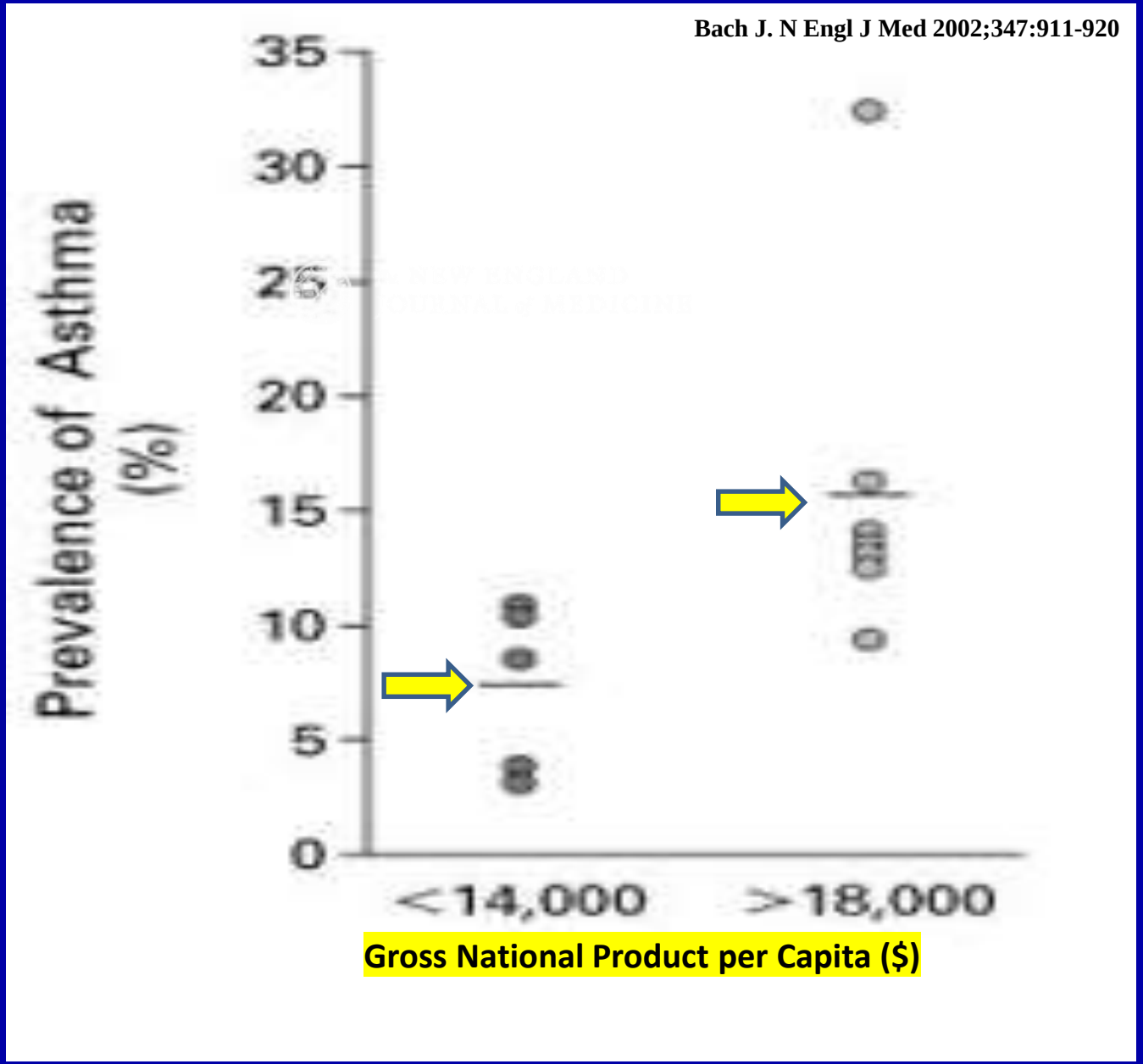


Type 1 Diabetes Mellitus Frequency
12 EU Countries and GNP per Capita

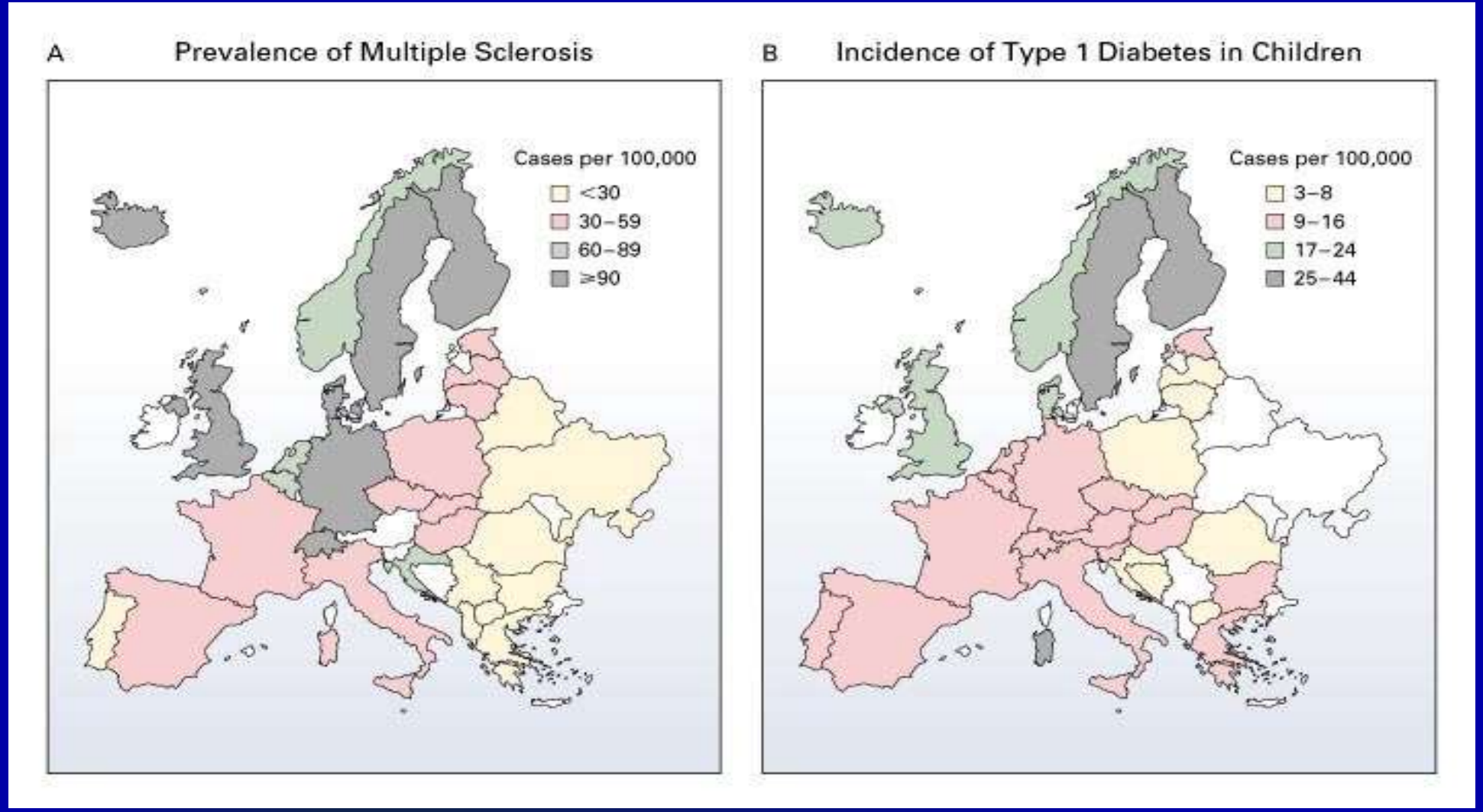
Bach J. N Engl J Med 2002;347:911-920



Asthma Frequency
12 EU Countries According to GNP per Capita



North South Gradient
Multiple Sclerosis and Type 1 Diabetes



Bach J. N Engl J Med 2002;347:911-920.

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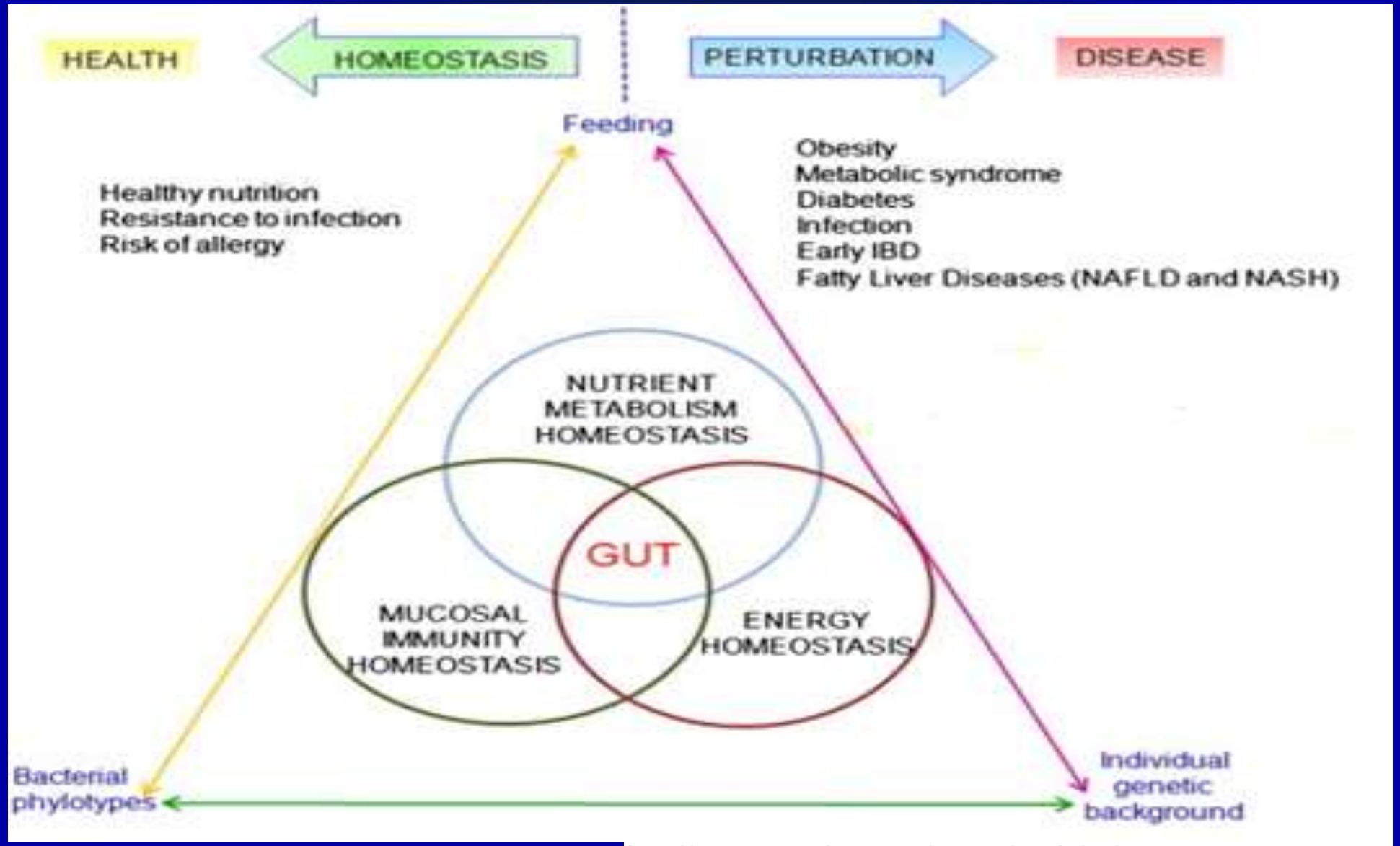
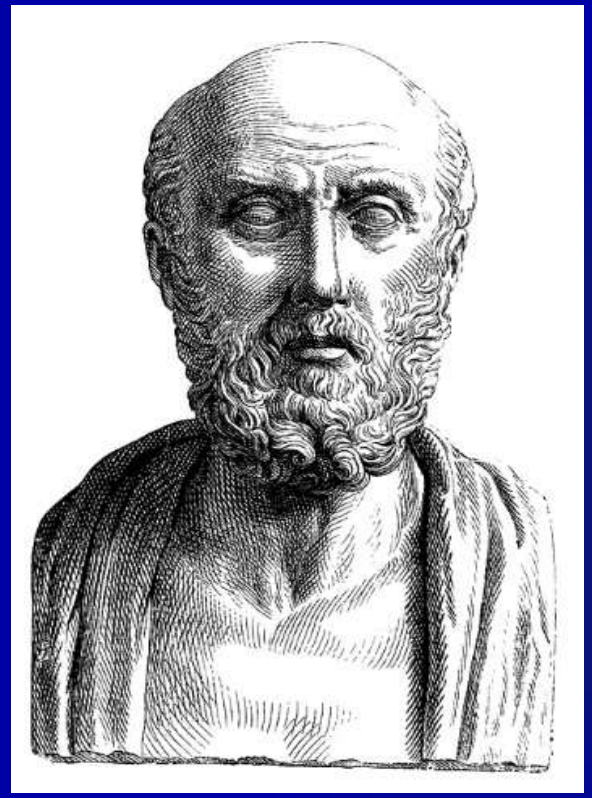
Gut Homeostatsis vs Perturbation Balance

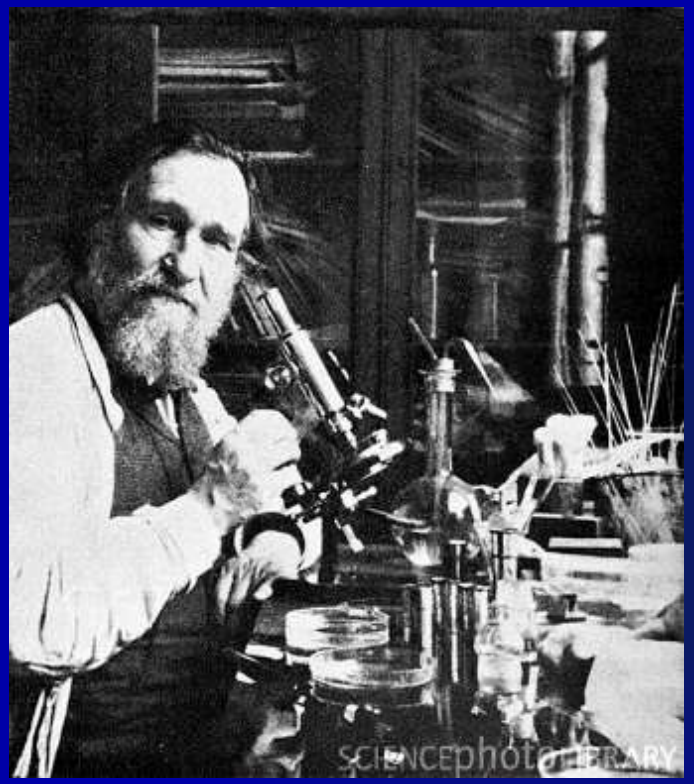


http://www.sciencedirect.com/science/article/pii/S1874391912001029?np=y



Hippocrates

Let food be thy medicine and medicine be thy food



Elie Metchnikoff, 1907
Nobel recipient

The dependence of the intestinal microbes on the food makes it possible to adopt measures to modify the flora in our bodies and to replace the harmful microbes by useful microbes

The protective effect of farm milk consumption on childhood asthma and atopy: The GABRIELA study

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Background: Farm milk consumption has been identified as an exposure that might contribute to the protective effect of farm life on childhood asthma and allergies. The mechanism of action and the role of particular constituents of farm milk, however, are not yet clear.

Objective: We sought to investigate the farm milk effect and determine responsible milk constituents.

Methods: In rural regions of Germany, Austria, and Switzerland, a comprehensive questionnaire about farm milk consumption and other farm-related exposures was completed by parents of 8334 school-aged children, and 7606 of them provided serum samples to assess specific IgE levels. In 800 cow's milk samples collected at the participants' homes, viable bacterial counts, whey protein levels, and total fat content were analyzed. Asthma, atopy, and hay fever were associated to reported milk consumption and for the first time to objectively measured milk constituents by using multiple regression analyses.

Results: Reported raw milk consumption was inversely associated to asthma (adjusted odds ratio [aOR], 0.59; 95% CI, 0.46-0.74), atopy (aOR, 0.74; 95% CI, 0.61-0.90), and hay fever (aOR, 0.51; 95% CI, 0.37-0.69) independent of other farm exposures. Boiled farm milk did not show a protective effect. Total viable bacterial counts and total fat content of milk were not significantly related to asthma or atopy. Increased levels of the whey proteins BSA (aOR for highest vs lowest levels and asthma, 0.53; 95% CI, 0.30-0.97), α-lactalbumin (aOR for interquartile range and asthma, 0.71; 95% CI, 0.52-0.97), and β-lactoglobulin (aOR for interquartile range and asthma, 0.62; 95% CI, 0.39-0.97), however, were inversely associated with asthma but not with atopy.

Conclusions: The findings suggest that the protective effect of raw milk consumption on asthma might be associated with the whey protein fraction of milk. (J Allergy Clin Immunol 2011;128:766-73.)

Key words: *Allergic diseases, asthma, atopy, children, farming, hay fever, microorganism, farm milk, risk, whey protein*

RANDOMISED CONTROLLED TRIAL OF EFFECT OF RAW AND HOLDER PASTEURISED HUMAN MILK AND OF FORMULA SUPPLEMENTS ON INCIDENCE OF NEONATAL INFECTION

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N. S. MURTHY
K. PRAKASH
V. V. GUJRAL

Kalawati Saran Children's Hospital and Department of Microbiology, Lady Hardinge Medical College, and Indian Council of Medical Research, New Delhi, India

Summary Supplementary formula feeds inhibited the protective effect of expressed raw and pasteurised human milk in 226 high-risk neonates in a randomised controlled trial. The infection rate in the group given pasteurised human milk and formula (33%) was significantly higher than the rates in the groups given raw human milk (10·5%), pasteurised human milk (14·3%), and raw human milk and formula (16%). This accords with the impressions that some of the association of infection with artificial feeding is partly attributable to the lack of the protective effect of human milk. Heating expressed human milk to 62·5°C for 30 min significantly reduces its protective effect.

The Lancet · Saturday 17 November 1984

CLINICAL REVIEWS IN ALLERGY AND IMMUNOLOGY

Series editors: Donald Y. M. Leung, MD, PhD, and Dennis K. Ledford, MD

The gut microbiota and inflammatory noncommunicable diseases: Associations and potentials for gut microbiota therapies

Christina E. West, MD, et al

Ume0a and Linko€ping, Sweden, Marburg, Germany, Edmonton, Alberta, Canada, Melbourne, Geelong, Perth, Clayton, and Sydney, Australia, Turku, Finland, Hong Kong, China, Copenhagen, Denmark, Tokyo, Japan, and Nice, France

(J Allergy Clin Immunol 2015;135:3-13.)

JLB

Editorial

Editorial: Celiac disease and intestinal bacteria: not only gluten?

Mauro Rossi[1] *and Kathryne B. Schwartz*

Institute of Food Sciences, NRC, Avellino, Italy

RECEIVED DECEMBER 5, 2009; REVISED DECEMBER 30, 2009; ACCEPTED DECEMBER 31, 2009. DOI: 10.1189/jlb.1209784

▶ SEE CORRESPONDING ARTICLE ON PAGE 765

CD is a widespread, immune-mediated food intolerance to gluten that exhibits autoimmune

ated innate-immune response involves activation of IEL with an induction of the nonclassical class I molecule MICA

people on a gluten-free diet, and counts for *Enterobacteriaceae* and *Escherichia coli* were increased [5].

ORIGINAL ARTICLE

Alterations in Diversity of the Oral Microbiome in Pediatric Inflammatory Bowel Disease

Michael J. Docktor, MD, Bruce J. Paster, PhD,[†,‡] Shelly Abramowicz, DMD, MPH,[§,‖] Jay Ingram, BS,* Yaoyu E. Wang, PhD,[¶] Mick Correll, BS,[¶] Hongyu Jiang, PhD,** Sean L. Cotton, BS,[†] Alexis S. Kokaras, BS,[†] and Athos Bousvaros, MD, MPH**

Autoimmunity Reviews 14 (2015) 269–276

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Behçet's syndrome patients exhibit specific microbiome signature

Clarissa Consolandi [a,*,1], Silvia Turroni [b,1], Giacomo Emmi [c,1], Marco Severgnini [a], Jessica Fiori [b], Clelia Peano [a], Elena Biagi [b], Alessia Grassi [c], Simone Rampelli [b], Elena Silvestri [c], Manuela Centanni [b], Fabio Cianchi [e], Roberto Gotti [b], Lorenzo Emmi [d,**], Patrizia Brigidi [b], Nicola Bizzaro [f], Gianluca De Bellis [a], Domenico Prisco [c,d], Marco Candela [b], Mario M. D'Elios [c,d]

Curr Stem Cell Rep (2015) 1:53 59
DOI 10.1007/s40778 014 0006 9

MICROBIOME AND STEM CELL FUNCTION (KE NELSON AND MB JONES, SECTION EDITORS)

The Microbiome and Allogeneic Stem Cell Transplantation

Daniela Sporrer · Andre Gessner · Thomas Hehlgans ·
Peter J. Oefner · Ernst Holler

Less diversity associated with Graft versus Host disease

Our Actions Now Are Our Future


Rx
PATIENT NAME
ADDRESS
Prescription:
Date
Signature


A NIVERS

Just the Very Beginning

The Economist

The Catholic church's unholy mess

Paul Ryan: the man with the plan

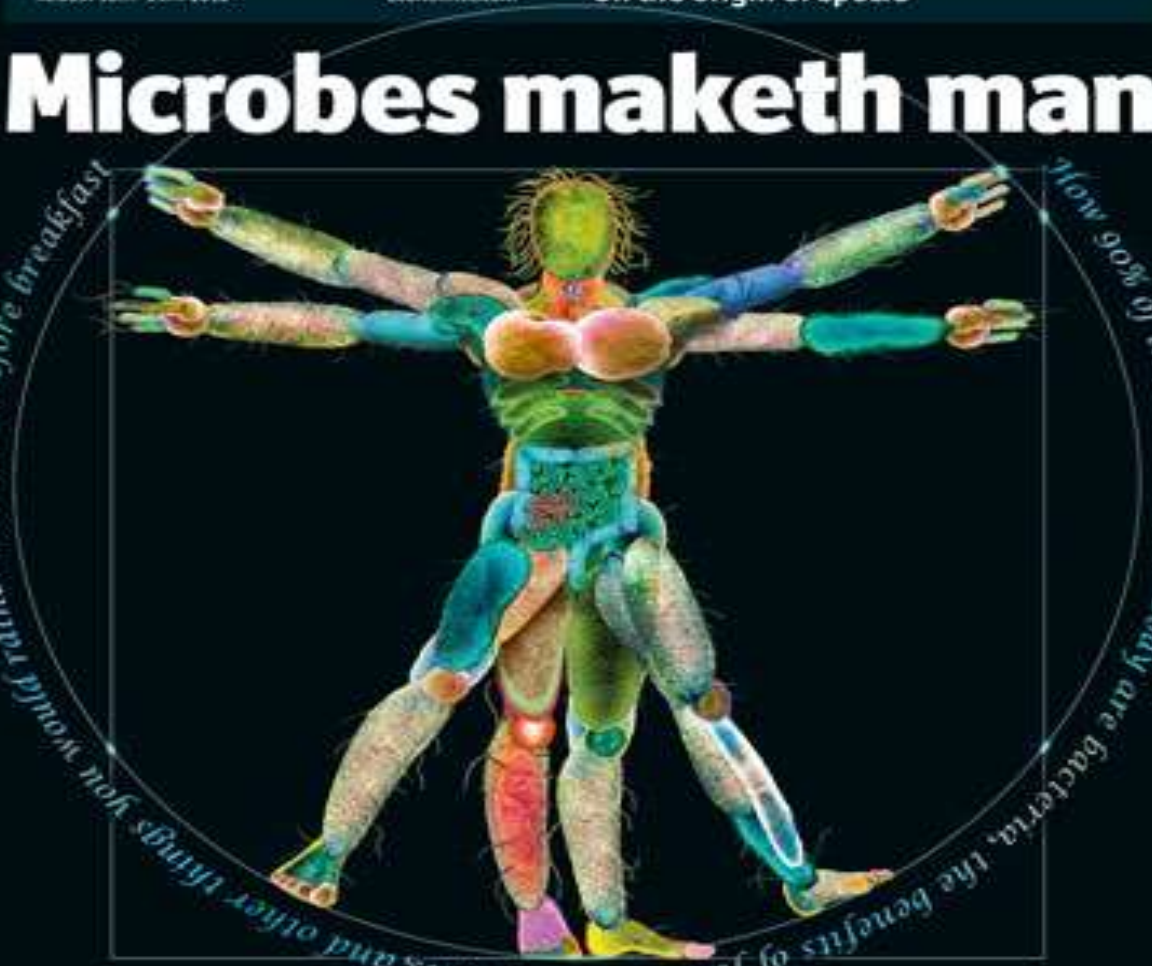
Generation Xhausted

China, victim of the Olympics?

On the origin of specie

AUGUST 18TH–24TH 2012 Economist.com

Microbes maketh man



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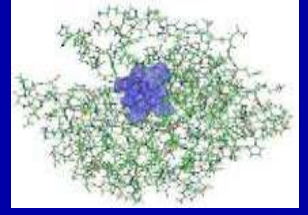
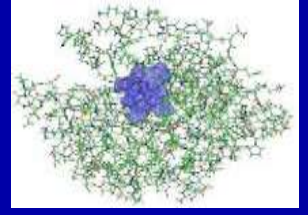


Thoughts to Ponder (1)

- **Does human Host cell hormonal communication interact with Bacterial quorum sensing??**

- **Quorum sensing bacterial communication could we ever learn to be as sociable?**

- **<u>Life did not take over the globe by combat but by networking and cooperation</u>**



Thoughts to Ponder (2)

- We are highly complex ‘super-organisms’
- 90% of cells in our body are not human
- Our bacteria contribute so much
  where does our body end & the microbes begin??

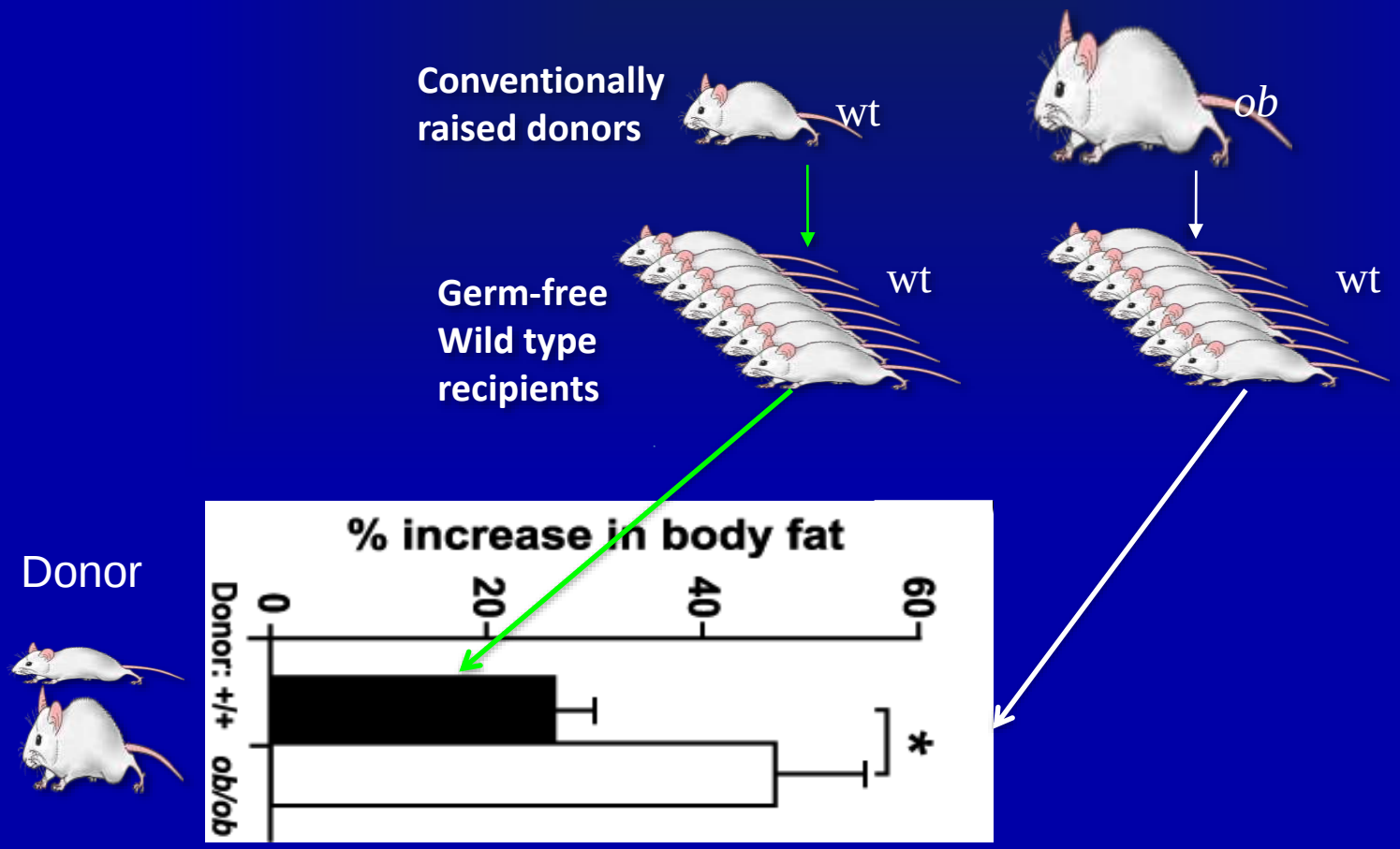
Effect of probiotics on central nervous system functions in animals and humans - a systematic review

These probiotics showed efficacy in improving psychiatric disorder-related behaviors including anxiety, depression, autism spectrum disorder (ASD), obsessive-compulsive disorder, and memory abilities, including spatial and non-spatial memory.

Because many of the basic science studies showed some efficacy of probiotics on central nervous system function, this background may guide and promote further preclinical and clinical studies. ... According to the qualitative analyses of current studies, we can provisionally draw the conclusion that B. longum, B. breve, B. infantis, L. helveticus, L. rhamnosus, L. plantarum, and L. casei were most effective in improving CNS function, including psychiatric disease-associated functions (anxiety, depression, mood, stress response) and memory abilities

Wang H, Lee IS, Braun C, Enck P (July 2016 *J. Neurogastroenterol Motil*. doi:10.5056/jnm16018.PMID 27413138.

Faecal Transplantation



Turnbaugh *et al*., Nature 444: 1027-1031

Implications for prevention and treatment of disease

- Avoid disruption by antibiotics
- Faecal transplant
- “Probiotics”
- “Prebiotics”
  - Dietary modification
- “Probiomics”
  - Helminthic therapy

Lyn Jolly, helminth-therapy pioneer, is treating her autoimmune disorder with live parasites.
CHRIS MCKEEN / FAIRFAX NZ

There's a colony of hookworms living inside Lyn Jolly – and she says they're the best thing that's ever happened to her.

Worms tried

- *Trichuris trichiura*
- *Trichuris suis*
- *Hymenolepis diminiuta*
- *Necator americanus*
- *Ancylostoma duodenale*

WormTherapy

Helminth Induced Immune Modulation

FOR MORE INFO (888) 898-WORM 9676

HOME | PRODUCTS | THEORY | FAQ | FORUMS | CONTACT

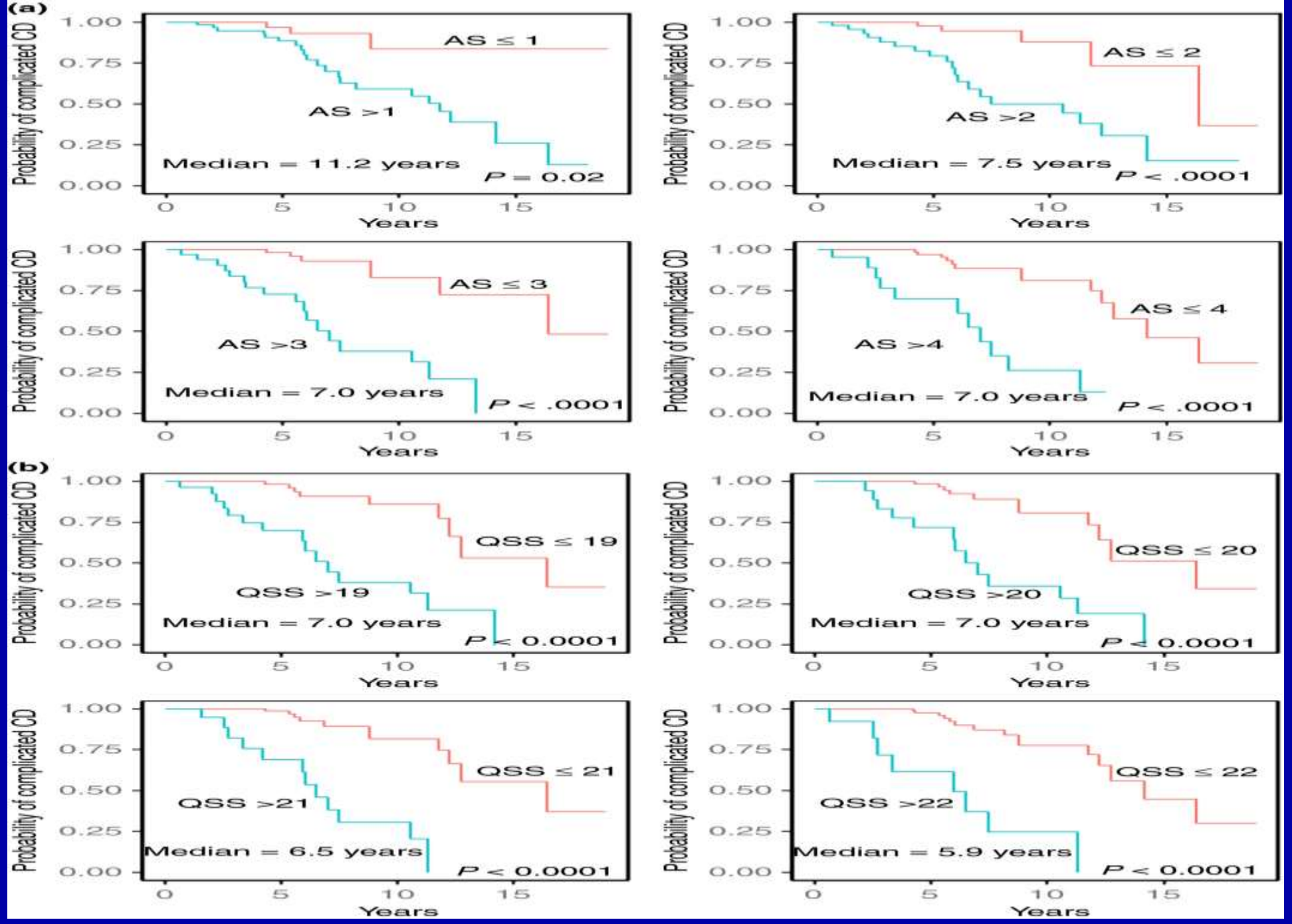
Treatments Available:

Hookworm

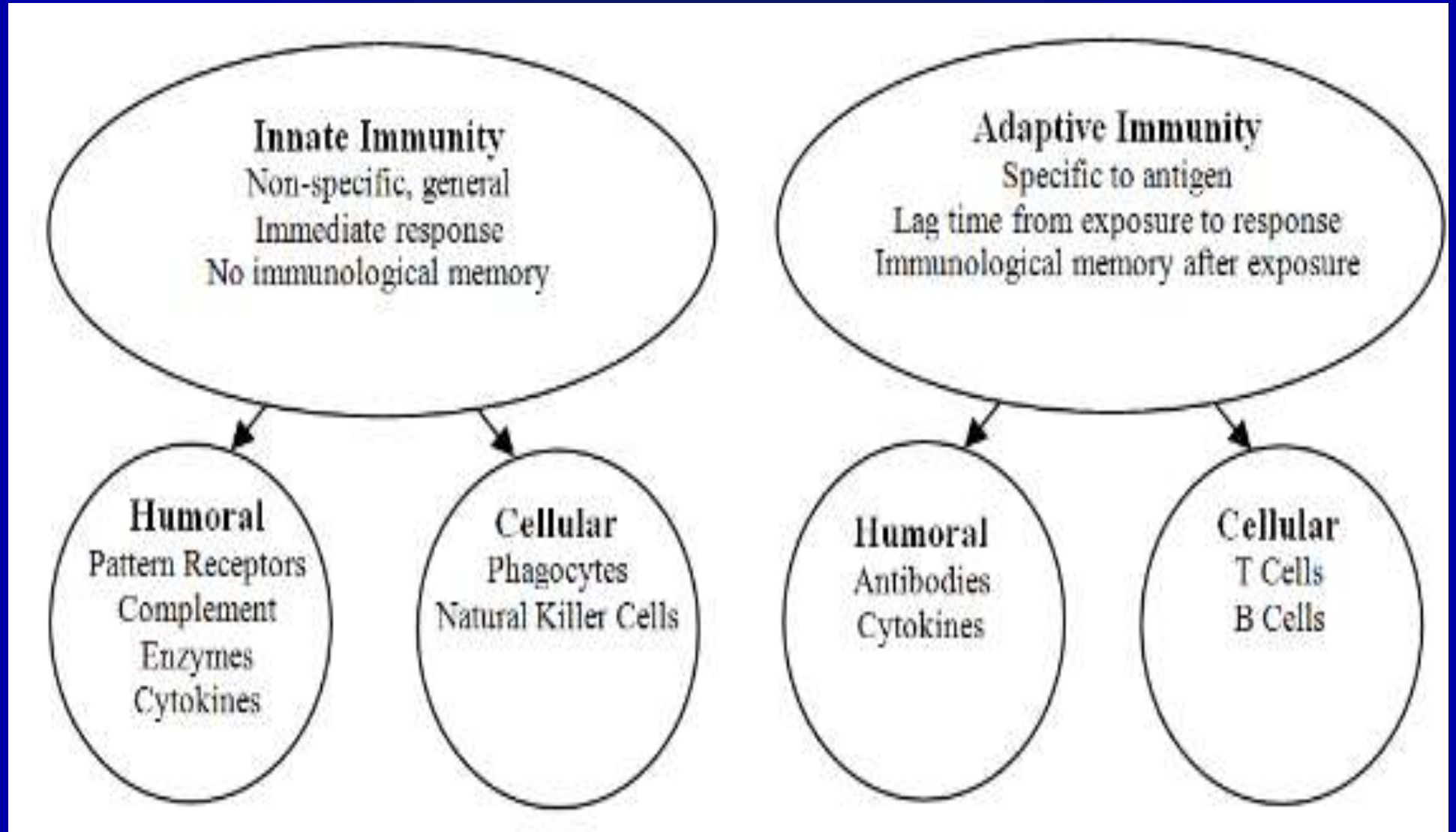
Whipworm

Combination Therapy

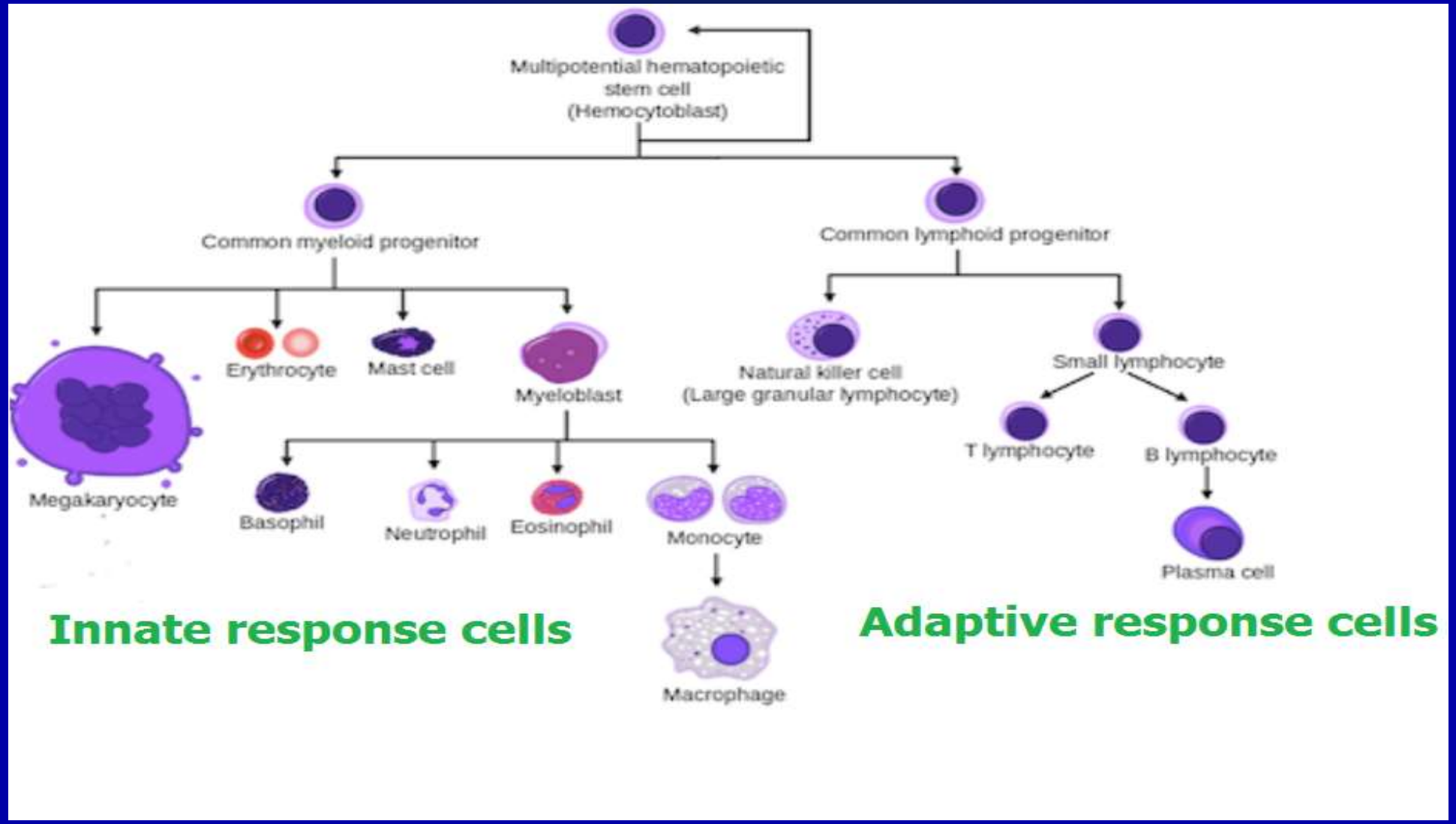
wormtherapy.com


(a)
Probability of complicated CD
1.00
0.75
0.50
0.25
0.00
0
5
10
15
Years
AS ≤ 1
AS >1
Median = 11.2 years
P = 0.02
AS ≤ 2
AS >2
Median = 7.5 years
P < .0001
AS ≤ 3
AS >3
Median = 7.0 years
P < .0001
AS ≤ 4
AS >4
Median = 7.0 years
P < .0001
(b)
QSS ≤ 19
QSS >19
Median = 7.0 years
P < 0.0001
QSS ≤ 20
QSS >20
Median = 7.0 years
P < 0.0001
QSS ≤ 21
QSS >21
Median = 6.5 years
P < 0.0001
QSS ≤ 22
QSS >22
Median = 5.9 years
P < 0.0001

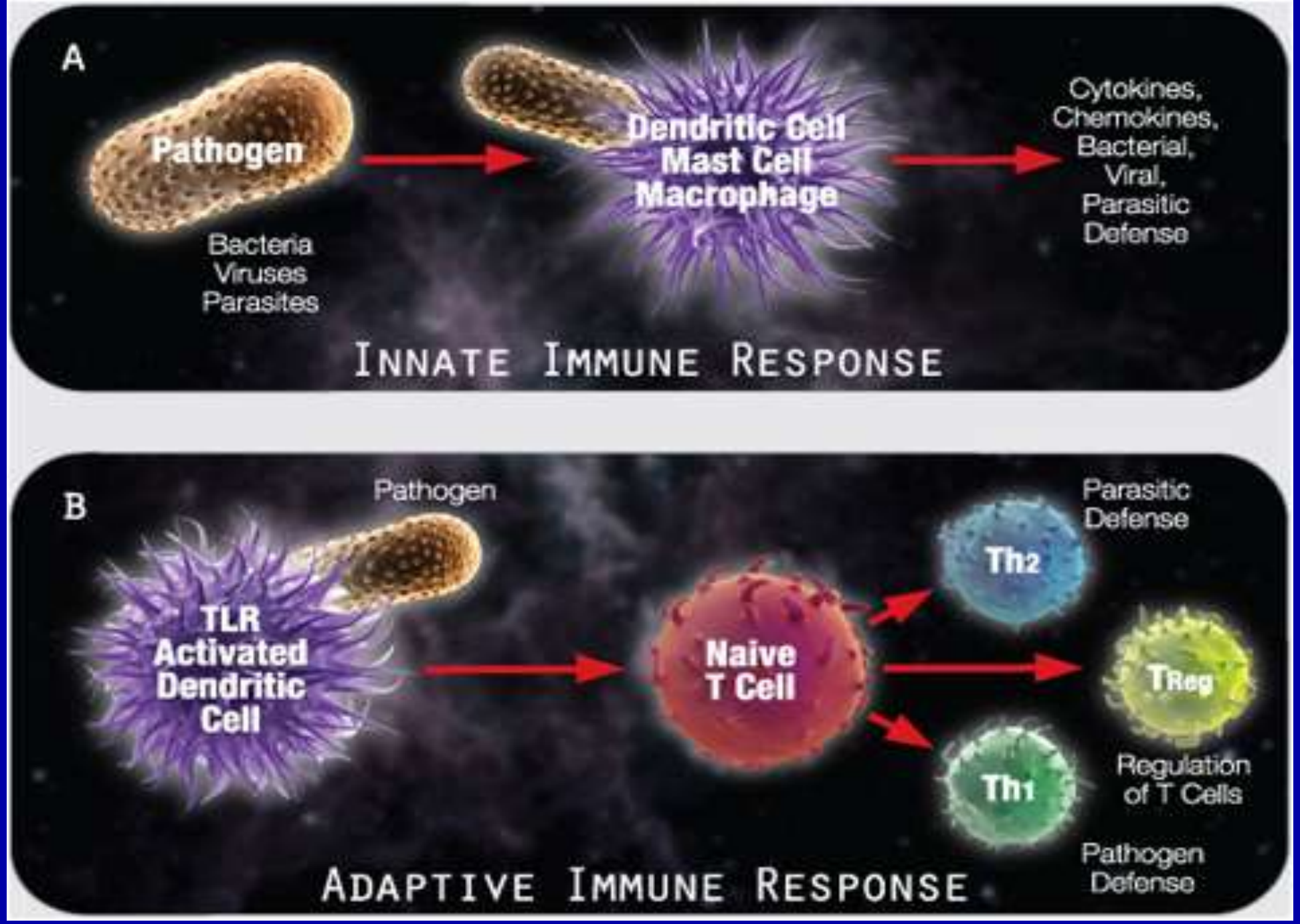
Our Immune System



Innate vs Adaptive Cell Immunity



www.khanacademy.org/test-prep/mcat/biological-sciences-practice/biological-sciences-practice-tut/e/innate-vs-adaptive-immunity



http://www.sabiosciences.com/pathwaymagazine/pathways7/toll-like-receptors-and-innate-immunity.php

The Gut Microbiome Affects Obesity

Humans & mice have different gut flora but the two largest microbial groupings are shared in common:

1. Bacteroidetes - Gram negatives
2. Firmicutes - Gram positives

These Groupings change in response to diet, obesity and genetics

Presence in Raw Cow's Milk of a Bactericidal Substance Specific for Certain Strains of Coliform Organisms

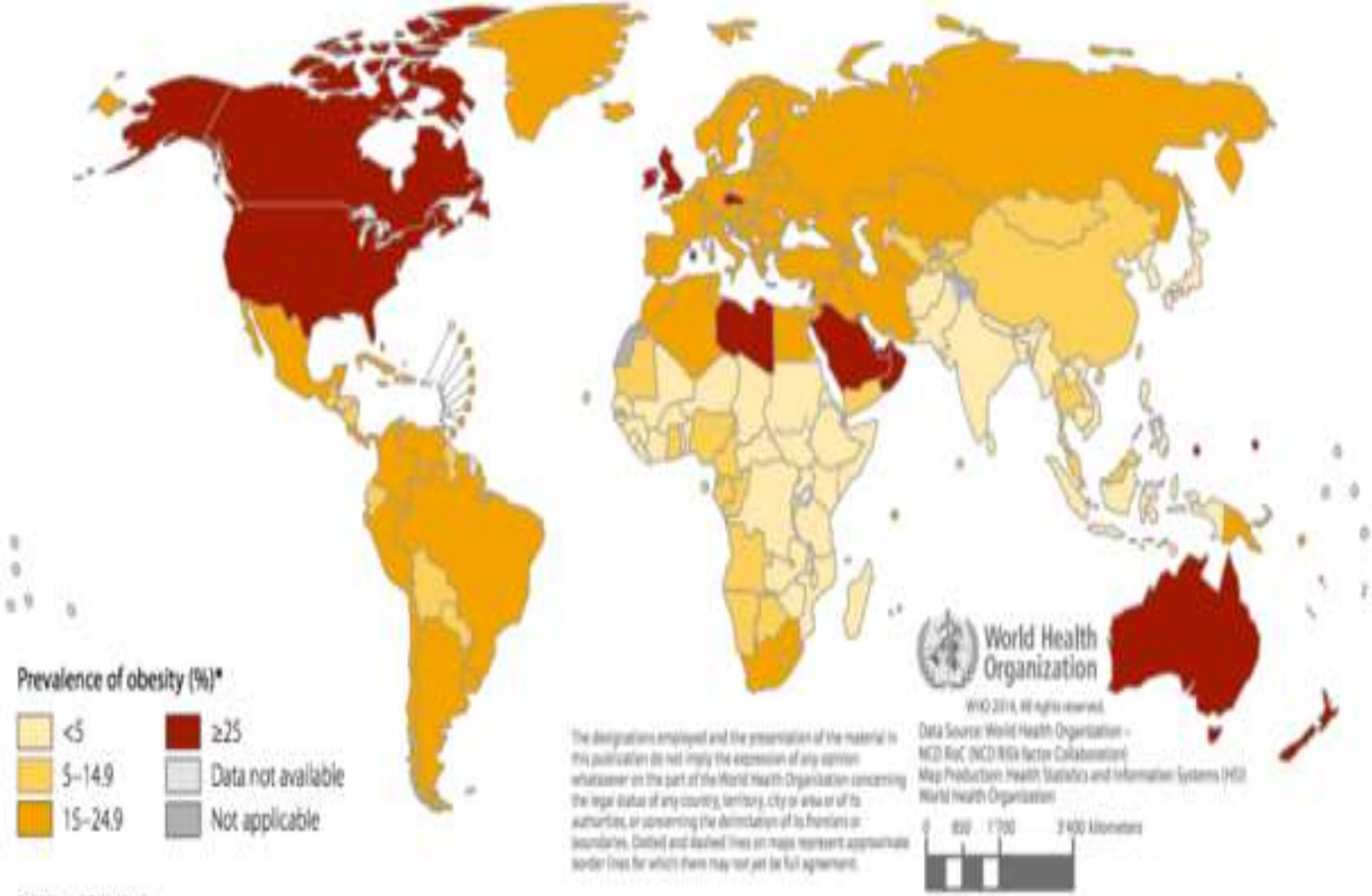
DURING the course of an investigation as to the reason why certain strains of coliform organisms when inoculated into raw 'sterile' milk did not reduce methylene blue or resazurin, it was found that these organisms were actually destroyed in milk held at 37° C. for six hours[1]. As all the tests for the presence of a bacteriophage in the raw milk were negative, it was considered that the destruction of the organisms

Plate counts on MacConkey's agar were carried out at inoculation, and after holding the inoculated milk in a water-bath at 37° C. for four hours, with the following results:

Temperature to which milk was heated (for half an hour) before inoculation		Count per ml. at inoculation	Count per ml. after 4 hours at 37° C.
Culture No. 1	52° C.	1,328,000	1,000
	53° C.	848,000	40,000,000
Culture No. 2	52° C.	316,000	31,000
	53° C.	640,000	28,000,000


COUNTY DISPENSARY
FOR FREE TREATMENT
HOOKWORM DISEASE.

Age-standardized prevalence of obesity in men aged 18 years and over (BMI ≥30 kg/m²), 2014



* BMI ≥ 30 kg/m²