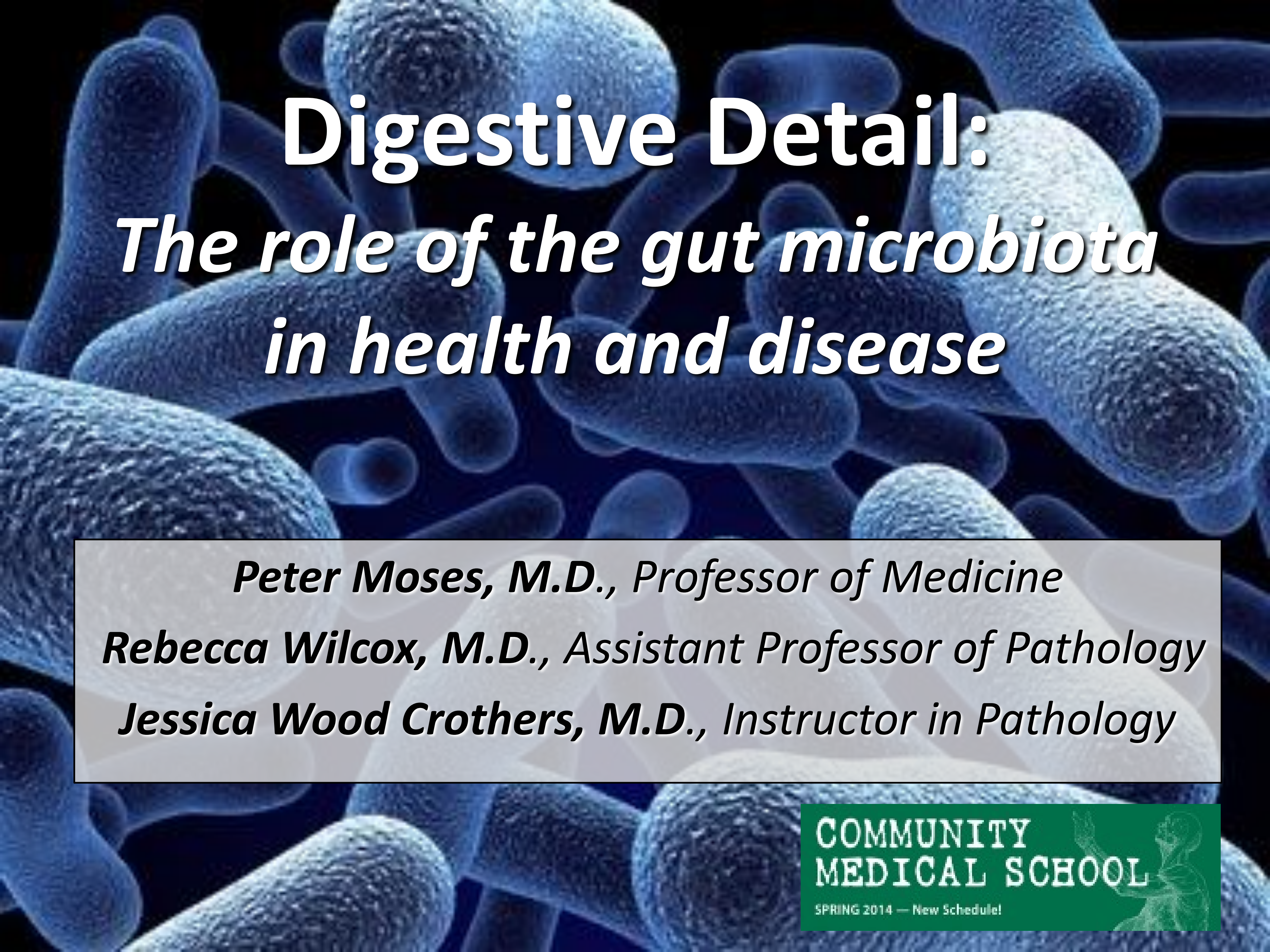


# Digestive Detail:

## *The role of the gut microbiota in health and disease*

***Peter Moses, M.D.**, Professor of Medicine*

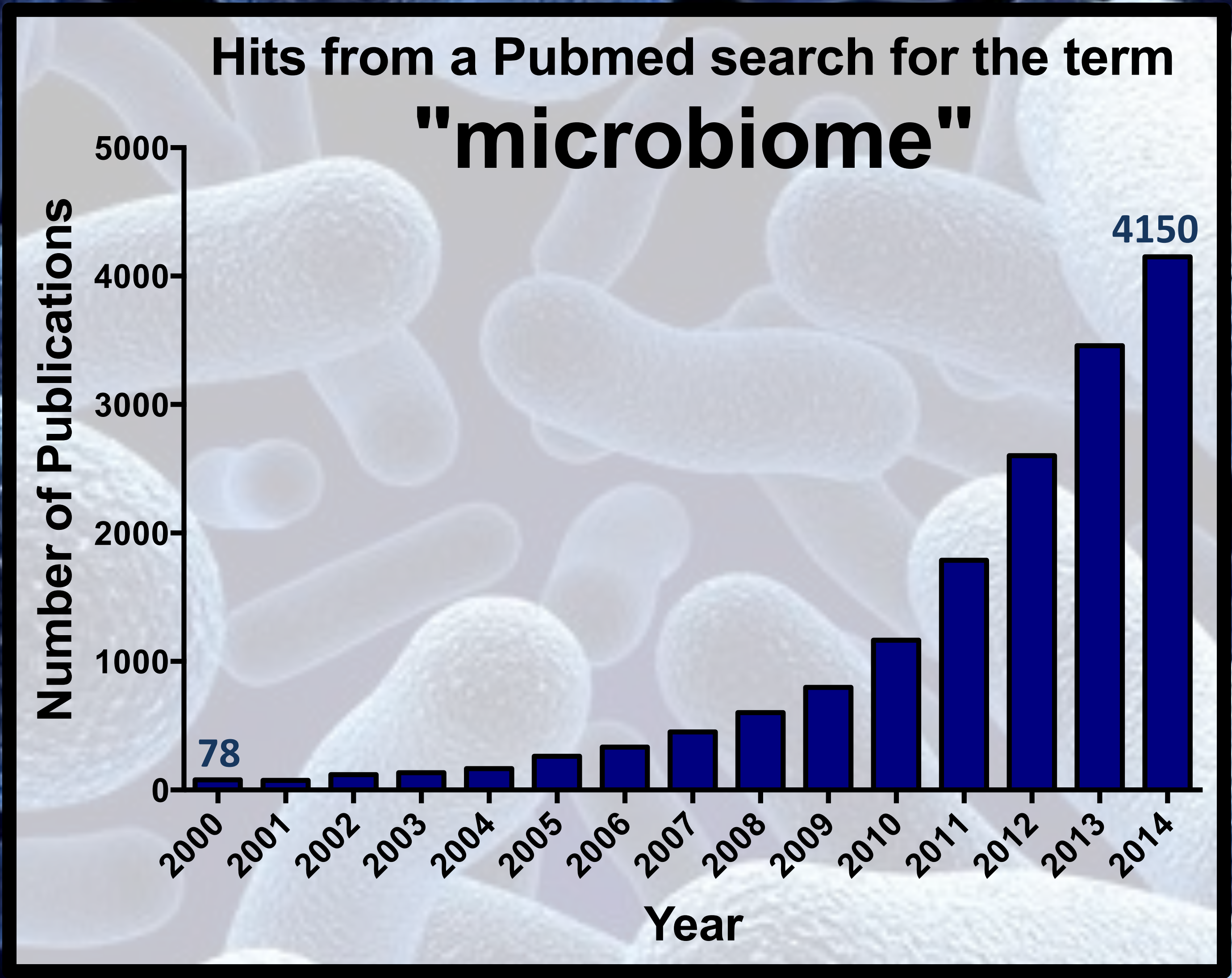
***Rebecca Wilcox, M.D.**, Assistant Professor of Pathology*

***Jessica Wood Crothers, M.D.**, Instructor in Pathology*

COMMUNITY
MEDICAL SCHOOL

SPRING 2014 — New Schedule!

# Hits from a Pubmed search for the term "microbiome"



**Peter Moses, M.D.**, Professor of Medicine

**Introduction to the microbiome:**

**What is it?**

**Why is it important?**

**Rebecca Wilcox, M.D.**, Assistant Professor of Pathology

**The microbiome in disease:**

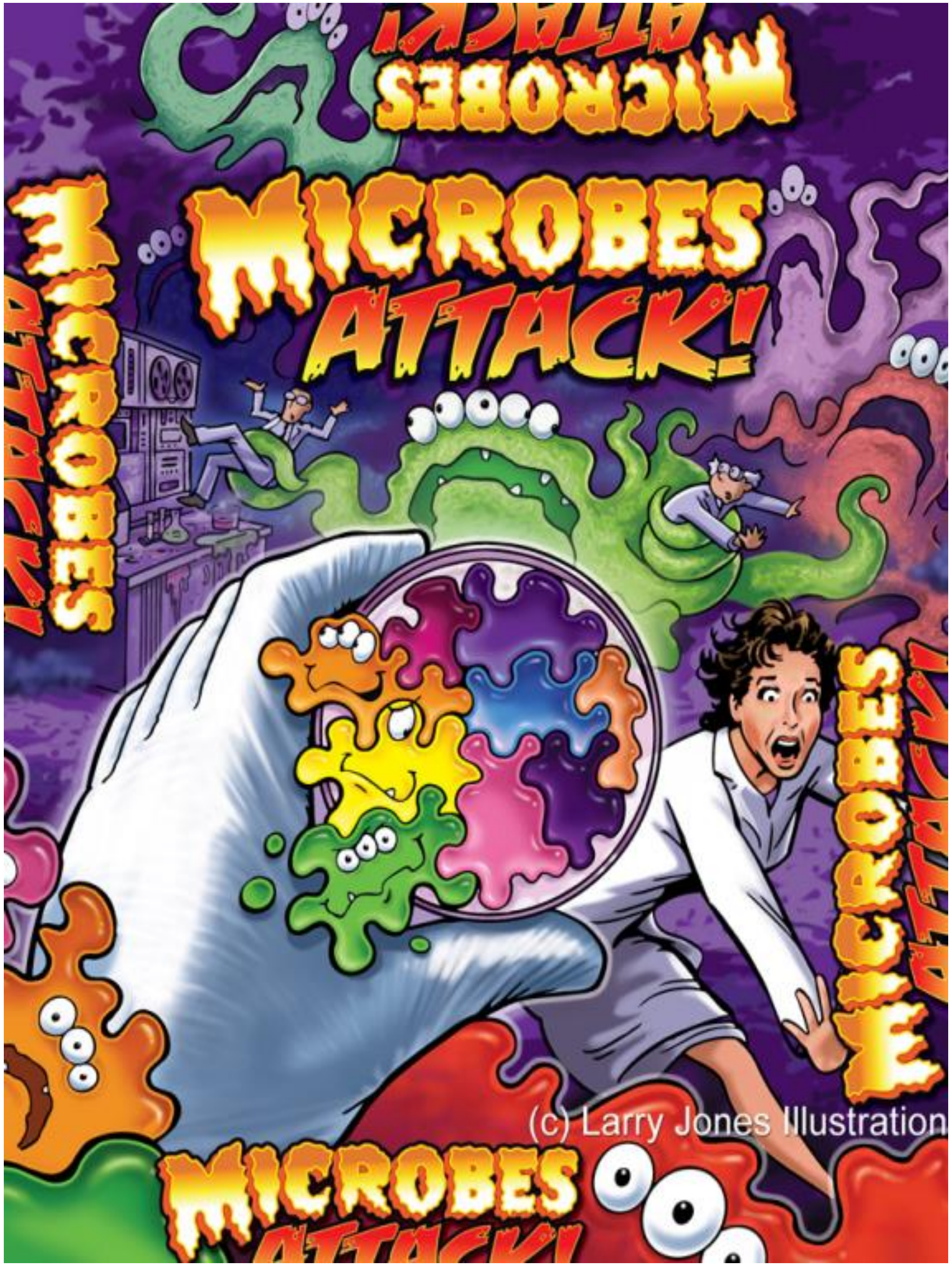
**When “bad bugs” get the upper hand.**

**Jessica Wood Crothers, M.D.**, Instructor in Pathology

**Why the interest now?**

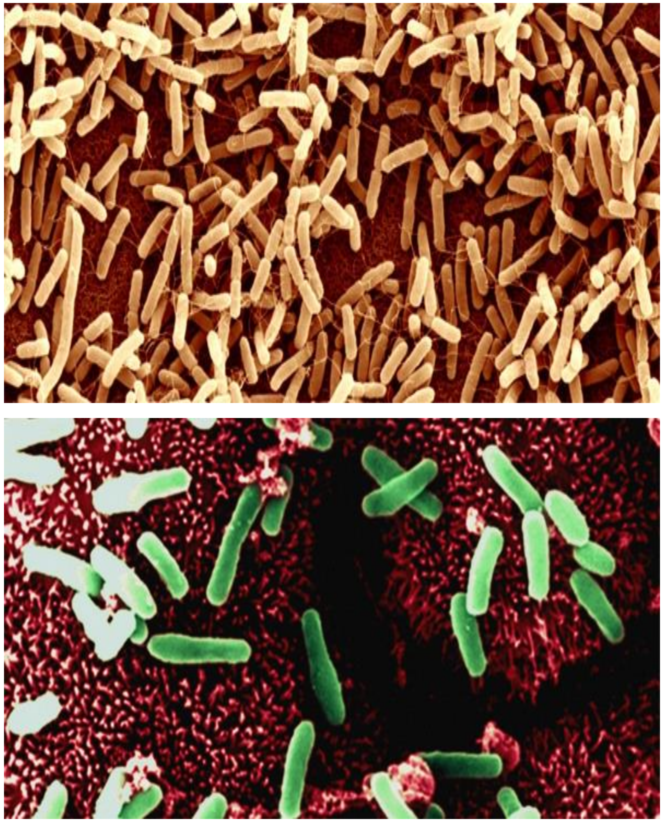
**Metagenomics: Analyzing the microbial community**

**Manipulation and alteration of the microbiome .**


MICROBES
ATTACK!

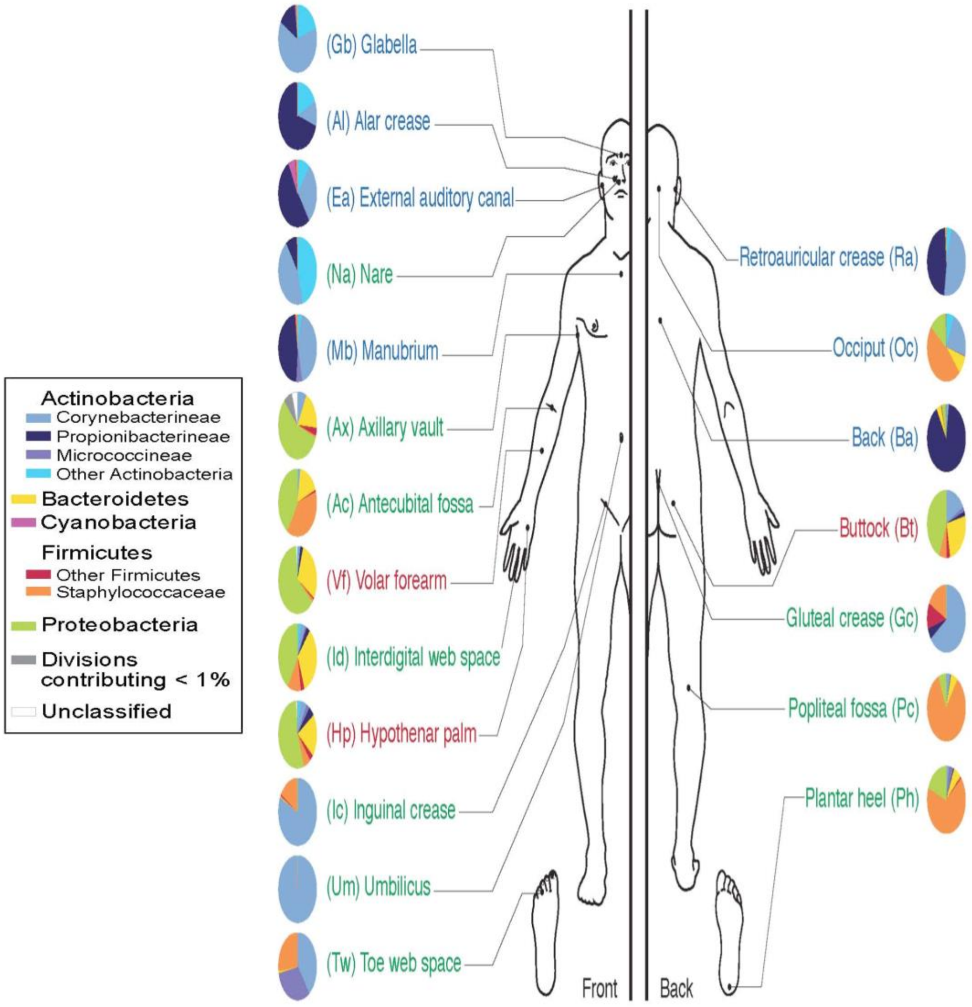
# The Microbiome

- The human body is made up of around ten trillion cells, and over 100 trillion total microbial organisms ($10^{14}$) .
  - We are 10 parts microbe for every 1 part Human
  - For every human gene, there are 100 microbial genes carried on and in our bodies.
- The microbiome has a significant impact on our health and on associated diseases.
- Everything from the food we eat to the way we are born influences the species of bacteria that take up residence in our bodies.

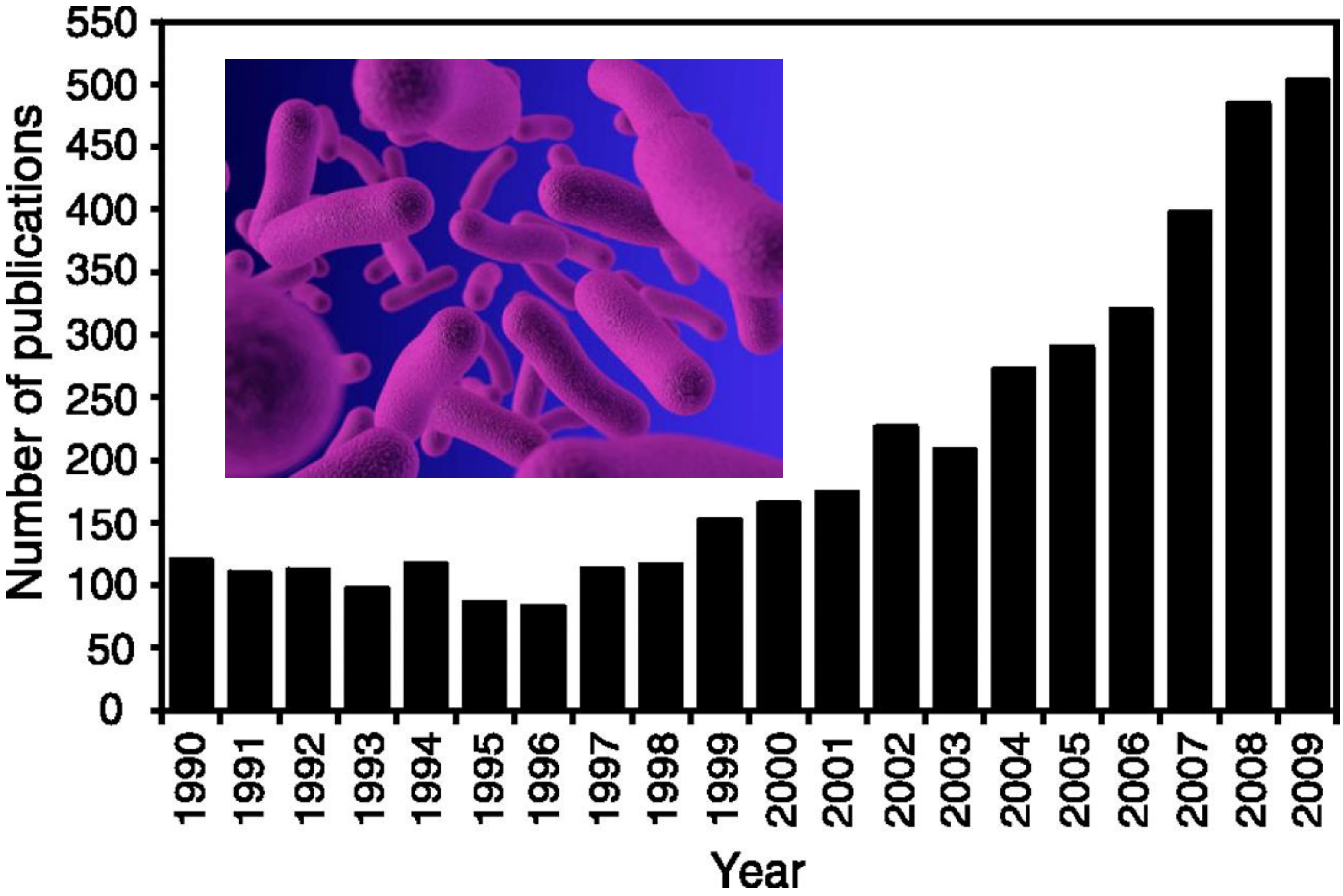


# We are More Microbe than Human

- Definitions:
  - Microbiome: *Aggregate of all microbial species on and in the human body.*
  - Microbiota: *Individual bacterial species in the biome specific to the organism.*
- The human microbiome weighs 5-7 pounds.
  - The gut houses the majority of these organisms.
  - Microbes harvest energy from food, provide us with nutrients, prevent the growth of harmful bacteria.
- Humans and their microbiome have co-evolved as a physiologic community.
- The sphere of influence of the human microbiome is just beginning to be understood.



# Publications Related to the Gut Microbiota (per year).

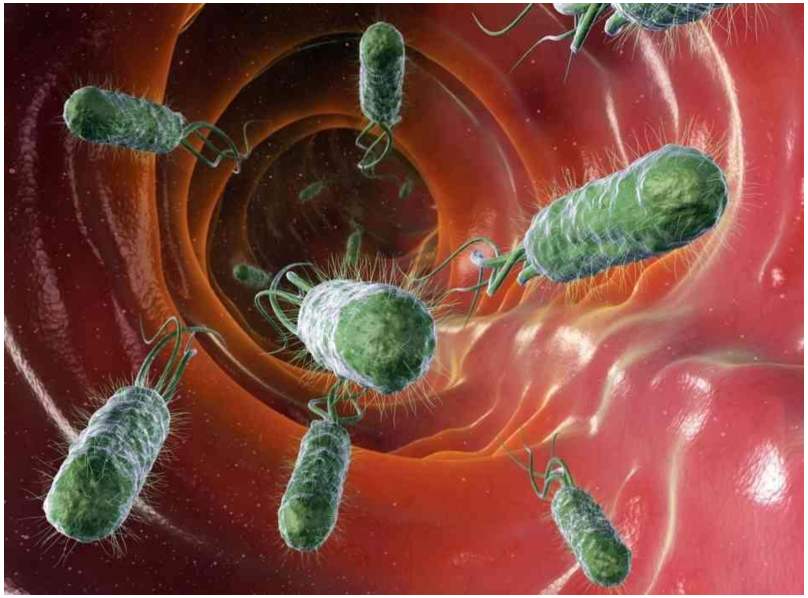


**Sekirov I et al. Physiol Rev 2010;90:859-904**

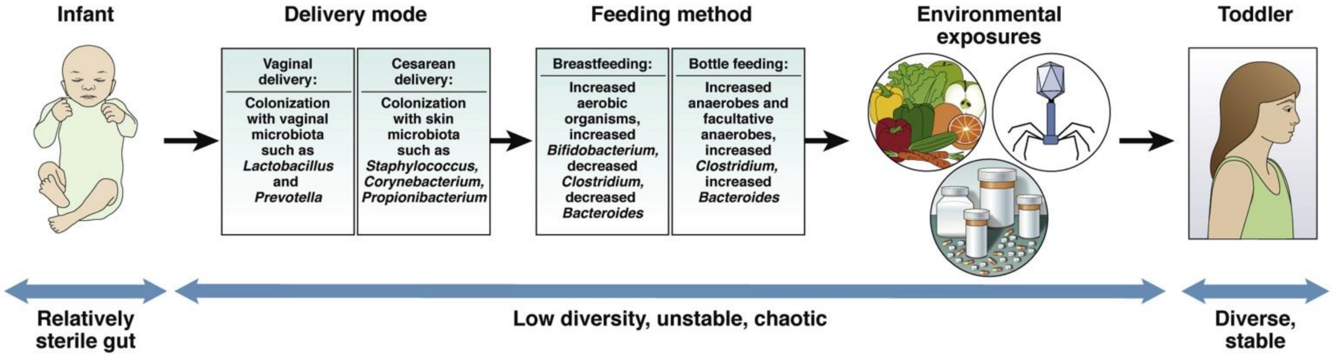
Physiological Reviews

# Microbial Content in Various Regions of the Gut

- Upper GI tract: $10^2 – 10^4$ cells/ml
  - Lactobacilli, streptococci, H pylori
- Ileum: $10^6$-$10^{12}$ cells /ml, upper bacteria plus
  - Faculative anaerobes: ***Enterobacteriaceae***
  - Obligate anaerobes: ***Bacteroides, Veillonella, Fusobacterium*** and ***Clostridium*** species
- Colon: distal human colon is the most biodense natural ecosystem known ($10^{10}$-$10^{12}$ cells/ml)
  - Complex and diverse
  - Comprise most of our bacterial biomass



# A Mutually Beneficial Life-long Relationship



**Infant**

**Delivery mode**

**Vaginal delivery:** Colonization with vaginal microbiota such as *Lactobacillus* and *Prevotella*

**Cesarean delivery:** Colonization with skin microbiota such as *Staphylococcus*, *Corynebacterium*, *Propionibacterium*

**Feeding method**

**Breastfeeding:** Increased aerobic organisms, increased *Bifidobacterium*, decreased *Clostridium*, decreased *Bacteroides*

**Bottle feeding:** Increased anaerobes and facultative anaerobes, increased *Clostridium*, increased *Bacteroides*

**Environmental exposures**

**Toddler**

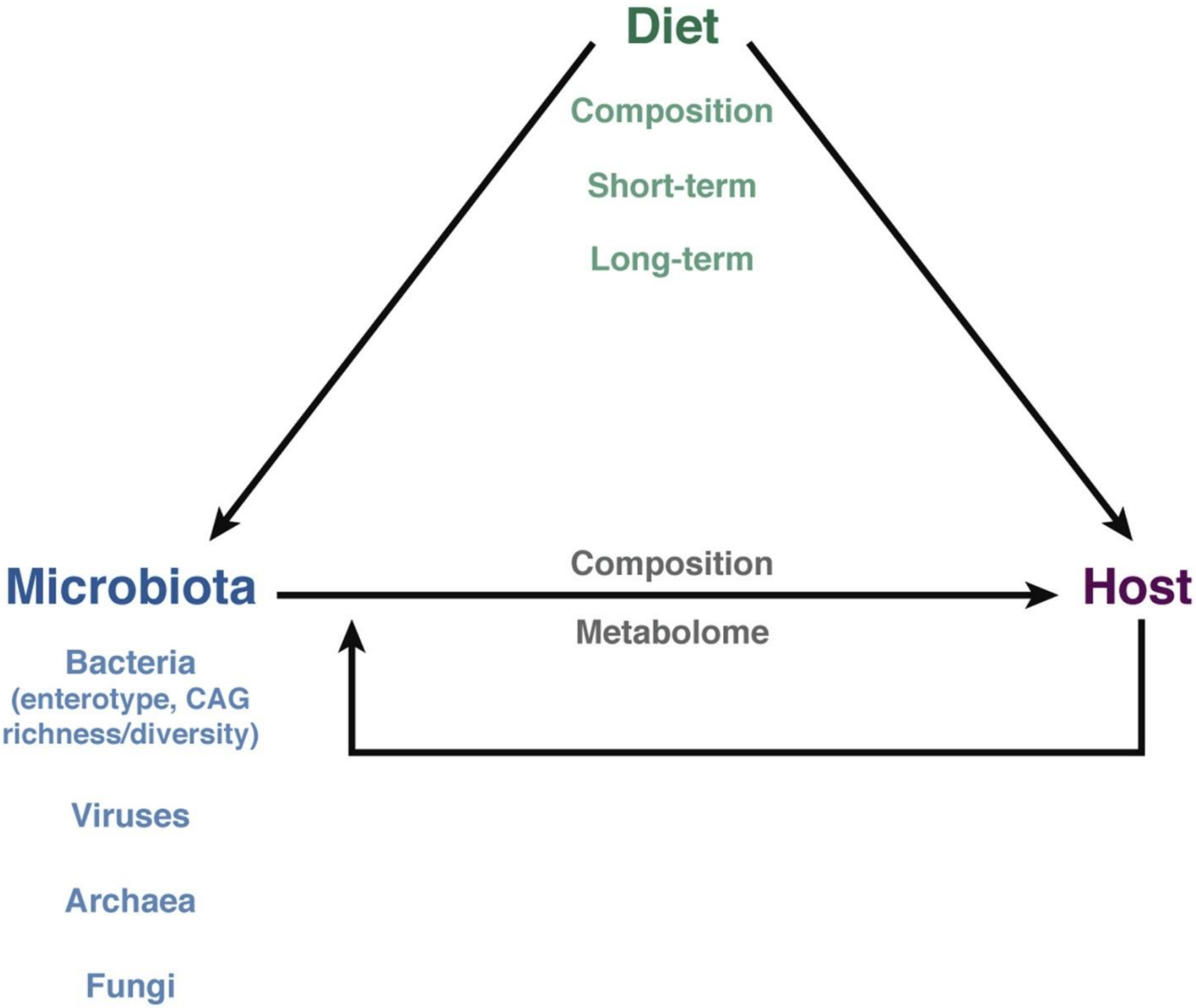
**Relatively sterile gut**

**Low diversity, unstable, chaotic**

**Diverse, stable**

*Gastroenterology* 2014 146, 1564-1572DOI: (10.1053/j.gastro.2014.01.058)

# Interaction of the Microbiome and Host



**Diet**

Composition

Short-term

Long-term

**Microbiota**

Bacteria
(enterotype, CAG
richness/diversity)

Viruses

Archaea

Fungi

Composition

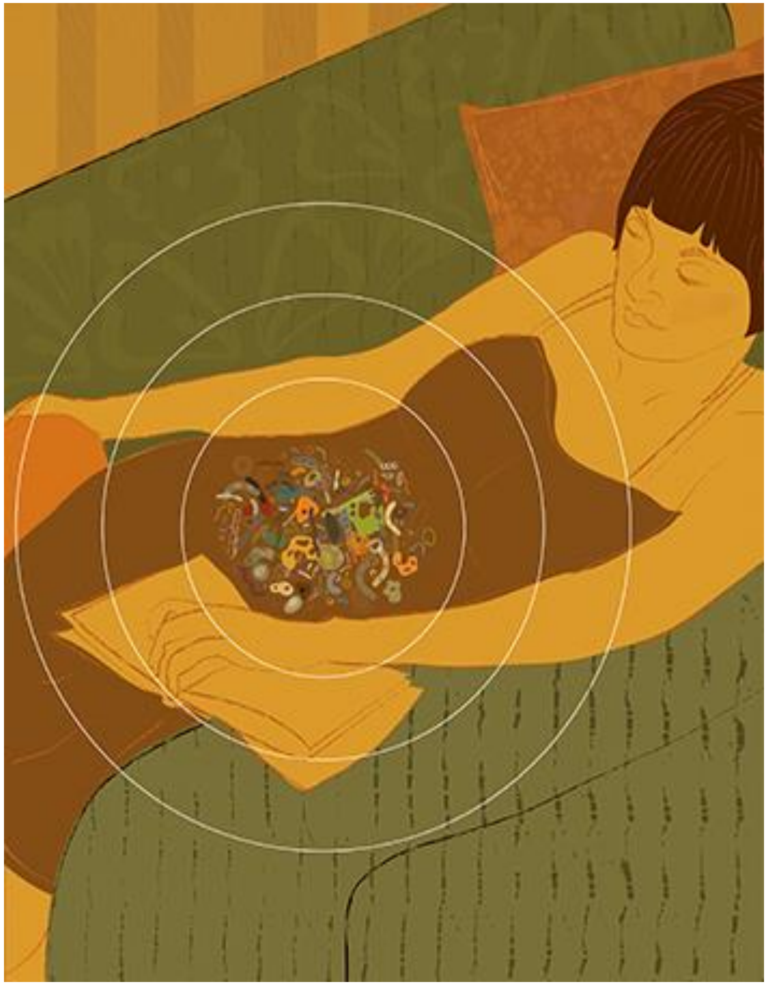
Metabolome

**Host**

*Gastroenterology* 2014 146, 1564-1572DOI: (10.1053/j.gastro.2014.01.058)

# Functions of Normal Bacterial Flora

- **Synthesize and modify vitamins**
  Vitamin K and Vitamin B12
- **Prevent colonization by pathogens**
  competing for attachment sites or for essential nutrients
- **May antagonize other bacteria**
  the production of substances which inhibit or kill non-indigenous species
- **Stimulate the development of certain tissues.**
- **Stimulate the production of cross-reactive antibodies**. Low levels of antibodies produced against components of the normal flora are known to cross react with certain related pathogens, and thereby prevent infection or invasion.



# Proposed Regulatory Functions of the Microbiome

- Metabolic
  - Obesity, Insulin resistance
- Inflammatory
  - IBD and possibly IBS
- Neuropsychiatric
  - Mood and temperament

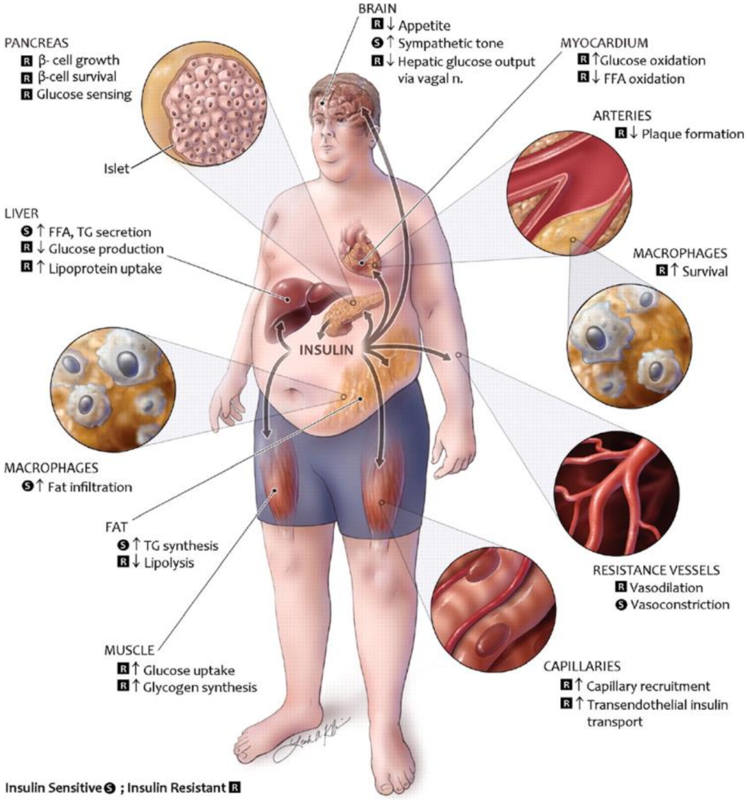
# Metabolism

# The Microbiome and Metabolic Syndrome

*Internal Medicine at the*
*Academic Medical Center in Amsterdam,*
*the Netherlands*

Max Neuwdorp, MD

*34% of American adults*



Lean donor’s microbiota transferred into guts of male patients with metabolic syndrome -> Increased sensitivity to insulin @ 6 wks.

# Experimental Design

- On day one: all subjects had insulin sensitivity, serum glucose, insulin, glucagon, free fatty acids and gluco-regulatory hormones.
- On day two: fasting subjects and donors produced morning stool. Study subjects were randomized to allogenic (n=9 from lean donors) or autologous (n=9) FMT by naso-duodenal tube.

# Results: Summary

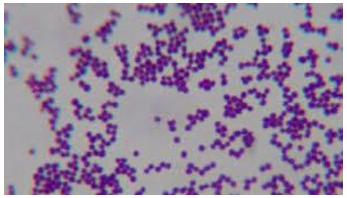
- No difference in bacterial abundance in either group.
- Microbiota of experimental subjects shifted toward that of the lean donors: More diverse, more energy efficient.
- Insulin sensitivity improved 6 weeks after FMT in patients with metabolic syndrome.
- Gut microbiota content was shifted toward that found in lean individuals by FMT.

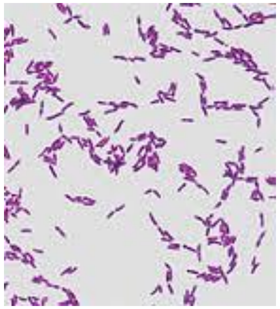
# Obesity is associated with changes in the relative abundance of Bacteroidetes and the Firmicutes

- **Phylum Bacteroidetes :**
  3 large classes of
  Gram-negative,
  Non-sporeforming,
  anaerobic,
  rod-shaped bacteria
- widely distributed in the environment

- **Phylum Firmicutes:**

Most are Gram-positive.
Listeria, Staphylococcus, Bacilli, Lactobacillales, Enterococcus, Lactobacillus.

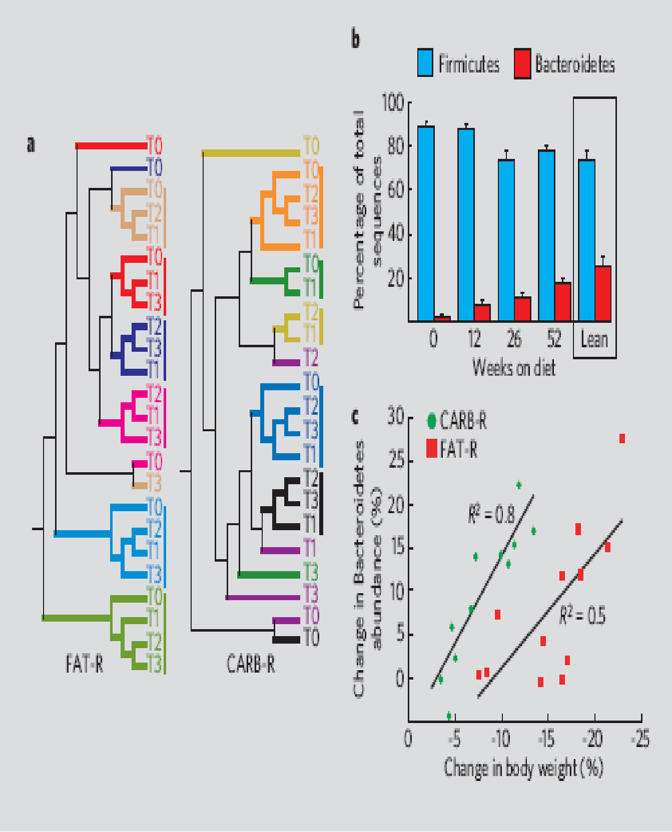




Nature 444, 1027-1031 (21 December 2006)
Turnbaugh, Ley, Mahowald, Magrini, Mardis & Gordon

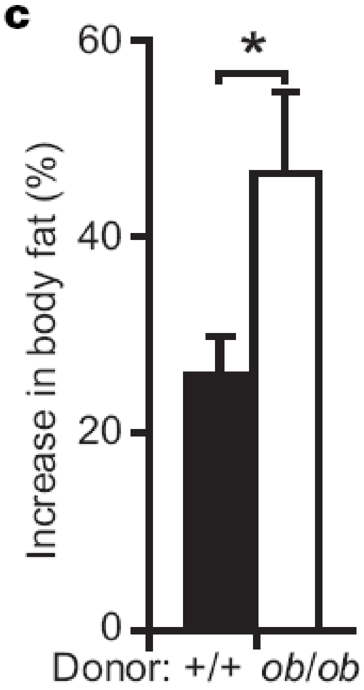
# An obesity-associated gut microbiome Demonstrates an increased capacity for energy absorption.

- 12 Obese people were assigned to a low carb or low fat diet over 1 year: Microbiota composition was monitored along with weight loss.
- Obesity associated with changes in the relative abundance of two dominant bacterial divisions: Bacteroidetes (B) and the Firmicutes (F).
- The "obese gut" has properties that tip the microbial balance toward the Firmicutes.
- Obese: F>B, Over time B increased and F decreased regardless of diet type.



Nature 444, 1027-1031 (21 December 2006)
Turnbaugh, Ley, Mahowald, Magrini, Mardis
& Gordon

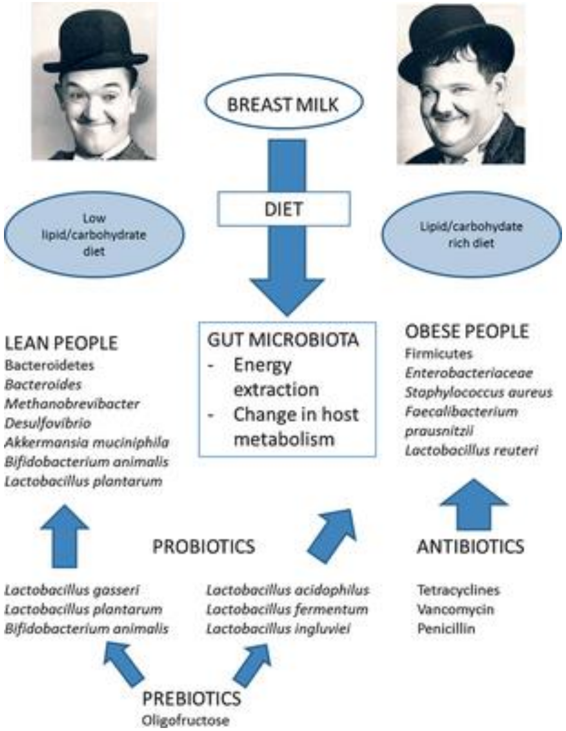
# The Microbiome: mouse transplant experiments



- Germ-free mice given ob/ob or wild-type flora
- Chow consumption and exercise the same for both groups
- Both sets had similar starting weight and % BF.
- ob/ob microbiota had significantly higher relative abundance of Firmicutes ($P < 0.05$).
- The ob/ob microbiota promote host adiposity

Turnbaugh, et al. Nature 2006; 444:1027

# Gut bacterial microbiota and obesity



BREAST MILK

DIET

Low lipid/carbohydrate diet

Lipid/carbohydrate rich diet

LEAN PEOPLE
Bacteroidetes
*Bacteroides*
*Methanobrevibacter*
*Desulfovibrio*
*Akkermansia muciniphila*
*Bifidobacterium animalis*
*Lactobacillus plantarum*

GUT MICROBIOTA
- Energy extraction
- Change in host metabolism

OBESE PEOPLE
Firmicutes
*Enterobacteriaceae*
*Staphylococcus aureus*
*Faecalibacterium prausnitzii*
*Lactobacillus reuteri*

PROBIOTICS

*Lactobacillus gasseri*
*Lactobacillus plantarum*
*Bifidobacterium animalis*

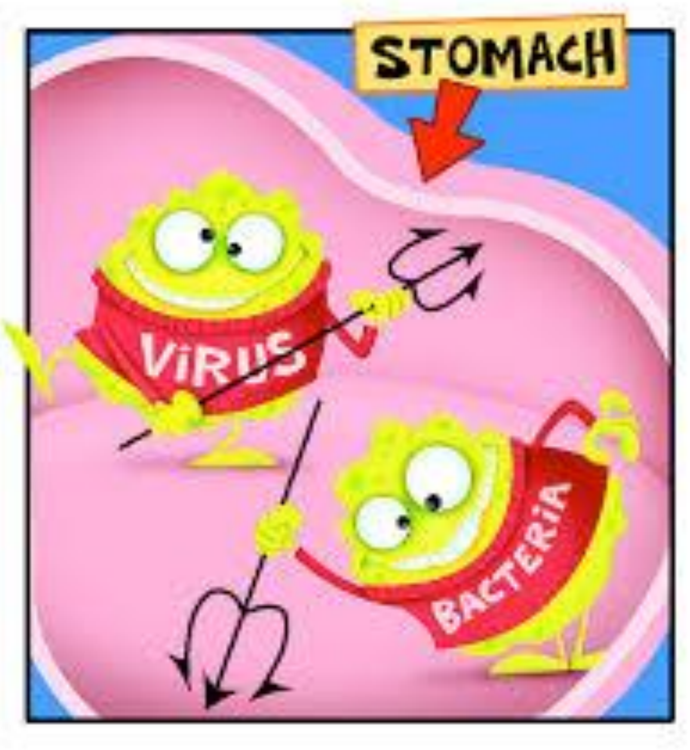
*Lactobacillus acidophilus*
*Lactobacillus fermentum*
*Lactobacillus ingluviei*

ANTIBIOTICS
Tetracyclines
Vancomycin
Penicillin

PREBIOTICS
Oligofructose

**Clinical Microbiology and Infection**
Volume 19, Issue 4, pages 305-313, 2 MAR 2013 DOI: 10.1111/1469-0691.12172
http://onlinelibrary.wiley.com/doi/10.1111/1469-0691.12172/full#clm12172-fig-0001

# Inflammatory and Functional GI Disorders

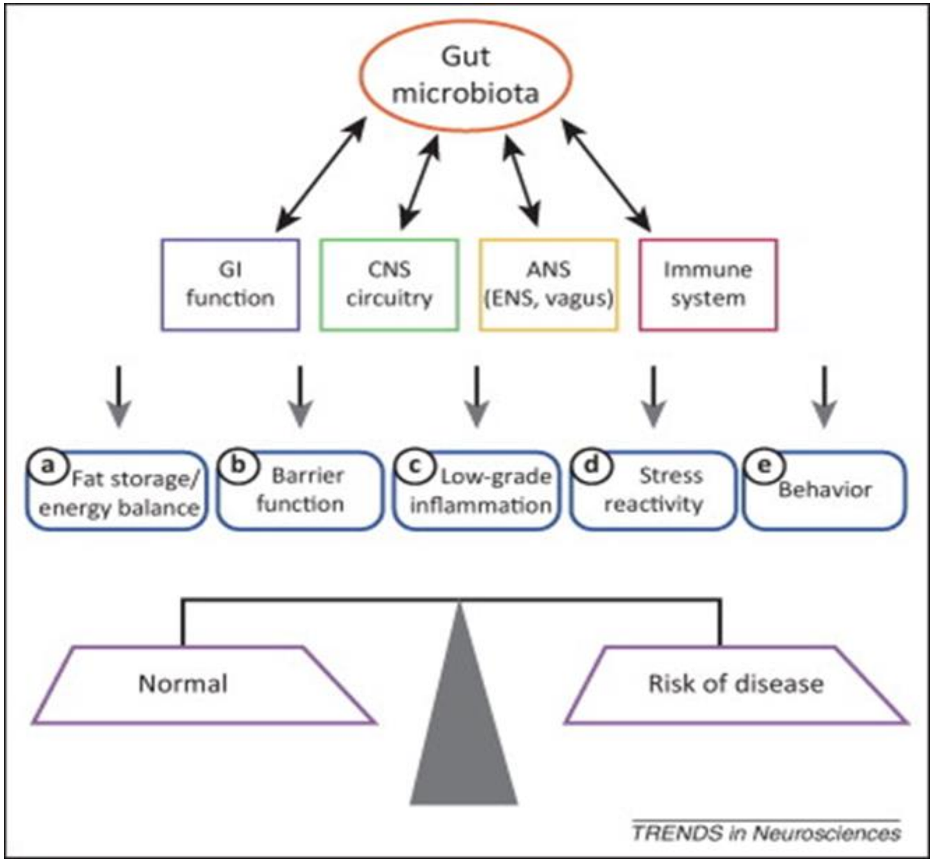


# Irritable Bowel Syndrome

- Bile acid alteration by microbes may affect stool volume and consistency.
- Changes in fermentation affect gas production.
- Antibiotics, prebiotics and Probiotics have been demonstrated to have an effect in clinical GI symptoms.
- Gut–Brain Axis may be altered by the microbial environment.

Shen et al. Inflammatory bowel diseases; 20 (1) January 2014

# The brain-Gut Axis

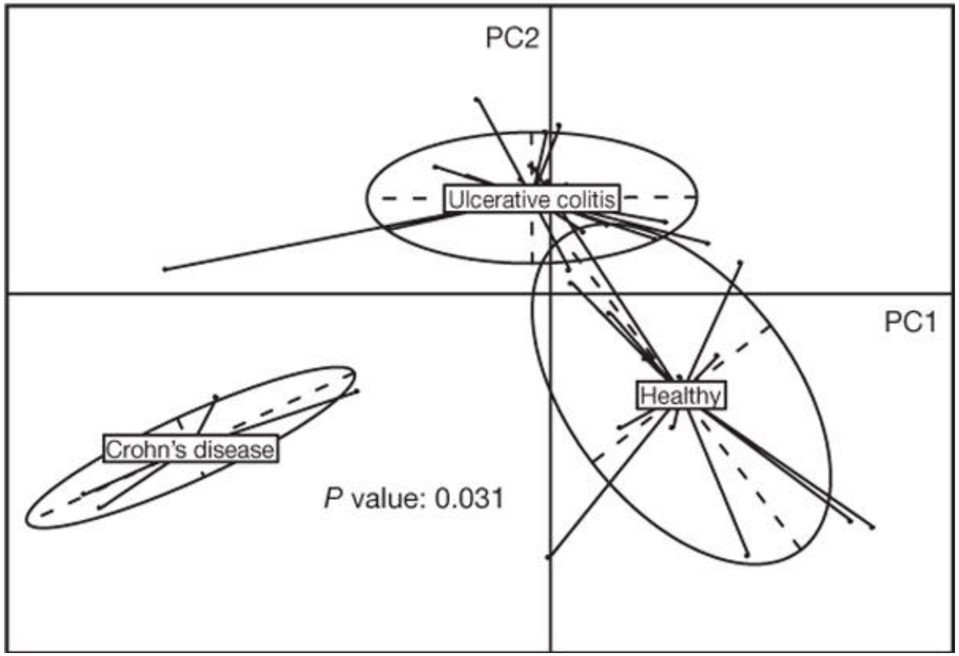


Jane A. Foster, Karen-Anne McVey Neufeld. Trends in Neuroscience. Volume 36, Issue 5, p305–312, May 2013

# Bacterial species abundance differentiates IBD patients and healthy individuals

## IBD individuals: 25% fewer genes and lower bacterial diversity

14 healthy individuals and 25 IBD patients (21 ulcerative colitis and 4 Crohn's disease)



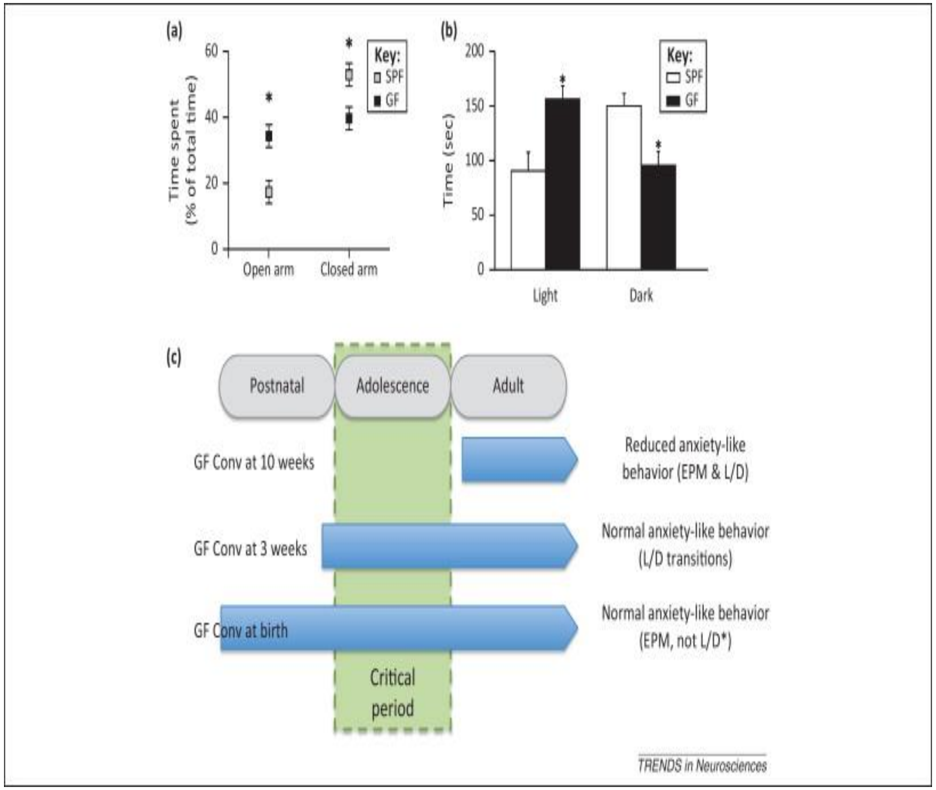
nature

JJ Qin *et al. Nature* **464**, 59-65 (2010) doi:10.1038/nature08821

# Behavioral Disorders

# **Your Microbes May Affect Your Behavior:** Germ-Free (GF) mice, raised without exposure to microbes, show reduced anxiety-like behavior

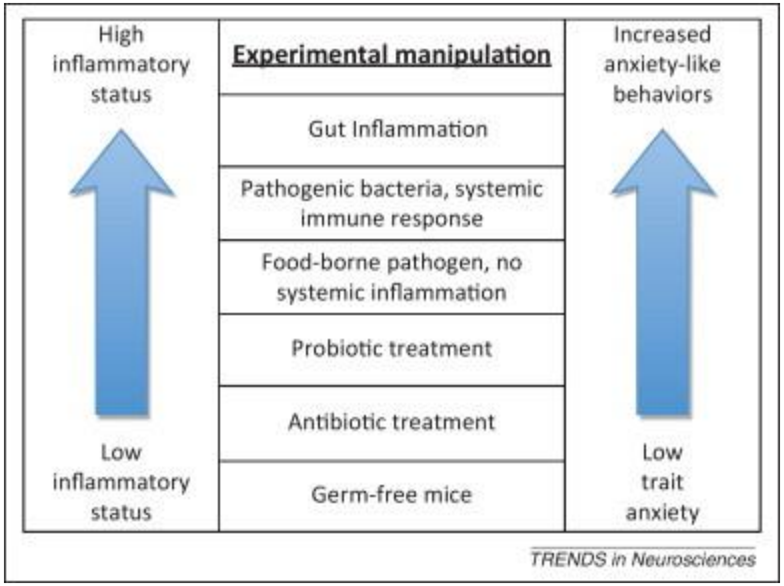
- Germ-free demonstrated reduced anxiety-like behavior than normal (SPF) in maze and light-dark box.
- FMT early in life normalizes anxiety-like behavior.
- GF mice undergoing FMT at 10 weeks (later) continue to demonstrate reduced anxiety-like behavior.
- These data suggest that behavioral modification with FMT is “time-sensitive”.
- Hypothesis: Adolescence is a critical period where the gut–brain axis influences adult anxiety-like behavior.



Jane A. Foster, Karen-Anne McVey Neufeld. Trends in Neuroscience. Volume 36, Issue 5, p305–312, May 2013

# Microbiota may play a role in the relation between inflammation and anxiety-like behaviors

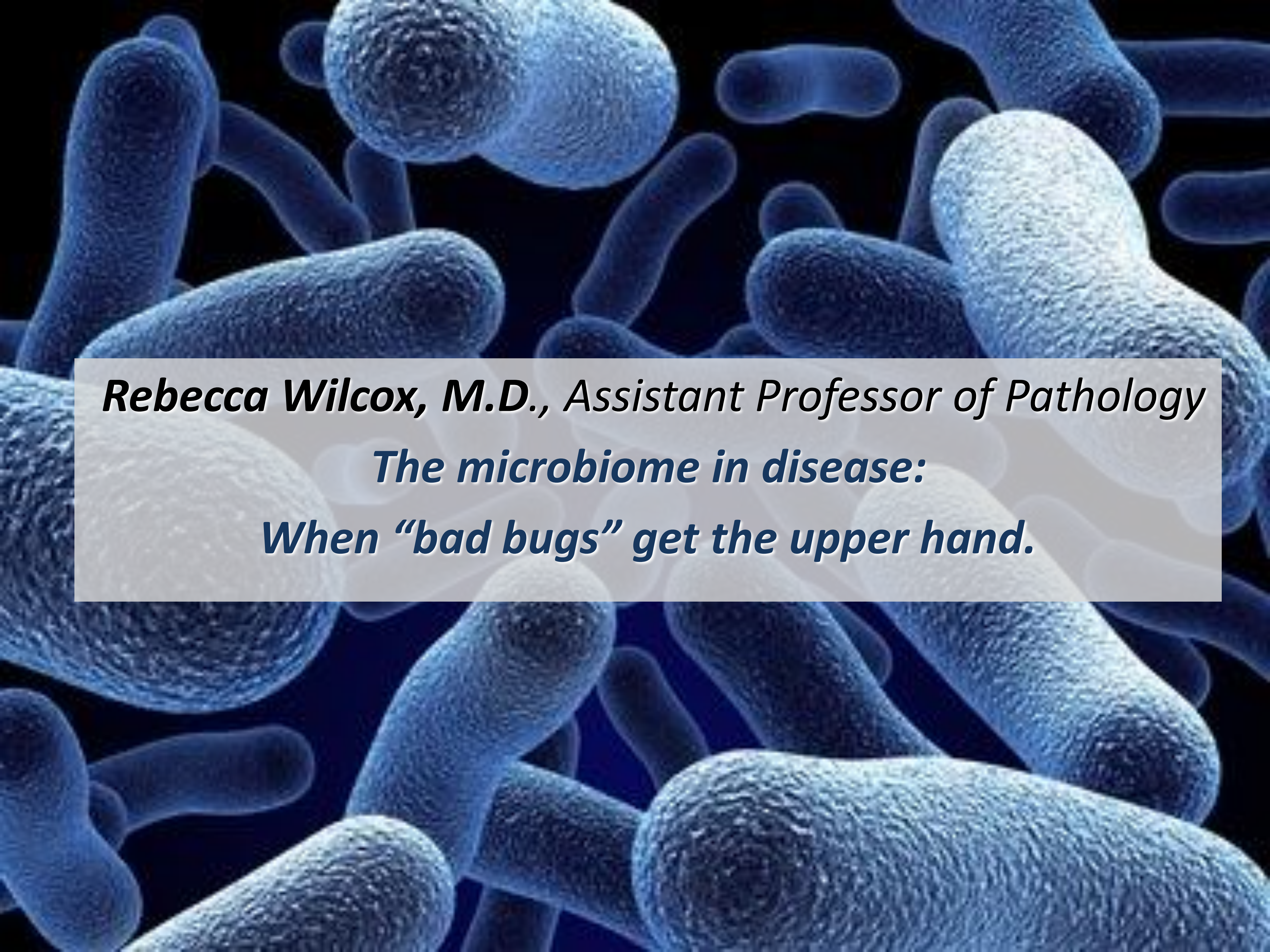
- Experimental manipulations that alter intestinal microbiota impact anxiety-like behavior.
- The observed behavioral changes relate to inflammatory status and are associated with differences in the microbiota profile in the gastrointestinal tract.



Jane A. Foster, Karen-Anne McVey Neufeld. Trends in Neuroscience. Volume 36, Issue 5, p305–312, May 2013

# Summary

- The microbes in your gut may affect the size of your belly.
- Microbiological manipulation may impact anxiety, depression and emotion.
- The more abundant and variable the microbiota the better.
- Lack of microbial diversity has been linked to allergy, GI disorders, inflammation and other diseases.



***Rebecca Wilcox, M.D.****, Assistant Professor of Pathology*

# *The microbiome in disease: When "bad bugs" get the upper hand.*

# Gastrointestinal (GI) Pathology

Fletcher Allen
HEALTH CARE

In alliance with
The University of Vermont

GI Pathologist: Surgical Pathology

Gastroenterologists: Endoscopy

# Patterns

- Disease Burden
- Quality of Life
- Cost

CENTERS FOR DISEASE CONTROL AND PREVENTION

**Helicobacter Pylori (H. Pylori) related Peptic Ulcer Disease**

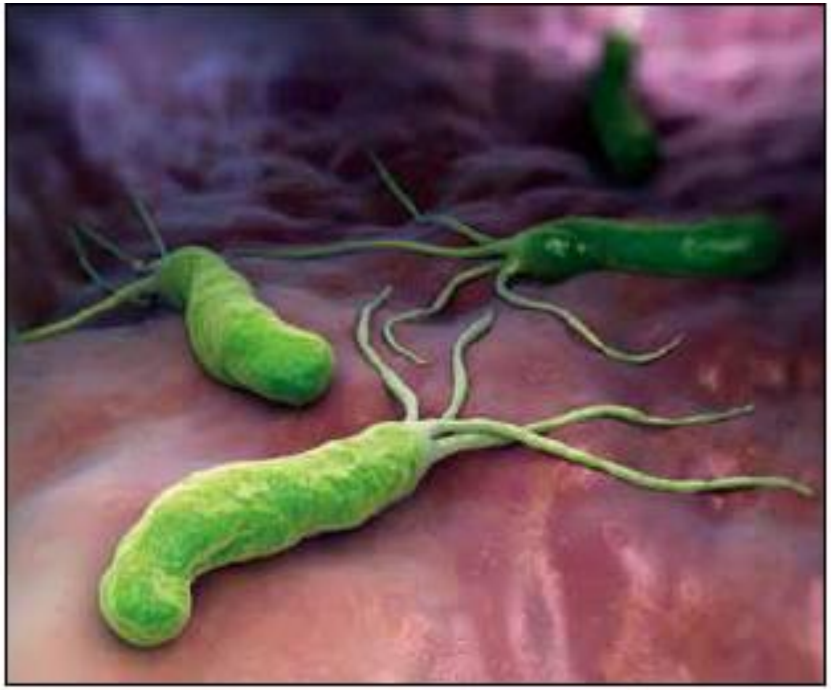
- **6,500 deaths per year**
- **Annual Health Care Costs:**
    - **~6 billion**
        - **3 b Hospital Costs**
        - **2 b Physical Office Visits**
        - **1 b Decreased Productivity**

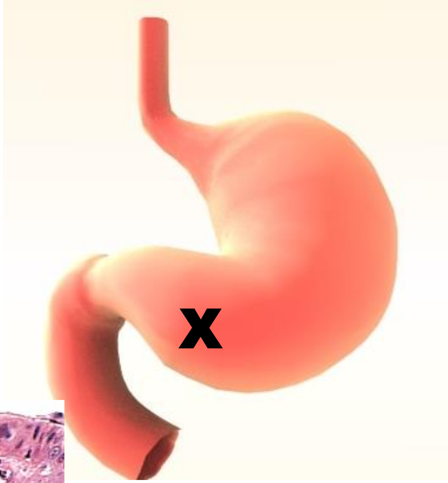
**Clostridium Difficile (C. Diff) Colitis**

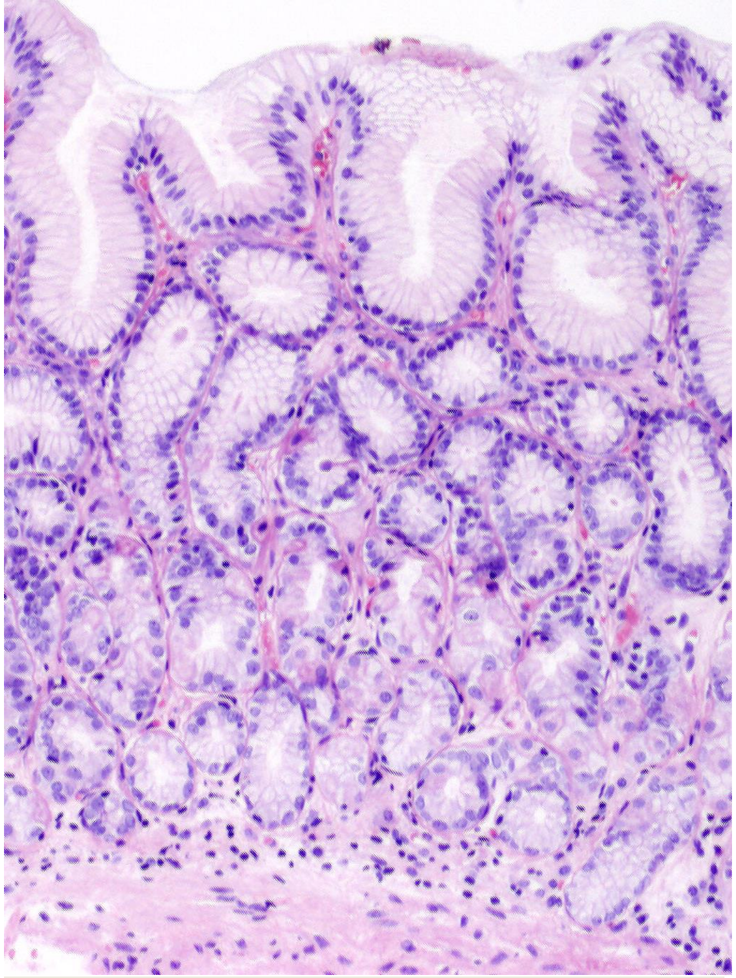
- **14,000 deaths per year**
- **Annual Health Care Costs:**
    - **AT LEAST 1 billion Hospital Costs**

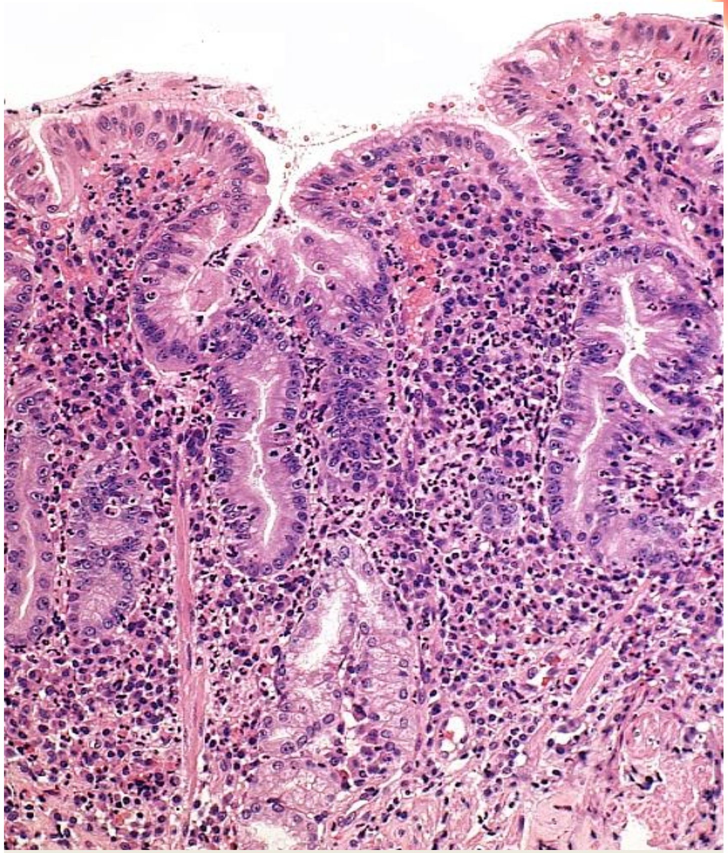
# H. Pylori Gastritis

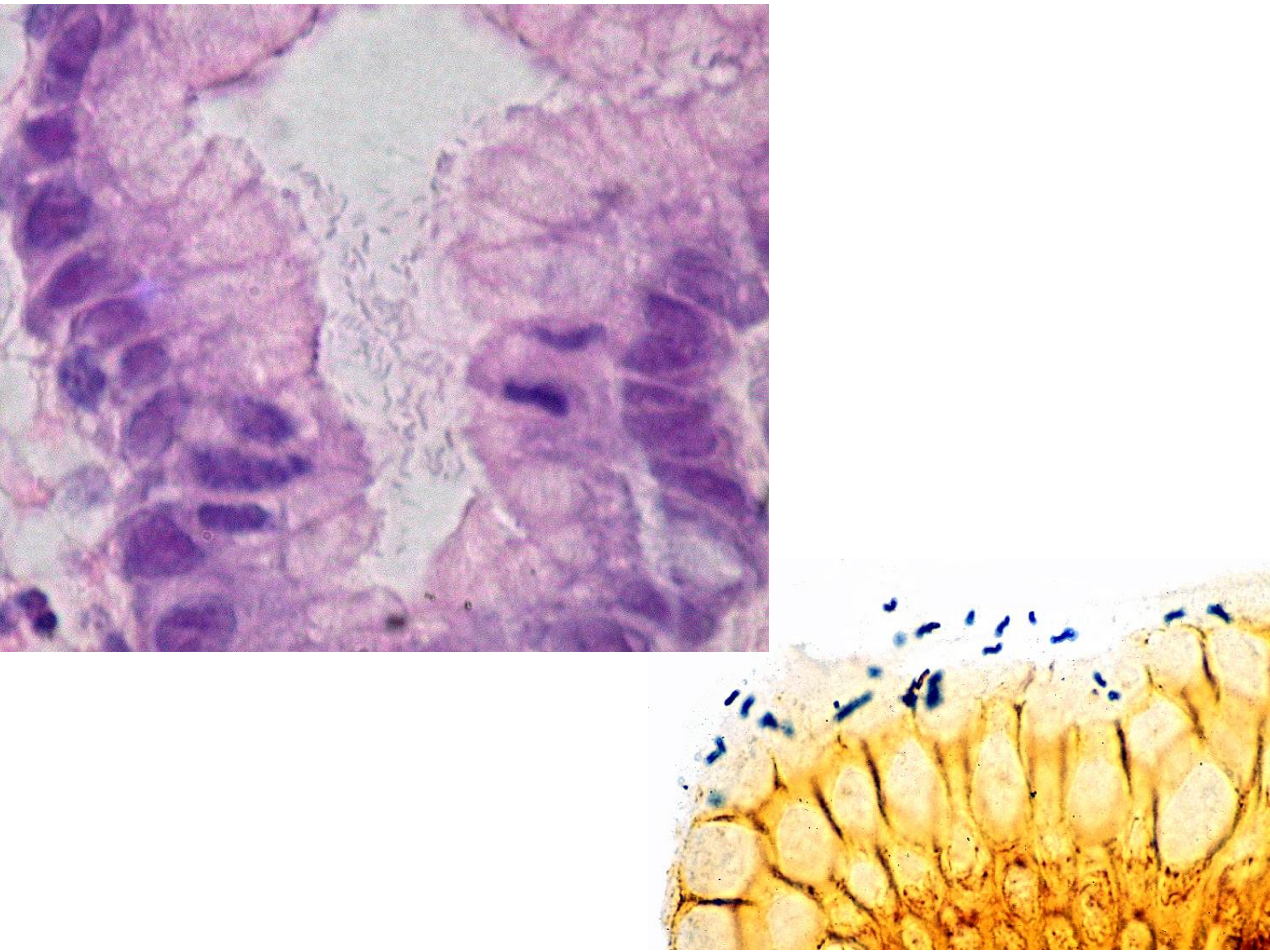
- Spiral-shaped bacterium that colonizes the stomach
  - 50% of humans
- Typically contracted in childhood
- Chronic infection
- Usually asymptomatic
- 10-15% of infected individuals develop peptic ulcer disease
- H. pylori associated malignancies
  - Gastric Cancer
  - Lymphoma (MALT)

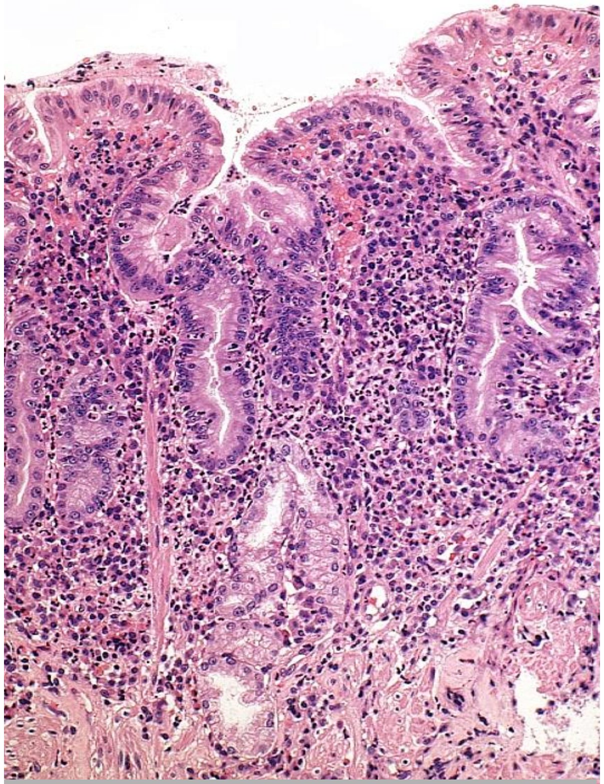




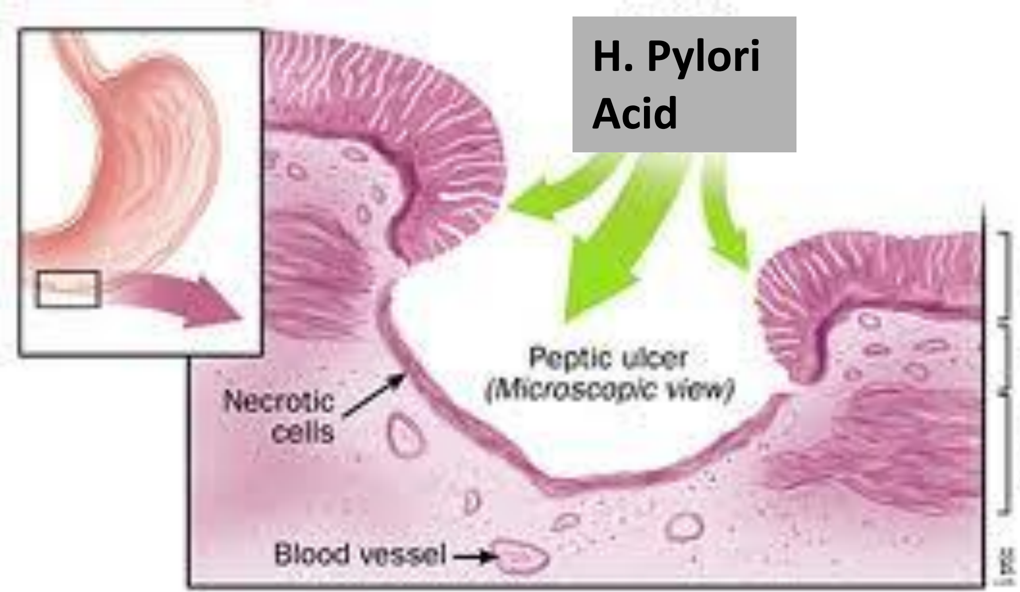

Normal Stomach Biopsy


Stomach Biopsy with H.Pylori Gastritis





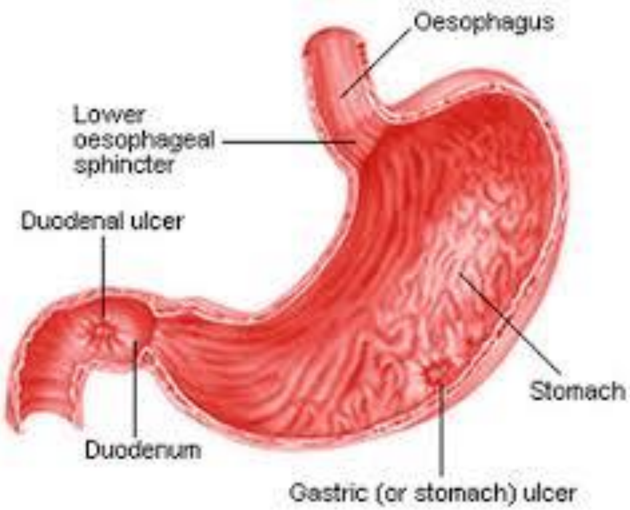
Stomach Mucosa with
Chronic  H. Pylori Gastritis



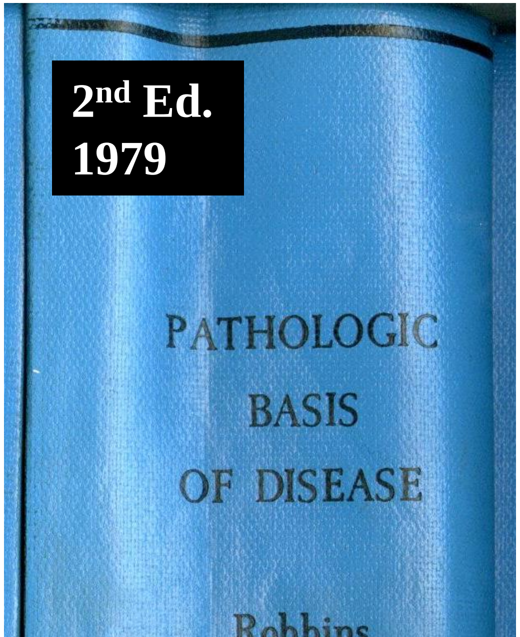
**H. Pylori**
**Acid**

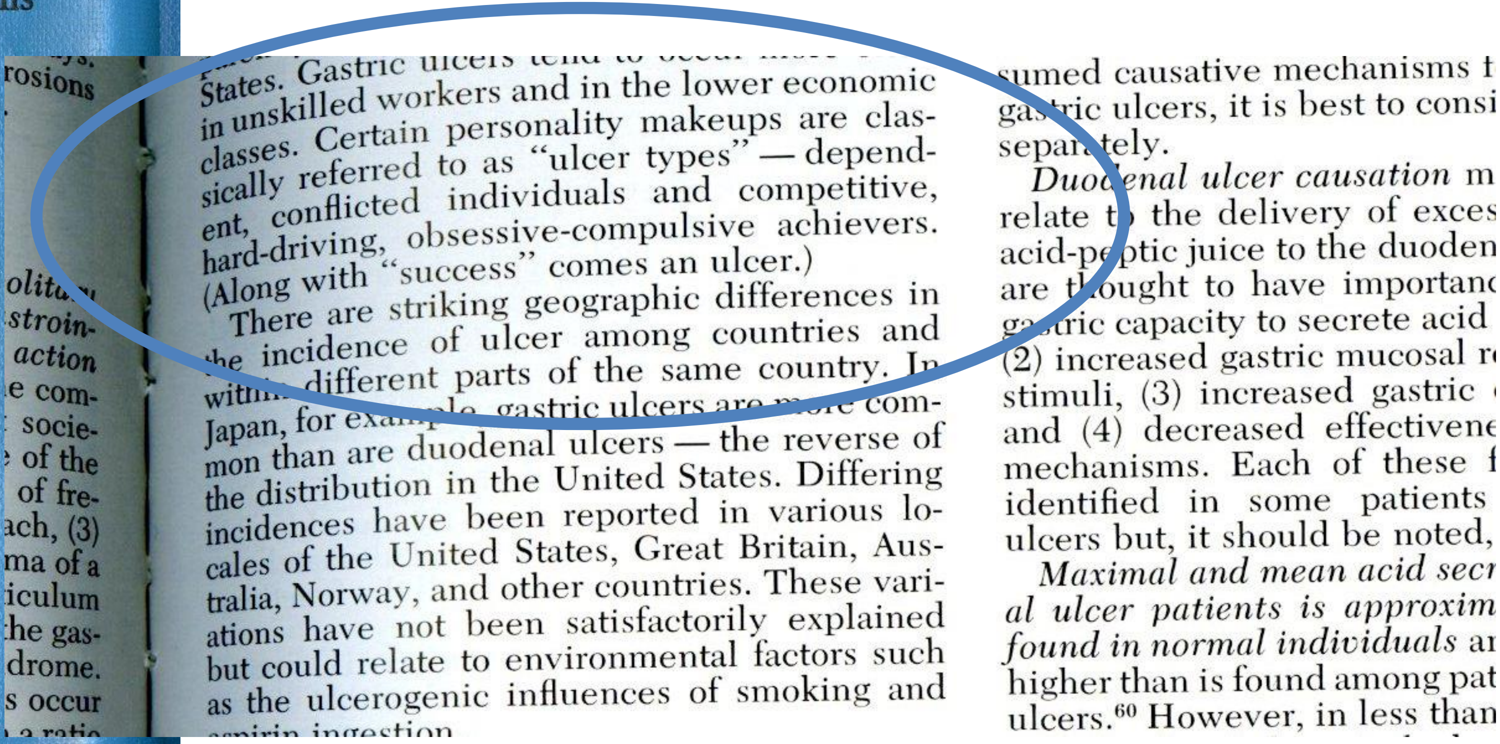
Peptic Ulcer Disease

**<u>Bacteria Pathogenicity</u>**
**Chronic inflammation (Host Response) Leads to:**
**Peptic Ulcer Disease**
**Lymphoma**
**Gastric Cancer**



# 2nd ed. (1979): On Gastric Ulcers





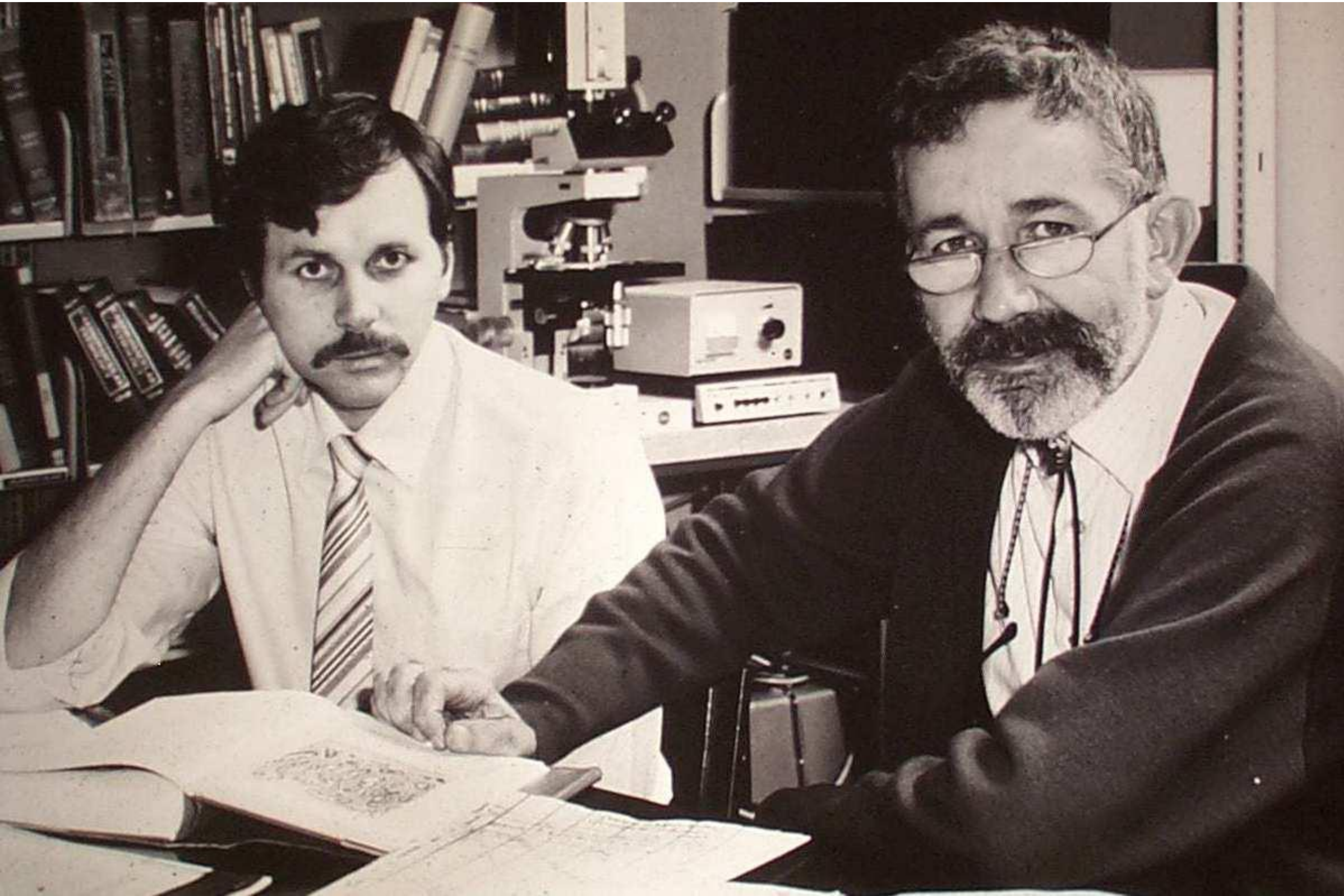
rosions
olita
stroin-
action
e com-
socie-
of the
of fre-
ach, (3)
ma of a
iculum
he gas-
drome.
s occur
a ratio

States. Gastric ulcers tend to occur more in unskilled workers and in the lower economic classes. Certain personality makeups are classically referred to as "ulcer types" — dependent, conflicted individuals and competitive, hard-driving, obsessive-compulsive achievers. (Along with "success" comes an ulcer.)

There are striking geographic differences in the incidence of ulcer among countries and within different parts of the same country. In Japan, for example, gastric ulcers are more common than are duodenal ulcers — the reverse of the distribution in the United States. Differing incidences have been reported in various locales of the United States, Great Britain, Australia, Norway, and other countries. These variations have not been satisfactorily explained but could relate to environmental factors such as the ulcerogenic influences of smoking and aspirin ingestion.

sumed causative mechanisms
gastric ulcers, it is best to consi
separately.
*Duodenal ulcer causation* m
relate to the delivery of exces
acid-peptic juice to the duoden
are thought to have importan
gastric capacity to secrete acid
(2) increased gastric mucosal r
stimuli, (3) increased gastric
and (4) decreased effectivene
mechanisms. Each of these
identified in some patients
ulcers but, it should be noted,
*Maximal and mean acid secr*
*al ulcer patients is approxim*
*found in normal individuals* a
higher than is found among pat
ulcers.[60] However, in less than

Dr. Barry Marshall, a young resident physician (internal medicine), and Dr. Robin Warren, a staff pathologist, at Royal Perth Hospital (Australia).



# *H. pylori* gastritis

- Responsible for most gastric and duodenal ulcers (not "type A" personality)
- Responsible for significant morbidity and mortality in the past due to bleeding from ulcers
- Responsible for most gastric adenocarcinomas and lymphomas
- Easily curable with antibiotics!

# *Clostridium difficile* Colitis

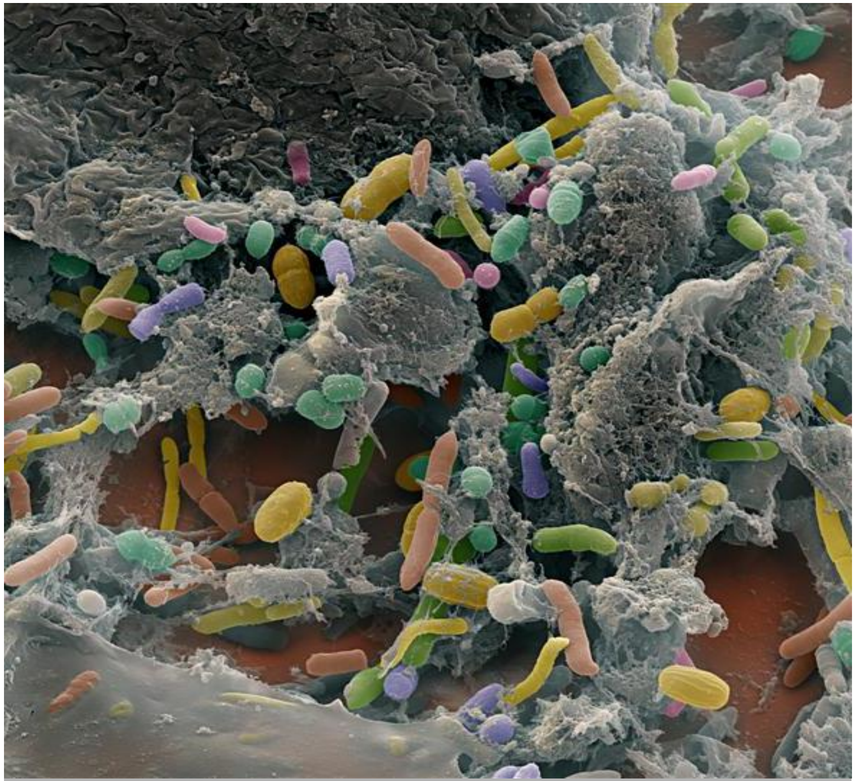
## (AKA antibiotic-associated colitis)

- Among the most common health-care associated infection
- Significant cause of morbidity and mortality among elderly hospitalized patients

- **20% of hospitalized adults are C. *difficile* carriers**
- **In long-term care facilities, carriage rate can approach 50%**

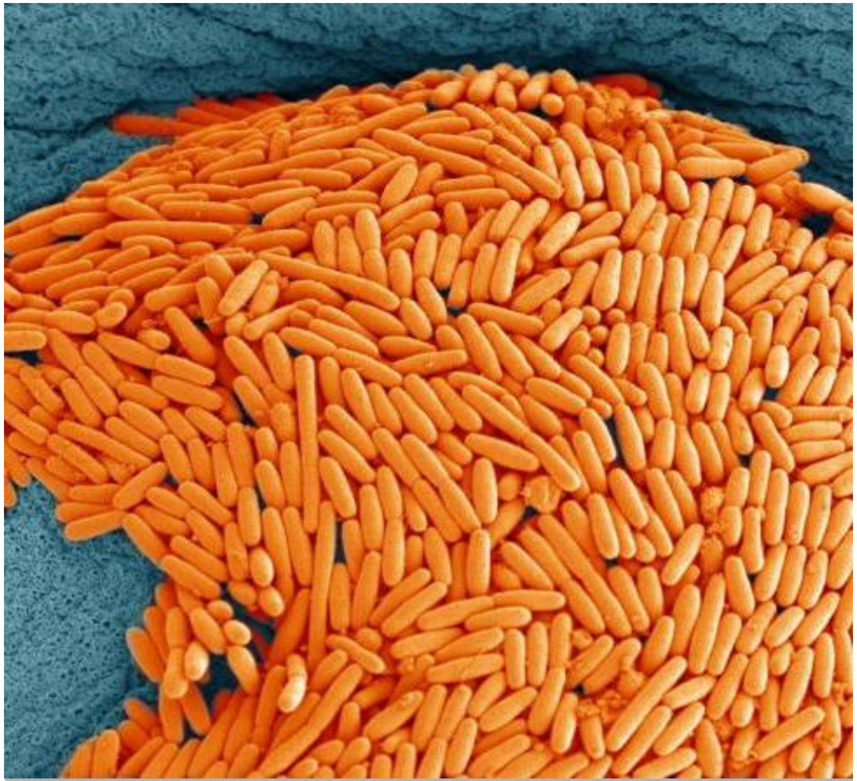
# C. *difficile* Colitis

## Symbiosis



C. *difficile* present in small numbers in ~20% of patients: kept "in check" by the rest of the "community"

## Dysbiosis

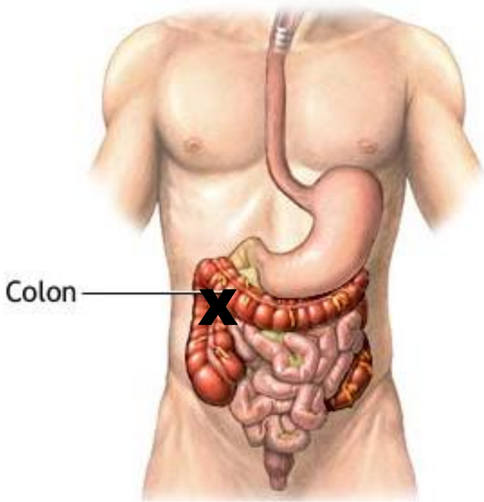


Antibiotics alter the normal gut flora: C. *difficile no longer kept "in check" and able to grow/colonize the colon*

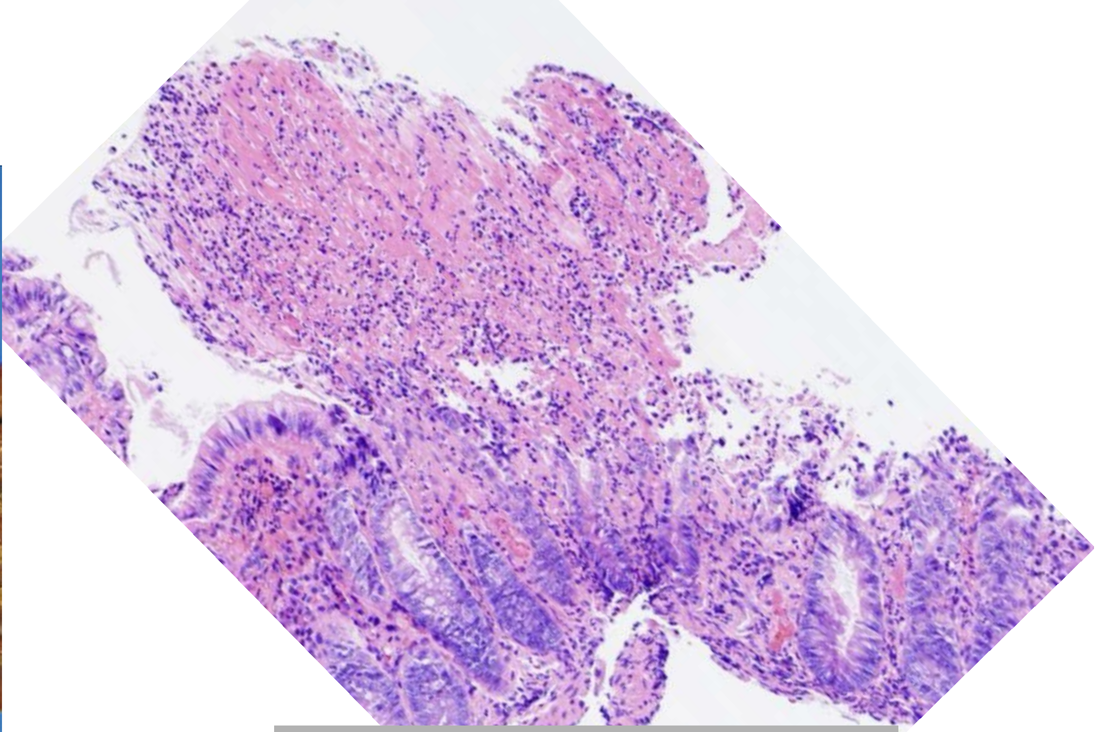
# C. *difficile* colitis

- Proliferation of C. difficile leads to **toxin** production
- Characteristic presentation
  - Fever, severe **diarrhea** and abdominal pain
  - **Recent antibiotic** use

**Normal Colon Biopsy**

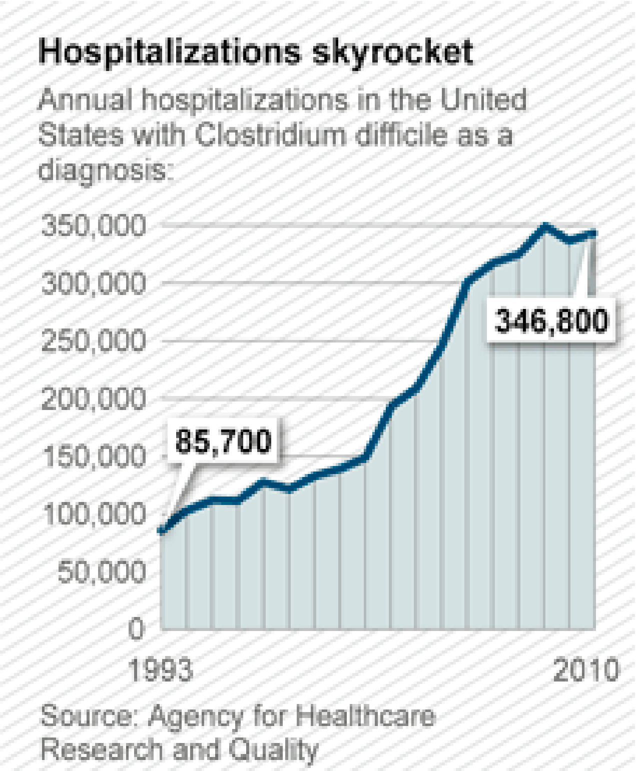


**Colon resection in patient with C. *difficile* colitis**



**Colon Biopsy with C. *difficile* colitis**

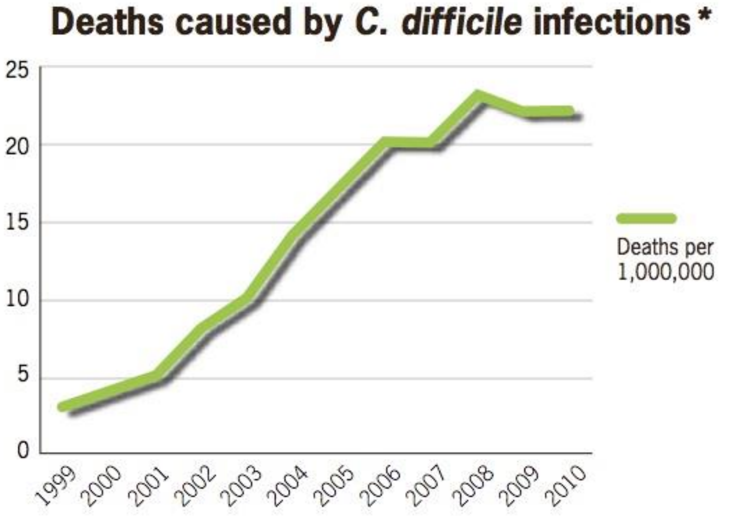
# C. *difficile* Colitis
# Increasing Incidence & Severity



**Hospitalizations skyrocket**

Annual hospitalizations in the United States with Clostridium difficile as a diagnosis:

Source: Agency for Healthcare Research and Quality



**Deaths caused by *C. difficile* infections***

*Age-adjusted rate of *C. difficile* as the primary (underlying) cause of death.

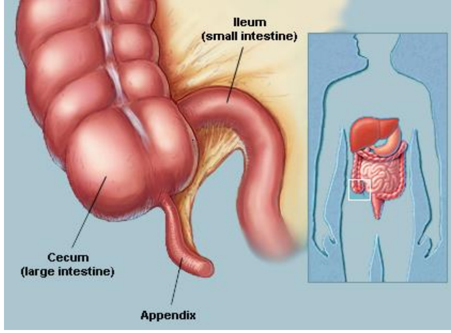
SOURCE: CDC National Center for Health Statistics, 2012

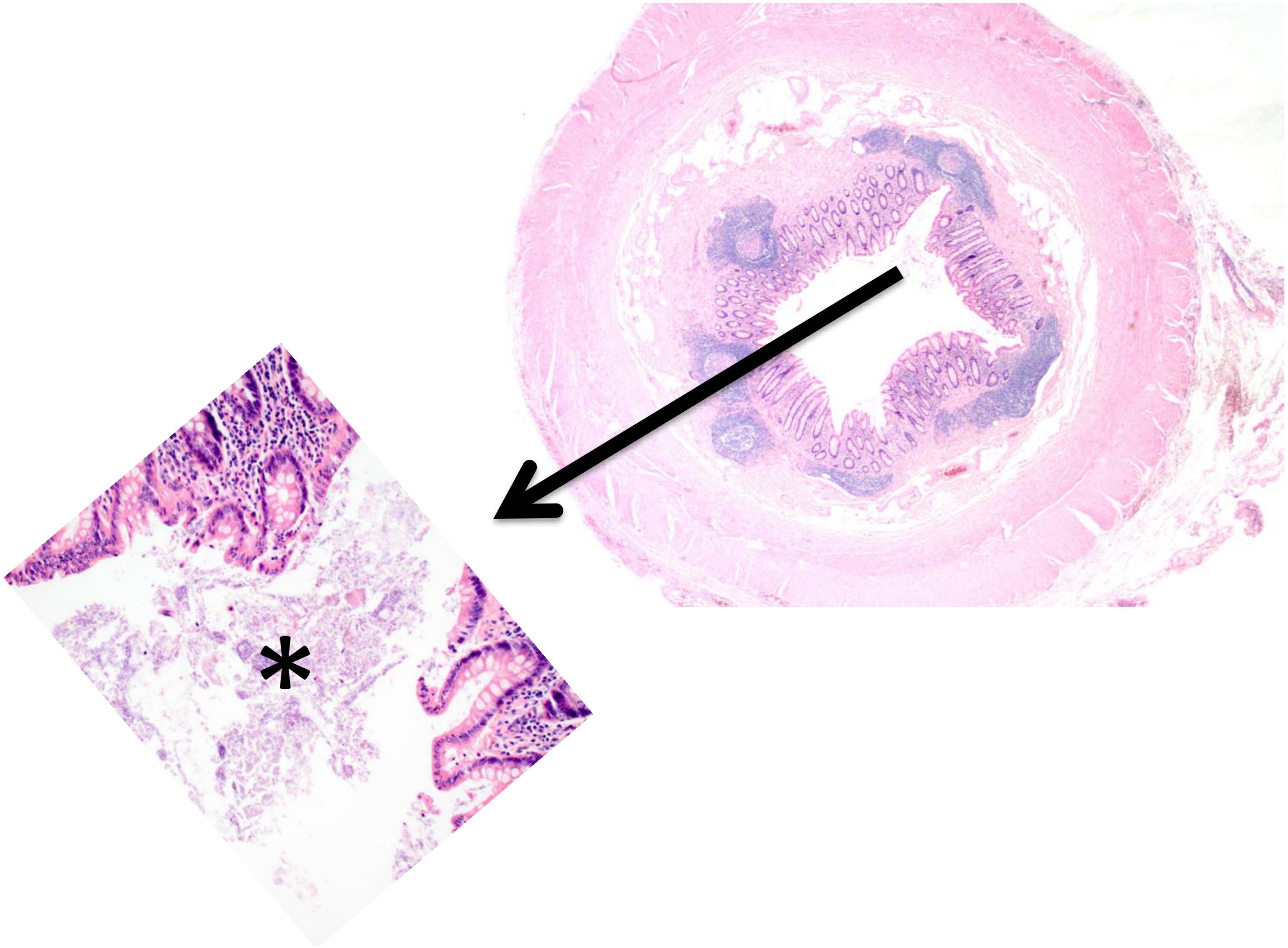
**2002: Hypervirulent strain of C .difficile colitis (NAP1) emerged**

# Limitations

*in daily practice*

“Normal”





**Cross-Section of Normal Appendix**

# Limitations

*in daily practice*

- **Which Bacteria?**
  - **~400-500 species make up the gut microbiota**
- **Symbiosis**

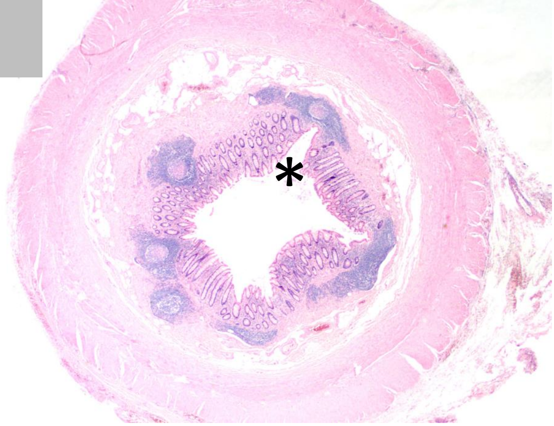
  **vs.**

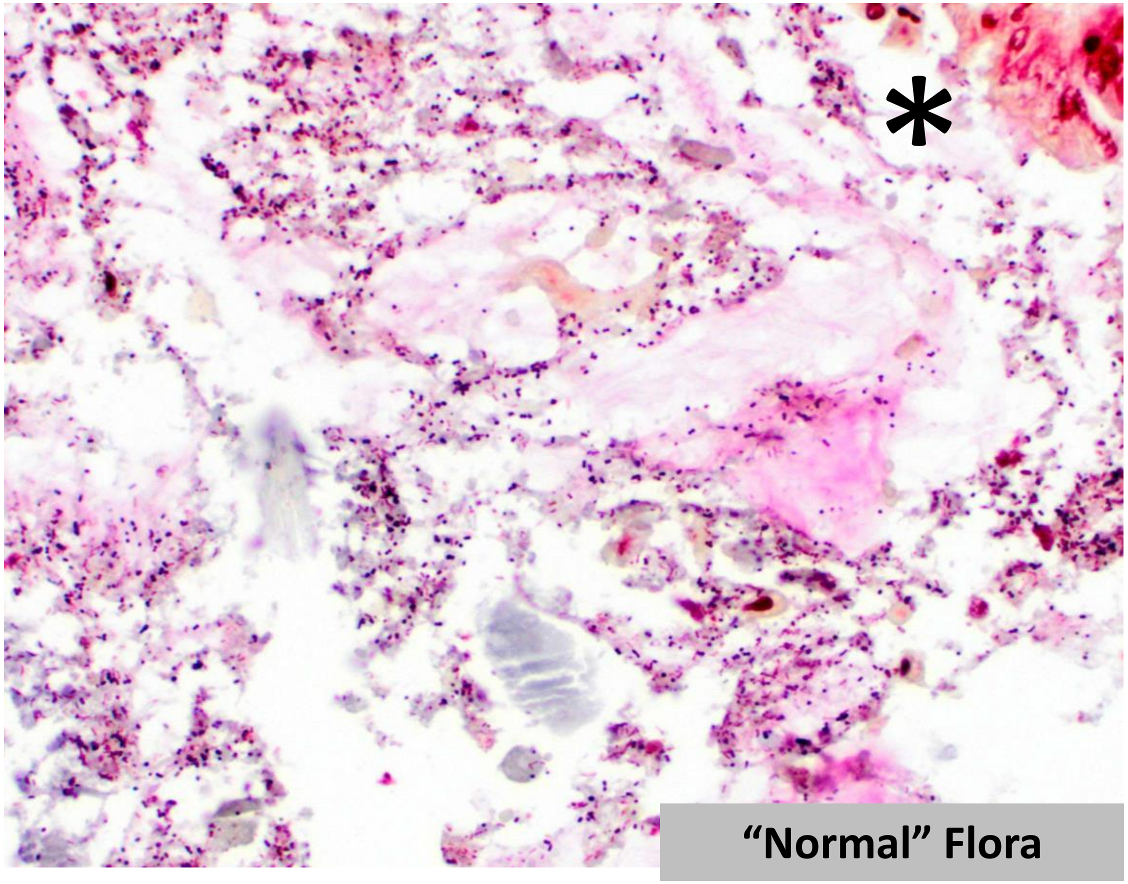
  **Dysbiosis**
- **Disease State**

  **vs.**

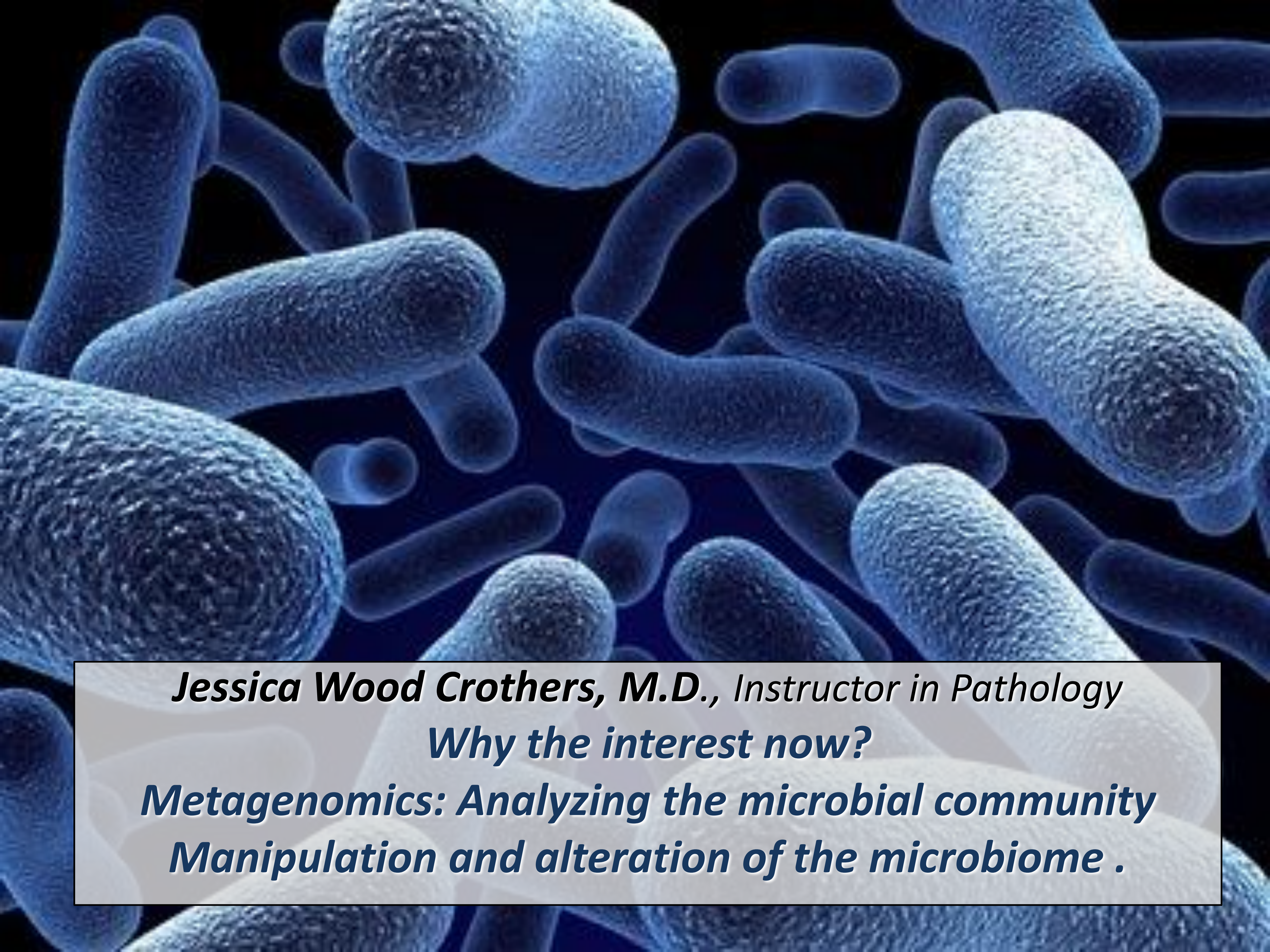
  **Dysbiotic State**

**Normal Appendix**





**“Normal” Flora**



***Jessica Wood Crothers, M.D.****, Instructor in Pathology*

## *Why the interest now?*

## *Metagenomics: Analyzing the microbial community*

## *Manipulation and alteration of the microbiome .*

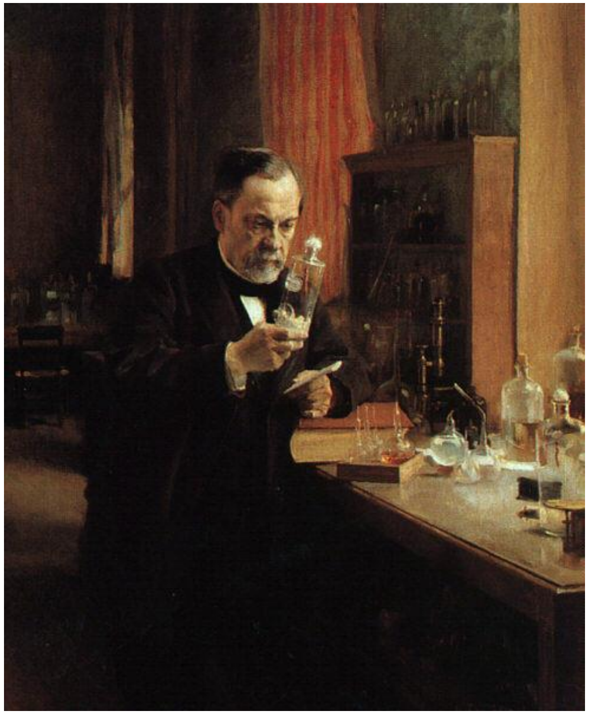
# Old Friends

- Ancient relationship btwn our bodies and microbes.
  - Immune system must do more than recognize self vs not self

# Microorganisms as Foe:

## Germ Theory

- Edward Jenner (1796)
- Louis Pasteur (1860-64)
  - Growth of microorganisms in nutrient broths did not proceed by spontaneous generation.



# The Age of Antibiotics

- 1928: First observation of the mold Penicillium’s ability to kill colonies of Staph aureus
- 1942: Mass manufacturing of Penicillin begins
- 1943: Streptomycin isolated from soil bacteria
- 1945: Nobel Prize for medicine given for work on penicillin
- 1955: Tetracycline patented and is most prescribed broad spectrum antibiotic in US
- 1957: Nystatin patented for treatment of fungal infections.

# And The War on Bugs

# Killing Bad Bugs is Good

- Pneumonia, diarrhea and malaria accounted for one third of all under-five deaths (WHO, 2011)

# Unintended Consequences

American kids receive 10-20 rounds of Abx by age 18

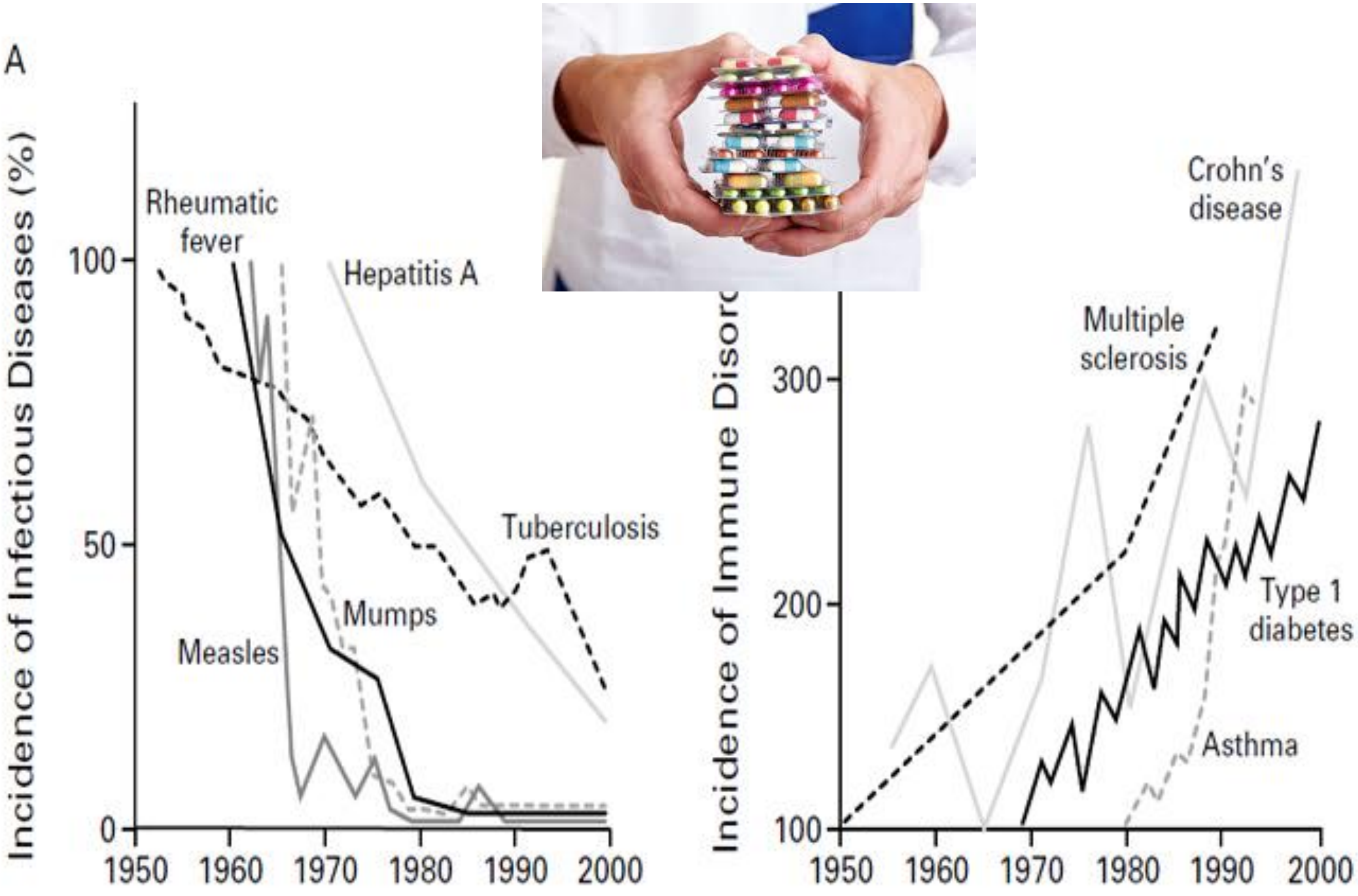


**Figure 1.** Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

- 1980s (Strachan)
  - Risk of allergic rhinitis inversely linked to birth order and the size of the family.

## Microflora Hypothesis (Nocerr and Huffnagle)

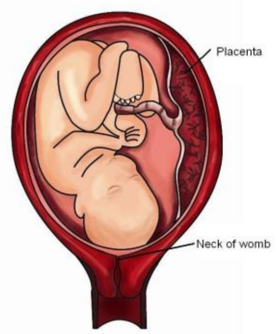
- Reduced exposure (family, diet, Abx) ->

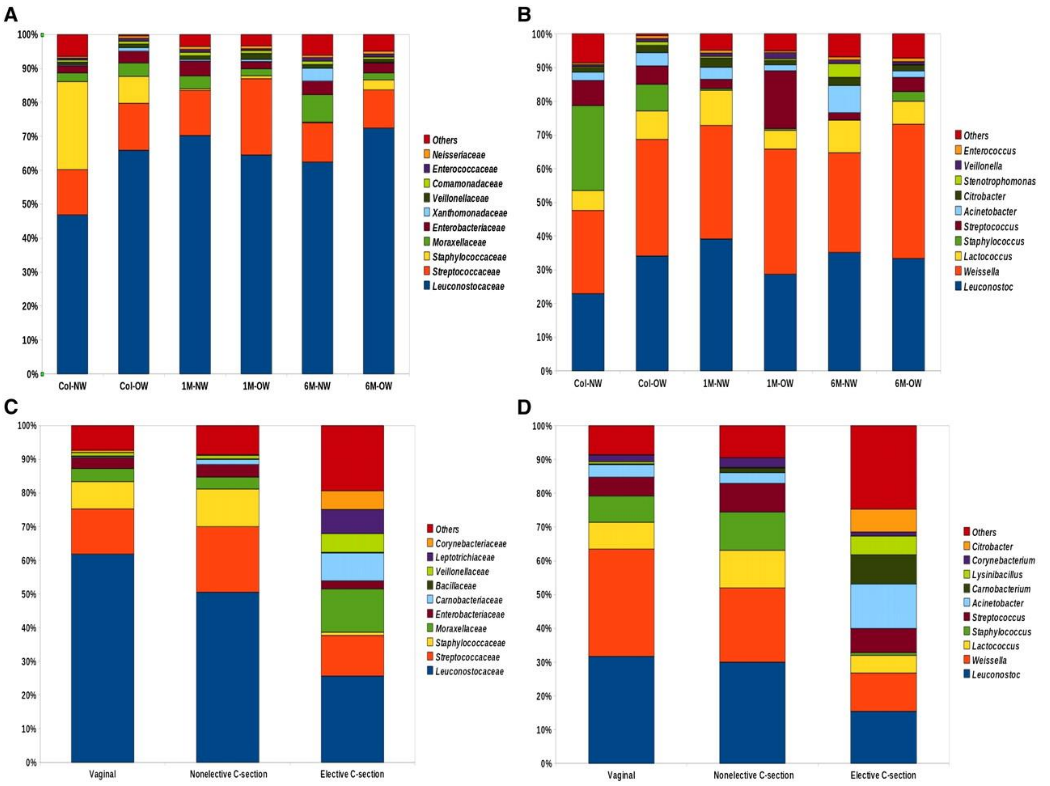
  "Immature" Microbiota ->

  Abnormal immunologic tolerance -> Atopy/Allergy

# The Building of Your Microbiome

- Stable microbiome established by ~ age 3
- Mode of delivery
- Breast feeding
- Environmental exposures (dogs, Abx)

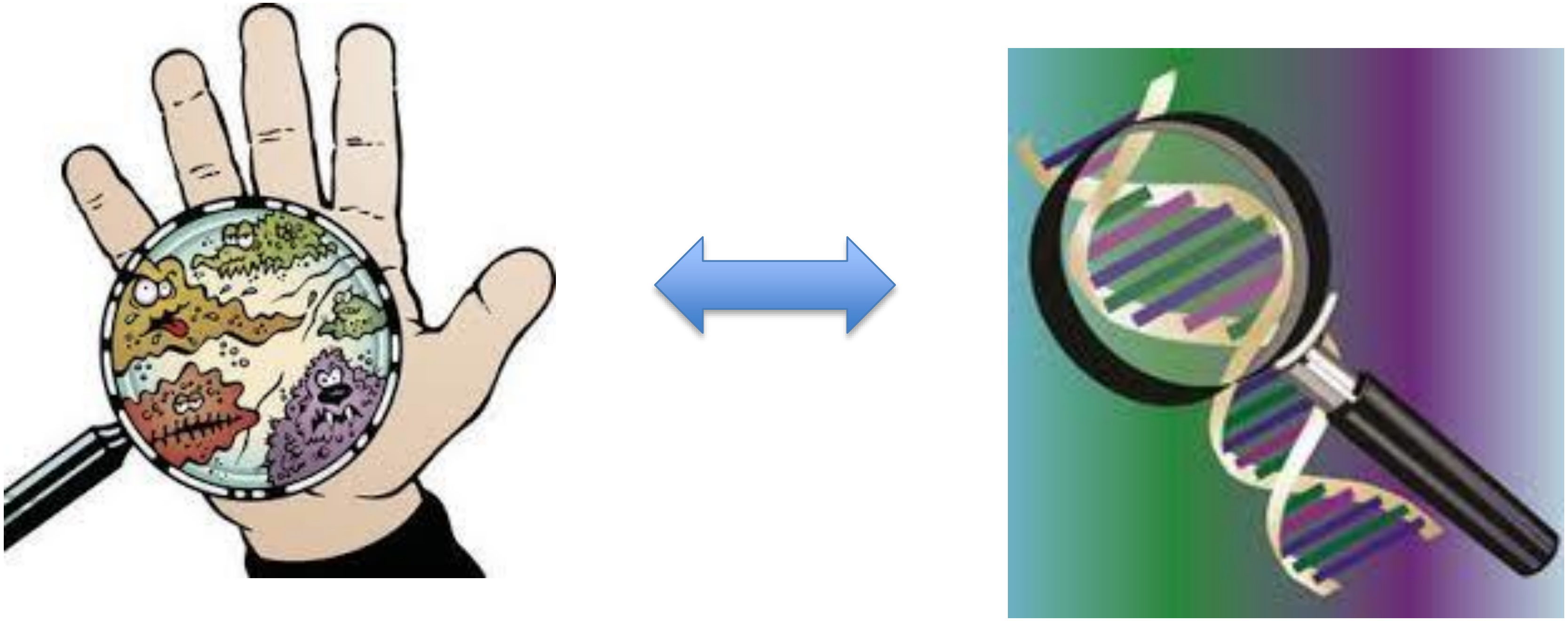




**Bacterial taxonomic composition of human breast milk.**

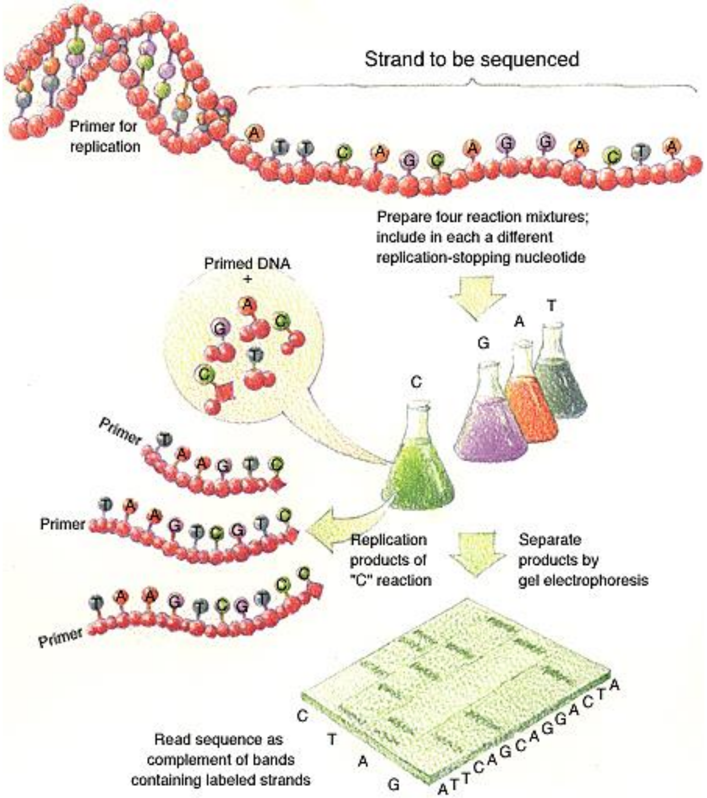
**Cabrera-Rubio R et al. Am J Clin Nutr 2012;96:544-551**

# How do we know?
# …..Genomics



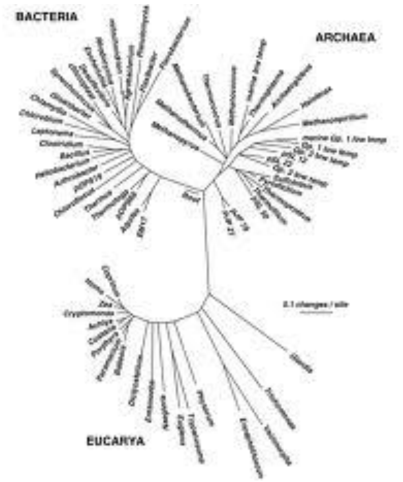
# Sanger Sequencing

- Chain termination sequencing
- 1975
- Very expensive
- Need large amount of DNA



# Marker Gene: 16s Ribosomal RNA

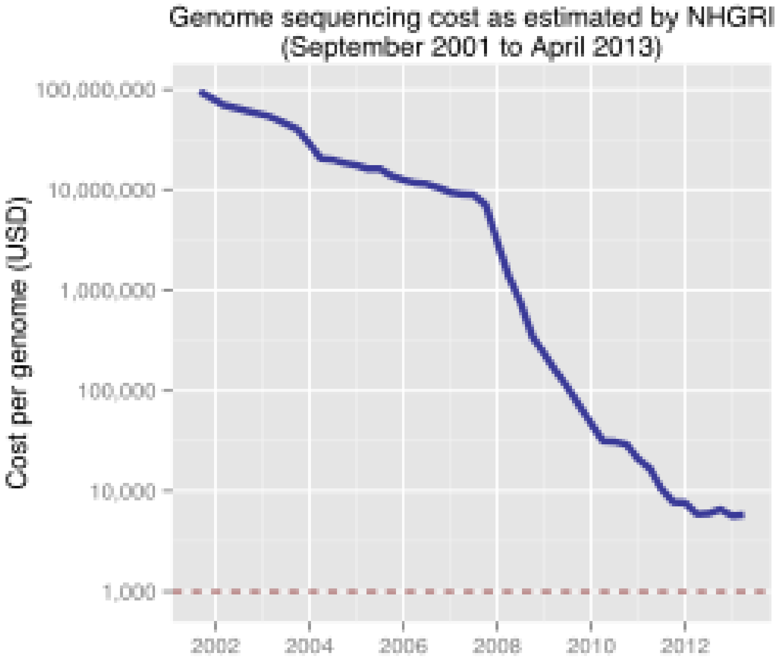
- Relatively short
- Highly conserved and different between species.
  - Norman Pace (Indiana Univ) late 1980’s



- Early studies discovered novel rRNA, indicating new, previously uncultured species present
  - 2-20% of organisms are culturable.

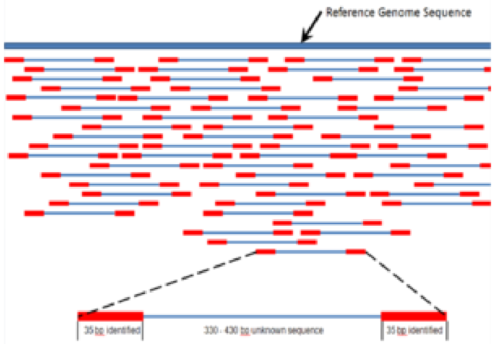
# Race is On

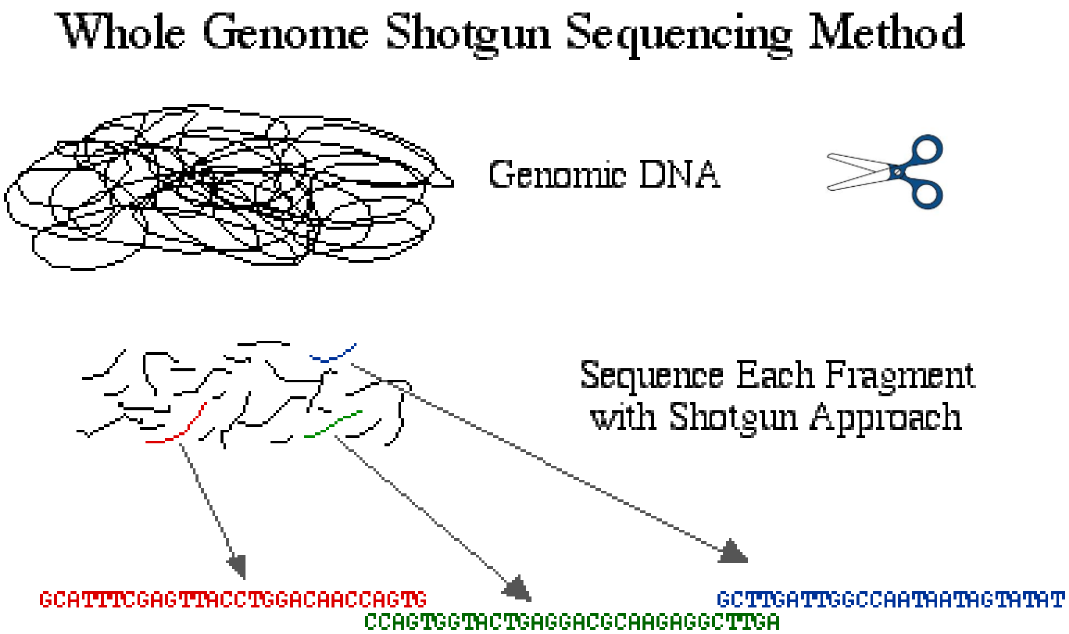
- 1995: first bacterial genome published (*Haemophilus influenzae*)
- 2000: *Drosophila* (fruit fly) genome
- 2003: Human genome



# Shotgun Sequencing

- Randomly shear DNA into "fragments"
- Together, "fragments" = DNA "library"
- Reconstruct reads into a 'consensus sequence' based on overlapping regions ("Contig")

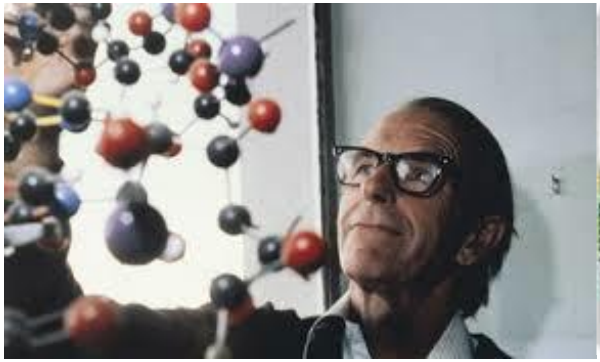




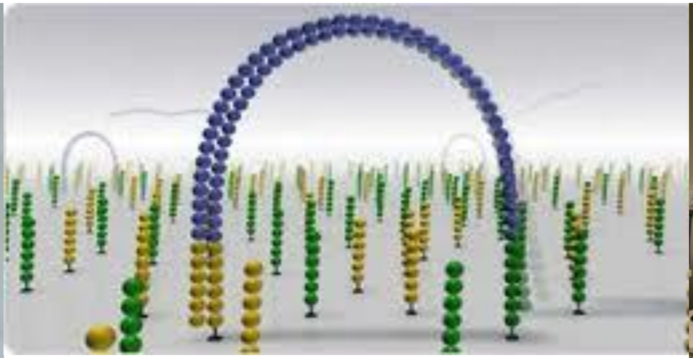
# Sanger to Next Generation

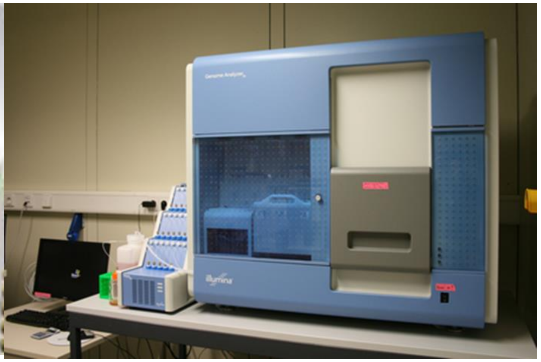
- Sequencing a single human genome:

  3 years to 3 days



*Frederic Sanger*





# Metagenomics

- First in print: 1998 ~ "Beyond"
- *"The application of modern genomics techniques to the study of microbial organisms directly in their natural environments, bypassing the need for isolation and lab cultivation of individual species."*
  - Kevin Chen and Lior Pachter (UC Berkely)

- 0.1 -20% of organisms are 'culturable'

# Community by Genomics

# Environmental Samples

200L of seawater contains > 5K different viruses.

Mya Breitbart

# Human Microbiome Project

- NIH funded ($170 million)
- 2007 (5 years project)

  Deep sequencing of PCR-amplified 16S rRNA
  Whole Genome (a single community and species specific)
  Metagenomics (Community)
  Skin, mouth, nose, colon, vagina

- Databases
- Tools
- Software
- Methods and systems for assembly

HMP

NIH HUMAN
MICROBIOME
PROJECT

# Gut MetaMicrobiome

>99 % of the gut biome is bacterial:

Total of ~1000 species in the collective sample (124 ind)

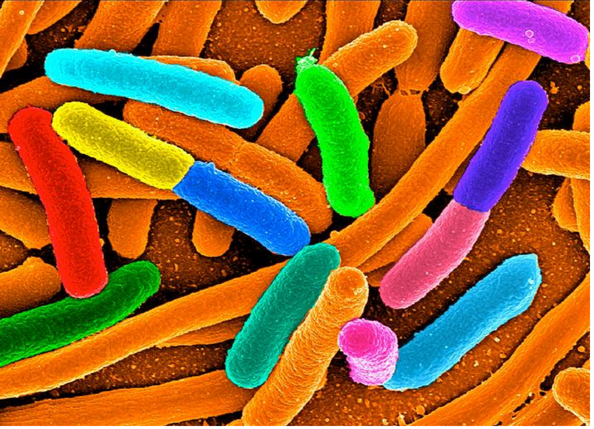
~ 160 species in each sample

18 species found in all individuals

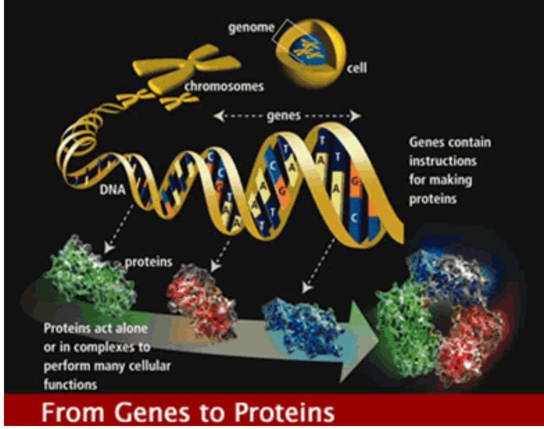
57 species found in >90% of individuals

75 species in 50% of individuals

- Prominent clusters of Bacteroidetes, *Dorea*/*Eubacterium*/*Ruminococcus* groups, bifidobacteria, Proteobacteria and streptococci/lactobacilli groups.



# Gut MetaGenome

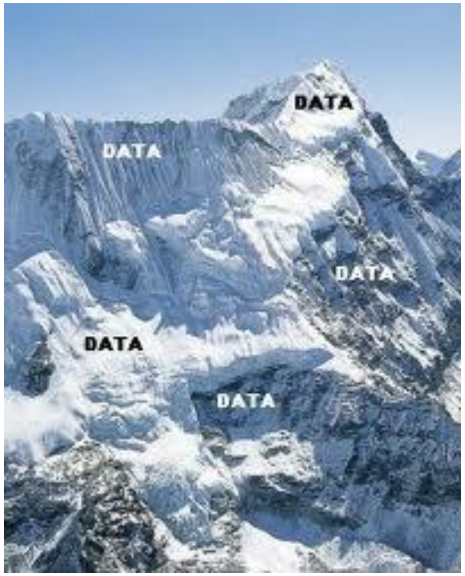


- 3.3 million gene sets (124 ind)
- Each individual harbors >500K genes
- Common Genes:
  - 60% present in ~ 50%
  - Encoded across many species
  - Homeostasis of the whole ecosystem (metab., phages)

- Novel Genes:
  - 60% present in < 20% of ind.
  - Many not well characterized

# Data Analysis

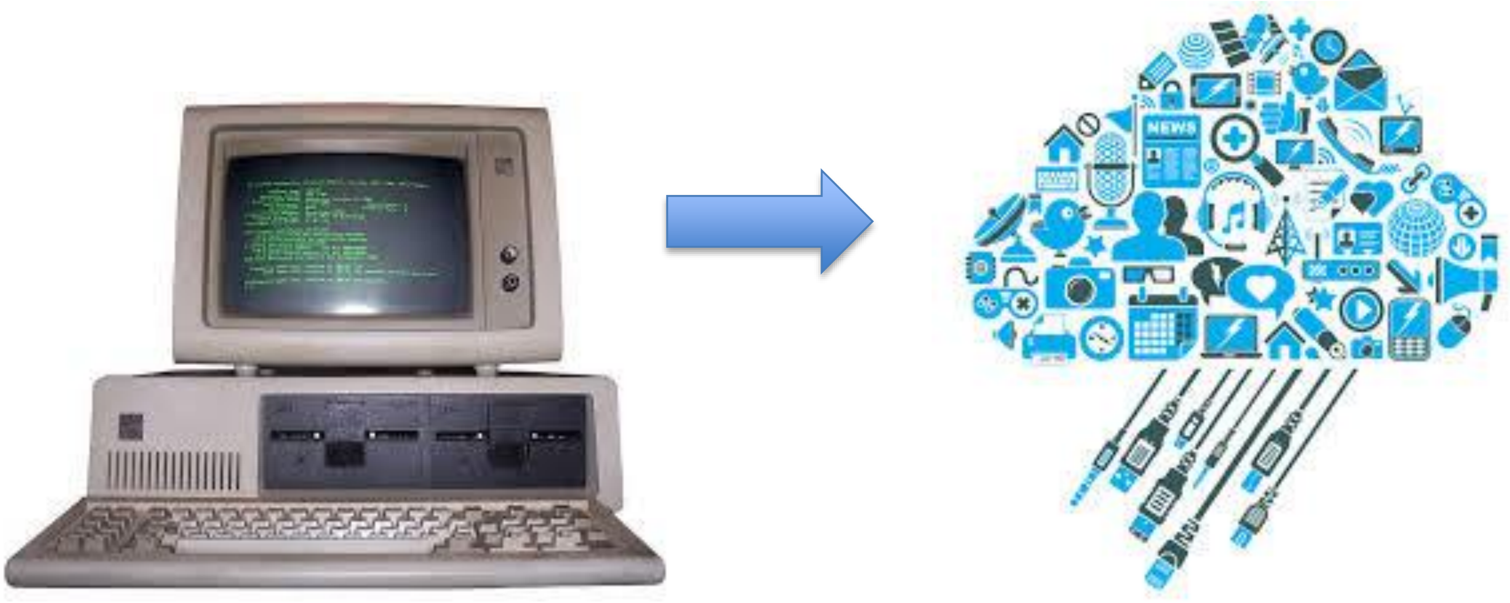
- Human genome => 21,000 genes
  - 6 billion base pairs
- Human gut => 3.3 million genes
  - 567 billion base pairs



# Cloud Computing

Amazon Web Services (AWS)

- Bioinformatics tool
- Open-source, freely available software
- Able to cluster ~ 69 million sequences in 3 hours.



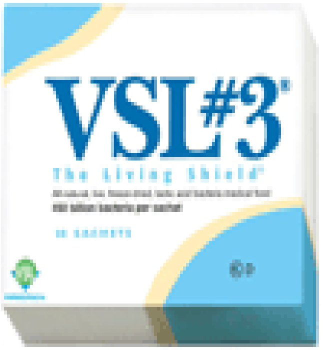
*On a standard desktop machine: 20 days of computation*

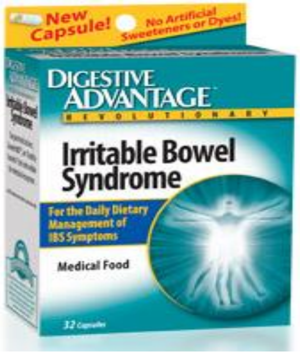
# Truly Translational

# *Can You Buy a New Microbiome?*
# Probiotics

- Live microorganisms which when ingested in adequate amounts confer a health benefit to host.

- Majority of probiotics are Gram +, lactic acid producers
  - Bifidobacterial species and *Lactobacillus* species
  - Survive transit through stomach and duodenum

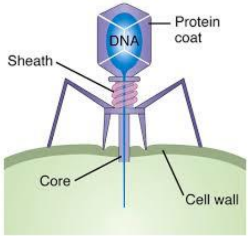




# Problems with Probiotics

- Poor quality studies
  - Small populations, different IBS subgroups, variable end points, different organisms
- Not all strains are the same!
- Products NOT regulated by FDA
  - Presence, viability of organisms variable
- Don’t colonize… must be taken indefinitely

- IBS > Ulcerative colitis > Crohn’s Disease



# Live Culture Foods

- Earliest evidence of humans fermenting food for preservation and storage: 7000–6600 BCE, China
  - Coevolution
- Extremely diverse
  - >200 organisms isolated in a serving of kimchi
  - Microbes of live culture foods do not take on permanent residence
  - Exchange of genetic material via bacteriophages

*Can you feed your microbiome?*

# Prebiotics

- Ingested substances that selectively stimulate the proliferation and/or activity of desirable bacterial populations present in the host intestinal tract……*Feed your gut!!*

- Non-digestible oligosaccharides (NDOs)
  - Lactulose, galacto-oligosaccharides, lactosucrose…

# Prebiotics = Fiber

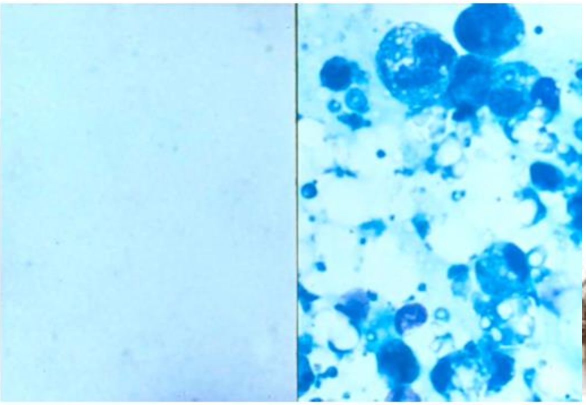
- Inulin: Plant polymers mainly comprising fructose units, usually have a terminal glucose
- Indigestible fiber
- Gut flora produce H2, CO2, methane gas from inulin

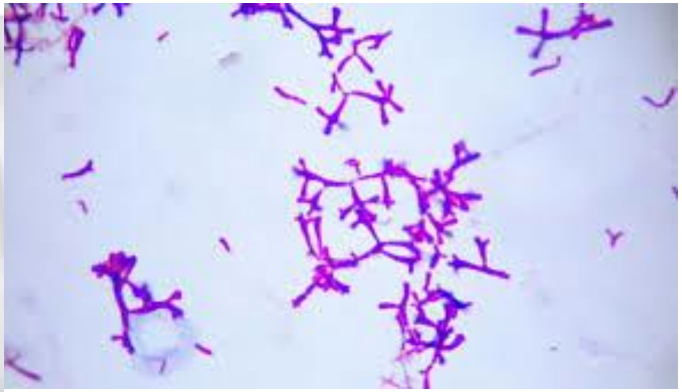
# Prebiotics = Food = Fiber

Less cooked foods (al dente, steel-cut, raw) have more insoluble fiber than cooked, or processed foods

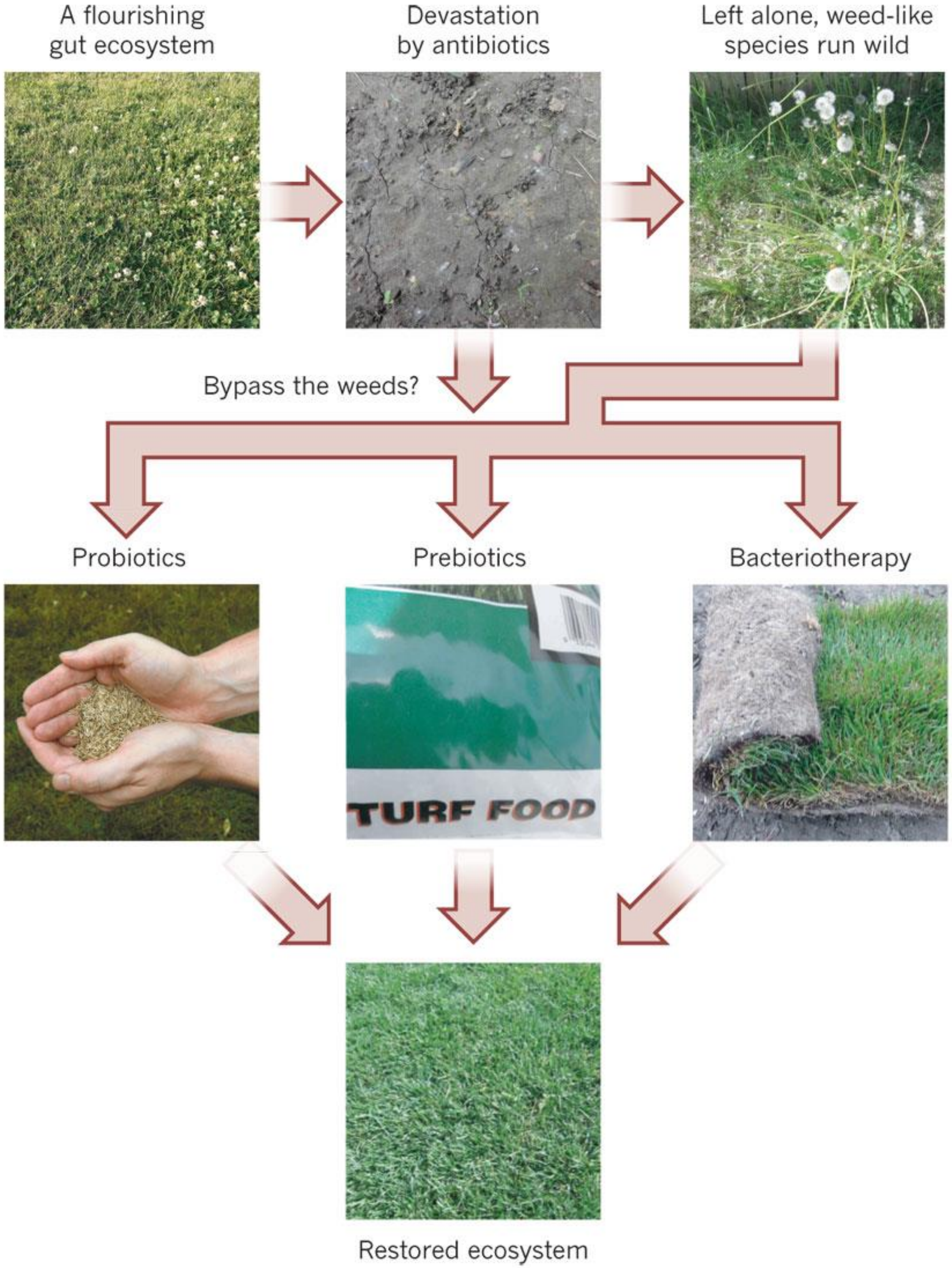
# Breast Milk: The First Prebiotic

- Breastfeeding: Human milk oligosaccharides (~21%) and Bifidobacterium longum
  - Grab and flush “bad bacteria”
  - Selectively feed “good” bacteria (enzyme to eat HMO)





HMOs → Bifidobacterium longum


A flourishing gut ecosystem
Devastation by antibiotics
Left alone, weed-like species run wild
Bypass the weeds?
Probiotics
Prebiotics
Bacteriotherapy
TURF FOOD
Restored ecosystem

A flourishing gut ecosystem

Devastation by antibiotics

Left alone, weed-like species run wild

Bypass the weeds?

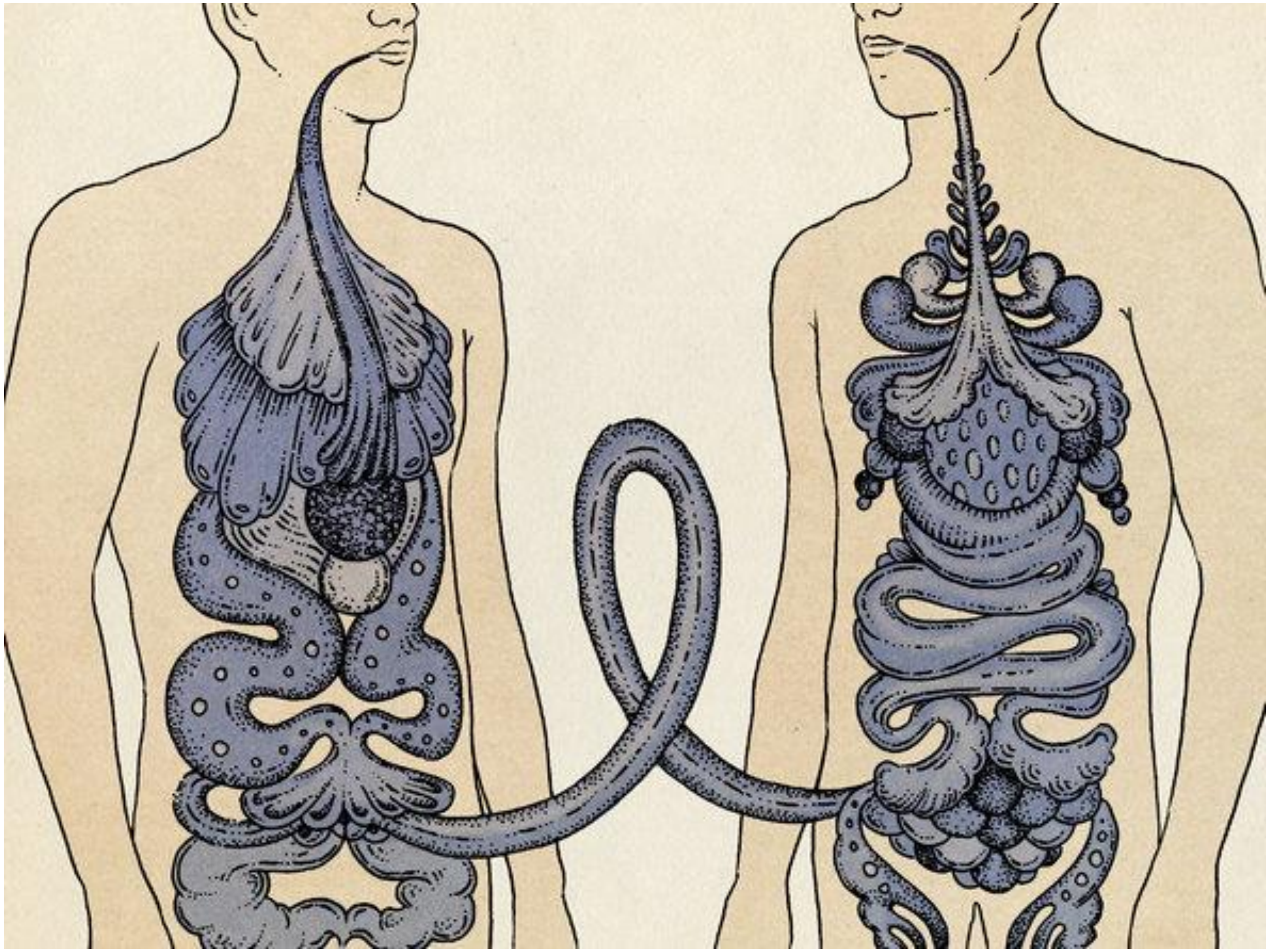
Probiotics

Prebiotics

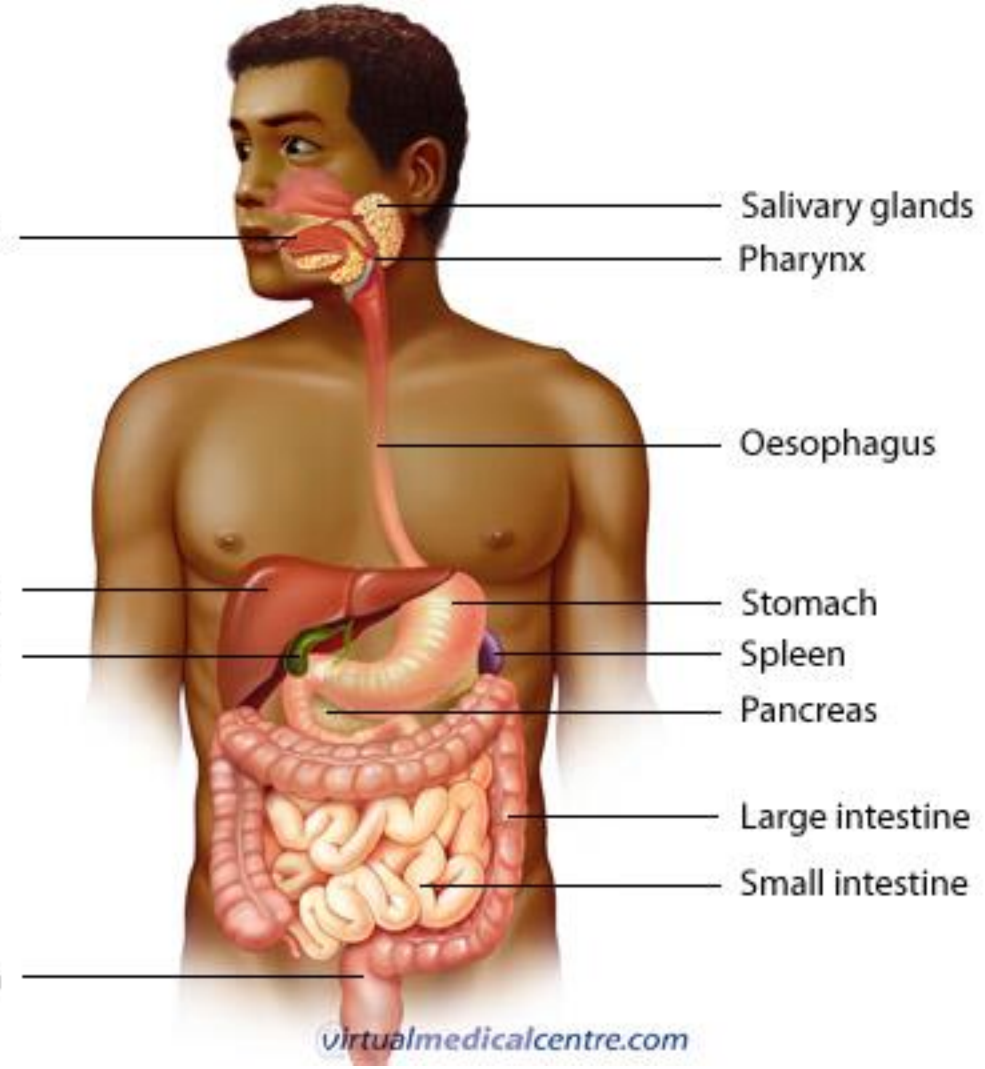
Bacteriotherapy

Restored ecosystem

# Fecal Microbiota Transplant (FMT)



# FMT: The Details



- Donor stool (fresh, <6 hrs)
  - Screened for infectious disease
  - Hepatitis, HIV, *C. diff*, parasites
- Bowel prep for recipient
- Stool mixed with saline into a "slurry" consistency
- Infusion of mixture into recipient
  - NG tube, Enema or Colonoscope

# …A Bit of History

- 16th c. Ming dynasty, traditional Chinese medicine
  - "yellow soup": fermented fecal concoctions used for digestive problems.
- 17th c. German physician Christian Franz Paullini compiled a stool recipe book for treating dysentery and other digestive ailments.
- 20th c. Fecal therapy used to treat GI disease in livestock

# Ben Eiseman, MD

- Chief of Surgery at Denver General Hospital
- 1958: Journal of Clinical Gastroenterology
  - 4 pts cured of pseudomembraneous colitis via fecal enemas

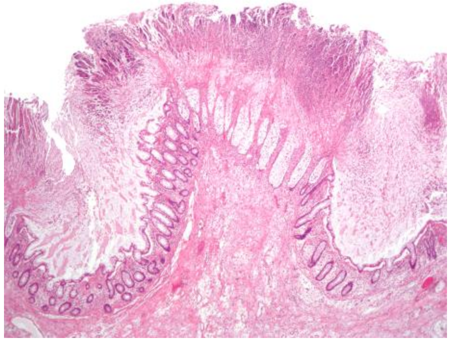
The NEW ENGLAND JOURNAL of MEDICINE

- **Prospective, randomized, controlled trial**

1) **FMT**: Short-course of vancomycin (500 mg orally q6 x 4d) =>FMT

2) **Standard vancomycin**: 500 mg orally q6 x 14 days)

3) **Vancomycin with bowel lavage**: Bowel lavage performed on d 4



van Nood E, Vrieze A, Nieuwdorp M, et al.

**Duodenal infusion of donor feces for recurrent Clostridium difficile.**

N Engl J Med 2013;368(5):407-415.

The NEW ENGLAND JOURNAL of MEDICINE

- The **study was stopped** after an interim analysis.
  - 13/16 (81%) of FMT patients had resolution after first infusion.
  - 3 remaining patients received a second infusion with feces from a different donor, resolution occurred in 2 patients.
- Recurrence rate 5 weeks following treatment:
  - 62% in vancomycin alone
  - 54% in vancomycin + bowel lavage
  - 1 patient (6%) in FMT

# FMT for rCDI

- Average cure rate: 92%
- No serious adverse events to date have been reported.

~500 rCDI pts worldwide have received FMT

~3,000 F.M.T.'s have been performed worldwide

# How does FMT work?

- Antibiotics, environment and/or other iatrogenic factors => disturbed natural colonic flora
- Loss of healthy gut flora allows proliferation of pathogenic organisms such as *C. difficile* (Loss of repressive forces).

- Reestablishing a healthy microbial population enables gut to suppress *C. difficile.*

# FMT at FAHC

# Future Horizons: “Bugs to Drugs”

- Genomic Technology + Quality studies ➔ New Therapeutic Agents:

  *Anti-inflammatory*

  *Immune modulators*

  *Cytoprotective agents*

  *Antimicrobial agents*

  *Disease prevention*

# Conclusions

- Emerging knowledge of the micrbobiome is changing the way we think about ourselves, our health and how we live and interact with the world around us.

- Old world view:

  Bacteria = Pathogen

- New world view:

  Some Bacteria = Pathogen (cause disease)

  Some Bacteria = Co-resident (mutually beneficial)

  Some Bacteria = Targeted therapy (help fight or prevent disease)

# Conclusions

- We build and sustain our microbiomes over time
  - Delivery method and breast feeding
  - Probiotics, Prebiotics, Live culture foods
  - Antibiotics

- Alterations in the microbiome are related to various disease states
  - Diabetes, IBD, Obesity
- Changing the microbiome can treat and/or prevent disease
  - Metabolic syndrome, Obesity, *C. difficile* infx

# Conclusions

- Metagenomics + High Quality Studies => Bourgeoning New Field of Medicine
  - Chronic diseases (Metabolic syndrome, Diabetes, Obesity)
  - Autoimmune diseases (IBD, Allergy)
  - Behavioral/Psychiatric disease (Depression, Anxiety)

# Questions?

# The Mighty Microbiome

- Irinotecan and bacterial glucuronidase
  - Reactivation in GIT causes dose-limiting diarrhea
  - Prevented with Rx inhibitors of microbial enzyme


www.cookingkorean.com


MADHUR JAFFREY'S
World Vegetarian
heart of the artichoke
and other kitchen journeys
david tanis
AUTHOR OF
A Platter of Figs and Other Recipes
PLENTY

# *Eat real food, not too much, mostly plants.*