THE MICROBIOME

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Bioscience in the 21st Century
11/28/16
LEARNING OBJECTIVES

• Define the microbiome

• Discuss the diversity in the human microbiome

• Explain the effect of antibiotics on the microbiome

• Describe the relation of the microbiome to autoimmune diseases like Crohn’s Disease
You are mostly microbe...

- Microbe: bacteria, archea fungi, viruses etc.
- #bacterial cells: 100 trillion
- # human cells: 37 trillion
- 5:1
  - microbial :human cells
The Human Microbiome

- All the microbes that live in/on us
  - All of their genetic material

- Thousands of different species
  - 2.5 lbs/3 pints
  - Skin, nasal passages, lungs, digestive and urogenital tracts
  - Most in in gut
The Microbiome Has An Important Role in Human Health

• Various roles:
  – Keep away pathogens
  – Needed for oral health
  – Helping to extract energy/nutrients from food

• Co-evolved
  – ~1 million bacterial species
Microbial Communities Are Diverse

They may look alike, but the two species of bacteria *Bacteroides fragilis* and *Escherichia coli* are about as similar at the genetic level as humans and nematode worms.
Microbial Communities Are Diverse
Adult Microbial Communities Similar Between People Based On Position
Initial Microbial Community Established From Mother to Child
Baby’s Microbial Communities Similar To Mother’s For Several Years

adapted from Gonzalez et al. 2011, EMBO reports
Microbial Diversity In Gut During First 15 Months Of Life

- **ALL** baby’s microbial communities similar, resemble mother’s skin or vaginal
- Does not gain diversity of adult until ~ 3 years

Microbial Dysbiosis
Microbial Dysbiosis

Introduction of pathogens and/or disease leads to dysbiosis and inflammation.
Pattern of Gut Microbiome Dysbiosis Observed In Autoimmune Disease

• Autoimmune diseases
  – e.g. systemic lupus erythematosus, celiac disease, Type I diabetes, Crohn’s disease

• Underlying cause of most poorly understood

• Genetic link; environment critical whether predisposition will lead to disease

• Gut bacteria differ from healthy individuals
Crohn’s Disease

• Chronic inflammatory bowel disease

• Immune cells overly sensitive to bacteria
  – pathologic inflammation in GI tract lining

• Often onset of disease follows course of antibiotics

Approximately 700,000 people in the United States
Long-term Effects of a Course of Antibiotics on an Adult Gut

## Rates for Asthma, Allergic, and Autoimmune Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence</th>
<th>Country</th>
<th>Year</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>4%</td>
<td>UK</td>
<td>1964</td>
<td>Devenny et al. 2004</td>
</tr>
<tr>
<td>Asthma</td>
<td>24%</td>
<td>UK</td>
<td>1999</td>
<td>Devenny et al. 2004</td>
</tr>
<tr>
<td>Asthma</td>
<td>3%</td>
<td>Nepal</td>
<td>2003</td>
<td>Masoli et al 2004</td>
</tr>
<tr>
<td>Asthma</td>
<td>8%</td>
<td>Pakistan</td>
<td>2003</td>
<td>Masoli et al 2004</td>
</tr>
<tr>
<td>Asthma</td>
<td>28%</td>
<td>Australia</td>
<td>2003</td>
<td>Masoli et al 2004</td>
</tr>
<tr>
<td>Crohn's Disease</td>
<td>64.9/100,000 (men)</td>
<td>USA</td>
<td>1980</td>
<td>Gollop et al. 1988</td>
</tr>
<tr>
<td>Crohn's Disease</td>
<td>90.5/100,000 (women)</td>
<td>USA</td>
<td>1980</td>
<td>Gollop et al. 1988</td>
</tr>
<tr>
<td>Crohn's Disease</td>
<td>241.3/100,000</td>
<td>USA</td>
<td>2008–2009</td>
<td>Kappelman et al. 2013</td>
</tr>
<tr>
<td>Crohn's Disease</td>
<td>1.38/100,000</td>
<td>China</td>
<td>1950–2002</td>
<td>Zheng et al 2011*</td>
</tr>
<tr>
<td>Crohn's Disease</td>
<td>2.29/100,000</td>
<td>China</td>
<td>2003–2007</td>
<td>Zheng et al 2011*</td>
</tr>
<tr>
<td>Eczema</td>
<td>5%</td>
<td>UK</td>
<td>1964</td>
<td>Devenny et al. 2004</td>
</tr>
<tr>
<td>Eczema</td>
<td>21%</td>
<td>UK</td>
<td>1999</td>
<td>Devenny et al. 2004</td>
</tr>
<tr>
<td>Type 1 Diabetes</td>
<td>0.35/1000 (boys)</td>
<td>USA</td>
<td>1935–1936</td>
<td>Gale 2002</td>
</tr>
<tr>
<td>Type 1 Diabetes</td>
<td>1.2/1000</td>
<td>USA</td>
<td>1989–1992</td>
<td>Gale 2002</td>
</tr>
<tr>
<td>Type 1 Diabetes</td>
<td>1.93/1000</td>
<td>USA</td>
<td>2009</td>
<td>Dabelea et al 2014</td>
</tr>
</tbody>
</table>

Source: Chunco & Uno. National Center for Case Study Teaching in Science, University at Buffalo, State University of New York

### What patterns of disease occurrence can you observe from the table above and the paper referenced? List three hypotheses that might explain these patterns.
The Hygiene Hypothesis

• Current hypothesis:
  - *In the absence of exposure to a species-rich environment full of pathogens and parasites, the human body will tend to shift toward a more inflammatory state associated with allergies, asthmas, and autoimmune diseases*

• Developed in 1980s
  • increasing incidence of asthma/allergic disorders in industrialized countries
Factors Linked To Lower Rates of Asthma and/or Allergies in Children

• Include:
  ① being raised on a farm
  ② vaginally delivered babies (versus C-section)
  ③ attending daycare or having older siblings
  ④ living in a home where dishes are hand-washed (versus in a dishwasher)
Amelia's Case

Amelia just returned to the US from a family vacation in Mexico. By the trip’s end they all had begun to suffer from nausea and diarrhea. They were diagnosed with food poisoning and placed on antibiotics. While her family started feeling better relatively quickly, Amelia continued to suffer from gastrointestinal distress. She found that she couldn’t leave her home because she was constantly running to the bathroom (10–12 times per day), felt tired, had severe abdominal cramping, and had lost her appetite.

After visiting a gastroenterologist, Amelia was diagnosed with Crohn’s disease.

Do you think the hygiene hypothesis could be applicable to Amelia’s Crohn’s diagnosis? Why or why not?
Treatment For Crohn’s Disease: Steroids

• Well established treatment for Crohn’s and other autoimmune conditions

• Suppresses immune system by decreasing the production of inflammatory proteins
  – Decreases general immune cell activity in body.

• Can cause weight gain, high risk for secondary infection.
Experimental New Treatments: Fecal Microbiota Transplant

- Transplant from healthy donor restores more diverse microbial community

- Stool collected from tested donor, administered rectally or orally

- 2013: FDA classified fecal matter as an Investigational New Drug (IND)

- Success for other inflammatory GI disorders (not Crohn’s)

[Link to NPR article](http://www.npr.org/sections/health-shots/2014/10/11/355126926/frozen-poop-pills-fight-life-threatenin-ginfections)
Experimental New Treatments: Helminthic Treatment

- Deliberate infection with parasitic worm, orally or through the skin.

- Hypothesized to change immune system activity

- Because of co-evolution, proponents argue worms needed for healthy immune system

- Mouse studies with IBD; clinical trials (MS); anecdotes

- **Not** FDA approved.

Chunco & Uno. National Center for Case Study Teaching in Science, University at Buffalo, State University of New York
Steroids, fecal transplants, and helminth therapy are three very different approaches to the same disease.

① What do you think the major differences are in these three different approaches?

② If you were deciding on a treatment plan, what additional information would you need to make an informed choice?
If we think of the human body as an ecosystem, what ecological parallels can you draw between the consequences of decreased biodiversity in nature and your body?

*(For example, imagine you were looking at fish species in a coral reef or species of birds in a tropical forest rather than species of bacteria in the gut of a person.)*

What are some possible implications of decreased biodiversity for human health?
Preserving The Microbiome

• Diet rich in fiber, fruits and vegetables

• Consuming microbes
  – Fermented foods like yogurt, cheese, sauerkraut & kimchi

• Probiotics (use with caution)
YOU SHOULD NOW BE ABLE TO

• Define the microbiome

• Discuss the diversity in the human microbiome

• Explain the effect of antibiotics on the microbiome

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