Host-Pathogen Interaction and Human Disease

Part 1. What is a Pathogen?

Trying to Understand Human Biology by the Study of Pathogenic Bacteria

Humans are Heir to a Veritable Sea of Smaller Creatures

Bacteria – the smallest free-living organisms

Viruses – Obligate Intracellular Parasites

Parasites like the Protozoa, Worms and Flukes

And even insects that live in your eyebrows, hair and elsewhere
90% of the Cells Humans Carry are Microbes

1. The makeup of our flora depends upon various factors, including genetics, age, sex, stress, nutrition, and diet of the individual.

2. Our flora synthesize and excrete vitamins that can be absorbed as nutrients by the host.

3. The flora often reflects specific anatomic sites.

4. The Normal Microbial Flora contributes to the first line of innate immune defense against incursion by ‘foreign’ microorganisms.
What is the Difference Between a Pathogen and a Commensal?

Pathogens can establish themselves in a niche usually devoid of commensal microbial populations.

Pathogens possess the inherent ability to cross anatomic barriers or breach other host defenses that limit commensals.

What is the Difference Between a Pathogen and a Commensal?

It’s in the Genes!

The Pathogen–Commensal–Host Ecological Landscape

Three Phases of Host Defense

Phase 1 Non-induced Innate Immunity

- Removal of pathogens utilizing microorganisms by innate defense
- Normal flora competes with pathogens
- Microbes, e.g., lactobacilli, etc., which prevent colonization of gram-negative bacteria
- Normal flora inhibits microbial growth
- Mucus and protective mucus
- Interleukin-1 β (IL-1 β) inhibits microbial growth
- Normal flora competes with pathogens
Bacteria and Other Microbes Have Unique Structures

That form the basis for how host's detect microbes who 'go to far'

Phase 2 induced Innate Immunity
Phase 3: Induced Adaptive Immunity

Thus, a significant part of human evolution has gone into developing ways to thwart microbial intrusion.

And, of course the type of host matters.

Bacterial pathogenicity – A “Lifestyle”

Entry into Host

Humans have nine “Portals” serve as a point of entry for one or more pathogenic microbes.

Entry into Host
Colonize

Attachment to a unique host cellular target usually determines the niche.

They may get there by swimming

Many bacterial pathogens are motile

Colonize

To avoid physical and immunological removal, bacteria must adhere near or to host cells
Persist- Despite Host Defenses
Avoid- hide, mimic

Persist- Despite Host Defenses
Circumvent the host
Enzymes and toxins allow local tissue spread and perturb immune function

Persist- Despite Host Defenses

The Streptococcus Strategy to Circumvent the host

Hide- Microbial Invasion

The Streptococcus Strategy to Circumvent the host
**Hide-Microbial Invasion**

**Why?**
- escape immune surveillance
- nutrients
- parasitize host cell machinery
- transportation

**How?**
- tight adherence
- pick right receptor (internalization)
- provoke a “disturbance” at cell surface

**What do you do once you’ve gotten in?**

- Break-out of the vacuole and even swim around

**Subvert the Host’s Defense**

- Bacterial Toxins
Some Bacterial Components trigger inflammation

Bacterial Exotoxins

The toxic part
Helps solubilise Lipid A
Somatic antigen

Lipopolysaccharide (LPS)

Some Bacterial Components trigger inflammation

Subvert the Host’s Defense

Bacterial Exotoxins

The “Floppy’ Baby Syndrome – Infant Botulism
Subvert the Host’s Defense
Bacterial Exotoxins
Are Among the Most Potent Poisons Known

Yet, from a biological viewpoint, they are extraordinary in their variety and mode of action.

All in All, Pathogens are Impressive Cell Biologists
Pathogenic bacteria interfere or manipulate for their own benefit normal function(s) of the host cell

Replicate
“Every bacterium’s dream is to be bacteria”
Exit the Host

Sooner or later you have to find a new host

The Corollaries of Pathogenicity

Bacterial Pathogens Use Elaborate Regulatory Mechanisms to Key on Biochemical “Cues” From Their Host

pH, temperature, O₂, CO₂, osmolarity etc.

The Corollaries of Pathogenicity

Pathogens Respond to a Host’s Biological and Social Behavior

The Corollaries of Pathogenicity

Some Diseases of Human Progress

Legionnaire’s Disease
Toxic Shock Syndrome
HIV/AIDS
Lyme Disease
E. coli Hemorrhagic Fever
The Corollaries of Pathogenicity

Legionnaire's Disease

Legionella Really Likes to Grow in Fresh Water Protozoa

Legionnaire's Disease

We Changed Some of Our Habits Over Time

Legionella Really Likes to Grow in Fresh Water Protozoa

And so Did Legionella

So a Human Alveolar Macrophage Looks Pretty Good Too!
The Corollaries of Pathogenicity

Some Diseases of Human Progress

Legionnaire's Disease
Toxic Shock Syndrome
HIV/AIDS
Lyme Disease
*E. coli* Hemorrhagic Fever

Toxic Shock Syndrome

Women Changed Their Habits

And it provided Staphylococci with a 'new opportunity'

And Human Misery

Human – Microbe Interactions is Still a “Work in Progress”
Bacterial Pathogenicity can evolve in genetic quantum leaps

A Single Genetic Event can Change a Commensal into a Pathogen

E. coli that cause urinary tract infection differ from those that are commensal inhabitants of the bowel because they inherited several blocks of genes.
Overt Clinical Disease Need Not be the Outcome of a Host-Pathogen Interaction

Asymptomatic Infection Rates

- *M. tuberculosis* - 90%
- *Salmonella typhi* – 80%
- *Helicobacter pylori* - 80%

Disease is the more the Exception than the Rule

Pathogenicity is the reflection of ongoing evolution between a parasite and a particular Host

When we study pathogens we learn as much about ourselves as we do about them