Principles of Infection
Advanced Pathophysiology
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Infections
Modern advances in health have nearly eradicated smallpox
Vaccines, ABX treatments and public health initiatives
Despite many widespread immunizations and policies, infection still cause a significant mortality and morbidity –WHY?

b/c of emergence of new infectious processes
Re-emergence of old processes
Drug resistant processes

https://www.youtube.com/watch?v=uGeWspeMzFk

Smallpox (variola virus)
Origin is unknown; can be traced back to the Egyptian empire in 3rd century B.C. initially on average 3 per 10 people who acquired the infection died.
Can be traced to growth and expansion of civilizations

By 1959 WHO (World Health Organization) developed initiative to eradicate. By 1975 they thought that was the last case, but 2 other patients had developed it in 1978.
Classified as ERADICATED
Why?
Cast rapid urbanization
resulting in breakdown of public health facilities and more rapid spread of infection

Poverty and social inequality
War and famine
Global travel
Encroachment on wildlife areas contact with sequestered illnesses
Abx resistance and over prescribing, under utilizing

History of infectious diseases was primary source of mortality many years ago
14th century "The Black Death" killed more than 50 million
Spanish influenza killed 50-100 million in 1918-1919

A dynamic relationship?
MOs and humans usually live-in symbiosis
Very hospitable environment for MOs
Normal flora
Colonization in many systems
Breached and infection ensues
Protective barriers are broken normal flora leaked into blood stream
sepsis shock --->death

True pathogens vs. Opportunistic infections
TRUE pathogens:
Designed to invade
Devised to circumvent your natural systems
Successful infection is related to # of invaders vs weakened response (like in an opportunistic)

Opportunistic pathogen:
MO's that may cause disease if the physical barrier or defensive system is weakened
alterations in microbiome (from Abx) may allow overgrowth of flora

Factors that influence the cause of disease

These factors affect the ability of the infectious agent to cause disease

1. Communicability
2. immunogenicity
3. infectivity
4. mechanism of action
5. pathogenicity
6. portal of entry
7. toxigenicity
8. virulence

Process of infection: 4 distinct stages

1. Colonization
2. Invasion
3. Multiplication
4. Spread

Colonization

MOs usually are present in reservoirs (standing water, soil, contaminated environment, animals and other humans)
Zoonotic vs vectors vs direct transmission
After transmission and deposition, colonization begins, MOs adhere to tissues through specific receptors
Specificity of adherence results in particular organisms being limited to where it can adhere (tissue tropism)

Invasion

Invades surrounding areas and can move to other sites
Direct confrontation with the organisms immunity
Complement, antibodies, phagocytes (neutrophils and macrophages)
Evasion of immunity may lead to MOs transported through the blood (bacteremia) and even multiply in blood (septicemia)

Pathogen evasion techniques
Destroy or block immune response
Produce endo & exotoxins
Produce protease to digest IgA
Produce surface molecules that mimic receptors
Change antigenic profile

Multiplication

Within the warm and nutrient rich environment of the human host the MOs grow and undergo rapid multiplication
Viral usually replicated within the cell
Bacterial mainly intracellular (but can be extracellular biofilm)
Produce many progeny bacterial cells
Spread
Many are localized
Some are highly invasive and may enter lymphatics

Virulence factors

Virulence factors include:

Adhesion molecules

Toxins

Inflammation & Immune protection

Infectious organisms

1. Directly cause tissue damage
2. Produce exotoxin
3. Produce endotoxin
4. Direct damage with invasion
5. Indirectly cause tissue damage
6. Produce immune complexes
7. Cause cell-mediated immunity

Clinical process of infection

4 distinct phases

1. Incubation period
2. Prodromal stage
3. Invasion period
4. Convalescence

Will vary in degree and severity dependent on host systems and affected systems

Bacterial infections

Aerobic or anaerobic

Motile or immotile

Gram positive vs negative

3 layers – plasma membrane /cell wall / capsule
Cell wall: thick peptidoglycan (Gram – have another plasma membrane)
Gram + = easier to treat because less protection
Gram - = more difficult to treat and resistant
Gram stain: pink stain on gram + bacteria due to retaining the dye

Viral infections

Simple MOs with nucleic acid containing the viral genome protected from environment by layer or layers of proteins
Most common affliction of humans
Short life span outside the cell
Sensitive to many environmental factors

Viral replication

Do not have organelles therefore no metabolism
Incapable of independent replication must penetrate host cell to perform this function and use host cells own organelles

6 distinct phases

Adsorption / penetration / uncoating / replication / assembly / release

Fungal infection

Large MOs that have thick walls
2 basic structures
Single celled yeasts -spheres
Multicelled molds –filaments or hyphae
Transmitted usually by inhalation or or contamination of wounds; majority are commensals and cause mild infections (superficial mycoses)
Human to human concern with dermatophytes (tinea) and yeasts (candida)
Diseases are called mycoses

Fungal infection

Candida >> normal flora residing in skin, mouth, vagina and GI tract >> opportunistic when decreased immunity or ABX therapy destroys normal flora.
Morphological changes from unicellular yeast to filamentous hyphal forms when pH altered, elevated temp*, changes in host serum factors
Candida adheres >> secrete enzymes, tissue destruction, damage to cell membrane>> suppresses cell immune system by producing GM-CSF and alters complement response and opsonization and chemotaxis

Parasitic & protozoal infection

Establish symbiosis in which parasite benefits at hosts' expense
Can be unicellular to large worms (parasitic)
Unicellular MOs with nucleus and cytoplasm (protozoa)
Use vectors for transmission, rarely human to human
Tissues damage can be primary or 2/2 to inflammatory response

Parasitic infection

Malaria >> 4 species of plasmodium parasites --> transmission from female mosquito enters blood stream, travels to liver >> invades liver parenchyma and after several round of division liver cells explodes and several 1000 parasites enter blood and infect RBCs multiplication occurs in RBCs resulting in daughter cells re-infecting RBCs
CD4+ & CD8Tc and lymphocytes diminish and immunosuppression is present
gene switching aids in resistance

In Western countries, almost all malaria occurs in travelers; therefore, the diagnosis may be missed if a history of travel is not elicited.

Countermeasures

1. Environmental
2. Sewage removal
3. Breeding ground eradication
4. Antimicrobials (issues with resistance)
5. Vaccine administration
6. Passive immunotherapy
   Reduction since vaccines

"the great new debate" to vaccine or not to vaccine?? That is the question

Herd immunity
https://vaccines.procon.org/

The Centers for Disease Control (CDC) estimated that 732,000 American children were saved from death and 322 million cases of childhood illnesses were prevented between 1994 and 2014 due to vaccination.

https://antiantivax.flurf.net

The basis of the "MMR vaccine causes autism" argument is a flawed study (retracted by The Lancet on February 2, 2010) by Andrew Wakefield, who had several ethics breaches, including failure to disclose financial compensation from a lawyer representing families claiming MMR cause their children's autism, failure to disclose financial interests in patents for MMR alternatives, failure to include data which contradicted his conclusions, use of contaminated samples to support his conclusions. Furthermore, on January 28, 2010, Wakefield and two of his co-authors, John Angus Walker-Smith and Simon Harry Murch, were found by the UK.'s General Medical Council to have acted irresponsibly, dishonestly and not in the clinical interests of the children involved in the study. The basis for this decision included, among other things, colonoscopies, MRIs and lumbar punctures (spinal taps) when such procedures were not clinically indicated. On May 24, 2010, the General Medical Council issued a determination that Wakefield and Walker-Smith (PDF links) were guilty of professional misconduct and should be erased from the Medical Register in the U.K. (meaning that his license to practice medicine in the U.K. has been revoked).

Peer reviewed ……
Lack of Association Between Measles-Mumps-Rubella Vaccination and Autism in Children: A Case-Control Study
Mrożek-Budzyn, Dorota PhD; Kiełtyka, Agnieszka PhD; Majewska, Renata MSc
The Pediatric Infectious Disease Journal: May 2010 - Volume 29 - Issue 5 - p 397-400
doi: 10.1097/INF.0b013e3181c40a8a
Original Studies

Presentation of infection
- Systemic Manifestations of the infection
- Fever, chills, malaise, fatigue, weakness, loss of concentration, generalized achiness and anorexia
- Usually caused by our own systems- inflammation and immune

When do we as practitioners get concerned with fevers?
- Sepsis, PNA and influenza leading causes
- Neutropenic fever is an emergency
- A returning traveler (from malaria/surrounding areas) is malaria until proven otherwise

SIRS

Systemic inflammatory response syndrome
Screening tool for SEPSIS

Temp <36* or >38* C
HR >90 BPM
Tachypnea >20 BPM or PaCo2 <32
WBC <4000 or >12000 or >10% immature neutrophils

+ if 2 or more qualify
sepsis
Constitutional changes: fevers/hypothermia, diaphoresis, rigors, myalgias, and malaise
CV changes: hypotension, cold, clammy skin, mottling, decreased cap refill, tachycardia, decreased urine output.
Resp: hypoxia, dyspnea, and tachypnea cough, pleuritic chest pain
GI: abd pain, n/v//d, dec bowel sounds, GIB
GU: dysuria, frequency, hematuria, pyuria, CVA tenderness, pain, vag dc
Neuro: MS changes, agitation, HA

References

Up to date-per disease process
Epocrates- per disease process
Family medicine notebook –per disease process
Tkacs, Hermann and Johnson: Advanced physiology and Pathophysiology
McCance and Huether- Pathophysiology: the biologic basic for disease in adults and children
Sattar- Fundamentals of Pathology
Hammer and McPhee- Pathophysiology Of disease. An introduction to clinical medicine