Immunocompromise III

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Adaptive immunity

- recall that the innate immune system is designed to protect the host against normally colonizing endogenous flora (microflora)
- the adaptive immune system, on the other hand, is designed to protect the host against new, exogenous pathogens (macroflora)
  - viruses
  - non-colonizing bacteria
  - non-colonizing fungi
  - parasites
- also recall that public health measures can best impact the immune system's interactions with macroflora
B cells & IgGs

Macrophages

T cells

Macro Flora

Classical Immune System

Adaptive
Recall: The innate immune system is designed to protect the host against its own naturally-occurring microflora and commonly encountered (exogenous) macroflora.
B cells & IgS

S. pneumoniae (sinopulmonary), Group A strep and S. aureus (skin), and GI pathogens

Classical Immune System

Adaptive
Immunoglobulins

- Immunoglobulins protect:
  - Respiratory tract from pneumococcal infections
  - GI tract from Giardia (parasite), Campylobacter (bacterium), and enteroviruses
  - Skin from Group A Strep and Staphylococcal infections
Addition of type-specific Abs facilitate phagocytosis

A. M protein-rich group A streptococci after rotation at 37°C in tubes of whole blood from a non-immune donor. In the absence of type-specific antibody, the organisms are highly resistant to phagocytosis by PMNs and multiply greatly.

B. After the addition of type-specific antibody, the organisms are avidly phagocytosed.
Immunoglobulin deficiency

- hypogammaglobulinæmia (deficiency in all Ig$s$) is more common than dysgammaglobulinæmia (deficiency in some Ig$s$)

- there are a host of rare but congenital immunoglobulin disorders (e.g. SCID)
Immunoglobulin deficiency: acquired causes

- nephrotic syndrome (due to renal loss)
- malabsorption or protein-losing enteropathy (due to GI)
- cirrhosis (due to reduced production)
- chronic lymphocytic leukemia (CLL)
Cirrhosis

- Patients with cirrhosis—who have ascites—are most at risk for spontaneous bacterial peritonitis.
- Ascites is a collection of peritoneal fluid without flow.
- Because of portal hypertension (where pressure in the portal system causes “backup” in the gut), there are leaky vessels in the gut.
- Ascitic fluid due to cirrhosis has low Ig levels.
patients with untreated CLL are at risk for the expected infections with Ig deficiency:
- sinus infections
- respiratory infections
- bacteræmia (due to encapsulated organisms)

patients with treated CLL often have cell-mediated immunocompromise (cf Lecture IV)
Asplenia

- The spleen plays a role in clearing encapsulated bacteria.
- Patients may have surgical or functional (e.g., from Sickle Cell Disease) asplenia.
- Functional asplenia is recognized by Howell-Jolly and Heinz bodies.
patients with asplenia are at greatest risk for overwhelming post-splenectomy infection (OPSI)

the risk is highest in children (esp. HbSS)

OPSI is usually due to S. pneumoniae, although N. meningitidis (meningocococcus) is also an important cause of OPSI

patients with asplenia are at risk for a select few other infections: Babesia, Malaria, Capnocytophaga canimorsus (due to dog bites)
Overwhelming pneumococcal infection following splenectomy for lymphoma staging

Capnocytophaga canimorsus infection (GN bacilli) following a dog bite


Asplenia

- because of the high risk of severe infections, prevention with vaccination (pneumococcal and meningococcal) is of high importance
- patient education regarding travel risks, dog exposure, and measures to take when febrile are also important aspects of management
macrophages

exogenous bacteria and fungi, viruses, parasites

T cells

Classical Immune System

Adaptive
Cell-mediated immunity

- T lymphocytes and macrophages protect us against exogenous pathogens which our innate immune system would not have encoded:
  - most viruses
  - most fungi
  - mycobacteria
  - some uncommon exogenous bacteria
  - most parasites
Case

- 47 yo M presents with diplopia (double vision)
- there has been a 1-year history of weight loss and diarrhea
- he reports multiple sexual partners
Case

Step 1: What is the nature and severity of his immunocompromise?
Case

History:
- sexual history puts him at ↑risk for syphilis, gonorrhea, hepatitis B, HIV, other STIs
- would also want to know:
  - travel/immigration history (e.g. TB)
  - history of IVDU (e.g. hepatitis B/C, HIV)
  - exposure to animals (e.g. toxoplasma)
  - crowded conditions (e.g. First Nations reservations, jails)
Case

Pt’s history:

- has history of sex with men (mostly) and women
- previous gonorrhea
- never tested for HIV, viral hepatitis, etc
- grew up and lives on Aboriginal reservation, where he is a social worker
- has been managed with traditional medicines for depression, wt. loss
- has never seen an MD
Case

Physical exam:

- patient requires a thorough physical exam
- requires special attention to:
  - causes of diplopia
  - causes of wt. loss (e.g. cancer)
  - evidence of sexually-transmitted infections
  - evidence of immunocompromise
Pt’s physical exam:

- afebrile
- neck supple with no papilledema
- right homonymous hemianopsia, L CN VI palsy
- thrush
- cachectic (i.e. VERY thin)
- no features of liver disease
- findings of Kaposi’s sarcoma

N Engl J Med 342:1027
What is the nature of this man's immunocompromise?

- physical exam strongly suggestive of advanced HIV infection (thrusht, wasting, KS)
- social history also puts him at risk for TB, syphilis (and other infections)
HIV and CD4

- although viral load is clinically useful in terms of initiating and monitoring treatment of HIV, it is not useful vis-à-vis diagnosis

- \( CD_4 (T_4) \) count is inversely correlated with the risk of opportunistic infection

- TB and KS (which can occur at almost any \( CD_4 \) count) are exceptions
# HIV and CD4

<table>
<thead>
<tr>
<th>CD4 count (x 10^6/L)</th>
<th>Risk of opportunistic infections/cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>No significant increase</td>
</tr>
<tr>
<td>200-499</td>
<td>Increased risk, esp. of reactivation (e.g. thrush, HSV, VZV)</td>
</tr>
<tr>
<td>&lt;200</td>
<td>Very increased risk</td>
</tr>
<tr>
<td>&lt;50</td>
<td>Dramatically high risk</td>
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</tbody>
</table>
HIV and CD4

adapted from BMJ 2001;322;1290
HIV and Opportunistic Infections

- there are so many possible infections and infectious cancers that doctors (and EVEN STUDENTS) find it overwhelming
- at your stage, knowing the categories is what is important
- patients with clinical AIDS can't just get "anything"
HIV and OIs: The Big Picture

- Viruses
- Bacteria
- Fungi
- Protozoa
HIV and OIs: The Big Picture

- Viruses
  - reactivation/cancer from latent viruses (herpesviruses, papillomaviruses)
  - severe or complicated community-acquired viruses (e.g. influenza, hepatitis C)
HIV and OIs: The Big Picture

- Bacteria
  - Mycobacteria (TB, MAI)
  - other weird bacteria
HIV and OIs:
The Big Picture

- Fungi
  - mucosal candidiasis
  - Pneumocystis jirovecii
  - dimorphic fungi
HIV and OIs: The Big Picture

- Protozoa
  - Toxoplasma
  - Intestinal protozoa
## Herpesviruses and Disease

<table>
<thead>
<tr>
<th>Virus</th>
<th>Reactivation</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-1/2</td>
<td>oral and genital ulcers</td>
<td>???</td>
</tr>
<tr>
<td>VZV</td>
<td>shingles</td>
<td>???</td>
</tr>
<tr>
<td>EBV</td>
<td>oral hairy leukoplakia</td>
<td>lymphoma</td>
</tr>
<tr>
<td>CMV</td>
<td>retinitis*</td>
<td>???</td>
</tr>
<tr>
<td>HHV-6/7</td>
<td>???</td>
<td>???</td>
</tr>
<tr>
<td>HHV-8</td>
<td>???</td>
<td>Kaposi’s, 1° effusion lymphoma, multicentric Castleman’s</td>
</tr>
</tbody>
</table>
HPV and disease

- HPV reactivation causes warts (verrucae vulgaris)
- HPV oncogenesis causes cervical cancer and anal cancer
39 yo M living on a First Nations reserve with high-risk sexual activity

- acute neurological illness superimposed on wasting illness
- thrush, KS and cachexia on examination
HIV serology +
CD$_4$ count: $310 \times 10^9$/L
VL 6.9 log (i.e. very high)
CT Head and MRI ...
imaging shows L MCA stroke, meningeal enhancement (i.e. inflammation)

spinal fluid:
- 418 WBCs (67% monos), 4 RBCs
- high protein, low glucose
- negative for bacteria, TB, cryptococcus, viruses (HSV, EBV)
- + for syphilis
Diagnoses

- advanced chronic HIV infection (AIDS)
  - wasting illness
  - chronic diarrhea
  - Kaposi’s sarcoma
  - thrush
  - neurosyphilis (meningovascular)
Additional points on HIV

- Cell-mediated immunocompromise often does not tell the whole story with chronic HIV infection:
  - Persons who acquired HIV sexually are (by definition) at risk for other STIs
  - Persons who acquired HIV from IV drug use are at risk for hepatitis B/C, MRSA, endocarditis
  - Persons from developing countries are at risk for TB, parasitic infections, etc
Last thoughts on HIV

- although treatment and prognosis for chronic HIV infection in developed (and developing) world have changed dramatically, we continue to see AIDS

- now, complications of treatment and diseases of aging are an important domain of the HIV specialist (FP, general internist, ID specialist)