M13 - Infections in the Immunocompromised Patient

3 more properties

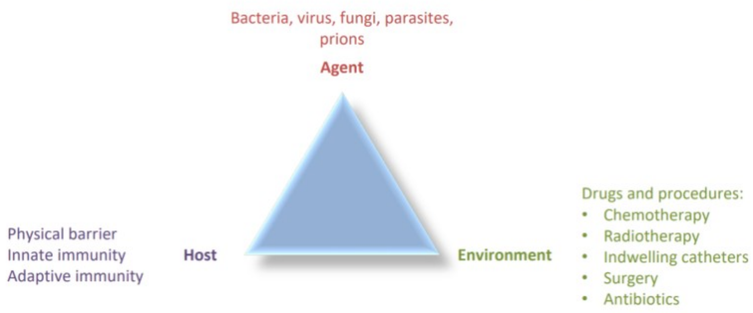
Learning Objectives

- Components of the host immune system
- Common infections and complications associated with different types of immunodeficiencies
- List the microbes typically associated with Neutropenic fever
- List the microbes typically associated with Solid organ or haemopoietic stem cell transplantation

Recap

Introduction to the "Infective Triad"

> Set of 3 influential factors that play a significant role in development and spread of infectious diseases.



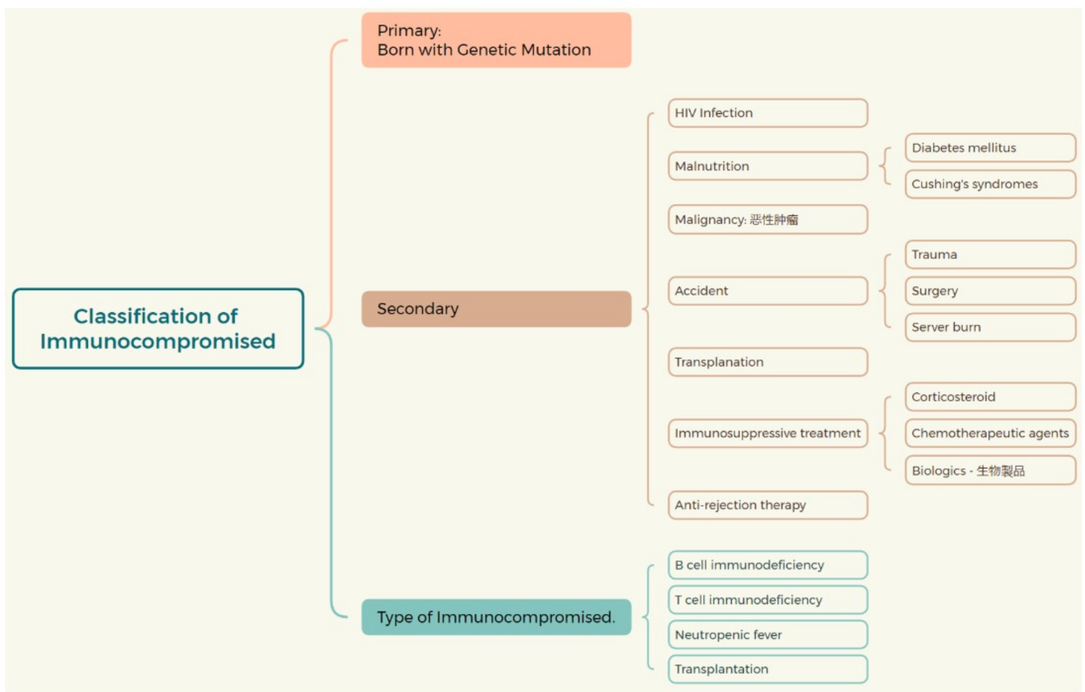
Text Version:

Agents: Bacteria, Virus, Fungi, Parasites, Prions

Host: Barrier, Innate Immunity, Adaptive Immunity

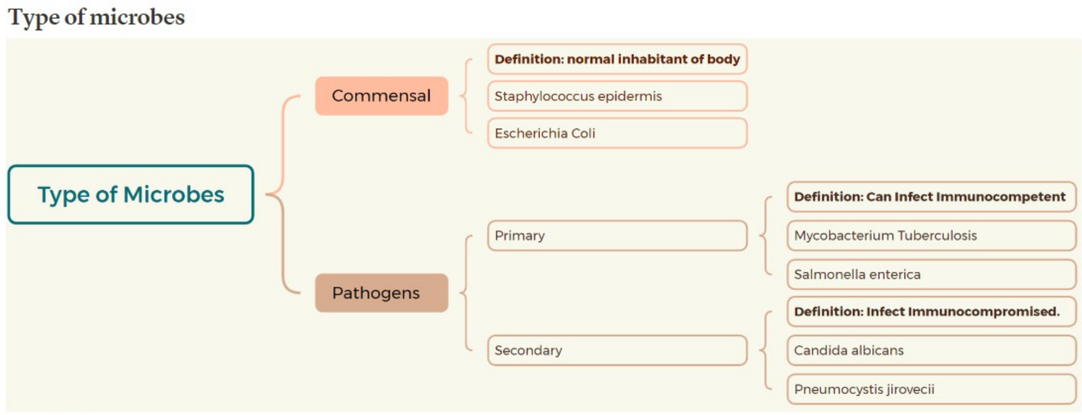
Drugs: Chemotherapy, Radiotherapy, Indwelling catheters, Surgery, Antibiotics

Host Status



- Immunocompetent: having the ability to mount a normal immune response.
- Immunocompromised: having a weakened immune system
  - Primary: Born with Genetic Mutation
  - Secondary:
    - Infection: e.g., human immunodeficiency virus (HIV) infection.
    - Malignancy: e.g., leukemia, lymphoma.
    - Haemopoietic stem cell or solid organ transplantation and anti-rejection therapy.
    - Immunosuppressive treatment: e.g., chemotherapeutic agents, corticosteroid, biologics.
    - Trauma or surgery, severe burn.
    - Malnutrition and other metabolic disruption: e.g., diabetes mellitus, Cushing's syndrome.

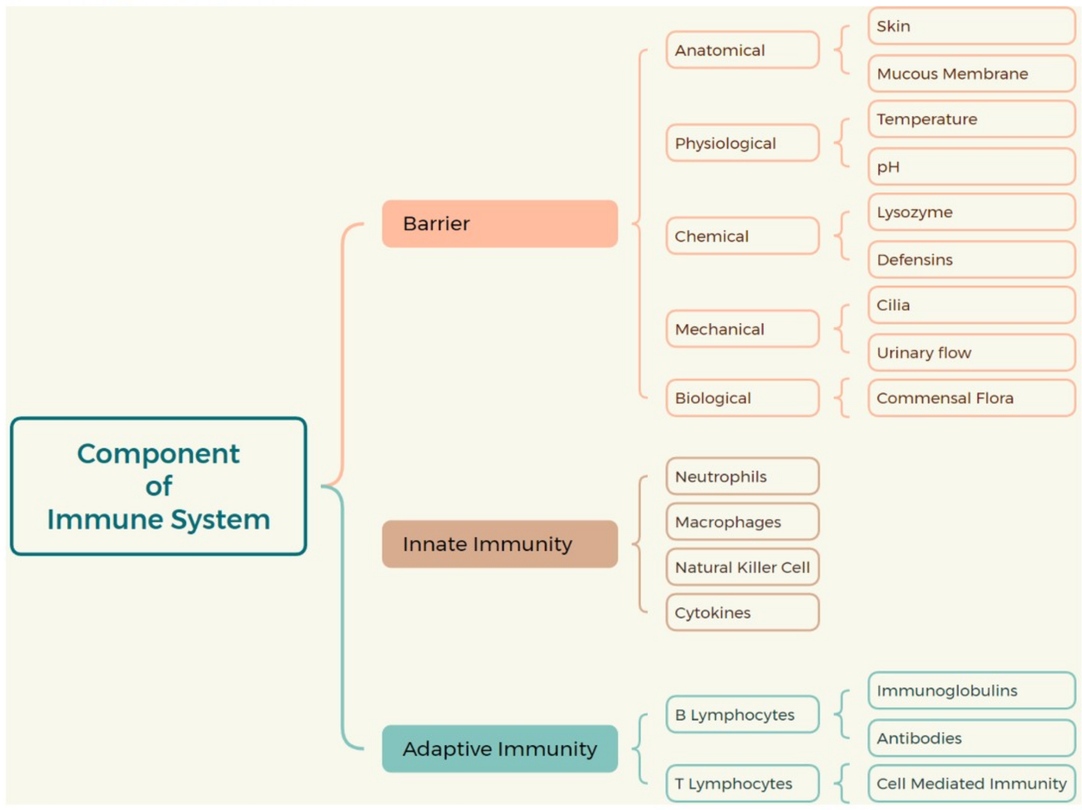
Type of microbes



Text Version

- Commensal: a normal inhabitant of the human body.
  - Staphylococcus epidermidis, Escherichia coli
- Pathogen: Capable of causing disease.
  - Streptococcus pneumoniae, Influenza virus
- Primary pathogen: A pathogen that regularly causes disease in some proportion of immunocompetent patient.
  - Mycobacterium tuberculosis, Salmonella enterica
- Opportunistic pathogen: An opportunistic pathogen causes disease mostly in immunocompromised individuals.
  - Candida albicans, Pneumocystis jirovecii [HIV Indicate Disease]

Immune System - Refer to M6



Comparison of Innate Immunity & Adaptive Immunity

	Innate Immunity	Adaptive Immunity
Mechanism	Pre-existing barriers and induced mechanisms	All mechanisms are induced
Recognition Pattern	Small Pattern Recognition → Cover Large Range of Pathogens	Recognize specific antigen
Rate of Response	Fast response	Slower response
Proliferation	Responding cells don't proliferate.	Responding cells proliferate
Life Cycle	Short-lived	Long-lived
Re-infection	Level of response similar	Level of response is stronger & faster

Immunodeficiencies: Common infections & Complications

[CD19] - B cell Immunodeficiency

> Example: B-cell lymphoma on chemotherapy including rituximab (anti-CD20 monoclonal antibody).
> 患有B 细胞淋巴瘤的病人接受化療中

- Defects in immunoglobulin production → Predisposes to infection by:

	Encapsulated bacteria	Enterovirus	Campylobacter spp.	Salmonella spp.	Giardia lamblia
Examples	Streptococcus pneumoniae				
	Haemophilus influenzae				
	Neisseria meningitidis				

Remarks - Case Study:

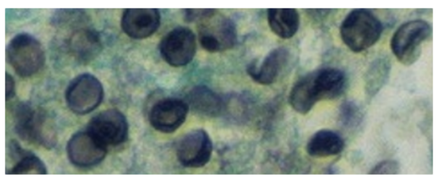
A 38-year-old male with B-cell lymphoma, undergoing chemotherapy including rituximab (anti-CD20 monoclonal antibody), presented with persistent right lower quadrant abdominal pain, chronic diarrhea, and weight loss for 4 months. Colonoscopy and biopsy revealed inflammation and ulcer in the caecum. Despite repeated courses of ciprofloxacin and oral budesonide, there was no improvement. Stool culture and multiplex PCR identified Campylobacter spp. The patient was treated with intravenous ertapenem followed by oral azithromycin for 10 days. Additionally, he started receiving replacement intravenous immunoglobulin every 4 weeks. Following the treatment, the diarrhea and abdominal pain subsided.

一个38岁的男性患有B细胞淋巴瘤，正在接受包括利妥昔单抗（抗CD20单克隆抗体）在内的化疗，出现持续性右下腹痛、慢性腹泻和体重减轻已有4个月。结肠镜检查和活检显示盲肠炎症和溃疡。尽管反复使用环丙沙星和口服布地奈德，但没有改善。粪便培养和多重PCR鉴定出弯曲菌属。患者接受了静脉注射依他必利，随后口服阿齐霉素治疗10天。此外，他开始每4周接受静脉免疫球蛋白替代治疗。治疗后，腹泻和腹痛缓解了。

[CD3/4/8] - T cell Immunodeficiency

> Example: Newly diagnosed HIV infection, not yet started on combined antiretroviral treatment (cART)
> 新诊断的艾滋病毒感染，尚未开始抗逆转录病毒联合治疗（cART）

- Defects in T cells and cell-mediate immunity → Predisposes to infection by:



Bacteria	Fungi	Virus	Parasites
Mycobacteria Listeria monocytogenes Salmonella	P. jirovecii Cryptococcus Talaromyces marneffei	Cytomegalovirus Herpes simplex virus Adenovirus	Toxoplasma gondii

> If the patient is diagnosed of these pathogens, esp. Pneumocystis jirovecii, the patient maybe a HIV carrier.

▼ Remarks - Case Study:

A 40-year-old male was newly diagnosed with HIV infection and had a CD4 count of 50 cells/μL. He had not yet started combined antiretroviral treatment (cART). He presented with a low-grade fever, dry cough, and increasing shortness of breath for one week. The patient was found to have Pneumocystis jirovecii infection in the bronchoalveolar lavage (BAL) sample. He was treated with trimethoprim-sulfamethoxazole with steroid cover, which resulted in improved oxygenation and radiological appearance. The patient has since started cART.

一名40岁的男性最近被诊断出患有HIV感染，并且CD4细胞计数为50个/μL。他尚未开始联合抗逆转录病毒治疗（cART）。他出现了低热、干咳和呼吸困难逐渐加重的症状已有一周。在支气管肺泡灌洗（BAL）样本中发现患者患有肺孢子虫感染。他接受了三联噻嗪-磺胺甲噁唑治疗，并加用类固醇，结果呼吸氧合改善并且影像学表现有所改善。之后患者已经开始了cART治疗。

Neutropenic fever

Neutropenia	Severe neutropenia	Profound neutropenia
Absolute neutrophil count (ANC) <1,000 cells/μL	ANC <500 cells/μL or expected to decrease to <500 cells/μL over the next 48 hours	ANC <100 cells/μL

> Characteristic of Neutropenic Fever:
> Single oral temperature of ≥38.3°C (101°F) or a temperature of ≥38.0°C (100.4°F) sustained over a one-hour period.

Spectrum of organisms

Bacteria: skin, GI tract	Gram (+) Bacteria: S. aureus S. epidermidis Viridans streptococci Enterococcus spp.
	Enterobacteriaceae: E. coli Klebsiella spp. Enterobacter spp.
	Non-fermenters: Pseudomonas aeruginosa Acinetobacter spp.
Yeasts: GI tract, GU tract	Candida spp.
Moulds: air	Aspergillus spp., Mucorales, Fusarium spp.

Common Sites of infection

- Primary bacteremia
- Catheter-related bloodstream infection
- Oral mucositis
- Neutropenic enterocolitis (typhlitis)
- Pulmonary infection
- Urinary tract infection

Investigation

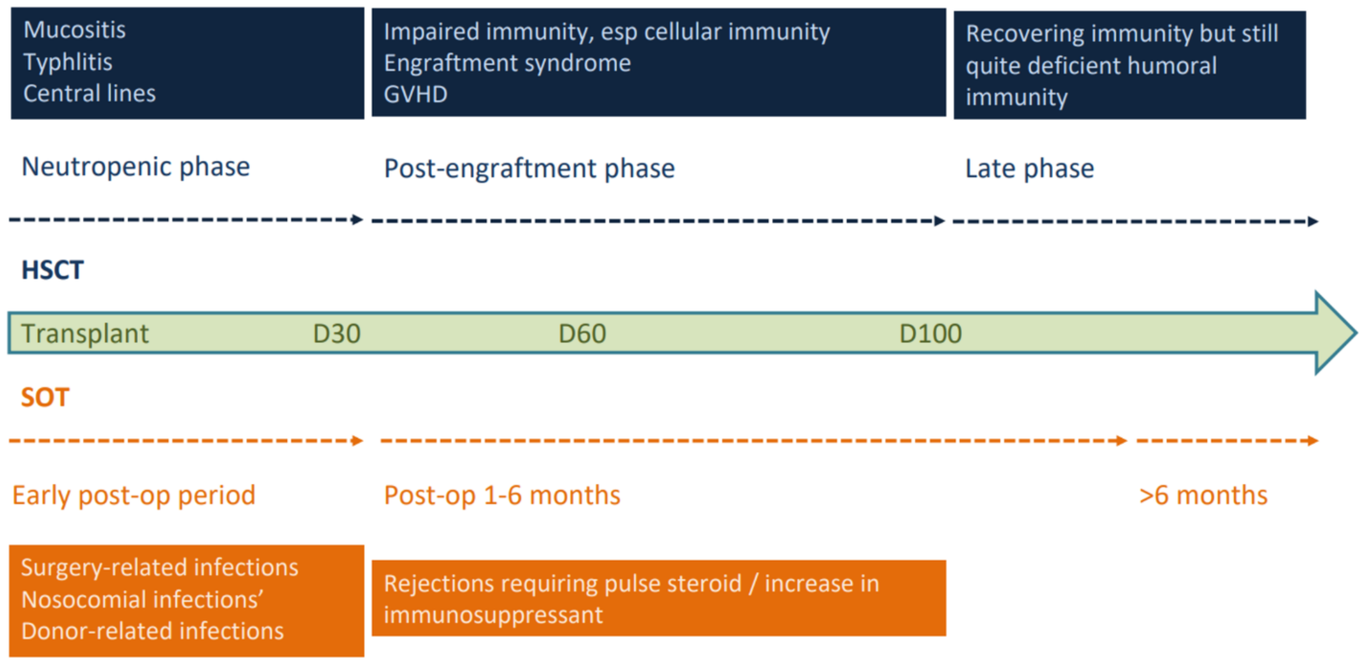
Physical	Microbiological	Radiological
Pulmonary abdominal skin sinuses mucosa	Blood culture Urine culture sputum culture	Chest X-ray CT thorax CT abdomen

▼ Remark - Case Study

A 60-year-old female with acute myeloid leukemia undergoing chemotherapy presented with sudden onset fever and chills 10 days after chemotherapy, without any specific symptoms of infection. She developed septic shock and required high-dose inotropic support. Her absolute neutrophil count was extremely low at 0.02 x 10^9/L. Blood culture revealed Pseudomonas aeruginosa infection. Initially, she was treated with intravenous meropenem, which was later switched to ceftazidime and amikacin based on antibiotic susceptibility results (as the organism was resistant to meropenem). Unfortunately, she did not survive due to overwhelming sepsis.

一位60岁的女性患有急性髓系白血病，正在接受化疗治疗。化疗后的第10天，她突然出现发热和寒战，没有任何特定的感染症状。她发展为败血症休克，并需要高剂量的强心药支持。她的绝对中性粒细胞计数极低，为0.02 x 10^9/L。血液培养显示铜绿假单胞菌感染。最初，她接受静脉注射美罗培南治疗，后根据抗生素敏感性结果（由于细菌对美罗培南耐药），改用头孢他啶和阿米卡星。不幸的是，由于严重败血症，她未能幸存。

Transplant-related infections



SOT - Solid Organ Transplant

- Early post-op period:
  - Surgery-Related Infection
  - Nosocomial Infection
  - Donor-related infection
- Post-Op:
  - Rejections requiring pulse steroid → Immunocompromised

HSCT - Hematopoietic Stem Cell

- Neutropenic Phase - 中性粒细胞减少期
  - Mucositis, Typhlitis, Central Lines Inflammation
    口腔炎，盲肠炎，中央静脉导管
- Post-engraftment phase - 植入后阶段
  - Impaired immunity → Cellular Immunity Engraftment syndrome
- Late Phase - Deficient humoral immunity

> More about Transplant-related infections
>
> ▼ Remark
>
> - SOT stands for Solid Organ Transplant. It refers to the transplantation of organs such as the heart, liver, kidney, lung, or pancreas from a donor to a recipient.
> - HSCT stands for Hematopoietic Stem Cell Transplantation. It is a procedure in which stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood, are transplanted to replace damaged or destroyed bone marrow. HSCT is commonly used in the treatment of various hematologic malignancies, such as leukemia and lymphoma, as well as certain non-malignant conditions, to restore the patient's immune system and blood cell production.
>   HSCT 代表 造血干细胞移植。这是一种将通常来自骨髓、外周血或脐带血的干细胞移植以替换受损或破坏的骨髓的过程。HSCT常用于治疗各种血液系统恶性肿瘤，如白血病和淋巴瘤，以及某些非恶性疾病，以恢复患者的免疫系统和血细胞生成。
> - Cellular Immunity Engraftment syndrome (CIE) is thought to result from an immune response mediated by donor T-cells against host tissues. The exact mechanism of CIE is not fully understood, but it is believed to be related to the interactions between the donor immune cells and the recipient's tissues. CIE can manifest as skin rash, liver dysfunction, gastrointestinal symptoms, and other systemic manifestations. Treatment usually involves immunosuppressive therapy to control the immune response and supportive care to manage symptoms.
>   细胞免疫移植综合征（CIE）是造血干细胞移植（HSCT）后可能发生的一种疾病。它的特点是在移植后的前几周内突然发热、皮疹和器官功能障碍。CIE被认为是由供体T细胞介导的免疫反应对宿主组织产生的。CIE的确切机制尚不完全清楚，但据信与供体免疫细胞与受体组织之间的相互作用有关。CIE可以表现为皮疹、肝功能障碍、胃肠症状和其他全身症状。治疗通常包括免疫抑制疗法以控制免疫反应和支持性护理以管理症状。

Spectrum of organisms

Bacteria (usually intracellular)	Listeria monocytogenes Salmonella spp. Legionella pneumophila Mycobacteria Nocardia spp.
Fungi	Pneumocystis jirovecii Cryptococcus neoformans Aspergillus spp.
Viruses	Herpesviruses - 疱疹病毒: VZV, CMV (Cytomegalovirus), EBV, HSV 1/2, HHV-6 BK virus
	Respiratory viruses: adenovirus
Parasites	Toxoplasma gondii

Pitfalls in transplant recipients - 移植受者的陷阱

> 'One man one disease' may not hold true.
>
> The concept that each individual typically has one specific disease or condition. However, in the context of transplant recipients, this concept may not hold true. Due to their weakened immune system and the potential for opportunistic infections, transplant recipients may experience multiple infections or complications simultaneously, making it challenging to attribute each symptom to a single disease.
> 每个人通常只患有一种特定的疾病或病症。然而，在移植受者的情况下，这个概念可能不适用。由于他们的免疫系统受损并可能出现机会性感染，移植受者可能同时经历多种感染或并发症，这使得将每个症状归因于单一疾病变得具有挑战性。

- Immune response is dampened, leading to atypical presentation or atypical radiological/histological findings.
  免疫反应受到抑制，导致非典型表现或非典型放射学/组织学結果。
- Fever is a poor indicator of infection.
- Serological assays: False-positive/negative reactions
- Antibody detection is unreliable