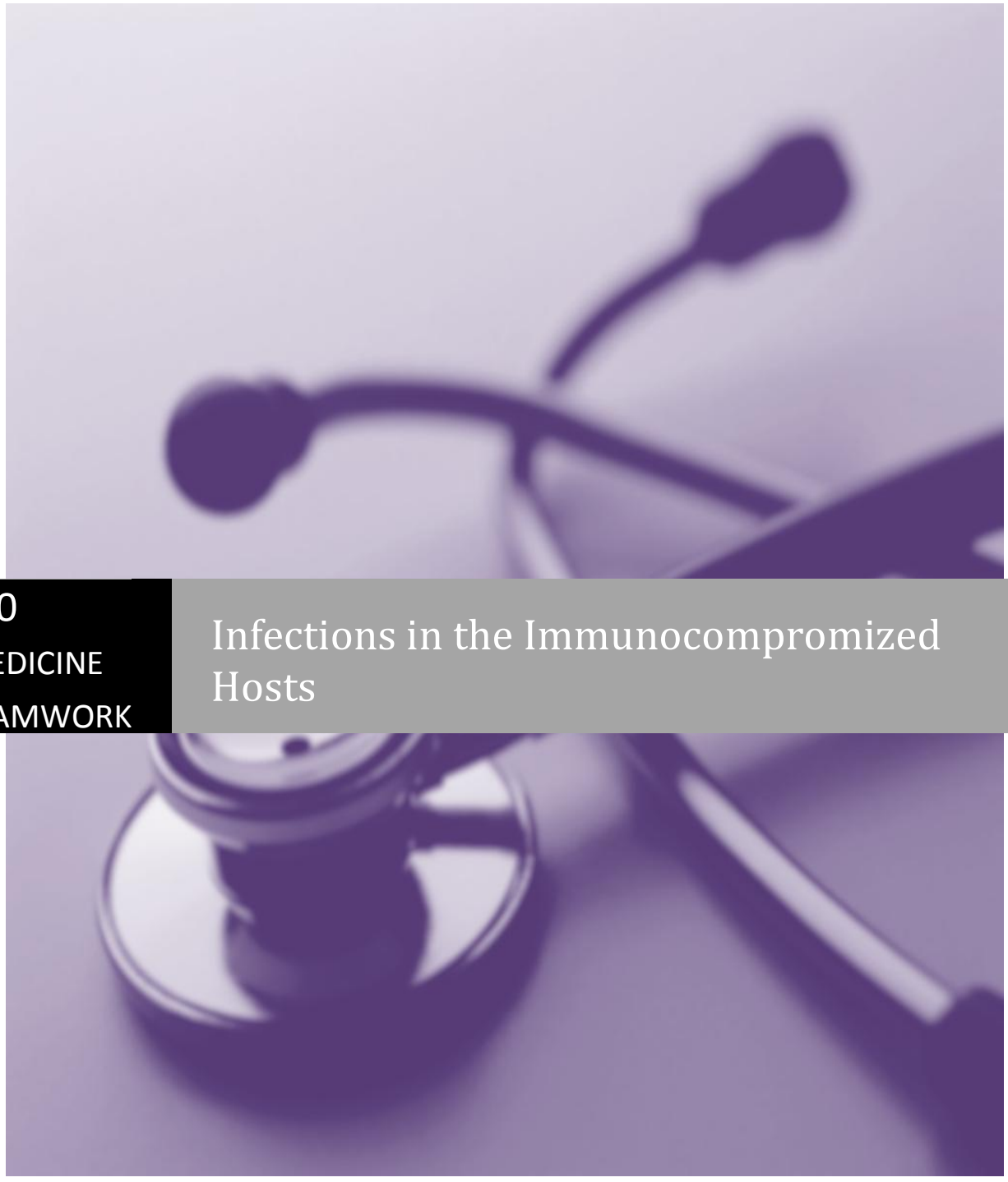
"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." – William Osler



430
MEDICINE
TEAMWORK

Infections in the Immunocompromized Hosts

Done by: Reem AlAhmadi

Infections In The Immunocompromized Hosts

Definition of immunocompromized:

A state in which a person's immune system is weakened or absent.

Components of Host Defenses:

- **Mechanical barriers**:
  Skin {Trauma might cause skin removal which puts the person in great risk of infections}, mucous membranes, epiglottis {Food or water my go to the lungs and cause infections}, cilia. {Cilia and mucus in the airways prevent foreign bodies from entering the body}
- **Granulocytes:** {their main function is to attack foreign bodies engulf them and kill them.}
- **Immune system:**
  Cell mediated Immunity:
  Macrophages, T-lymphocytes (Main cells), NKC, cytokines
  Humoral Immunity
  B-lymphocytes (Main cells), immunoglobulins, complement.
- **Spleen**

Any defect in any of these components will make the person immunocompromized.

The importance of infections in immunocompromized host:

- Increasing numbers of immunocompromized patients. {Hospital admissions put patients in this state by e.g. Central lines, cancer therapy cause immunosuppression, and organs transplant}
- Seriousness of infections in those patients.
- Infections with unusual, nonpathogenic microorganisms. {The opportunistic infections}
- Atypical presentation of infections by common pathogens.
  {Gonorrhea in infected normal individual will cause urethritis and will present as urethral discharge. However, in immunocompromized hosts it will cause bacteremia and eventually septic shock}

Causes of immune deficiency:

- **Primary (congenital):**
  Rare, more common in children e.g chronic granulomatus disease, combined immunedifiency syndrome, specific Ig deficiency, and others.
- **Secondary (acquired):**
  The commonest, there are many causes like:
  Extremes of age, pregnancy, infections, malignancy, chemotherapy, steroids, burns, trauma, procedures, connective tissue diseases, chronic diseases like DM,CRF etc.

Host Defects and Associated Prevalent Pathogens:

Defect	Pathogen
Granulocytopenia	Staph. Aureus,CNSS, V strep, Enterococci, E. coli, Pseudomonas aeruginosa, K.pneumoniae, other gram –ve bacilli, Aspergillus spp
Damaged skin and mucous membrane	CNSS, Staph. Aureus, pseudomonas aeruginosa and other gram-ve bacilli, candida spp, V. strep, enterococci, HSV.

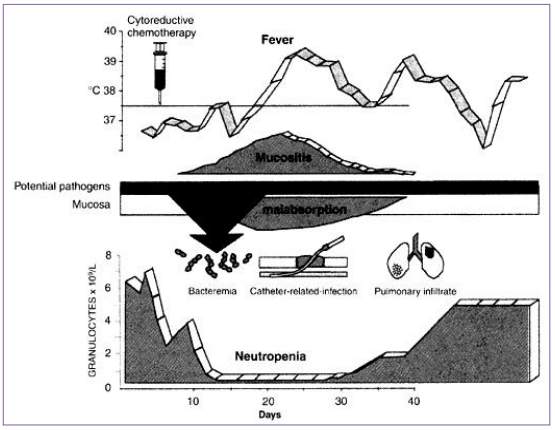
Impaired CMI	HSV, VZ, EBV, CMV, RSV, M. tuberculosis, Aspergillus spp and other fungi, Toxoplasma gondi.
Impaired humoral immunity	Streptococcus pneumoniae, Haemophilus influenzae
Spleen dysfunction	Streptococcus pneumoniae, Haemophilus influenzae Neisseria meningitides.
Complement deficiency	Neisseria meningitides, Neisseria gonorrhea

Fever in neutropenic patients:

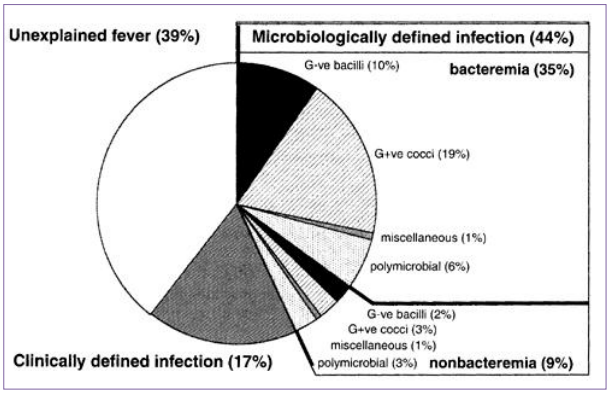
- **Definitions:**
  Fever: Oral temperature of 38c for more than two hours or single temperature of 38.3 C° or more.
  Neutropenia: A Neutrophil count of <500 cells/mm^3 or a count of <1000 cells/mm^3 with a predicted decline to 500/mm.

- **Approach to patient:**
  Careful history and examination, investigations {blood cultures, urine culture, CXR, others}, then start antibiotic therapy to cover the most likely organisms. {The whole assessment should not take more than half an hour or an hour before you start treatment or the patient will deteriorate}

- **Sequential infective events:**
  - A patient with diagnosed metastatic cancer started chemotherapy the usual total white blood cells and granulocytes will be normal at day one. After few days when the chemotherapy will start to kill bone marrow cells, the neutrophil count will decrease.
  Chemotherapy also affects other sells like in mucus membrane and the patient may have some ulcers in the mouth, which could be a route for bacteria and eventually cause bacteremia.
  - Most of these patients will remain febrile until the neutrophils go up.



- **Causes of fever in neutropenic patients:**
  The commonest cause of fever in these patients is infections.
  Sometimes the organism causing the fever is known and other times it is not. It could be an unknown organism, or an underlying disease or it could be drugs.



- **How to approach neutropeniac patients:**

The doctor skipped both table 3 and 4 and went through graphs very quickly.

Table 3. Factors that favor a low risk for severe infection among patients with neutropenia.

Absolute neutrophil count of ⩾100 cells/mm^3
Absolute monocyte count of ⩾100 cells/mm^3
Normal findings on a chest radiograph
Nearly normal results of hepatic and renal function tests
Duration of neutropenia of <7 days
Resolution of neutropenia expected in <10 days
No intravenous catheter–site infection
Early evidence of bone marrow recovery
Malignancy in remission
Peak temperature of <39.0°C
No neurological or mental changes
No appearance of illness
No abdominal pain
No comorbidity complications[a]

NOTE. Data are adapted from [4, 42–49, 51–53].

[a] Concomitant condition of significance (e.g., shock, hypoxia, pneumonia or other deep-organ infection, vomiting, or diarrhea).

Table 4. Scoring index for identification of low-risk febrile neutropenic patients at time of presentation with fever.

Characteristic	Score
Extent of illness[a]	
No symptoms	5
Mild symptoms	5
Moderate symptoms	3
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumor or no fungal infection	4
No dehydration	3
Outpatient at onset of fever	3
Age <60 years[b]	2

NOTE. Highest theoretical score is 26. A risk index score of ⩾21 indicates that the patient is likely to be at low risk for complications and morbidity. The scoring system is derived from [50].

[a] Choose 1 item only.

[b] Does not apply to patients ⩽16 years of age. Initial monocyte count of ⩾100 cells/mm^3, no comorbidity, and normal chest radiograph findings indicate children at low risk for significant bacterial infections [46].

- **Treatment algorithms**:

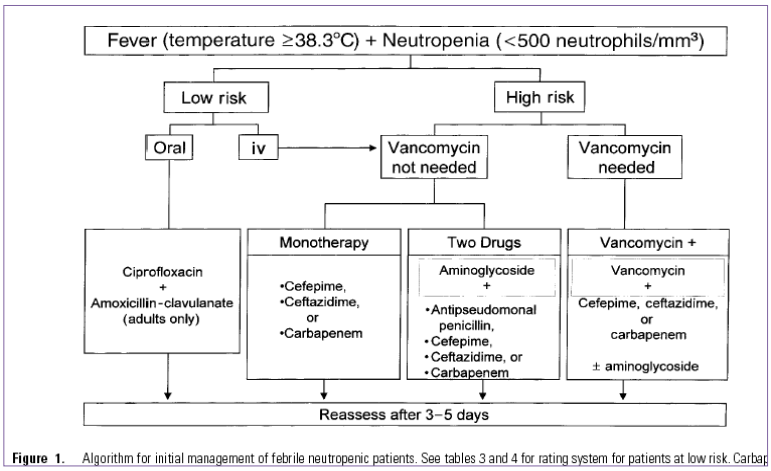
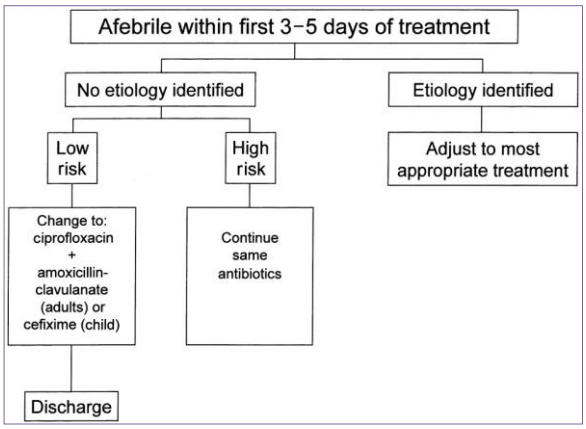
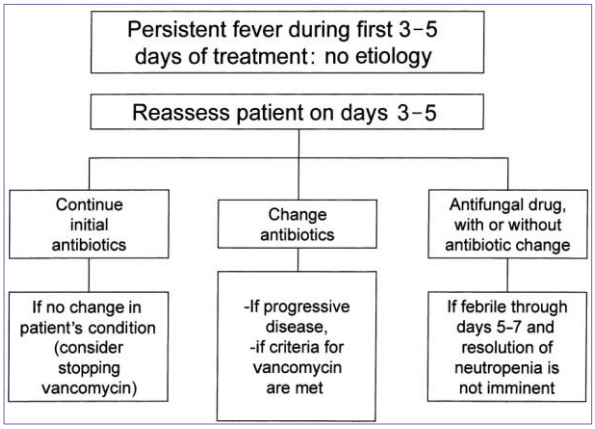
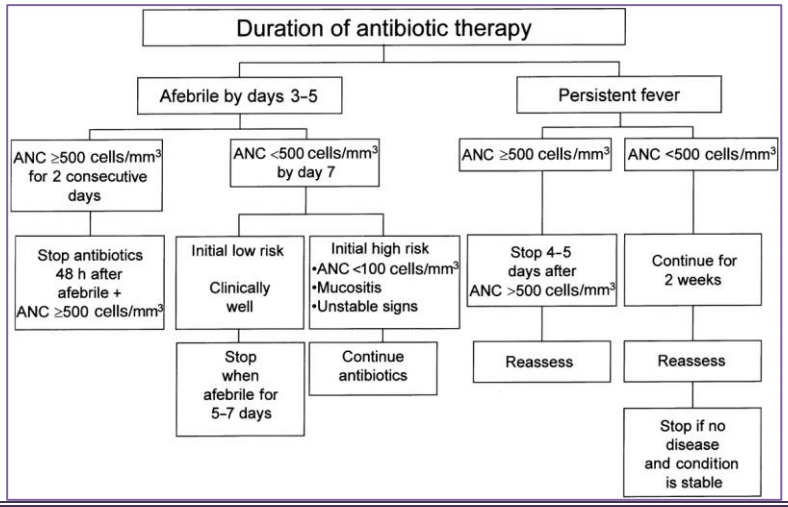


Figure 1. Algorithm for initial management of febrile neutropenic patients. See tables 3 and 4 for rating system for patients at low risk. Carbap







- **Treatment:**
  - Antibacterials**:** pipracilline+ aminoglycoside or ceftazidime+ aminoglycoside or Imipenem, vancomycine.
  - Antifungal: Amphotericine B, Fluconazole.
  - Antiviral: Acyclovir.
  - Granulocyte stimulating factors.

Common infection in specific organ transplant:

- **Bone marrow transplant**: Bloodstream infections, pneumonia, and viral infections. {The worst because patients who are assigned to have bone marrow transplant are already immunocompromized and the procedure itself requires destroying the normal bone marrow.}
- **Kidney transplant:** Urinary tract infections.
- **Liver transplant:** Intra-abdominal infections.
- **Heart and Heart-Lung transplant:** Chest, and mediastinitis.

TABLE 1. Evolving risk of infection in the bone marrow recipient

Time	Infectious agent
Early (neutropenic period)	Bacteria Common gram-positive and gram-negative pathogens Fungi *Candida* spp. *Aspergillus* spp. *Fusarium* spp. Viruses HSV RSV Protozoa *T. gondii*
Middle (following marrow recovery)[a]	Viruses CMV VZV HHV-6 Adenovirus RSV Fungi *Aspergillus* spp. *P. carinii* Protozoa *T. gondii*
Late (>100 days post-transplantation)	Bacteria *S. pneumoniae* *S. aureus* Viruses VZV CMV RSV Fungi *P. carinii* Protozoa *T. gondii*

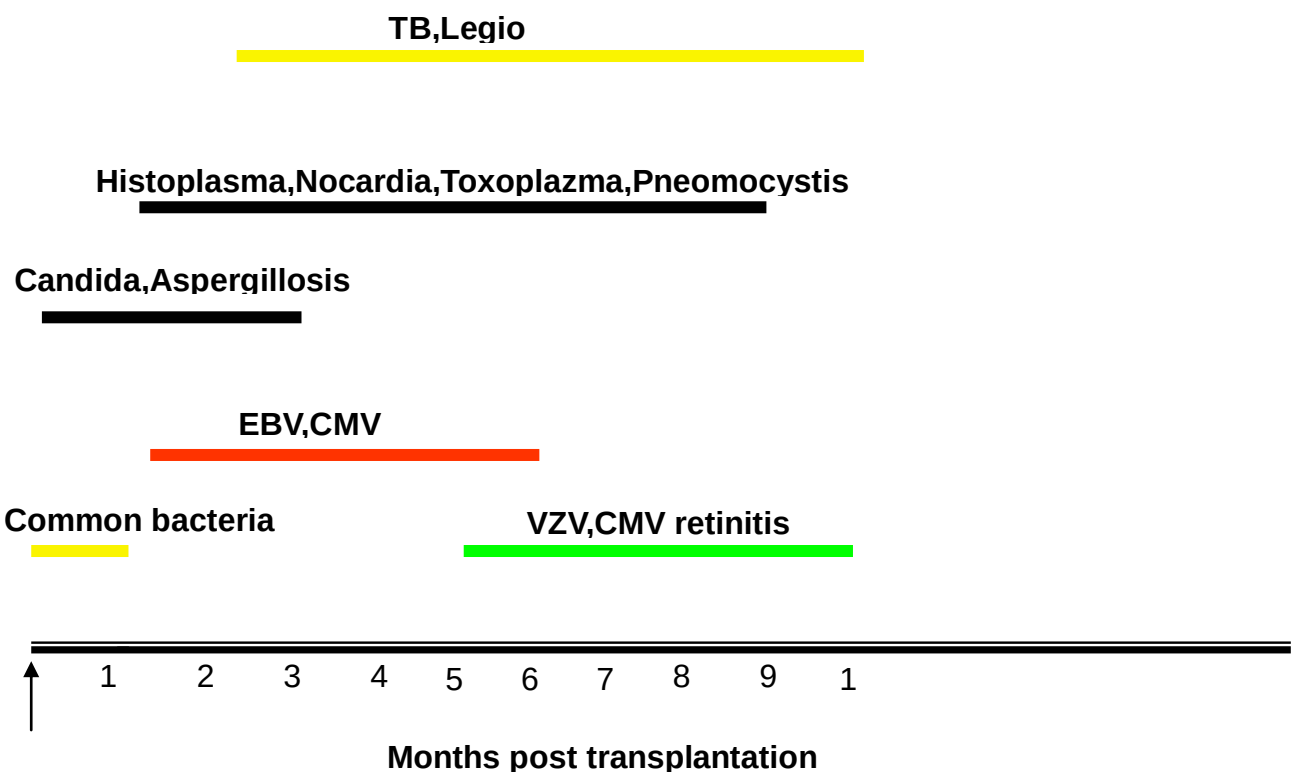
[a] More common in patients experiencing GVHD or infection with immunomodulating viruses.

Because the main suppression is cell-mediated immunity these patients will have reactivation of viral and fungal infections and some of the bacteria.

The initial few days, the patient usually in the ICU and they are prone to have severe bacterial infections but later on after few months the cell mediated immunity deficiency will start to show by reactivation of the common viral symptoms.

Factors affecting the incidence of infections:

- The type of organ transplanted.
- The degree of immunosupression.
- The need for additional antirejection therapy. {If the body rejects the transplanted organ}
- The occurrence of surgical complications.
- Presence of latent infection in the donor or recipient.



Graph explanation:

The first month after transplant, the patients usually in the ICU and they are prone to have severe bacterial infections (Bacteremia from staph aureus for example), sever fungal infections, etc. During this period the patient will be treated like any febrile person. After that, the patient will be discharged and the effect of immunosuppressive drugs like steroids, cyclosporines will take place as reactivation of viral infections (CMV, HSV and EBV), also some of the fungi (Candida), and protozoas (Pneumocystis). At this stage patients resemble HIV infected patients. Usually if the patient is doing well, they will start tapering and reducing the doses of immunosuppression and the risk of infections will gradually decrease with time.