

Team Medicine

29. Infections in
immunocompromised
patient

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■ Slides ■ Doctors notes ■ Additional



(The reference is mainly from the slides)

- Definitions:

- Immunodeficient: No cell-mediated or humoral immunity
- Immunocompromised: Any form of defect, e.g. burned skin, or patient treated with immunosuppressive therapy.

- Components of Host Defenses:

- Mechanical barriers: Skin (defective skin → bacteria will go directly to tissue and then to blood and cause an infection. Trauma may cause skin removal which puts the person in great risk of infections), mucous membranes, epiglottis (protects the lung from secretions) & cilia. (Cilia and mucus in the airways prevent foreign bodies from entering the body) >> Kartagener syndrome: ciliary immotility
- Granulocytes: (their main function is to attack foreign bodies engulf them and kill them)
- Immune system:
 - Cell mediated Immunity: Macrophages, T-lymphocytes (Main cells), NK cells, cytokines
 - Humoral Immunity (production of antibodies): B-lymphocytes (Main cells), immunoglobulins, complement (they help in phagocytosis). (Antibodies: 1-general immunoglobulins → defend against any foreign material. 2-specific antibodies for specific microorganisms e.g. IgG against measles or chicken pox...)
- Spleen.

- 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 organ transplant)
- Seriousness of infections in those patients. (Because immunocompromized patients can quickly deteriorate and die.)
- Infections with unusual, nonpathogenic microorganisms
- 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. (Most of these children do not survive because they usually die of infections)
 - E.g. chronic granulomatous disease, combined

immunodeficiency syndrome, specific Ig deficiency, others. (Primary “congenital” can be very specific e.g. IgG deficiency or it can be mixed like combination of immune deficiency of cell mediated immunity and humeral immunity and one of the commonest is combined immunodeficiency syndrome)

- (Chronic granulomatous disease is an inherited disorder in which immune system cells called phagocytes “neutrophils and macrophages” do not function properly. This leads to ongoing and severe infection. neutrophils number is normal but their function is defiant, so they phagocytose ‘ingest’ but they do not kill the organism due to failure in making hydrogen peroxide and other oxygen metabolites)
- other disease can cause immune deficiency like kartageners syndrome, situs inversus “it’s a condition in which the internal organs lie in mirror image of their normal body” and cystic fibrosis.)
- Secondary (acquired):
 - The commonest, there are many causes.
 - Extremes of age, pregnancy, infections, malignancy, chemotherapy, steroids, burns, trauma, procedures, connective tissue diseases, chronic diseases like DM, CRF etc.
 - (Mechanical barriers defects → Surgeries, trauma, burns, intubation, urinary catheters and intravenous catheters... all these make the patient more susceptible to infections. 30% of intubated patients will get pneumonia)
 - (Cell mediated immunity → typical examples are HIV/AIDS because it directly affects T-lymphocytes and transplant patients because of their medication that suppresses the cell mediated immunity.)
 - Humeral immunity → there are many causes particularly cancer chemotherapy which will lead to suppression of bone marrow and hematopoietic cells
 - Patients with chronic diseases → diabetes, chronic renal failure and liver failure. All these patient are prone to infections due non-specific decrease in immunity.)
 -

Host Defects and Associated Prevalent Pathogens:

(Patients with immunodeficiency can have any infection but certain defects are known to be associated with certain pathogens/infections. Its summarized in the table bellow.)

Granulocytes main function is to engulf bacteria (notice that almost all the pathogens are bacterial in that specific defect)

In CMI, the major problem is usually reactivation of viral infections. In IHI, the main bacterial infections are due to those bacteria, which require immunoglobulins for

Spleen plays role in opsonizing the capsulated bacteria. Defect in spleen results in susceptibility to encapsulated bacterial infection

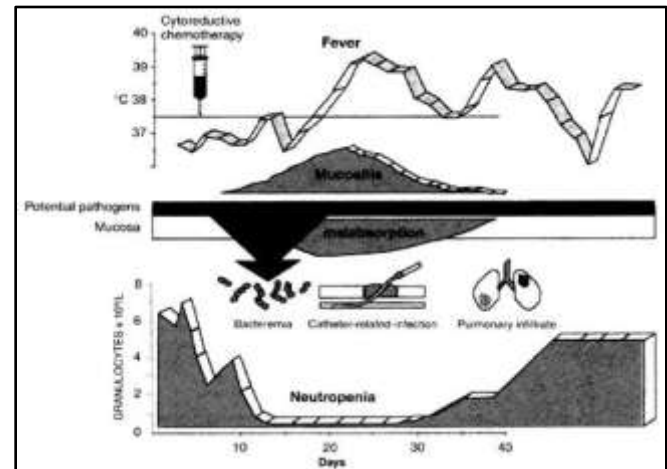
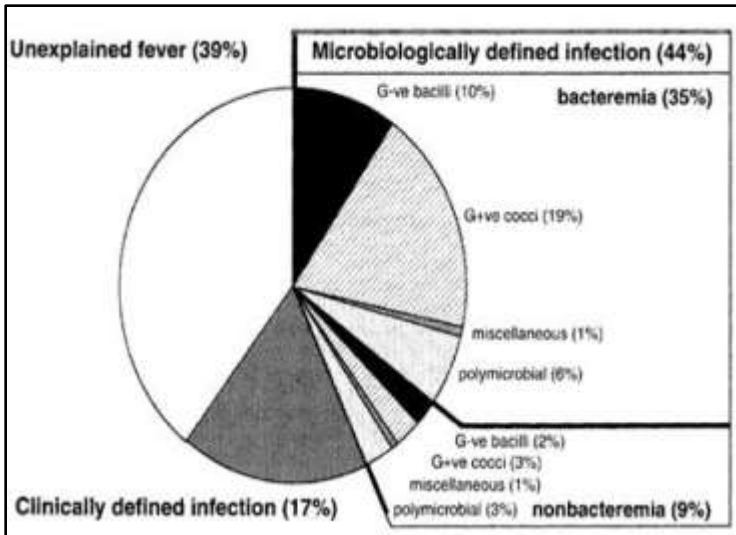
Defect	Pathogen
Granulocytopenia Chemotherapy is the main cause	Staph. Aureus, CNSS, V strep, Enterococci, E. coli, Pseudomonas aeruginosa, K.pneumoniae, other gram -ve bacilli, Aspergillus spp
Damaged skin and mucous membrane	CNSS (Coagulase negative staph species.), Staph. Aureus, pseudomonas aeruginosa 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 → congenital (Usually) or connective tissue disease e.g. SLE	Neisseria meningitides, Neisseria gonorrhoea

Fever In Neutropenic Patients: (two major categories of immunodeficiency, which are relatively common. So is HIV/AIDS.)

- Definition: (this is a specific clinical condition. its very common in hospitals especially in cancer patients due to the treatment which leads to neutropenia, and then they develop fever because of an infection.)
- Fever
 - Oral temperature of 38c for more than two hours or single temperature of 38.3c or more. (Temperature of 38.3 in an immunocompromised patient must be taken seriously and immediate action should be taken to evaluate and treat these patients.)
 - Neutropenia : A Neutrophil count of <500 cells/mm³ or a count of <1000 cells/mm³ with a predicted decline to 500/mm. (normal neutrophils > 1000 cells/mm³) (normal level of neutrophils is above 1000 so anything below it is considered neutropenia, and the seriousness of the infection correlates with the level. The lower the level the more likely the patient will have an infection. Usually serious infections will start occurring when the level is below 500)
- Approach to patient:
 - Careful history and examination, investigations (like blood cultures (most important culture), urine culture, CXR, others), then start antibiotic therapy to cover the most likely organisms. (usually these patients will have an infection related to their IV lines so we should examine the site of intravenous catheters, look for any evidence of cellulitis, pneumonia → xray, UTI and so on.)

The commonest cause of fever in these patients is infections and the most common cause of infection is bacteremia. 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.

A patient with metastatic cancer > chemotherapy > few days and chemotherapy will start to kill (active multiplying cells e.g. bone marrow cells > neutrophil count decrease. Chemotherapy also affects other cells like in mucus membrane > ulcers in the mouth > bacteria > bacteremia. Most of these patients will remain febrile until the



The doctor skipped table 3 and 4 and went through the graphs (algorithms) by reading them quickly!

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

- Absolute neutrophil count of ≥ 100 cells/mm³
- Absolute monocyte count of ≥ 100 cells/mm³
- 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/mm³, no comorbidity, and normal chest radiograph findings indicate children at low risk for significant bacterial infections [46].

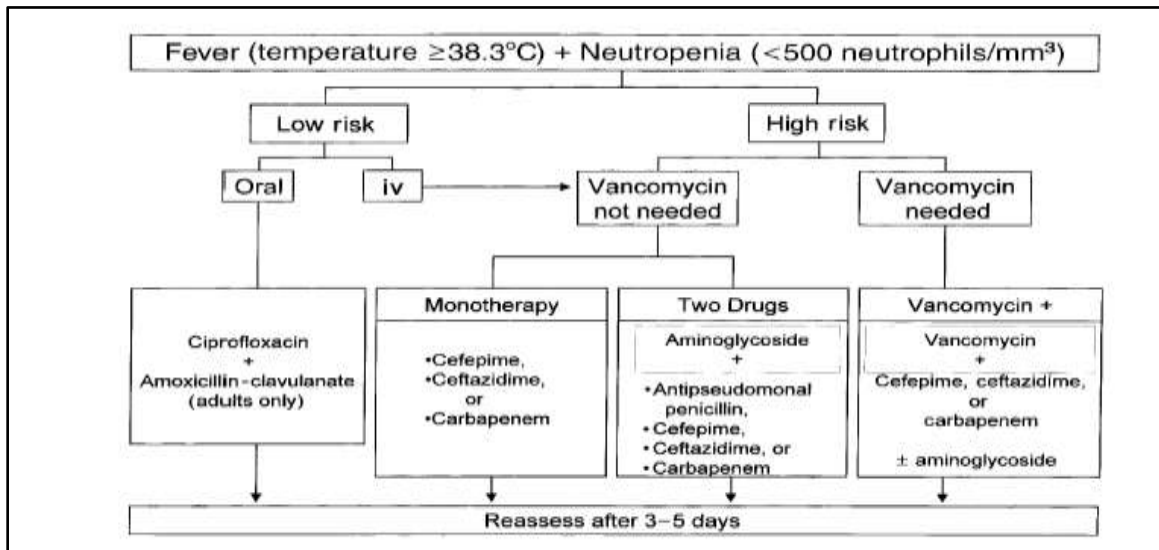
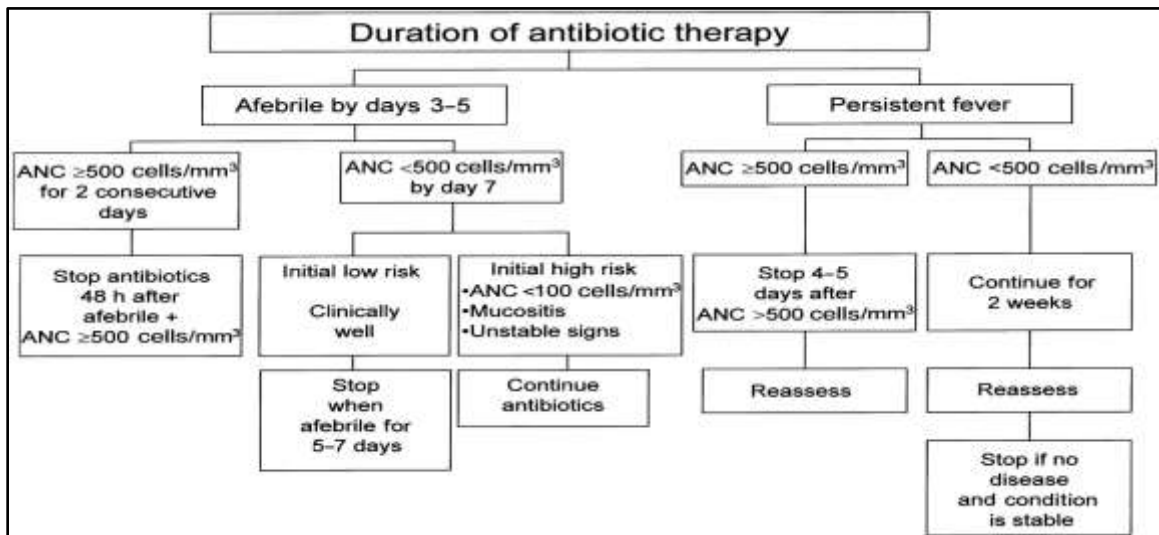
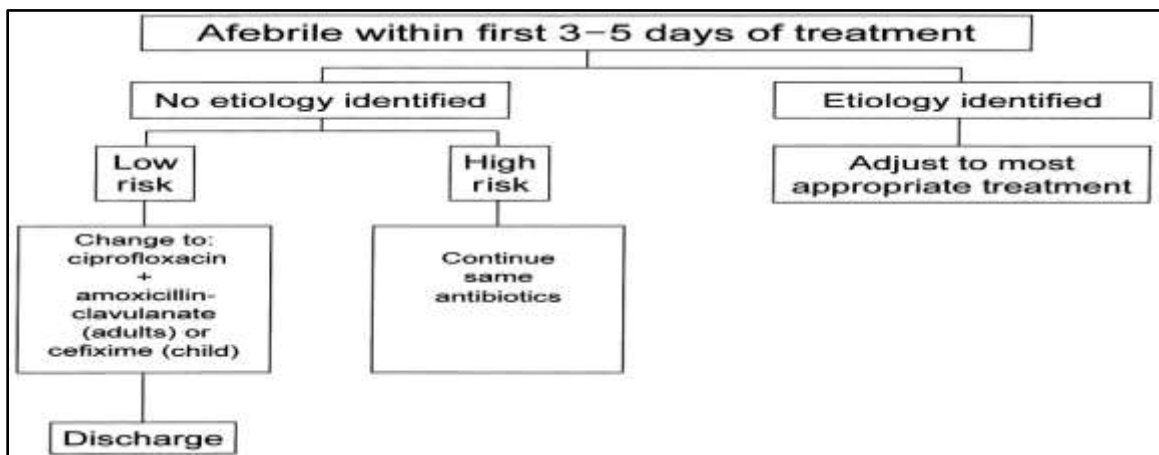


Figure 1. Algorithm for initial management of febrile neutropenic patients. See tables 3 and 4 for rating system for patients at low risk. Carbap



Treatment:

- Antibacterial like: piperacilline+ aminoglycoside or ceftazidime + aminoglycoside or Imipenem, vancomycine.
- Antifungal like: Amphotericine B, Fluconazole.
- Antiviral like: Acyclovir. (Antiviral not usually used)
- Granulocyte stimulating factors. → not antibiotics. They stimulate bone marrow to produce neutrophils to shorten the duration of neutropenia.
- Duration of treatment is variable. If there is abscess, drain it, send aspiration to lab, then start antibiotic

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 normal bone marrow)
- Kidney transplant: Urinary tract infections.
- Liver transplant: Intra-abdominal infections.e.g. cirrhosis
- Heart and Heart-Lung transplant: Chest, and mediastinitis

Factors affecting the incidence of infections:

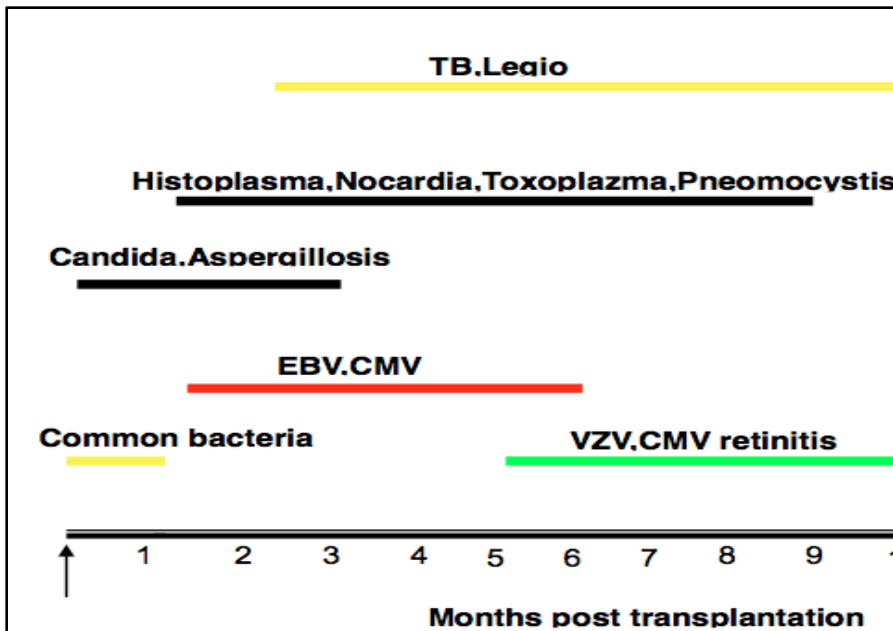
- The type of organ transplanted.
- The degree of immunosuppression.
- The need for additional antirejection therapy. (If the body rejects the transplanted organ)
- The occurrence of surgical complications.
- Presence of latent infection in the donor or recipient.

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.

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

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



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), severe 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.

Summary:

- Components of Host Defenses: Mechanical barriers, Granulocytes, Immune system and spleen.
- Causes of immune deficiency:
 1. Primary (congenital):
 - Rare, more common in children.
 - Ex. chronic granulomatous disease, combined immunodeficiency syndrome, specific Ig deficiency, others.
 2. Secondary (acquired):
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- Treatment:
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- Liver transplant → Intra-abdominal infections. e.g. cirrhosis
- Heart and Heart-Lung transplant → Chest, and mediastinitis
- Factors affecting the incidence of infections:
- type of organ transplanted, degree of immunosuppression, need for additional antirejection therapy, occurrence of surgical complications and presence of latent infection in the donor or recipient.

Questions:

- A 25 year old girl with leukemia , received the first cycle of chemotherapy ,one week before she came to the emergency department complaining of fever for about 3 hours . Her temperature is 39C and pulse is 102 beats / minutes the rest of the physical examination is normal .Total WBC are 0.1×10^9 cells/L. the patient was admitted .

which one of the following management should we do ?

- A. oral ciprofloxacin
- B. IV piperacillin / tazobactam +amikacin
- C. take blood culture and wait for the result
- D. Anti pyretic

- 27 years old man with acute leukemia, developed fever while in hospital 4 day after he received chemotherapy. His temperature is 39 c. total white blood cells count is 0.1×10^9 cells/l (Normal range 4-11 cells x 10^9 /L). The most likely cause of his fever is:

- A. Related to leukemia
- B. Viral infection
- C. Bacterial infection
- D. Fungal infection

Answers :

- 1. B
- 2. C