MEDICINE

432 Team

57 Infections in Immunocompromised Host

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

Not Given!

Introduction:

- Components of Host Defenses:
1. Mechanical barriers: Skin, mucous membranes, epiglottis, cilia.
2. Granulocytes
3. Cell mediated Immunity: Macrophages, T-lymphocytes, NKC, cytokines
4. Humoral Immunity: B-lymphocytes, immunoglobulins, complements
5. Spleen

The importance of infections in IC host:

- Increasing numbers of immunocompromised patients.
- Seriousness of infections in those patients.
- Infections with unusual, nonpathogenic microorganisms.
- Atypical presentation of infections by common pathogens

Causes of immune deficiency:

Primary (congenital)	Secondary (acquired)
Rare, more common in children	The commonest, there are many causes like:
e.g chronic granulomatus disease, combined immunedifiency syndrome, specific Ig deficiency, others.	HIV, 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:

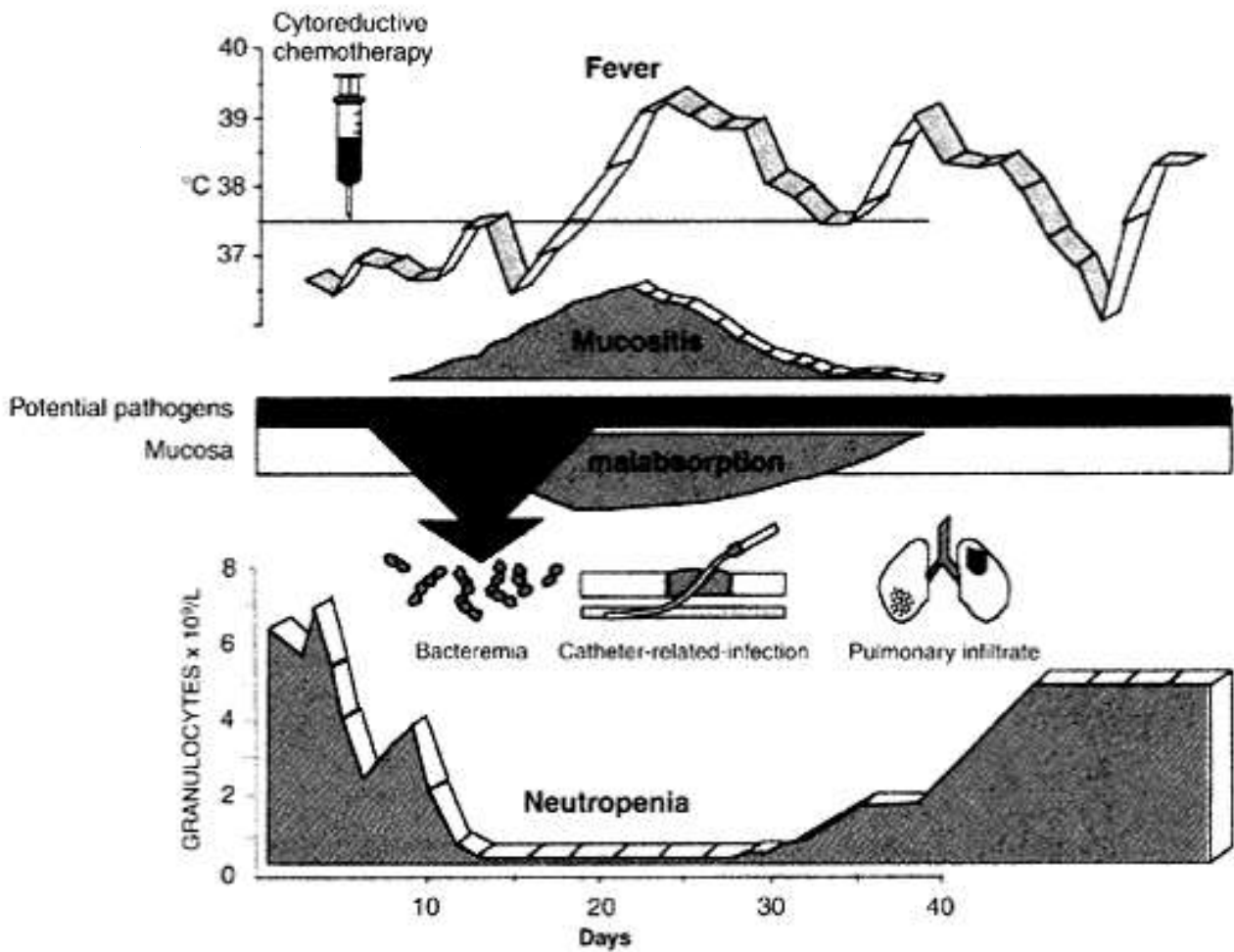| Defect	Pathogen
Granulocytopenia	Staph. Aureus, CNSS, V strep, Enterococci, E. coli, Pseudomonas aeruginosa, K.pneumoniae, other gram –ve bacilli, Aspergillus spp
Damaged skin and mucous membrane	CNSS, Staph. Aureus, pseudomonas aeruginosa and other gram-ve bacilli, candida spp, V. strep, enterococci, HSV.
Impaired CMI	HSV, VZ, EBV, CMV, RSV, M. tuberculosis, Aspergillusspp and other fungi, Toxoplasma gondi.
Impaired humoral immunity	Streptococcus pneumoniae, Haemophilusinfluenzae
Spleen dysfunction	Streptococcus pneumoniae, Haemophilusinfluenzae Neisseria meningitides.
Complement deficiency	Neisseria meningitides, Neisseria gonorrhea

Fever in Neutropenic Patient:

Definitions:

Fever: Oral temperature of 38c for more than two hours or single temperature of 38.3c or more.
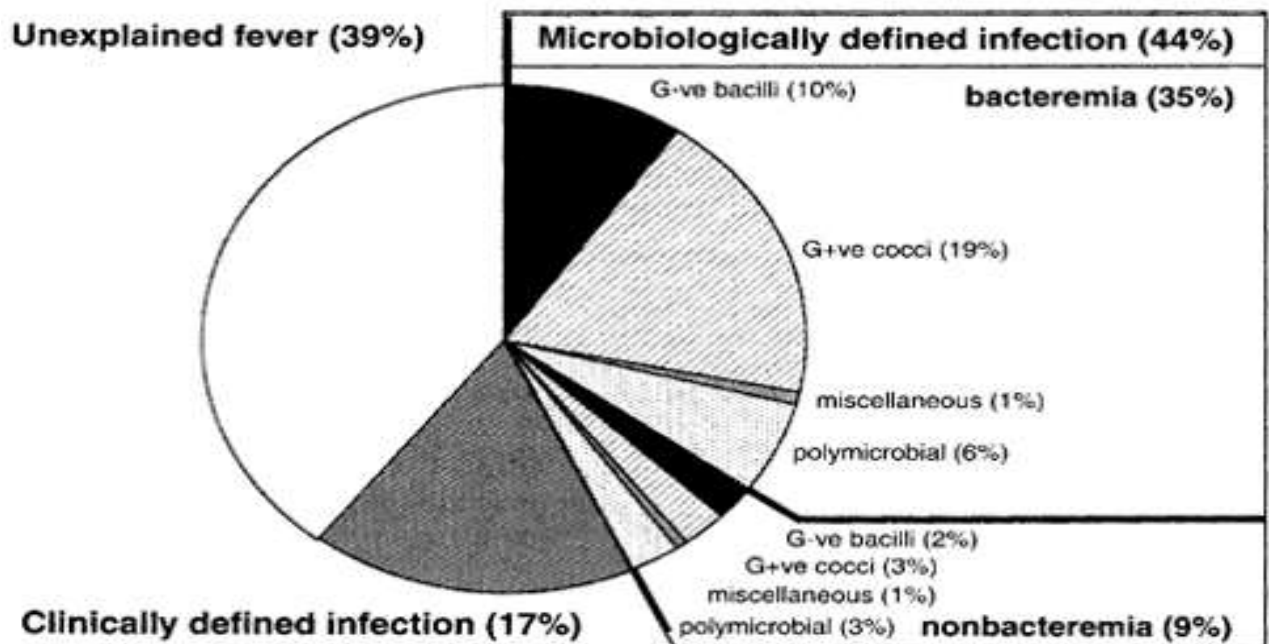
Neutropenia: A Neutrophil count of<500 cells/mm³ or a count of <1000 cells/mm³ with a predicted decline to 500/mm

Approach to patient: Careful history and examination, investigations (like blood cultures, urine culture, CXR, others), then start antibiotic therapy to cover the most likely organisms.

SEQUENTIAL INFECTIVE EVENTS

Causes of fever in neutropenic patients

IDSA guidelines CID

Fever (temperature ≥38.3°C) + Neutropenia (<500 neutrophils/mm³)

Low risk

High risk

Oral   iv   →   Vancomycin not needed

Vancomycin needed

Ciprofloxacin + Amoxicillin-clavulanate (adults only)

Monotherapy
•Cefepime,
•Ceftazidime, or
•Carbapenem

Two Drugs
Aminoglycoside +
•Antipseudomonal penicillin,
•Cefepime,
•Ceftazidime, or
•Carbapenem

Vancomycin +
Vancomycin +
Cefepime, ceftazidime, or carbapenem
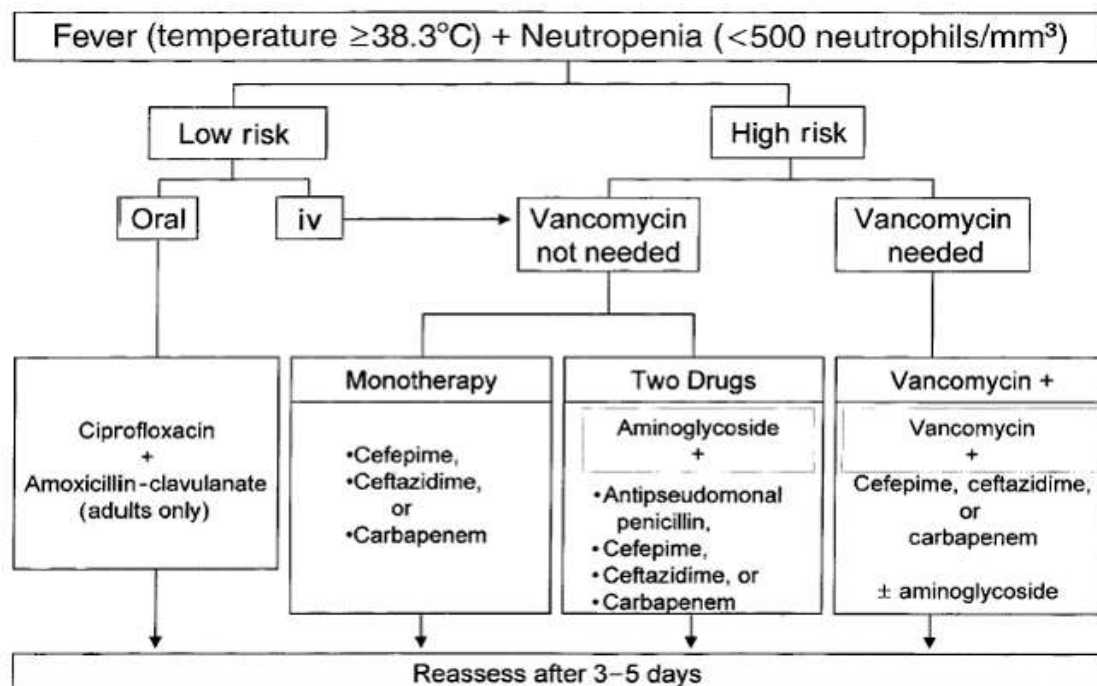± aminoglycoside

Reassess after 3–5 days

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

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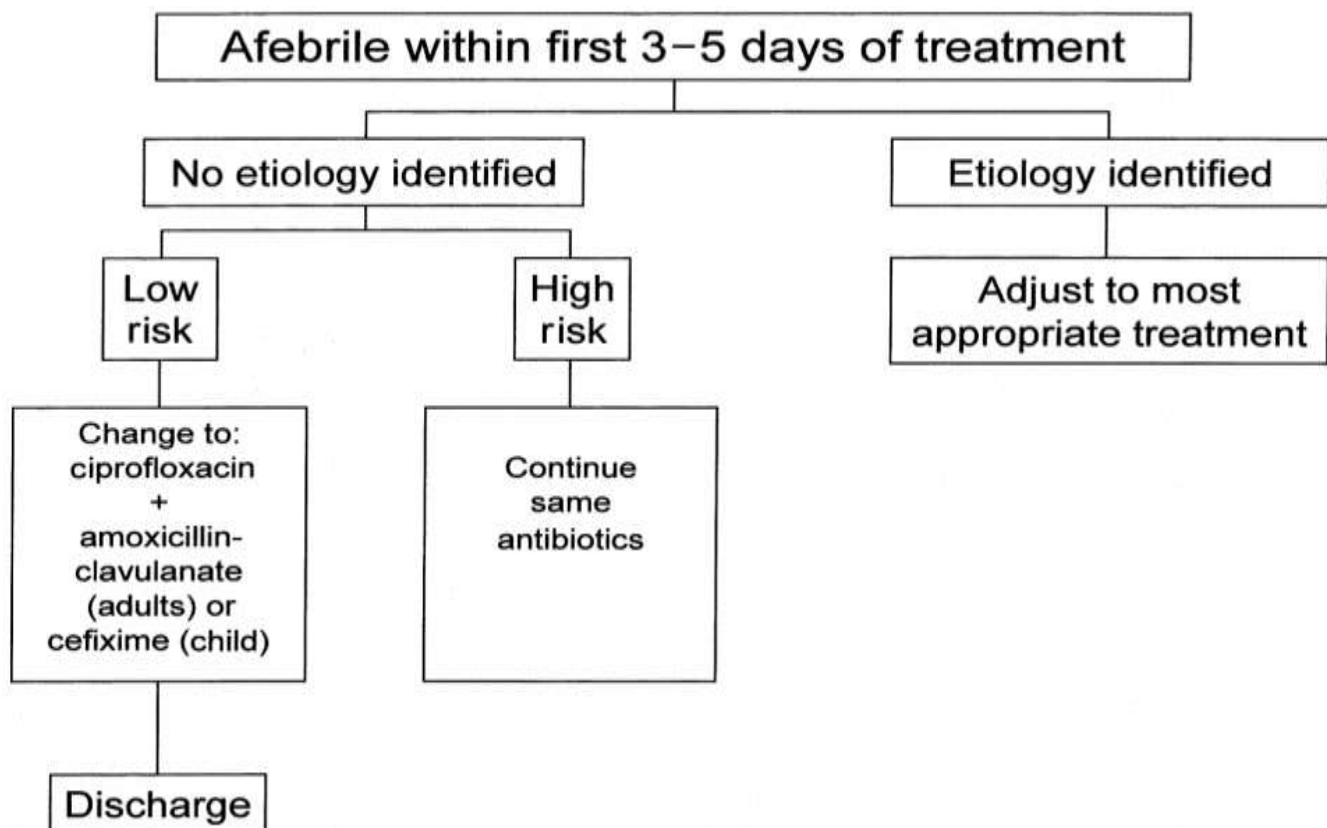
Table 4. Scoring index for identification of low-risk febrile neutropenic patients at time of presentation with fever.

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].
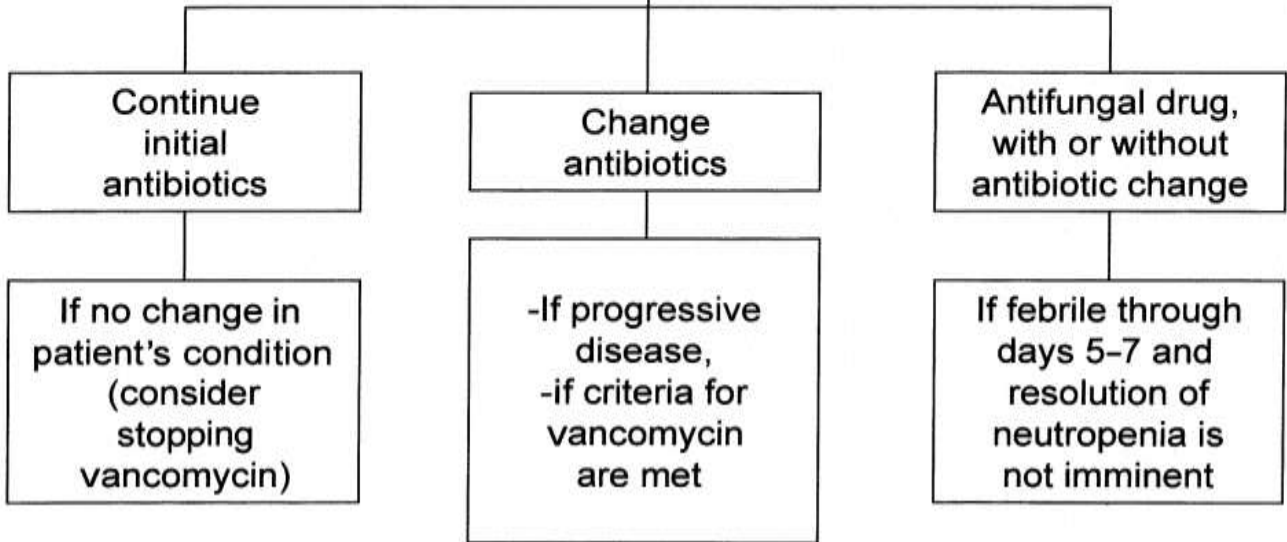
[a] Choose 1 item only.

[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].

Afebrile within first 3–5 days of treatment

- **No etiology identified**
  - **Low risk**
    - Change to: ciprofloxacin + amoxicillin-clavulanate (adults) or cefixime (child)
      - **Discharge**
  - **High risk**
    - Continue same antibiotics
- **Etiology identified**
  - Adjust to most appropriate treatment

Persistent fever during first 3-5 days of treatment: no etiology

Reassess patient on days 3-5

Continue initial antibiotics

If no change in patient's condition (consider stopping vancomycin)

Change antibiotics

-If progressive disease,
-if criteria for vancomycin are met

Antifungal drug, with or without antibiotic change

If febrile through days 5-7 and resolution of neutropenia is not imminent

Duration of antibiotic therapy

Afebrile by days 3-5

ANC ≥500 cells/mm³ for 2 consecutive days

Stop antibiotics 48 h after afebrile + ANC ≥500 cells/mm³

ANC <500 cells/mm³ by day 7

Initial low risk

Clinically well

Stop when afebrile for 5-7 days

Initial high risk
•ANC <100 cells/mm³
•Mucositis
•Unstable signs

Continue antibiotics

Persistent fever

ANC ≥500 cells/mm³

Stop 4-5 days after ANC >500 cells/mm³

Reassess

ANC <500 cells/mm³

Continue for 2 weeks

Reassess

Stop if no disease and condition is stable

Treatment:

- **Antibacterial like:** Pipracilline + Aminoglycoside or Ceftazidime + Aminoglycoside or Imipenem, Vancomycine.
- **Antifungal like:** Amphotericine B, Fluconazole, Voriconazole
- **Antiviral like:** Acyclovir, Granulocyte stimulating factors

Infections in Organ Transplant Recipients:

Common infection in Specific Organ transplant:

| Bone marrow transplant	Bloodstream infections, pneumonia, viral infections
Kidney transplant	Urinary tract infections.
Liver transplant	Intraabdominal infections.
Heart and Heart-Lung transplant	Chest, 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 immuno-modulating viruses.

Factors affecting the incidence of infections:
I.   The type of organ transplanted.
II.   The degree of immunosuppression.
III. The need for additional antirejection therapy.
IV.   The occurrence of surgical complications.
V.   Presence of latent infection in the donor or recipient.
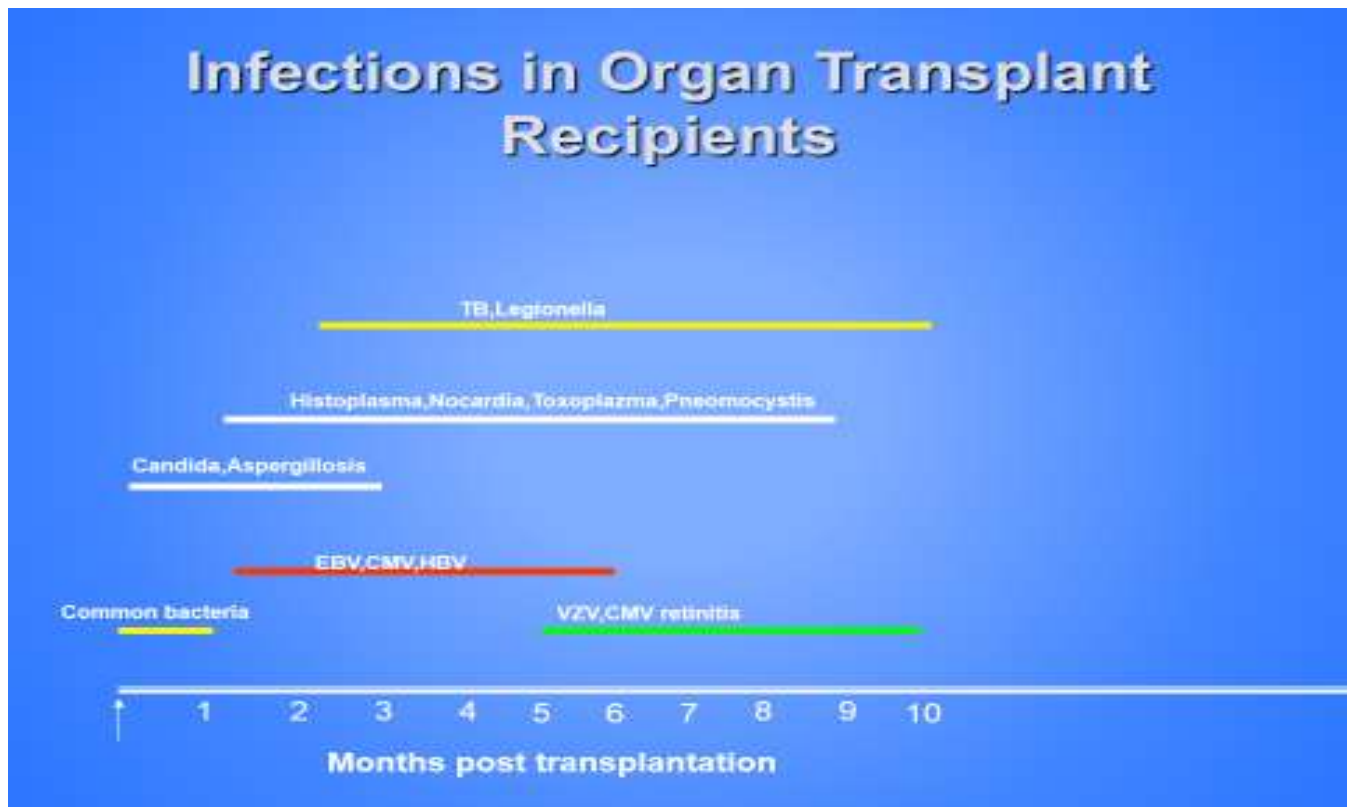
SUMMARY

1. **Immunocomprised Infections** are increasing in number, serious, with unusual organisms and atypical presentation.

2. It could be **congenital** (chronic granulomatus disease, combined immunedifiency syndrome, specific Ig deficiency) or **acquired** (due to other cause; infection, pregnancy, malignancy ...)

3. It comes with immune barrier defect (granulocytopenia , damaged skin and mucus membrane , impaired CMI or Humoral immunity , complement deficiency and spleen dysfunction)

4. **Fever in neutropenia**: (fever while neutrophils < 500, could be bacteriogenic or idiopathic) approach: Hx, PE and investigation (Blood, urine, radiology) then start antibiotics.

5. **Infection in organ transplant recipient**: Bone marrow (bloodstream, pneumonia, viral), Kidney (UTI) , Liver (intra-abdominal infections) , heart & lung (Chest, mediastinitis)

6. Factors affecting the incidence of infections:
   1) The type of organ transplanted.
   2) The degree of immune-suppression.
   3) The need for additional anti-rejection therapy.
   4) The occurrence of surgical complications.
   5) Presence of latent infection in the donor or recipient.
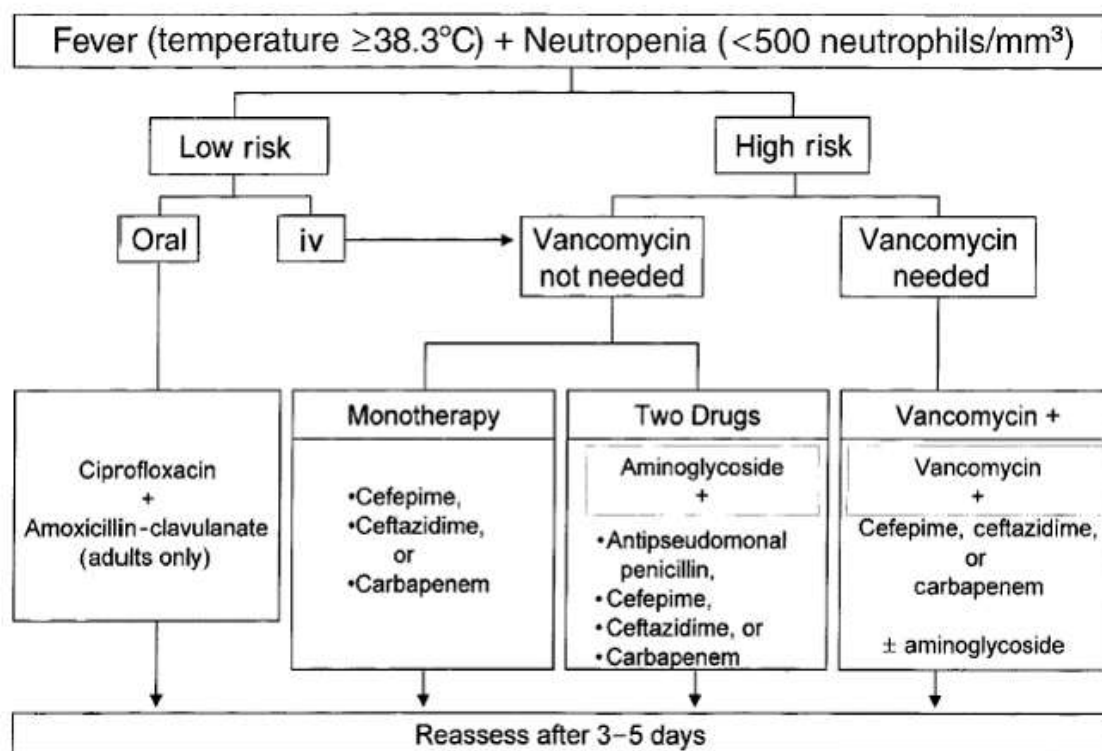

Figure 1. Algorithm for initial management of febrile neutropenic patients. See tables 3 and 4 for rating system for patients at low risk. Carbap

Questions

1) A 30 years old patient had kidney transplant one year ago. He is doing well on standard immunosuppressive therapy. He is at high risk to develop which of the following infections?

    a. Urinary tract infections
    b. Infectious mononucleosis
    c. Pulmonary tuberculosis
    d. Recurrent cellulites

2) Which one is a likely infection in immunocompromised patient?

    a. Glomerulonephritis
    b. Osteomyelitis
    c. Pulmonary TB
    d. Thyroiditis

432 Medicine Team Leaders

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Answers:

1st Questions: A

2nd Questions: C