

**Infections in the Immunocompromised:**  
**MANAGEMENT IN CHILDREN WITH**  
**HEMATOLOGIC MALIGNANCIES**

**JULIUS A. LECCIONES, MD, MHSA, MPM, CEO VI**

**Executive Director**

**Philippine Children's Medical Center**

**Quezon Avenue, Quezon City**

# Management of Infections in Children with Hematologic Malignancies

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- Childhood cancer is a major cause of mortality
- Leukemia and lymphoma constitute approximately 50-60% of all malignancies in children
- More than 80% of hematologic malignancies attain long-term survival
- Chemotherapy as the cornerstone of treatment is responsible for this high cure rate

# Management of Infections in Children with Hematologic Malignancies

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- Infections have become the expected sequelae of cancer chemotherapy
- Magnitude of infection risk varies closely with the depth and duration of neutropenia

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- Fewer than 30% of patients whose duration of neutropenia is less than 1 week have fever or evidence of infection
- Almost 100% of patients who receive chemotherapy and have neutropenia will have fever and/or infections

*Pizzo PA, Robichaud KJ, Edward BK et al: J Pediatr 1983; 102: 125;  
Pizzo PA, Commers JR, Cotton DJ, et al: Am J Med 1984; 76: 436*

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- Extent of cancer closely correlates with intensity and duration of chemotherapy and contributes to increased infection rate
- Once in remission, risk of infection-related morbidity and mortality declines

*Young LS: Clinical Approaches to Infections in the Compromised Host.  
New York: Plenum, 1998: 439*

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- Fever remains the most important indicator of infection in children with cancer
- Almost 75% of patients with F+/N+ could eventually be shown to have a clinically or microbiologically documented site of infection
- Less than 20% had defined infectious cause in those with F+/N-

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The NCI study helped to delineate the association of fever and neutropenia with infection in children with cancer and supported the use of empiric antibiotic treatment in the overall management

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- During the 1980s – empiric antibiotic treatment in F+/N+ limited ability to define infectious origin of febrile episode
- Late 1980s – only 30%-40% of cases of F+/N+ had definable infectious cause
- Early 1990s – increased use of indwelling IV catheters; increased G+ bacterial infections and decline in G-, particularly *Pseudomonas aeruginosa*
- Today, management in neutropenic children initially revolves around the management of fever as a manifestation of infection

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- Recent guidelines define fever as a single oral temperature  $>38.3^{\circ}\text{C}$ , or  $38.0^{\circ}\text{C}$  over at least an hour
- Fever in N+ patients should not be attributed to blood products reactions, neoplasms or drugs
- The absence of fever should not delay therapy when infection is suspected

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- N+ is defined as absolute count  $<500/\mu\text{L}$  of blood, or  $1,000/\mu\text{L}$  with predicted decline to below  $500/\mu\text{L}$
- ANC  $<100/\mu\text{L}$ , an ANC  $<500/\mu\text{L}$  for  $>10$  days, and rapidly falling ANC are associated with occurrence of infection

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- Customary signs and symptoms of localized infection may be diminished or absent in the setting of N+
- Pain does not seem to be diminished in N+ and therefore becomes a more important symptoms
- Fever, chills or rigors within 2 hrs following accessing or flushing of indwelling line should increase suspicion

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The physical examination generally can be focused on common sites of infection, including the oral cavity, skin, nails, catheter exit sites, lungs, abdomen, and the perirectal area

Whitecar JPJ, Luna M, Bodey GP: Am J Med Sci 1970; 60: 216-223

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- Cultures should be obtained while the initial dose of antibiotics are being prepared
- Minimum of 2 blood cultures from separate locations
- If with indwelling line, blood culture must be obtained from each of the lumen, and from a peripheral site
- Cultures of other suspected sites

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- Newer studies cast doubt on the utility of routine chest xray
- Chest xray must be obtained in those with respiratory symptoms at onset of fever or when symptoms developed while N+
- CT of chest and abdomen especially helpful in identifying disseminated fungal disease

# Principles of Antibiotic Therapy in the Neutropenic Host

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- Empiric, broad-spectrum antibiotic therapy is necessary at the outset of fever in the neutropenic patient
- Initial empiric therapy should be based on the likely infecting organisms. Cover pathogens with high morbidity and mortality. Be familiar with the local susceptibility patterns

# Principles of Antibiotic Therapy in the Neutropenic Host

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- Analysis of factors associated with the specific patient may guide empiric therapy
- Take into account the host factors, including mucositis, presence of an indwelling catheter, or an antecedent viral infection
- Know patient's flora and inquire regarding exposures
- Examine for focus of infection

# Principles of Antibiotic Therapy in the Neutropenic Host

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- Antimicrobial regimens should minimize toxicity and emergence of resistance. Withdraw antibiotics when they are not needed
- Minimize number and duration of antimicrobials while maintaining broad spectrum coverage

# Principles of Antibiotic Therapy in the Neutropenic Host

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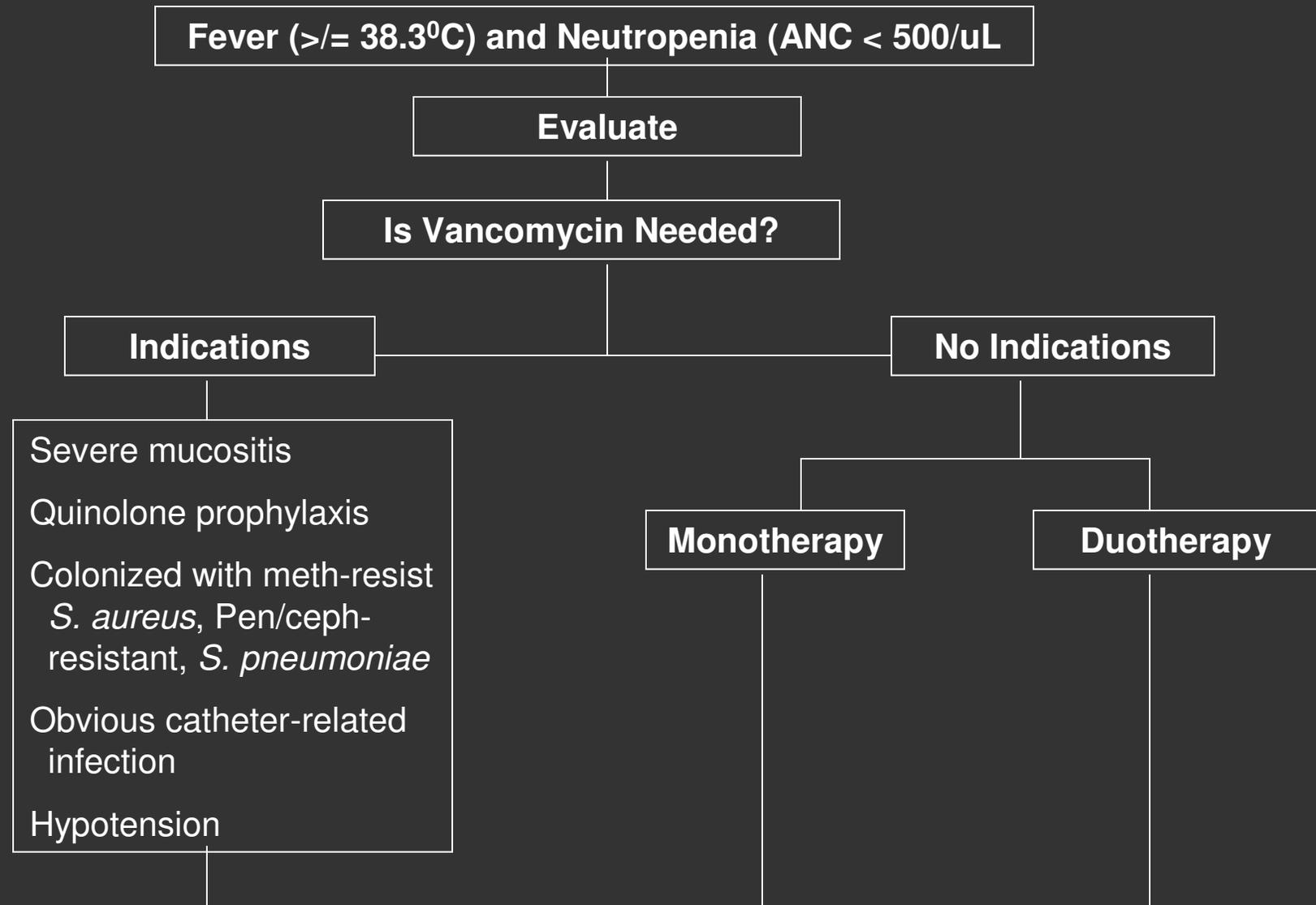
- Empiric therapy should be modified to reflect the changing pattern of infections during therapy
- Deterioration should prompt change to optimize both G+ and G- coverage
- Isolation of a specific pathogen may allow directed therapy while maintaining broad-spectrum coverage. Withdraw unnecessary antibiotics when practical
- Add antifungal coverage when needed

# Principles of Antibiotic Therapy in the Neutropenic Host

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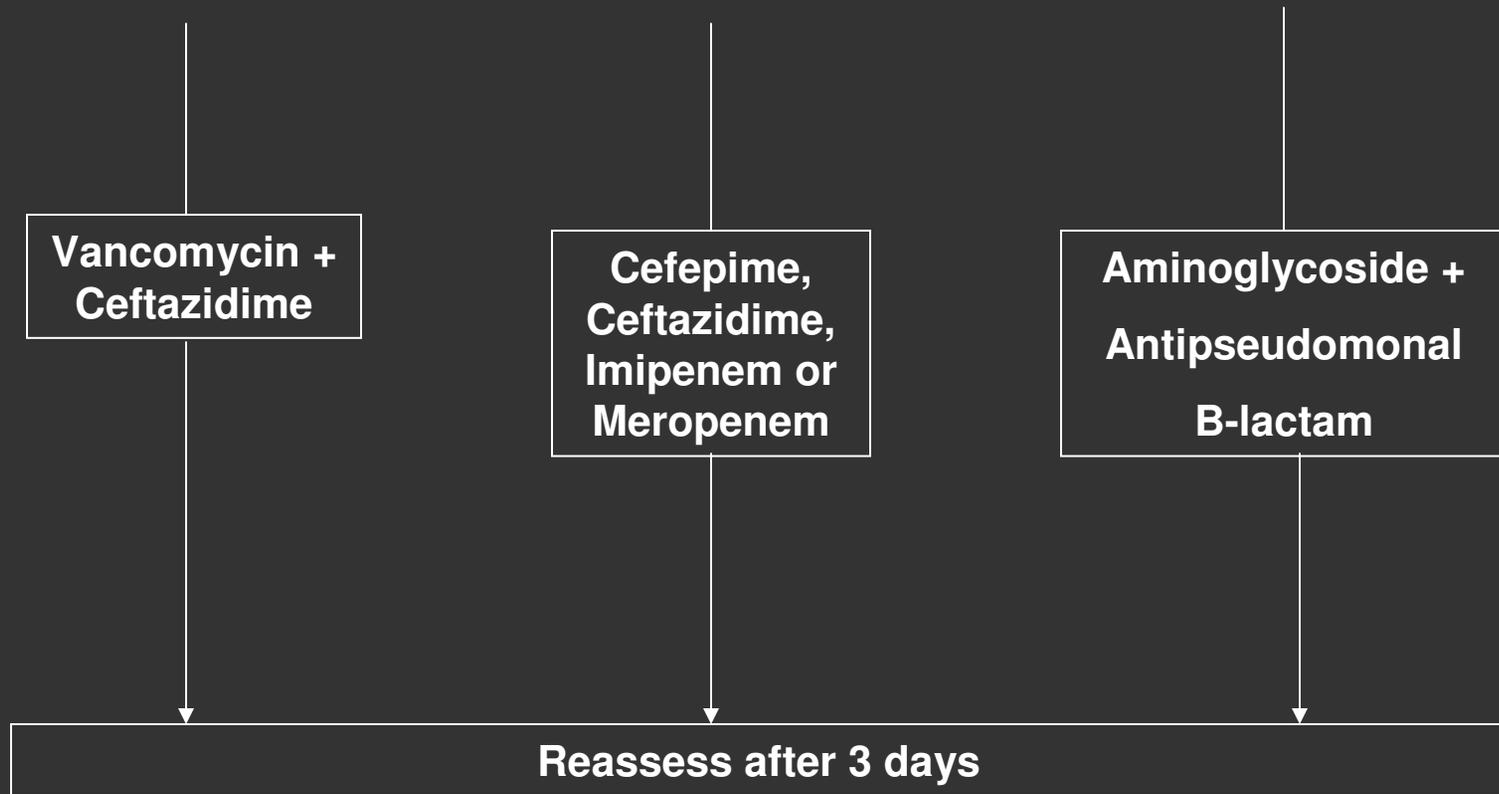
- Optimal therapy requires balancing need to reduce morbidity and mortality against the goal of minimizing use of antibiotics
- Prevention of infection is preferable to treatment of infection

# Three General Approaches



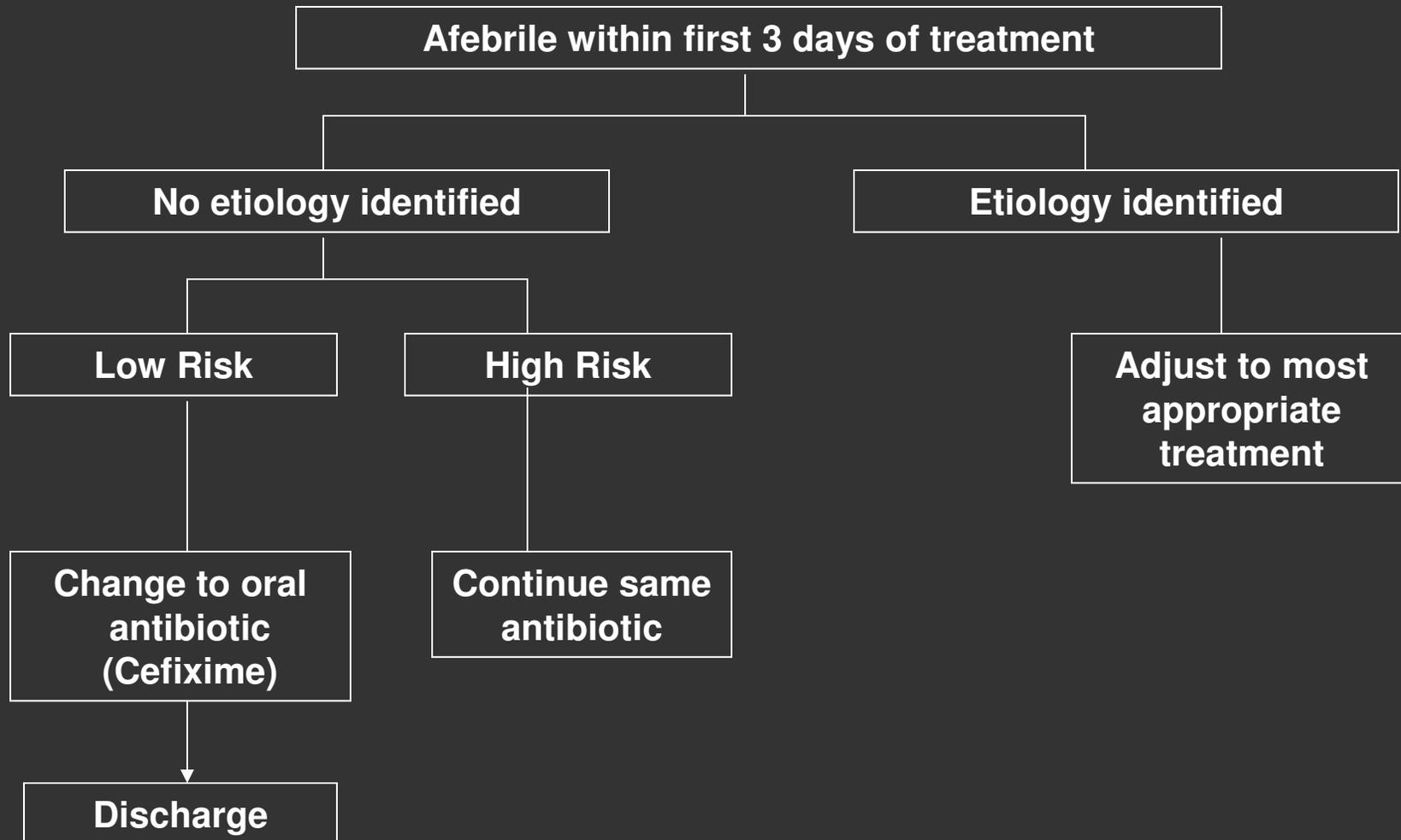
# Three General Approaches

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Persistent fever during 3 days of treatment: no etiology

Reassess patient on day 4-5

Continue initial antibiotics

If no change in patient, consider stopping vancomycin

Change antibiotics

If progressive disease, add vancomycin + G- bacillary coverage

Add Amphotericin B with or without antibiotic change

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

# Three General Approaches

