Febrile Neutropenia in Immunocompetent Patients

Fever[1]: a single oral temperature ≥ 38.3°C or a temperature ≥ 38°C sustained over 1 hour

Neutropenia[2]: Based on Absolute Neutrophil Count (ANC = neutrophils + bands + myelocytes + metamyelocytes)

- **Mild**: 1.0 x 10^9/L to 1.5 1.0 x 10^9/L
- **Moderate**: 0.5 x 10^9/L to 1.0 x 10^9/L
- **Severe**: < 0.5 x 10^9/L

Risk of Invasive Bacterial Infection (IBI)

Immunocompetent Patients

- Risk of IBI is ~1.9%, similar to febrile patients *without* neutropenia.[4]
- Many of these patients do not require admission or antibiotics[2] (see management algorithm).

Oncologic Patients

- Risk of IBI is ~30%.[3]
- Guidelines clearly recommend IV antibiotics and admission. (Note: Febrile Neutropenia)

Etiology of Neutropenia[5]

Immunocompetent Host	Immunocompromised Host
▪ Viral suppression*	▪ Malignancy (i.e. leukemia)
▪ Non-chemotherapy drug induced (i.e. NSAIDs, antibiotics, antiepileptics)	▪ Chemotherapy induced
▪ Autoimmune	▪ Severe or invasive bacterial infections
▪ Neonatal Alloimmune Neutropenia (from mother's antibodies)	▪ Cyclic Neutropenia (genetic, ~21-day cycles)
▪ Nutritional (B12 or folate deficiencies)	▪ Severe congenital neutropenia
▪ Duffy-Null phenotype (Genetic neutropenia seen in individuals of African or Middle Eastern descent)	▪ Bone marrow failure syndromes (i.e. Fanconi Anemia, Blackfan Diamond)
	▪ Primary Immunodeficiencies

***Most cases of neutropenia are transient (< 1 month) and caused by a viral illness[6].**

⚠ Risk Factors for IBI

History

- ❑ Immunocompromised
- ❑ History of neutropenia
- ❑ Previous severe/recurrent infection (i.e. sepsis, meningitis, severe pneumonia, etc.)
- ❑ Intravascular device
- ❑ Significant comorbidities (i.e. failure to thrive, genetic condition, chronic medical condition)
- ❑ Not up-to-date on vaccines for encapsulated bacteria
- ❑ Family history of: immunodeficiency, neutropenia, bone marrow failure, leukemia

Physical

- ❑ Ill-appearing
- ❑ Hepatosplenomegaly
- ❑ Diffuse lymphadenopathy
- ❑ Dysmorphic features

Investigations

- ❑ High mean corpuscular volume
- ❑ Suppression of other cell lines on CBC

MANAGEMENT[2]

> 6 months old, well-appearing, with febrile neutropenia

No → Exit Pathway

Yes ↓

- History and physical exam (Assess for IBI risk factors and etiology of neutropenia)
- Peripheral blood culture
- Other investigations as needed (i.e. urine culture)

≥ 1 risk factor for IBI	No risk factors for IBI
High risk of IBI	**Low risk of IBI**
Individualized care, Consider antibiotics +/- admission	Do not need admission and may not need empiric antibiotics.

ANC > 1	Manage as if normal ANC.
ANC 1 - 0.5	Do not routinely require empiric abx. Repeat CBC in 1-3 months.
ANC < 0.5	Empiric abx not usually required but may be considered if ANC < 0.2. Close follow up in 24-48 hours. Repeat CBC in 4-6 weeks and seek urgent care if new fevers develop.

Educate all parents on signs of sepsis (pallor, lethargy, altered LOC, persistent vomiting or fever)

Refer to Pediatric Hematology if: 1) ANC remains < 0.5 after 4-6 weeks, 2) there are other cell line abnormalities

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