



Neutropenic Fever

Antibiotics within 60 minutes · This is sepsis until proven otherwise

DOOR TO NEEDLE < 1 h
the quality standard

DEFINE IT AND MOVE *a single temperature is enough — do not wait for a second*

THE DEFINITION

ANC < 500/ μ L, or < 1,000 and expected to fall below 500, plus a single oral temperature $\geq 38.3^{\circ}\text{C}$ or $\geq 38.0^{\circ}\text{C}$ sustained over an hour. Fever may be the **only** sign — there is no pus, no infiltrate and no localizing inflammation without neutrophils.

ACT IN THE FIRST HOUR

Cultures then antibiotics within 60 minutes of presentation. Do not wait for the neutrophil count if the clinical suspicion is high in a recently treated patient. **Delay to antibiotics is directly associated with mortality.**

EXAMINE THE HIDDEN SITES

Mouth (mucositis), **perianal area** — but **no rectal examinations or suppositories**, which risk bacteremia — **indwelling line sites**, skin, and perineum. **Avoid instrumentation** in the neutropenic patient.

RISK-STRATIFY *not everyone needs admission*

Tool / group	Detail
MASCC score	≥ 21 is low risk; ≤ 20 is high risk. The MASCC index or Talcott's rules are the recommended tools for identifying candidates for outpatient management.
Low risk — outpatient option	Oral fluoroquinolone plus amoxicillin-clavulanate (or clindamycin if penicillin-allergic) is recommended empirical outpatient therapy — unless fluoroquinolone prophylaxis was already being taken, in which case a quinolone must not be used.
Outpatient prerequisites	Clinically stable, no significant comorbidity, able to tolerate oral intake, reliable transport and a carer , close follow-up, and living within reasonable distance of the hospital. If any of these fail, admit.
High risk	Anticipated prolonged (> 7 days) and profound neutropenia, hemodynamic instability, mucositis interfering with swallowing, gastrointestinal symptoms, new neurological change, line infection, or hepatic or renal impairment. Admit for intravenous therapy.

CHOOSE THE ANTIBIOTIC *monotherapy is standard — and vancomycin is not routine*

- 1 **Monotherapy with an antipseudomonal beta-lactam** is recommended — **cefepime**, **piperacillin-tazobactam**, or a **carbapenem** (meropenem or imipenem-cilastatin). Pseudomonal cover is non-negotiable.
- 2 **Do not add vancomycin routinely.** These monotherapy regimens give **excellent coverage of viridans streptococci** and are adequate as sole agents **even with oral mucositis** — which removes the traditional reason people reach for vancomycin.
- 3 **Add vancomycin only for: hemodynamic instability, skin or catheter-site infection**, suspected **MRSA pneumonia**, or **gram-positive organisms on blood culture** pending identification and susceptibilities. **If no gram-positive infection is confirmed, stop it after 48 hours.**
- 4 **Broaden for specific concerns** — add an aminoglycoside or switch to a carbapenem for suspected resistant gram-negatives or septic shock, and cover anaerobes for perianal or intra-abdominal sources. **Consult the local antibiogram**, which should drive empirical choice.
- 5 **Consider antifungal cover for persistent or recurrent fever after 4–7 days** of broad-spectrum antibacterials with anticipated prolonged neutropenia. Send galactomannan or beta-D-glucan and image the chest and sinuses.

DE-ESCALATE AND STOP *the part most people get wrong*

DURATION

If **all cultures are negative and the fever has resolved**, it is appropriate to consider **stopping intravenous antibiotics 72 hours after the last fever**, and to reinstate prophylaxis if applicable — **regardless of the neutrophil count**. Waiting for count recovery before stopping is an outdated practice that prolongs exposure, drives resistance and increases *C. difficile* risk.

IF A SOURCE IS FOUND

Treat for the **duration appropriate to that infection** rather than an arbitrary neutropenic-fever course. **Remove infected lines** for tunnel infection, port-pocket infection, septic thrombophlebitis, persistent bacteremia, or infection with *S. aureus*, *Pseudomonas*, *Candida*, or rapidly growing mycobacteria.

PREVENTION *who should never have got here*

Measure	Detail
G-CSF prophylaxis	Primary prophylaxis when the regimen carries a febrile neutropenia risk of $\geq 20\%$, and considered at 10–20% with additional patient risk factors — age, prior episode, poor performance status, comorbidity. It prevents; it does not treat established fever, where routine use is not recommended.
Antibacterial prophylaxis	A fluoroquinolone in high-risk patients with anticipated prolonged profound neutropenia , typically acute leukemia and stem cell transplant. Not for standard solid-tumor chemotherapy — the resistance and <i>C. difficile</i> cost outweighs benefit.
Antifungal & antiviral	Antifungal prophylaxis for prolonged neutropenia and transplant. Aciclovir for HSV-seropositive patients receiving intensive therapy. Pneumocystis prophylaxis with sustained steroid exposure or specific regimens.
Patient education	Every patient starting chemotherapy needs a thermometer, written instructions, and an alert card with a 24-hour number . They should be told to present immediately with fever and to say they are on chemotherapy at the door — this is what shortens door-to-antibiotic time.

PEARLS & PITFALLS

- **Empiric doses**, since the sheet names the agents but the clock is 60 minutes: cefepime 2 g IV q8h, piperacillin-tazobactam 4.5 g IV q6h, or meropenem 1 g IV q8h. **Vancomycin 15–20 mg/kg q8–12h is not routine**: add it only for a suspected line infection, skin or soft-tissue source, hemodynamic instability, severe mucositis, or known MRSA colonization.
- **Antibiotics within an hour**. Every delay costs survival, and this is the single measured standard for the condition.
- **Do not add vancomycin reflexively** — not even for mucositis. It has defined indications, and stopping it at 48 hours when cultures are negative is part of the protocol.
- **No rectal examinations, suppositories or enemas** in neutropenia — they can seed bacteremia.
- **Fever may be the only sign**. Absence of infiltrate, pus or erythema means nothing without neutrophils.
- **Stop at 72 hours afebrile with negative cultures**, without waiting for count recovery.
- **Give G-CSF for prophylaxis, not as treatment** of established fever, where routine use is not recommended.

