

Neutropenic Fever

Neutropenic fever means fever when you cannot make pus. Start broad antibiotics within one hour or bacteria win.

THE ONE-LINE TRUTH

Fever in a patient whose neutrophil count is below 500 cells per microliter—no white blood cell army left to fight infection.

The chain — how it unfolds

1. Chemotherapy kills bone marrow stem cells. — why: Chemotherapy targets all fast-dividing cells to stop cancer, but it cannot tell cancer cells from the stem cells in bone marrow that make neutrophils, so both are destroyed.
2. The absolute neutrophil count (ANC) drops below 500 cells per microliter within days to weeks. — why: Neutrophils only live a few hours in the bloodstream, so once the marrow stops making new ones, the circulating count falls fast—below 500 is the danger zone where infection risk skyrockets.
3. Bacteria from the gut (*E. coli*, *Klebsiella*, *Pseudomonas*), skin, or central line (*Staph aureus*, coagulase-negative staph) enter the bloodstream unopposed. — why: Healthy neutrophils kill bacteria within minutes of contact. With fewer than 500 neutrophils per microliter, there is no army to stop the invaders, so bacteria spread from the gut or catheter site into the blood.
4. Fever appears—often the only sign of infection. — why: Bacteria in the bloodstream trigger the hypothalamus (the brain's thermostat) to raise body temperature through cytokines (immune alarm chemicals). There is no swelling, redness, or pus because neutrophils are needed to make those signs.
5. The body releases epinephrine, norepinephrine, and cortisol (stress hormones) to hold blood pressure steady. — why: These hormones squeeze blood vessels, speed the heart, and keep blood flowing to the brain and heart. This buys time, so vital signs can look deceptively normal for a short window even as bacteria multiply.
6. Bacteria double every twenty to thirty minutes in the bloodstream, releasing endotoxins (poisons from bacterial cell walls). — why: Without neutrophils to kill them, bacteria grow exponentially. Endotoxins trigger a massive inflammatory cascade that damages blood vessel linings and makes vessels leak fluid into tissues.

7. Blood vessels leak, the heart pumps weakly, and blood pressure crashes into septic shock. — why: Endotoxins activate the endothelium (the inner lining of blood vessels), causing widespread leaking. Fluid shifts out of vessels into tissues, the heart cannot pump enough blood forward, and blood pressure collapses.
8. Organs starve for oxygen—kidneys fail, lungs fill with fluid (ARDS), the brain becomes confused, and the liver cannot clear toxins. — why: Every organ depends on steady blood flow and oxygen delivery. When blood pressure drops and vessels leak, oxygen does not reach tissues, so cells switch to anaerobic metabolism (making energy without oxygen), which produces lactic acid and fails quickly. Multi-organ failure follows.

Spot it — what you see, and why

- Fever (temperature at or above 100.4°F / 38°C once, or 100.4°F for one hour or longer): When white blood cells drop too low (neutropenia), the body cannot fight off germs that sneak in from the skin, gut, or lungs. Even a small infection that would normally be stopped right away can now spread quickly. The immune system raises the body's heat to try to slow the germs down — this is the fever. Because there are so few fighter cells, this fever is a serious alarm: something is wrong and help is needed fast.
- Chills and sweating: The hypothalamus (the brain's thermostat, sitting deep in the middle of the brain) resets the body's target temperature higher to fight infection. Muscles shake (chills) to make heat and raise the temperature up to the new set point. Once the body gets there, sweating cools it back down. In neutropenic fever, these swings can be intense because even a tiny infection can trigger a big inflammatory surge.
- Redness, warmth, swelling, or pus around central line sites (where IV catheters enter the skin): A central line is a tube placed into a big vein to give medicines or draw blood. Skin bacteria (like *Staphylococcus*) can crawl down the outside of the catheter and infect the tunnel under the skin or the bloodstream itself. The body tries to send immune cells to the spot, causing redness and warmth, but with so few white cells available, the infection spreads easily instead of being walled off.
- Pain, redness, or sores in the mouth or throat: The lining of the mouth and throat sheds and regrows constantly. Chemotherapy damages the fast-growing cells that rebuild that lining, leaving raw spots (mucositis). Bacteria and fungi that normally live in the mouth can now invade those raw areas. With dangerously low infection-fighting cells (neutropenia), the body has no troops to keep them in check, so sores spread and infections take hold quickly.

- Pain or tenderness around the rectum (perirectal area): The skin around the anus and the lining just inside the rectum are thin and can tear easily, especially if stools are hard or if the area is irritated. Bacteria from stool can enter those tiny breaks. Normally white blood cells rush in and seal the infection off into a small abscess, but in dangerously low infection-fighting cells (neutropenia) there are not enough cells to do that, so the infection can spread into deeper tissues and the bloodstream.
- New cough or shortness of breath: Bacteria or fungi (like *Aspergillus*, a mold that lives in the air and soil) can settle into the lungs. With low white blood cells, the lungs cannot clear out these invaders, and patches of infection (pneumonia) form. Inflamed lung tissue gets stiff and fills with fluid, making it hard to breathe. Because neutropenic patients cannot mount a strong immune response, the usual thick phlegm and infiltrates on X-ray may be missing at first, but the infection is still dangerous.

Red flags — act now

- Temperature at or above 100.4°F (38°C) in anyone with known low white blood cells (absolute neutrophil count below 500 cells per microliter)
- Signs of septic shock: confusion, very low blood pressure, fast breathing, cold or mottled skin, or little to no urine output
- Severe pain, redness, or drainage around a central line, port, or catheter site
- New trouble breathing, chest pain, or coughing up blood
- Severe belly pain or inability to have a bowel movement, which may signal a perirectal abscess or infection in the gut wall

Treat it — in this order

1. Broad-spectrum antibiotic with anti-pseudomonal coverage (cefepime, piperacillin-tazobactam, or meropenem) within 60 minutes of presentation → Kills the most dangerous bacteria—gram-negative organisms like *Pseudomonas aeruginosa* and *E. coli* from the gut, and gram-positive organisms like *Staphylococcus* from skin and lines—before they multiply unchecked in the bloodstream. Without neutrophils, the body cannot slow the bacteria down, so the antibiotic must do all the work. Every hour of delay increases the risk of septic shock and death.

2. Add vancomycin (or linezolid if vancomycin-resistant) if the patient is hemodynamically unstable (low blood pressure, high lactate), central line infection is suspected, MRSA is known or common in your hospital, or there is skin/soft tissue involvement → Covers methicillin-resistant *Staphylococcus aureus* (MRSA) and other resistant gram-positive bacteria that the first antibiotic may not kill. Central lines are coated with skin bacteria, and MRSA is especially dangerous in neutropenic patients because it can cause aggressive bloodstream infection or endocarditis (infection of the heart valves). Adding vancomycin closes the gap when the infection is more severe or when the source is likely the line or skin.
3. Blood cultures (before antibiotics), careful physical exam of central line sites, perirectal area, mouth, and lungs; chest X-ray → Identifies the source of infection (line, gut, mouth, lungs) and the exact organism growing in the blood. This guides whether to remove a contaminated central line, switch antibiotics based on culture sensitivities, or add antifungals if cultures stay negative but fever persists. The exam and imaging tell you where to look; the cultures tell you what you are fighting.
4. Add empiric antifungal therapy (echinocandin like micafungin or caspofungin, or voriconazole) if fever persists beyond 4–7 days on broad-spectrum antibiotics and dangerously low infection-fighting cells (neutropenia) continues → Kills fungi—especially *Candida* (yeast) and *Aspergillus* (mold)—that grow when neutrophils stay low for a long time. Fungi are slower to cause symptoms than bacteria, so they are not the first suspect, but they become the main suspect if fever does not break after several days of antibiotics. Adding an antifungal stops a second, hidden infection from taking over while the bone marrow is still recovering.
5. IV fluids (crystalloid like normal saline or lactated Ringer's, 30 mL/kg bolus) and vasopressors (norepinephrine) if blood pressure drops, lactate rises, or signs of shock appear → Restores blood volume and squeezes blood vessels to maintain blood flow to vital organs (brain, heart, kidneys) when septic shock causes vessels to leak fluid and lose tone. Fluid alone often is not enough—norepinephrine (a medication that mimics adrenaline) tightens blood vessels and keeps pressure up while antibiotics work. This buys time for the immune system (and the antibiotics) to catch up.

Your top priorities at the bedside

1. Notify the provider immediately and prepare to draw two sets of blood cultures from different sites before any antibiotics are given. — why: Blood cultures identify the exact bacteria causing infection so antibiotics can be adjusted later. Drawing before antibiotics gives the best chance of growing bacteria in the lab. Two separate draws reduce false positives from skin contamination.

2. Administer broad-spectrum antibiotics within 60 minutes of fever recognition, using cefepime, piperacillin-tazobactam, or meropenem as ordered. — why: Neutropenic patients have almost no white blood cells to fight infection. Every hour of delay increases risk of septic shock and death. Broad-spectrum antibiotics kill many different bacteria types until culture results identify the specific bug.
3. Take full vital signs including blood pressure, heart rate, respiratory rate, oxygen saturation, and temperature every 1 to 2 hours until stable. — why: Neutropenic patients can progress to septic shock quickly because they lack the white blood cells that usually contain infection. Low blood pressure, high heart rate, fast breathing, or low oxygen signal deterioration requiring immediate intervention.