

Multiple Myeloma

Multiple myeloma is one type of plasma cell (an antibody-making white blood cell) taking over the bone marrow, breaking down bone, and squeezing out normal blood production.

THE ONE-LINE TRUTH

One clone of plasma cells has broken free and is flooding the blood with one antibody (the M-protein) while crowding out healthy blood cells, dissolving bone, and clogging the kidneys.

The chain — how it unfolds

1. One plasma cell breaks free and copies itself endlessly in the bone marrow. — why: Genetic mutations (such as t(4;14), t(14;16), deletion 17p, or gain of chromosome 1q) let one plasma cell ignore normal stop signals and divide without limit—this is the single upstream break that starts everything.
2. The malignant clone floods the blood with one antibody (the M-protein) and free light chains. — why: Unlike healthy plasma cells that make many different antibodies, the myeloma clone makes only one type (IgG, IgA, or light chain only) in huge amounts—this monoclonal protein shows up as an M-spike on serum protein electrophoresis and free light chains in urine (Bence Jones protein).
3. The clone secretes signals (RANKL and DKK1) that activate osteoclasts and block osteoblasts, dissolving bone. — why: RANKL tells osteoclasts (bone-eating cells) to work overtime; DKK1 blocks osteoblasts (bone-building cells)—so bone is dissolved but not rebuilt, leaving punched-out lytic lesions (visible as holes on X-ray) and releasing calcium into the blood (hypercalcemia).
4. Bones hurt and break from normal activity or minor bumps (pathologic fractures). — why: Dissolved bone is weak and full of holes; even small stress—lifting a bag, coughing, rolling over in bed—can break ribs, vertebrae (causing back pain and risk of spinal cord compression), or long bones.
5. Calcium rises in the blood (hypercalcemia), causing confusion, weakness, constipation, and kidney damage. — why: Dissolved bone dumps calcium into the bloodstream; high calcium slows the heart and brain (causing arrhythmias, confusion, and coma) and makes the kidneys lose water (leading to dehydration and worsening kidney injury).

6. The expanding plasma cell mass crowds the marrow, squeezing out red cell, white cell, and platelet production. — why: The marrow has limited space; as the myeloma clone fills it, there is less room for normal blood cell precursors—red blood cells drop (anemia, causing fatigue and shortness of breath), neutrophils drop (raising infection risk), and platelets drop (raising bleeding risk, though severe bleeding is less common).
7. Free light chains (pieces of the M-protein) are filtered by the kidneys and jam the renal tubules, causing cast nephropathy (myeloma kidney). — why: Light chains pass through the glomerulus (the kidney's filter), travel down the tubule, and bind to Tamm-Horsfall protein, forming dense casts that block the tubule, trigger inflammation, and scar the kidney—leading to acute kidney injury and, if untreated, permanent kidney failure.
8. The immune system weakens, and infections become frequent and severe. — why: The myeloma clone suppresses normal plasma cells (so the body cannot make a full range of antibodies), and marrow crowding lowers neutrophils—leaving the patient vulnerable to bacterial infections, especially pneumonia (*Streptococcus pneumoniae*, *Haemophilus influenzae*) and urinary tract infections.

Spot it — what you see, and why

- Bone pain, especially in the back or ribs: The cancer cells crowd into the bone marrow and release chemicals (cytokines like IL-6 and TNF- α) that wake up osteoclasts (the cells that break down bone). These osteoclasts chew away bone faster than the body can rebuild it, leaving weak spots that hurt and can crack easily.
- Getting tired easily and looking pale (anemia): The myeloma cells pack the bone marrow so tightly that there's no room left for the stem cells that normally make red blood cells. Fewer red blood cells means less oxygen reaches your muscles and brain, so you feel worn out and your skin looks pale.
- Breaking a bone from a tiny bump or fall (pathologic fracture): Because the osteoclasts have eaten away so much bone, the skeleton becomes brittle—like a cracker instead of a strong beam. Even a small knock or lifting something light can snap a rib or crack a vertebra in the spine.
- Getting infections often, like pneumonia or urinary tract infections: Myeloma cells are abnormal plasma cells that crowd out the healthy plasma cells, which are the body's antibody factories. Without enough normal antibodies (immunoglobulins), your immune system can't tag and kill germs as well, so bacteria and viruses take hold more easily.
- Feeling confused, very thirsty, or urinating a lot (high calcium): When osteoclasts break down bone, calcium floods into the bloodstream (hypercalcemia). High calcium slows down nerves and muscles, making you feel foggy or weak, and it also makes your kidneys dump extra water into urine to try to wash the calcium out, leaving you thirsty and peeing constantly.

- Foamy urine or swelling in the legs (kidney trouble): The myeloma cells dump huge amounts of abnormal antibody pieces (light chains, also called Bence Jones protein) into the blood. These light chains clog the tiny filters in the kidneys (the tubules), damaging them so they leak protein into the urine (making it foamy) and can't balance fluids well (causing swelling).

Red flags — act now

- New fracture or severe bone pain in the spine (could mean the vertebra is collapsing and pressing on the spinal cord)
- Sudden confusion, extreme thirst, or barely urinating (signs of dangerously high calcium or failing kidneys)
- Fever plus shaking chills in someone with known myeloma (weakened immune system makes infections life-threatening fast)
- Numbness, tingling, or weakness in the legs (could mean spinal cord compression from a collapsed vertebra)

Treat it — in this order

1. Triplet induction chemotherapy (proteasome inhibitor + immunomodulatory drug + corticosteroid, e.g. bortezomib + lenalidomide + dexamethasone, called VRd) → Attacks the myeloma plasma cells three ways at once. The proteasome inhibitor (bortezomib) stops the cells from breaking down old proteins, so trash piles up inside and the cell dies. The immunomodulatory drug (lenalidomide) wakes up the immune system's T cells and natural killer cells to recognize and kill myeloma cells, and also stops new blood vessels from feeding the tumor. The corticosteroid (dexamethasone) directly kills plasma cells and calms inflammation. Together, they shrink the myeloma clone so normal marrow cells can grow back, red blood cells rise, and symptoms ease.
2. Bisphosphonates (zoledronic acid 4 mg IV every 3–4 weeks, or pamidronate) → Blocks osteoclasts (bone-breaking cells) from dissolving more bone. It poisons the osteoclasts so they cannot respond to the myeloma's bone-breaking signals. This stops new lytic lesions from forming, lowers the risk of fractures, and reduces bone pain. Also lowers high calcium by stopping calcium release from bone.
3. Aggressive IV hydration (normal saline, often 200–500 mL/hour if the heart can handle it) and avoid nephrotoxic drugs (NSAIDs, contrast dye when possible) → Dilutes the M-protein and light chains in the blood so they are less likely to clog the kidney tubes. Keeps urine flowing fast to flush light chains out before they can settle and cause damage. Also helps lower high calcium by flushing it out through the kidneys.

4. Autologous stem cell transplant (after 3–4 cycles of induction therapy, in patients younger than 65–70 and fit enough) → High-dose melphalan (a chemotherapy drug) wipes out the marrow, including the myeloma plasma cells. Then the patient's own stem cells (collected before the big chemo dose) are put back in to rebuild healthy marrow. This pushes the myeloma deeper into remission and makes people live longer without the cancer coming back.
5. Maintenance therapy after transplant or induction (lenalidomide, continued for years) → Keeps the immune system turned on against any leftover myeloma cells. By blocking new blood vessel growth and keeping T cells active, it holds the myeloma in check longer and delays relapse. Extends the time people live without the cancer growing back.

Your top priorities at the bedside

1. Run IV normal saline at 200 to 300 mL per hour to keep urine output above 100 mL per hour — why: Aggressive hydration flushes light chains and calcium out through kidneys before they cause permanent tubular damage (blocked kidney filters); dehydration is the top cause of acute kidney injury in myeloma
2. Hold all NSAIDs like ibuprofen and all contrast dye procedures until renal function is checked — why: Nephrotoxic drugs (medicines that poison kidneys) plus light chains cause sudden irreversible kidney failure; even one dose of ibuprofen or CT contrast can push borderline kidneys into dialysis need
3. Check calcium level immediately if patient has confusion, severe constipation, or drowsiness — why: High calcium (Hypercalcemia) from bone breakdown causes life-threatening cardiac arrhythmias (irregular heartbeats) and coma; calcium above 12 mg/dL needs emergency treatment with IV fluids, calcitonin, and bisphosphonates within one hour