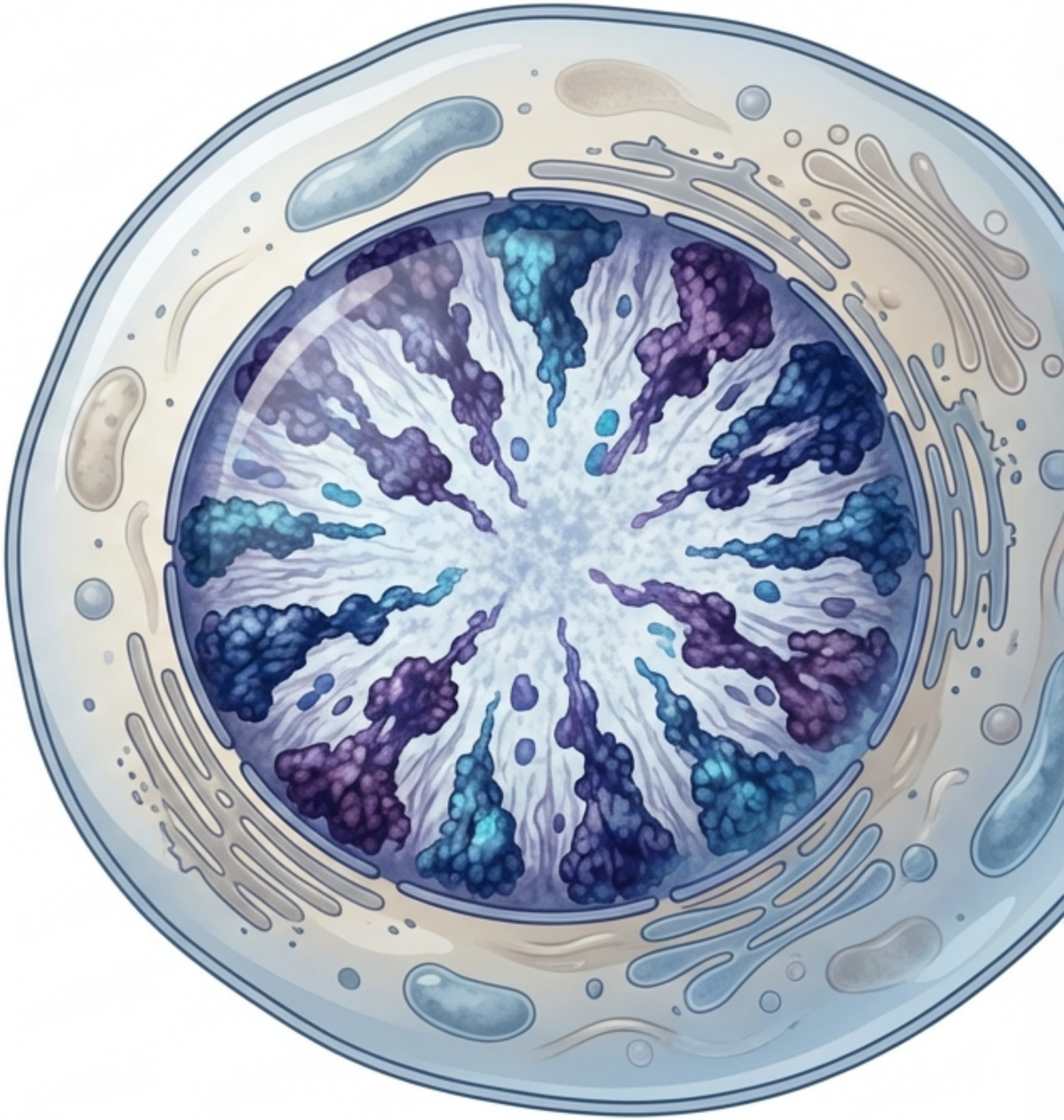
Multiple Myeloma: From Pathogenesis to Diagnosis

A Clinical & Pathophysiological Review



Source: [Medical Institutic NotebookLM

The Case Presentation

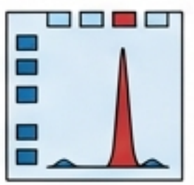
A 60-year-old gentleman presents with new exertional fatigue. He has no significant past medical history.

Lab Results
Hemoglobin: **10.6 g/dL (Low - Anemia)**
Creatinine: **1.8 mg/dL (High - Renal Insufficiency)**
Calcium: **11.2 mg/dL (High - Hypercalcemia)**
Total Protein: **11 g/dL (High)** vs. Albumin 3.1 g/dL (Low)

Clinical Blue

Investigative Clue

Serum protein electrophoresis demonstrates a monoclonal IgA protein of 60 g/dL.



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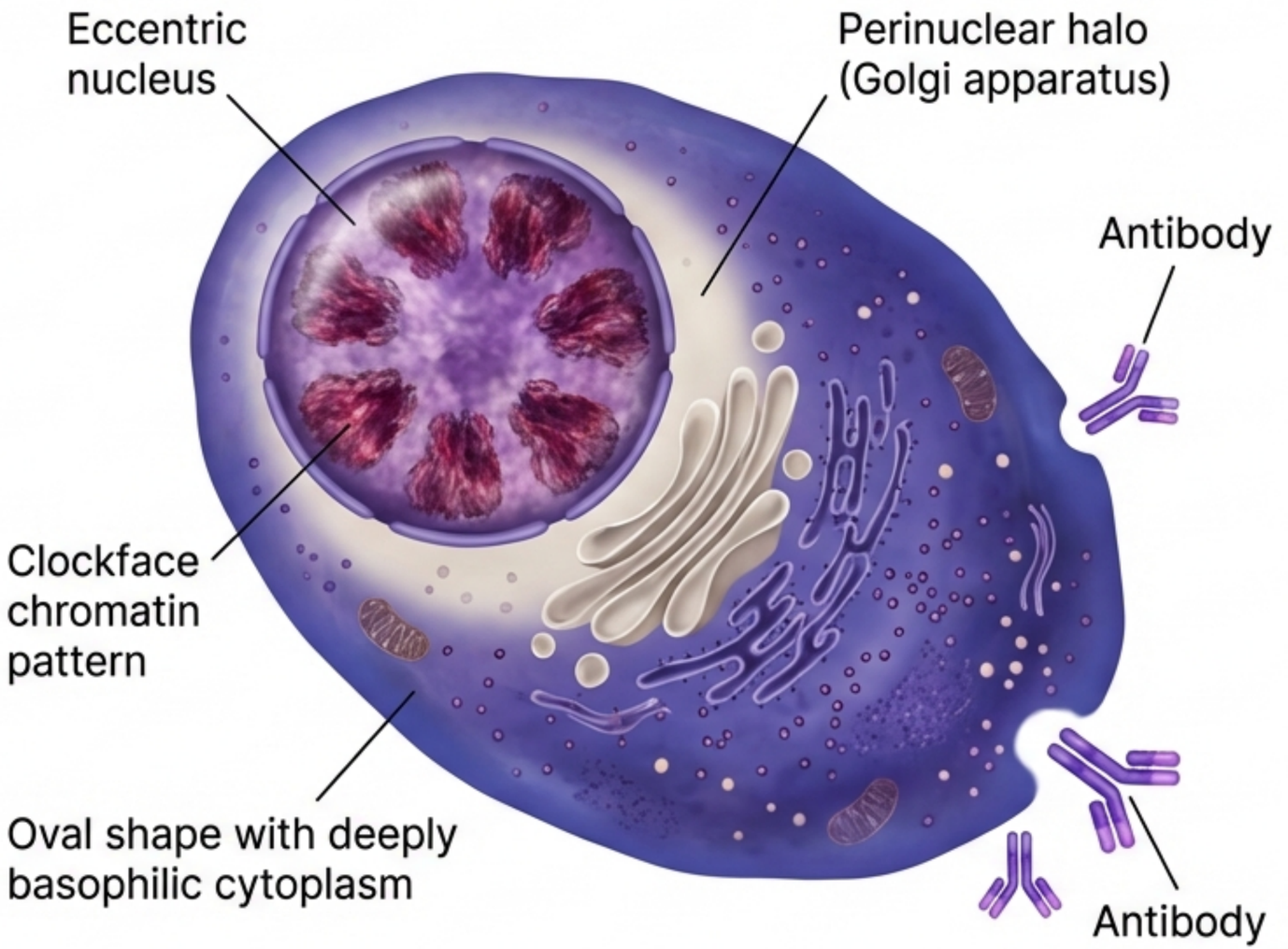
The Cell of Origin: The Plasma Cell

Plasma cells are the terminal differentiation of B-cells, primarily responsible for humoral immunity. They normally reside in the bone marrow (3-5%) and secrete polyclonal antibodies (IgG, IgM, IgA, IgD, IgE).



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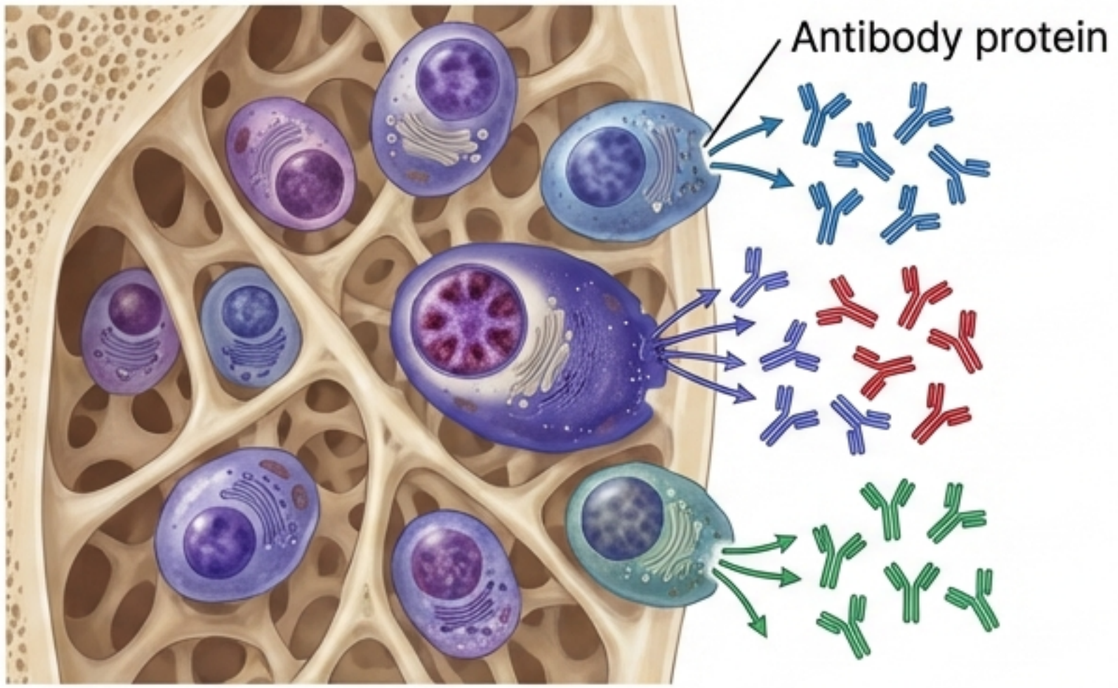
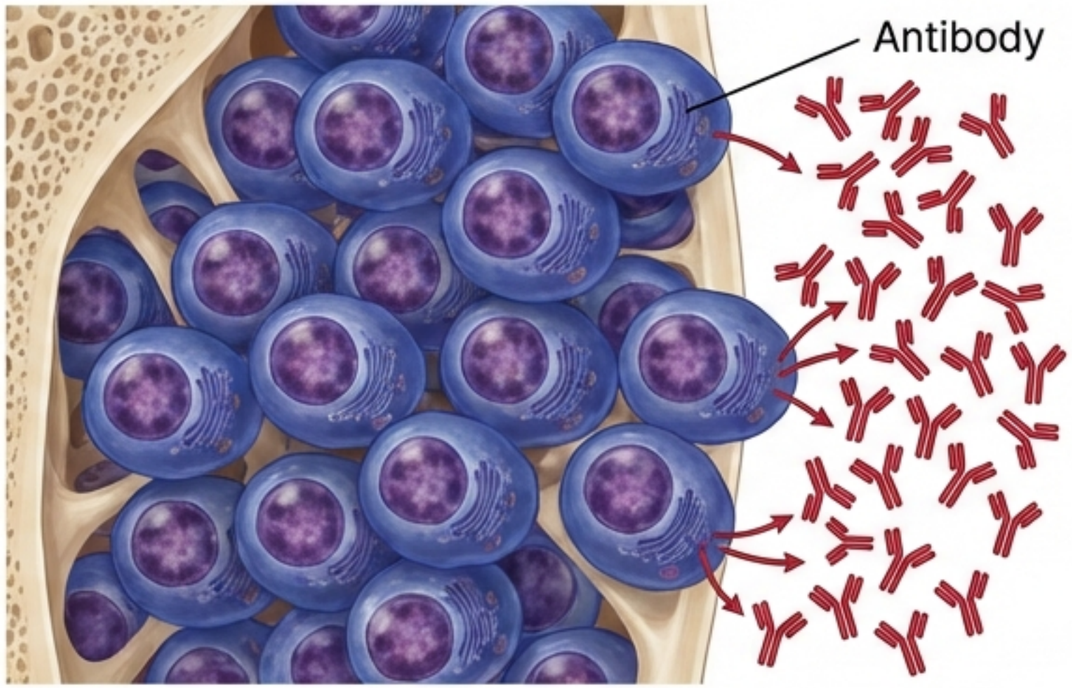
Pathogenesis: The Clonal Proliferation

Normal Response (Polyclonal)



Different plasma cells secrete a variety of immunoglobulins to fight infection.

Malignancy (Monoclonal)



A single malignant clone replicates uncontrollably. The clone secretes a single, identical immunoglobulin known as the Paraprotein or M-Protein.

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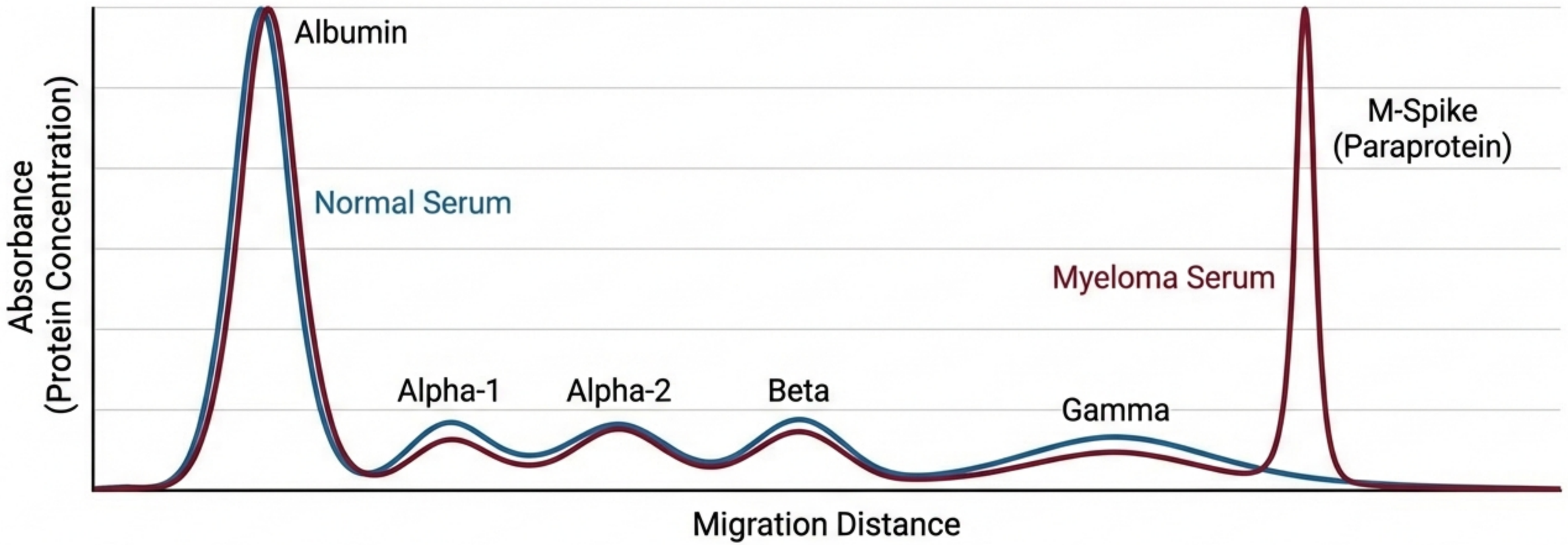
Detecting the Clone: Serum Protein Electrophoresis (SPEP)



Proteins are separated by charge. In Myeloma, the monoclonal protein accumulates in the gamma region, creating a tall, narrow spike.

Blue: Normal Serum, Red: Myeloma S

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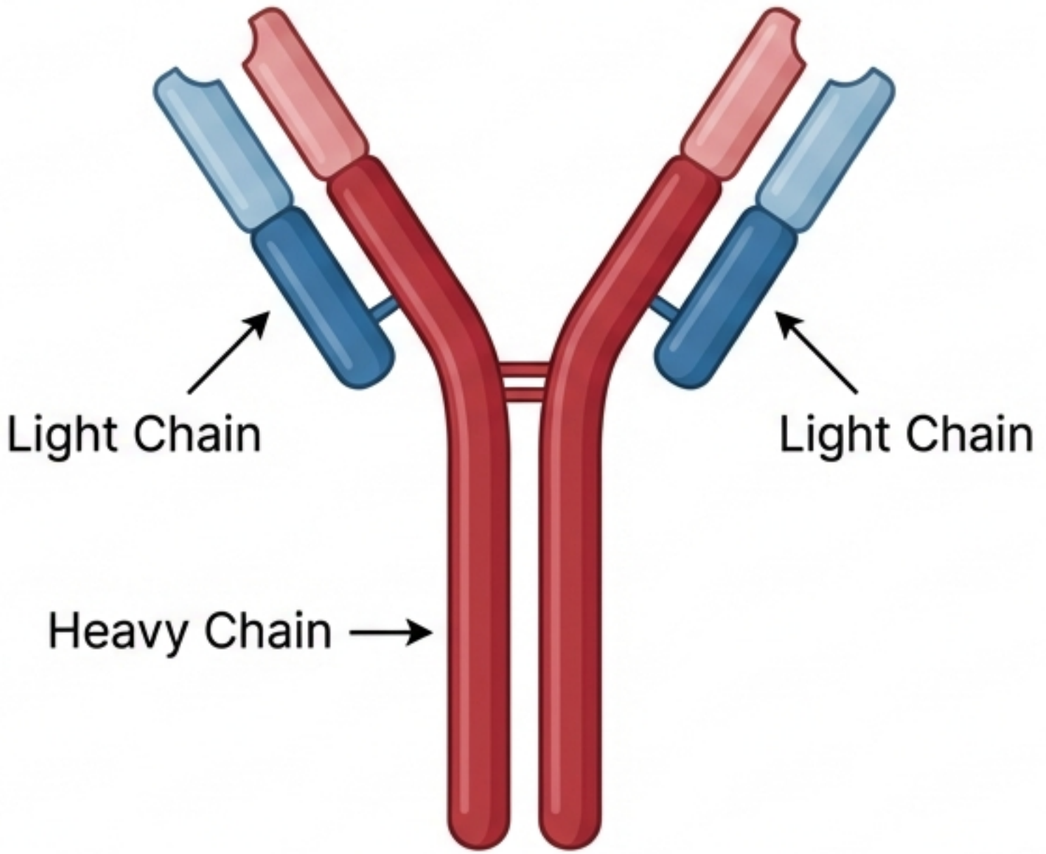
Decoding the M-Spike



The spike represents the physical quantity of the monoclonal protein. It is identified by its Heavy Chain and Light Chain.

- Common: IgG or IgA
- Rare: IgD or IgE
- Very Rare: IgM (Suggests Waldenström's)

Case Insight

Our patient has an IgA spike of 60 g/L—indicating a massive tumor burden.

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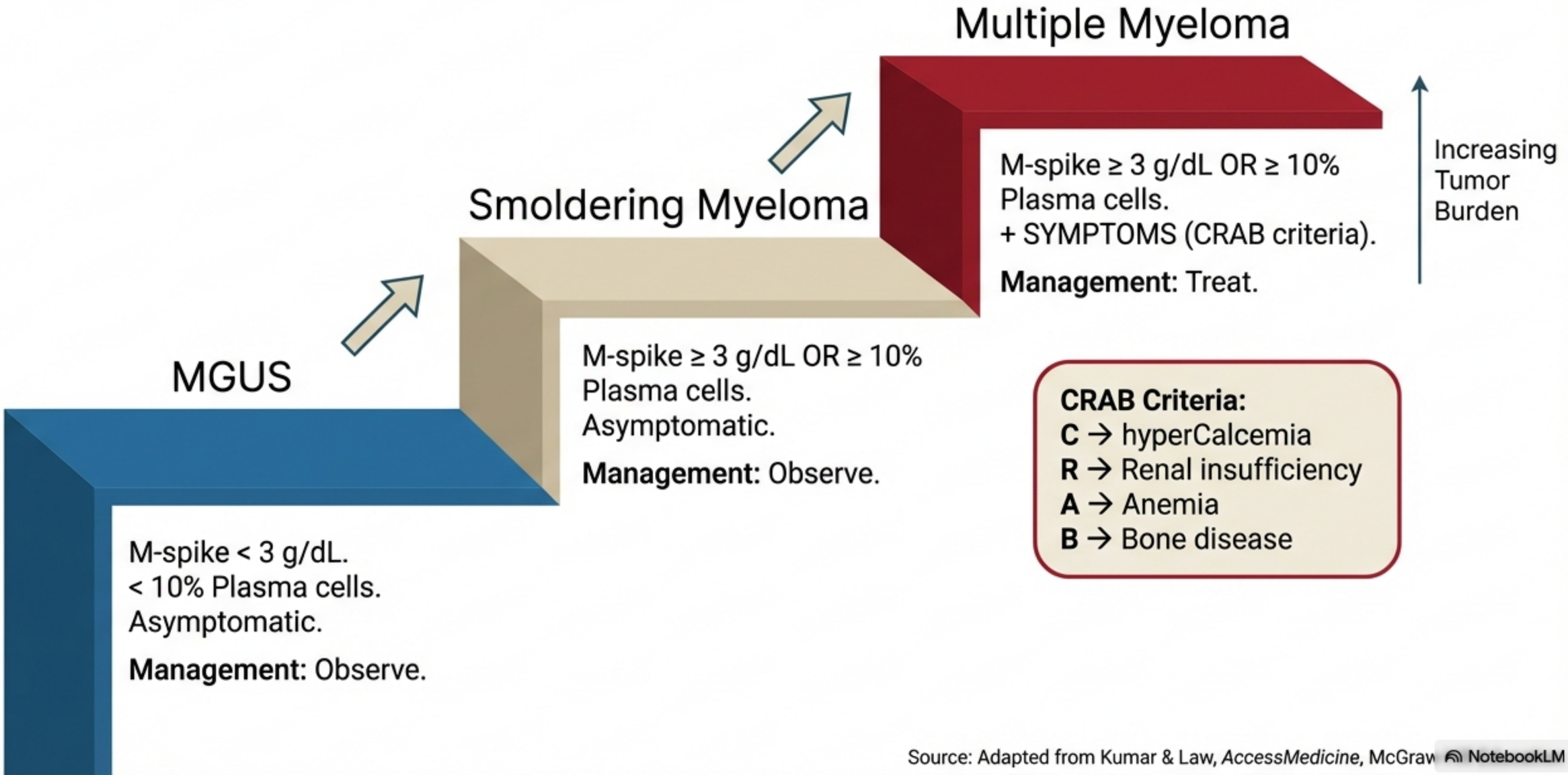
The Spectrum: From MGUS to Symptomatic Myeloma



Source: Adapted from Kumar & Law, *AccessMedicine*, McGraw

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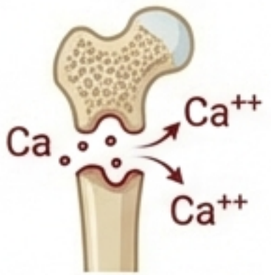
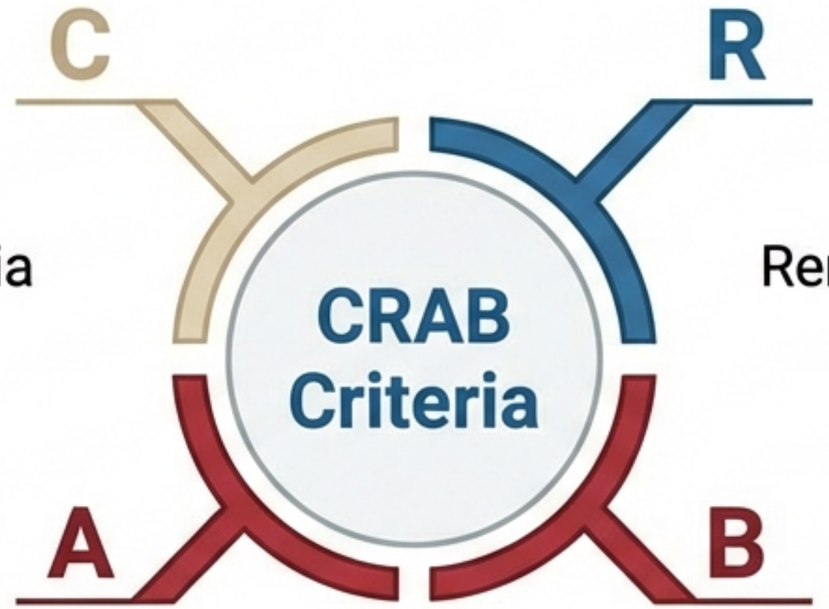
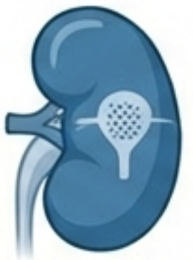
Clinical Manifestations: The CRAB Criteria

Symptomatic Myeloma is defined by end-organ damage.



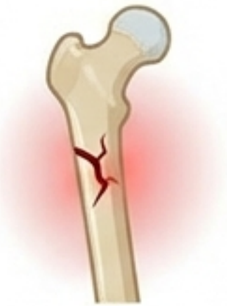
Hypercalcemia





Renal Insufficiency

Anemia



Bone Disease

These four pillars explain the constellation of symptoms in our patient case.

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Bone Destruction & Hypercalcemia

Myeloma cells disrupt bone remodeling by increasing **Osteoclast** activity (bone eating) and decreasing **Osteoblast** activity (bone building).

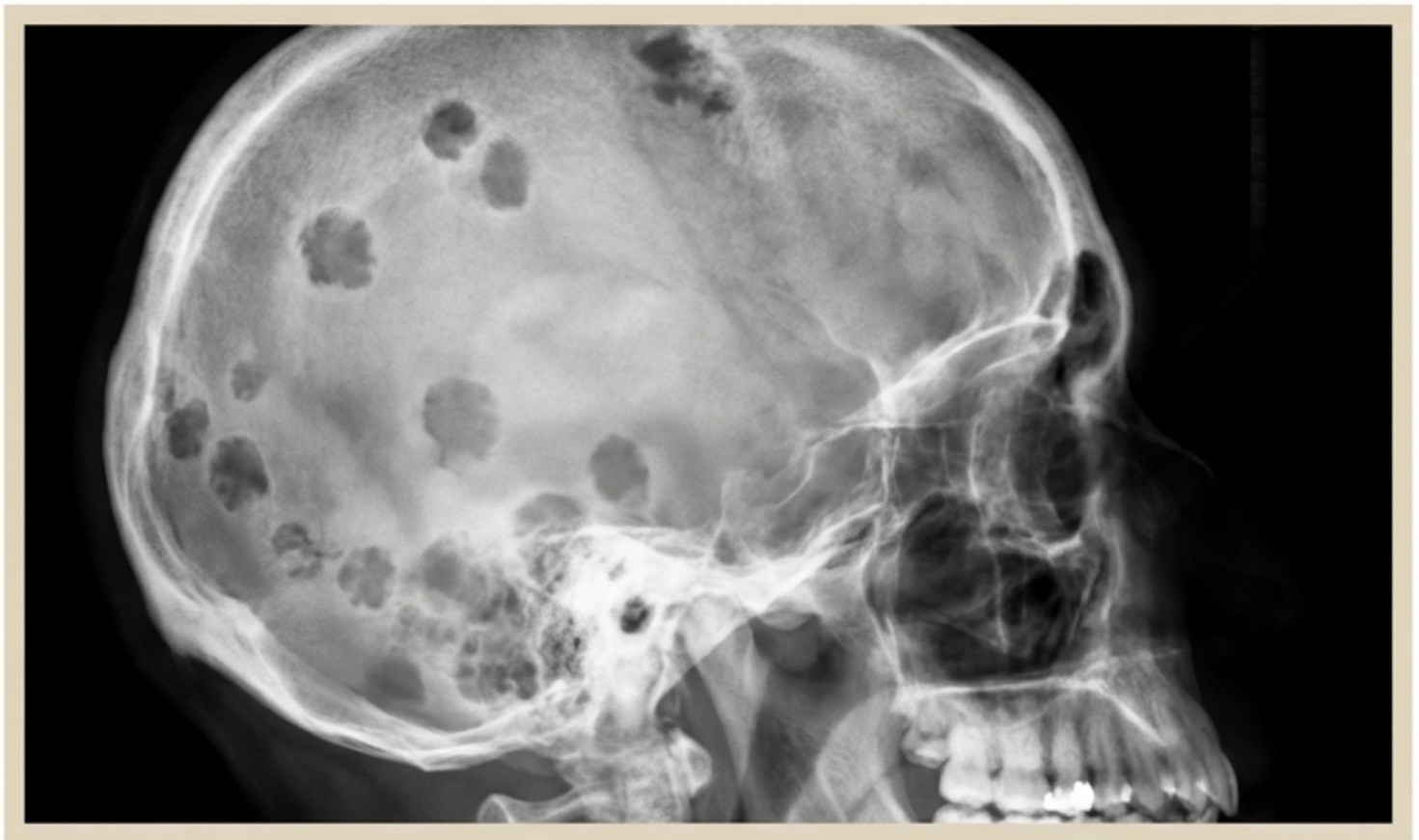

Figure X. Lateral skull X-ray demonstrating multiple "punched-out" lytic lesions characteristic of myeloma.

Consequences:

- Diffuse osteopenia
- Lytic Lesions ("Punched-out" appearance)
- Pathological fractures
- Hypercalcemia (leached from destroyed bone)

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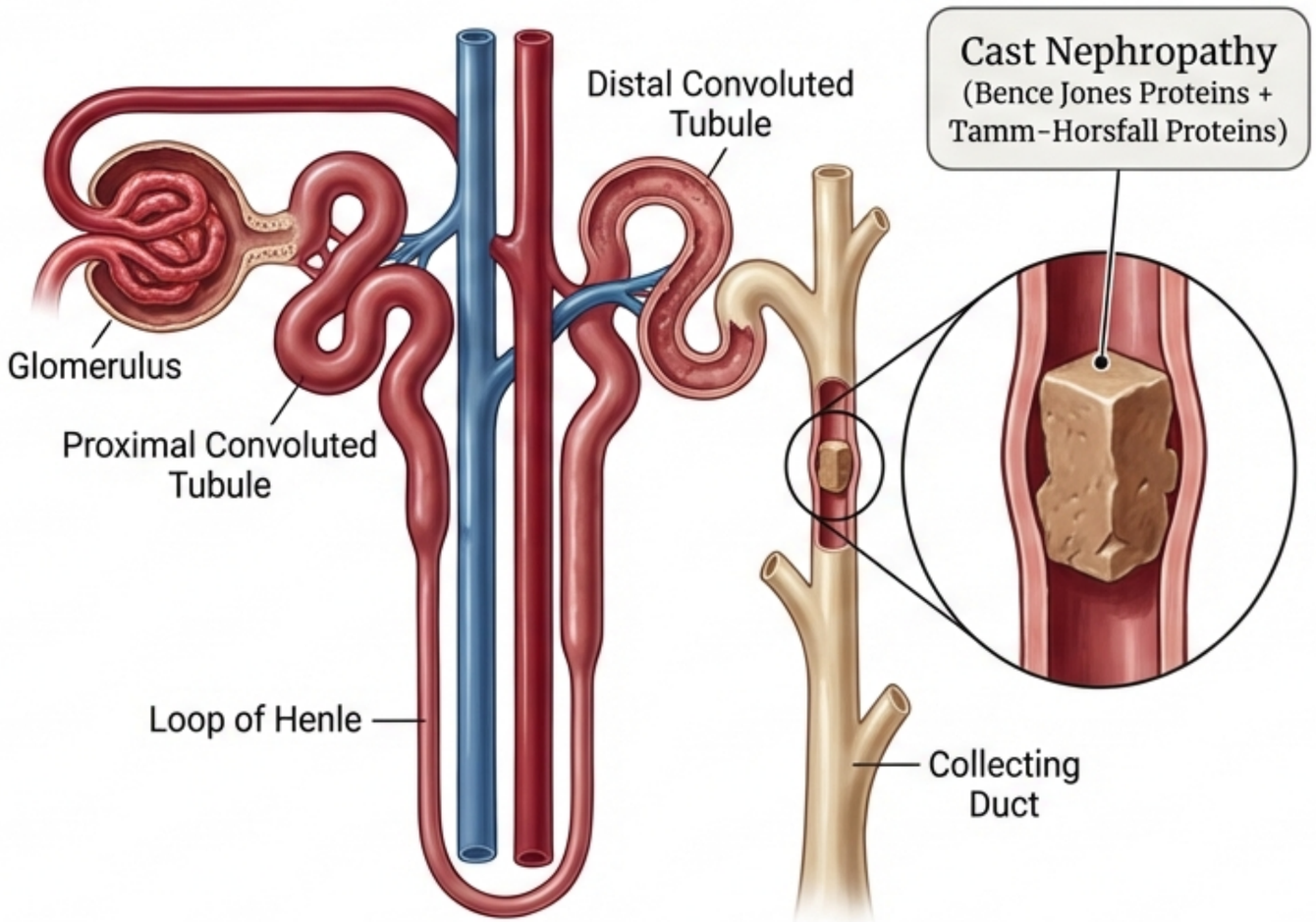
Renal Insufficiency: The Mechanism of Injury

Primary Cause:
Cast Nephropathy

Light chains bind with proteins in the tubules to form insoluble casts, obstructing flow.

Contributing Factors:

- Hypercalcemia
- Hyperviscosity
- NSAID use



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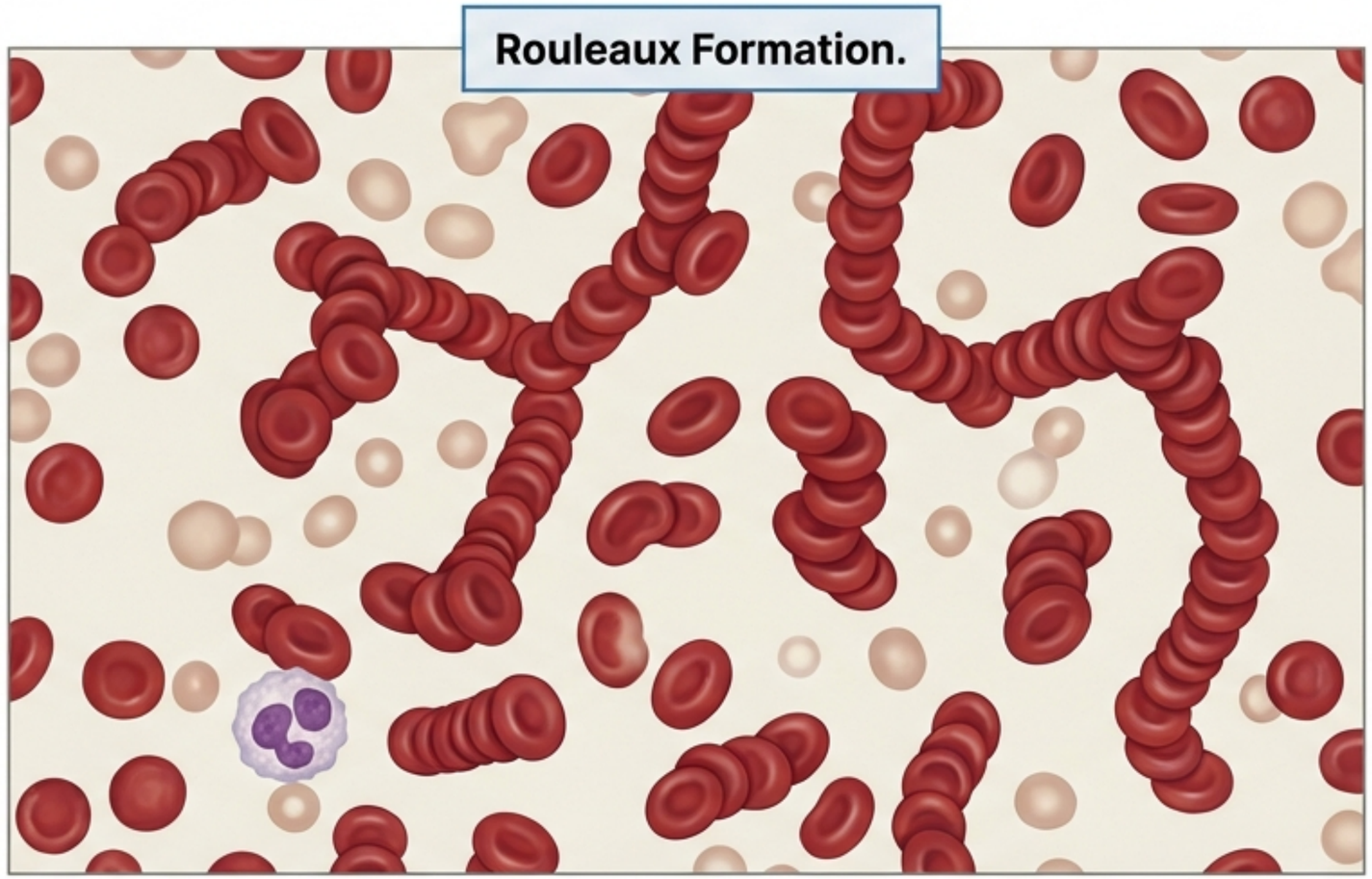
Anemia & Immunodeficiency

Normocytic Anemia: Caused by marrow infiltration (cancer cells crowding out RBC precursors) and renal failure (low EPO).

Infection: Patients are immunodeficient because the clonal antibodies are ineffective, and normal immunoglobulins are suppressed.



High protein levels reduce charge repulsion, causing RBCs to stack.

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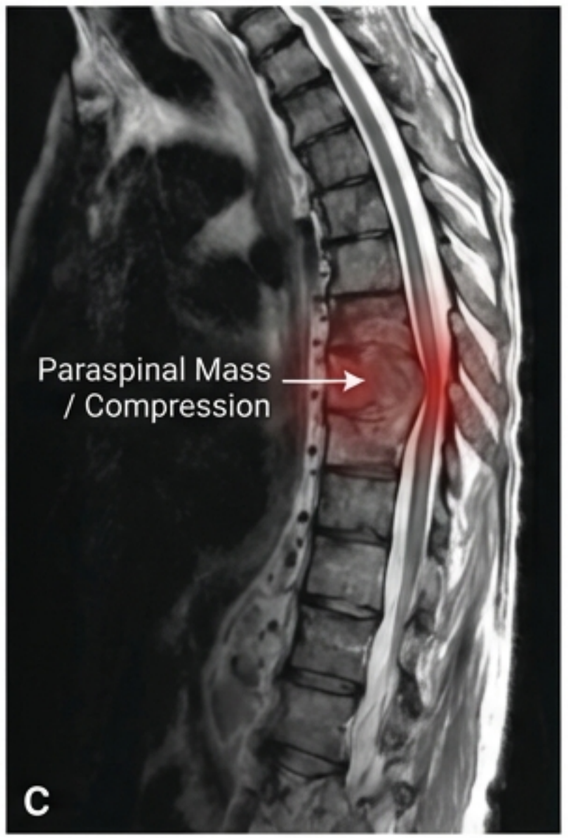
Neurological Complications

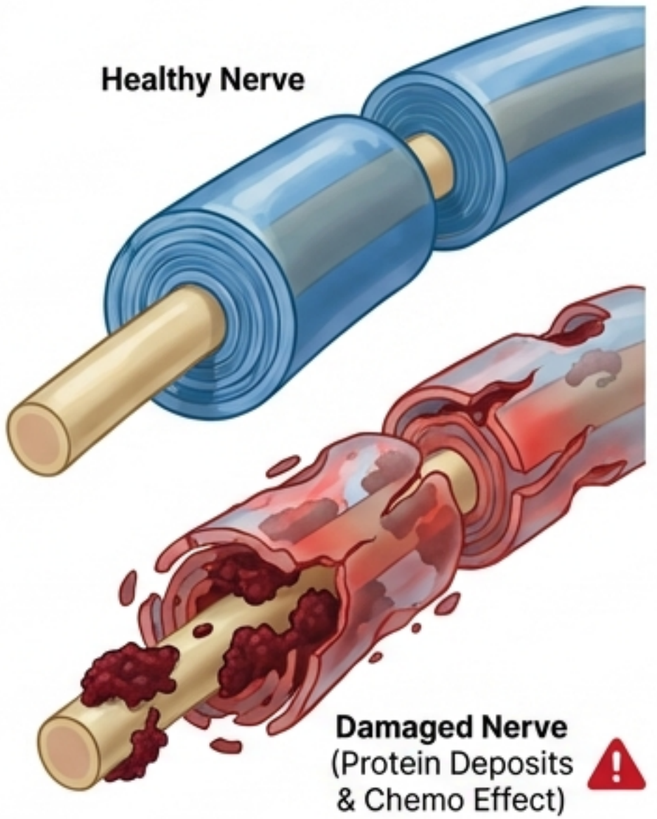
Spinal Cord Compression

Caused by paraspinal masses or vertebral body collapse. A medical emergency.



Peripheral Neuropathy

Direct damage to nerves by monoclonal proteins, or a side effect of chemotherapy.



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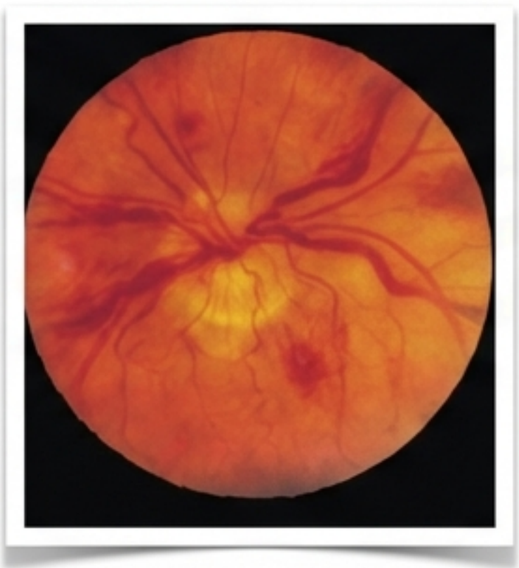
Differential Diagnosis: Waldenström's Macroglobulinemia

Multiple Myeloma	Waldenström's
• IgG or IgA • Lytic Bone Lesions present	• IgM (Pentameric - Large Molecule) • Hyperviscosity Syndrome • Organomegaly (Spleen/Liver) • NO Lytic Bone Lesions



Retinal Vein Engorgement ('Sausage Link' effect due to hyperviscosity).

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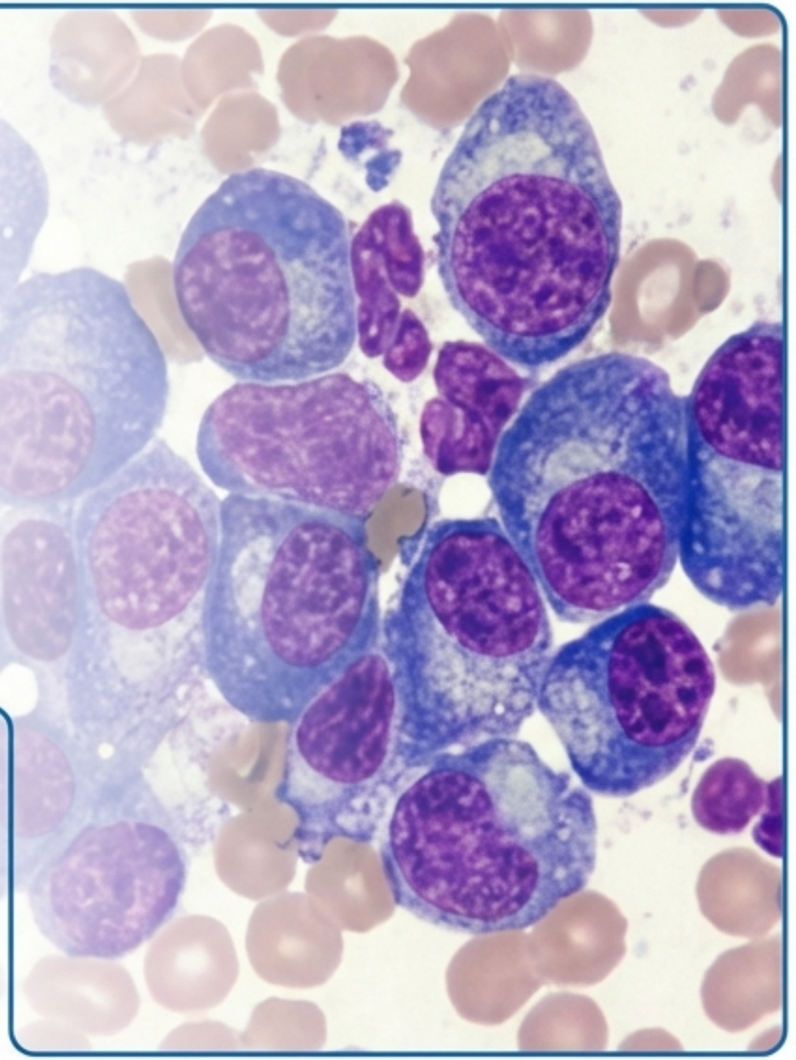
Confirming the Diagnosis: The Triad

Diagnostic Criteria (Must have all three):

- **Monoclonal Protein:** M-Spike > 3 g/dL (or Bence Jones protein in urine)
- **Bone Marrow Clones:** Biopsy showing >10% CD138+ Plasma Cells
- **End Organ Damage:** Presence of CRAB features



The Patient's Verdict

- ✓ M-Spike 60g/L [Check]
- ✓ Anemia + Renal + Hypercalcemia [Check]

Diagnosis: Symptomatic Multiple Myeloma requiring treatment.

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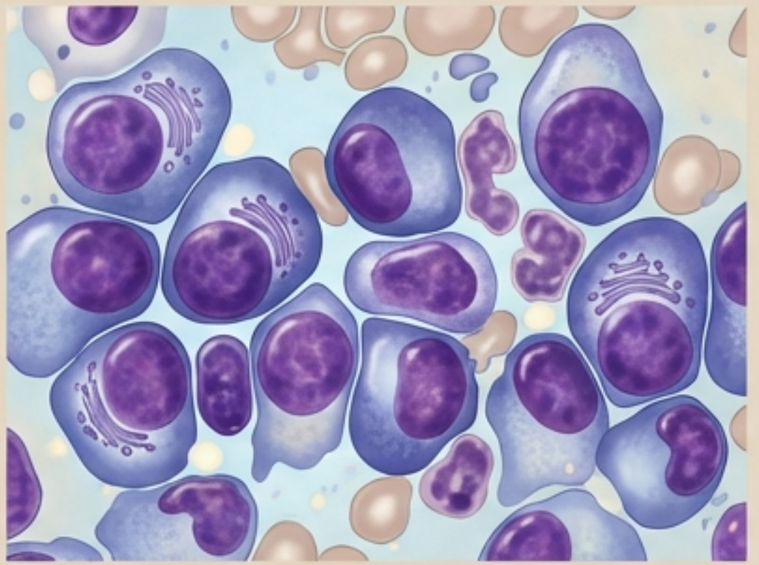
Summary & Epidemiology

- **Demographics:** Median age at diagnosis 65-70 years. Slight male predominance.
- **Incidence:** Represents 1% of all malignancies and 10% of hematologic malignancies.
- **Etiology:** Generally unknown; links to radiation, benzene, and chronic antigen stimulation.
- **Key Takeaway:** Recognize the progression from asymptomatic MGUS to the toxic, end-organ effects of Symptomatic Myeloma (CRAB).



American Society of Hematology
Kyle RA, et al. *Mayo Clin Proc.* 2003;78:21-33.

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