Multiple Myeloma: A Comprehensive Overview

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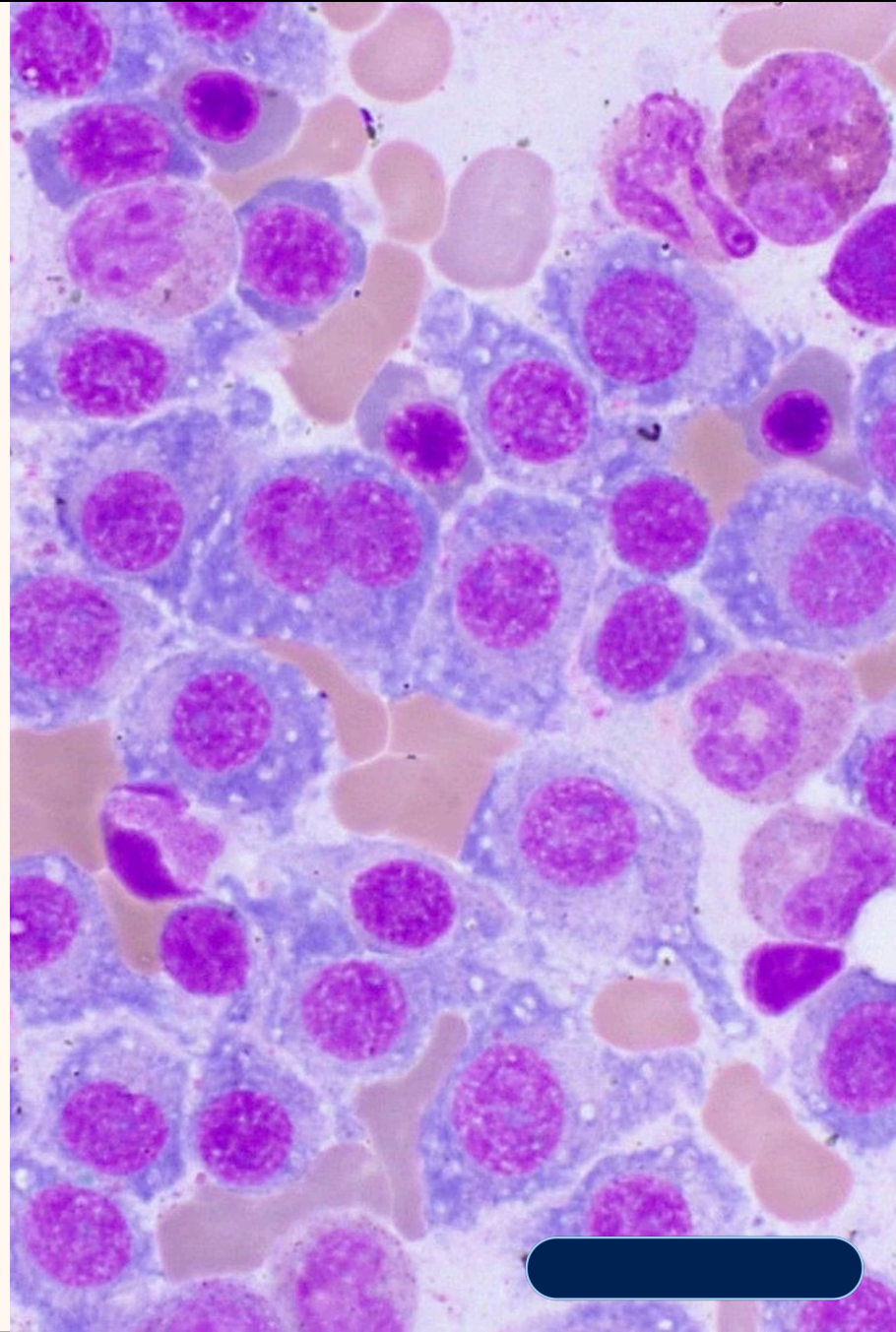
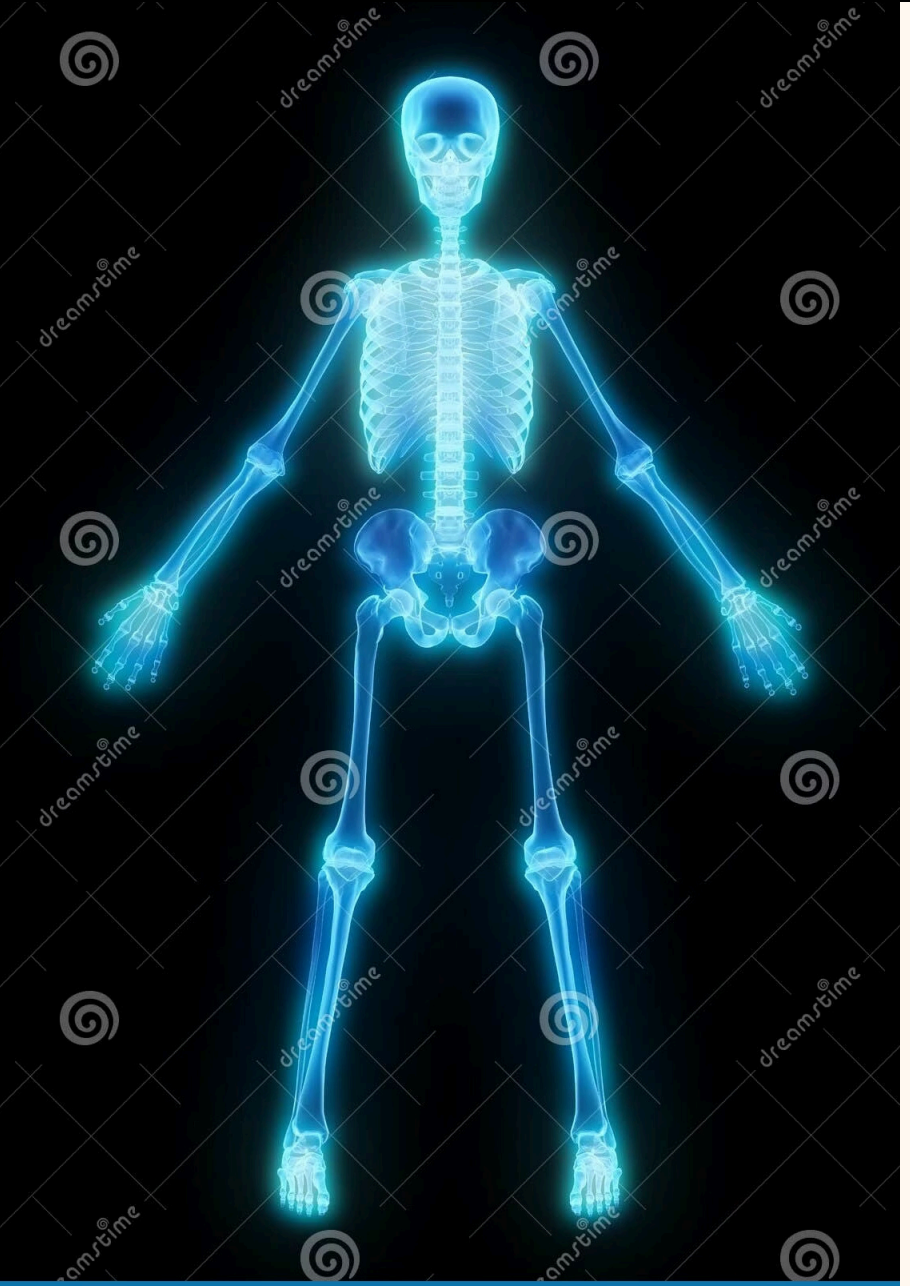




Agenda: Understanding Multiple Myeloma

01

Definition & Pathophysiology

What is MM and how does it develop?

02

Epidemiology & Classification

Incidence and types of the disease.

03

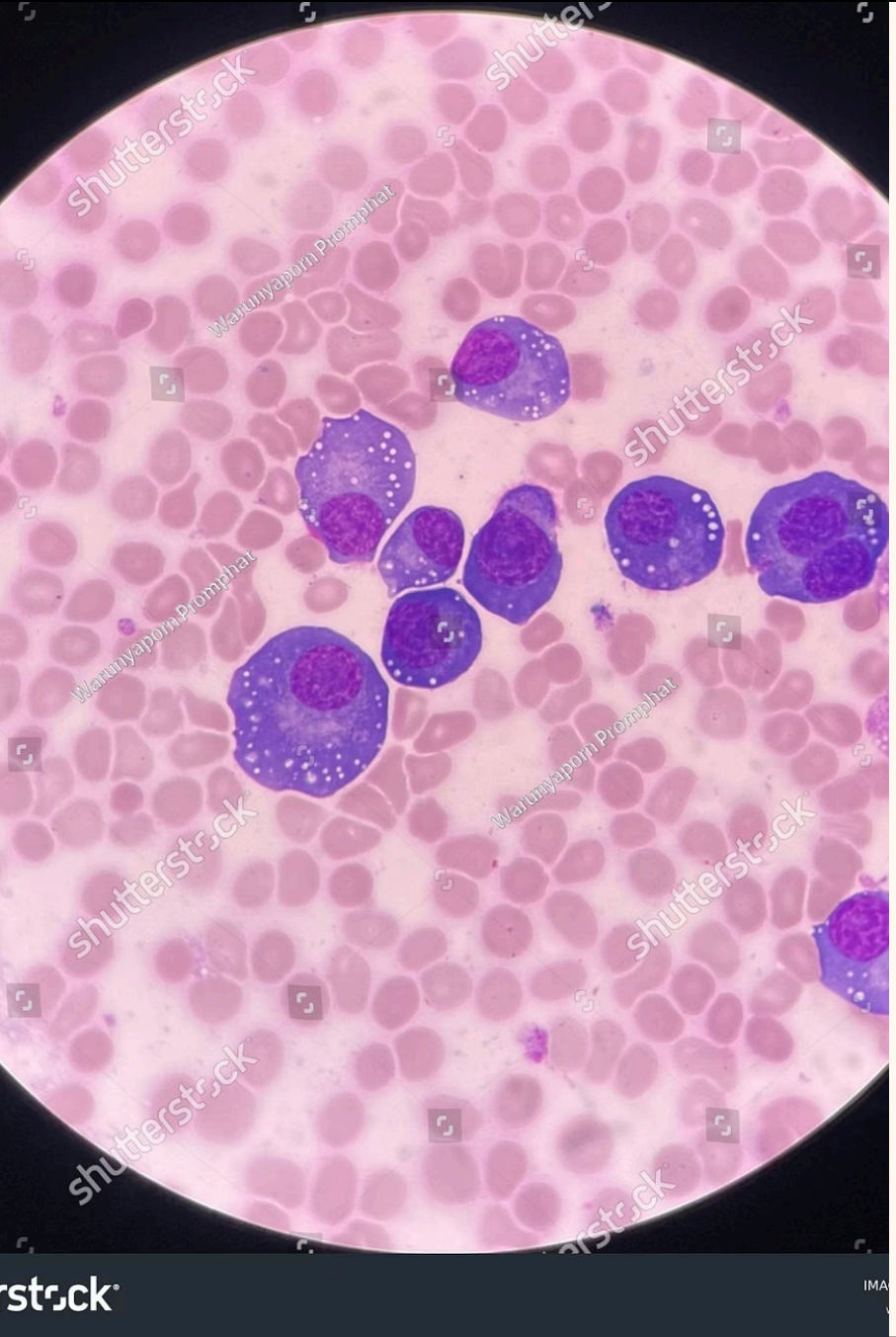
Clinical Picture & Diagnosis

Recognizing symptoms and diagnostic methods.

04

Staging & Management

Determining severity and treatment options.



Defining Multiple Myeloma (MM)

Malignant Plasma Cell Disorder

Uncontrolled proliferation and diffuse infiltration of monoclonal plasma cells in the bone marrow.

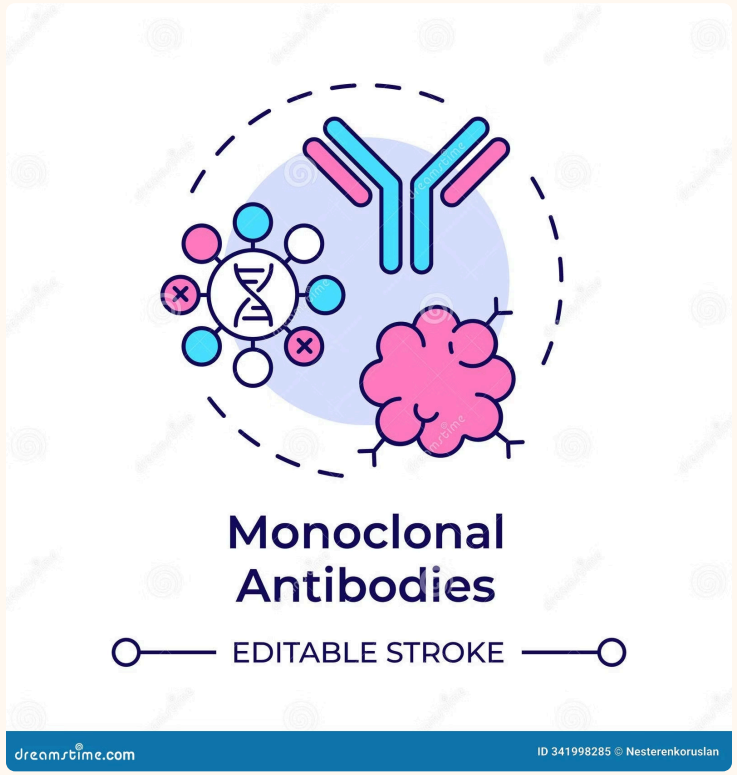
Plasma Cells

Activated B-cells producing Immunoglobulin (antibodies) against specific antigens.

Key Characteristic: Monoclonal Production

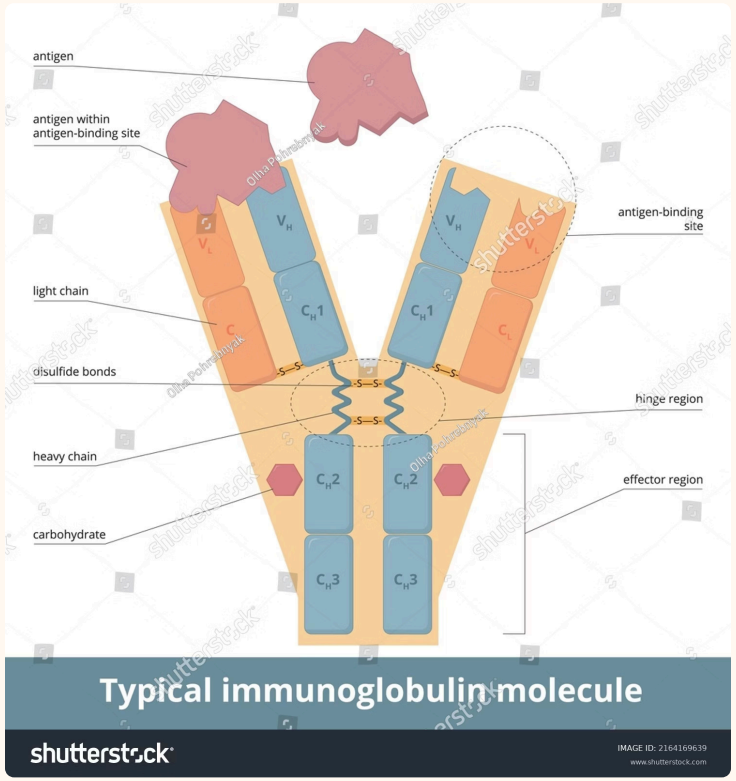
The main characteristic of MM is the high production of abnormal plasma cells.

Defined by the monoclonal production of antibodies (Abs), also known as **M protein**.



Immunoglobulins (Igs)

- Composed of heavy (IgG, IgA, IgM, IgE, IgD) and light chains (kappa, lambda).
- Normal Igs are **polyclonal** (variety of chains).
- MM Igs are **monoclonal** (single heavy and light chain type).



Genetic Basis: Chromosomal Translocations

Chromosomal Translocations

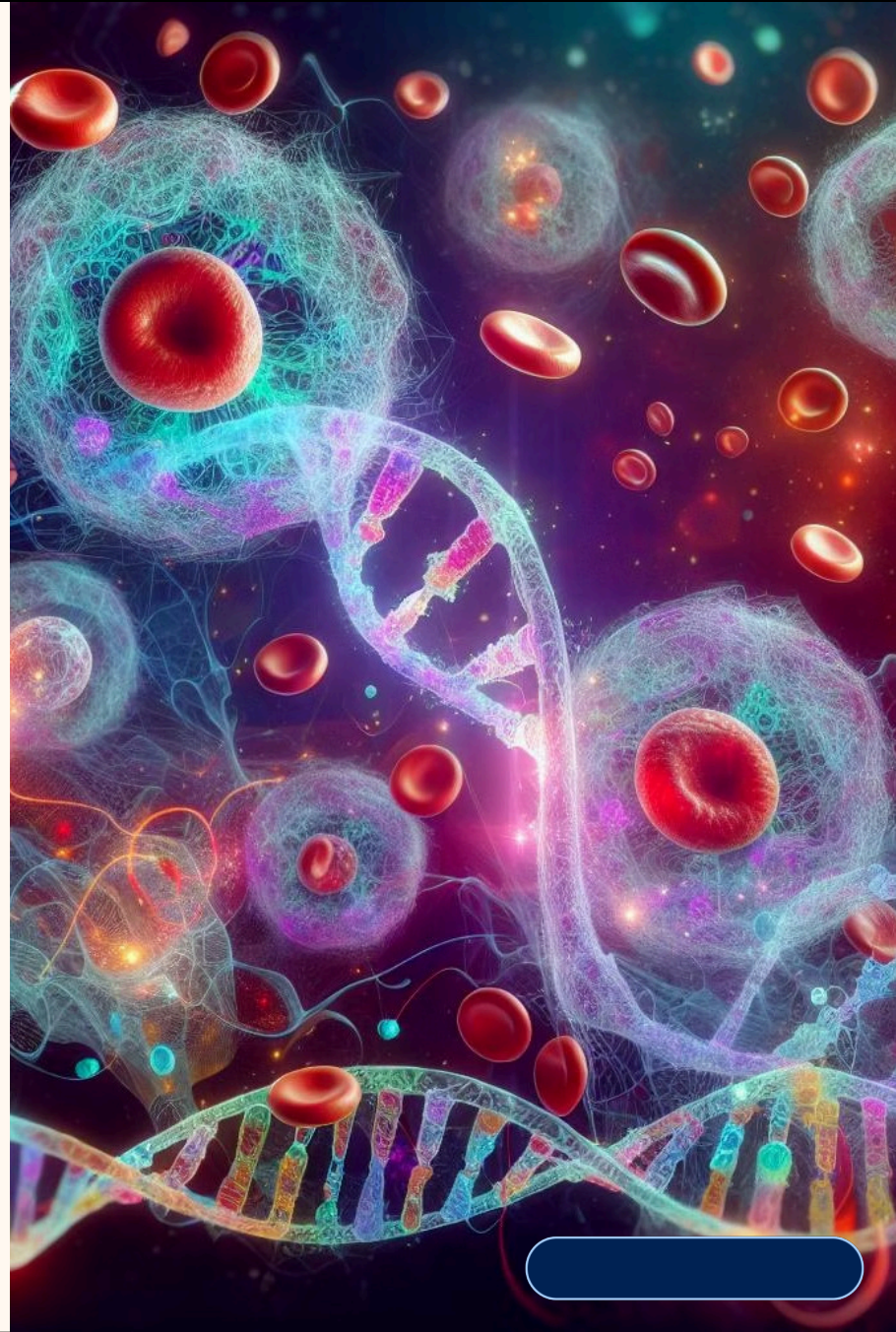
MM often involves genetic rearrangements.

IgH Locus

Translocations fuse the IgH locus on chromosome 14.

Oncogene Fusion

Fused to oncogenes like cyclin D1 and cyclin D3 genes.



Epidemiology: Key Statistics

4/100K

Incidence Rate

New cases per annum.

2:1

Gender Ratio

Male-to-female ratio.

60-70

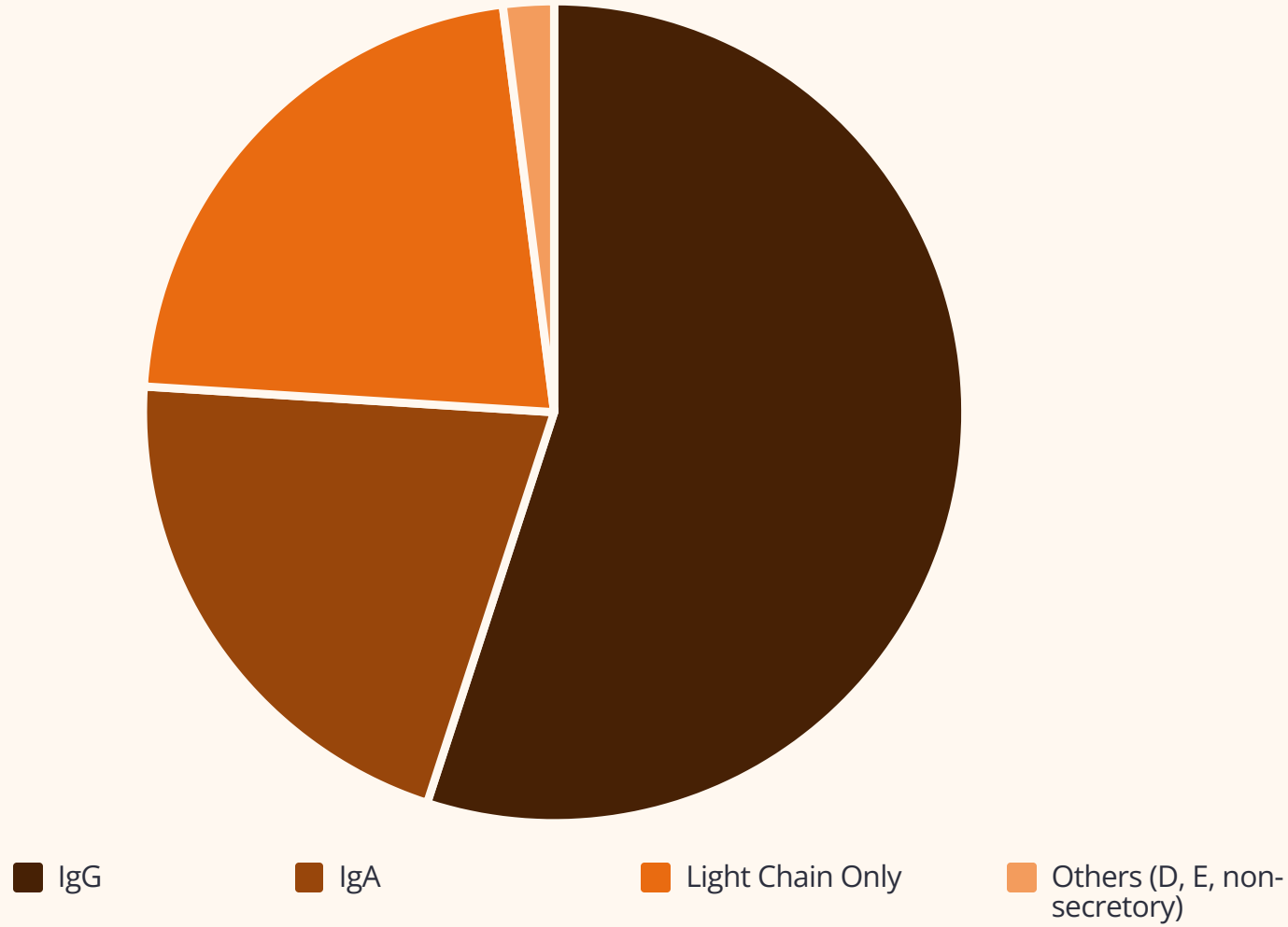
Median Age

Age range at diagnosis.

The disease is more common in people of African Caribbean origin.

Classification by M-Protein Type

Multiple Myeloma is classified based on the type of monoclonal (M)-protein produced by the malignant plasma cells.



Pathogenesis: Bone Destruction

Malignant Plasma Cells

Mostly in bone marrow.

Cytokine Production

Activate osteoclasts (pro-osteoclastogenic factors).

Bone Resorption

Leads to lytic lesions, bone pain, and hypercalcemia.

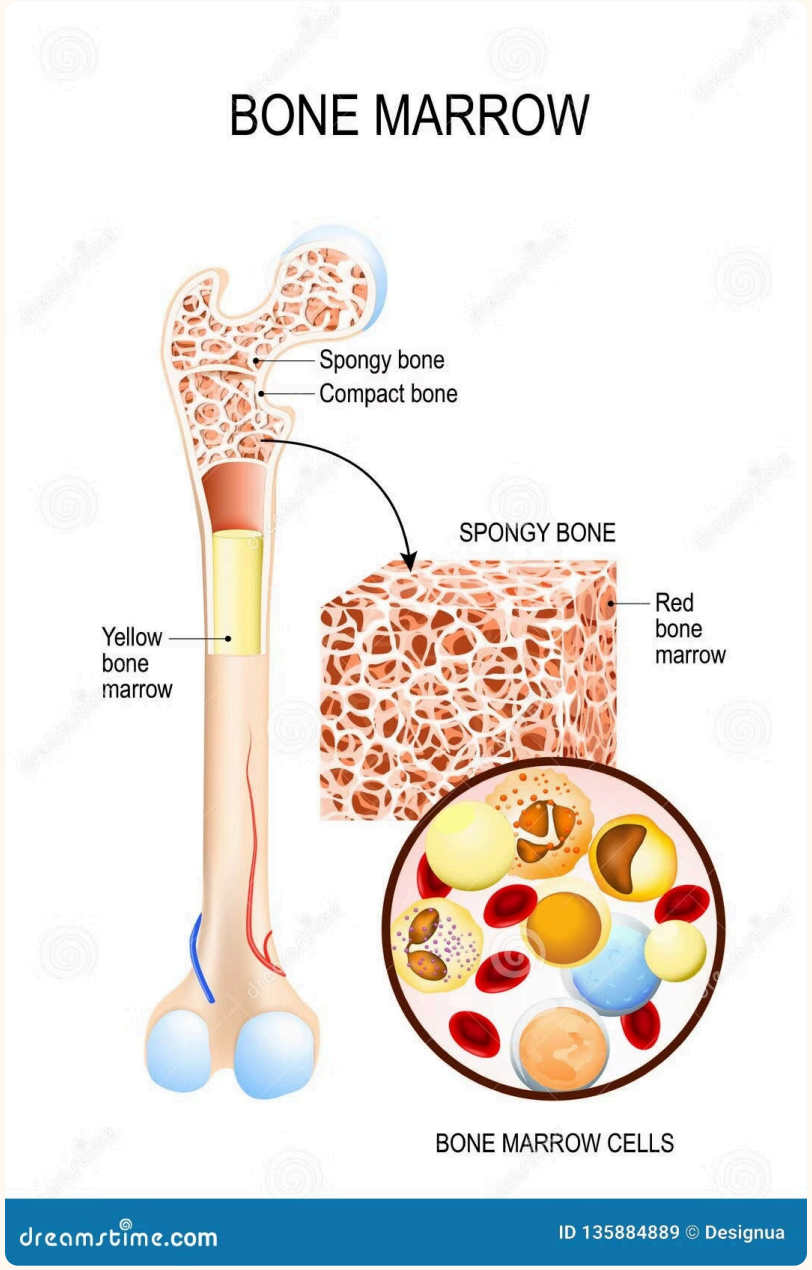
Pathogenesis: Bone Marrow Infiltration

Infiltration and Suppression

Increased malignant plasma cells infiltrate the bone marrow, suppressing normal hematopoiesis.

Result: Pancytopenia

- Leukopenia (low white blood cells)
- Thrombocytopenia (low platelets)
- Anemia (low red blood cells)



Bone marrow infiltration is a key driver of systemic symptoms.

Light Chains and Bence-Jones Proteins

1

Excess Light Chains

In most MM cases, an excess of light chains is produced; sometimes, only light chains are produced.

2

Low Molecular Weight

These light chains have a low molecular weight.

3

Excretion

Excreted in the urine as Bence-Jones proteins.

Clinical Picture: Asymptomatic vs. Symptomatic

Often Asymptomatic

Myeloma can be discovered incidentally during routine blood work.

Symptomatic Features

When symptoms occur, they are primarily related to four key areas: bone, marrow, renal function, and immunity.

1: Bone Resorption

Bone Pain

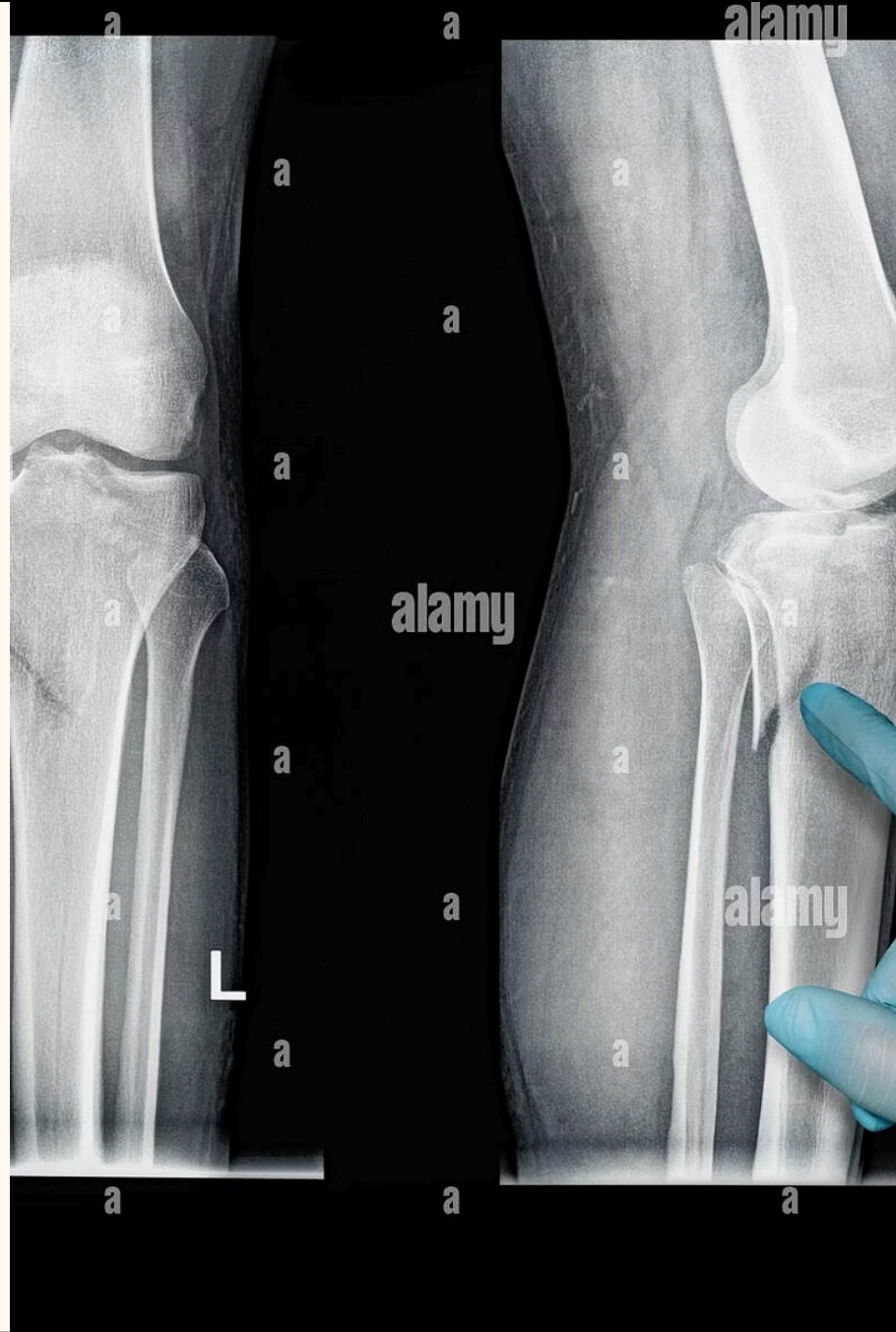
Mainly affects the back bones.

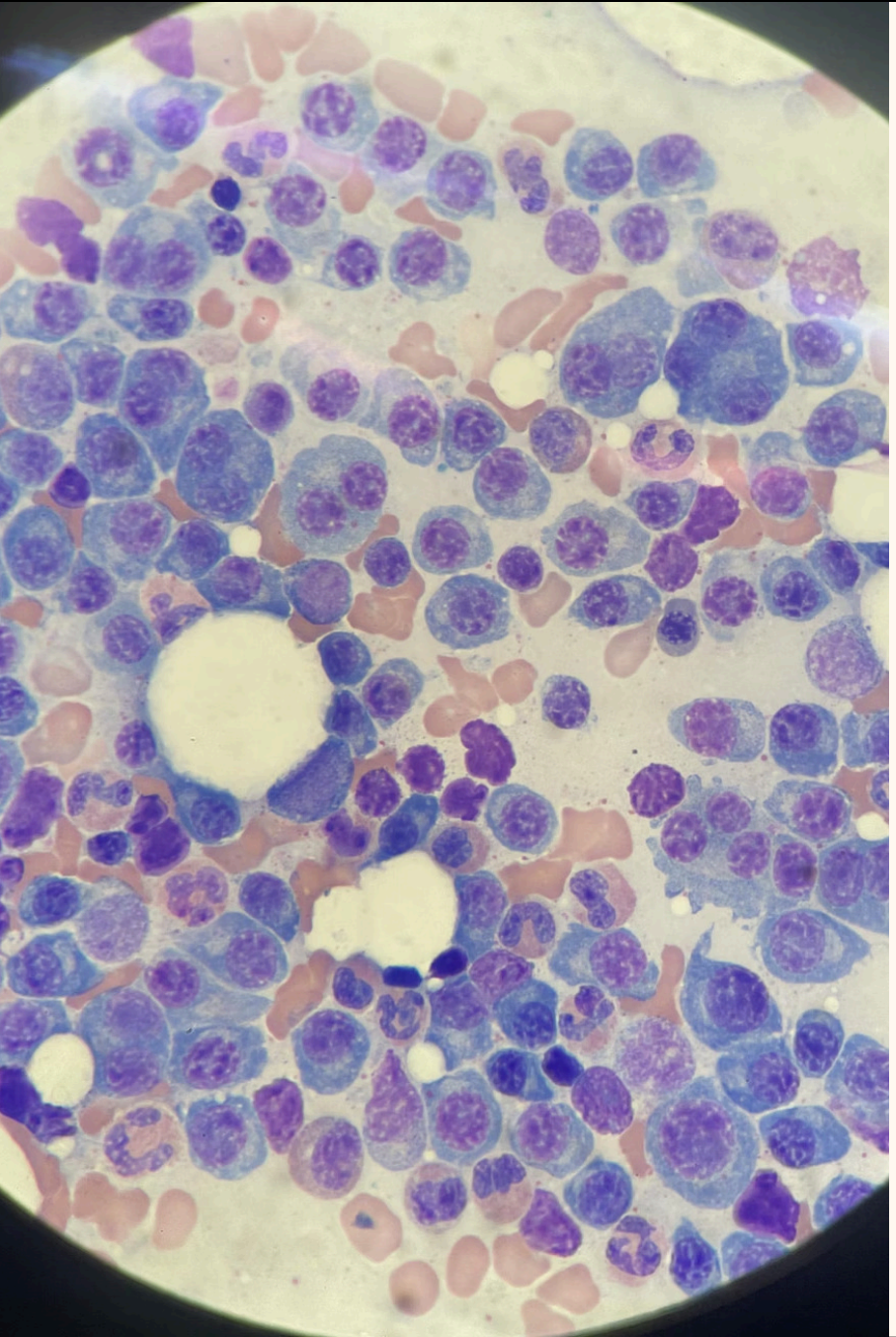
Spontaneous Fractures

Increased fragility due to bone damage.

Hypercalcemia

Elevated calcium levels leading to confusion, lethargy, and weakness (neurological manifestations).





2: Marrow Involvement

Overproduction of malignant plasma cells (>30% cellularity is common) in the bone marrow leads to pancytopenia.

1

Pancytopenia

Reduction in red cells, white cells, and platelets.

2

Anemia

Caused by decreased red blood cell production.

3

Bleeding Tendency

Due to low platelet count (thrombocytopenia).

3: Renal Dysfunction

Kidney damage is a significant complication, often caused by multiple factors:

1

Bence-Jones Protein

Light chain deposition causes direct renal damage.

2

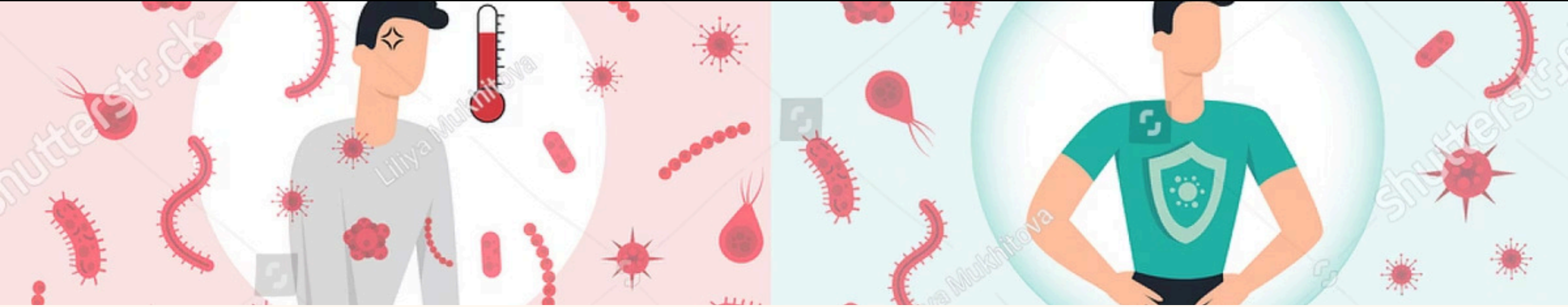
Hypercalcemia

Leads to dehydration and renal stones.

3

Infection Risk

Increased risk of pyelonephritis (kidney infection).



4: Depressed Immunity

> Immunity is depressed due to bone marrow involvement and the production of non-functional antibodies. The patient is at a high risk for infection.

Diagnosis: Initial Studies & Biomarkers

Initial Laboratory Studies

- Complete Blood Count (CBC)
- Comprehensive Metabolic Panel (CMP)
- Urinalysis

Myeloma Biomarkers

- Serum and Urine Protein Electrophoresis
- Free Light Chain Assay
- Lactate Dehydrogenase (LDH)

Key Diagnostic Lab Findings

1

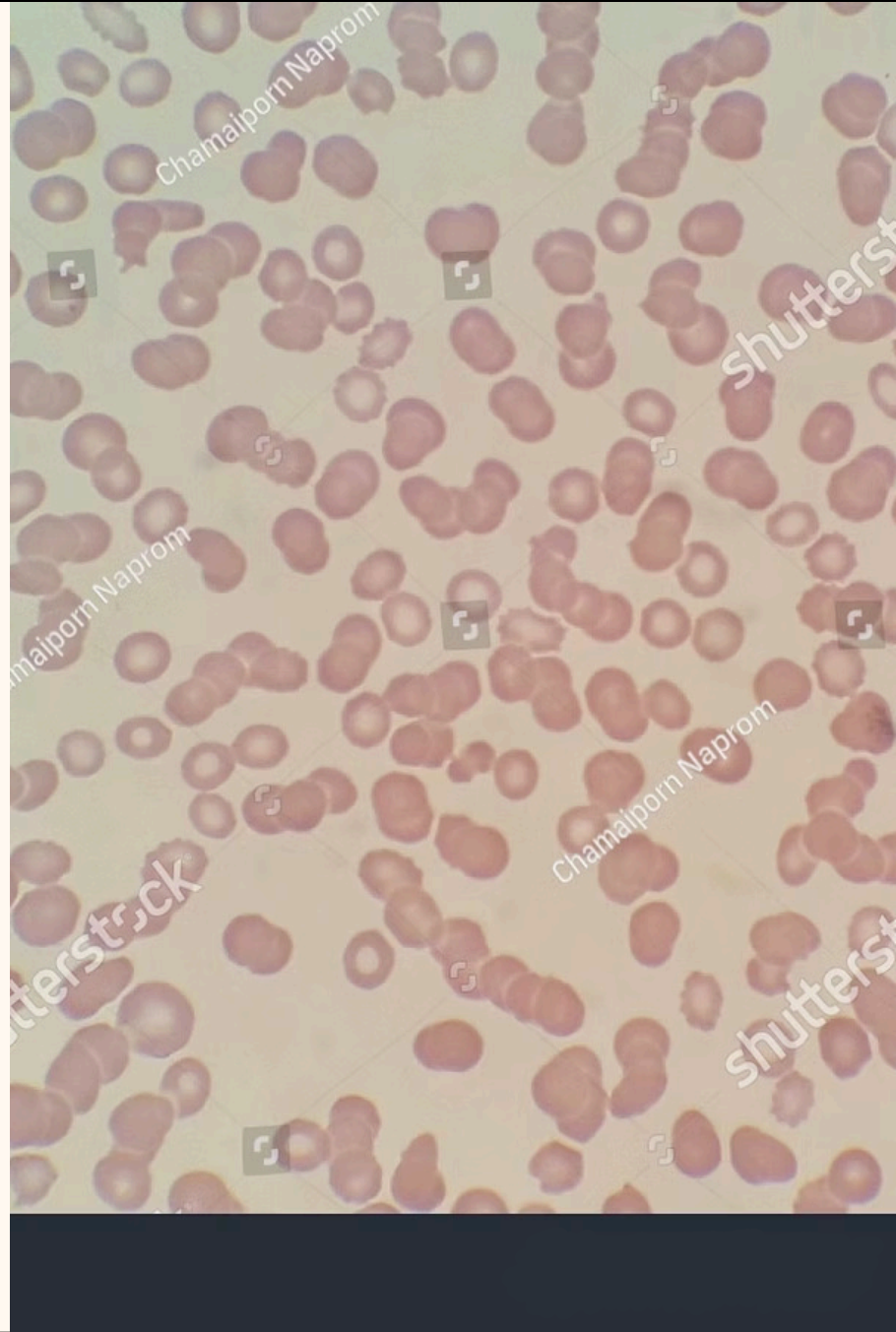
CBC with Blood Smear

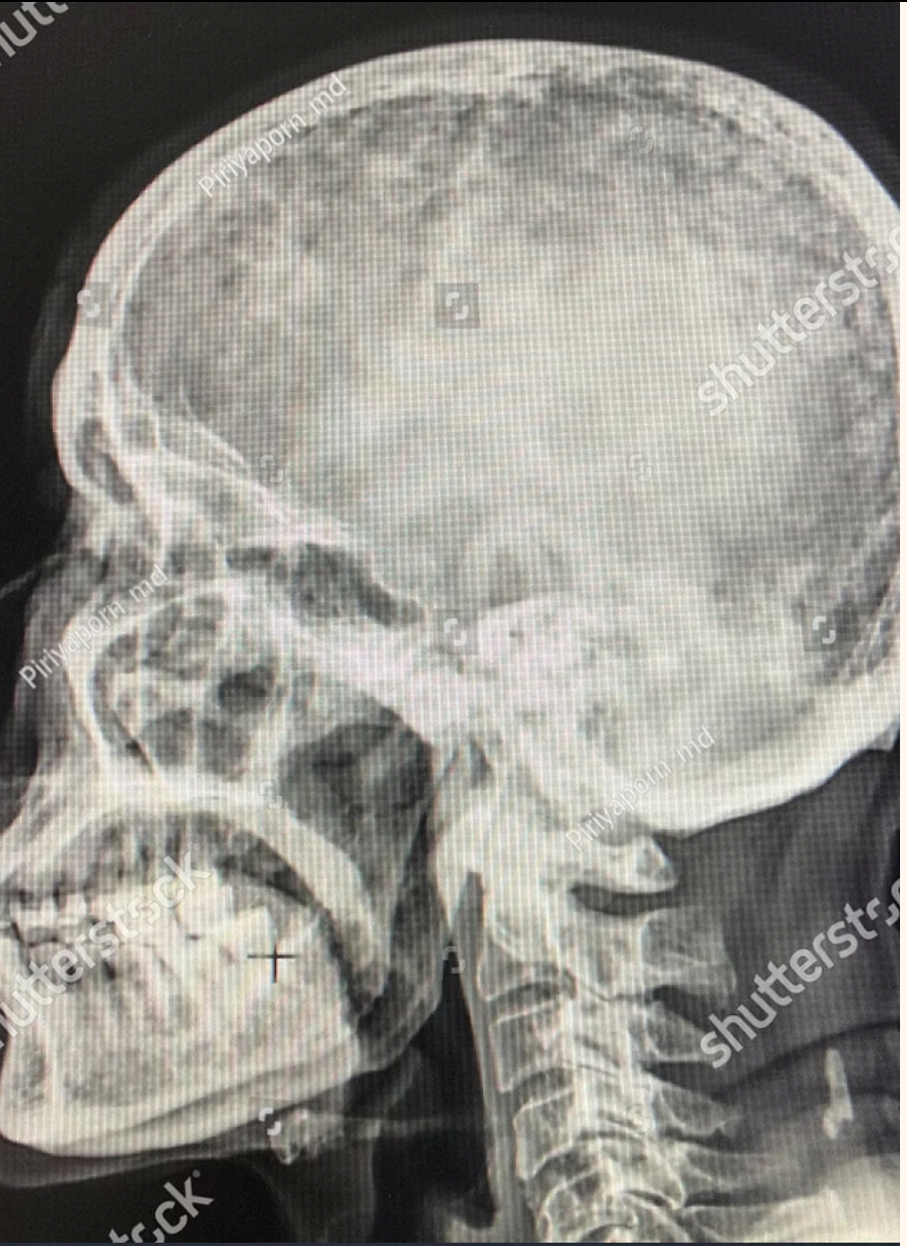
Shows anemia, thrombocytopenia, leukopenia, decreased reticulocyte count, and characteristic Rouleaux formation.

2

Bence Jones Proteins

Monoclonal immunoglobulin light chains produced by neoplastic cells. Their presence in urine is suggestive of plasma cell disorders.





Diagnostic Imaging Studies

Whole-Body Low-Dose CT (WBLDCT)

First-line test for bone surveillance. More sensitive than X-rays; detects osteolysis and osteopenia.

MRI (Whole-Body or Spine/Pelvis)

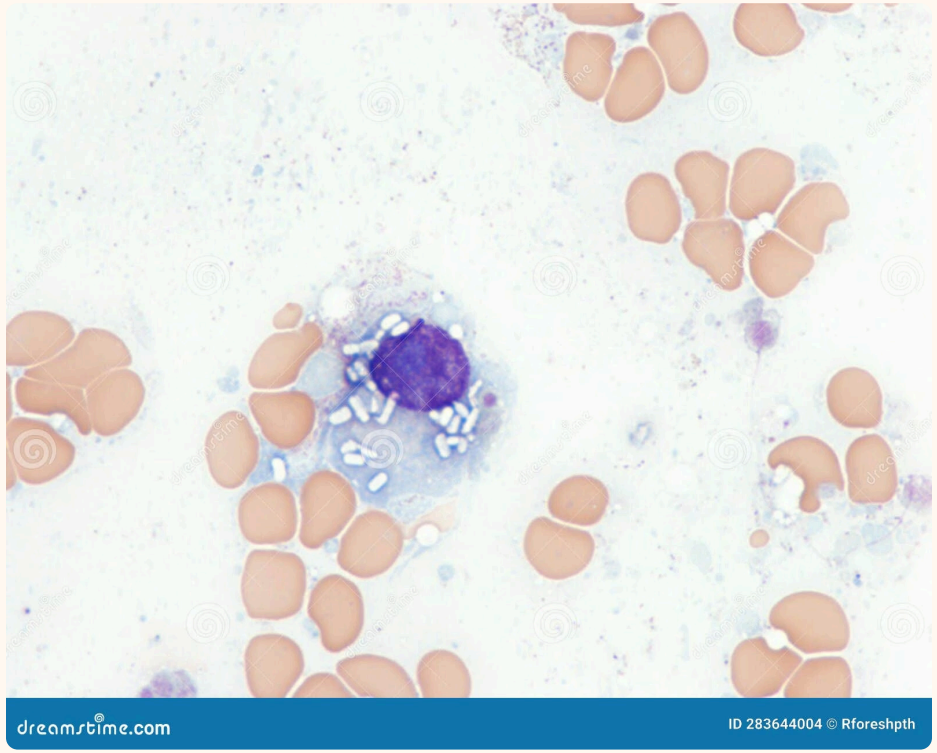
Highest sensitivity for detecting diffuse bone marrow involvement.

Plain X-Rays

Low sensitivity; no longer the best initial test. Findings include multiple lytic lesions ("punched-out" holes).

Bone Marrow Biopsy Findings

Microscopic examination of the bone marrow is crucial for diagnosis, showing an increased number of plasma cells (typically >30% cellularity).



Increased Plasma Cells

More than 10% is a feature for MM, usually >30% of cellularity.

Mott Cells

Plasma cells with spherical inclusions (Russell bodies) packed with Immunoglobulin (Ig) in their cytoplasm.

Clockface Nuclei

Chromatin at the periphery of the nucleus resembles a cartwheel or clock face arrangement.

CRAB Criteria: Indicators of Organ Damage

These four criteria indicate organ damage resulting from a plasma cell disorder and are essential for diagnosis.

C: Calcium Increased

Hypercalcemia.

R: Renal Insufficiency

Kidney damage or failure.

A: Anemia

Low red blood cell count.

B: Bone Lesions

Lytic lesions or fractures.

Staging and Management Strategy

The R-ISS (Revised International Staging System) is the most common staging system. Management focuses on remission and quality of life.

Goal of Therapy

Achieve the highest level of remission with the best possible quality of life.

Asymptomatic Myeloma

If no end-organ damage is present, treatment may not be required, but close monitoring is essential.

Treatment Choice

Based on R-ISS stage and eligibility for Autologous Hematopoietic Stem Cell Transplantation (HSCT).

Primary Treatment: Chemotherapy and HSCT

Patients are initially assessed for fitness and eligibility for HSCT, which forms a core part of the primary treatment strategy.

> Primary treatment involves chemotherapy with or without HSCT. Patient fitness and eligibility for autologous HSCT are key determinants.

Management of Complications: Bone and Renal

Effective management of complications is crucial for improving patient outcomes and quality of life.

Bone Pain & Skeletal Events

Use analgesia for pain. Bisphosphonates treat hypercalcemia and delay skeletal-related events.

Renal Impairment & Hypercalcemia

High fluid intake is recommended. Allopurinol is used for prevention of urate nephropathy.

Localized Pain

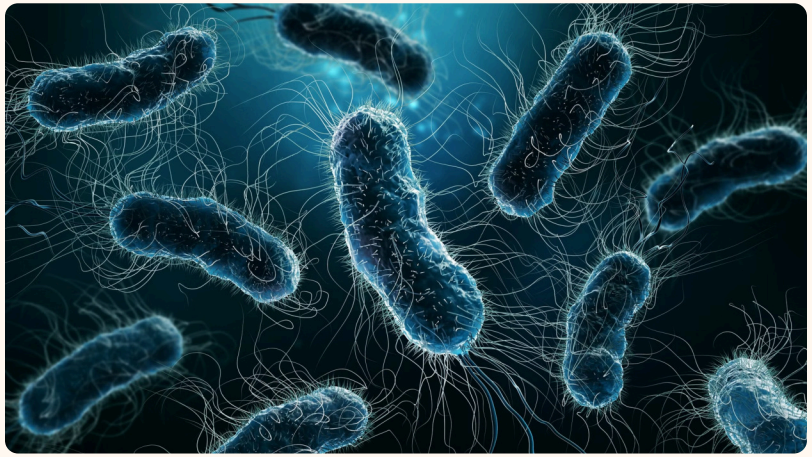
Radiotherapy is effective for localized bone pain not responding to simple analgesia, pathological fractures, or spinal cord compression.

Infection Prophylaxis and Risk

Infections are a major cause of death in MM patients, necessitating proactive measures.

Infection Risk

Infections are the major cause of death in Multiple Myeloma patients due to immunosuppression.



Antibiotic prophylaxis with levofloxacin is recommended during the first 3 months of therapy to mitigate infection risk.

Major Complications of Multiple Myeloma

Infections

Major cause of mortality.

Kidney Disease

Caused by hypercalcemia, dysproteinemia, analgesic nephropathy, or AL amyloidosis.

Hypercalcemic Crisis

Associated with chronically elevated calcium levels due to osteolysis.

Secondary Plasma Cell Leukemia

A potential progression of the disease.

Prognosis and Key Factors

The disease course is highly variable. While therapeutic options have improved, complete remission remains rare.

Advanced R-ISS Stage

Higher stage indicates poorer prognosis.

Advanced Age

Older patients face greater challenges.

Increased Biomarkers

High beta microglobulin, CRP, and LDH are poor signs.

Decreased Serum Albumin

Low albumin levels are associated with worse outcomes.

Thank You 👈

We appreciate your attention and engagement during this presentation on Multiple Myeloma.

Please feel free to ask any questions or connect for further discussion.