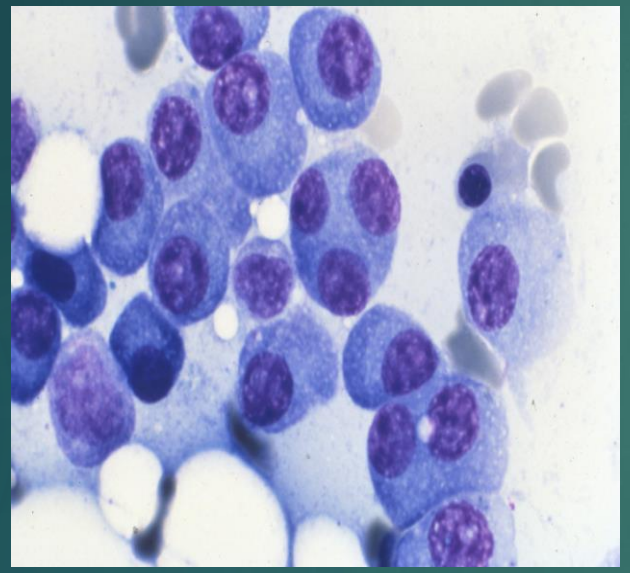
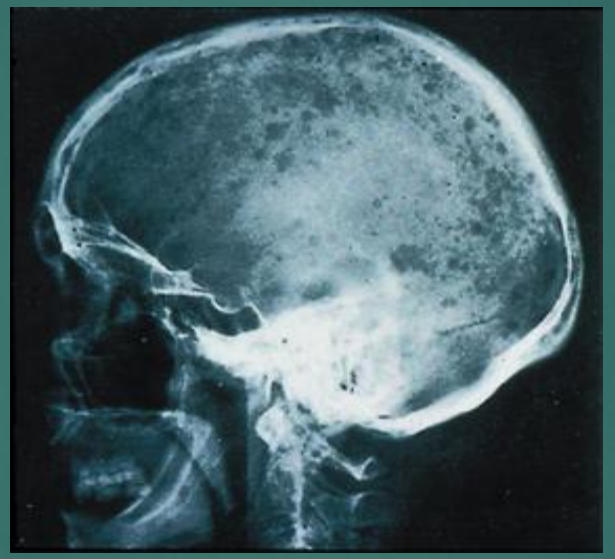
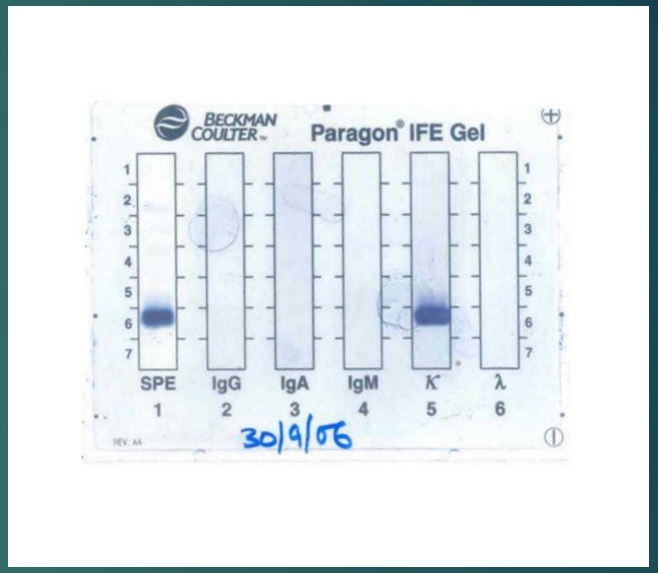
MULTIPLE MYELOMA



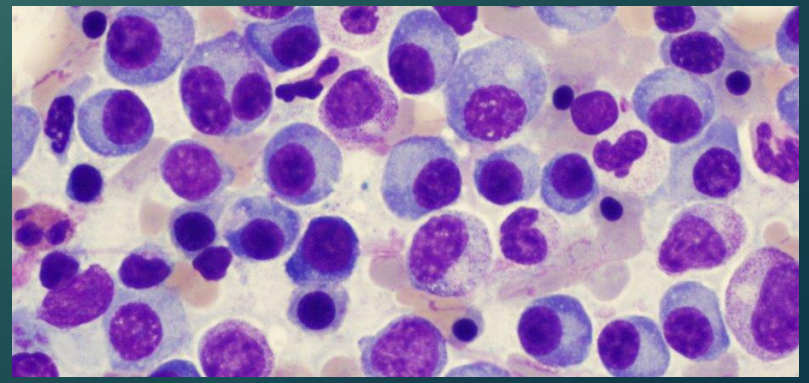




DR DURGA MORATUWAGAMA

Multiple Myeloma(MM)

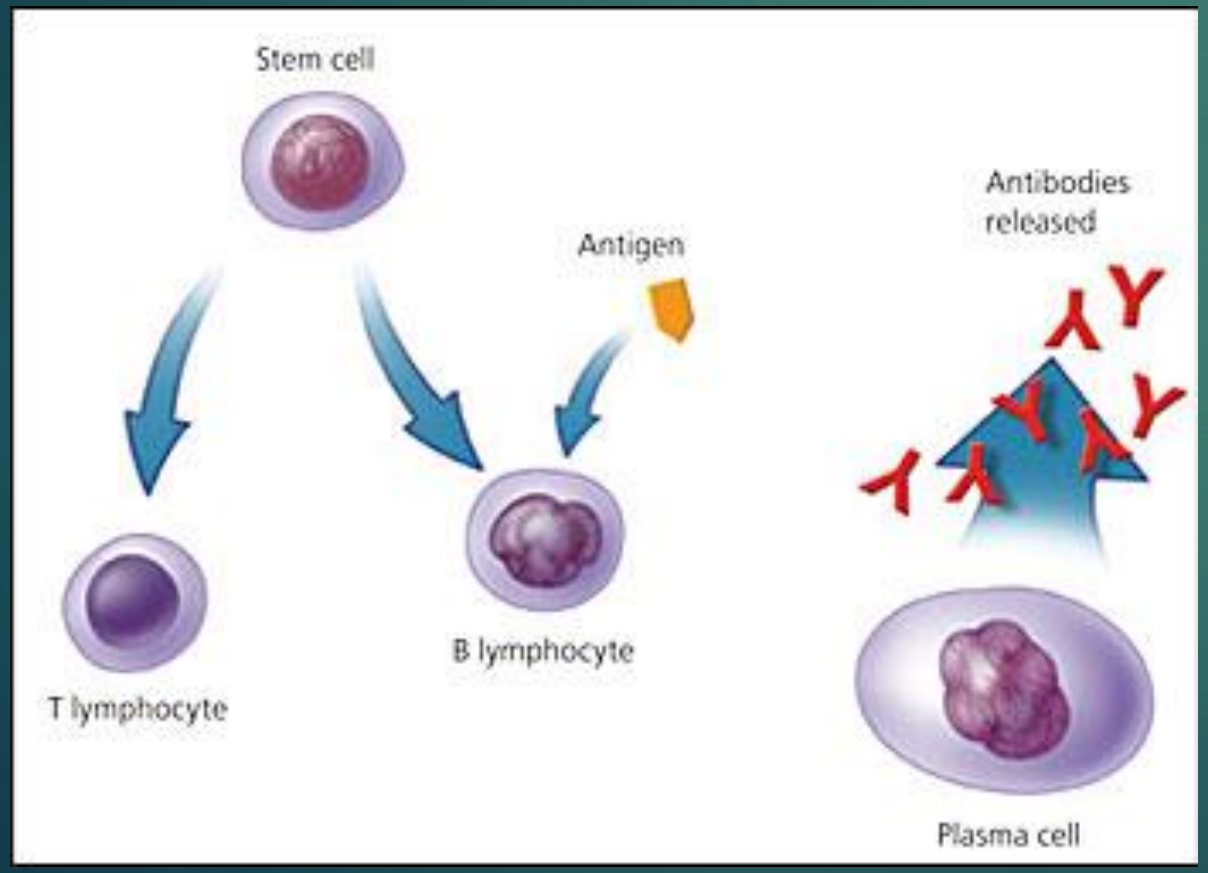
- At the end of this lecture student should be able to:
- Define Multiple myeloma
- Describe the clinical features of multiple myeloma and describe the pathophysiological basis
- Describe the laboratory investigations with expected results
- Describe the complications of MM
- Outline the basic principles in managing MM

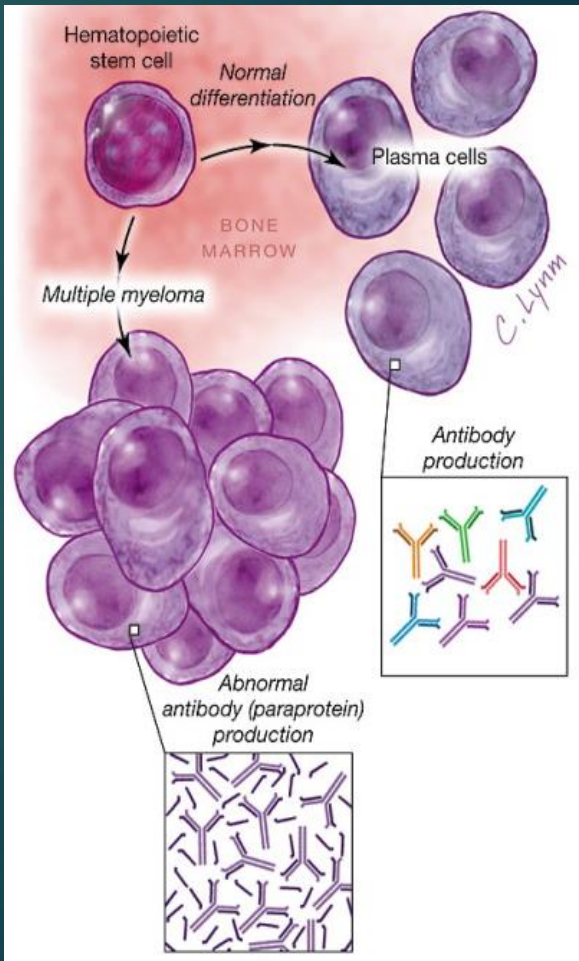


MULTIPLE MYELOMA

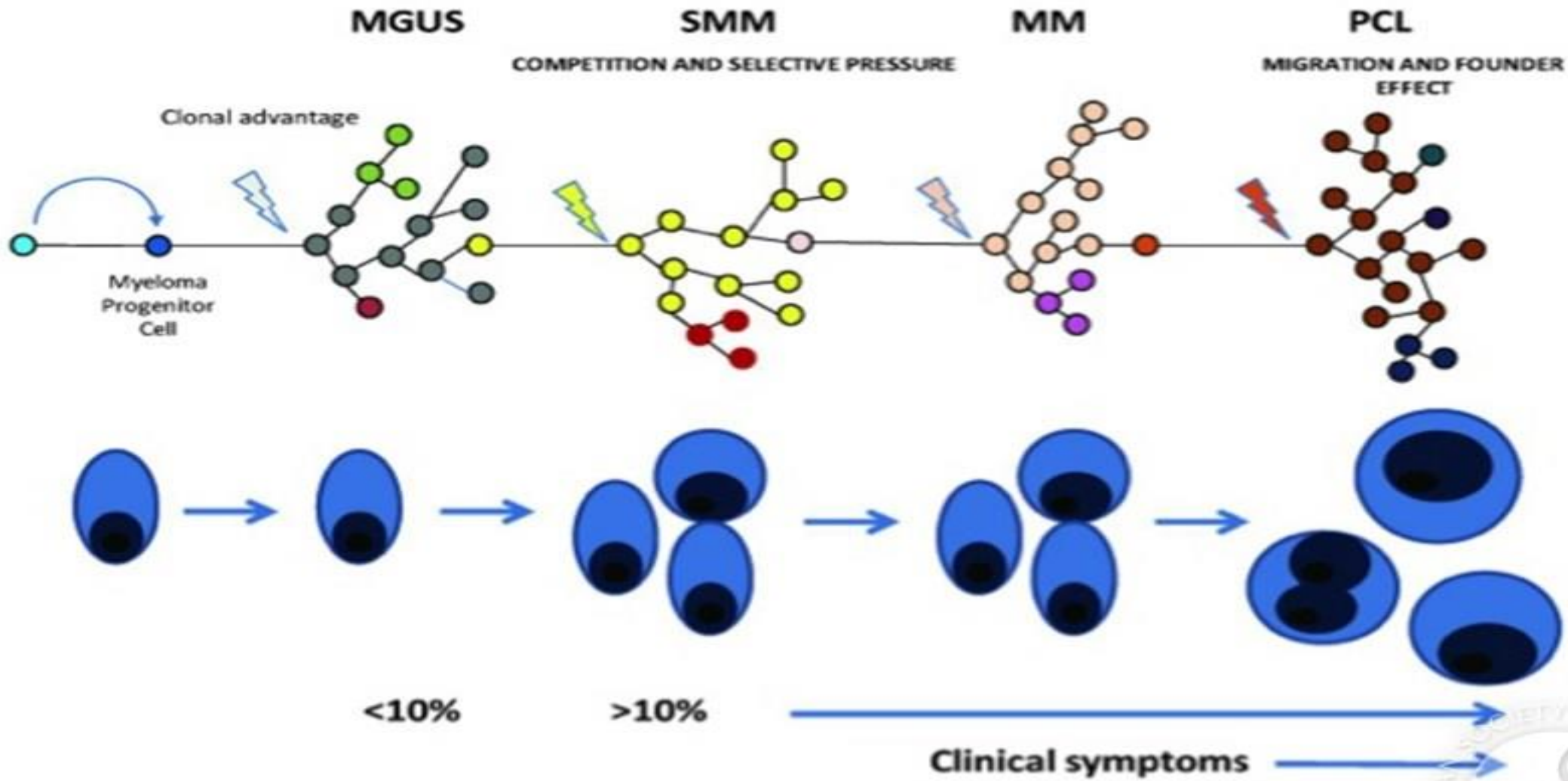
- Plasma cell neoplasm
- Median age-65-70 years
- Incurable

- Normal Plasma cells secrete normal immunoglobulins
- Normal Ig are polyclonal
- Clonal/Abnormal plasma cells- Abnormal Ig
- Monoclonal immunoglobulins- paraprotein/M-protein)





Clonal evolution in myeloma.



Morgan G J , and Kaiser M F Hematology 2012;2012:342-349

Clinical effects and laboratory abnormalities

- Effects due to plasma cell proliferation in the BM
- Effects due to the products secreted by plasma cells (ex:paraprotein)

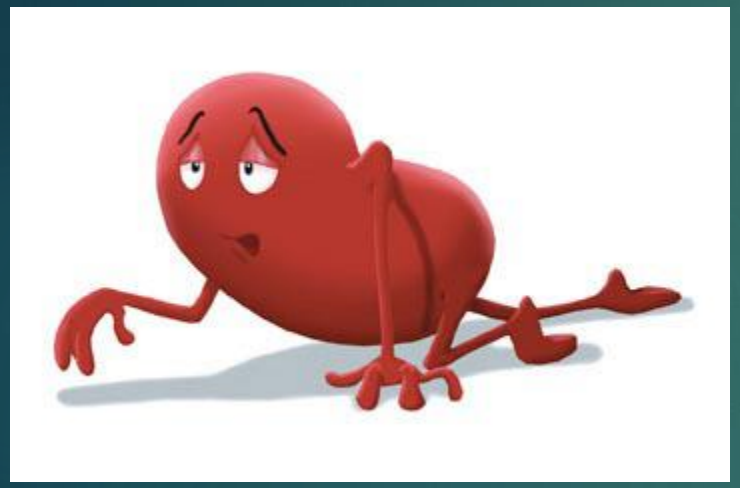
Early stage -Asymptomatic

CLINICAL PRESNTATION

- Bone pain -backache

BM failure

Symptoms of anaemia



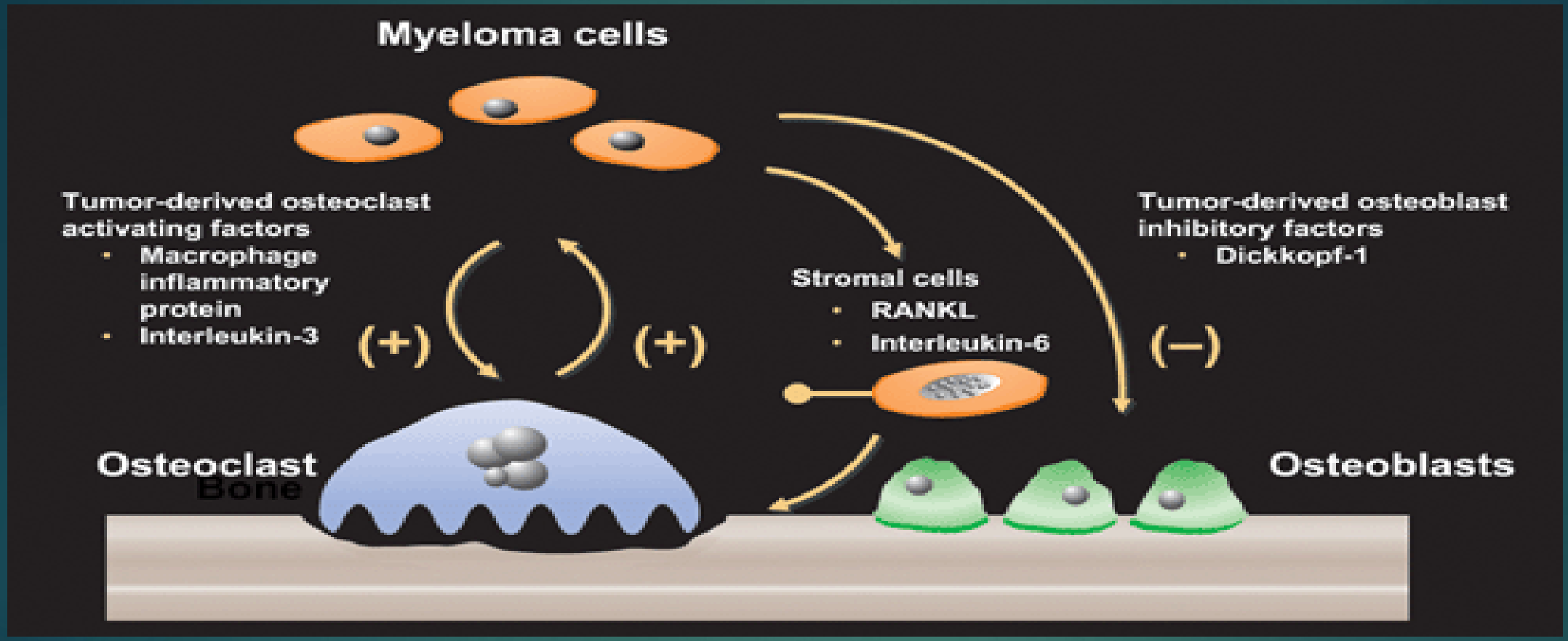
Recurrent Infections

Neutropenia
Hypogammaglobulinaemia

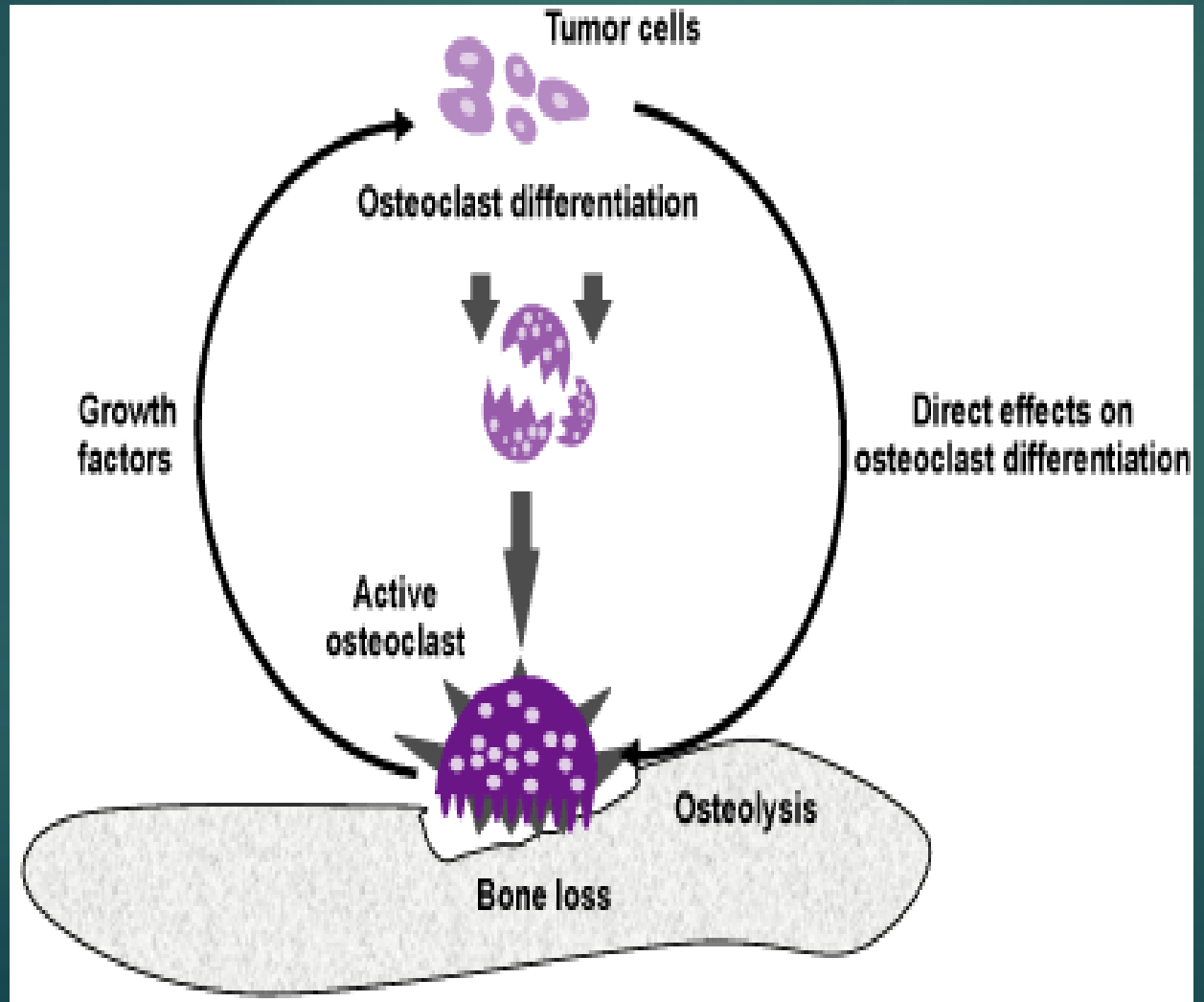
Bleeding

Thrombocytopenia
Acquired inhibitors
Platelet function defects due to paraproteins

Pathological fractures

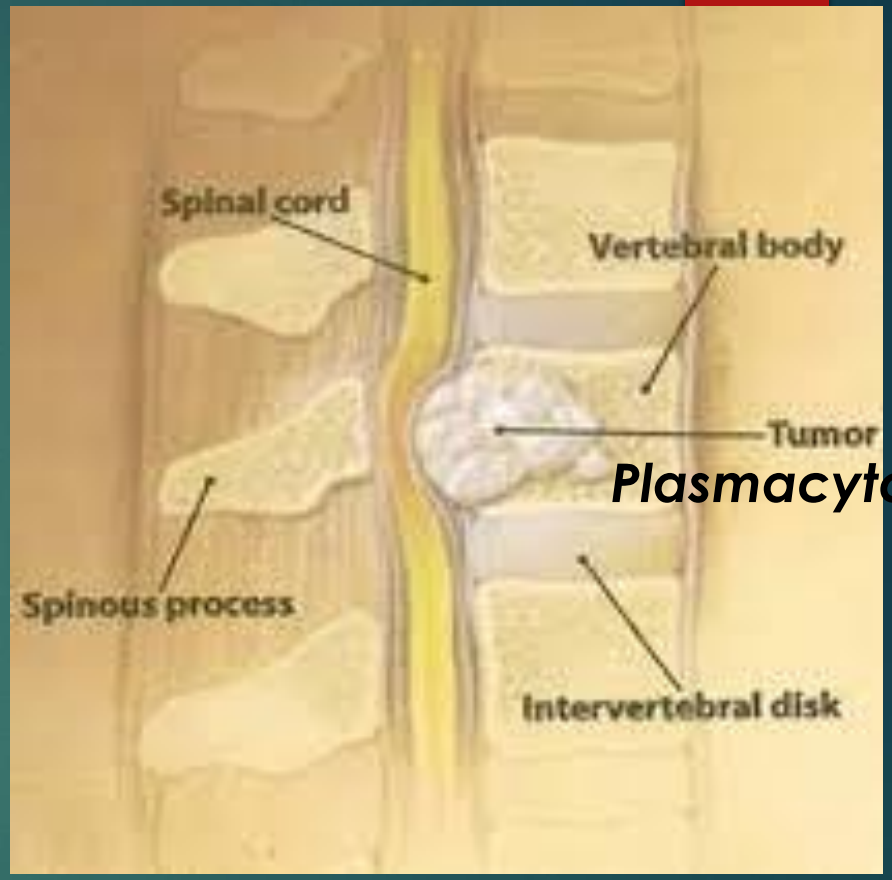


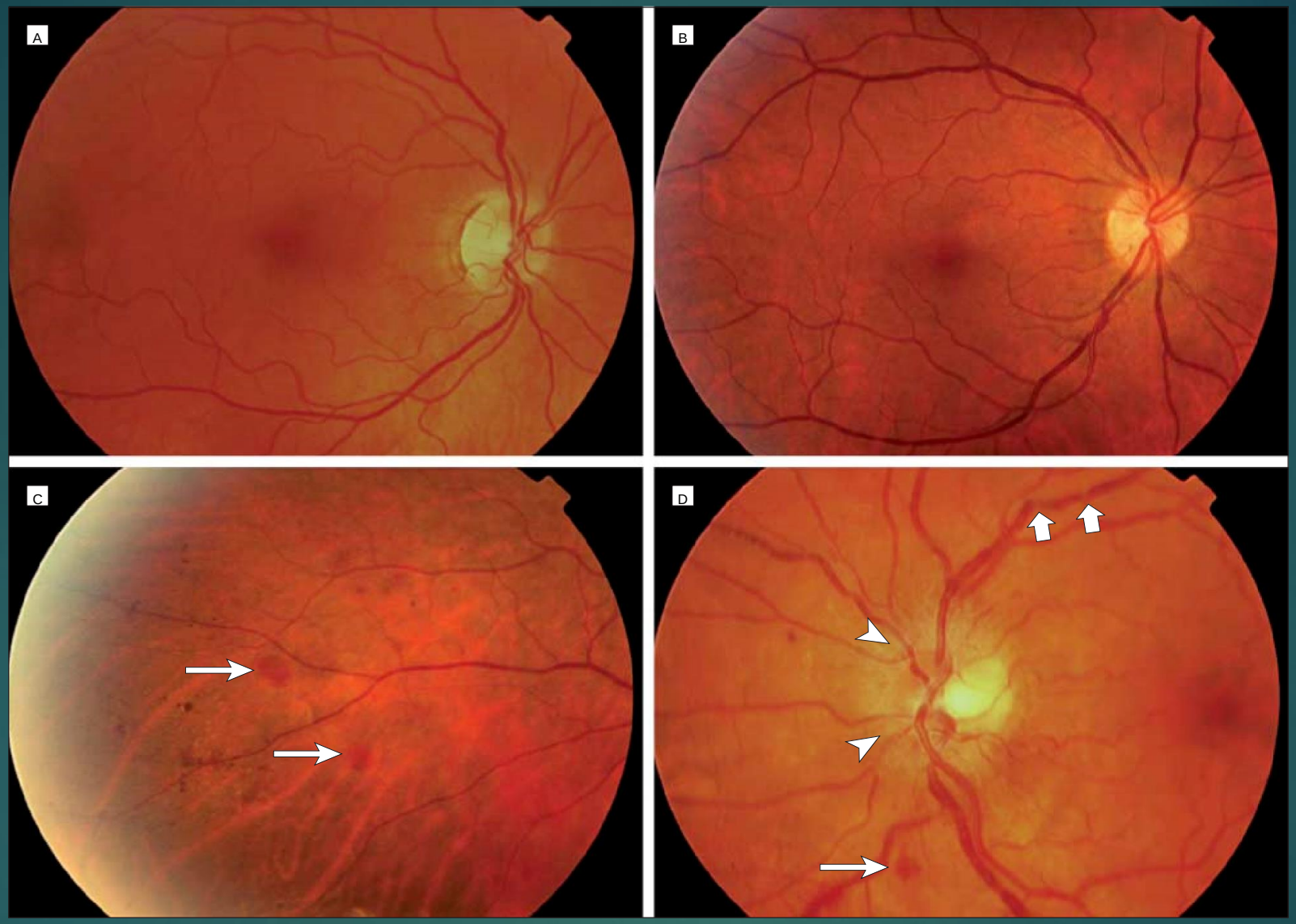
- Symptoms related to hypercalcaemia
- vomiting, weakness, confusion, polyuria, polydypsia or constipation



Nervous system manifestations

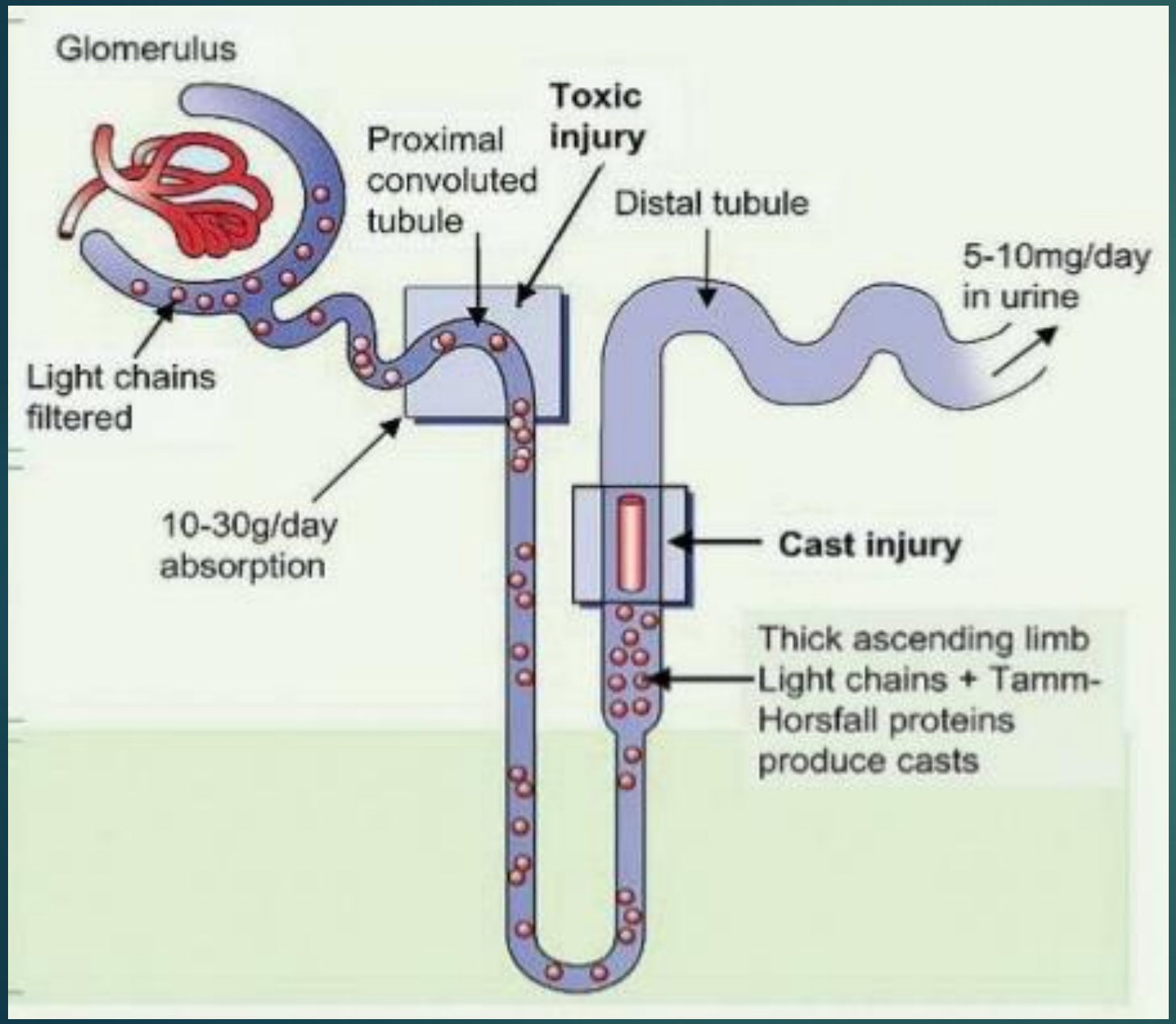
- Hypercalcaemia
- Spinal cord compression
- Hyperviscosity syndrome





Fundus images A, No retinopathy ; B, dilated veins ; C, peripheral retinal hemorrhages (arrows); and D, central retinal hemorrhage (thin arrow), optic disc edema (arrowheads), and venous sausaging (thick arrows)

Renal insufficiency



Cast nephropathy
Dehydration
Hypercalcaemia
Hyperurecaemia
Infections :Pyelonephritis
Use of NSAIDS
Amyloidosis

- Amyloidosis-Macroglossia, carpal tunnel syndrome, autonomic neuropathy,cardiomyopathy

DIAGNOSIS

- Clinical presentation

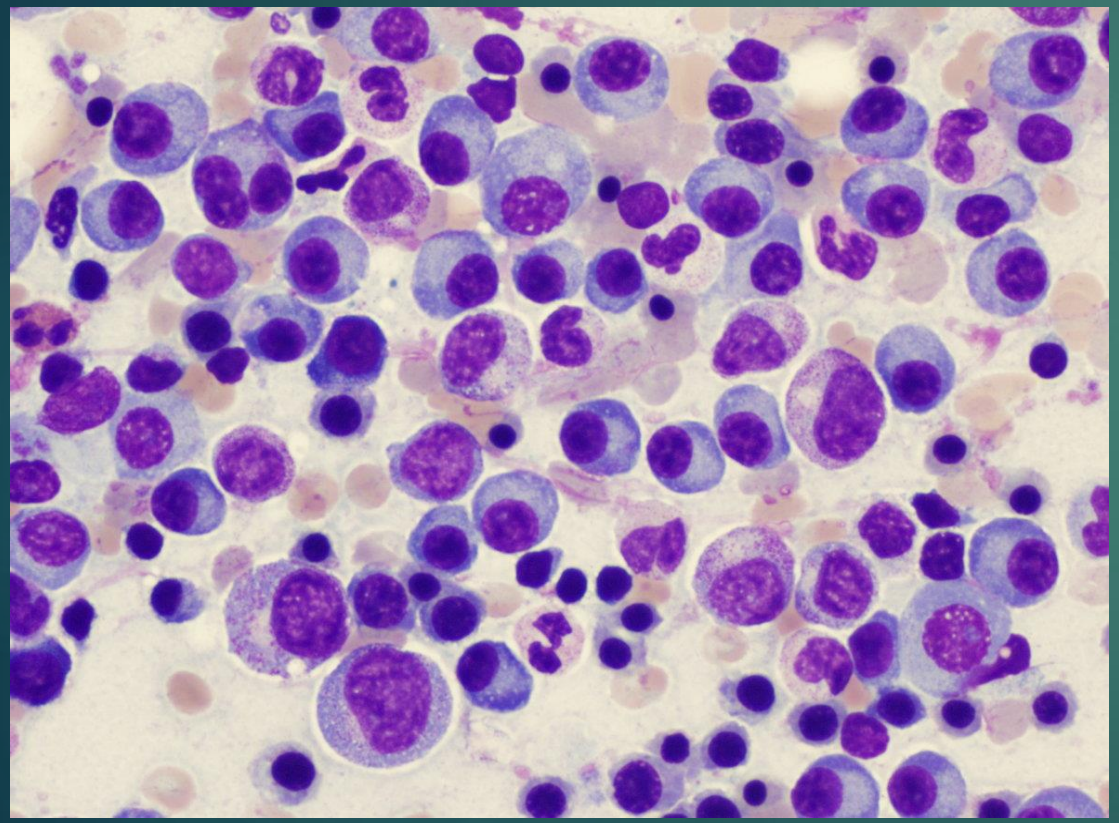
- Investigations-Haematological
  Bio-chemical
  Radiological

Investigations

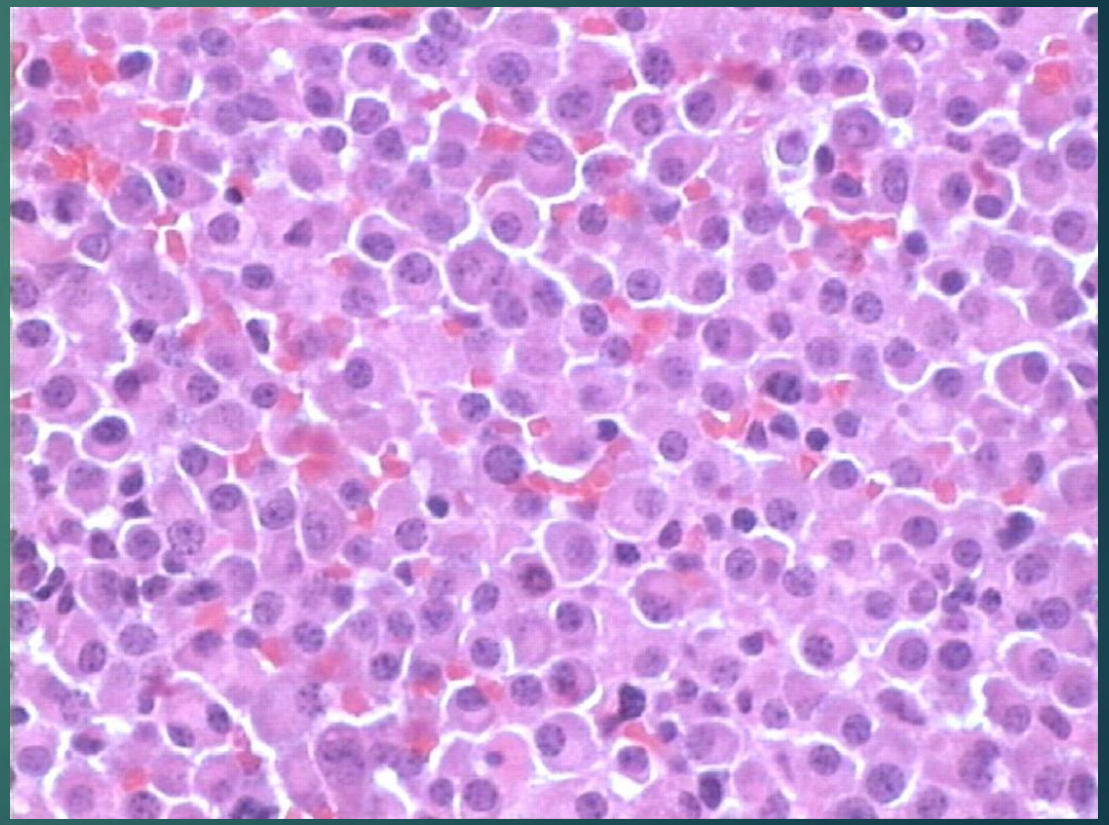
- Demonstrate plasma cell proliferation
- Demonstrate the effects of plasma cell proliferation

Demonstrate plasma cell proliferation

BM aspiration



Trephine Biopsy

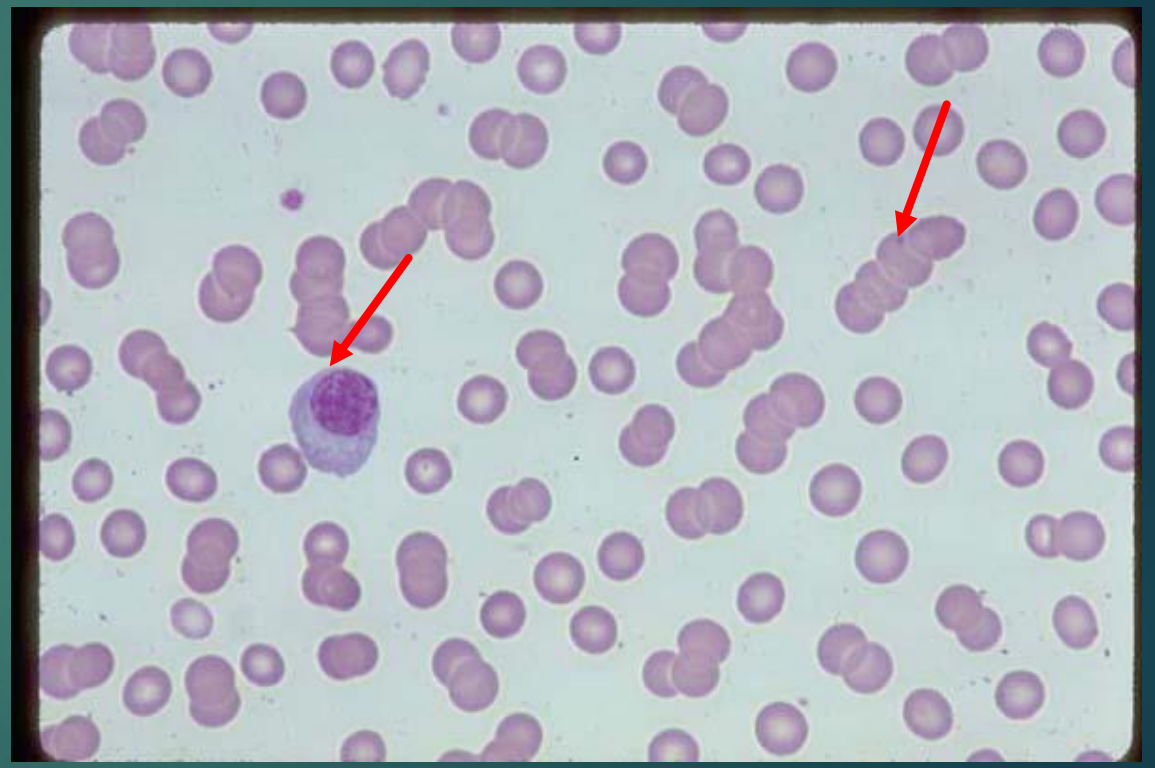


Demonstrate the effects of plasma cell proliferation

- BM failure
- Presence of paraprotein & its effects
- Other effects due to plasma cell proliferation

BM failure-FBC+BP

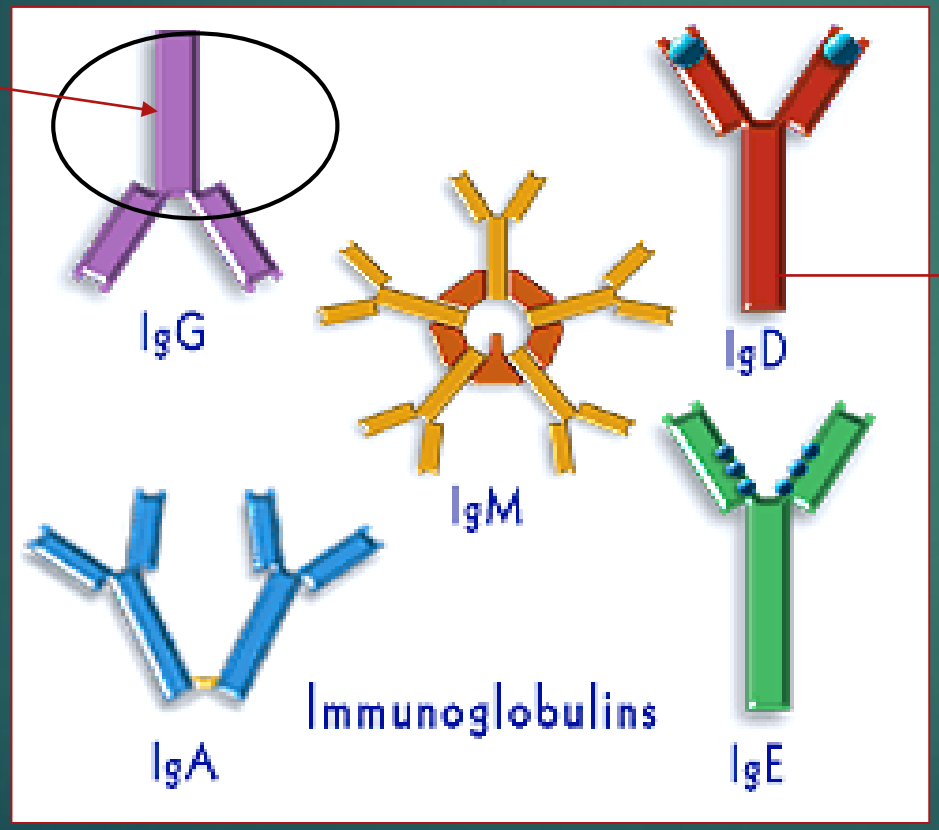
- Normochromic normocytic anaemia
- Marked rouleaux formation
- Back ground staining
- Plasma cells



Presence of paraprotein

- Serum protein electrophoresis
- Urine protein electrophoresis

60%



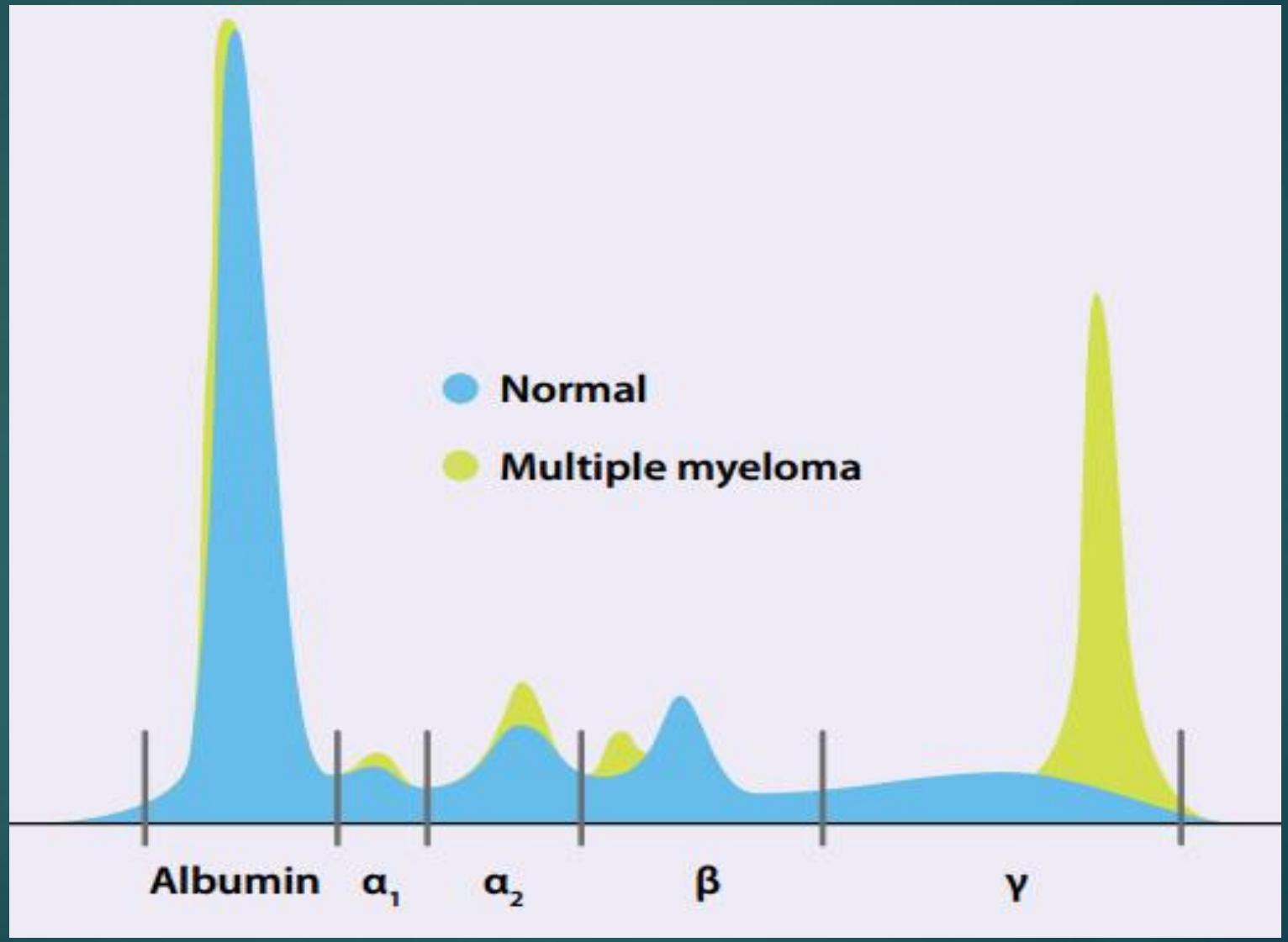
Negative

Serum/urine free light chains

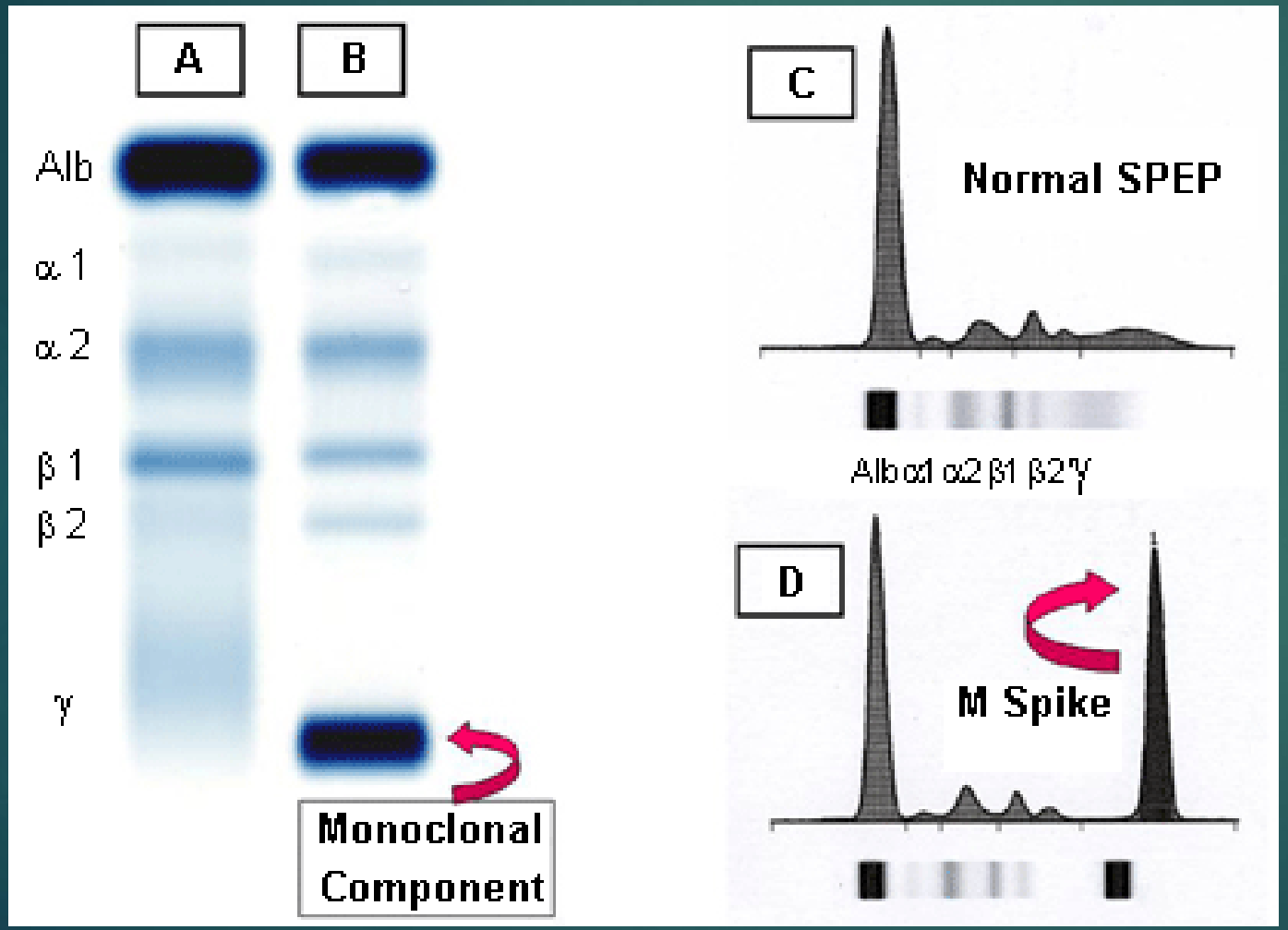
Negative

Non secretory-01%

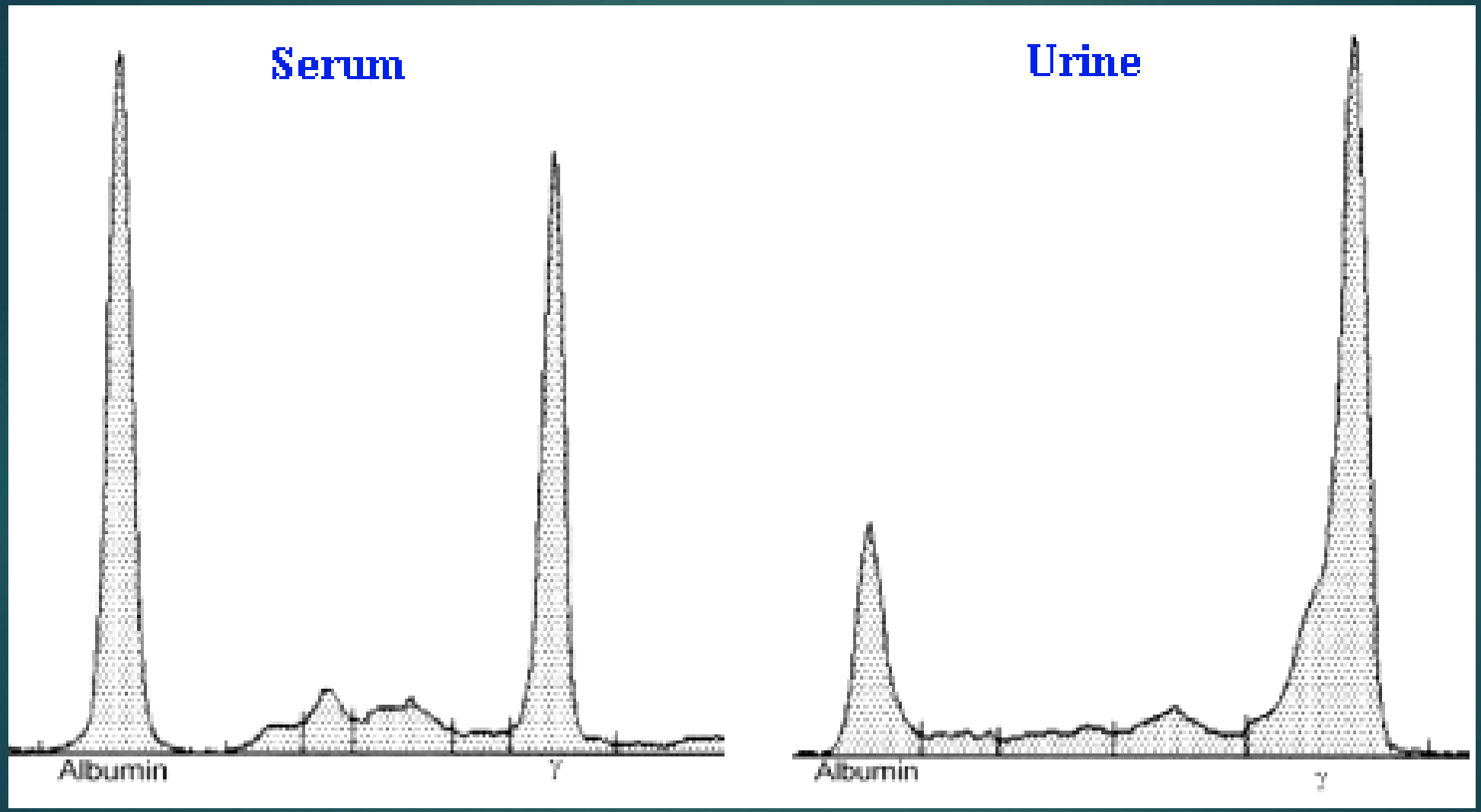
Serum protein electrophoresis

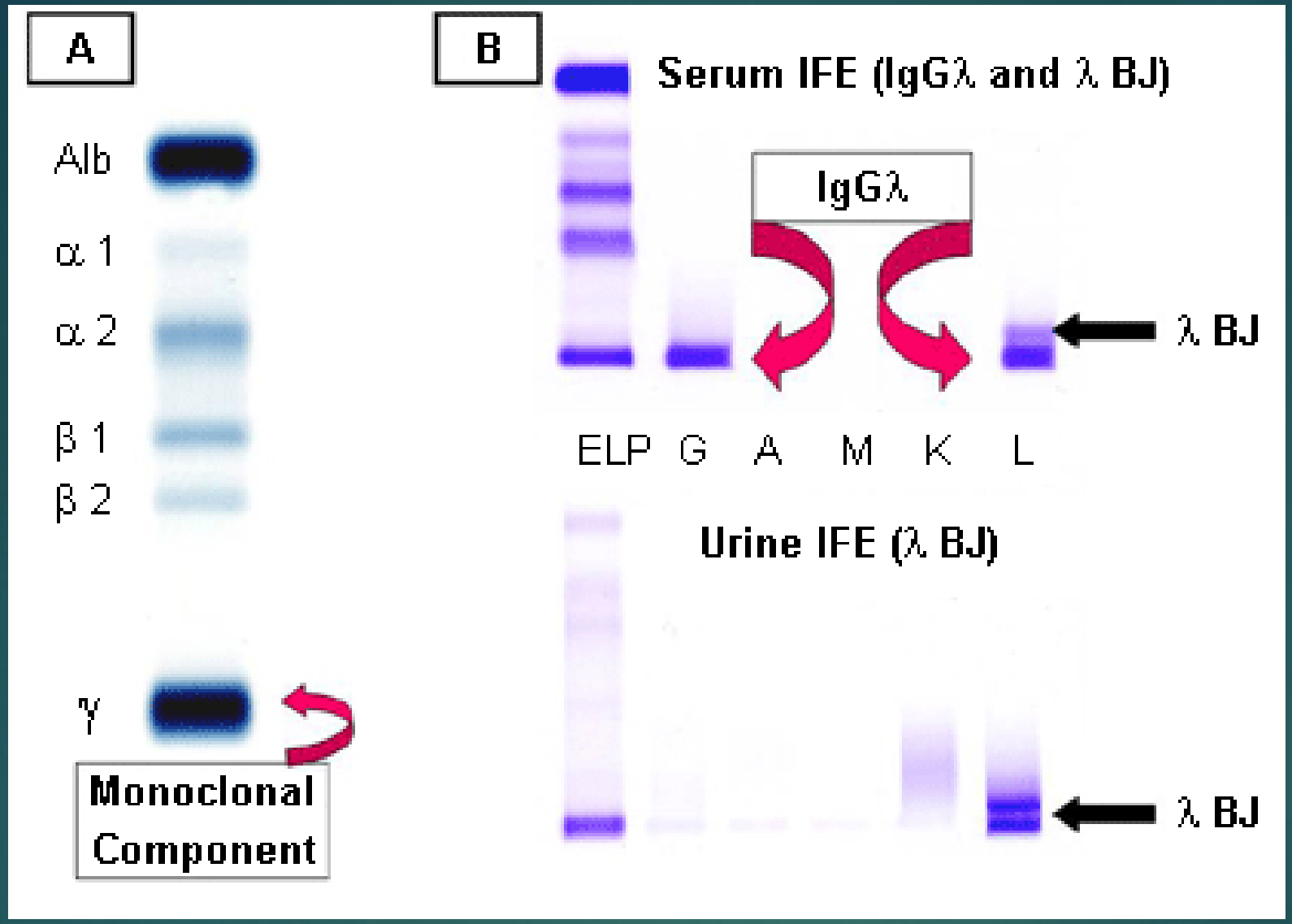


Serum protein electrophoresis



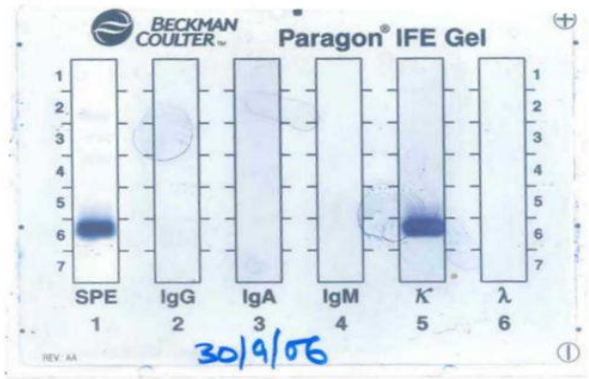
M band
Immune paresis
Reversed A/G

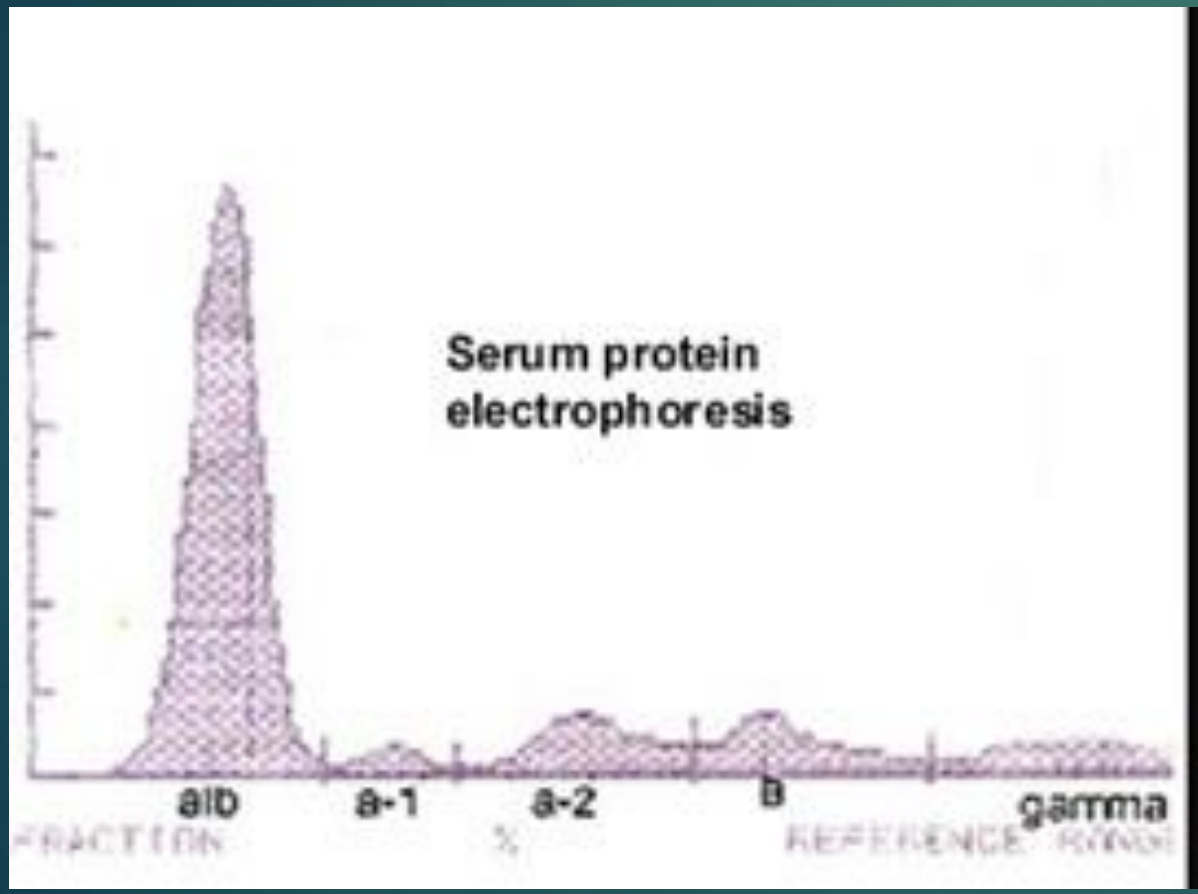

Serum
Albumin
γ
Urine
Albumin
γ

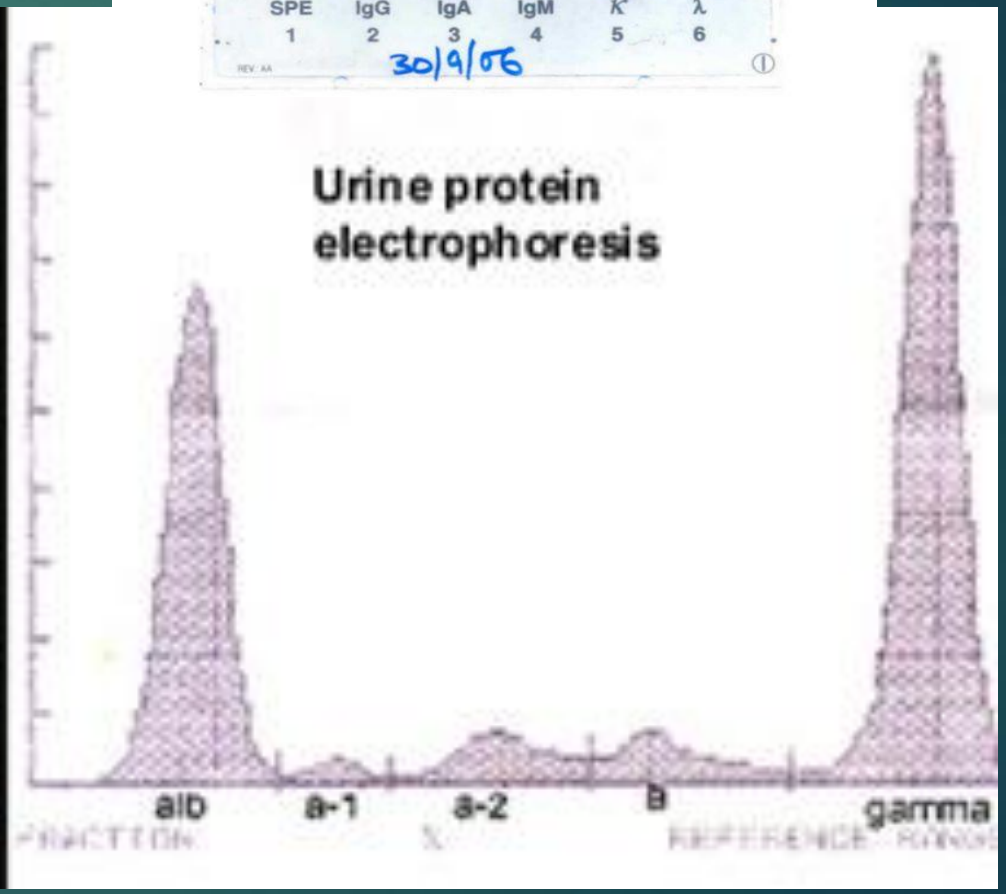


A: serum protein electrophoresis demonstrating the M component.

B: serum and urine immunofixation electrophoresis







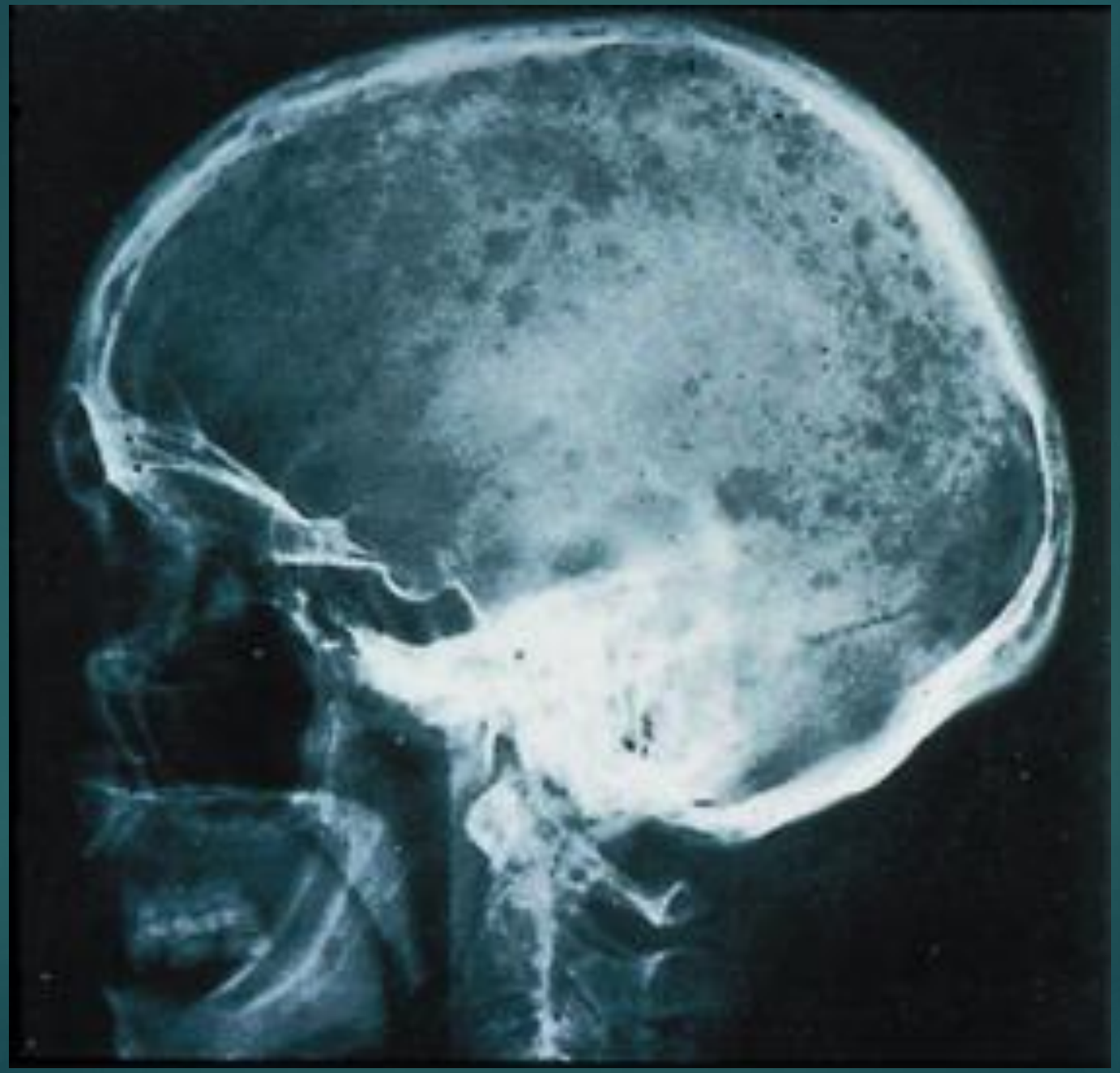
Light chain MM

Effects of paraprotein

- High ESR
- Hyperviscosity
- Renal insufficiency

Other effects due to plasma cell proliferation

- Bone lesions-lytic bone lesions
  - Osteopenia
  - Pathological fractures
- Hypercalcaemia
- Hyperuricaemia

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INVESTIGATION OF PATIENTS WITH SUSPECTED MYELOMA

1. Screening tests
2. Diagnostic tests
3. Tests to establish tumor burden and prognosis
4. Tests which may be useful in some patients

1.SCREENING TESTS

- ESR
- FBC+BP
- Urine BJP
- Serum protein electrophoresis
- Urine protein electrophoresis
- X ray sites of bone pain
- S.creatinine
- S.calcium
- S Uric acid

2.DIAGNOSTIC TESTS

- BM Aspirate
- Radiological skeletal survey
- Serum/Urine protein electrophoresis/SFL assay

3.TESTS TO ESTABLISH TUMOR BURDEN AND PROGNOSIS

S.$\beta_2$microglobulin
S. Albumin
BM Cytogenetics

STAGE	VALUES
Stage 1	$ß_2$M <3.5 mg/dL ALB ≥3.5 g/dL
Stage 2	Not Stage 1 or 3
Stage 3	$ß_2$M >5.5 mg/dL

International Staging System for Symptomatic MM

4.TESTS WHICH MAY BE USEFUL IN SOME PATIENTS

- MRI/CT
- Serum free light chain assay

  -diagnosis and monitoring light chain only myeloma

Diagnostic criteria for MGUS, Asymptomatic myeloma and Symptomatic myeloma

Diagnostic Criteria for Plasma Cell Disorders

Plasma Cell Disorder	Bone Marrow Plasma Cells		Circulating M-Protein	Clinical Manifestations
MGUS	< 10%	and	< 3 g/dL	Absent
SMM	≥ 10%	and/or	≥ 3 g/dL	Absent
MM	≥ 10%	and/or	≥ 3 g/dL	Present[a]

[a] CRAB symptoms (hypercalcemia, renal insufficiency, anemia, lytic bone lesions), recurrent infection
MGUS = monoclonal gammopathy of unknown significance; SMM = smoldering myeloma; MM = multiple myeloma.

Myeloma-related organ or tissue impairment (ROTI)

One or more of the following (**CRAB** criteria):

- **C**alcium elevation (>0.25 mmol/l above NL >2.75 mmol/l or>11mg/dl)
- **R**enal insufficiency (attributable to myeloma Cr>2mg/dl)
- **A**nemia (hemoglobin <10 g/dL or 2 g/dL<normal)
- **B**one disease (lytic lesions or osteopenia with compression fractures)
- Other –Symptomatic hyperviscosity, amyloidosis recurrent bacterial infections

Management

- **Specific**
- Chemotherapy

Thalidomide/lenolidomide.

bortezomib/steroids/Melphalan

- Autologous BM transplantation
- Radiotherapy

- **Supportive**
- BM failure
- Renal disease
- Hypercalcaemia
- Spinal cord compression
- Hyperviscosity
- Bone disease

- Multiple myeloma-Plasma cell neoplasm
- Back pain, anaemia and high ESR
- Increase plasma cells in the BM, Paraprotein,Bone lesions
- Complications- BM failure/renal failure /Hypercalcaemia /hyperviscosity/spinal cord compression

THANK YOU