

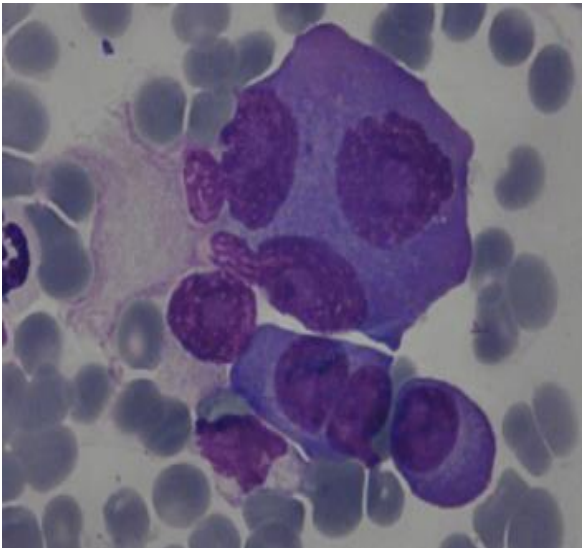
Gambaran, Diagnosis & Penegakkan Diagnosis Multiple Myeloma

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Apa itu Multiple Myeloma ?

MYELOMA

- Sel ganas yang berasal dari sel plasma , berdiferensiasi dari sel B
- Penyakit keganasan sel plasma yang memiliki karakteristik proliferasi klonal dari sel plasma yang ganas di dalam sumsum tulang dengan mikroenvironment, protein monoklonal di dalam darah atau kencing dan berhubungan dengan disfungsi organ



Manifestasi Klinis

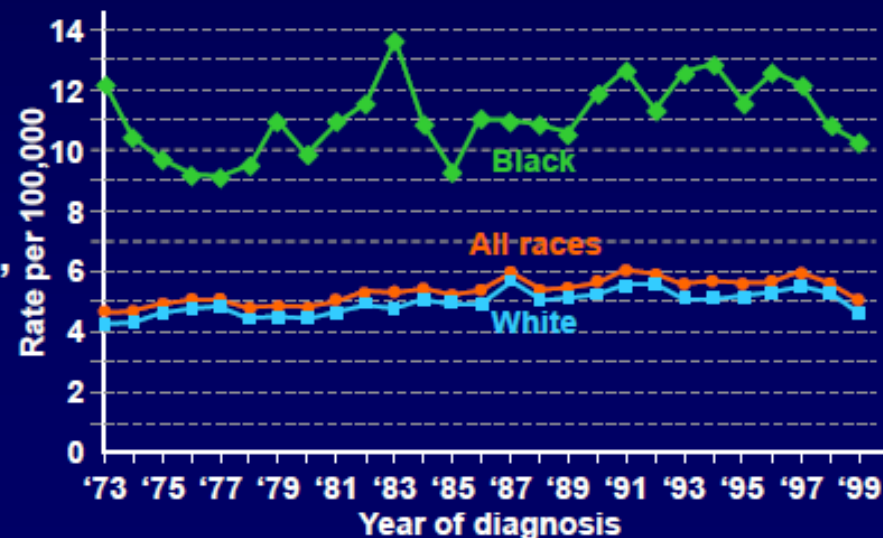
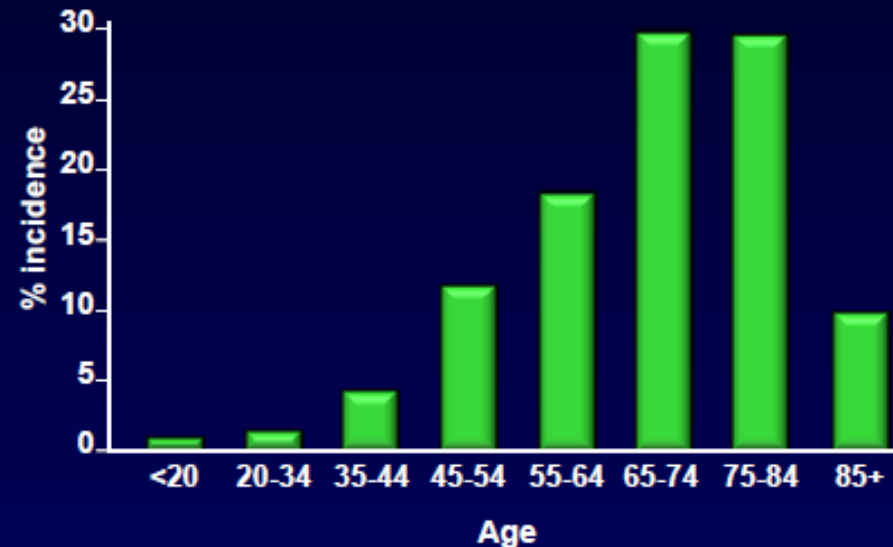
Tidak Spesifik

- Nyeri pada tulang (lesi litik, osteoporosis, vertebral collapse)
- Lemah dan mudah lelah
- Infeksi
- Perdarahan
- Kelainan saraf
- Gangguan Ginjal
- Hiperkalsemia
- Pucat
- Pembesaran Organ
- Nyeri dan bengkak disekitar bagian yang mengalami patah tulang atau plasmositoma
- Kelainan pada kulit

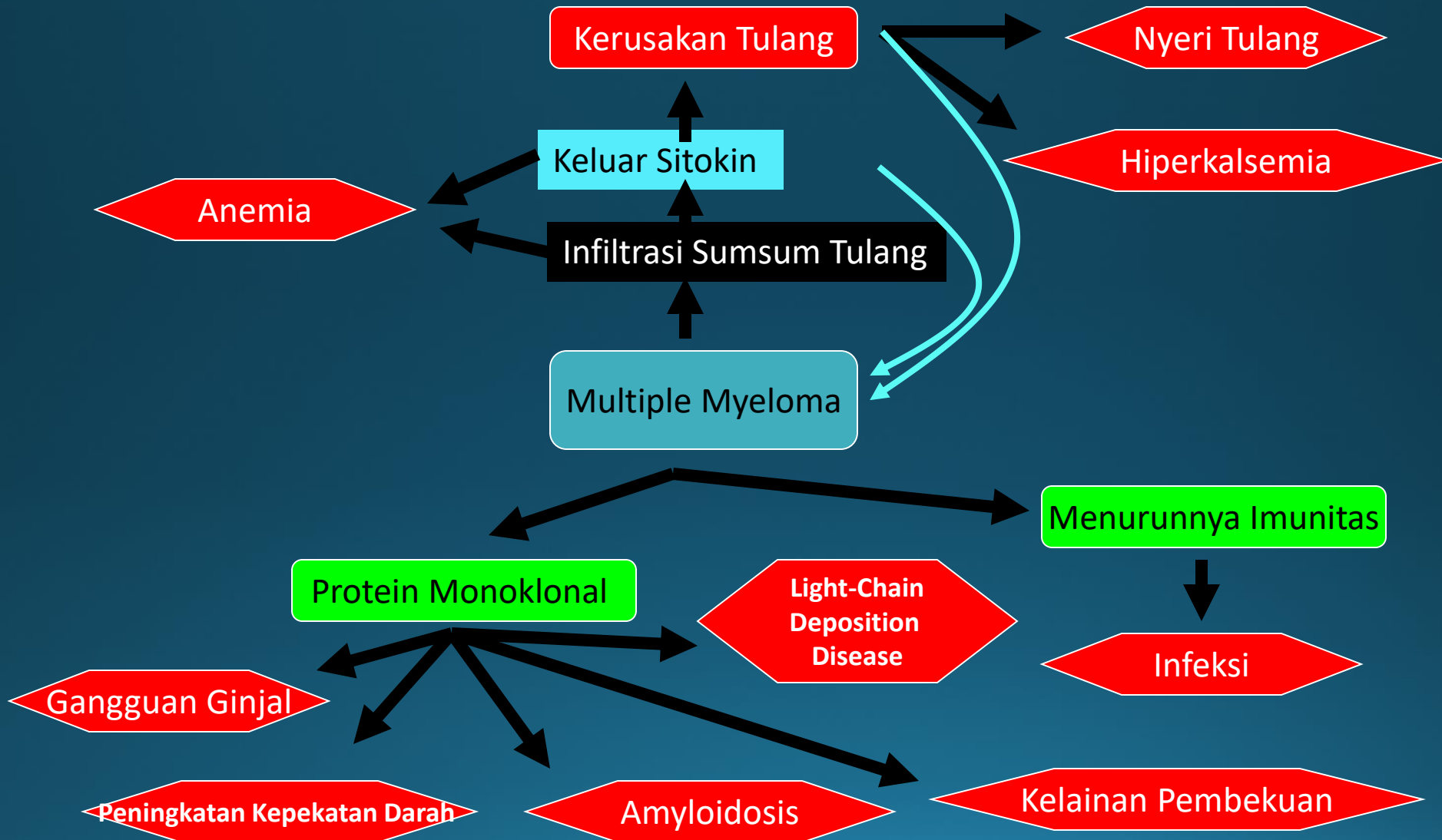


Epidemiologi Multiple Myeloma

- **Approximately 1% of all cancers**
 - second most prevalent hematologic cancer
- **Median age at diagnosis: 71 years**
 - 74 years (community population)
 - 62 years (hospital population)
 - 2% of cases <45 years
- **Risk factors**
 - age
 - male gender
 - African descent
 - occupational exposure to herbicides, insecticides, petroleum products, heavy metals, plastics, asbestos
 - exposure to radiation



Manifestasi Klinis dari Multiple Myeloma



Bagaimana mendeteksi awal Multiple Myeloma ?

Aware CRAB symptoms if present on patient IS CRITICAL

Requires one or more of following CRAB Symptoms :

CRAB



Calcium elevation

Serum Ca > 11.5 mg / dL
or > 2.65 mmol/l



Anemia

HB < 10 g / dl



Renal Disease

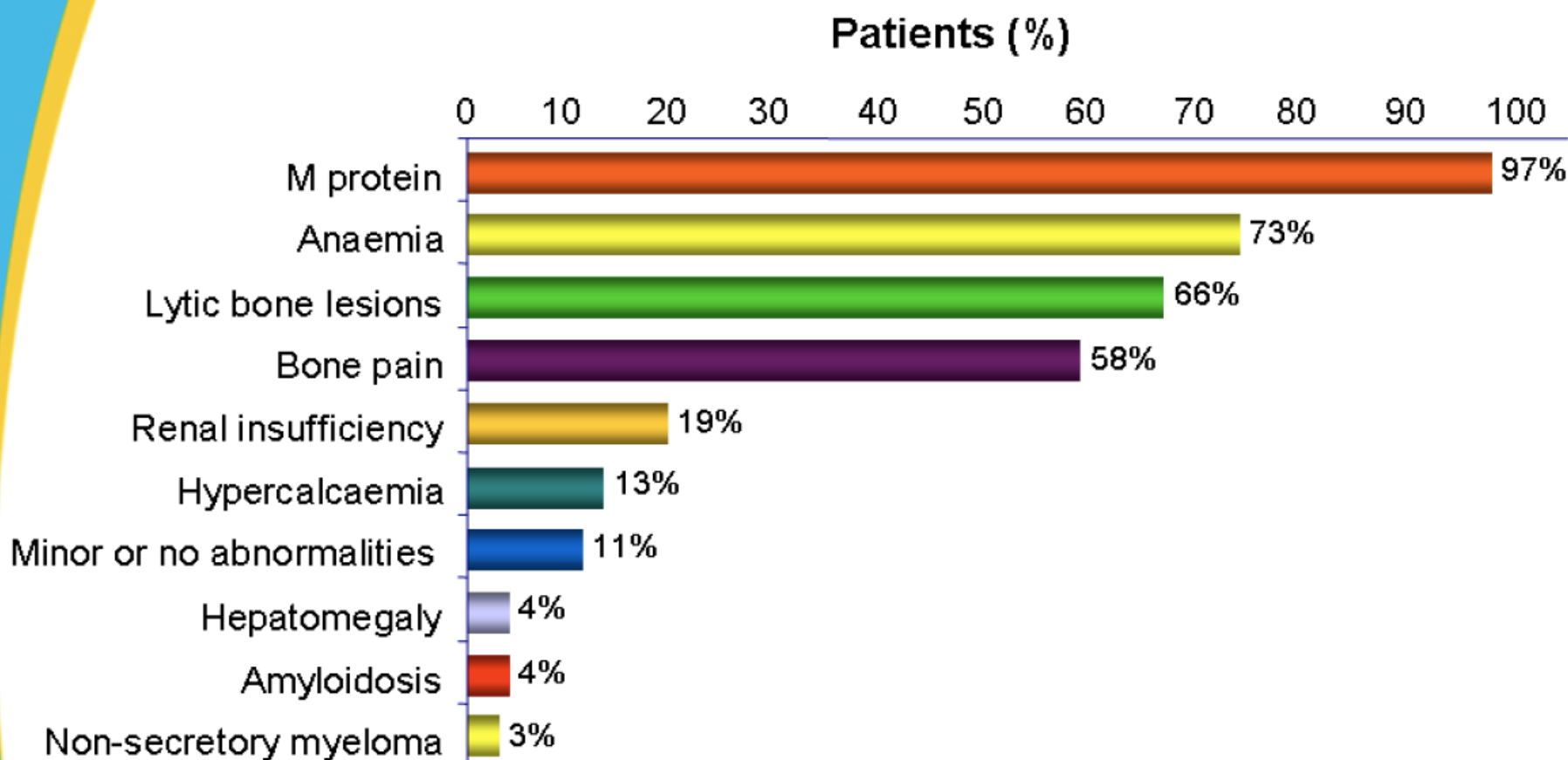
Creatinine > 177 mmol / l
OR Creatine > 2 g / dl



Bone Disease

Lytic lesions or osteoporosis with compression fractures (MRI or CT will clarify)

Pasien dengan Multiple Myeloma berdasar persentase Manifestasi Klinis



Kriteria Diagnosis Multiple Myeloma berdasarkan International Myeloma Working

Panel: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smouldering multiple myeloma

Definition of multiple myeloma

Clonal bone marrow plasma cells $\geq 10\%$ or biopsy-proven bony or extramedullary plasmacytoma* and any one or more of the following myeloma defining events:

- Myeloma defining events:
 - Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
 - Hypercalcaemia: serum calcium >0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (>11 mg/dL)
 - Renal insufficiency: creatinine clearance <40 mL per min† or serum creatinine >177 μ mol/L (>2 mg/dL)
 - Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L
 - Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT‡
 - Any one or more of the following biomarkers of malignancy:
 - Clonal bone marrow plasma cell percentage* $\geq 60\%$
 - Involved:uninvolved serum free light chain ratio§ ≥ 100
 - >1 focal lesions on MRI studies¶

Definition of smouldering multiple myeloma

Both criteria must be met:

- Serum monoclonal protein (IgG or IgA) ≥ 30 g/L or urinary monoclonal protein ≥ 500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%
- Absence of myeloma defining events or amyloidosis

Kelainan Multiple Myeloma berdasarkan International Staging System

STAGE	VALUES
Stage 1	$\beta_2M < 3.5$ mg/dL ALB ≥ 3.5 g/dL
Stage 2	Not Stage 1 or 3
Stage 3	$\beta_2M > 5.5$ mg/dL

β_2M =serum β_2 microglobulin in mg/dL; ALB=serum albumin in g/dL

Evaluasi Pemeriksaan Diagnosis Multiple Myeloma

Test	Finding (s) With Myeloma
CBC with differential counts	↓ Hgb, ↓ WBC, ↓ platelets
Electrolytes	↑ Creat, ↑ Ca+, ↑ Uric acid, ↓ Alb
Serum electrophoresis with quantitative immunoglobulins	↑ M protein in serum, may have ↓ levels of normal antibodies
Immunofixation	Identifies light/heavy chain types M protein
β ₂ -microglobulin	↑ Levels (measure of tumor burden)
24-hour urine protein electrophoresis	↑ Monoclonal protein (<i>Bence Jones</i>)
Bone marrow biopsy	≥ 10% plasma cells
Skeletal imaging	Osteolytic lesions, osteoporosis
Serum free light chain	↑ Free light chains
MRI	Evaluation of involvement of disease

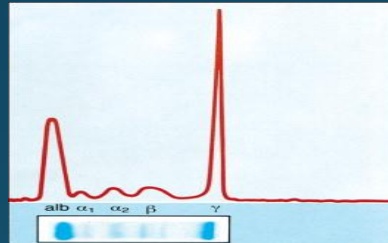
Alb = albumin; CBC = complete blood count; Creat = creatinine; Hgb = hemoglobin; MRI = magnetic resonance imaging; WBC = white blood cell.

Multiple Myeloma

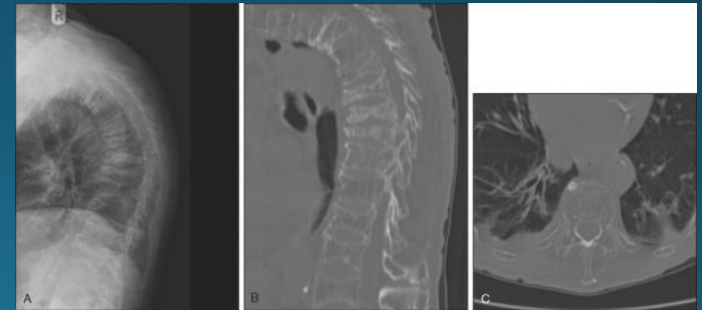
Sel Plasma Klonal
di Sumsum Tulang



M-Protein pada
Darah / Air Seni



(Kelainan Organ/
Jaringan) CRAB



Biomarker sebagai penunjang diagnosis Multiple Myeloma

	2-year probability of progression
High levels of circulating plasma cells	80% ⁹³
Abnormal plasma cell immunophenotype $\geq 95\%$ plus immunoparesis	50% ^{28,38,94,95}
Evolution of smouldering multiple myeloma*	65% ⁹⁶
Cytogenetic subtypes: t (4;14), 1q amp, or del 17p	50% ^{97,98}
High bone marrow plasma cell proliferative rate	80% ⁹⁹
Unexplained decrease in creatinine clearance by $\geq 25\%$ accompanied by a rise in urinary monoclonal protein or serum free light-chain concentrations	Not known

*Increase in serum monoclonal protein by $\geq 10\%$ on each of two successive evaluations within a 6-month period.

Table 2: Potential future biomarkers for diagnosis of multiple myeloma

Waktu yang digunakan untuk menegakkan diagnosis Multiple Myeloma

Journey to diagnosis

Munculnya keluhan

- Sendi / Tulang / Nyeri Dada / Lelah

→ *Uncertainty*

Periksa ke Dokter Umum

- Keluhan yang muncul dengan penyakit lain
- Pemeriksaan penunjang dasar

→ *Anxiety, concern*

Rujuk Dokter Spesialis

- Merujuk ke spesialis sesuai dengan keluhan yang berkaitan; Orthopaedics, Rheumatology, Nephrology

→ *Confused*
Confident, looked after

Rujuk Konsultan Hemato-Onko

- Diagnosis tetap belum dapat ditegakkan
- Pemeriksaan untuk menegakkan diagnosis
- Pemeriksaan untuk mengkonfirmasi diagnosis dan memberitahukan kepada pasien kemungkinan diagnosis

→ *Khawatir, confused, fear,*
Tidak percaya

Diagnosis

- Pemberitahuan Diagnosis Pasti

→ *Shocked, scared, devastated*
Hope

Oncologists concur with patients that diagnosis is too long but try not to place blame on colleagues as symptoms often hard to distinguish



Improvement / opportunity:
To raise awareness of MM in the referring physicians mind to ensure they think about it / suspect it earlier when considering cause of symptoms

Take Home Messages

- MM membutuhkan kolaborasi dari beberapa dokter
- Pendidikan Kedokteran Berkelanjutan dan kolaborasi antar dokter dibutuhkan untuk menghasilkan hasil terapi yang diinginkan
- Membutuhkan kesadaran dalam diri terkait dengan gejala Multiple Myeloma
- Untuk meningkatkan hasil terapi yang maksimal, pikirkan Multiple Myeloma apabila tidak sesuai dengan Diagnosis Banding yang lain



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