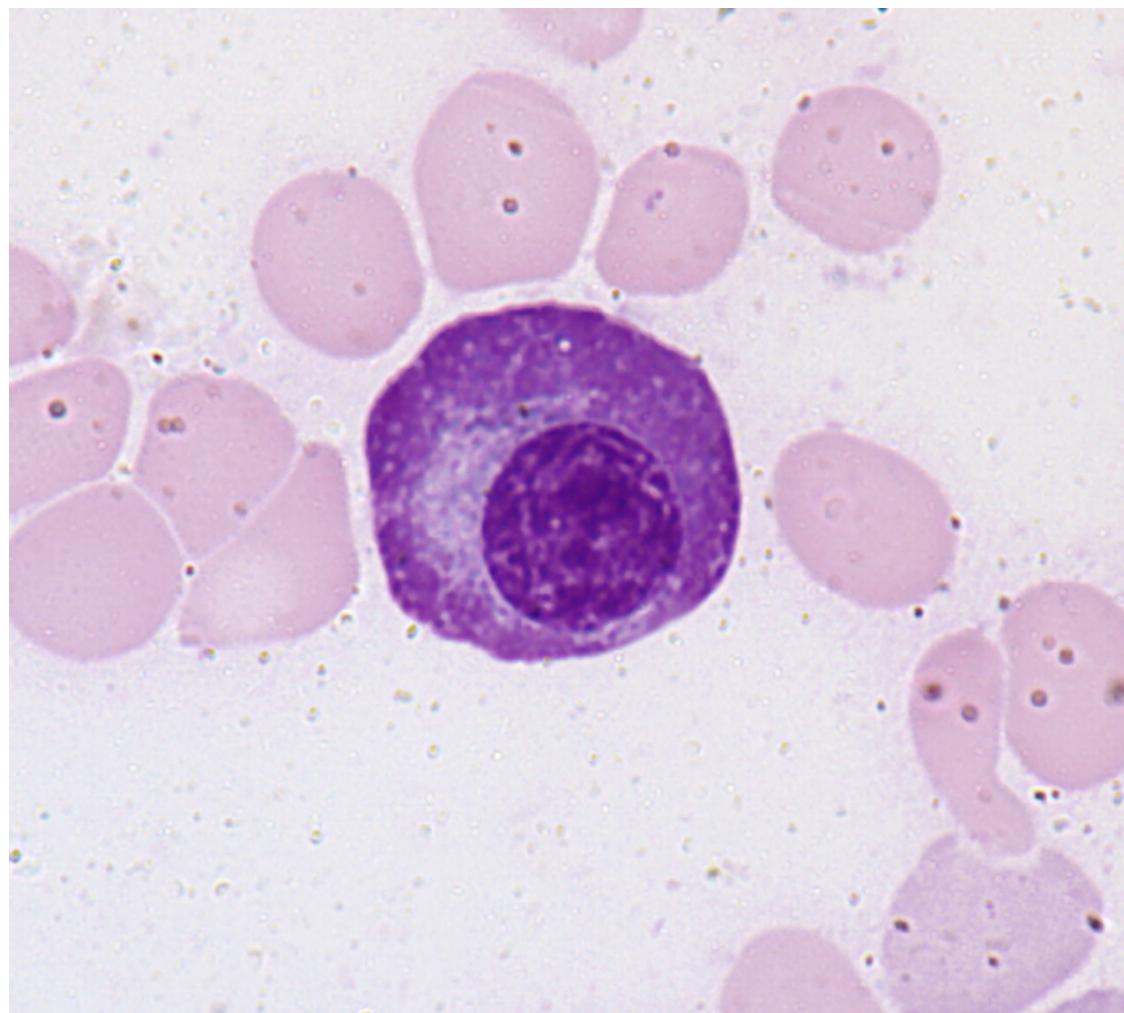


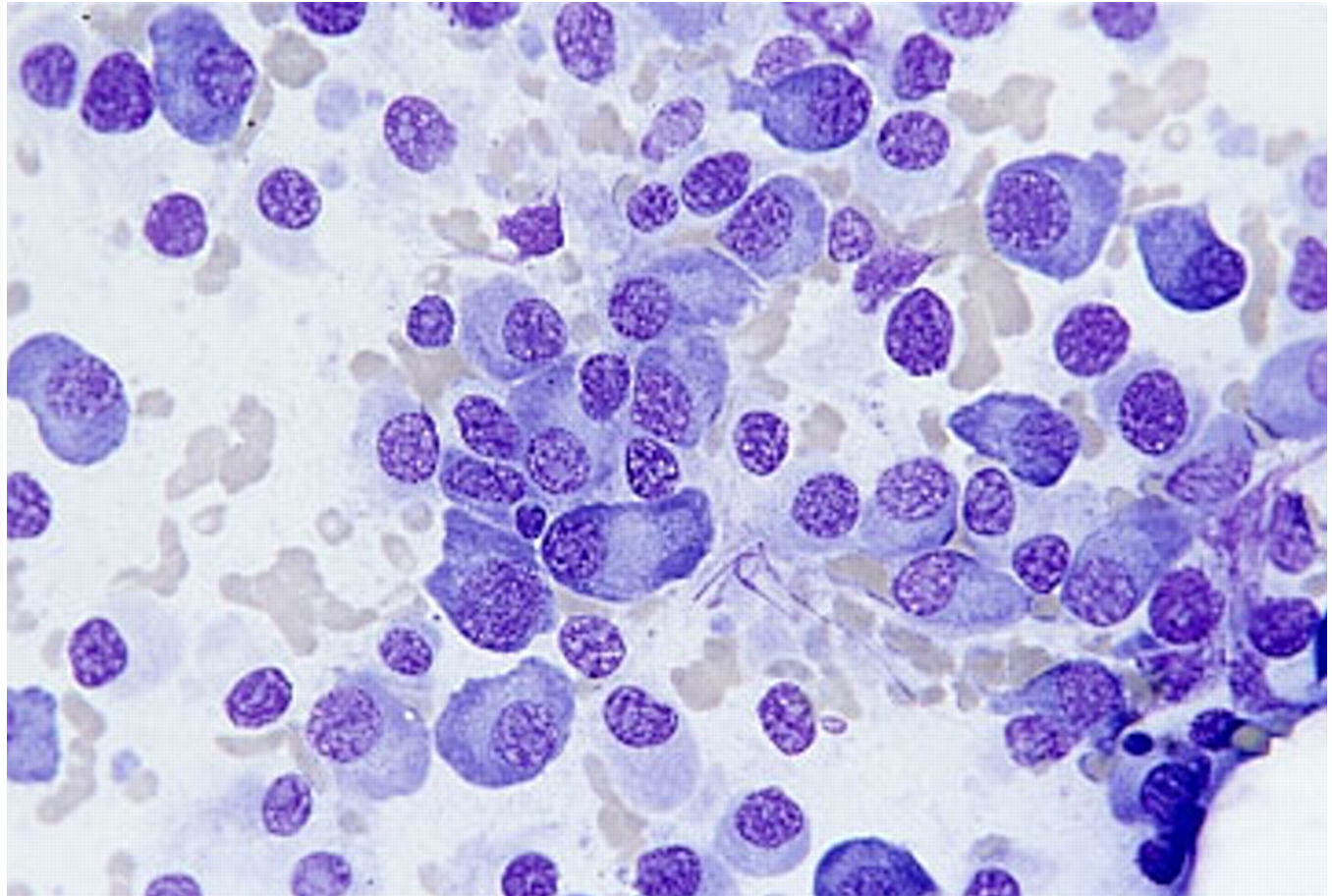
Flame cell - 1.



Peter Maslak, ASH Image Bank 2011; 2011-4174



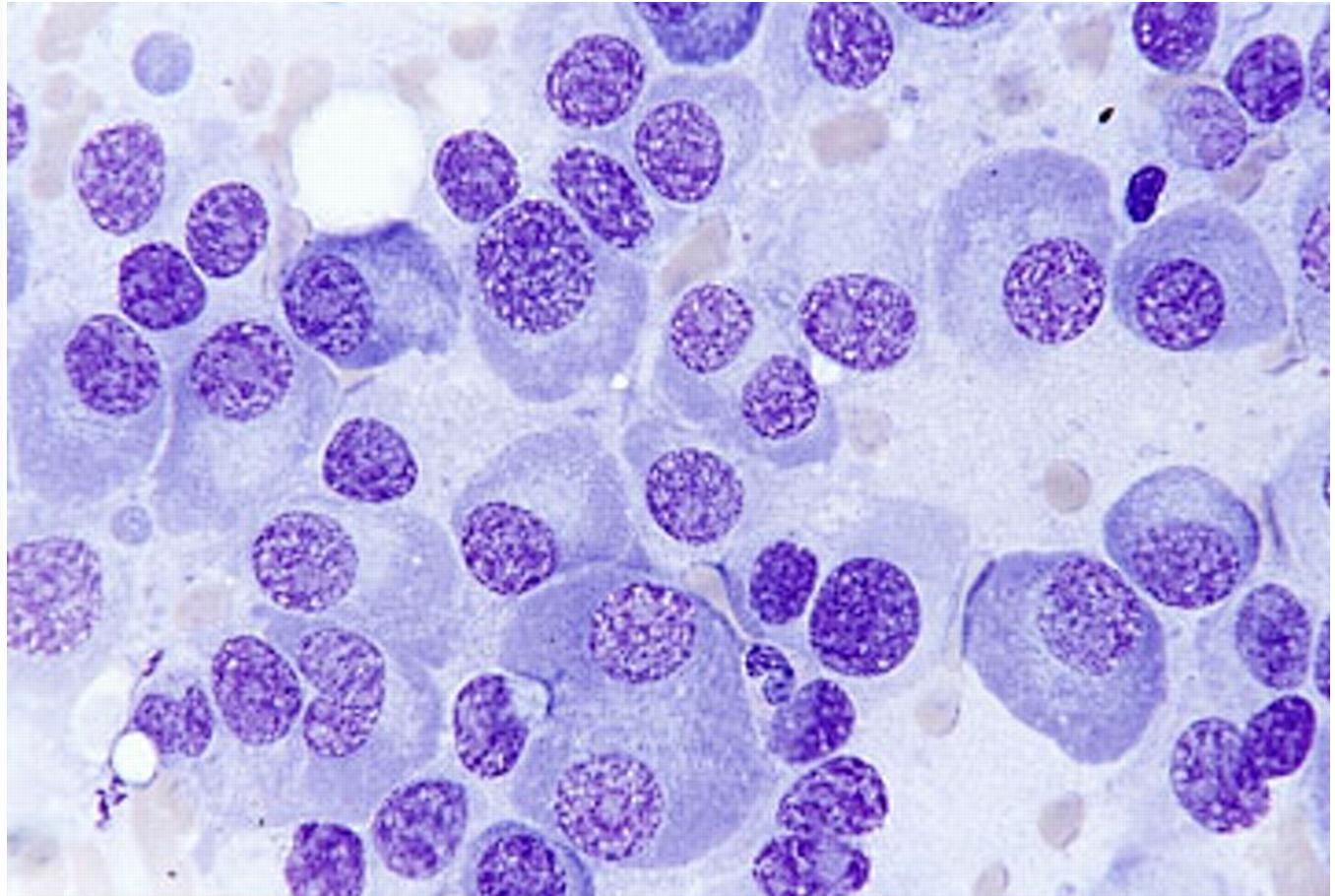
Multiple Myeloma - 1.



Stanely Schrier, ASH Image Bank 2011; 2011-1814

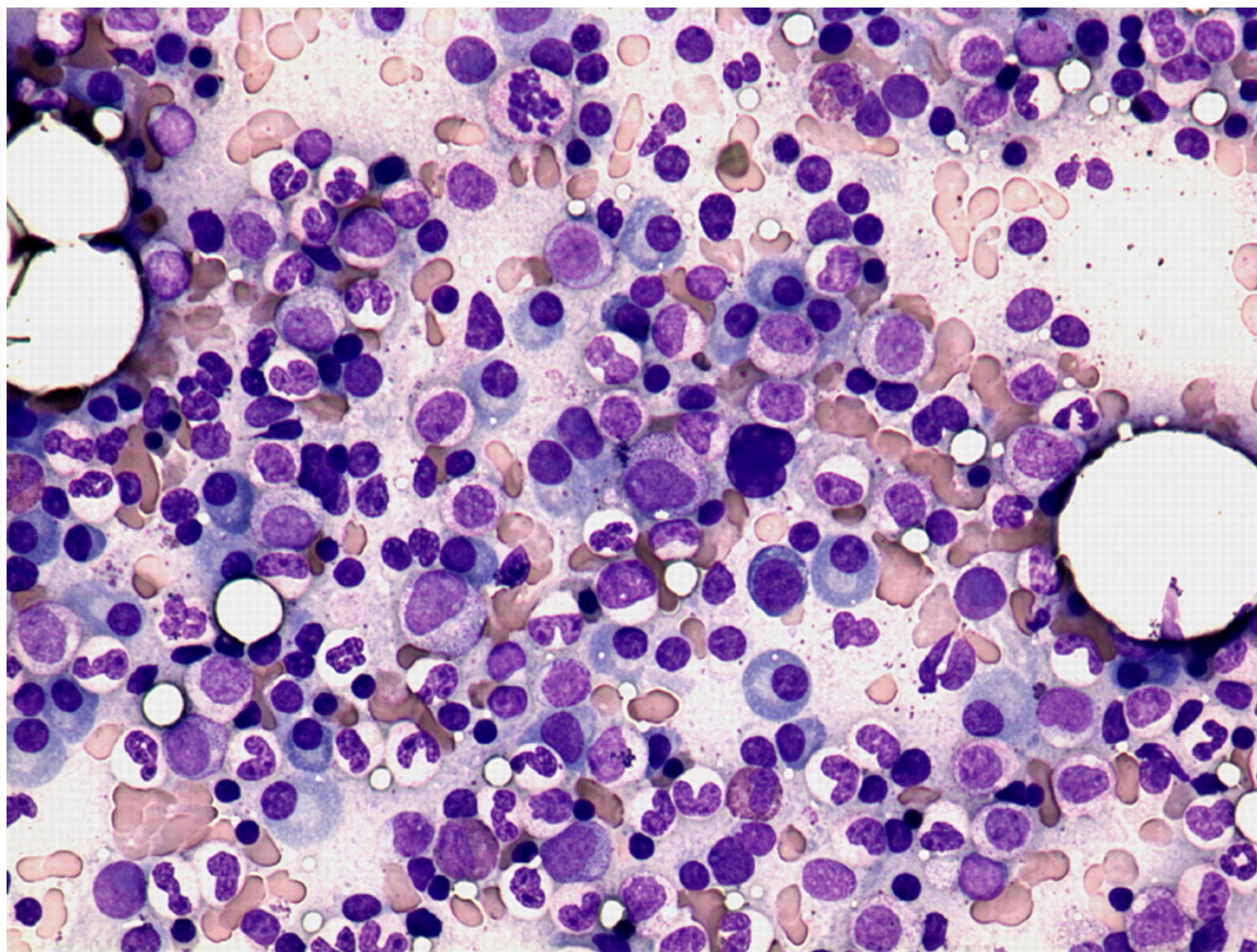


Multiple Myeloma - 2.



Stanely Schrier, ASH Image Bank 2011; 2011-1815

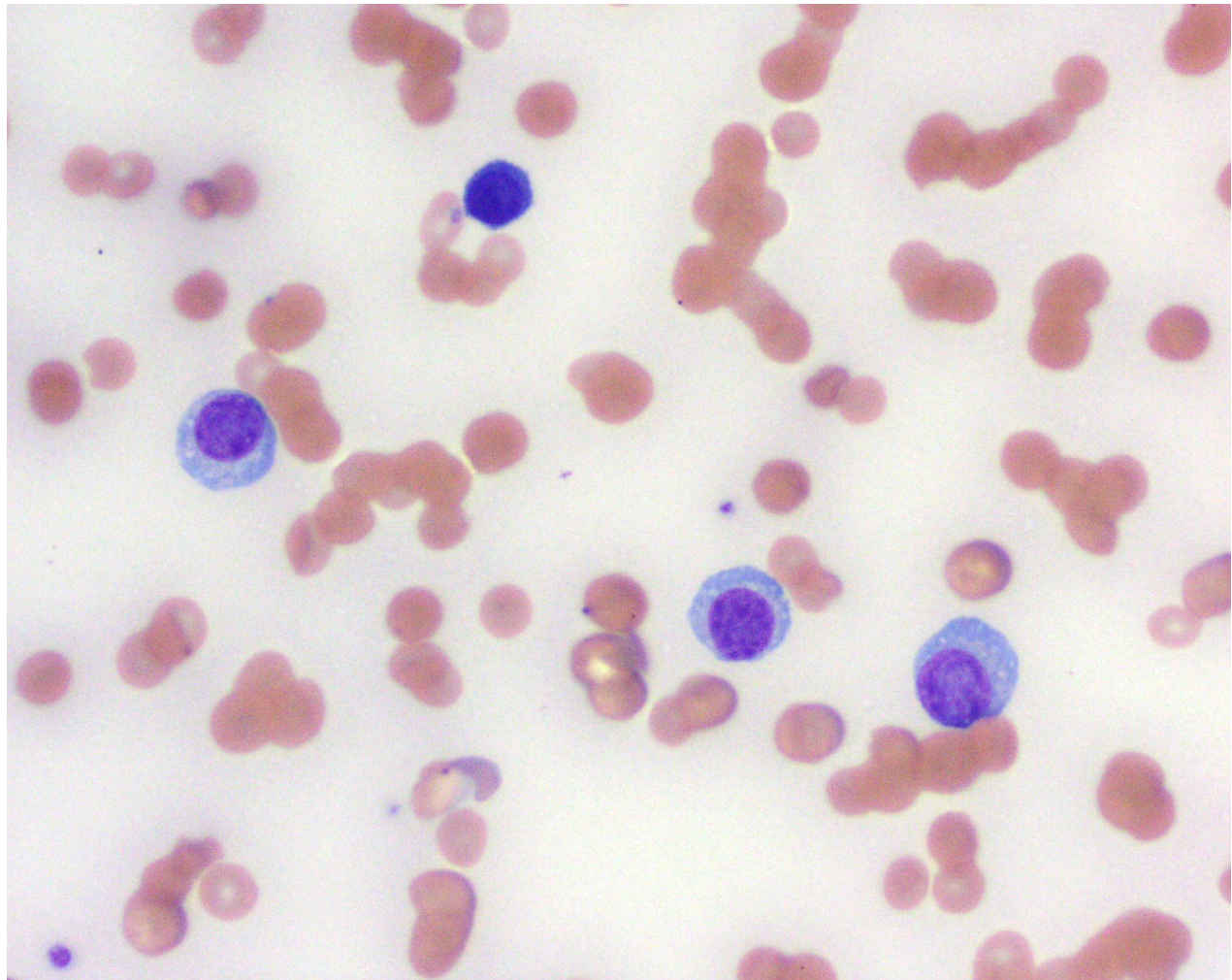
Relapsed multiple myeloma - 1.



Peter Maslak, ASH Image Bank 2013; 2013-3990

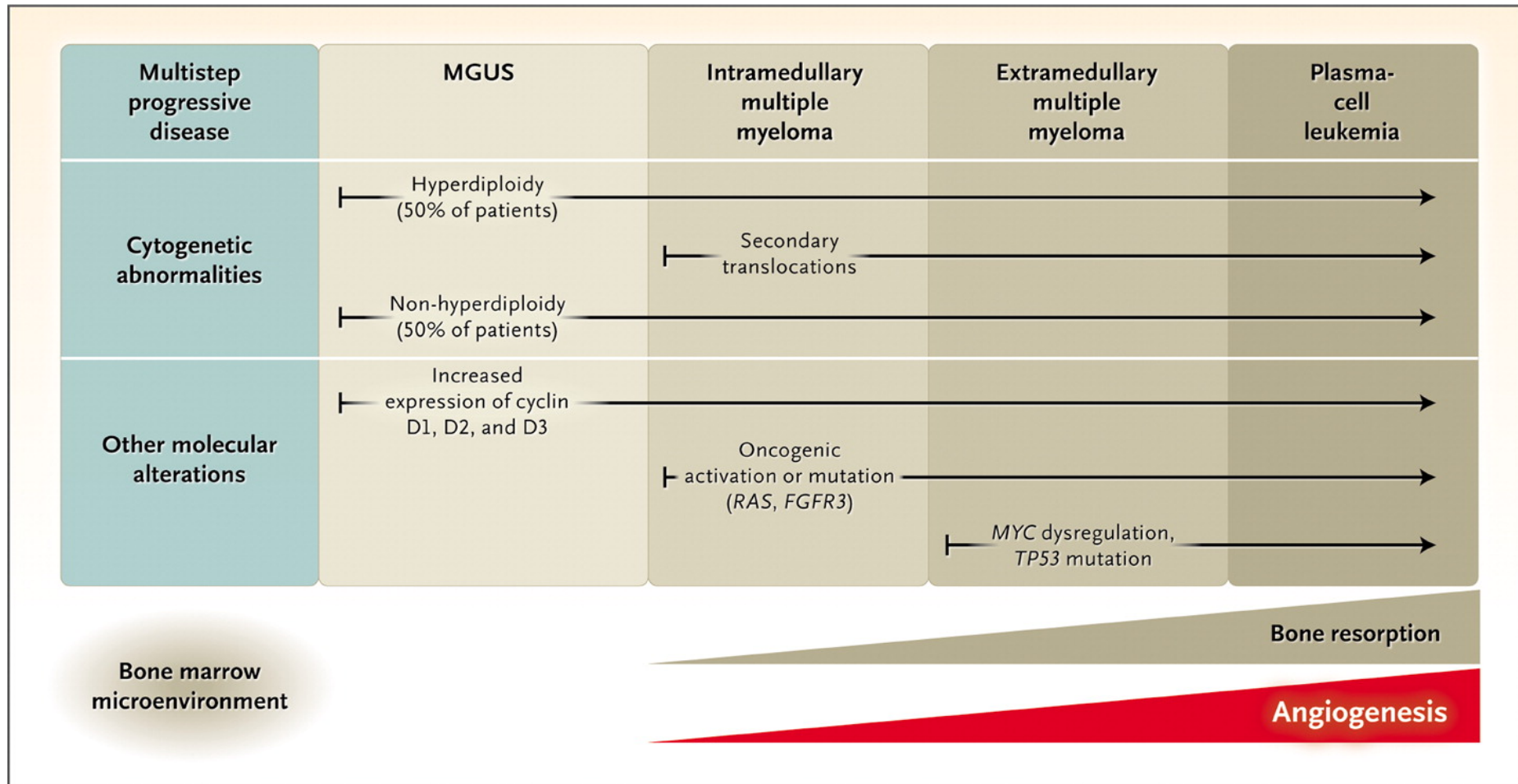


Leukemic phase of multiple myeloma - 2.



John Lazarchick, ASH Image Bank 2011; 2011-4095

Multistep pathogenesis of multiple myeloma



Cellular interactions in marrow in multiple myeloma

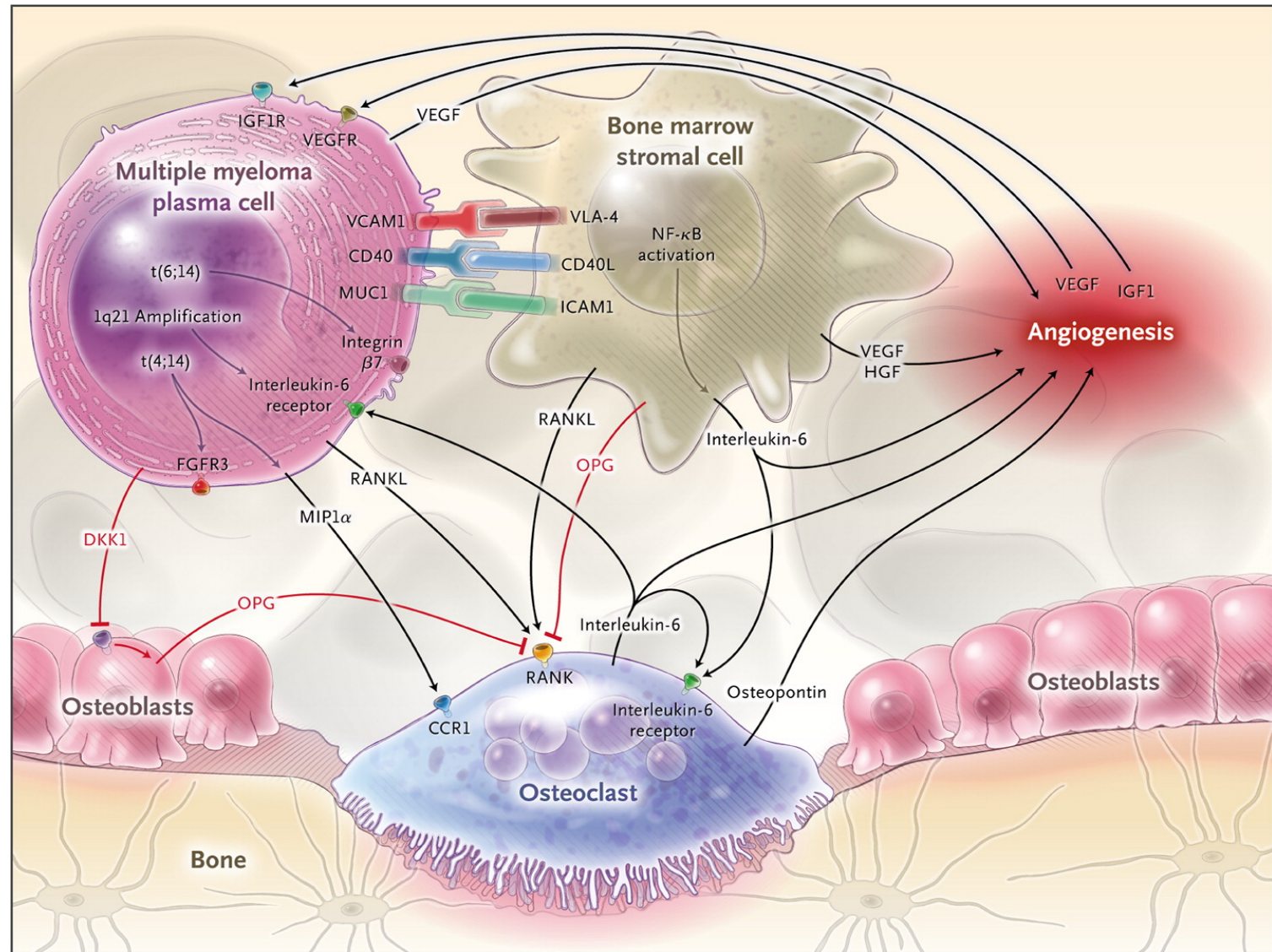


Table 1. Diagnostic Criteria, Diagnostic Evaluation, and Staging System for Multiple Myeloma.

Diagnostic criteria

Diagnosis of myeloma

- At least 10% clonal bone marrow plasma cells
- Serum or urinary monoclonal protein

Myeloma-related organ dysfunction (CRAB criteria)

- Hypercalcemia (serum calcium >11.5 mg/dl [2.88 mmol/liter])
- Renal insufficiency (serum creatinine >2 mg/dl [177 μ mol/liter])
- Anemia (hemoglobin <10 g/dl or >2 g/dl below the lower limit of the normal range)
- Bone disease (lytic lesions, severe osteopenia, or pathologic fracture)

Diagnostic evaluation

Diagnosis

- Medical history and physical examination
- Routine testing: complete blood count, chemical analysis with calcium and creatinine, serum and urine protein electrophoresis with immunofixation, quantification of serum and urine monoclonal protein, measurement of free light chains
- Bone marrow testing: trephine biopsy and aspirate of bone-marrow cells for morphologic features; cytogenetic analysis and fluorescence in situ hybridization for chromosomal abnormalities
- Imaging: skeletal survey, magnetic resonance imaging if skeletal survey is negative

Prognosis

- Routine testing: serum albumin, β_2 -microglobulin, lactate dehydrogenase

Staging

International Staging System

- Stage I: serum β_2 -microglobulin <3.5 mg/liter, serum albumin \geq 3.5 g/dl
- Stage II: serum β_2 -microglobulin, <3.5mg/liter plus serum albumin <3.5 g/dl; or serum β_2 -microglobulin 3.5 to <5.5 mg/liter regardless of serum albumin level
- Stage III: serum β_2 -microglobulin \geq 5.5 mg/liter

Chromosomal abnormalities

- High-risk: presence of t(4;14) or deletion 17p13 detected by fluorescence in situ hybridization
- Standard-risk: t(11;14) detected by fluorescence in situ hybridization

Table 2. Commonly Used Therapy Regimens in Newly Diagnosed Multiple Myeloma.

Regimen	Schedule	Complete Response Rate after Induction %	Progression-free Survival	Overall Survival	Serious Toxic Effects Occurring in ≥10% of Patients
Bortezomib–dexamethasone	Bortezomib: 1.3 mg/m ² given as bolus intravenous infusion on days 1, 4, 8, 11 every 3 wk for a total of 4–8 cycles; dexamethasone: 40 mg/day given orally on days 1–4 and 9–12 every 3 wk for a total of 4–8 cycles ⁵³	21*	Median, 36 mo	At 3 yr, 81%	Infection (10%)
Bortezomib–dexamethasone–cyclophosphamide	Bortezomib: 1.3 mg/m ² given as bolus intravenous infusion on days 1, 4, 8, 11 every 4 wk for a total of 4–12 cycles; dexamethasone: 40 mg/day given orally on days 1–4, 9–12, and 17–20 or on days 1, 2, 4, 5, 8, 9, 11, 12 every 4 wk for a total of 4–12 cycles; cyclophosphamide: 300 mg/m ² given orally on days 1, 8, 15, 22 every 4 wk for a total of 4–12 cycles ⁵⁶	46*	Not reported	Not reported	Thrombocytopenia (25%), neutropenia (13%), anemia (12%), hyperglycemia (13%)
Bortezomib–dexamethasone–lenalidomide	Bortezomib: 1.3 mg/m ² given as bolus intravenous infusion on days 1, 4, 8, 11 every 3 wk for a total of 4–8 cycles; dexamethasone: 20 mg/day given orally on days 1, 2, 4, 5, 8, 9, 11, 12 every 3 wk for a total of 4–8 cycles; lenalidomide: 25 mg/day given orally on days 1–14 every 3 wk for a total of 4–8 cycles ⁵⁸	29	At 18 mo, 75%	At 18 mo, 97%	Lymphopenia (14%)
Lenalidomide–dexamethasone	Lenalidomide: 25 mg/day given orally on days 1–21 every 4 wk for a total of 4 cycles or until progression or intolerance; dexamethasone: 40 mg/day given orally on days 1, 8, 15, 22 every 4 wk for a total of 4 cycles or until progression or intolerance ⁵⁴	24†	Median, 25 mo	At 1 yr, 96%	Neutropenia (20%), deep-vein thrombosis (12%)
Melphalan–prednisone–thalidomide	Melphalan: 0.15 mg/kg given orally on days 1–7 every 4 wk for a total of 6 cycles ⁶⁶ or 0.25 mg/kg on days 1–4 every 6 wk for a total of 12 cycles ⁶⁷ ; prednisone: 1.5 mg/kg given orally on days 1–7 every 4 wk for a total of 6 cycles ⁶⁶ or 2 mg/kg on days 1–4 every 6 wk for a total of 12 cycles ⁶⁷ ; thalidomide: 100 mg/day given orally continuously until progression or intolerance ⁶⁶ or 200 mg/day continuously for a total of 12 cycles of 6 wk ⁶⁷	13–16	Median, 22–28 mo	Median, 45–52 mo	Neutropenia (16–50%), deep-vein thrombosis (12%), peripheral neuropathy (6–10%), infection (10–13%)
Melphalan–prednisone–bortezomib	Melphalan: 9 mg/m ² given orally on days 1–4 every 5–6 wk for a total of 9 cycles ^{73,76} ; prednisone: 60 mg/m ² given orally on days 1–4 every 5–6 wk for a total of 9 cycles ^{73,76} ; bortezomib: 1.3 mg/m ² given as bolus intravenous infusion on days 1, 4, 8, 11, 22, 25, 29, 32 (cycles 1–4) and on days 1, 8, 22, 29 (cycles 5–9) every 6 wk for a total of 9 cycles ⁷³ or 1.3 mg/m ² on days 1, 8, 15, 22 every 5 wk for a total of 9 cycles ⁷⁶	24–30	Median, 22–27 mo	At 2 yr, 85–87%	Neutropenia (28–40%), thrombocytopenia (20–37%), anemia (10–19%), peripheral sensory neuropathy (5–14%)
Melphalan–prednisone–lenalidomide	Melphalan: 0.18 mg/kg given orally on days 1–4 every 4 wk for a total of 9 cycles; prednisone: 2 mg/kg given orally on days 1–4 every 4 wk for a total of 9 cycles; lenalidomide: 10 mg/day given orally on days 1–21 every 4 wk for a total of 9 cycles; by the 10th cycle, maintenance with lenalidomide at 10 mg/day on days 1–21 every 4 wk until progression or intolerance ⁴⁷	16	At 2 yr, 55%	At 2 yr, 82%	Neutropenia (71%), anemia (24%), thrombocytopenia (38%), infection (10%)

* In these trials, the response is reported as immunofixation-negative complete response plus immunofixation-positive complete response.

† In this trial, the response is reported as immunofixation-negative complete response plus very good partial response.

