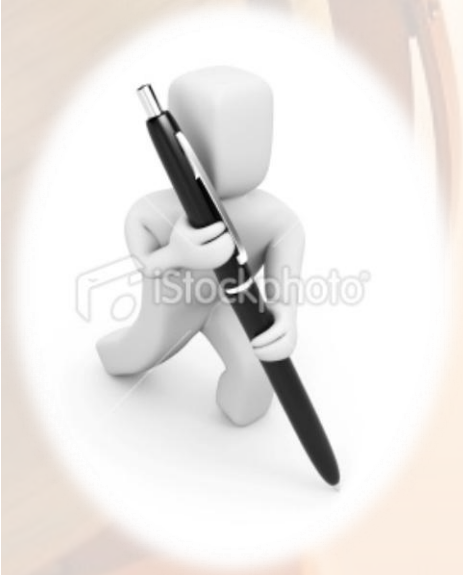
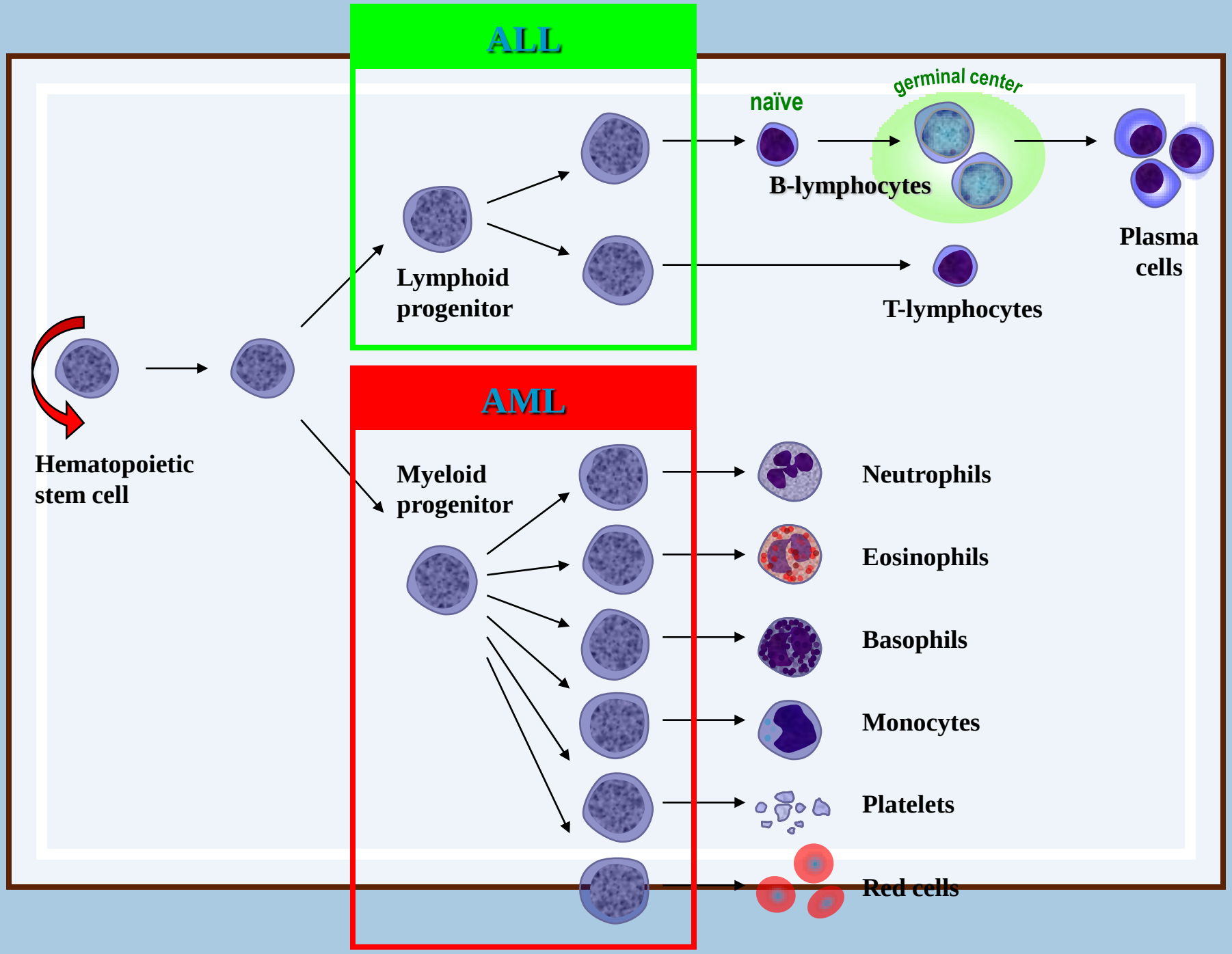
In the Name of God

"Hematologic Malignancies"

Definition & Classification



- Arising from hematopoietic cells & lymphoid tissues
- Myeloid: granulocytes, monocytes, erythrocytes, platelets
- Lymphoid: B & T lymphocytes


ALL
germinal center
naïve
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
AML
Myeloid progenitor
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells

Classification

- Leukemia
- Lymphoma
- Plasma Cell Disorders

- Uncommon < 10% of all cancers
- Chemotherapy
- Surgery and/or radiation is not used
- Growth rate; Rapid

Leukemia

- Myeloid or lymphocytic
- Acute (immature) or chronic (mature)

Acute Myeloid Leukemia (AML) Adults	Acute lymphocytic Leukemia (ALL) Children
Appear suddenly; progress rapidly	Death due to infection or bleeding within weeks to months

Classification of acute leukemias

ALL

- mainly children
- M > F
- curable in 70% of children
- curable in minority of adults

AML

- mainly adults
- M > F
- curable in minority of adults

Leukemia

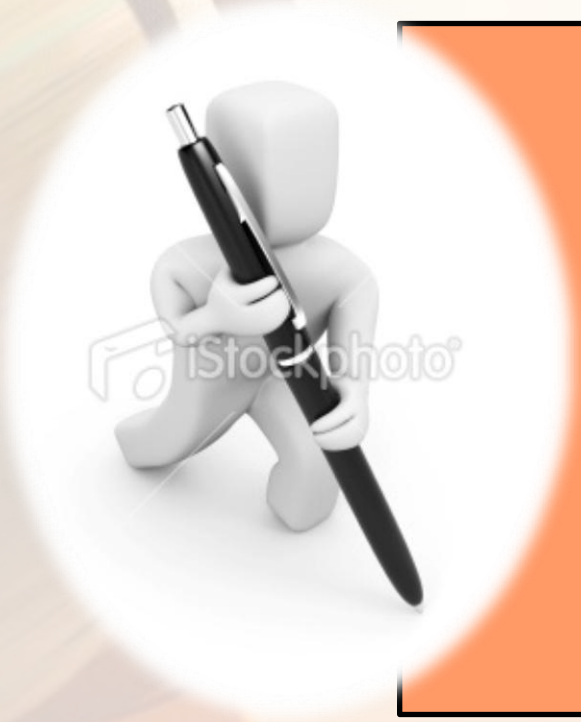
CLL	• Chronic Lymphocytic Leukemia
CML	• Chronic Myeloid Leukemia
Survive for Years	• Curable in only a fraction

Lymphoma

- Two major types
- Hodgkin disease (HD)
- Non- Hodgkin Lymphoma (NHL)
- NHL seven times more than HD

Plasma Cell Disorders

- Antibody-secreting B cells
- Most common form;
  - ❖ Multiple Myeloma (IgG & IgA)
  - ❖ Waldenstorm Macroglobulinemia (IgM)



Leukemia

Acute Myeloid Leukemia

1
- Signs & Symptoms; Increasing fatigue, fever, anemia, ↓plt

2
- Poor prognostic signs; Age>60 yo, pre-existing hematologic disorder, prior exposure to chemotherapy, poor baseline performance

3
- FAB Classification System; French-American-British M_0-M_7

4
- ↑WBC; Incapable of fighting infection; stroke, blindness, headache

Treatment

- *First decrease WBC count;*
  - Hydroxyurea 2-4 g Po or Leukapheresis
  - 7+3; idarubicin on days 1-3 + cytarabine on days 1-7
- *Exception;* AML-M3: ATRA or tretinoin starting 2 days before
- *ATRA ADR;* Retinoic acid syndrome (RAS); fever, weight gain, respiratory distress, lung infiltrates, pleural effusion, hypotension, ARF
- Dexa 10 mg BD for 3d

Treatment

- *Other ADRs of ATRA;* dryness of mouth/skin, hair loss, skin rash, conjunctivitis, muscle weakness, depression, elevated liver enzymes, high cholesterol *but patients may alive for 3-5 years*

- *Arsenic trioxide (ATO);* QT prolongation, RAS, N/V, rash, hypokalemia, hyperglycemia

Complication

- Tumor Lysis Syndrome (TLS);
  - Hyperuricemia, hyperphosphatemia, hypocalcemia, uremia => arrhythmia & ARF
- *Allopurinol;* before chemotherapy 300-600 mg/d
- *Rasburicase;* catalyst in enzymatic oxidation of uric acid to allantoin - effect within 4 hours; expensive

Complications

- Myelosuppression;
  - Filgrastim
  - Sargramostim esp. in older > 55 yo
- Thrombocytopenia;
  - ❖ Plt < 10000/mm3 ; tranfusion
  - ❖ premenopause; ocp or medroxyprogestrone 10-20 mg/d

Postremission Therapy

- High-Dose Cytarabine, low dose in elderly
  - Cerebellar
  - Ocular (artificial tears, corticosteroid eye drops in case of conjunctivitis)
  - Dermatologic Toxicity

Refractory or resistant AML

- Gemtuzumab; anti CD33 antibody

CML (Chronic Myeloid Leukemia)

- Signs & Symptoms; 30-40% asymptomatic, splenomegaly
- Initial treatment; Reduce WBC; Hydroxyurea to WBC <20000/mm^3
- Curative therapy; Allogeneic HCT; best result in young patients within 1 year of diagnosis
- Complete response; WBC<10000/mm3 and Plt<450000/mm^3

Treatment

- Imatinib mesylate (Gleevec); max 400 mg BD
- Most common toxicities; superficial edema, nausea, muscle cramps, rash
- Refractory or intolerant of Imatinib; Dasatinib 70 mg BD

ALL (Acute lymphocytic Leukemia)

- Poor prognostic factors; ↑WBC, very old or very young
- Treatment for children; vincristine, prednisone, asparginase ± anthracycline
- Treatment for adults; vincristin, prednisone, anthracycline ± asparginase
- Prophylactic therapy to prevent CNS disease (HD/IT/ cranial irradiation)
- Long term MD for 2-3 years; MTX/ MP

CLL (Chronic Lymphocytic Leukemia)

- Signs and symptoms; Lymphocytosis> 5000 lymph/mm3 with the absence of fever or signs of infection
- Most common type of leukemia in adults
- In 90% cases; age> 50 yo
- 40% asymptomatic

Indications for treatment

- Significant anemia and/or thrombocytopenia
- Lymphadenopathy, hepatomegaly, splenomegaly, L×2<6mo
- Recurrent Infections

Initial Therapy

- Elderly; Chlorambucil
- Fludarabine; ADR; fever, myelosuppression, immunosuppression
- Cladribine
- Rituximab; anti-CD20; pretreatment with acetaminophen & diphenhydramine
- Prophylaxis; pcp, herpes simplex/ zoster, IVIg
- Alemtuzumab; anti- CD52 monoclonal Ab

Lymphomas

Non- Hodgkin Lymphoma

- Signs and symptoms; LAP, extranodal involvement; fever (>38˚C), night sweats, weight loss (>10% body weight over 6mo) : B symptoms
- Indolent vs aggressive
- CHOP; cyclophosphamide, doxorubicin, vincristine, prednisone
- R-CHOP; Rituximab
- Antiemetic, bowel regimen, GCSF

Non- Hodgkin Lymphoma

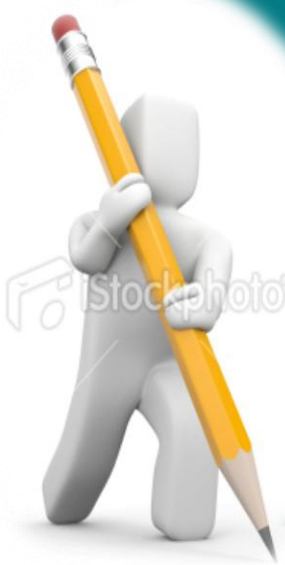
- Radioimmunotherapy
- If Plt>100000/mm^3

- ***For preservation of thyroid what do you suggest?***
- 2 drops of KI PO TID 24h before the first dose for 14d after therapy
- Avoid social contact up to 7 days
- Hematologic toxicity up to 9 wks

Hodgkin Lymphoma

- Curable even in advanced stages
- Painless lymph node, most commonly neck (cervical or supraclavicular)
- ABVD; doxorubicin, bleomysin, vinblastine, dacarbazine
- ADR; Pulmonary complication

Plasma cell Disorders

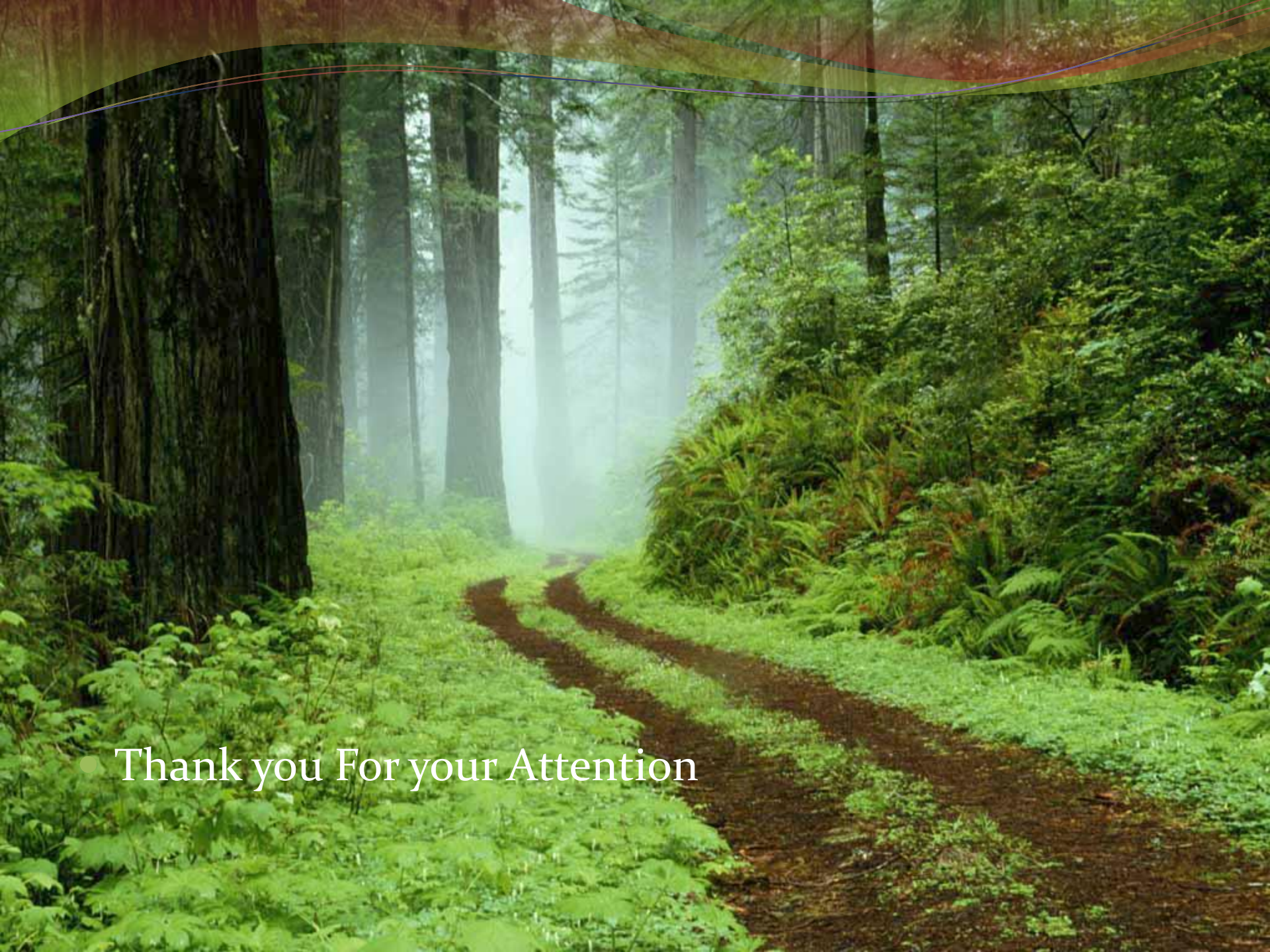


Multiple Myeloma

- Prevalent in men and older; >40yo
- Bone pain & skeletal disease
- Hypercalcemia, renal dysfunction
- Treatment;
  - Thalidomide; immunomodulator, antiangiogenic, 200-800 mg/d
    - ✓ADR; sedation, constipation, thrombotic evenets and neuropathy
  - Dexamethasone or a combination

Treatment of Choice in MM

- HCT (Hematopoietic Cell Transplantation)
- What about significant bone loss?
  - Pamidronate 90 mg over 2 hours
  - Zoledronic acid 4 mg over 15 min
- Bisphosphonates can precipitate renal failure
- Osteonecrosis of jaw (ONJ); rare but serious
- More common with Zoledronic acid
- Discontinue after 2 years



- Thank you For your Attention