CHRONIC LEUKEMIA

OBJECTIVES :-

- INTRODUCTION TO LEUKEMIA .
- CHRONIC LYMPHOCYTIC LEUKEMIA :-

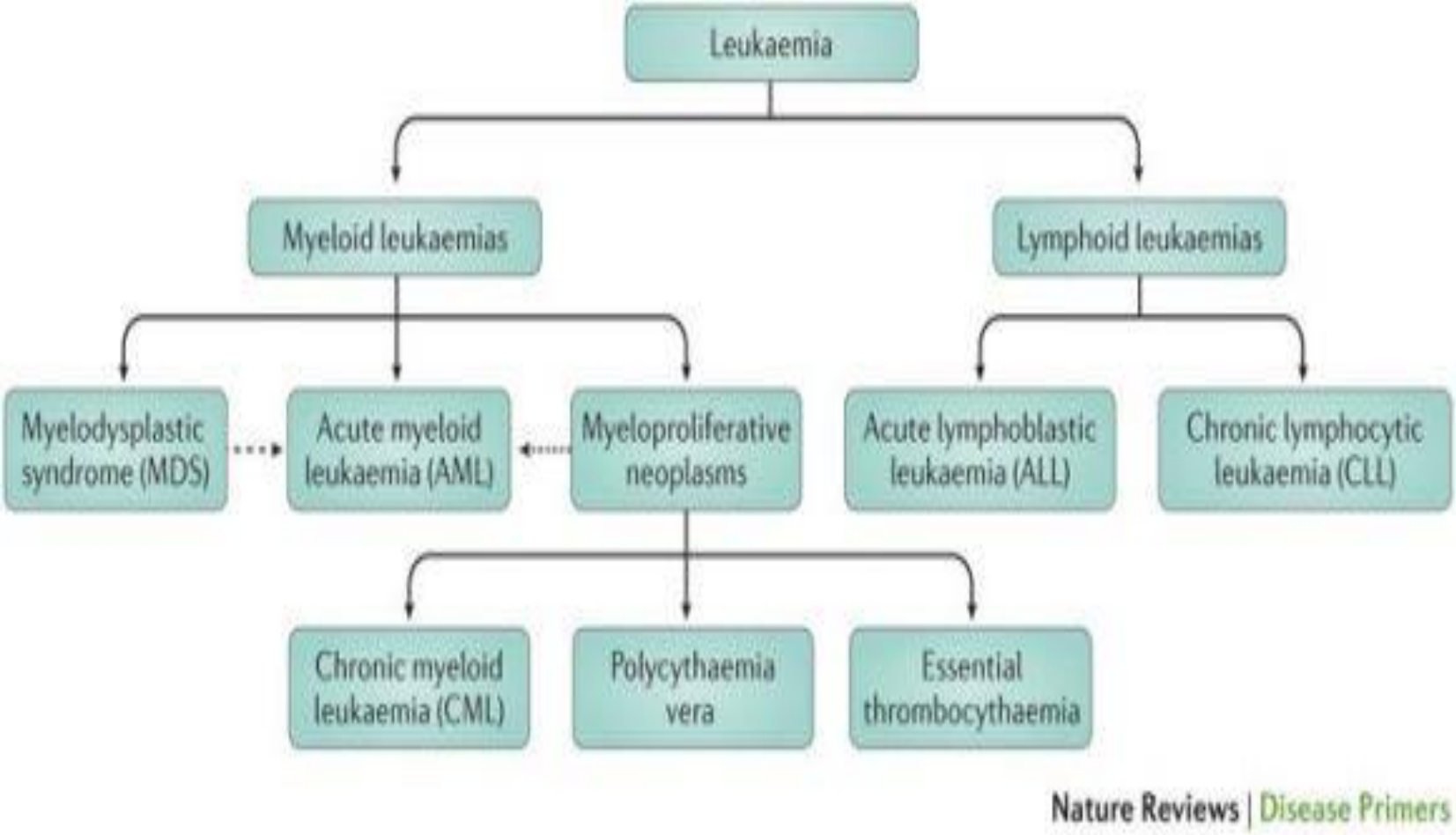
  definition , epidemiology , classification

  treatment .
- CHRONIC MYELOID LEUKEMIA :-

  staging , clinical features , investigation

  treatment .

CHRONIC LEUKEMIA



CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Definition :-

lymphproliferative disorder in which there is progressive accumulation of mature – appearing, functionally incompetent, long lived B-lymphocytes in PB, BM ,LNs, Spleen, liver other sites.

mostly of B origin, in less than 5% of T-cell origin constitute the prolymphocytic variant.

Epidemiology & incidence :-

*CLL is the most common variety of leukemia accounting for 30% of cases.

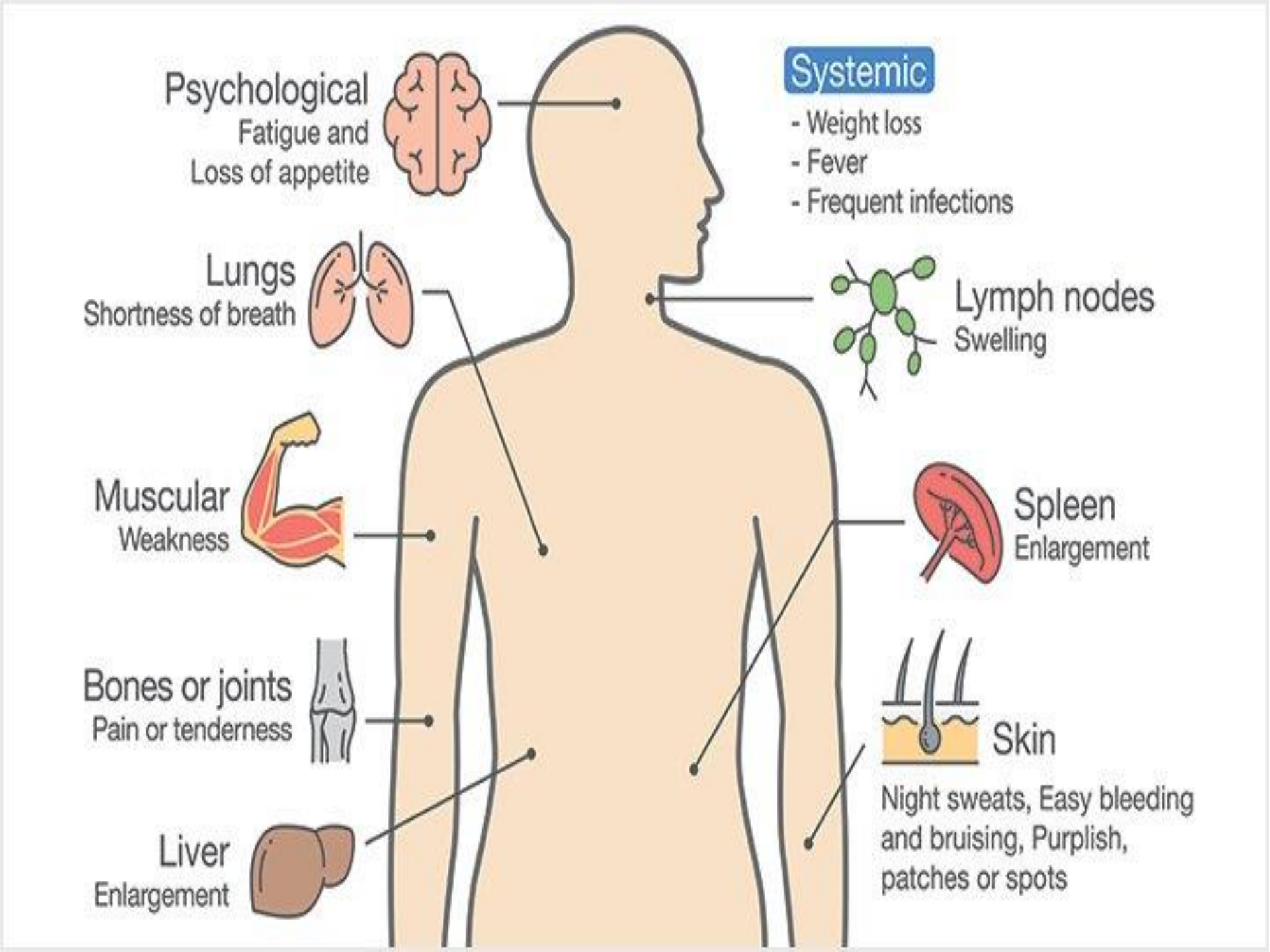
* annual incidence is : 2.5/ 1oo,ooo .

* predominantly disease of elderly (> 70 yrs.) .

* male to female ratio 2:1.

Clinical features & Presentation:-

- the onset is usually insidious, often the patient is Asymptomatic .
- recurrent infections (viral) .
- anemia.
- lymphadenopathy “painless,symmetrical”
- splenomegaly , hepatomegaly .
- systemic B symptoms (wt. loss ,sweating)
- autoimmune phenomena (AIHA , ITP) .

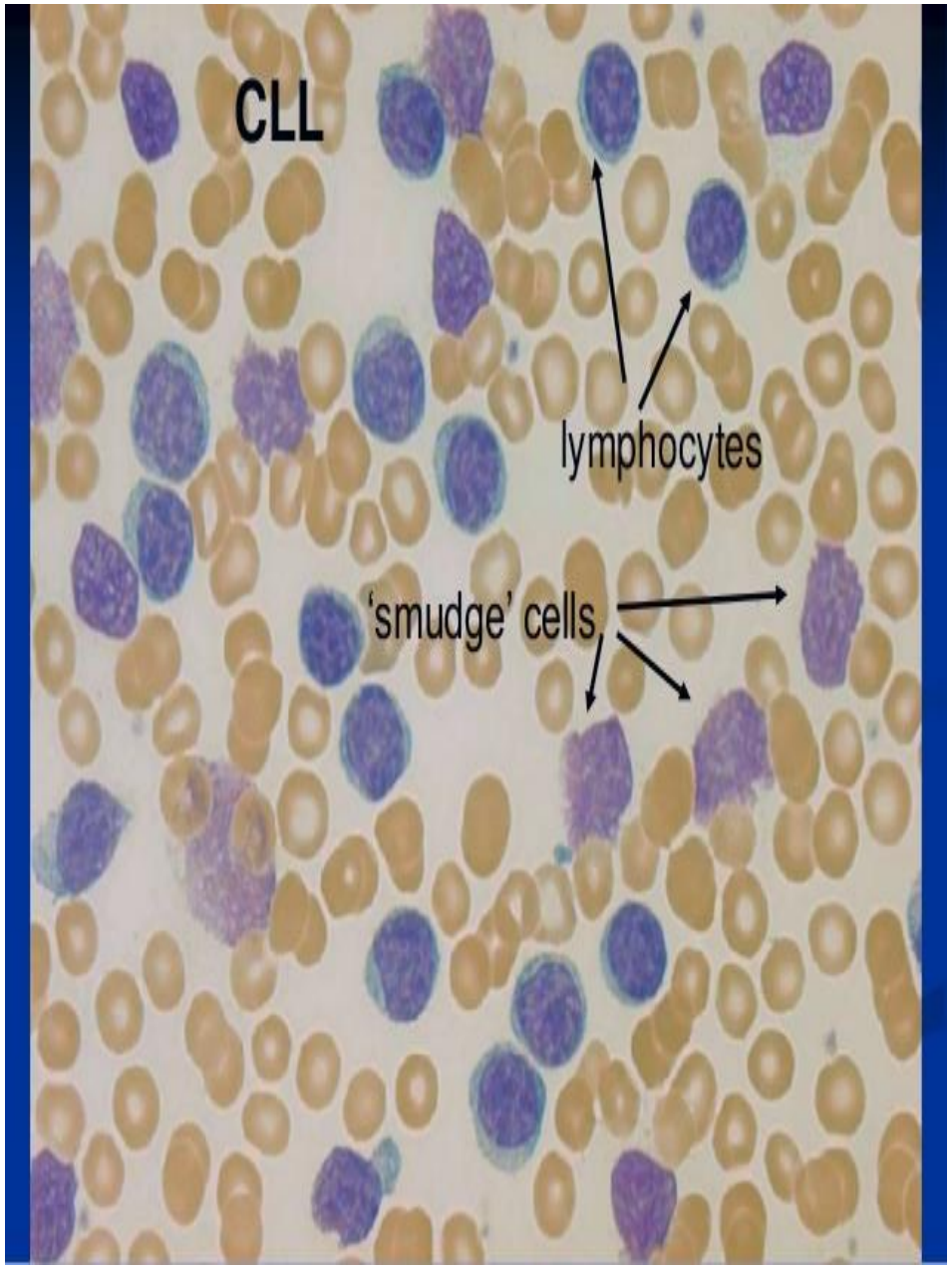

Psychological
Fatigue and
Loss of appetite
Systemic
- Weight loss
- Fever
- Frequent infections
Lungs
Shortness of breath
Lymph nodes
Swelling
Muscular
Weakness
Spleen
Enlargement
Bones or joints
Pain or tenderness
Skin
Night sweats, Easy bleeding
and bruising, Purplish,
patches or spots
Liver
Enlargement

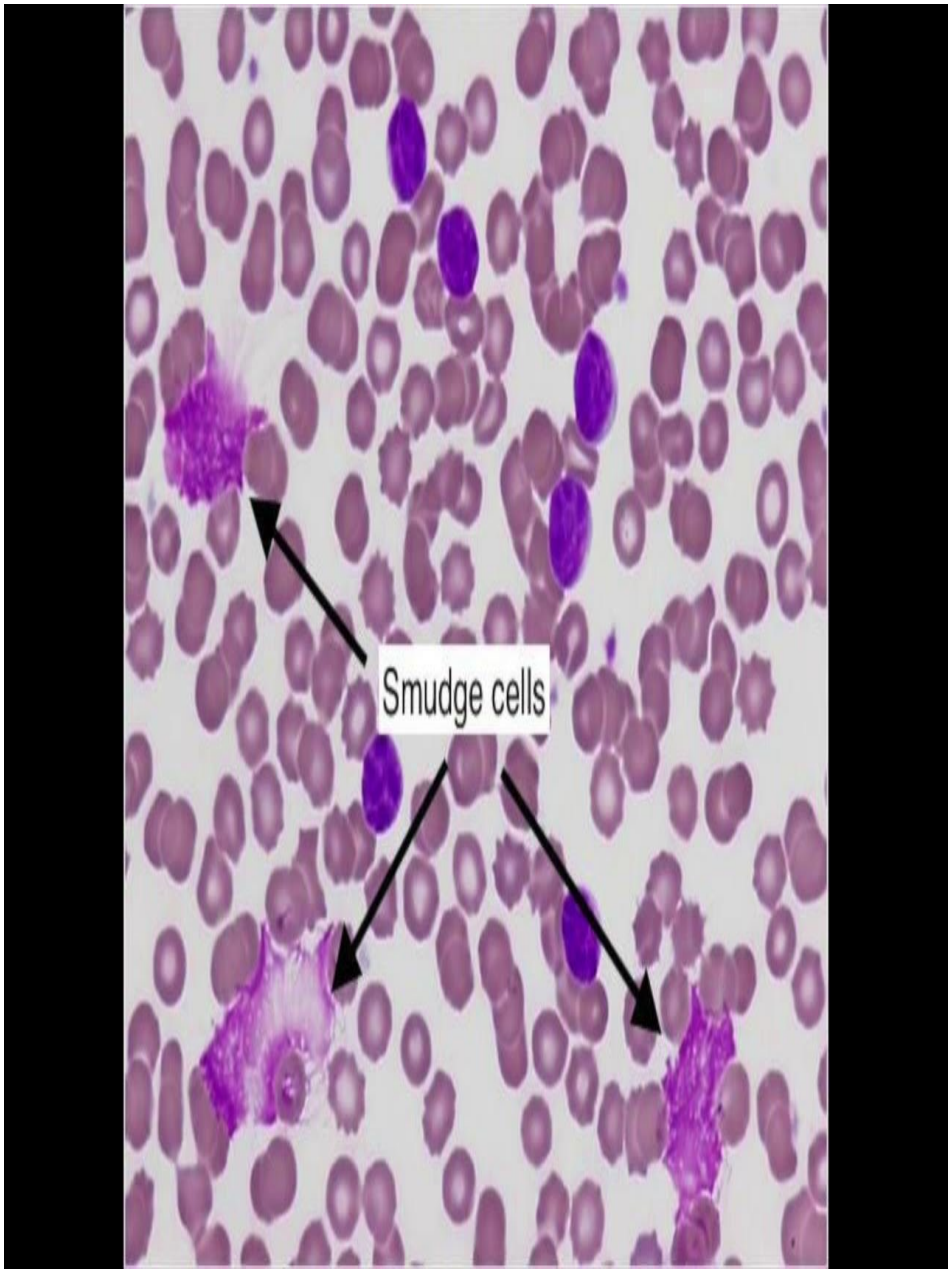
Investigations :-

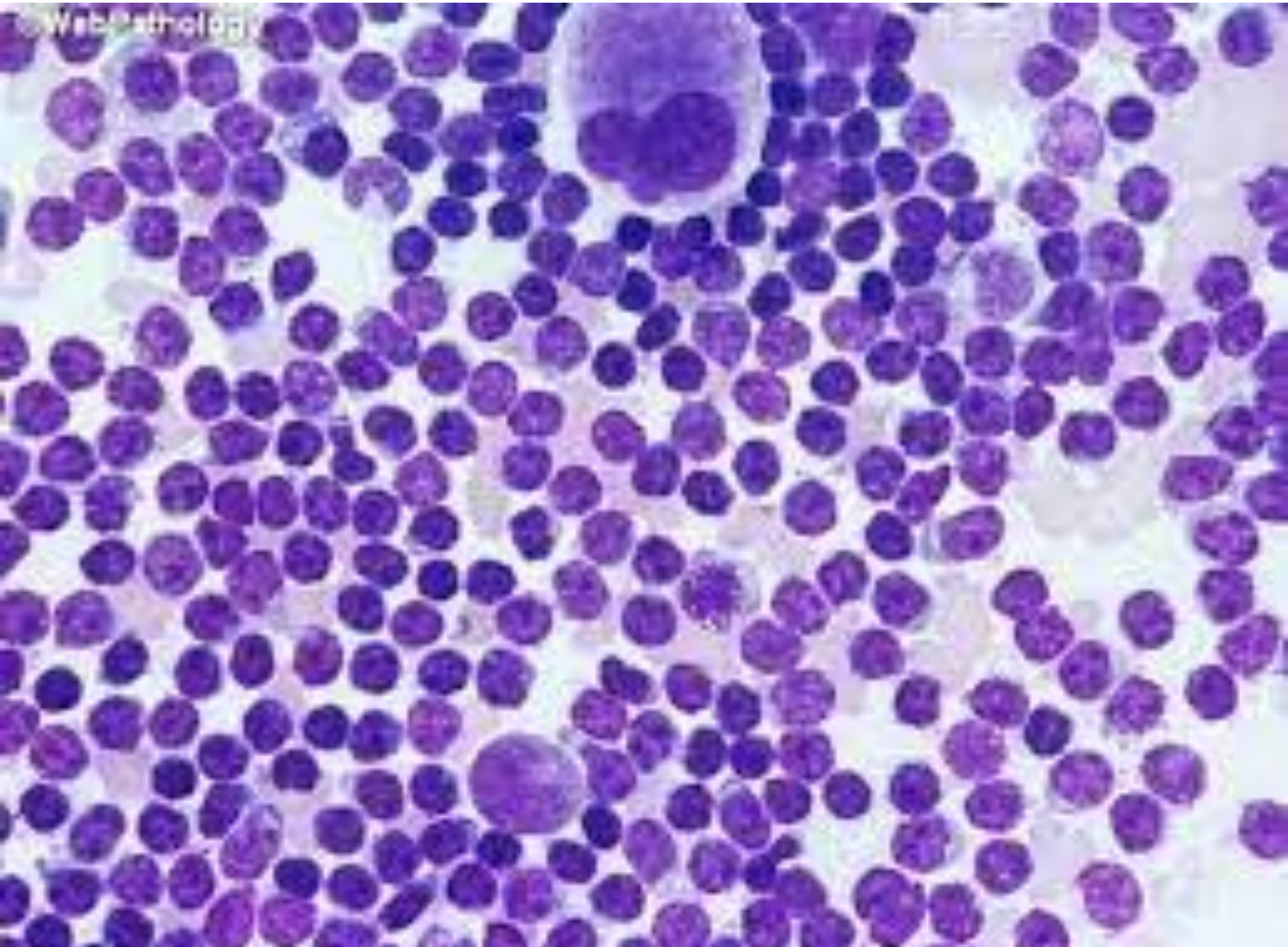
- CBC& PBF : Anemia (NNA ,Hemolytic) .
  Leukocytosis : mature lympho-
  cytes (absolute count >5x109/l)
  smear cells , plts N or low .
- Immunophenotyping : " flowcytometry"
  expression of CD19 ,,CD23,
  CD5, weak expression of CD79b
  and SmIg .

cll case should score = 3/5 .

peripheral blood film







- s protein electrophoresis : hypogammgloblinemia
- s.immunoglobulin levels .
- coomb's test (D) , reticulocyte count .
- BMA& BX : to assess the degree and type of infiltration (nodular or diffuse) .
- Cytogenetics : loss of chr. 17p.
  mutation in the TP53 gene.
  (predictor of response, prognosis).
- Radiology , RFT ,LFT ,UA .

Stages of CLL : Binet Staging

- clinical stage A :no anemia or thrombocyto-penia, <3 areas of lymphoid enlargement. (60%)
- clinical stage B :no anemia or thrombocyto-penia ,3or more areas of lymphoid enlargement. (30%)
- clinical stage C :anemia and/or thrombocyto-penia ,regardless of No. of areas of lymphoid enlargement. (10%)

TABLE 3. Binet Staging System[24]

Stage A	Hemoglobin ≥10 g/dL, platelets ≥100,000/μL, and <3 enlarged sites
Stage B	Hemoglobin ≥10 g/dL, platelets ≥100,000/μL, and ≥3 enlarged sites
Stage C	Hemoglobin <10 g/dL, platelets <100,000/μL, any number of enlarged sites

RAI CLASSIFICATION

Stage	Lymphocytosis	Enlarged lymph nodes	Enlarged Liver/Spleen	Anemia	Low platelets
0	+	-	-	-	-
1	+	+	-	-	-
2	+	+/-	+	-	-
3	+	+/-	+/-	+	-
4	+	+/-	+/-	+	+

Table 1
Rai and Binet staging systems in CLL

Rai 0: Lymphocytosis alone	Binet A: <3 groups of enlarged lymph nodes
Rai I: Stage 0 with enlarged lymph nodes	Binet B: ≥3 groups of enlarged lymph nodes
Rai II: Stage 0–I with palpable organomegaly	Binet C: Hemoglobin <10 g/dL and/or platelets counts <100 × $10^3/\mu L$
Rai III: Stage 0–II with hemoglobin <11 g/dL	
Rai IV: Stage 0–III with platelet counts <100 × $10^3/\mu L$	

Adapted from Binet JL, Auquier A, Dighiero G, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer 1981;48:198–206; and Rai KR, Sawitsky A, Cronkite EP, et al. Clinical staging of chronic lymphocytic leukemia. Blood 1975;46:219–34.

Management :

- clinical stage A : No specific treatment.
- stage B,C, or progressive A :

the treat.is based on Age, Fitness, TP53 mutational status .

* pt's<70, fit, TP53 mutation negative .

Fludrabine+cyclophosphamide+Rituximab (FCR) 6 –8 cycles every 28 days.

* pt's >70 , less fit

Rituximab + Bendamustine or oral chlorambucil.

*Relapsed, TP53 mutation+ pt's

IBRUTINIB , IDELALISIB (inhibitors of B cell pathway),

recommended for all stages.

* steroids for pt's with AIHA , ITP .
* Supportive Rx. By blood, plt transfusion ,IvIg for pt's with hypogammglobulinemia .
* Radiotherapy for bulky disease with compression and symptomatic splenomegaly .
* splenectomy for hypersplenism .

TABLE 3

Indications to initiate treatment for chronic lymphocytic leukemia

Constitutional symptoms attributable to the disease

Progressive marrow failure

Autoimmune anemia or thrombocytopenia poorly responsive to corticosteroids

Massive or progressive splenomegaly

Massive or progressive lymphadenopathy

Rapid lymphocyte doubling time

Based on information in reference 30.

Prognosis :

" non curable malignancy "

- the majority of clinical stage A cases have a normal life span .
- advanced cases are more likely to die from their disease or infectious complications.
- survival is influenced by the mutational status especially of TP53 .
- rarely CLL transforms to an aggressive high grade lymphoma called RICHTER'S SYNDROME