Chronic Lymphocytic Leukaemia.

When to Worry.

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Session Aims

01

CLL 101.

Overview of the disorder.

02

Diagnosing CLL.

How medics diagnose and manage CLL.

03

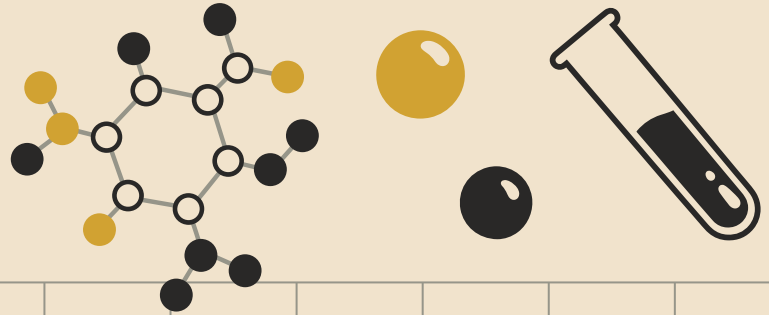
When is CLL NOT CLL?

Other factors relating to mature lymphocytosis.

04

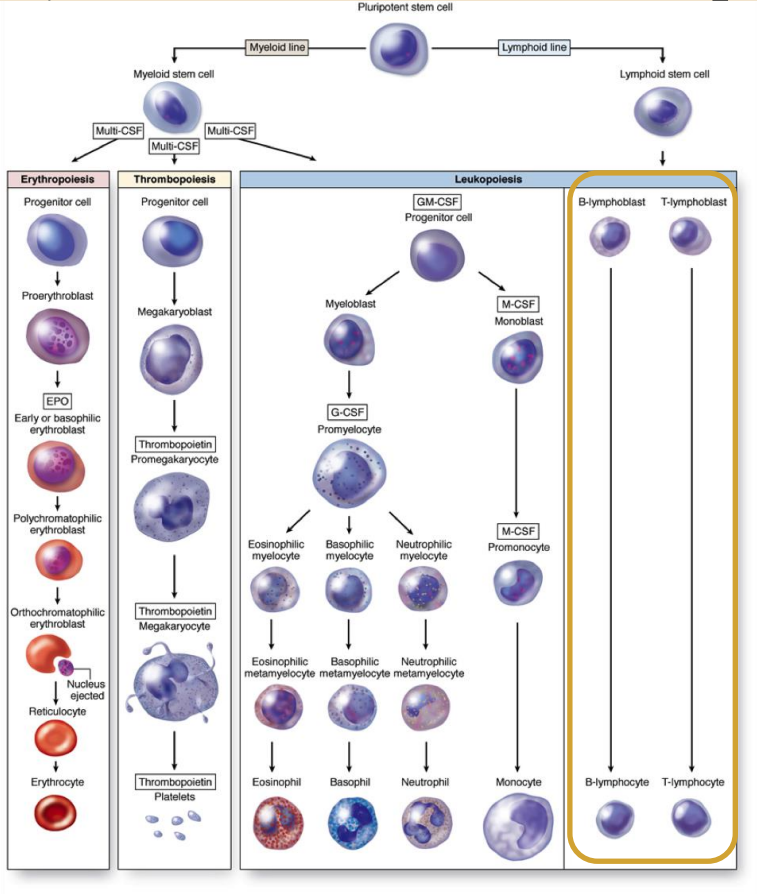
When should we worry?

When is a change significant, and when does it need urgent action?



Haematopoiesis Revision

01



Lymphocytes are made in the marrow.

T cells mature in the thymus, and B-cells mature lymph-nodes or organs.

B-cells undergo developmental changes when stimulated by antigen presenting cells, resulting in functional cells e.g. memory or plasma cells.

CLL is a disease of memory B-cells.

CLL Key Facts

01

01

Chronic Disorder

CLL is a chronic disorder. Blasts are always <20%.

02

Epidemiology

CLL is the most common leukaemia. The median age of onset is 70.

03

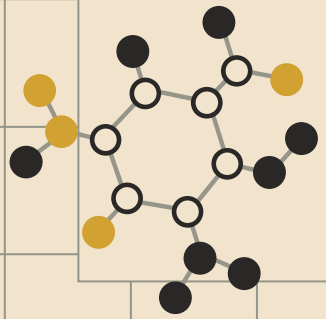
Incidental Finding

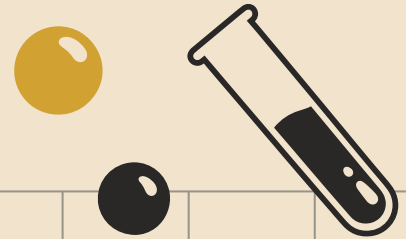
Often patients are asymptomatic and can remain stable for many years with no treatment.

04

Ethnic Association

CLL is uncommon outside of predominately white, western countries, this suggests that Caucasians have a genetic predisposition for CLL.





CLL and the FBC

02

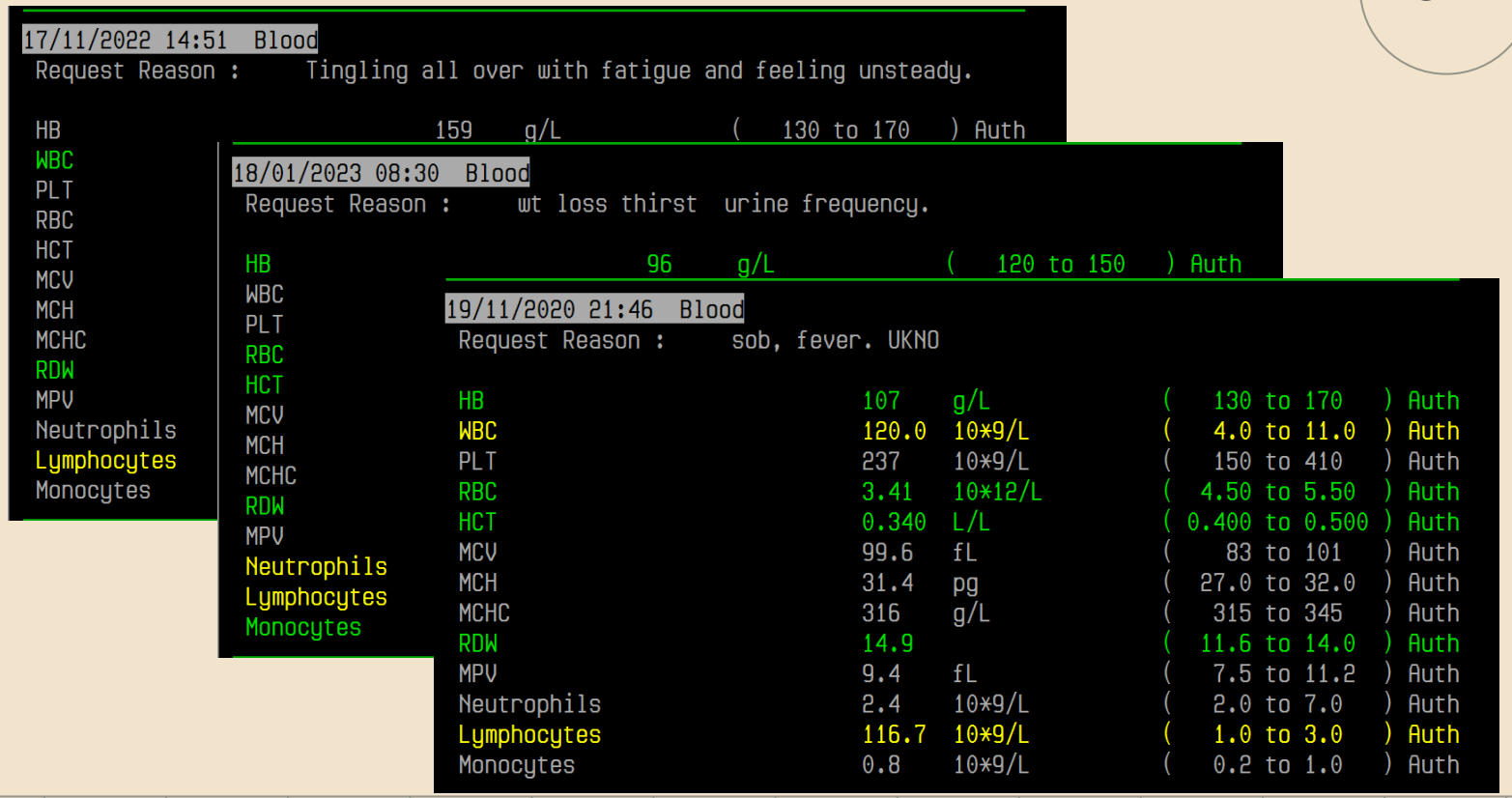
CLL typically presents as an isolated lymphocytosis.

The extent of the lymphocytosis can vary massively!

Patients with heavy marrow infiltration, or progressive disease at diagnosis may present with cytopenia’s.

CLL and the FBC

02



CLL and the Blood Film

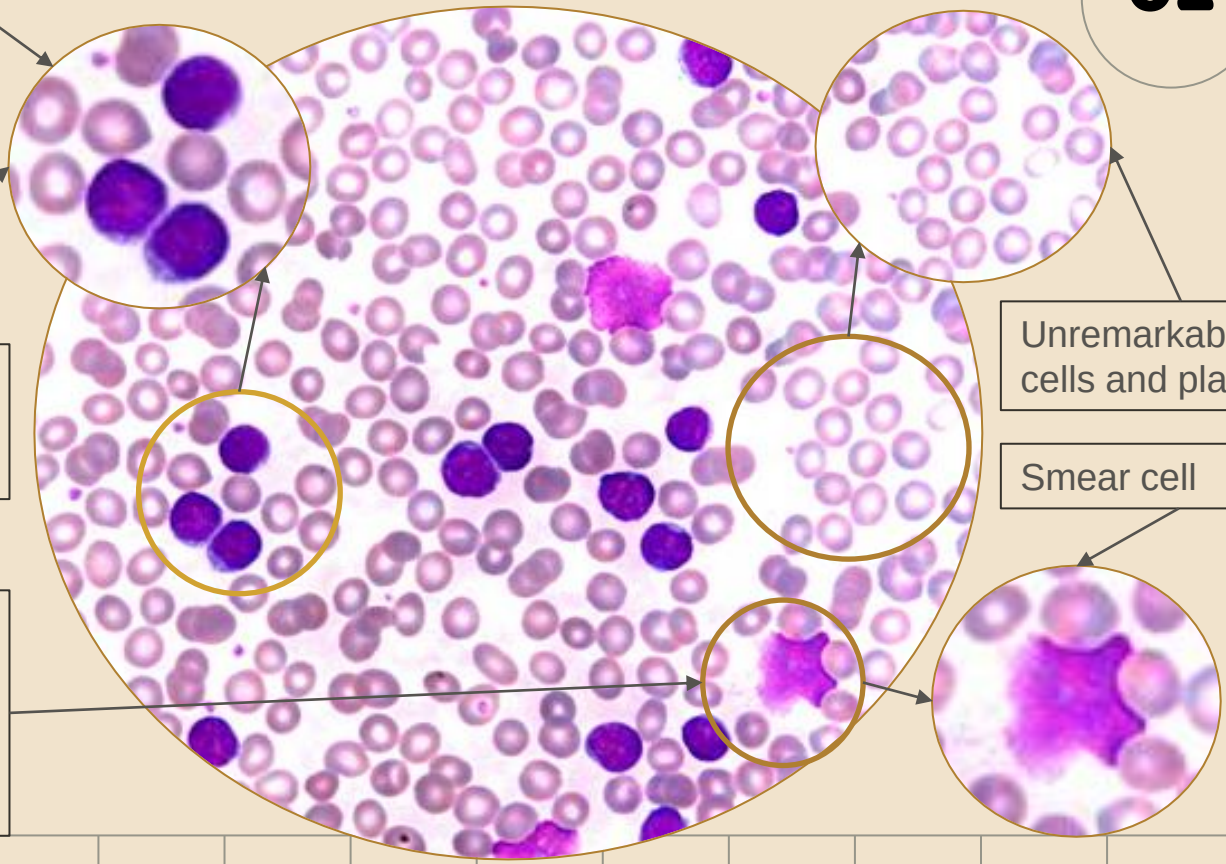
02

There is an excess of small lymphocytes.

Lymphocytes are small, with mature, clumped chromatin

This happens because the lymphocytes are fragile.

Smear cells are lymphocytes which have been damaged during the slide making process.



Unremarkable red cells and platelets.

Smear cell

CLL and Immunophenotyping

02

Marker	Lineage	Patient Result.
CD3+	T-Cell	CD3-
CD4+	T-Cell	CD4-
CD5+	T-Cell	CD5+
CD8+	T-Cell	CD8-
CD10+	Lymphocyte blast.	CD10-
CD34+	Generic Blast	CD34-
CD19+	B-Cell	CD19+
CD20+	B-Cell	CD20+
CD24+	B-Cell	CD24+
Surface Immunoglobulin	B-Cell	Surface Immunoglobulin+

Flow is often used to diagnose CLL.

Peripheral blood is often tested, and bone marrows are uncommon at diagnosis.

CLL and Immunophenotyping

02

The Matutes score is used to identify CLL and exclude other lymphomas.

Matutes score marker.	Patient Result.
CD5+	CD5+
FMC7-	FMC7-
CD79b-	CD79b-
CD24+	CD24+
Surface Immunoglobulin+ (weak expression)	Surface Immunoglobulin+ (weak expression)

A score of 4/5 or 5/5 is diagnostic of CLL. 3/5 and below is likely a different LPD.

CLL Scoring

02

B-Symptoms

- Organomegaly (spleen or liver)
- Night sweats (drenching)
- Unintentional weight loss (>10% of body weight in <6 months)

CLL Diagnosis

B Symptoms

Referal to haematology, usually via 2 week wait.

If patient is also cytopenic, or has a high WBCC, this may need to be expedited.

No B symptoms

Watch and Wait, usually through the primary care provider.

Referral to haem may still be needed if patient is anaemic or WBCC is very high.

CLL Transformation

02

Richter's Transformation

A rare syndrome where CLL transforms to a high grade lymphoma.

Diffuse Large B-cell Lymphoma

The most common high grade lymphoma for CLL to transform into.

Must it transform?

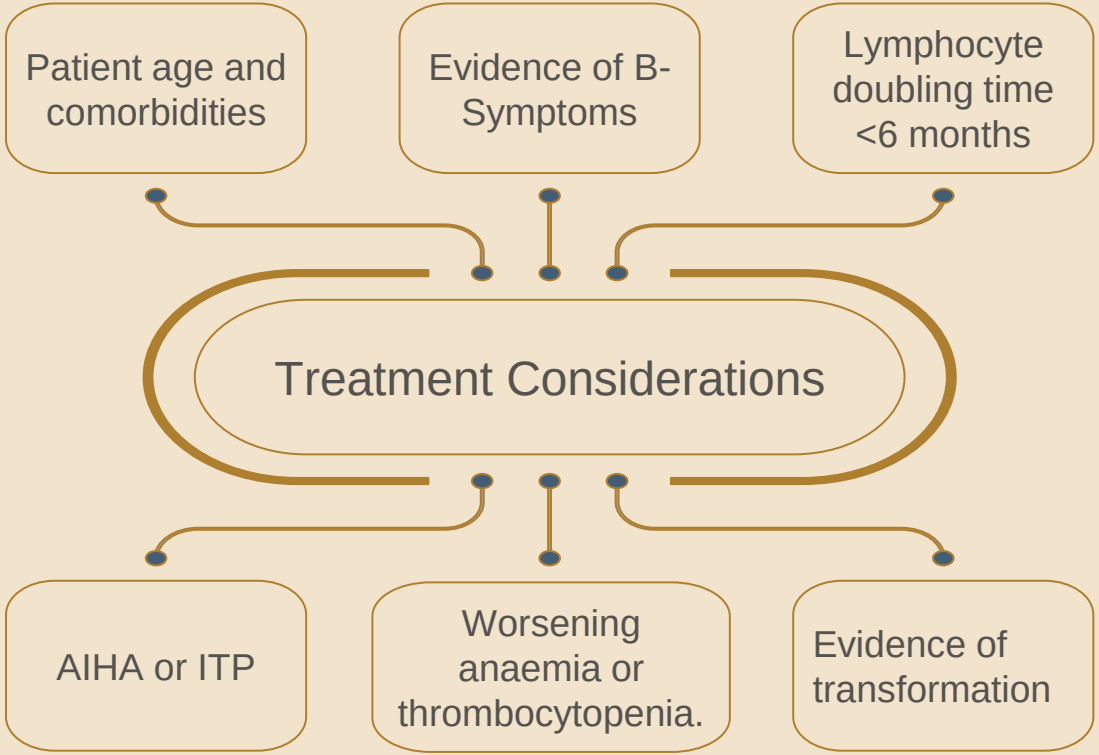
CLL can be highly proliferative, and can result in severe disease, even without transformation.

Can it transform to ALL?

Unlike chronic myeloid disorders, CLL does not transform to ALL.

Should we treat?

03



CLL and Treatment.

CLL

Classical chemotherapy drugs are less used now. They can cause cytopenia's (transfusion dependence) and organ/tissue damage.

Immunomodulatory drugs affect the cellular processes to

These drugs are more targeted, but can still have significant side affects such as neutropenia, thrombocytopenia etc.

Antibodies are an essential therapy in lymphoid disorders. Anti-CD20 targets a pan B-cell marker.

CLL, SLL and MBL

03

Features	CLL	SLL	MBL
Clonal Lymphocytosis	>5x10^9/L	>5x10^9/L	<5x10^9/L
Leukemic Phase	Yes	No	Yes
Cancer?	Yes	Yes	No?

CLL and Small Cell Lymphocytic Leukaemia (SLL) are the same disease, but in SLL, the lymphocytes are isolated in lymph nodes.

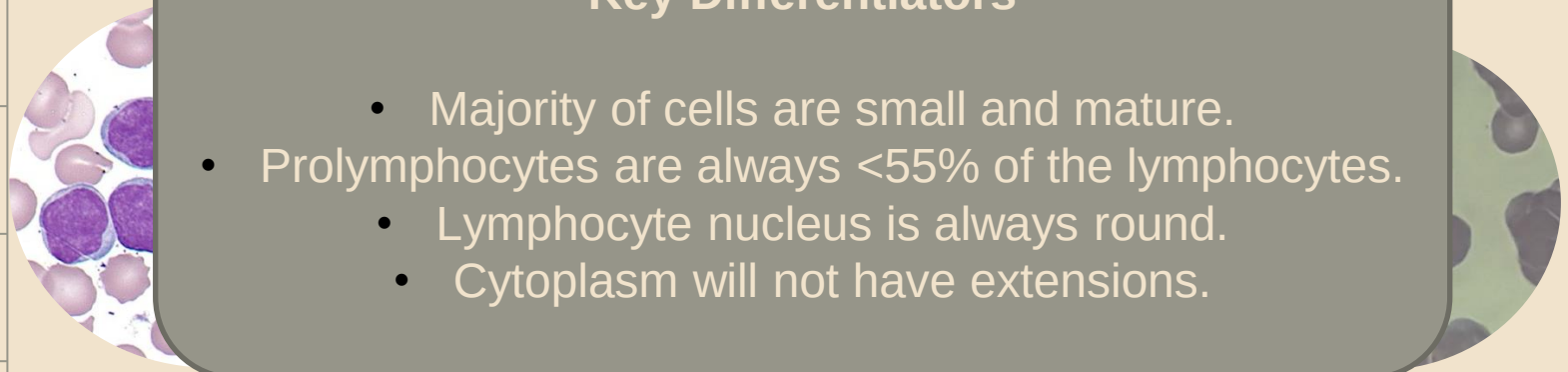
Monoclonal B-cell lymphocytosis (MBL) is a precursor disorder . Many patients will never progress.

CLL's evil siblings.

03

Prolymphocytic Le

Mantle cell



Key Differentiators

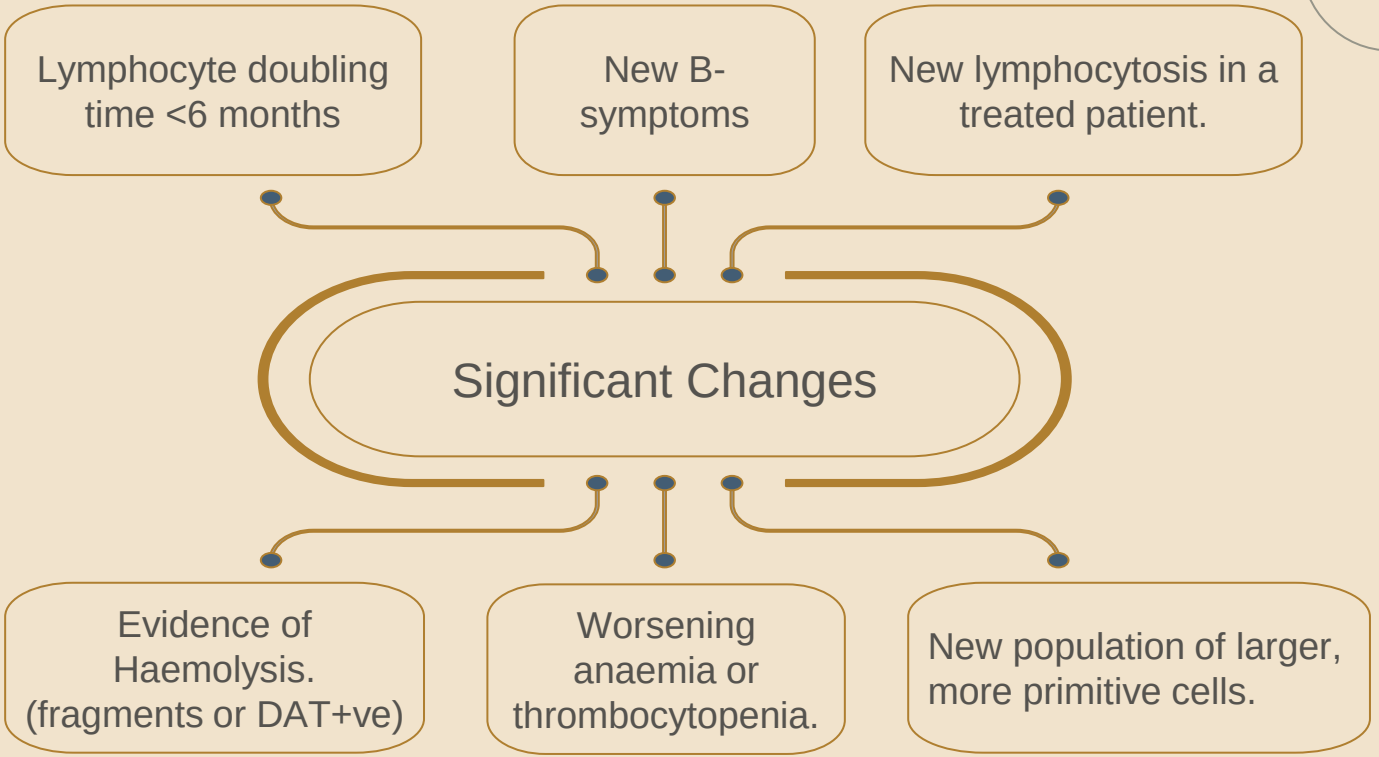
- Majority of cells are small and mature.
- Prolymphocytes are always <55% of the lymphocytes.
- Lymphocyte nucleus is always round.
- Cytoplasm will not have extensions.

Adult T-cell Lymphoma

Diffuse large B-cell lymphoma

What changes are significant?

04



When to Refer to HQ.

04

Any of these features should trigger a film before the HQ
eye o
morphologic

Lymphocyte doubling
<6 months

CLL does not need to be referred overnight. New, high WBCC (>100X10^9/l) should be referred in the AM.

New cytope
known CLL patient.

nphocytosis
nt, with no
other counts, can be authorised- no need for a film or HQ!

Thanks!

Do you have any questions?

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