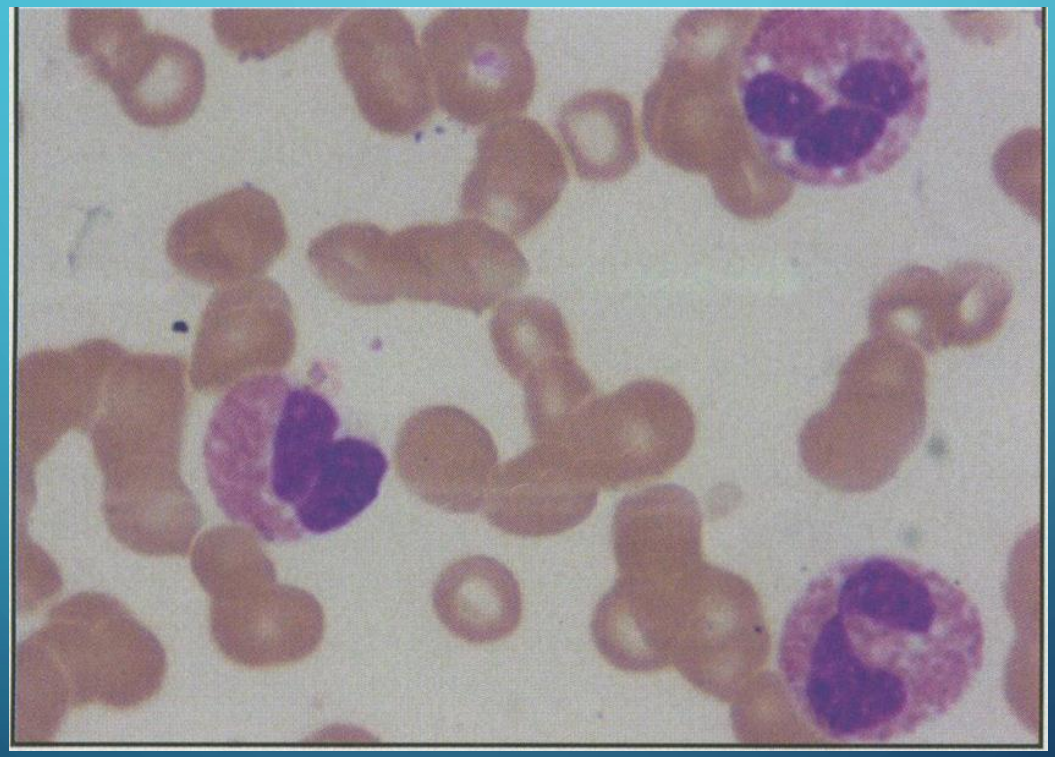
HYPEREOSINOPHILIA



- Eosinophils bilobed granulocyte derived from myeloid stem cell.

- "Eosin" is derived from "Eos," the rosy-fingered Titan goddess of the dawn.
- mature eosinophils are normally present in the (GI) tract (except the esophagus), lymphoid tissues (eg, thymus), uterus, and mammary glands.
- Whereas most surface markers expressed on eosinophils are expressed on other myeloid cells (CD45, CD15, CD66b), few are more specific to eosinophils, including EMR-1, Siglec-8, and CCR3 (CD193)

- Eosinophils persist in the circulation for 25h(compared with 10h for neutrophils) before migration to tissues.

- absolute eosinophil count (AEC) of 0.35–0.5 ×109/L , with a slight variation between measuring laboratories.

- the threshold of 1.5 × 109/L is arbitrary, and tissue infiltration by eosinophils and end-organ damage can be seen with a lower eosinophil count

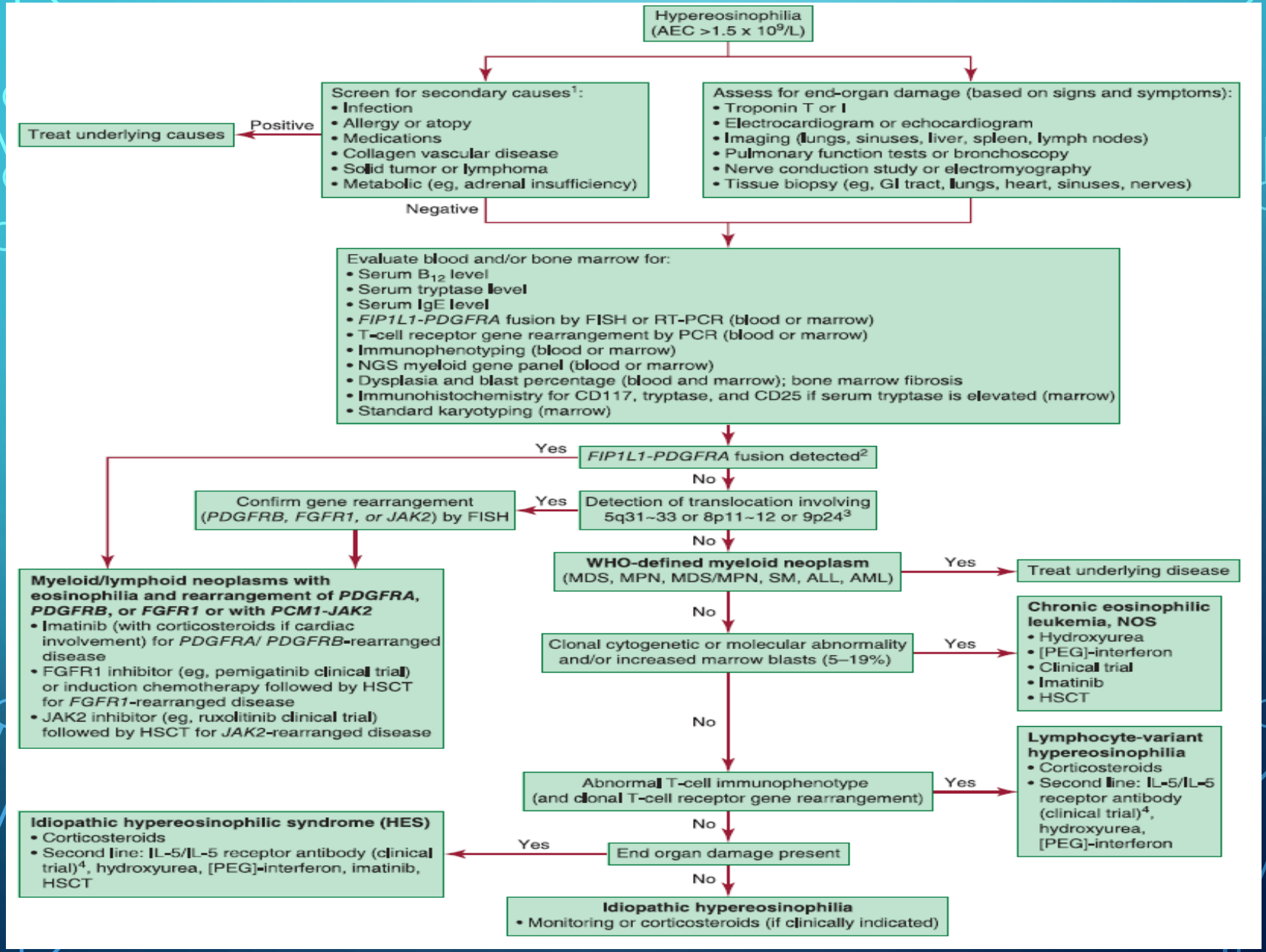
- requirement eosinophilia persists for more than 6 months is not practical today.

- many patients with an AEC greater than 1.5 × 109/L are asymptomatic with no end-organ damage, and in these patients, “idiopathic HE or HE of undetermined significance” is the preferred term.

- HE has been defined as persistent eosinophilia greater than 1.5 × 109/L.
- primary (clonal or neoplastic)
- secondary (reactive)
- Hereditary (familial)
- HE of undetermined significance when no underlying cause is identified.

- The term “hypereosinophilic syndrome” (HES) was first coined by Hardy and Anderson in 1968 to imply a syndrome of an unknown cause characterized by
- Eosinophilia
- organ infiltration by eosinophils
- and a spectrum of clinical manifestations involving the lungs, heart, liver, and spleen.

- Diagnostic workup:
- Evaluation for infections
- allergic and collagen vascular diseases
- prescription medications and supplements(ASA,NSAID…)
- physical examination that includes palpation of the lymph nodes and spleen because eosinophilia presenting sign in various malignancies
- Hodgkin disease
- T-cell lymphomas
- T-cell acute lymphoblastic leukemia/lymphoma
- solid malignancies


Hypereosinophilia (AEC >1.5 x 10⁹/L)
Screen for secondary causes[1]:
• Infection
• Allergy or atopy
• Medications
• Collagen vascular disease
• Solid tumor or lymphoma
• Metabolic (eg, adrenal insufficiency)
Positive
Treat underlying causes
Assess for end-organ damage (based on signs and symptoms):
• Troponin T or I
• Electrocardiogram or echocardiogram
• Imaging (lungs, sinuses, liver, spleen, lymph nodes)
• Pulmonary function tests or bronchoscopy
• Nerve conduction study or electromyography
• Tissue biopsy (eg, GI tract, lungs, heart, sinuses, nerves)
Negative
Evaluate blood and/or bone marrow for:
• Serum B_{12} level
• Serum tryptase level
• Serum IgE level
• *FIP1L1-PDGFRA* fusion by FISH or RT-PCR (blood or marrow)
• T-cell receptor gene rearrangement by PCR (blood or marrow)
• Immunophenotyping (blood or marrow)
• NGS myeloid gene panel (blood or marrow)
• Dysplasia and blast percentage (blood and marrow); bone marrow fibrosis
• Immunohistochemistry for CD117, tryptase, and CD25 if serum tryptase is elevated (marrow)
• Standard karyotyping (marrow)
FIP1L1-PDGFRA fusion detected[2]
Yes
No
Detection of translocation involving 5q31~33 or 8p11~12 or 9p24[3]
Yes
Confirm gene rearrangement (*PDGFRB, FGFR1, or JAK2*) by FISH
No
WHO-defined myeloid neoplasm (MDS, MPN, MDS/MPN, SM, ALL, AML)
Yes
Treat underlying disease
Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of *PDGFRA*, *PDGFRB*, or *FGFR1* or with *PCM1-JAK2*
• Imatinib (with corticosteroids if cardiac involvement) for *PDGFRA*/ *PDGFRB*-rearranged disease
• FGFR1 inhibitor (eg, pemigatinib clinical trial) or induction chemotherapy followed by HSCT for *FGFR1*-rearranged disease
• JAK2 inhibitor (eg, ruxolitinib clinical trial) followed by HSCT for *JAK2*-rearranged disease
No
Clonal cytogenetic or molecular abnormality and/or increased marrow blasts (5–19%)
Yes
Chronic eosinophilic leukemia, NOS
• Hydroxyurea
• [PEG]-interferon
• Clinical trial
• Imatinib
• HSCT
No
Abnormal T-cell immunophenotype (and clonal T-cell receptor gene rearrangement)
Yes
Lymphocyte-variant hypereosinophilia
• Corticosteroids
• Second line: IL-5/IL-5 receptor antibody (clinical trial)[4], hydroxyurea, [PEG]-interferon
No
End organ damage present
Yes
Idiopathic hypereosinophilic syndrome (HES)
• Corticosteroids
• Second line: IL-5/IL-5 receptor antibody (clinical trial)[4], hydroxyurea, [PEG]-interferon, imatinib, HSCT
No
Idiopathic hypereosinophilia
• Monitoring or corticosteroids (if clinically indicated)

- Further diagnostic testing depends on the organ involved and biopsy of the affected organ.

- In patients with a suspected malignancy, CT scan of chest, abdomen, and pelvis or positron emission tomography (PET)/CT is recommended.

- After excluding reactive causes, evaluation for a marrow disorder associated with eosinophilia should be pursued.

- Marrow evaluation includes looking for dysplasia, myeloproliferation, increased blasts, reticulin fibrosis, and immunohistochemical staining with CD117, tryptase, and CD25 to identify increased numbers of neoplastic mast cells.
- If a translocation involving 4q12, 5q31~33, 8p11~12, 9p24, or 13q12 is found on standard cytogenetics.
- then FISH testing for involvement of suspected genes (PDGFRA, PDGFRB, FGFR1, JAK2, or FLT3, respectively) should be performed to confirm gene rearrangement.

- This includes fluorescence in situ hybridization (FISH) testing for the CHIC2 deletion, a surrogate for FIP1L1-PDGFRA fusion gene on either blood or marrow.