Fred Hutch Cancer Center

UW Medicine

COMPREHENSIVE HEMATOLOGY & ONCOLOGY REVIEW

BENIGN WHITE CELL DISORDERS

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Associate Professor

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Land Acknowledgement

Fred Hutchinson Cancer Center acknowledges the Coast Salish peoples of this land, the land which touches the shared waters of all tribes and bands within the Duwamish, Puyallup, Suquamish, Tulalip and Muckleshoot nations.

DISCLOSURES

I have no disclosure or conflicts of interest

I will discuss off-label use of some medications

ACKNOWLEDGEMENT

Michael Linenberger, MD

OBJECTIVES

DIAGNOSE AND MANAGE CONGENITAL & ACQUIRED NETUROPENIA AND NON-CLONAL NEUTROPENIA

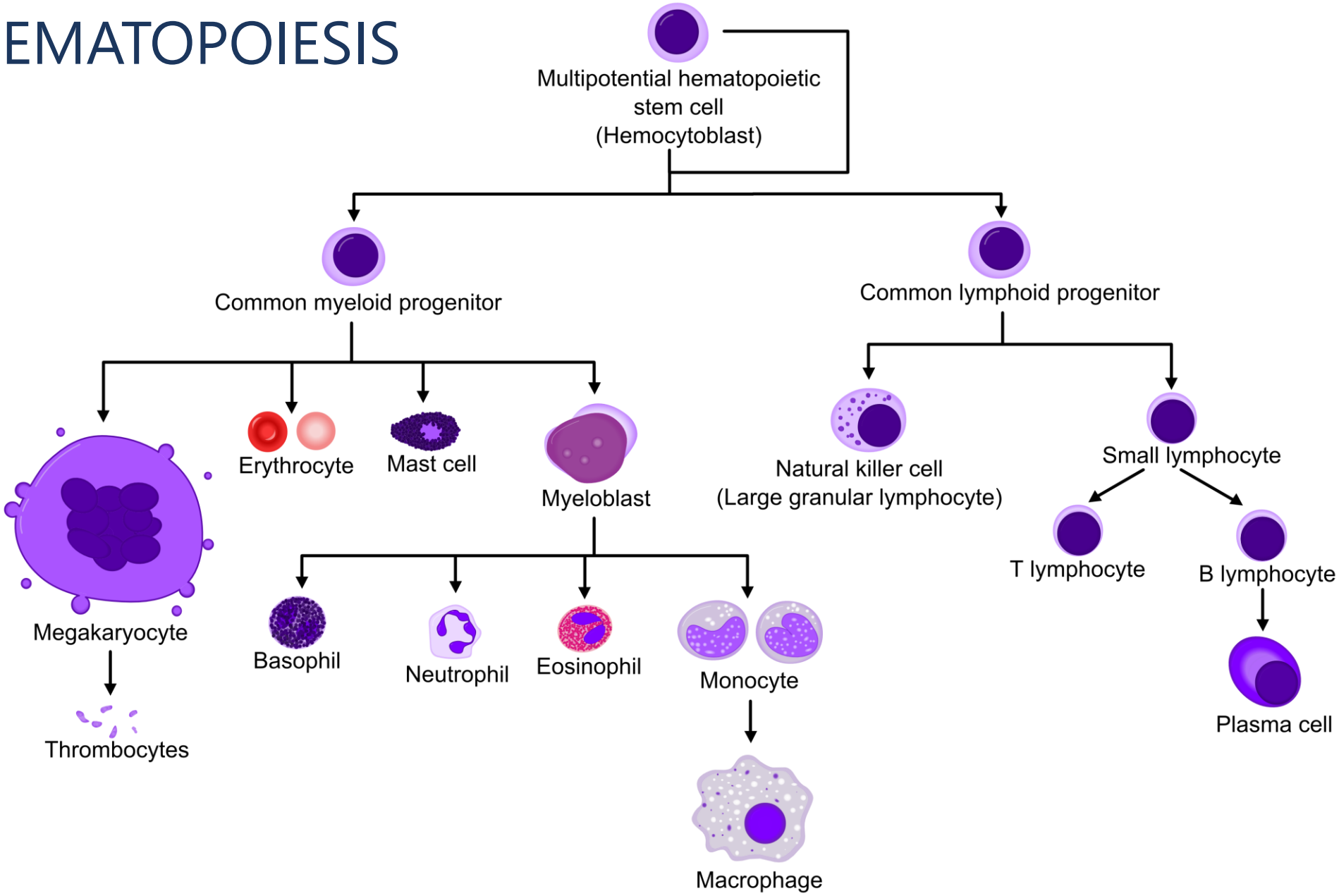
•

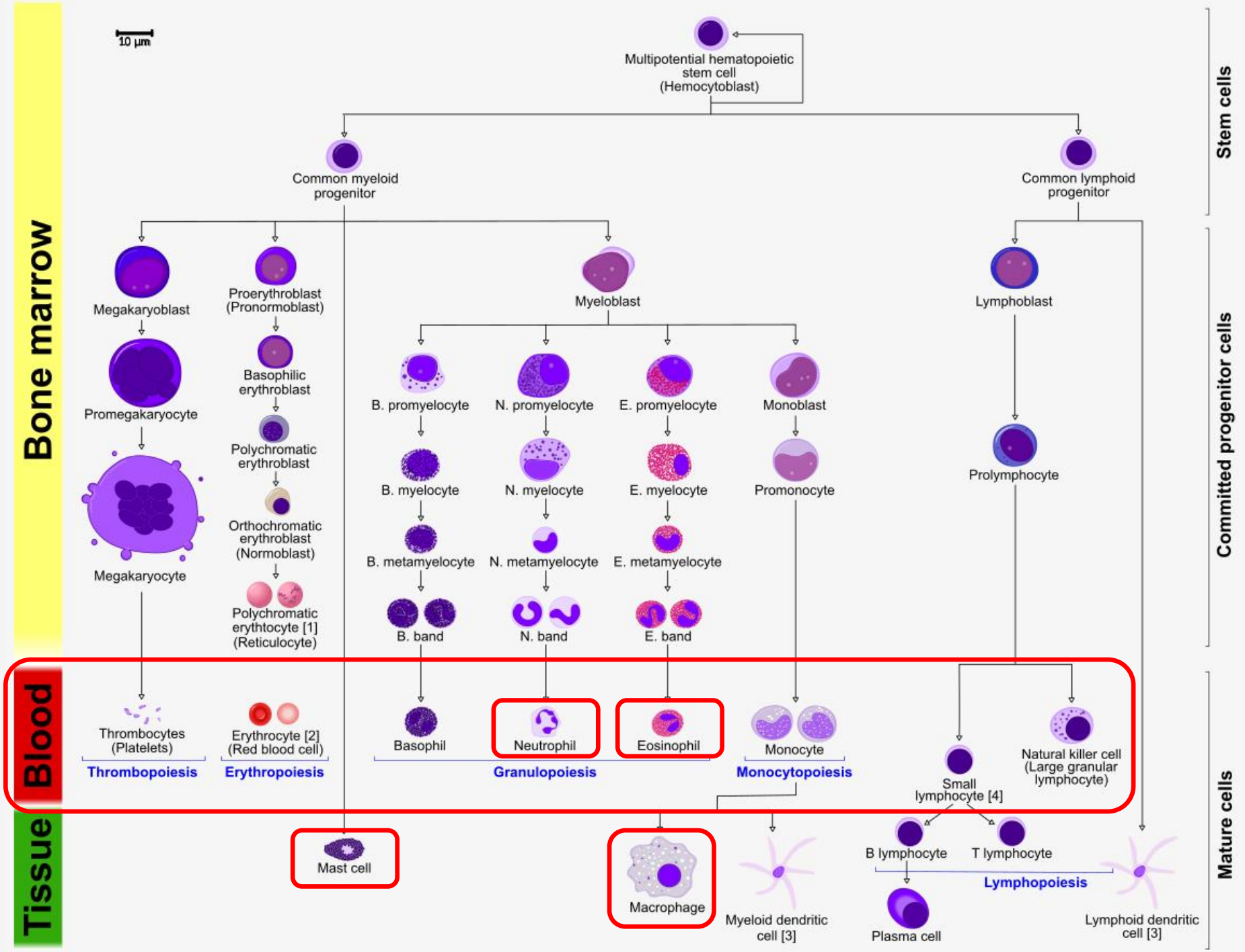
RECOGNISE CAUSES, EVALUATION AND TREATMENT OF EOSINOPHIL & MAST CELL DISORDERS

•

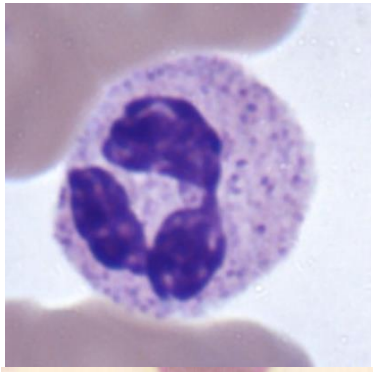
UNDERSTAND THE PATHOBIOLOGY & MANAGEMENT OF HLH AND MACROPHAGE ACTIVATION SYNDROMES

HEMATOPOIESIS

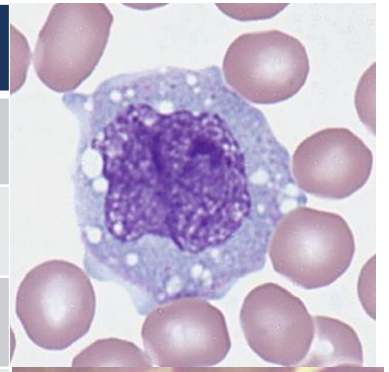


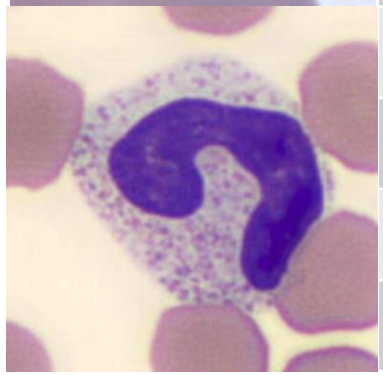

Bone marrow
Blood
Tissue
10 µm
Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Stem cells
Committed progenitor cells
Mature cells
Megakaryoblast
Promegakaryocyte
Megakaryocyte
Proerythroblast (Pronormoblast)
Basophilic erythroblast
Polychromatic erythroblast
Orthochromatic erythroblast (Normoblast)
Polychromatic erythtocyte [1] (Reticulocyte)
Myeloblast
B. promyelocyte
B. myelocyte
B. metamyelocyte
B. band
N. promyelocyte
N. myelocyte
N. metamyelocyte
N. band
E. promyelocyte
E. myelocyte
E. metamyelocyte
E. band
Monoblast
Promonocyte
Lymphoblast
Prolymphocyte
Thrombocytes (Platelets)
Thrombopoiesis
Erythrocyte [2] (Red blood cell)
Erythropoiesis
Basophil
Neutrophil
Eosinophil
Granulopoiesis
Monocyte
Monocytopoiesis
Small lymphocyte [4]
Natural killer cell (Large granular lymphocyte)
B lymphocyte
T lymphocyte
Lymphopoiesis
Plasma cell
Mast cell
Macrophage
Myeloid dendritic cell [3]
Lymphoid dendritic cell [3]

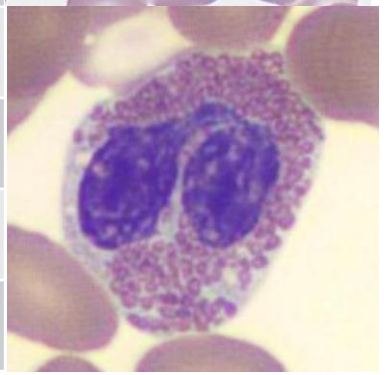
PERIPHERAL WHITE BLOOD COUNTS



WBC	RANGE (k/µL)	DIFFERENTIAL (%)
Total	4 - 10	
Neutrophils	1.8 - 7	42 -70
Neutrophilic bands	0 – 0.2	<2
Monocytes	0 – 0.8	0 – 8
Lymphocytes (T, B, NK)	1 – 4.8	10 – 40
Eosinophils	0 – 0.5	0 – 5
Basophils	0 – 0.2	0 - 2







CASE 1: NEUTROPENIA

- 42-year-old woman presents with fever and flank pain
- She had uncomplicated UTI about a week ago
- Past medical history:
  - Bipolar affective disorder, illicit substance and alcohol use, ? Rheumatoid arthritis
- Medications:
  - Ciprofloxacin (day 8), aspirin, risperidone (for the past 3 weeks) for recent acute maniac event, lithium, aspirin
- Exam:
  - Vitals: Temp: 38.6°C, BP: 110/66 mmHg HR: 110/min
  - Oriented, lethargic, left flank pain

CASE 1: DATA

- Lab results:
  - Hgb: 13 g/dL, MCV 89 fL, normal RPI. WBC 5.4 k/µL. Platelets: 395 k/µl
  - Diff: *neutrophils 0.3 k/µL*, monocytes 0.9 k/µL, lymphocytes: 3.9 k/µL, eosinophils: 0.3 k/µL
- Urinalysis:
  - Esterase +, no WBC, 3+ RBC
  - Gram stain: gram negative rods
- Radiology:
  - Chest X-ray: normal
  - KUB: No obstruction

ACQUIRED NEUTROPENIA

DECREASED PRODUCTION

Medications (dose-dependent & idiosyncratic)

Chronic idiopathic neutropenia (CIN)

Nutritional deficiency (B12, folate)

Infection (e.g. HIV, CMV, EBV, Parvo)

Infiltration (e.g. T-LGL, fibrosis, myeloma)

Primary hematopoietic disorders (MDS, AA)

INCREASED DESTRUCTION

Medication-related antibody mediated

Medication-related idiosyncratic

Post-infectious antibody mediated

Auto-immune (e.g. RA, SLE)

Immune (CIN)

INCREASED CONSUMPTION

Bacterial infection

Sepsis

SEQUESTRATION

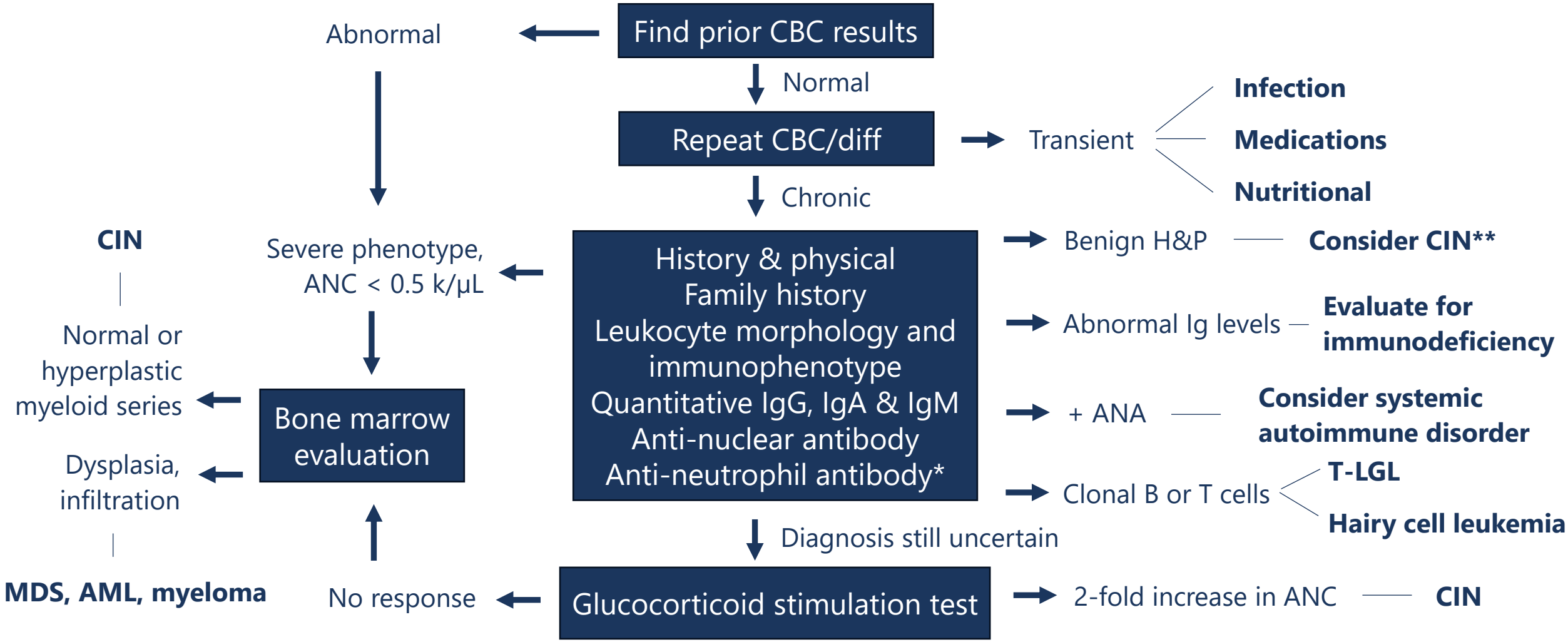
Hypersplenism

Splenomegaly

Myelokathexis (e.g. WHIM syndrome)

Hematology Am Soc Hematol Educ Program 2021. (1): 492–503

DIAGNOSTIC APPROACH TO NEUTROPENIA



*Granulocyte agglutinin & immunofluorescence test (GAT, GIFT): ~35%+ in adults with CIN

**CIN: chronic idiopathic/immune neutropenia

Hematology Am Soc Hematol Educ Program 2016. (1): 38-42

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  - Gram stain: gram negative rods
- Radiology:
  - Chest X-ray: normal
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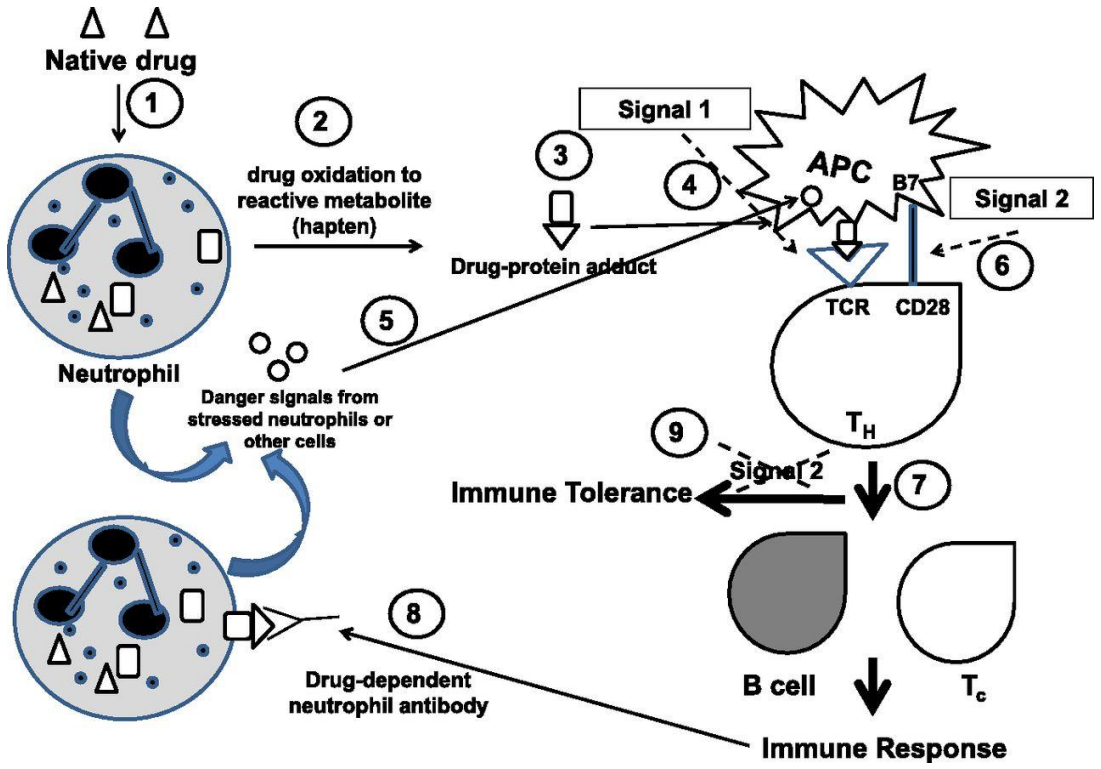
Several CBCs from the past: normal WBC/ANC

Repeat CBC 2 weeks later: normal ANC

IDIOSYNCRATIC DRUG-INDUCED NEUTROPENIA



Huber et al	Medrano-Casique et al
Carbamazepine†	Benzylpenicillin†
Clozapine†	Cefipime†
Metamizole (dipyrone)†	Linezolid
Sulfasalazine†	Meropenem†
Thiamazole†	Metronidazole
	Piperacillin-tazobactam†
	Teicoplanin
	Tobramycin
	Torsemide
	Vancomycin†

Andrés et al	Curtis
Amoxicillin†	Cefipime
Carbimazole†	Ceftriaxone‡
Clozapine†	Ciprofloxacin‡
Cotrimoxazole†	Clindamycin
Cefotaxime	Ibuprofen
Noramidopyrine	Levetiracetam
Piperacillin-tazobactam	Piperacillin-tazobactam‡
Salazopyrine	Quetiapine
Ticlopidine†	Sulfamethoxazole/trimethoprim‡
Valganciclovir	Tacrolimus
	Vancomycin‡
	Venlafaxine

†Five most frequently associated drugs.
‡Five most suspected drugs.

Hematology Am Soc Hematol Educ Program 2017. (1): 187-193

MANAGEMENT OF MEDICATION-INDUCED NEUTROPENIA

- Withdraw all non-essential medications, herbals and OTC meds
- Expect ANC recovery within 1-2 weeks of medications removal
- Slower recovery for ANC < 0.1 k/μL, sepsis or severe infection
- Broad-spectrum antibiotics as indicated for fever and infection or prophylaxis (case-by-case basis)
- Marrow biopsy:
  - If abnormal RBC/platelets or delayed recovery
- G-CSF:
  - Beneficial for ANC <0.1 k/μL (even without infection)
  - Consider for ANC < 0.5 k/μL in elderly w/wo infection, severe comorbidity, sepsis etc.

AUTO-IMMUNE NEUTROPENIA

- Commonly seen in patients with RA, SLE, Sjogren's
- Medications: PTU, rituximab
- Felty syndrome: RA (usually severe), splenomegaly (90%) & neutropenia
  - Anti-G-CSF ab (70%) ± increased oligoclonal CTLs (LGLs)
- SLE-associated neutropenia
  - 25-50% incidence
  - Anti-SSA/Ro, anti-SSB/La, TNF-related apoptosis
- Therapy:
  - Glucocorticoids, methotrexate, cyclosporine
  - Low-dose G-CSF; *beware of symptom flare, leukocytoclastic vasculitis, splenomegaly*

Nat Rev Immunol 2024. 24(3):161-177

CHRONIC IDIOPATHIC (IMMUNE) NEUTROPENIA

- Diagnosis of exclusion:
  - Chronic ANC < 0.5 k/μL
  - No associated auto-immune disorder, medication or infection
- Prevalence:
  - 1.7%, Females > males (2:1); adults > children; median age: 25 years
- Etiology:
  - Immune mechanism impairing neutrophil production in marrow
- Therapy:
  - Low dose G-CSF (1 μg/kg/day)*

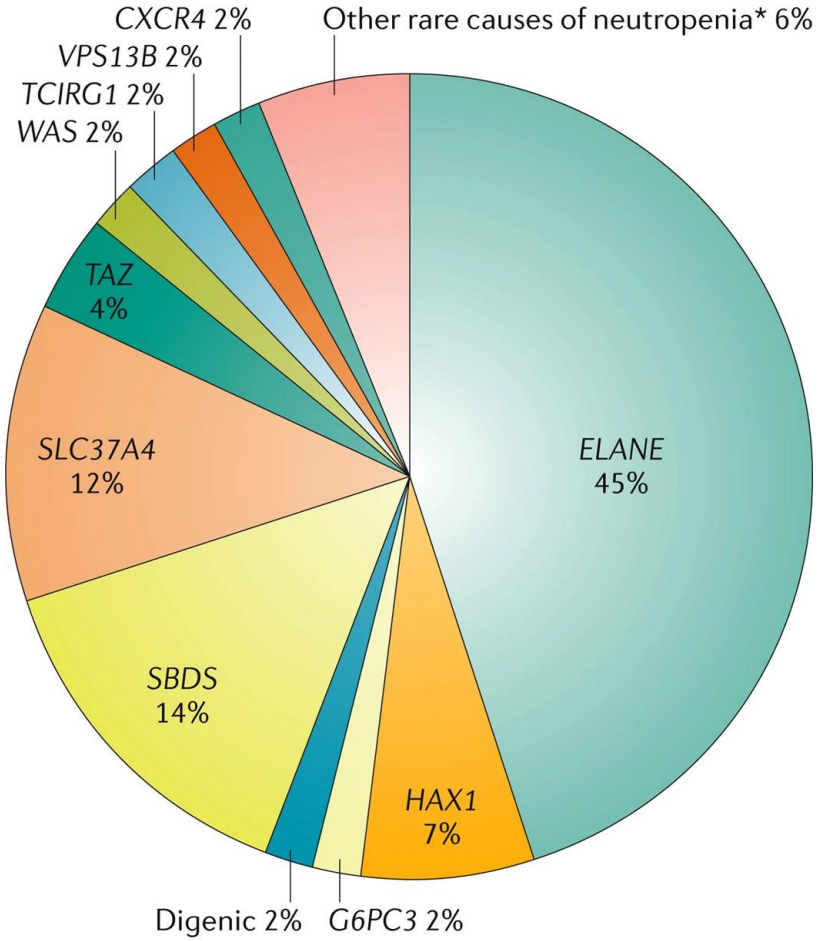
Events	Mouth ulcers	Otitis	Cellulitis	Skin abscesses	Pneumonia	Sepsis	Peritonitis
Before G-CSF	235	213	56	211	84	23	3
On G-CSF	82	73	18	44	22	1	0

*Data from SCNIR Registry

Current Opinion in Hematology 2017. 24(1): 46-53; Blood Adv 2022. 6 (13): 3861–3869

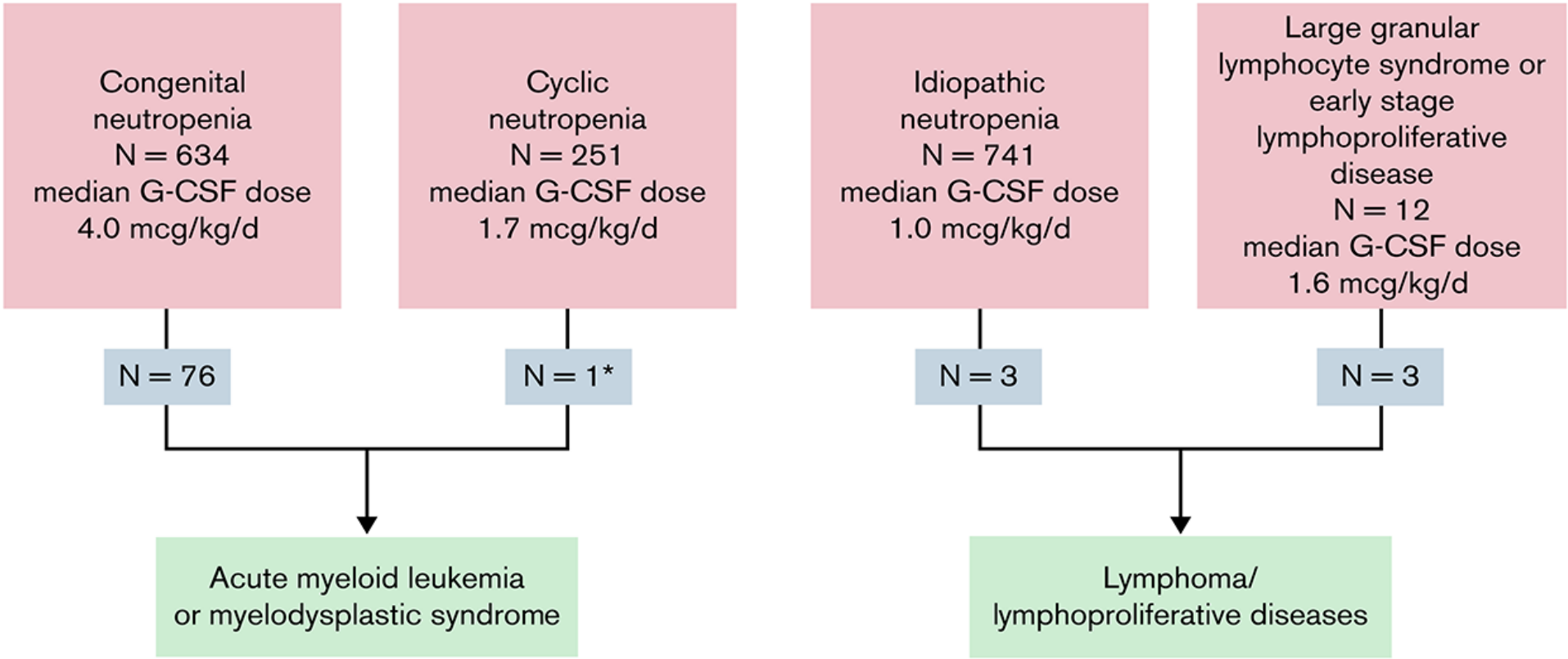
CONGENITAL NEUTROPENIA

- Severe congenital neutropenia (SCN)
- Cyclic neutropenia
- Other inherited neutropenia syndromes
  - Schwachman-Diamond syndrome
  - WHIM syndrome*
  - GATA2 deficiency/MonoMAC
  - Chediak-Higashi syndrome
  - Wiskott-Aldrich syndrome
  - Griscelli syndrome
- ACKR1/DARC-associated neutropenia (ADAN) (previously BEN & DANC)



Nat Rev Dis Primers 2017. (3):17032

OUTCOMES IN SEVERE CHRONIC NEUTROPENIA TREATED WITH G-CSF



*Patient also treated with cyclophosphamide

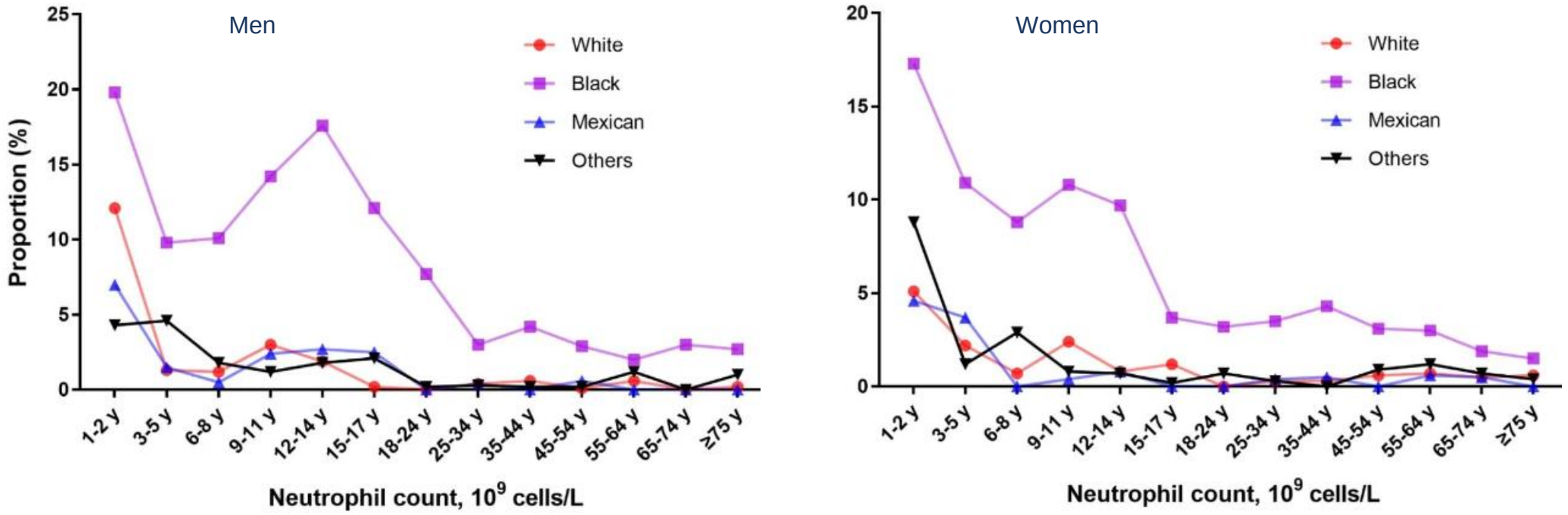
From SCNIR Registry; 1638 patients, >16,000 patient-years of prospective data

Blood Adv 2022. 6 (13): 3861–3869

PREVALANCE OF NEUTROPENIA IN US RESIDENTS

POPULATION BASED ANALYSIS OF NHANES 2011-2018

Neutrophil count < 1.0 k/μL



BMC Public Health 2023. 23(1):1254

CASE 2: NEUTROPHILIA

- 36-year-old man from Croatia presents with sporadic self-limiting abdominal pain for the past 15 years; more frequent episodes over the past year (~once a month). No triggers, but associated with fever, irritability, anxiety, muscle aches and testicular pain. Resolves over 2 days. Weight loss of around 10 lbs.
- Multiple ED visits; leukocytosis: WBC ~ 13-15 k/µL; ANC 9.6-11 k/µL
- Past medical history:
  - Bipolar affective disorder, illicit substance and alcohol use, ? Rheumatoid arthritis
- Medications:
  - Codeine
- Family/social history:
  - Living in the US for 10 years. Works at Microsoft. Non-smoker.
- Exam:
  - Afebrile. No organomegaly. No skin rash. No lymphadenopathy.

CASE 2: DATA

- Lab results:
  - Hgb: 13.6 g/dL, MCV 90 fL, normal RPI. *WBC 13.4 k/µL*. Platelets: 252 k/µl. *Neutrophils 10.1 k/µL.* No left shifted myeloid maturation.
  - ESR 45 mm/hr
  - Normal liver enzymes, lipase and renal functions
- Urinalysis:
  - 3+ protein
  - No WBC or RBCs
- Radiology:
  - CT abdomen: Prominent mesenteric lymph nodes. Normal liver, spleen and kidneys.

NON-CLONAL NEUTROPHILIA

SECONDARY /REACTIVE

Infections

Inflammation

Obesity, smoking

Tumor (secreting G-CSF)

Medications: lithium, steroids, G-CSF

DEMARGINATION/ DECREASED SEQUESTRATION

Asplenia

Corticosteroids

CONSTITUTIONAL

Down's syndrome

Transient myeloproliferative disorder *(GATA1)*

Hereditary chronic neutrophilia *(CSF3R)*

PRIMARY NEUTROPHIL DISORDERS WITH NEUTROPHILIA

Auto-activation: Familial mediterranean fever

Abnormal trafficking: Leukocyte-adhesion deficiency

Abnormal phagocytosis: Chronic granulomatous disease

Hematology Am Soc Hematol Educ Program 2012. (1): 475-484; Am J Hematol 2024. 99(7):1360-1387

CASE 3: EOSINOPHILIA

- 21-year-old man admitted to the hospital after having a cardiac arrest
  - Troponin I: 5.6 ng/mL, BNP: 10,050 pg/mL
  - Urine drug screen: + amphetamines
  - Echocardiogram: LVEF 15-20%, concentric LV hypertrophy, ballooning apex
  - On IABP

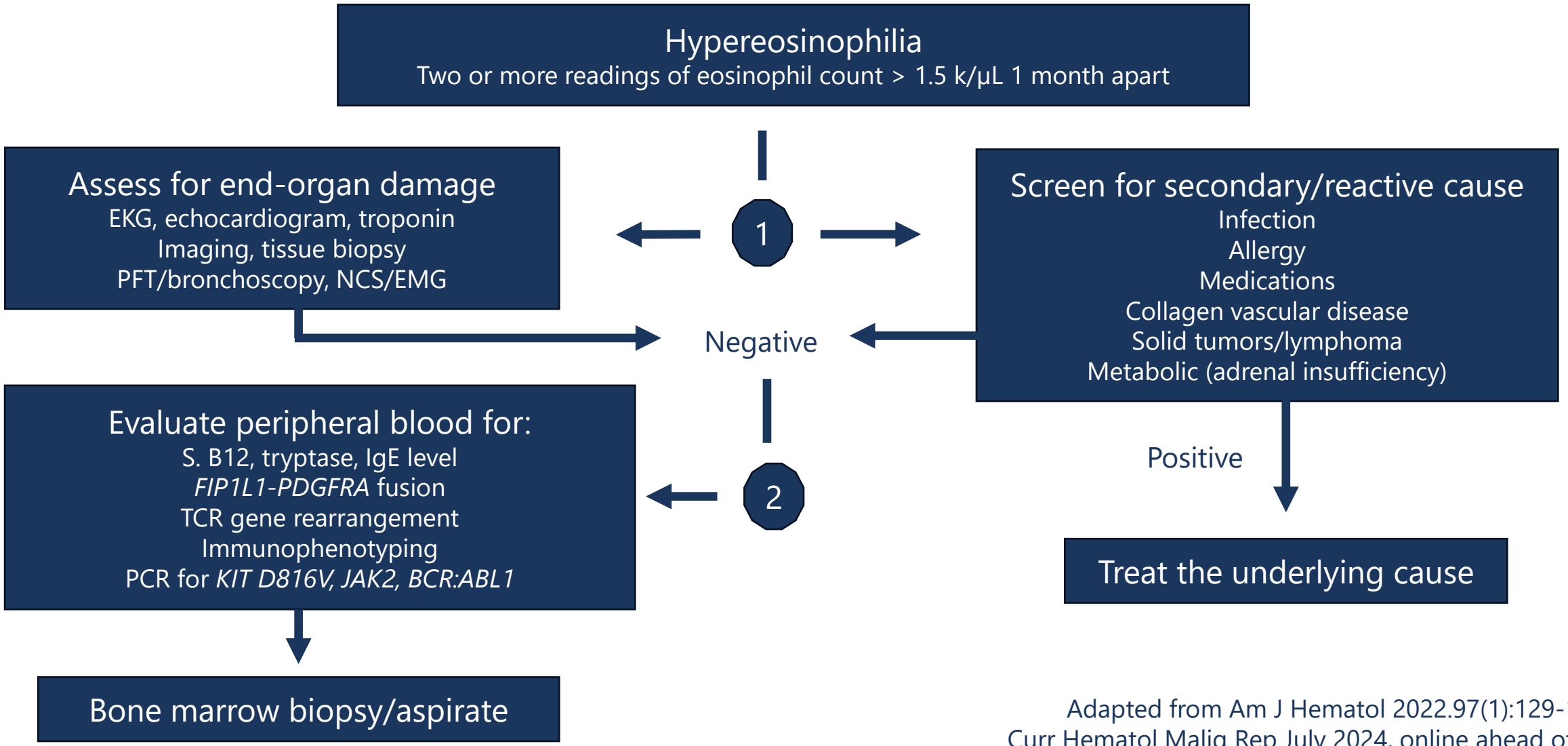
	DAY 1	DAY 2	DAY 3	1 month prior
WBC, k/μL	15.8	18.3	16.1	15
Hgb, g/dL	11.5	10.5	10	13
PLTs, k/μL	120	115	105	150
% neutrophils	40	42	38	35
% eosinophils	45	40	48	50
Eosinophil, k/μL	**7.11**	**7.32**	**7.73**	**7.5**

HYPEREOSINOPHILIA

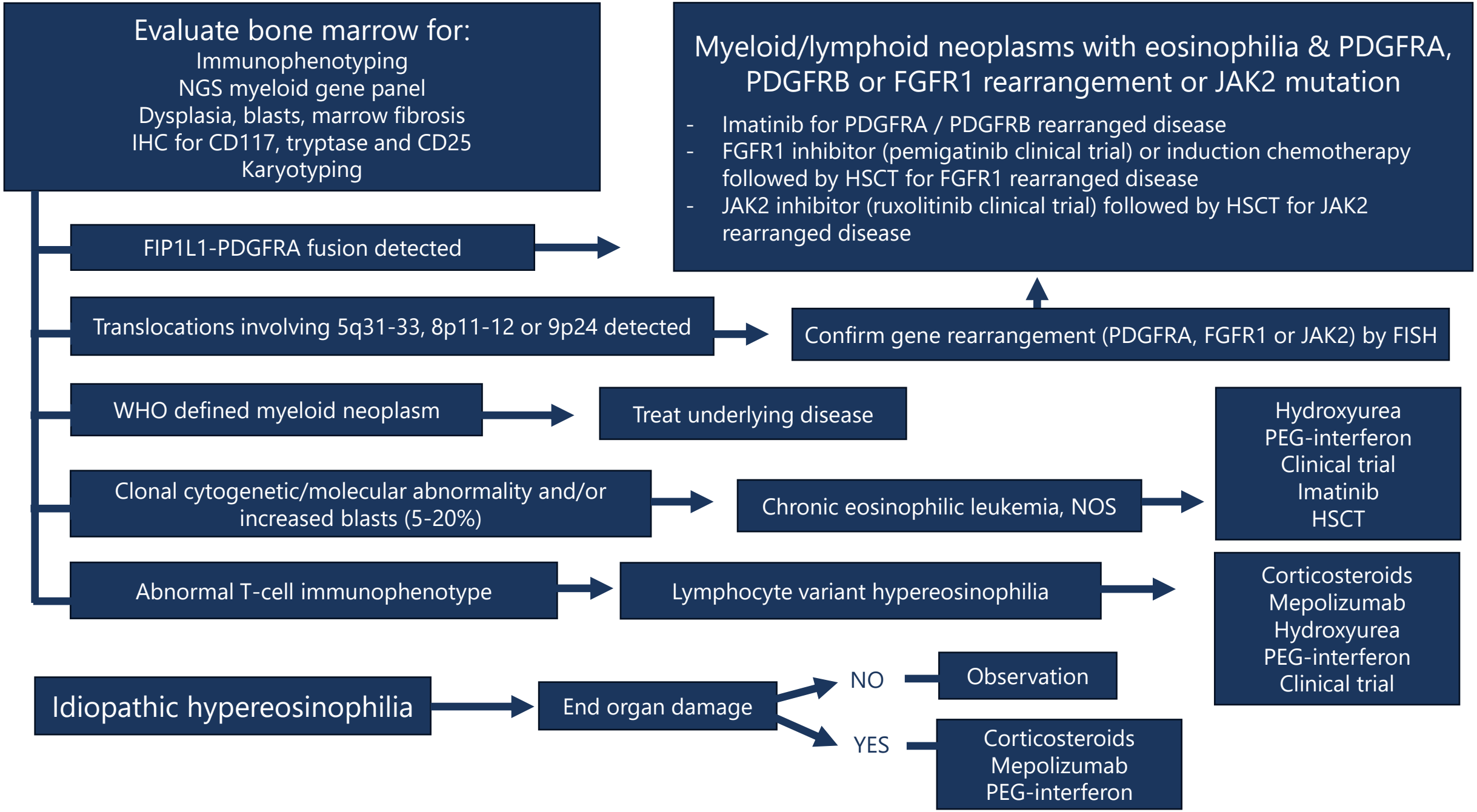
- Two or more readings of eosinophil count > 1.5 k/μL, 1 month apart and/or pathologic confirmation of tissue hypereosinophilia
  - > 20% eosinophils on bone marrow section
  - Extensive tissue infiltration
  - Marked deposition of eosinophil granule proteins in tissue (e.g. eosinophil peroxidase)
- Hypereosinophilic syndrome (HES)
  - Hypereosinophilia with eosinophil-mediated organ dysfunction
  - Other potential causes of tissue damage should be excluded
  - Primary (neoplastic): underlying clonal stem cell or myeloid/eosinophilic neoplasm
  - Secondary (reactive): infections, allergy, Addison's, collagen-vascular disorders (e.g.EGPA)
  - Idiopathic: cause remains unknown despite thorough work-up

Hematology Am Soc Hematol Educ Program 2022. (1): 47-54

APPROACH TO EOSINOPHILIA



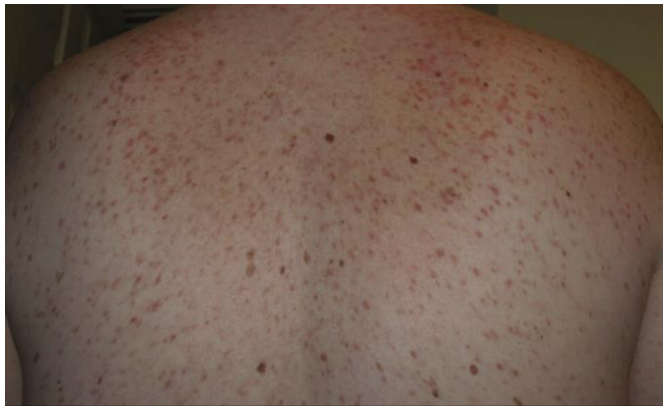
Adapted from Am J Hematol 2022.97(1):129-148 &
Curr Hematol Malig Rep July 2024, online ahead of print



Adapted from Am J Hematol 2022.97(1):129-148 & Curr Hematol Malig Rep July 2024, online ahead of print

CASE 3: MAST CELL DISEASE

- 60-year-old man with episodic cramping abdominal pain, nausea and diarrhea
- Likely triggers: stress and spicy food. Resolves over 5-7 days.
- Occasional episodes of flushing, presyncope, hive and itching
- Past medical history:
  - Gastric ulcer 6 months ago. Urticaria for 4-5 years
- Medications:
  - Omeprazole
- Exam:
  - Pigmented macular, dermatographism and Darier's sign +
- Labs:
  - Normal CBC & LFTs. Normal lipase and VIP
  - Tryptase 35 ng/mL; 24h urine histamine/creatine: 2100 nmol/g



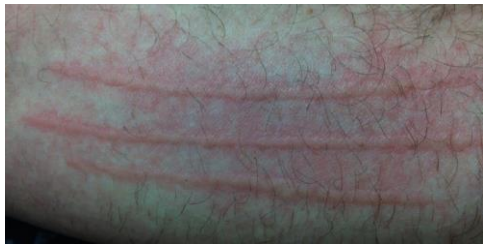
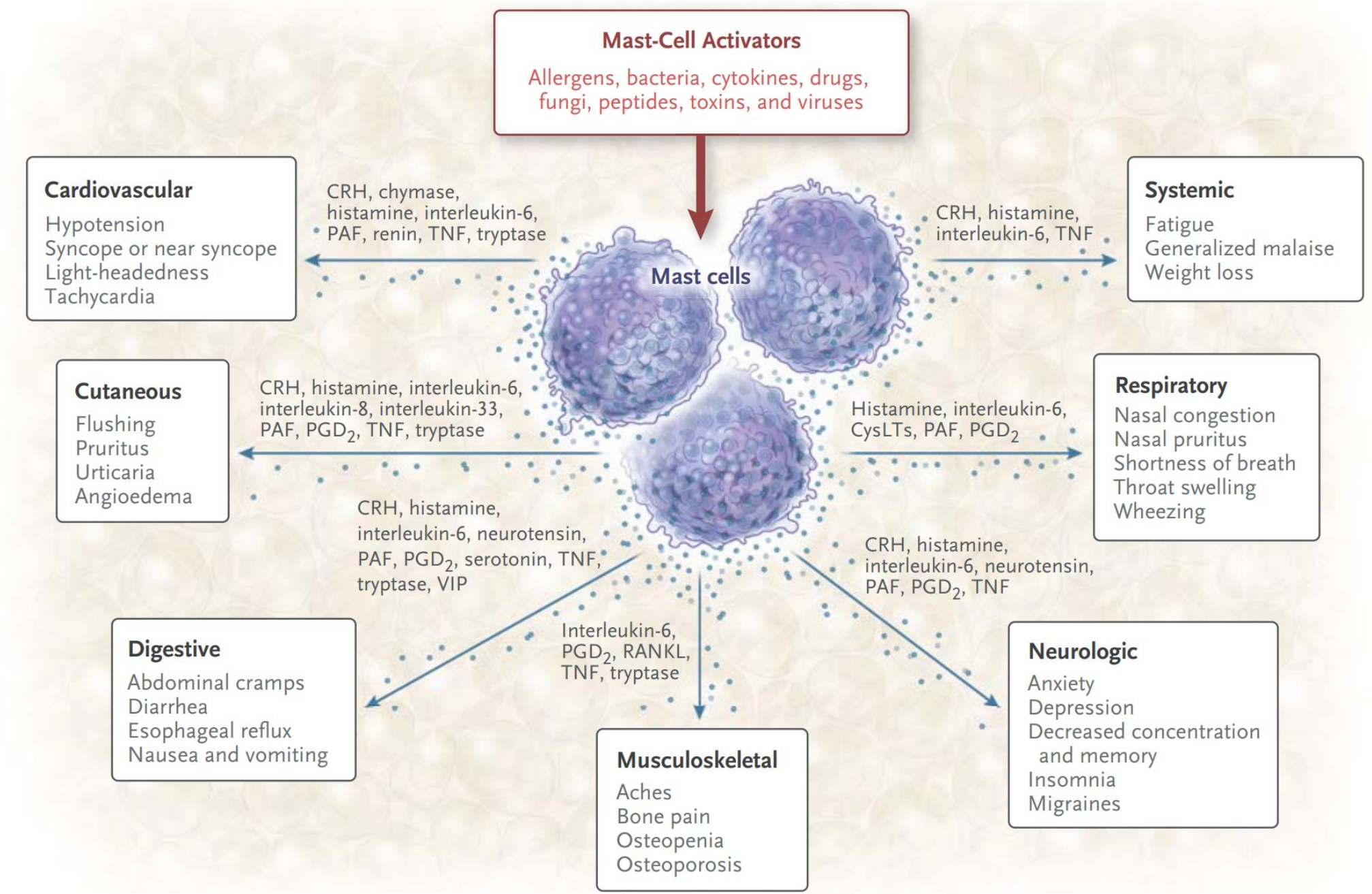


Image source: consultant360.com



The New England Journal of Medicine, 2015. 373 (2): 163-172

MAST CELL DISEASE

- Two categories: cutaneous mastocytosis (CM) and systemic mastocytosis (SM)
- Difficult to distinguish on clinical grounds, because both disorders can have the same skin lesions, systemic symptoms, and complications
- CM variants: usually indolent course
  - Maculopapular CM
  - Diffuse CM
  - Mastocytoma of the skin
  - *Telangiectasis macularis perstans**
  - *Nodular mastocytosis**
- SM variants: disparate clinical course
  - Indolent SM
  - Smoldering SM
  - SM with aggressive myeloid neoplasm
  - Aggressive SM
  - Mast cell leukemia

Am J Hematol 2023. 98(7):1097-1116

SYSTEMIC MASTOCYTOSIS: DIAGNOSIS

- WHO diagnostic criteria
  - Major
    - Multifocal mast cell infiltrates (>15 cells/infiltrate) in tissue other than skin
  - Minor
    a. Bone marrow or extracutaneous tissue infiltrates: >25% are spindle-shaped or have atypical morphology
    b. *KIT* D816V point mutation in bone marrow, blood or extracutaneous organ.
    c. Mast cells co-express CD25 ± CD2 in addition to normal mast cell markers
    d. Serum total tryptase persistently exceeds 20 ng/ml
  - Diagnosis requires 1 major + 1 minor, or 3 minor criteria
  - ICC and WHO subtype of SM variants: based on B* & C* findings
  - Risk scoring for SM: REMA & MAPS scores

Am J Hematol 2023. 98(7):1097-1116

SYSTEMIC MASTOCYTOSIS: TREATMENT

Indolent/smoldering SM

Avoid triggers of mast cell degranulation
Narcotics, EtoH, contrast dye, anesthetics

Symptom management
H1/H2 blockers, epinephrine, corticosteroids, leukotriene inhibitors, topical agents, ketotifen, cromolyn sodium, omalizumab,

Avapritinib
For patients with moderate-to-severe symptoms despite optimal symptom-directed therapies

Osteoporosis/osteopenia
Calcium & vitamin D, bisphosphonates, denosumab, vertebroplasty/kyphoplasty

Perioperative management

Clinical trials
(e.g. bezuclastinib, BLU-263, masitinib)

Aggressive SM

Avapritinib

Clinical trials
(e.g. bezuclastinib, BLU-263)

Midostaurin or cladribine
Cladribine preferred if rapid debulking is indicated; midostaurin as maintenance post-HSCT

Imatinib
Eosinophilia with FIP1L1-PDGFRA or KIT D816V-negative

Interferon-α
Pegylated forms likely better tolerated ±prednisone

Allogeneic hematopoietic stem cell transplant (AHSCT)

SM-AMN

Integrate clinical, histologic, and molecular data to assess which disease component (SM or AMN) warrants immediate treatment

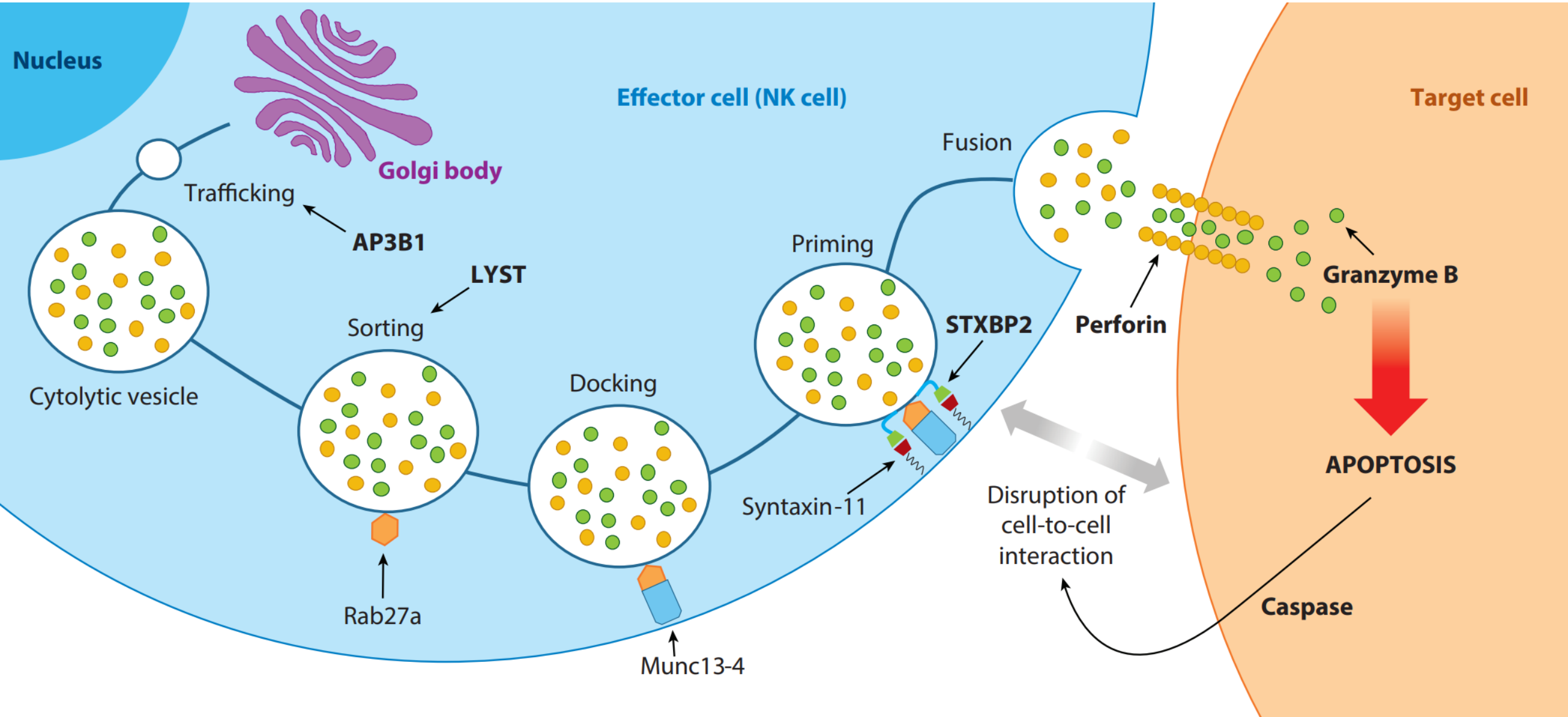
For aggressive AMN (with low burden SM): treat the AMN as per standard of care (e.g. AHSCT) with symptom management of SM as indicated

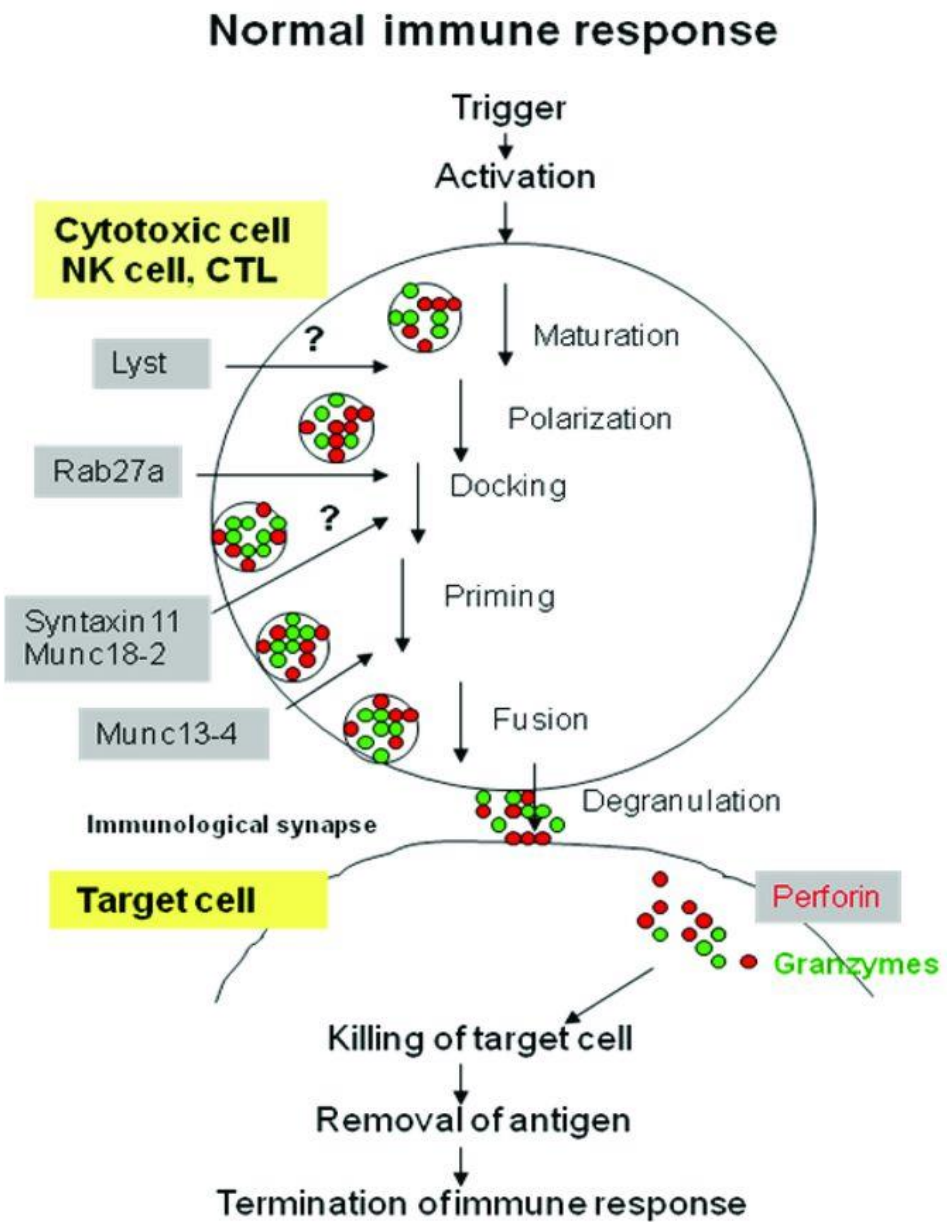
For SM causing organopathy (with indolent AMN): treat as aggressive SM; treat indolent AMN e.g. PV or ET with observation or treatment as per standard of care

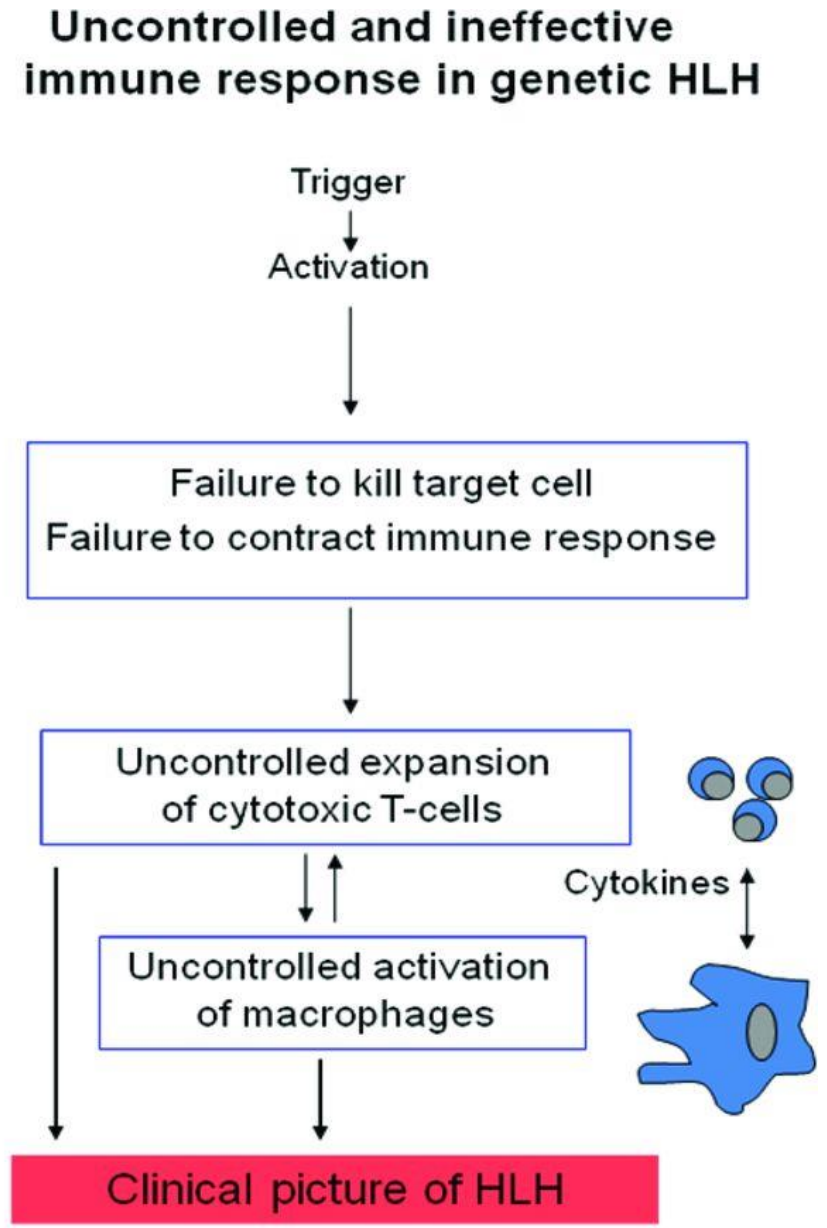
Disease progression
Restage to assess dominant component, SM or AMN; appropriate salvage therapy including AHSCT as indicated, molecular assessment may guide targeted therapy

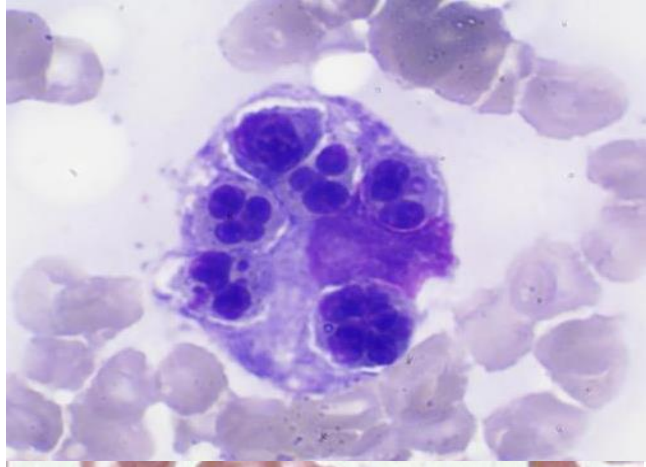
Adapted from Am J Hematol 2023. 98(7):1097-1116

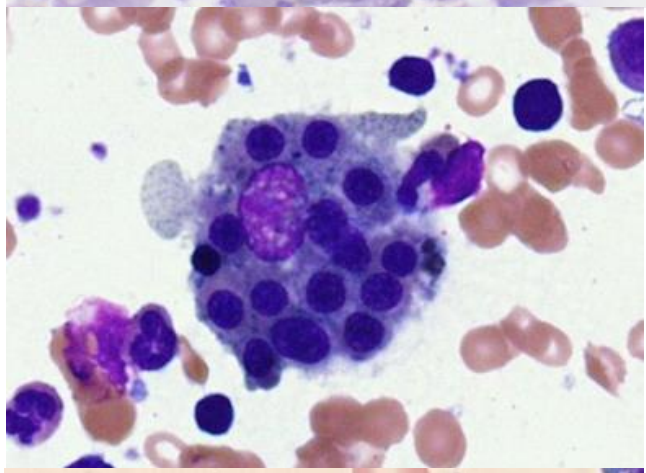
CTL & NK-CELL CYTOTOXICITY: 'KISS OF DEATH'

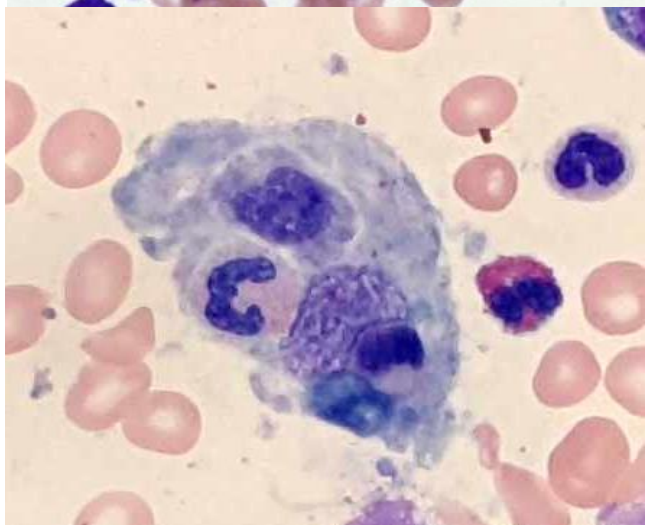










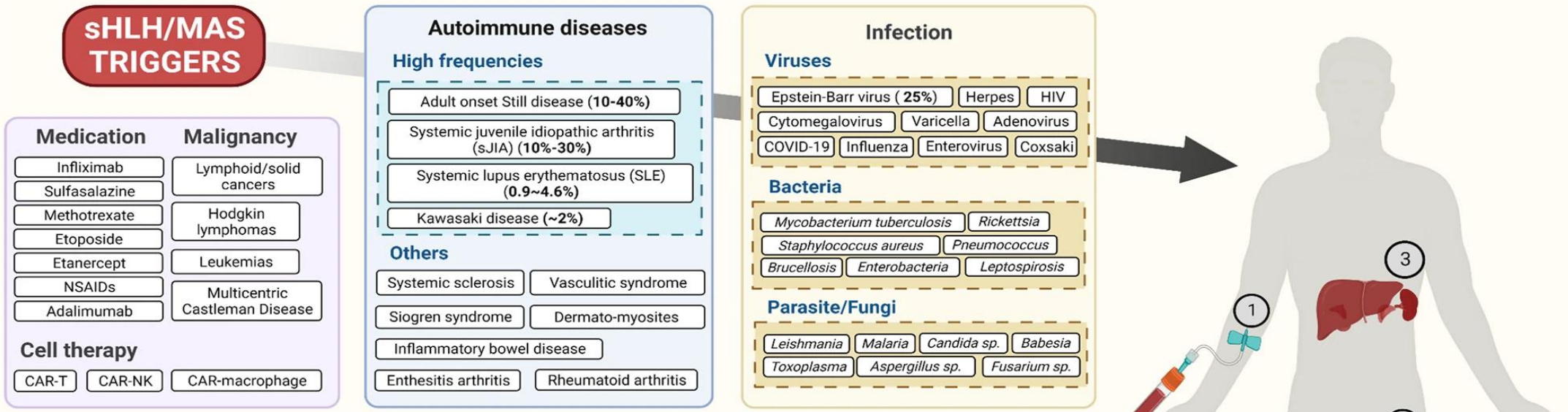


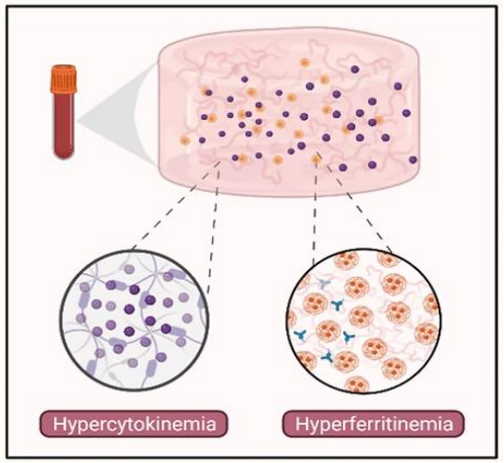
Hematology Am Soc Hematol Educ Program 2013 (1): 605-611
Image source of HLH: ASH imagebank, hematology.org/collection/

PRIMARY HLH: INHERITED CTL/NK-CELL DEFECTS

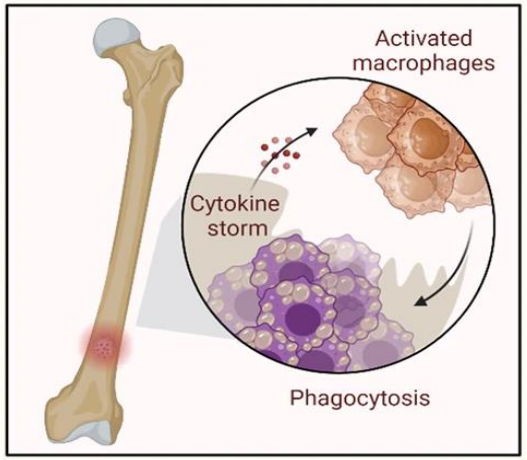
HLH ASSOCIATED WITH LYMPHOCYTE CYTOTOXIC DEFECTS
FHL1: Unidentified gene on chromosome 9
FHL2: Perforin (*PRF1*) mutation
FHL3: Munc13-4 (*UNC13D*) mutation
FHL4: Syntaxin 11 (*STX11*) mutation
FHL5: Syntaxin binding protein (*STXBP2*)
FHL WITH HYPOPIGMENTATION
Chediak-Higashi syndrome 1: *LYST* (=*CHS1*) mutation
Griscelli syndrome 2: *RAB27A* mutation
Hermansky-Pudlak syndrome: *HSP2 & AP3B1* mutation
FHL ASSOCIATED WITH INFLAMMASOME ACTIVATION DEFECTS
X-linked lymphoproliferative disorder type 1: *SH2D1A* mutation
X-linked lymphoproliferative disorder type 2: *BIRC4* mutation

Blood 2016.127(22):2672-81



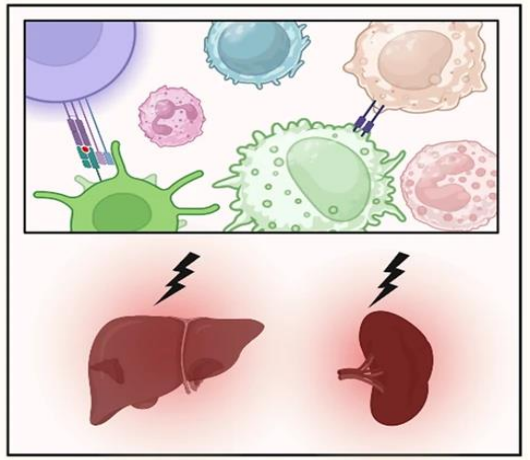


1) Ferritin > 500 ng/ml
2) Cytokine storms: ↑IFN-γ, TNF-α, IL-1, IL-6, IL-18, sCD25 (IL-2Rα)



2) HEMOPHAGOCYTOSIS

Bone marrow biopsy showing the phagocytosis of erythrocytes, lymphocytes or other hematopoietic precursors by activated macrophages as a result of cytokine storms

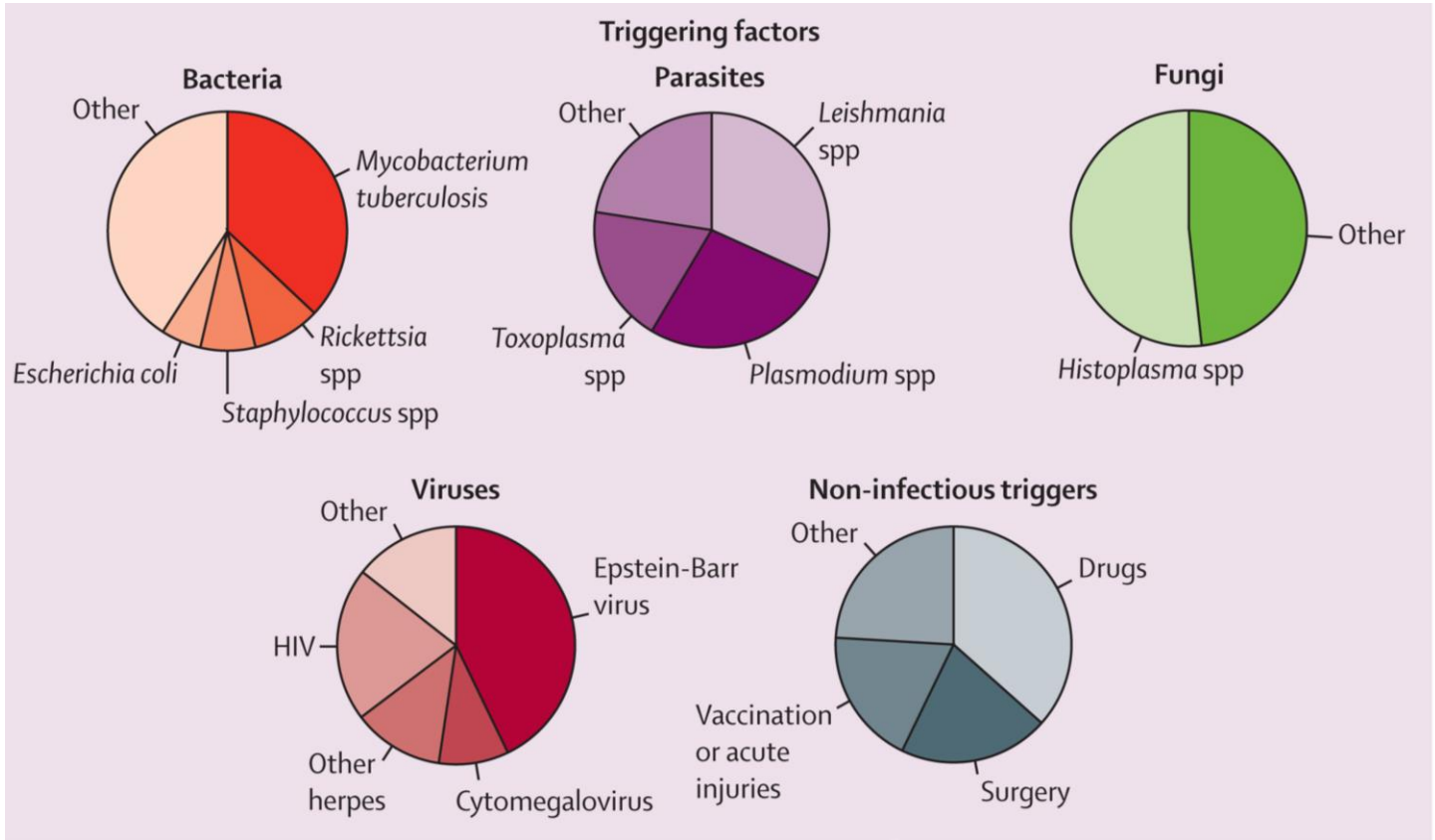


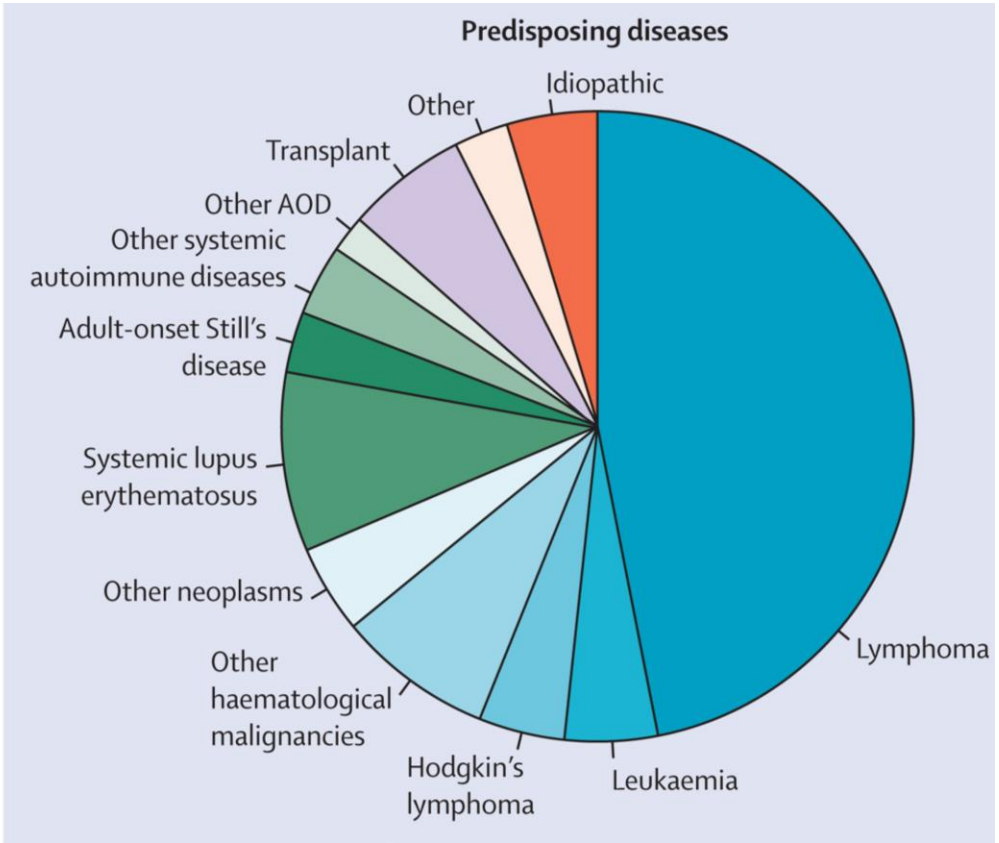
3) HEPATOSPLENOMEGALY

Cytokine storms caused by overaction and interactions of immune cells cause organ failure; enlargement of the liver and spleen is signature feature of MAS, correlation with ↑ALT, AST, TG , ↓ albumin and fibrinogen

Experimental & Molecular Medicine 2024. (56): 559–569

SECONDARY HLH: TRIGERRING FACTORS AND PREDISPOSING DISEASES





The Lancet 2014. 383(9927): 1503-1516

Criteria	HLH-04[a]	HScore[b]	2016 sJIA MAS	MS score
Fever (°C)	≥38.5	0 (<38.4), 33 (38.4–39.4), 49 (>39.4)	Degree not specified	NA
Ferritin (ng/mL)	≥500	0 (<2,000), 35 (2,000–6,000), 50 (>6,000)	>684	0.0001 × serum level
Organomegaly	Splenomegaly	0 (no), 23 (hepato- or splenomegaly), 38 (both)	NA	NA
Hematologic	Two or three out of three lineages	0 (one lineage), 24 (two lineages), 34 (three lineages)	Platelets ≤ 181 × 10^9/L	–0.003 × platelet count
Hemorrhagic	NA	NA	NA	1.54 (yes) or 0 (no)
Triglyceride	≥265 mg/dL[c]	0 (<1.5 mmol/L), 44 (1.5–4 mmol/L), 64 (>4 mmol/L)	>156 mg/dL	NA
Fibrinogen	≤1.5 g/L[c]	0 (>2.5 g/L), 30 (≤2.5 g/L)	≤360 mg/dL	–0.004 × serum level
LDH	NA	NA	NA	0.001 × serum level
AST	NA	0 (<30 IU/L), 19 (≥30 IU/L)	>48 units/mL	NA
CNS involved	NA	NA	NA	2.44 (yes) or 0 (no)
Arthritis active	NA	NA	NA	–1.3 (yes) or 0 (no)
Known immuno-suppression	NA	0 (no), 18 (yes)	NA	NA
Pathology	Hemophagocytosis	Hemophagocytosis: 0 (no), 35 (yes)	NA	NA
NK cell activity	Low or absent	NA	NA	NA
sCD25	≥2,400 units/mL	NA	NA	NA
Diagnosis	Five of eight criteria	Sum of scores > 169	Fever + sJIA + elevated ferritin + two of four criteria	Sum ≥ –2.1

[a]Hemoglobin < 90 g/L, platelets < 100 × 10^9/L, neutrophils < 1.0 × 10^9/L.
[b]Hemoglobin < 92 g/L, platelets < 110 × 10^9/L, leukocytes < 5.0 × 10^9/L.
[c]Either high triglyceride and/or low fibrinogen (counts as one criterion).

[b]https://saintantoine.aphp.fr/score/

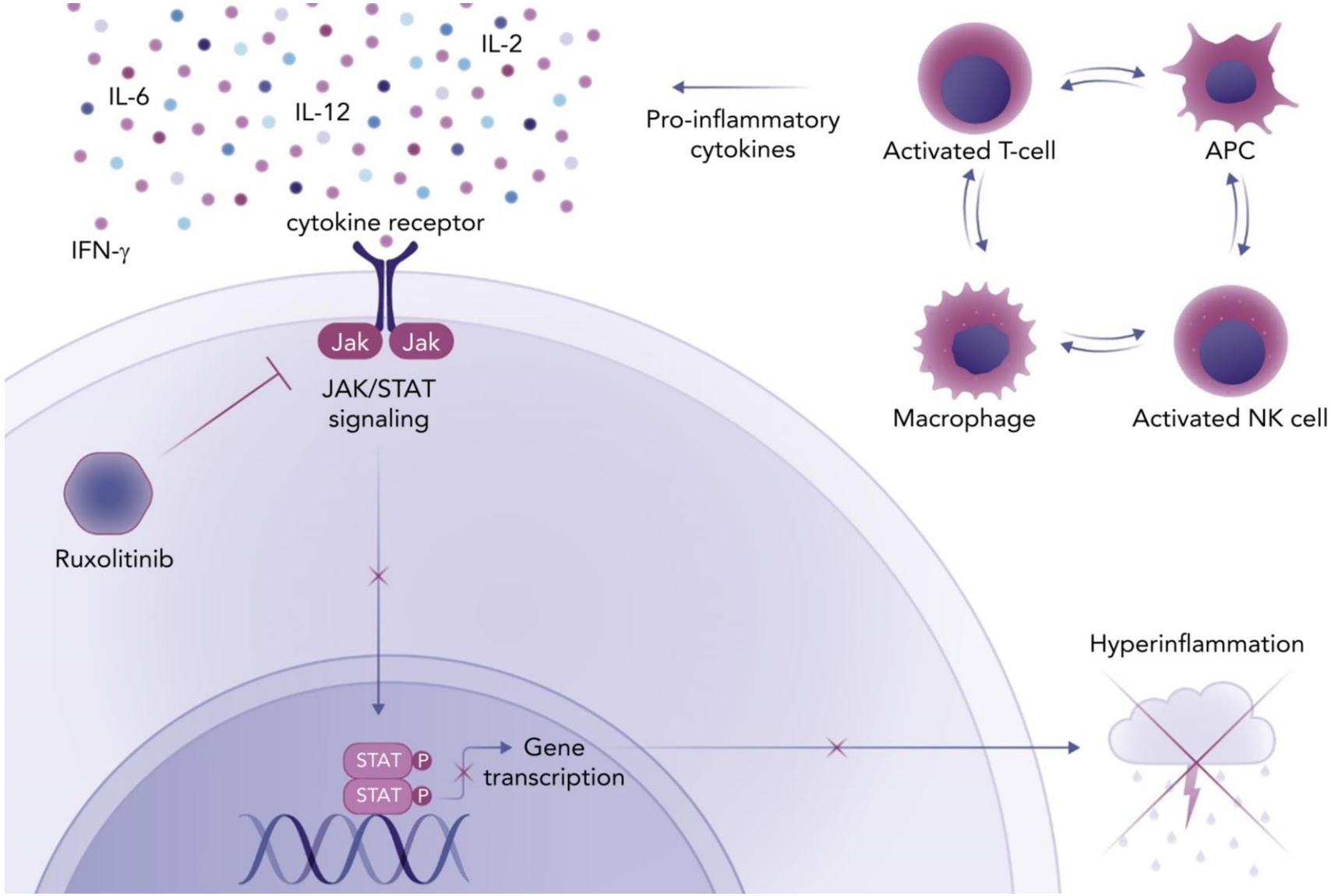
Annu. Rev. Med. 2023. 74:321–37

TREATMENT OPTIONS FOR HLH

Type	Example
Cytotoxic agents	Etoposide
	Cyclophosphamide
Glucocorticoids	Dexamethasone
	Methylprednisolone
Calcineurin inhibitors	Cyclosporin A
	Tacrolimus
Cytokine blockade	IL-1 (e.g., anakinra, a recombinant IL-1 receptor antagonist)
	IL-6 (e.g., tocilizumab, an anti-IL-6 receptor monoclonal antibody)
	IL-18 (e.g., tadekinig alfa, a recombinant IL-18 binding protein)
	IFN-γ (e.g., emapalumab, an anti-IFN-γ monoclonal antibody)
	Janus kinase inhibitor (e.g., ruxolitinib, which blocks signaling of multiple cytokines, such as IFN-γ, TNF, and IL-6)
Filtering	Plasmapheresis
	Cytokine-absorbing filter technologies
B cell depletion	Anti-CD20 monoclonal antibody (e.g., rituximab)

Annu. Rev. Med. 2023. 74:321–37

HLH TREATMENT: SMARTER, NOT HARDER



Newly diagnosed HLH patients (n=52) → RUX as frontline agent → Unfavorable responses → Intensive therapy

Frontline treatment with RUX

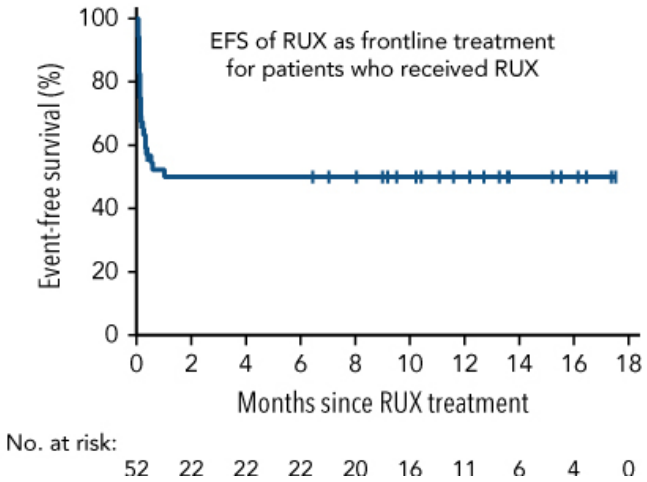
Overall response rate at day-28: 69.2%

- 42.3% (22/52) complete response
- 17.3% (9/52) partial response
- 9.6% (5/52) HLH improvement
- 30.8% (16/52) no response

Treatment response was associated with underlying etiology (p=0.009)

- EBV-HLH was most sensitive to RUX

12-month EFS rate: 50.1%

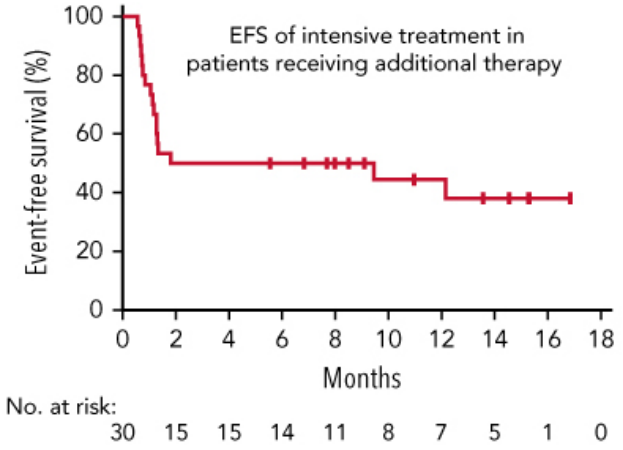


Intensive therapy with additional chemotherapy

Patients entered intensive therapy: 57.7% (30/52)

- 53.3 % complete response at week-8
- 46.7% refractory HLH at week-8 dominated by CAEBV-HLH

The 6-month EFS rate: 35.4%



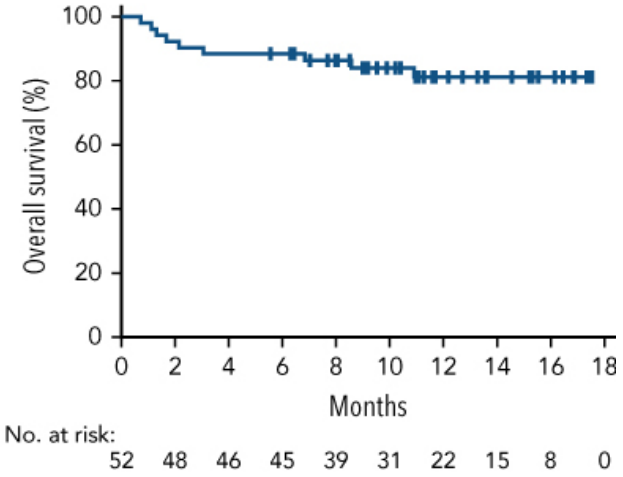
Treatment overall

Complete response: 73.1% (38/52)

Alive at last follow up: 82.7% (43/52)

- Death before HSCT: n=5
- Death after HSCT: n=4

One-year overall survival: 86.4±9.3



Blood 2022. 139 (24): 3493–3504

SUMMARY

Crucial to identify the causes and manage acquired neutropenias, while also considering the possibility of underlying primary congenital disorders

Reactive hypereosinophilia and mastocytosis can be pathological; targeted treatments now available for clonal disorders

HLH and MAS represent primary and acquired disorders driven by CTL/NK cell dysregulation and cytokine storms, resulting in multisystem complications. Early diagnosis is vital, and aggressive immunosuppression is key alongside treating the underlying cause

Fred Hutch Cancer Center

UW Medicine

Thank you