

A microscopic view of blood cells, showing numerous red blood cells (erythrocytes) and several white blood cells (leukocytes) against a reddish background. The red blood cells are biconcave discs, and the white blood cells are larger and more irregular in shape.

„Wenn Blut zur Gefahr wird“
Hämato-Onkologische Notfälle
auf der PICU

Dr. Anna Aichinger

PICU - Medizinische Universität Wien

WARD 6 ↑

ONCOLOGY →



„Wenn Blut zur Gefahr wird“

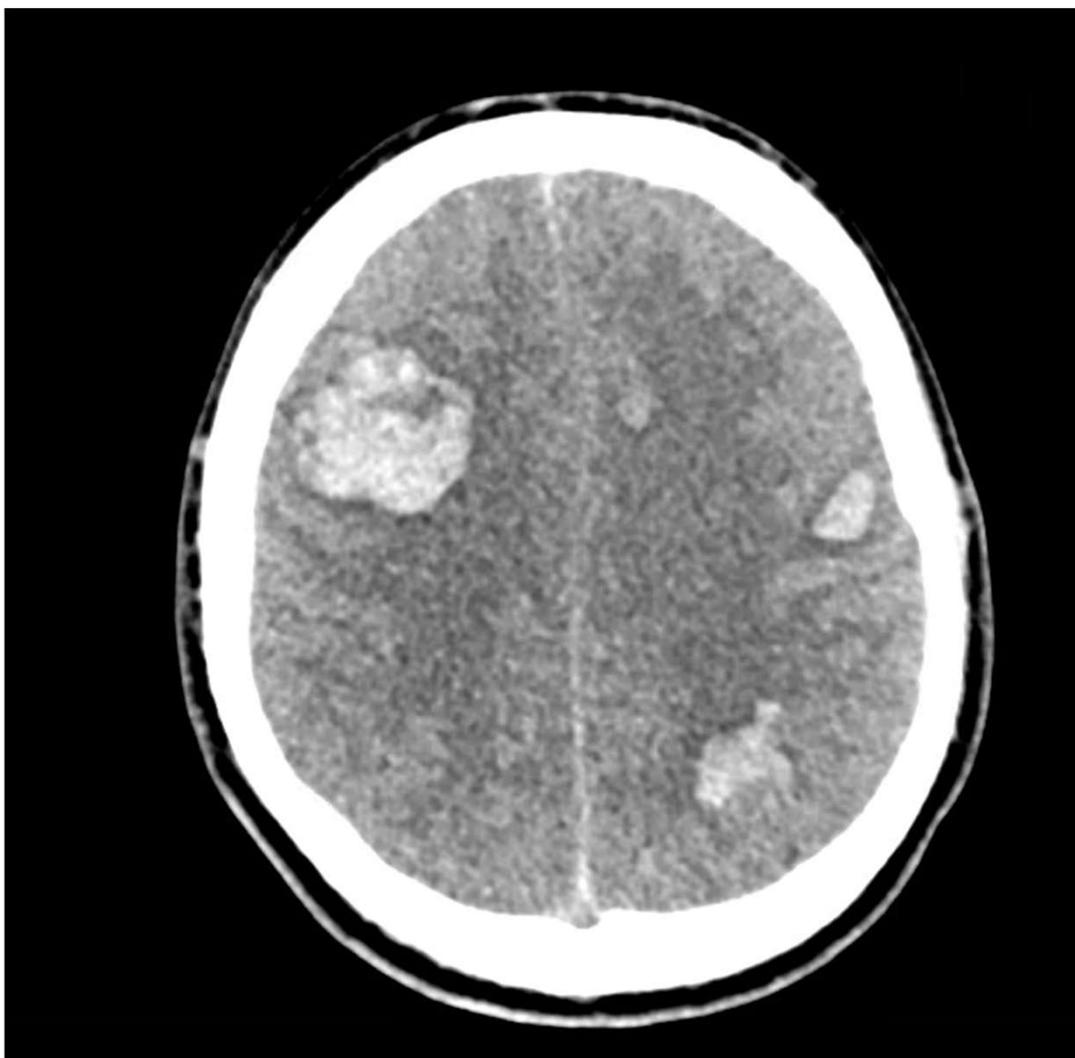
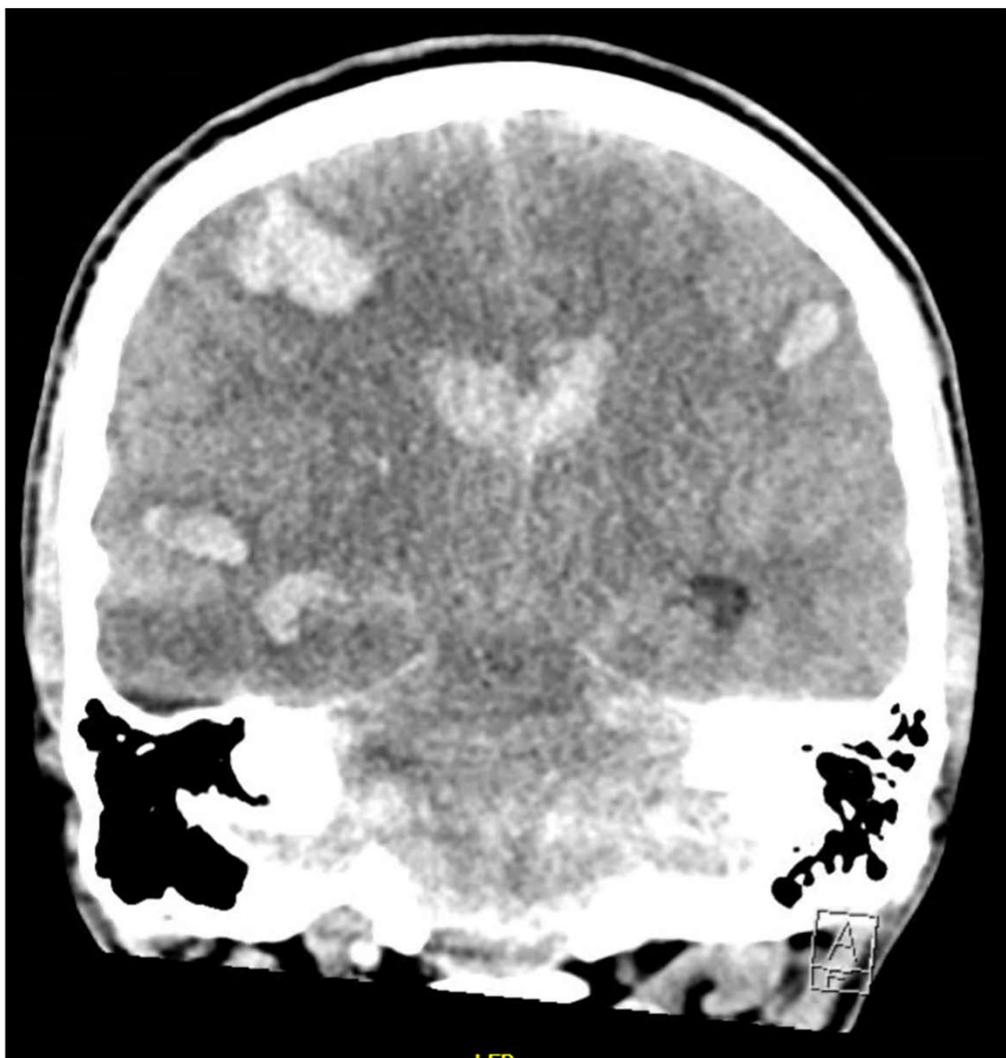
A microscopic view of several red blood cells, showing their characteristic biconcave disc shape and reddish color. The cells are arranged in a cluster, with some in the foreground and others in the background, creating a sense of depth. The lighting is dramatic, highlighting the texture of the cell membranes.

- zu viele Blutzellen
- zerfallende Blutzellen
- zu wenige Blutzellen
- verwirrte Blutzellen
- verformte Blutzellen

Fallpräsentation

- Anruf Rettungszentrale
- 16 Jahre, Krampfanfall, somnolent
- GCS 4, Schutzintubation
- cCT





BLUTBILD

> Erythrozyten #	↓	1.7	4.4 - 5.8	T/L
> Hämoglobin #	↓	4.9	13.5 - 18.0	g/dL
> Hämatokrit #	↓	18.0	40.0 - 52.0	%
> Thrombozyten #	↓	111	150 - 350	G/L
> Mittleres Thrombozytenvolumen #		10.5	7.0 - 13.0	fL
> Leukozyten #	↑	815.27	4.0 - 10.0	G/L
> ASAT (GOT)	↑	109	22 - 44	U/L
> ALAT (GPT)	↑	120	< 18	U/L
> Gamma - GT	↑	83	4 - 16	U/L
> LDH	↑	3143	< 240	U/L

Frage ans Auditorium

Welche Veränderung ist für den Patienten am problematischsten?

- A) erniedrigter Hb
- B) erniedrigte Thrombozytenzahl
- C) erhöhte LDH
- D) erhöhte Leukozytenzahl
- E) erhöhte GGT



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Welche Veränderung ist für den Patienten am problematischsten?

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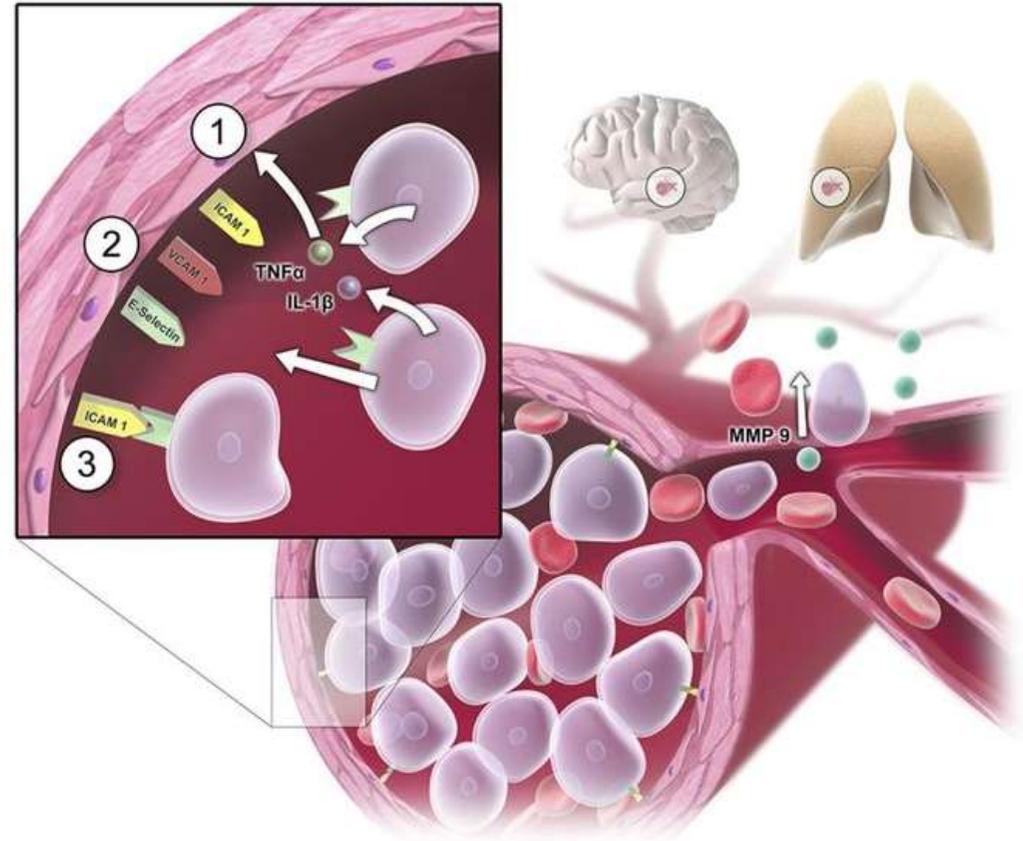
A microscopic view of several red blood cells, appearing as biconcave discs with a textured surface, set against a dark red background. The cells are illuminated from the side, creating a strong contrast and highlighting their three-dimensional structure.

„Wenn Blut zur Gefahr wird“

zu viele Blutzellen

Hyperleukozytose

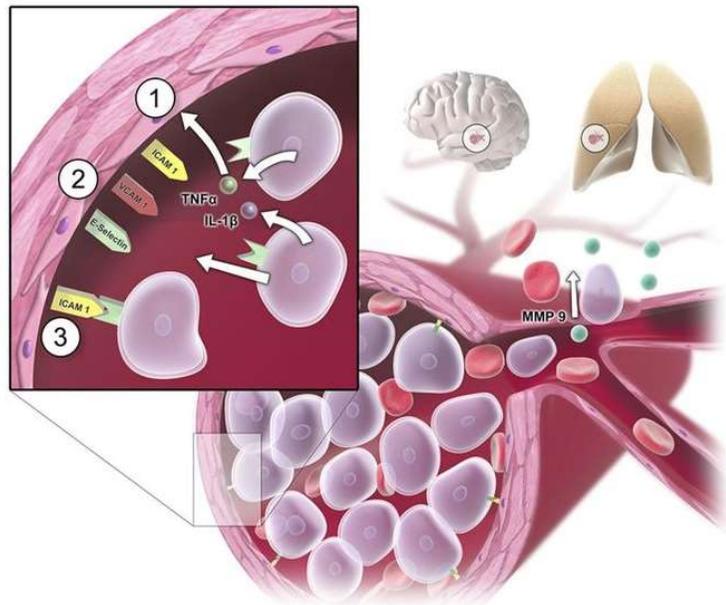
Leukozyten >100 G/L



Christoph Röllig, and Gerhard Ehninger *Blood*
2015;125:3246-3252

Frage ans Auditorium

Wann kann eine massive Hyperleukozytose auftreten?



Christoph Röllig, and Gerhard Ehninger Blood
2015;125:3246-3252



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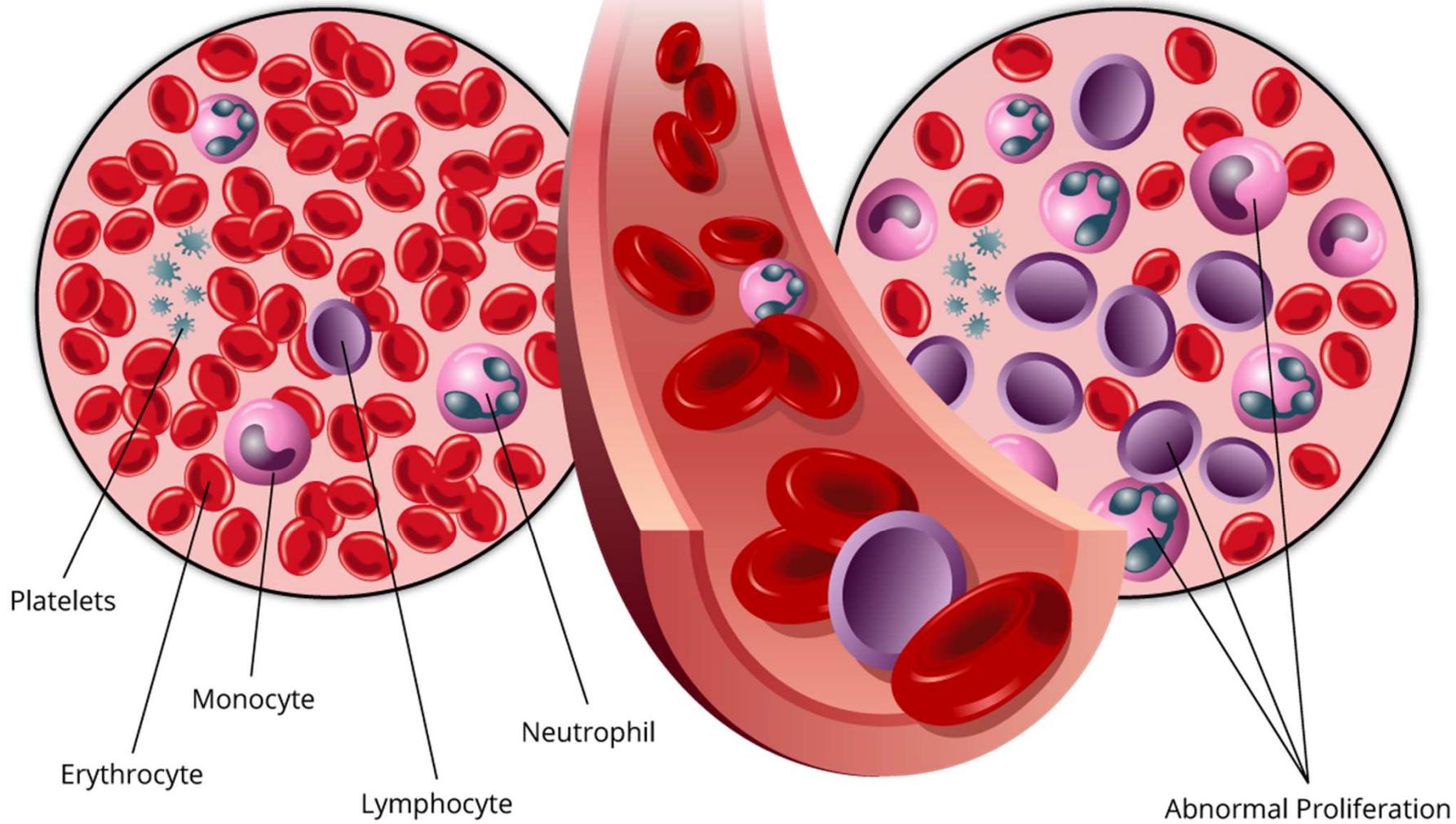


Wann kann eine massive Hyperleukozytose auftreten?

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Normal Blood

Leukemia

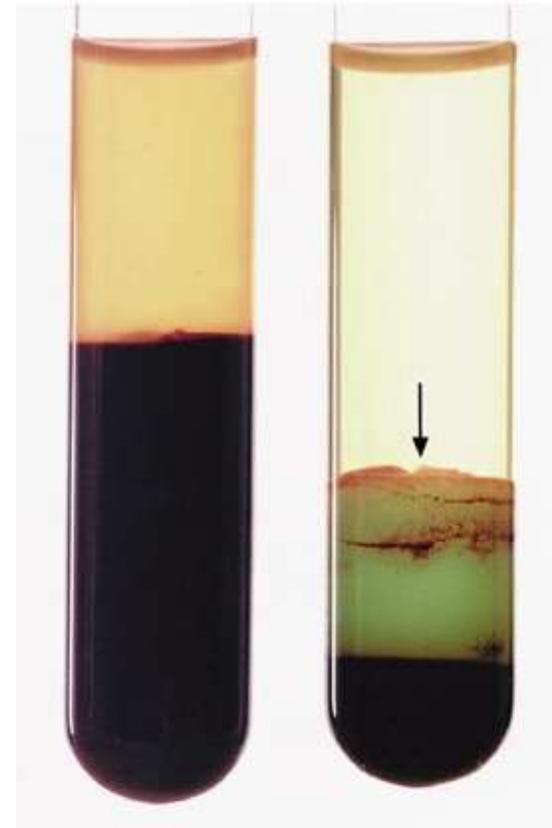


Hyperleukozytose

- **Leukozyten >100 G/L**

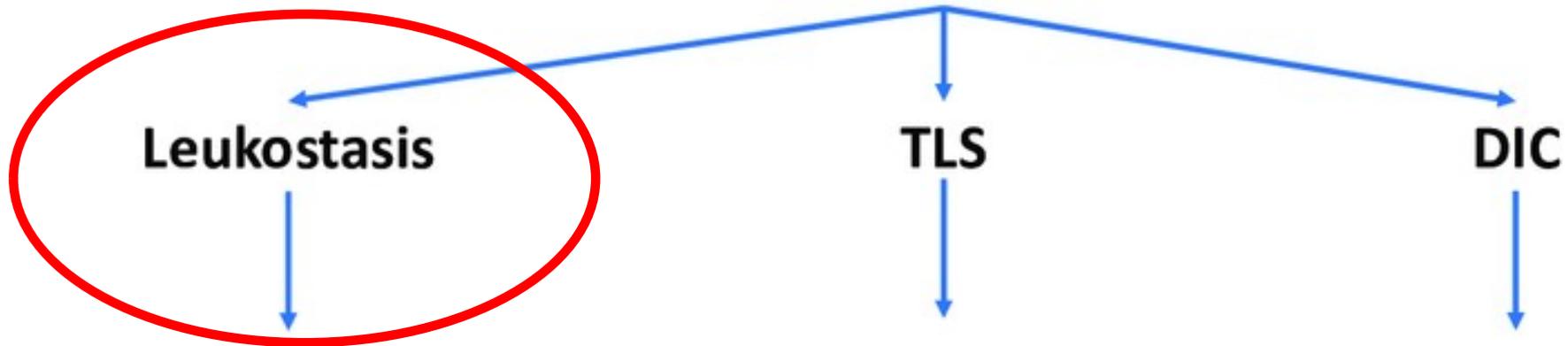
- **Leukämien und Lymphome**

- AML, ALL
- Burkitt Lymphom
- CLL, CML



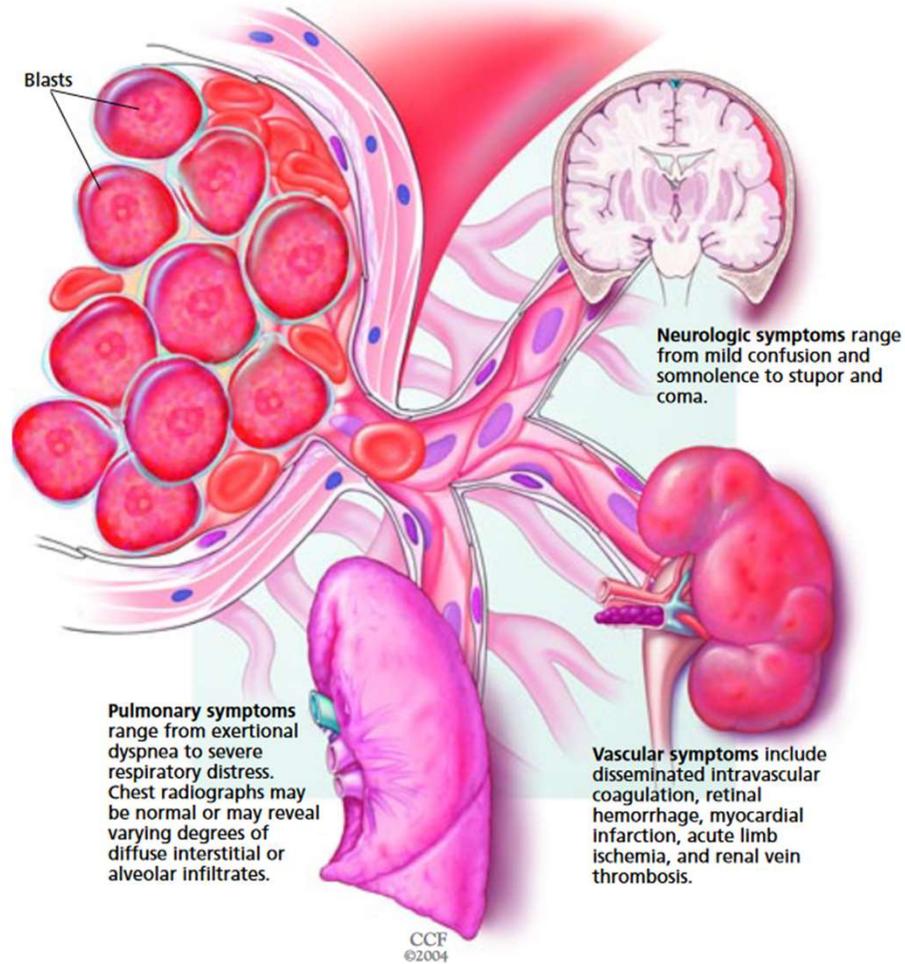
- **Das Risiko für Komplikationen hängt von der Biologie der Leukozytenzellen ab.**

Komplikationen bei Hyperleukozytose



■ Hyperleukocytosis, leukostasis, and sludging

Symptoms of hyperleukocytosis are mainly due to leukostasis, a clinicopathologic syndrome caused by the sludging of circulating leukemic blasts in tissue microvasculature.

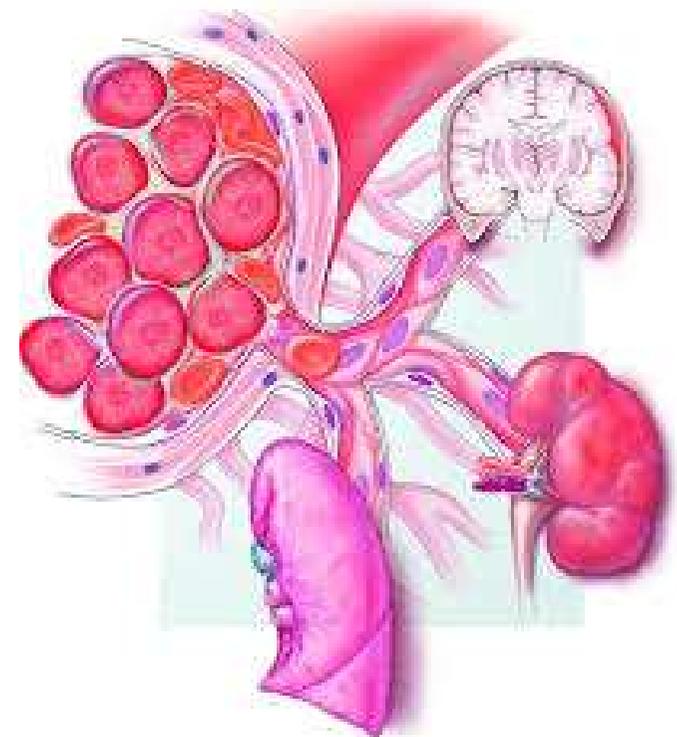


CLINICAL MANIFESTATIONS OF LEUKOSTASIS

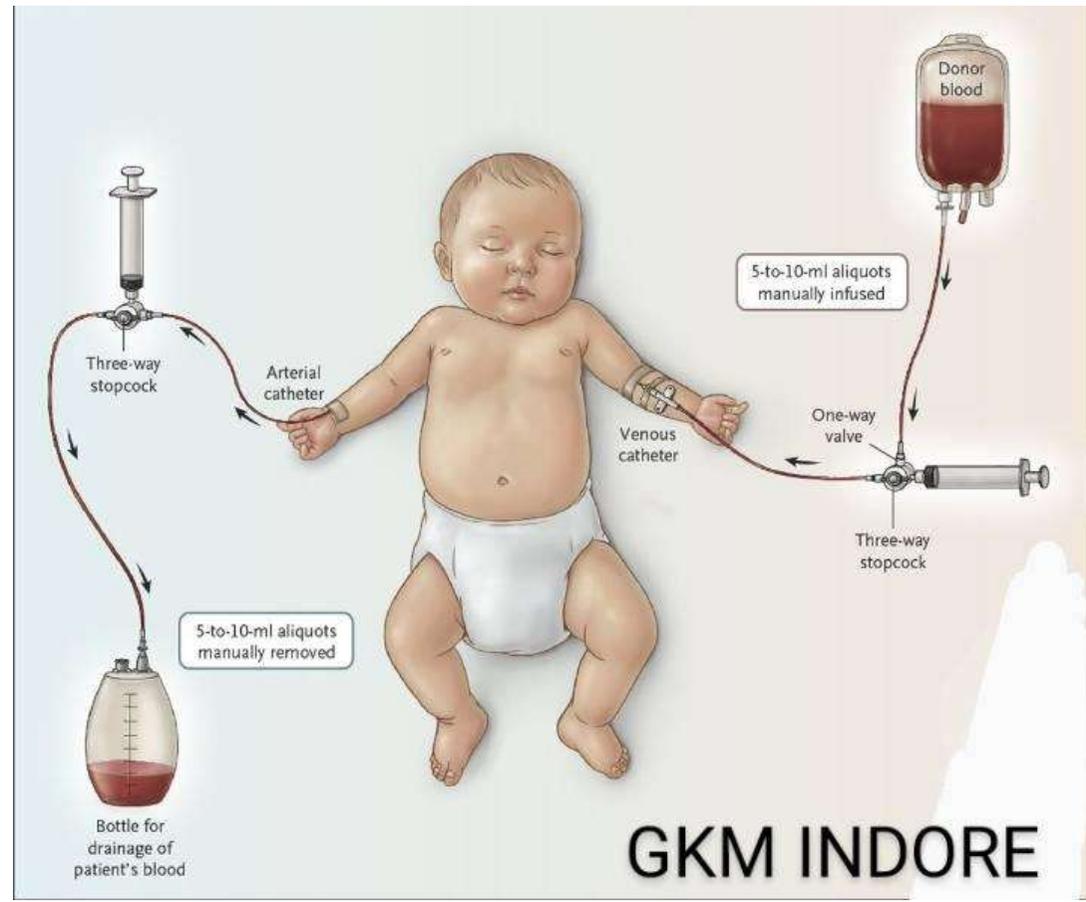
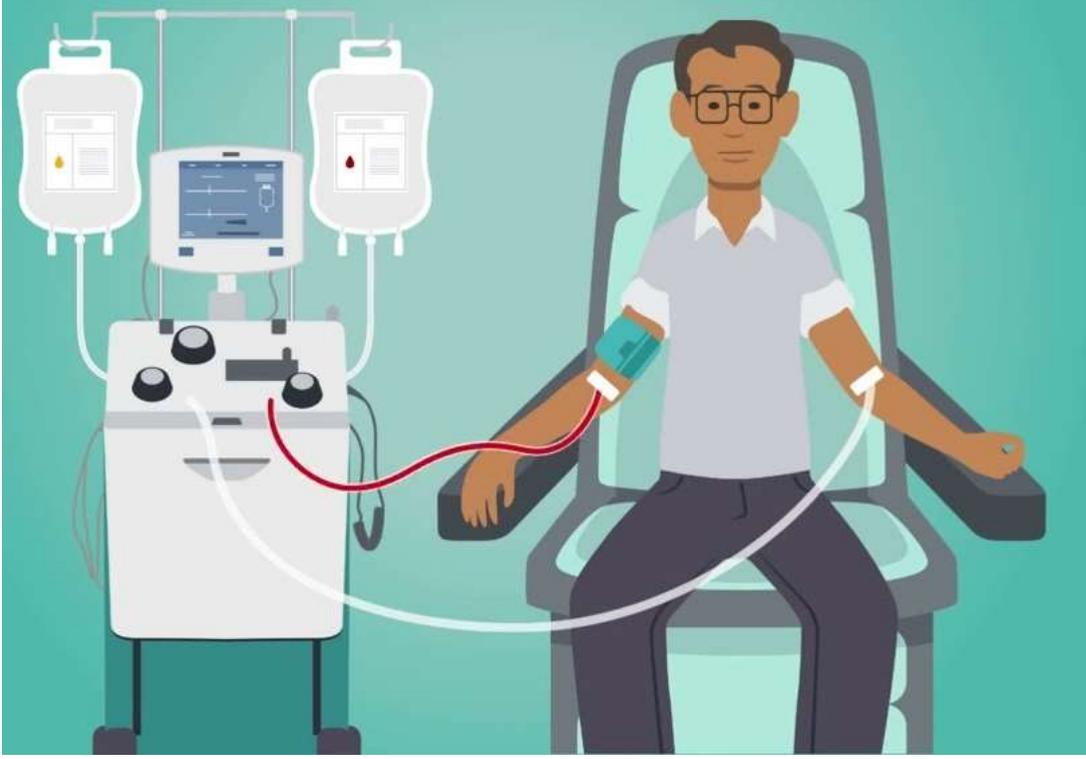
 PULMONARY	 NEUROLOGIC	 CARDIOVASCULAR
Hypoxia Dyspnea Tachypnea Respiratory Failure	Focal Deficits Seizures Delirium Papilledema	Chest Pain Myocardial Infarction Limb Ischemia
 SYSTEMIC	 RENAL	 HEMATOLOGIC
Fever Fatigue Generalized Weakness	Acute Kidney Injury Renal Vein Thrombosis	Bleeding Coagulopathy

Management der Leukostase

- **Multiorganversagen verhindern**
- **Verdünnung**
 - Hydratation mit IV-Flüssigkeit 2-3L/m²/d
- **CAVE Erythrozyten-Transfusion**
- **Reduktion der Leukozytenzahl**
 - Rascher Start Chemotherapie bzw. Cortison
 - Leukapharese wenn symptomatisch

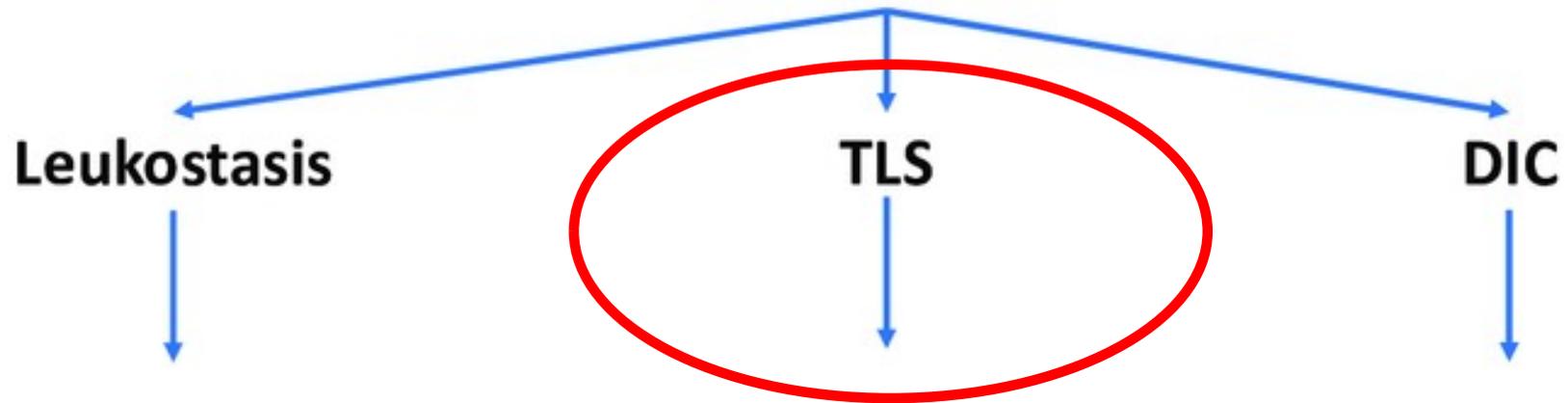


Leukapheresis Process

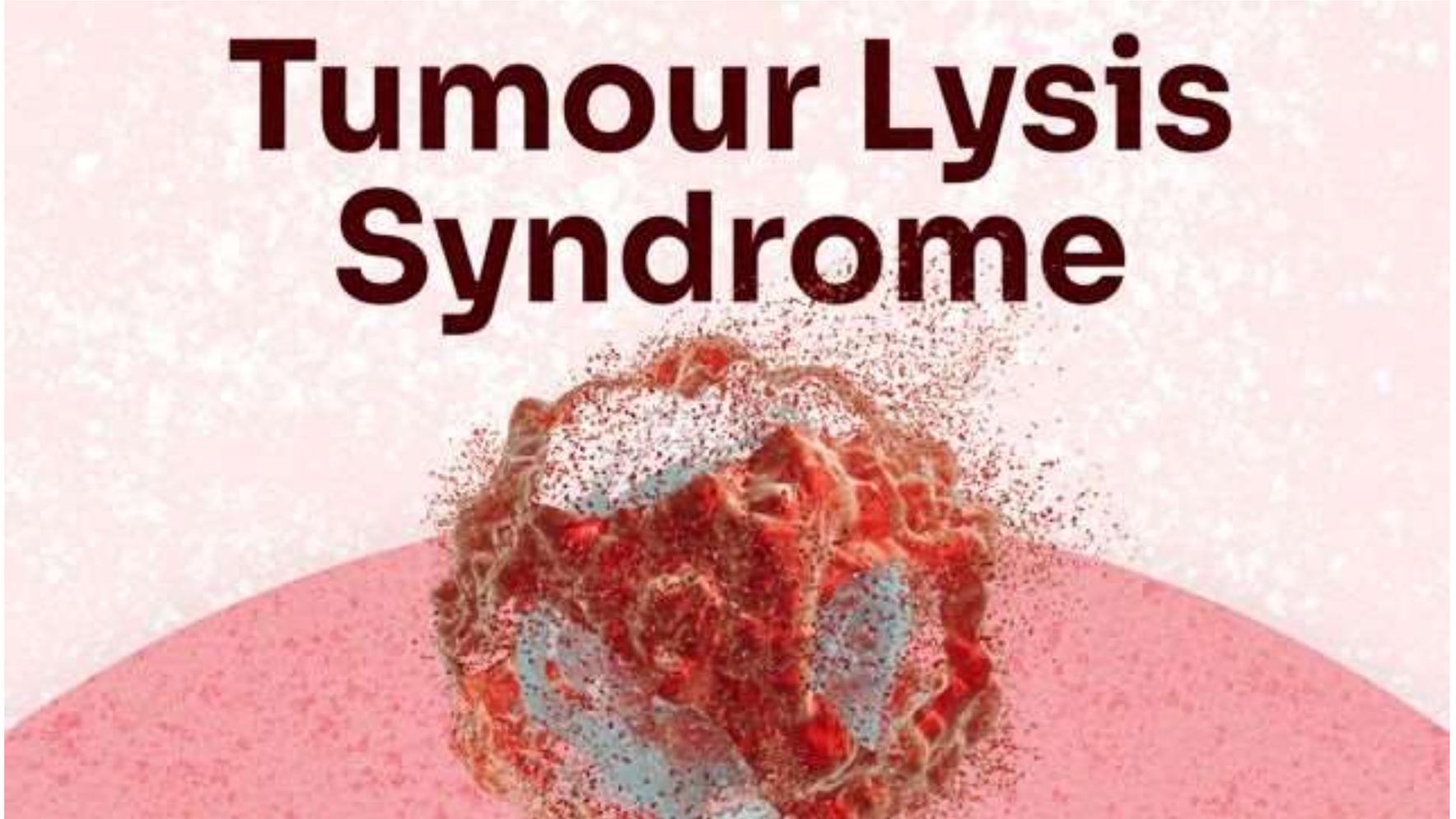


GKM INDORE

Komplikationen bei Hyperleukozytose



Tumour Lysis Syndrome

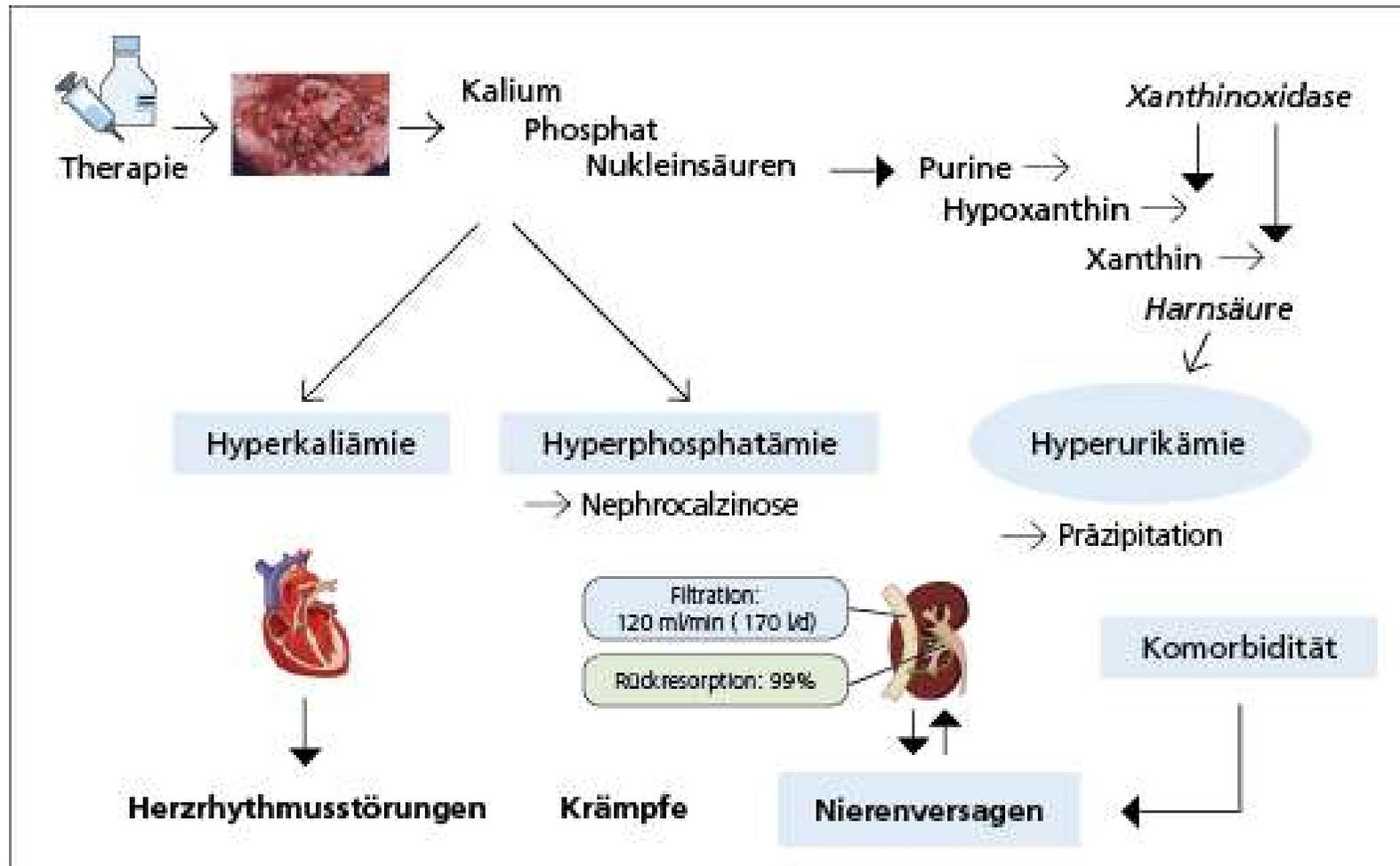


A microscopic view of several red blood cells, appearing as biconcave discs with a textured surface, set against a dark red background. The cells are illuminated from the side, creating a strong contrast and highlighting their three-dimensional structure.

„Wenn Blut zur Gefahr wird“

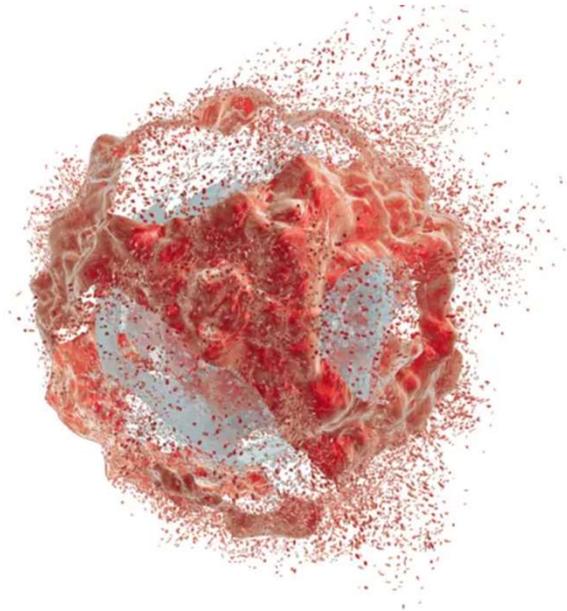
zerfallende Blutzellen

Tumorlysesyndrom (TLS)



Frage ans Auditorium

Bei welcher Tumorentität tritt das Tumorlysesyndrom am häufigsten auf?



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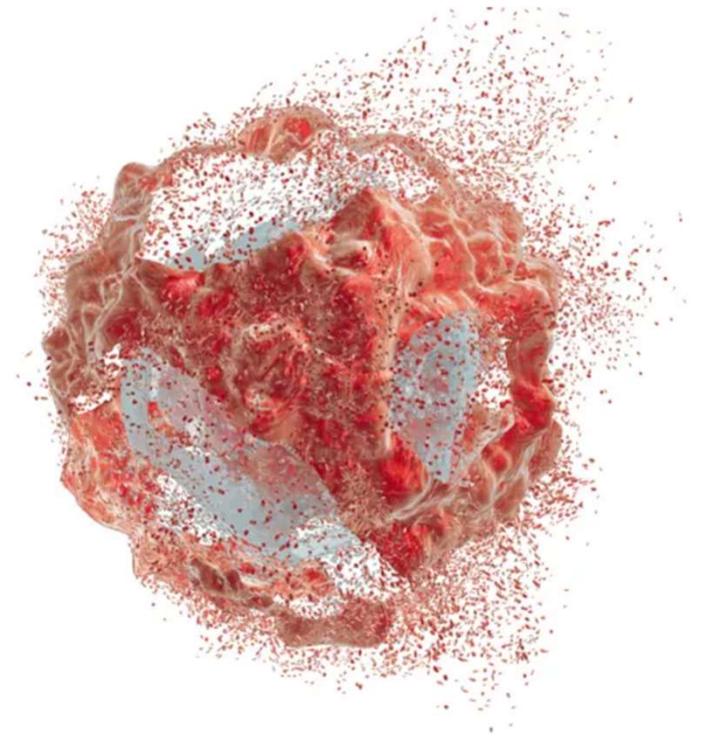


Bei welcher Tumorentität tritt das Tumorlysesyndrom am häufigsten auf?

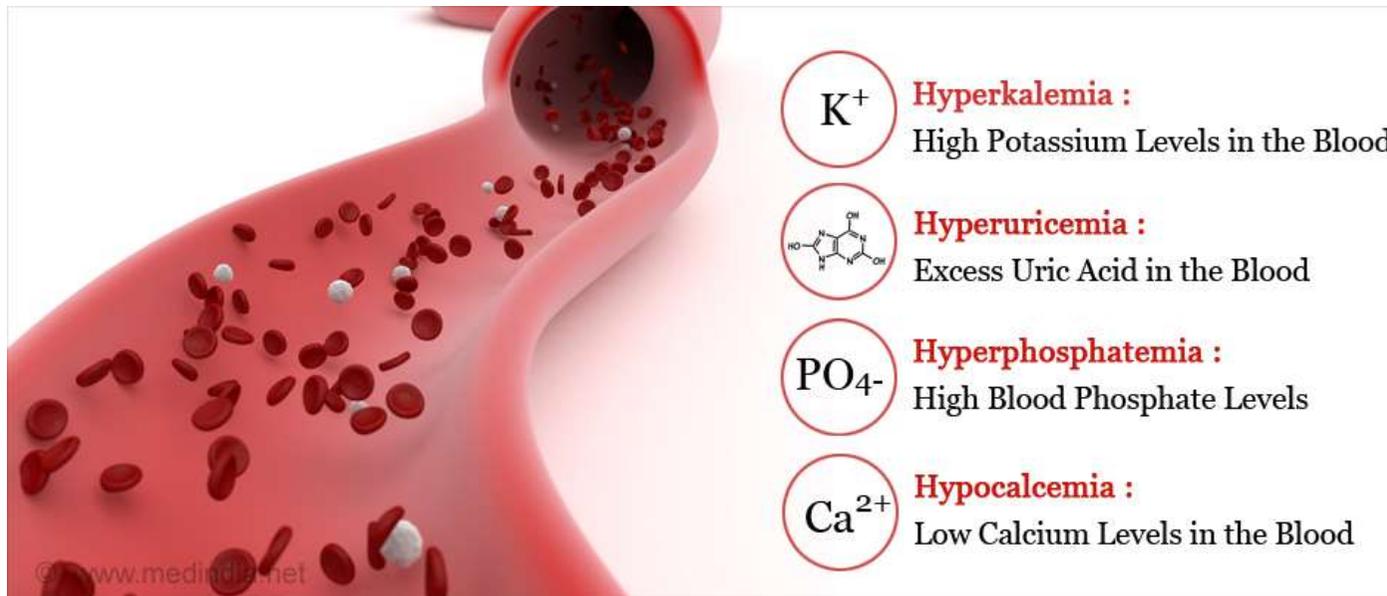
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Tumorlysesyndrom - Facts

- Leukämien und Lymphome
- Inzidenz: 5-6%
- Todesursachen: Blutung, akute Niereninsuffizienz
 - 15% versterben



Tumorlysesyndrom – Definition (Cairo-Bishop)



Clinical TLS: laboratory TLS and any of the following factors without any other obvious explanation:

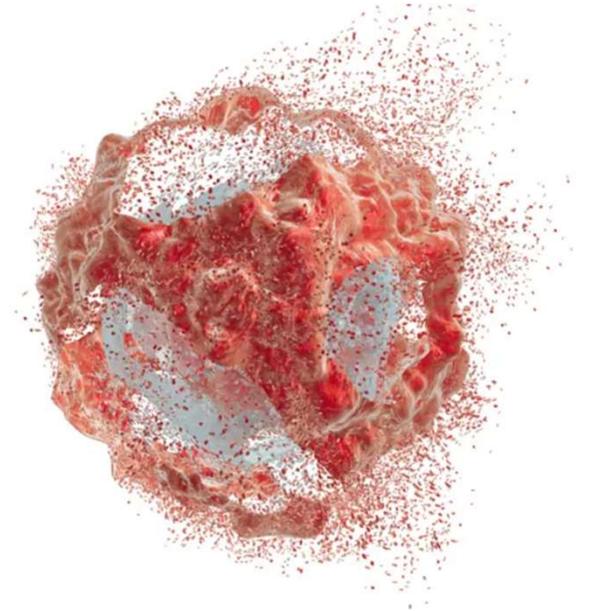
Creatinine: ≥ 1.5 -times upper limit of normal

Cardiac arrhythmia

Seizures

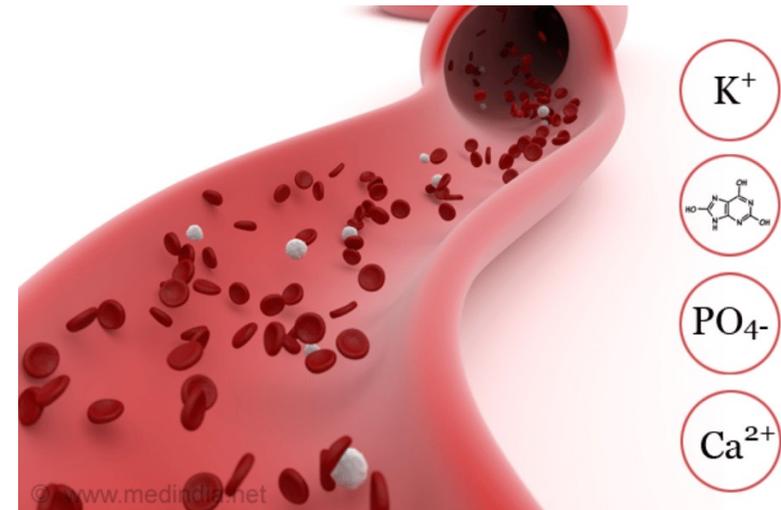
Prävention

- **Basismaßnahmen**
 - Laborkontrollen (Tumorlyseparameter), Vitalparameter
- **Hydrierung**
 - 2-3 L/m²/d
 - UO > 2ml/kg/h, Furosemid, Bilanz
- **Alkalisierung des Urins (Urin pH 7,0 – 8,0) mit NaBic**
 - Risiko der Ausfällung von Harnsäure in renalen Tubuli
- **Medikamente bei Hyperurikämie**
 - **Rasburicase (Fasturtec)** (0,2mg/kg) wiederholt - KI: G6PDH-Mangel
 - bei Rasburicase-Gabe Urin nicht alkalisieren (kein NaBic in Infusion)



Therapie des Tumorlysesyndroms

- **Start der Therapie** der Grunderkrankung trotz TLS (Chemotherapie, Cortison)
- **Hyperurikämie**
 - Rasburicase wiederholt
- **Management der Elektrolytabnormalitäten**
 - Hyperkaliämie
 - Hyperphosphatemie
 - Hypocalciämie
- **Nierenversagen → Nierenersatzverfahren**



Nierenersatzverfahren - Dialyse

- Protokoll B-NHL 2013

The indication for hemodialysis should follow local standards considering the individual course of the patient. The following criteria might serve as guidelines:

- potassium > 7 mmol/l or > 6 mmol/l and increasing, in spite of sufficient diuresis
- phosphate > 15 mg/100 ml (5 mmol/l) or product Ca x P > 6.4 mmol/l
- urine excretion: < 50 ml/m²/hr in spite of furosemide 10 mg/kg/d IV and fluid input 130-200 ml/m²/hr
- high-grade or complete urinary tract obstruction on both sides
- pulmonary edema (give oxygen and consider ventilation as immediate measures)
- creatinine > 10x upper normal limit
- uric acid > 10mg/dl (600 μmol/l)

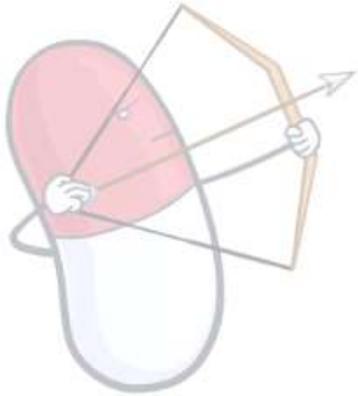


Prognose exzellent, wenn Dialyse frühzeitig begonnen wird

A microscopic view of several red blood cells, appearing as biconcave discs with a reddish-orange hue. The cells are scattered across the frame, with some in sharp focus and others blurred in the background. The overall lighting is a deep red, creating a dramatic and somewhat somber atmosphere.

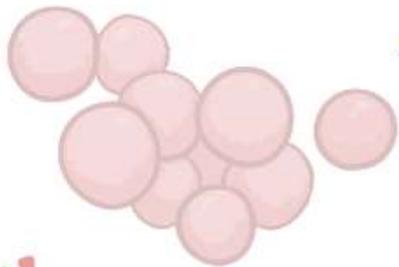
„Wenn Blut zur Gefahr wird“

zu wenige Blutzellen



FEBRILE NEUTROPENIA

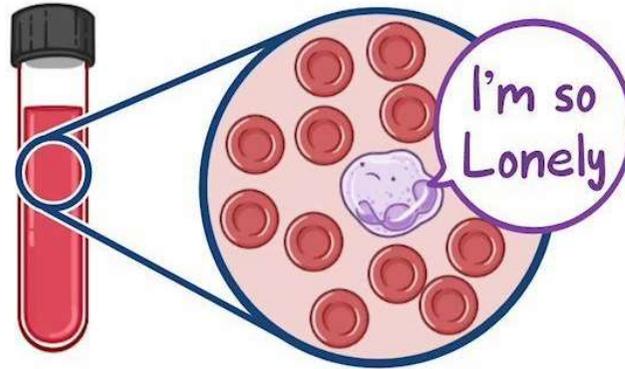
~ CLINICAL SCIENCE ~



FEBRILE NEUTROPENIA



ABSOLUTE NEUTROPHIL COUNT (ANC) < 1500 CELLS/ μ L



SEVERE NEUTROPENIA

ANC < 500 CELLS/ μ L

Frage ans Auditorium

Welche Therapie ist bei der febrilen Neutropenie rasch zu starten?

- A) Chemotherapie
- B) Cortison
- C) antibiotische Therapie
- D) Rasburicase-Gabe
- E) alle der genannten



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Welche Therapie ist bei der febrilen Neutropenie rasch zu starten?

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An illustration of a blood vessel, likely an artery, shown in a cross-section. The vessel is filled with red blood cells, which are depicted as small, biconcave discs. Interspersed among the red blood cells are several blue, rod-shaped bacteria, representing a bacterial infection. The vessel walls are shown in a reddish-brown color. The background is a soft, out-of-focus bokeh of light colors. A semi-transparent white rectangular box is overlaid on the center of the image, containing the text "Septic Shock" in a large, bold, black font.

Septic Shock

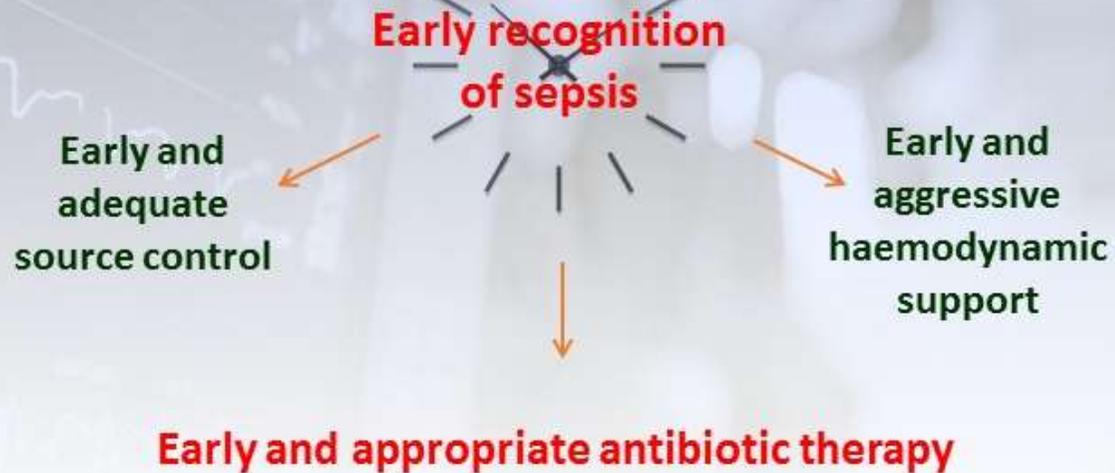
Febrile Neutropenie und Sepsis

- **Immunsuppression:**
 - nach Chemotherapiezyklus, Stammzell-Transplantation
- **Bakterielle oder fungale Infektion**
 - Kultur bleibt oft negativ
 - klinische Zeichen einer Sepsis



That Kids
Has No White
Blood Cells!
AND Has a
FEVER!
AWWW!

Antibiotics in patients with ongoing sepsis and septic shock



SEPSIS: time is survival

frühzeitiges Erkennen und **frühzeitige Therapie**

verbessern das Outcome



A microscopic view of several red blood cells, appearing as biconcave discs with a textured surface, set against a dark red background. The cells are illuminated from the side, creating a strong contrast and highlighting their three-dimensional structure.

„Wenn Blut zur Gefahr wird“

verwirrte Blutzellen

HAEMATOLOGY

IMMUNOLOGY





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Frage ans Auditorium

Was ist HLH?



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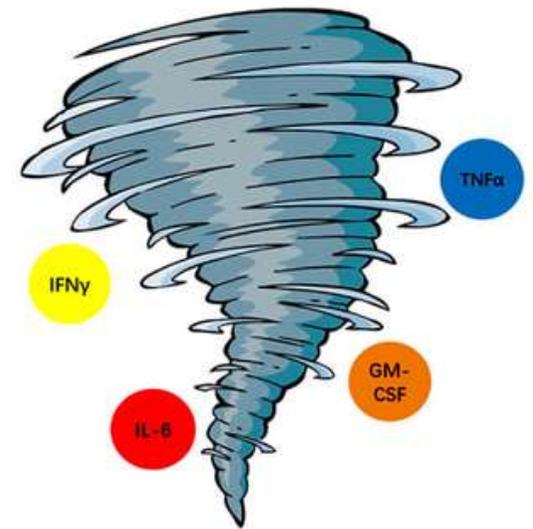
Was ist HLH?

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HLH – was ist das?

- selten – daran denken!!!!
- **lebensbedrohliches** Hyperinflammationssyndrom
- **unkontrollierte Immunantwort**
 - exzessive + unkontrollierte Aktivierung von Makrophagen + Zytokinsturm
- → **Muliorganversagen**

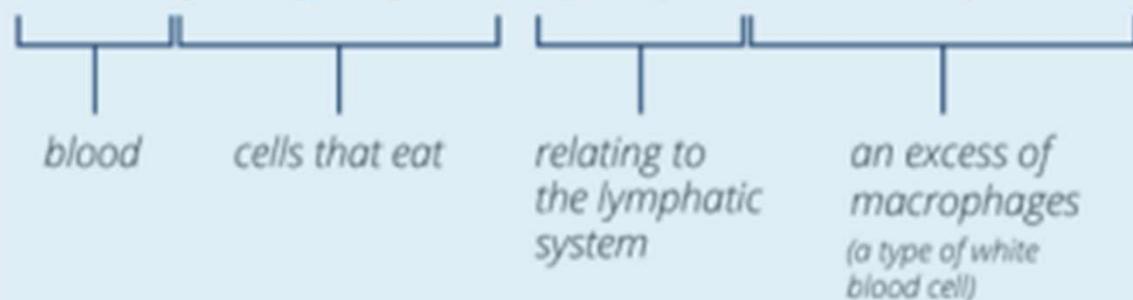
- schwierig in der Diagnosestellung
- Klinik:
 - kritisch krank
 - Sepsis-like



Cytokine storm

What does HLH stand for?

hemophagocytic lymphohistiocytosis



HLH: time is survival

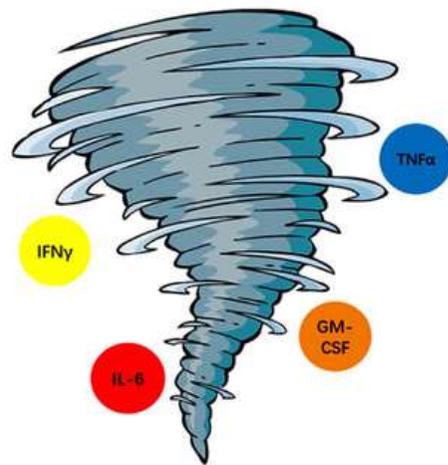
frühzeitiges Erkennen und **frühzeitige Therapie**

verbessern das Outcome



Frage ans Auditorium

Was können Ursachen bzw. auslösende Faktoren für HLH sein?



Cytokine storm



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Was können Ursachen bzw. auslösende Faktoren für HLH sein?

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Hemophagocytic disorders

Hemophagocytic lymphohistiocytosis (HLH)

Primary/genetic
(HLH)

**Familial
immunodeficiency**

Secondary/
acquired (HLH)

**Malignancy
infection
autoimmune (MAS)**

Macrophage activation syndrome (MAS)

Genetic/Familial HLH

DISEASE	GENE	FUNCTION
FHLH-1	UNKNOWN	UNKNOWN (9q21.3)
FHLH-2	PRF-1	INDUCTION OF APOPTOSIS
FHLH-3	MUNC13-4	VESICLE PRIMING
FHLH-4	STX11	VESICLE TRANSPORT
FHLH-5	STXBP2	VESICLE TRANSPORT
GS-2	RAB27A	VESICLE TRANSPORT
CHS-1	LYST	VESICLE TRANSPORT
XLP	SH2D1a	LYMPHOCYTE SIGNAL TRANSDUCTION

Sekundäre HLH

TRIGGERS



INFECTIONS

- EBV
- CMV
- HIV
- HSV
- VZV
- COVID-19
- MTB Complex
- Leishmania
- Malaria
- Histoplasma
- Brucella
- Anaplasma

Common



MALIGNANCY/Tx

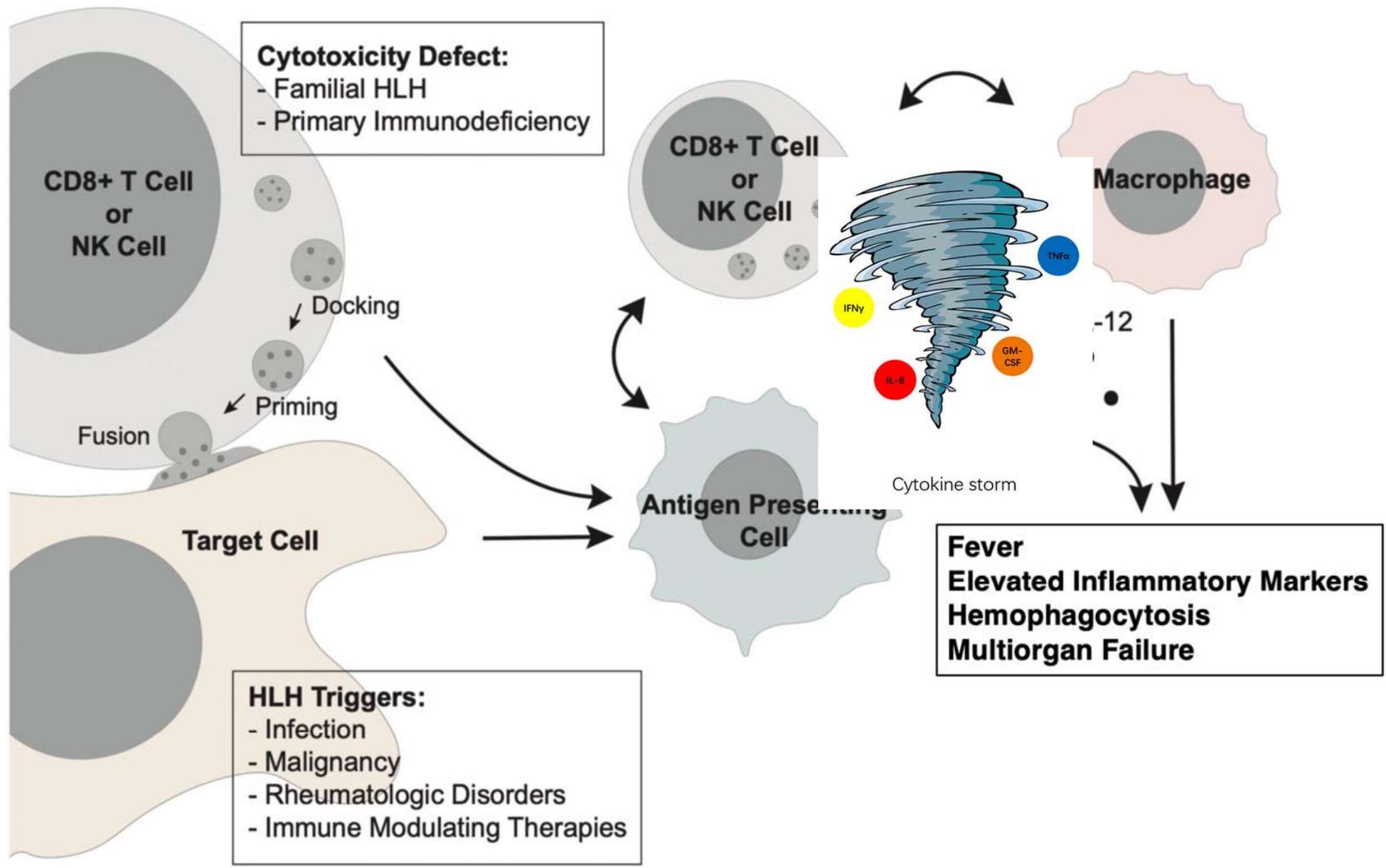
- B cell lymphoma
- T cell lymphoma
- NK cell lymphoma
- Leukemia
- Solid tumors
- Hematopoietic Tx
- Kidney, liver Tx



RHEUMATOLOGIC SX

- Systemic juvenile idiopathic arthritis
- Dermatomyositis
- Systemic sclerosis
- Antiphospholipid syndrome
- Sjogren's syndrome

Less common



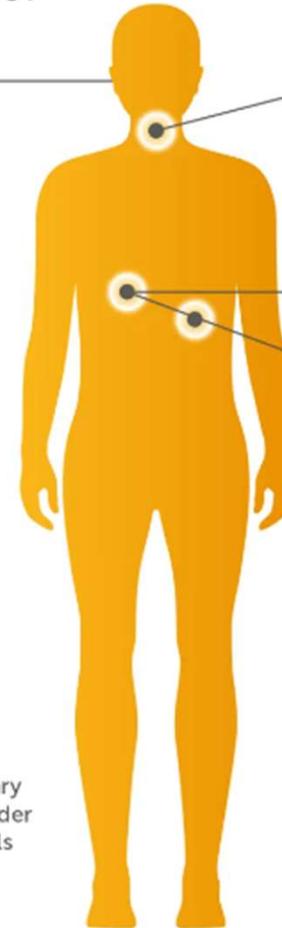
Haemophagocytic lymphohistiocytosis (HLH)

What are the symptoms?

WHOLE BODY

- **Fever**
The first, and most common, symptom of HLH is raised temperature or fever
- **Low blood cell counts**
Anaemia, low platelets, low white blood cells
- **Skin rashes**
- **Swollen lymph nodes**
- **Neurological symptoms**
Irritability, seizures, or altered mental status
- **Gastrointestinal symptoms**
Nausea, vomiting, diarrhoea

These symptoms can occur in both primary and secondary HLH. Their severity and order of appearance may vary among individuals and depending on the underlying causes.



Respiratory symptoms
Cough, shortness of breath

Elevated liver enzymes
Enlarged liver and spleen

The diagnostic of hemophagocytic lymphohistiocytosis can be established by fullfilling five of the eight following criteria.

Clinical criteria

Fever (> 7 days)

Spleen enlargment

Laboratory criteria

Bicytopenia without marrow hypoplasia, including

Hemoglobin<9g/L

Platelet count<100x10⁹/mm³

Neutrophil count<1x10⁹/mm³

Hypertriglyceridemia (>3,0mmol/L, fasting value) and/or hypofibrinemia (<1,5g/L)

Hyperferritinemia (>500µg/L)

Low/absent Natural Killer cell activity

Increased soluble CD-25 levels (>2400IU/mL)

Histological criteria

Hemophagocytosis

Ferritin level > 10.000 mcg/L

TREATMENT

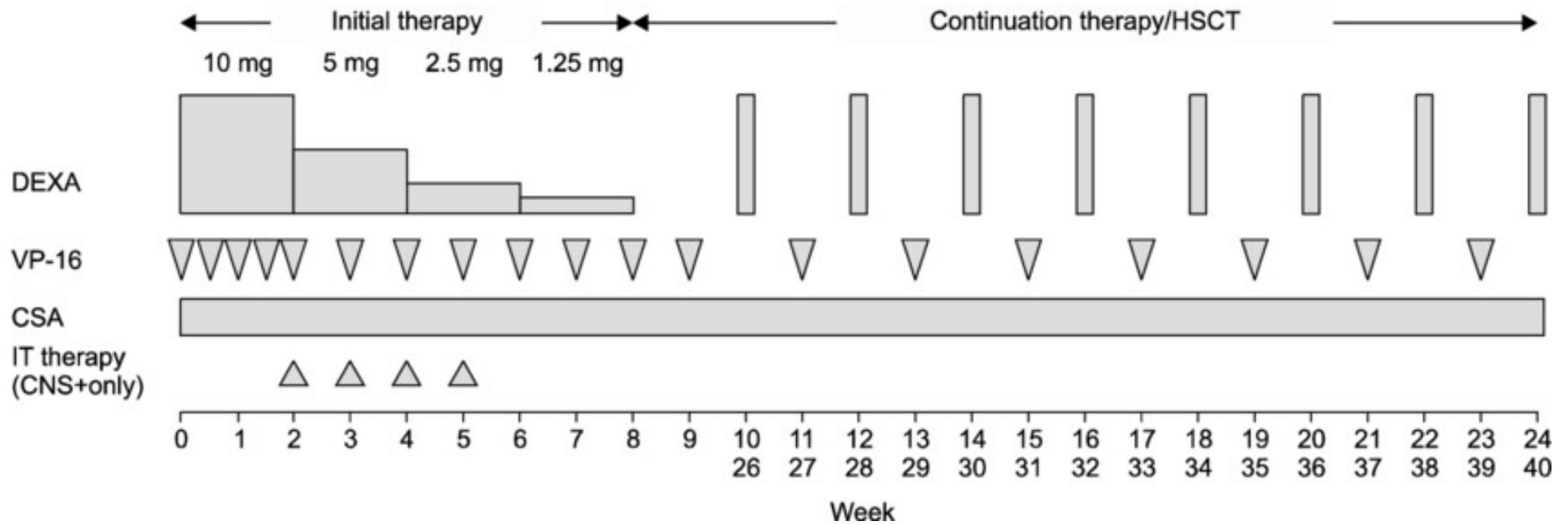
- Treatment requires a multidisciplinary team that includes infectious diseases, hematologist and critical care specialists. High mortality, up to 50%
- Infection should be diagnosed rapidly, and empiric antibiotic therapy should be initiated depending on the suspected organism
- Supportive measures and treating the insulting agent are the main goal of therapy. If no response HLH-94-based therapy with etoposide and dexamethasone is indicated

REVIEW

**HLH-2004: Diagnostic and Therapeutic Guidelines for
Hemophagocytic Lymphohistiocytosis**

Jan-Inge Henter, MD, PhD,^{1*} AnnaCarin Horne, MD,¹ Maurizio Aricó, MD,² R. Maarten Egeler, MD, PhD,³
Alexandra H. Filipovich, MD,⁴ Shinsaku Imashuku, MD,⁵ Stephan Ladisch, MD,⁶ Ken McClain, MD, PhD,⁷
David Webb, MD,⁸ Jacek Winiarski, MD, PhD,⁹ and Gritta Janka, MD, PhD¹⁰ for the Histiocyte Society

HLH-2004 Protocol



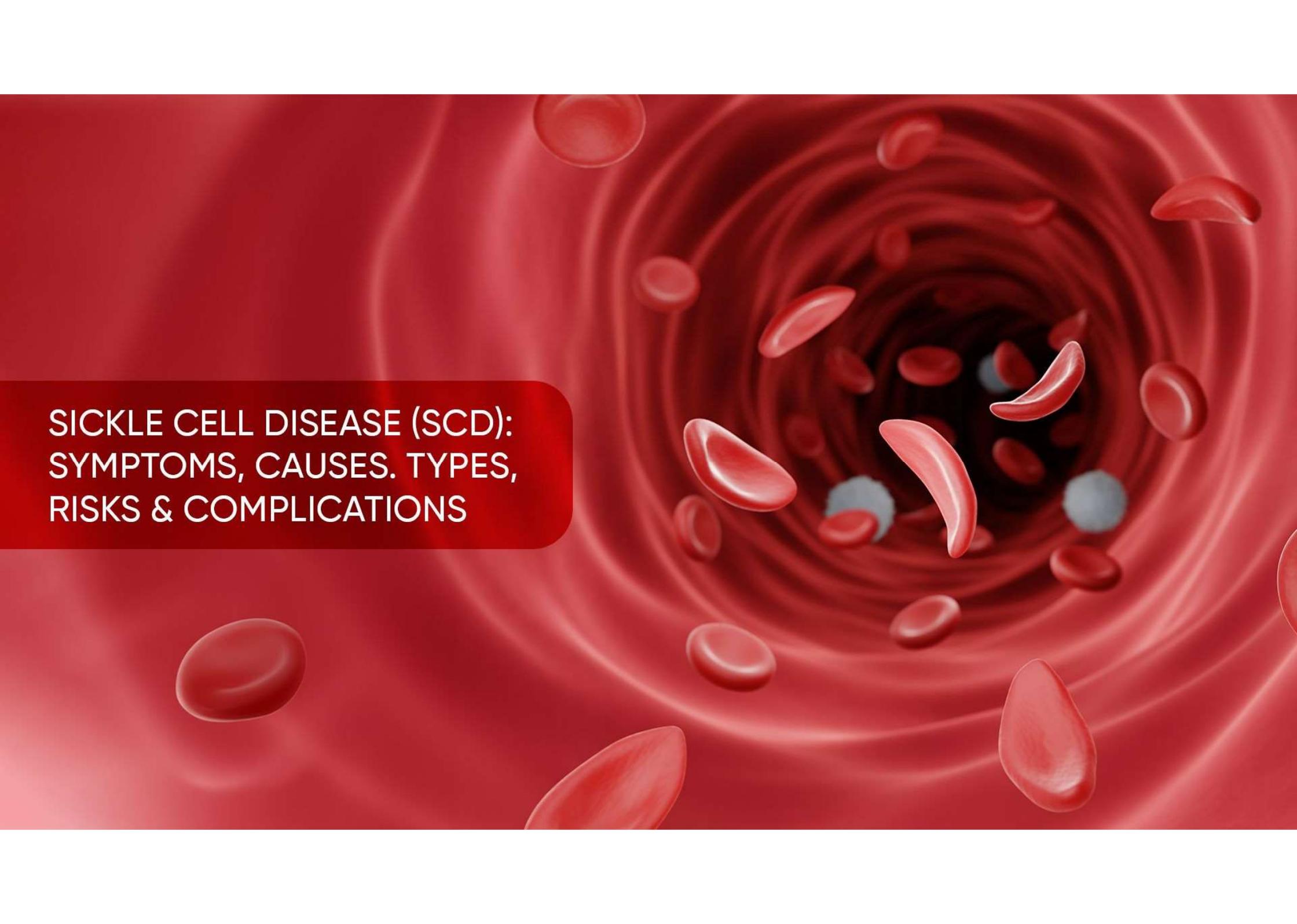
Milde Formen der sekundären HLH

- Hämato-Onkologie
- Steroide
- Therapie der Grunderkrankung (Infektion, Autoimmunologie)
- HLH 2004-Protokoll
- Anakinra, IVIG, Rituximab, Tacrolimus
- HSCT in refraktären Fällen

The background of the slide is a microscopic image of red blood cells. The cells are shown in various stages of deformation, appearing as irregular, bumpy spheres instead of the normal smooth, biconcave discs. The color is a deep, vibrant red, and the lighting creates a sense of depth and texture on the surface of the cells.

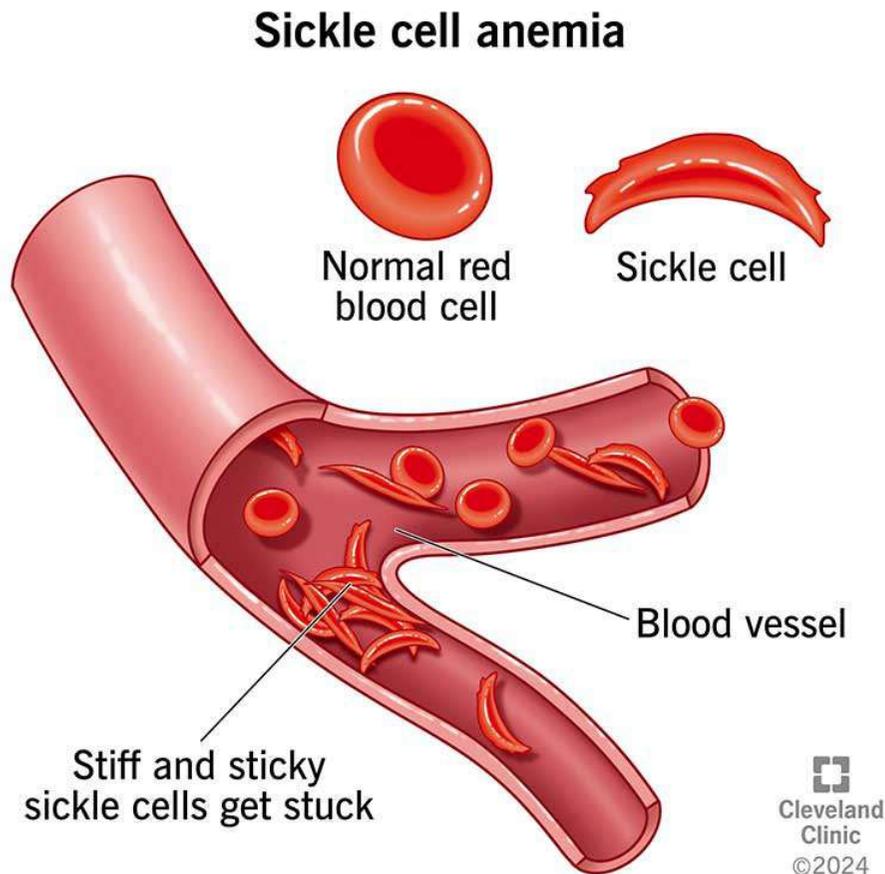
„Wenn Blut zur Gefahr wird“

verformte Blutzellen



**SICKLE CELL DISEASE (SCD):
SYMPTOMS, CAUSES, TYPES,
RISKS & COMPLICATIONS**

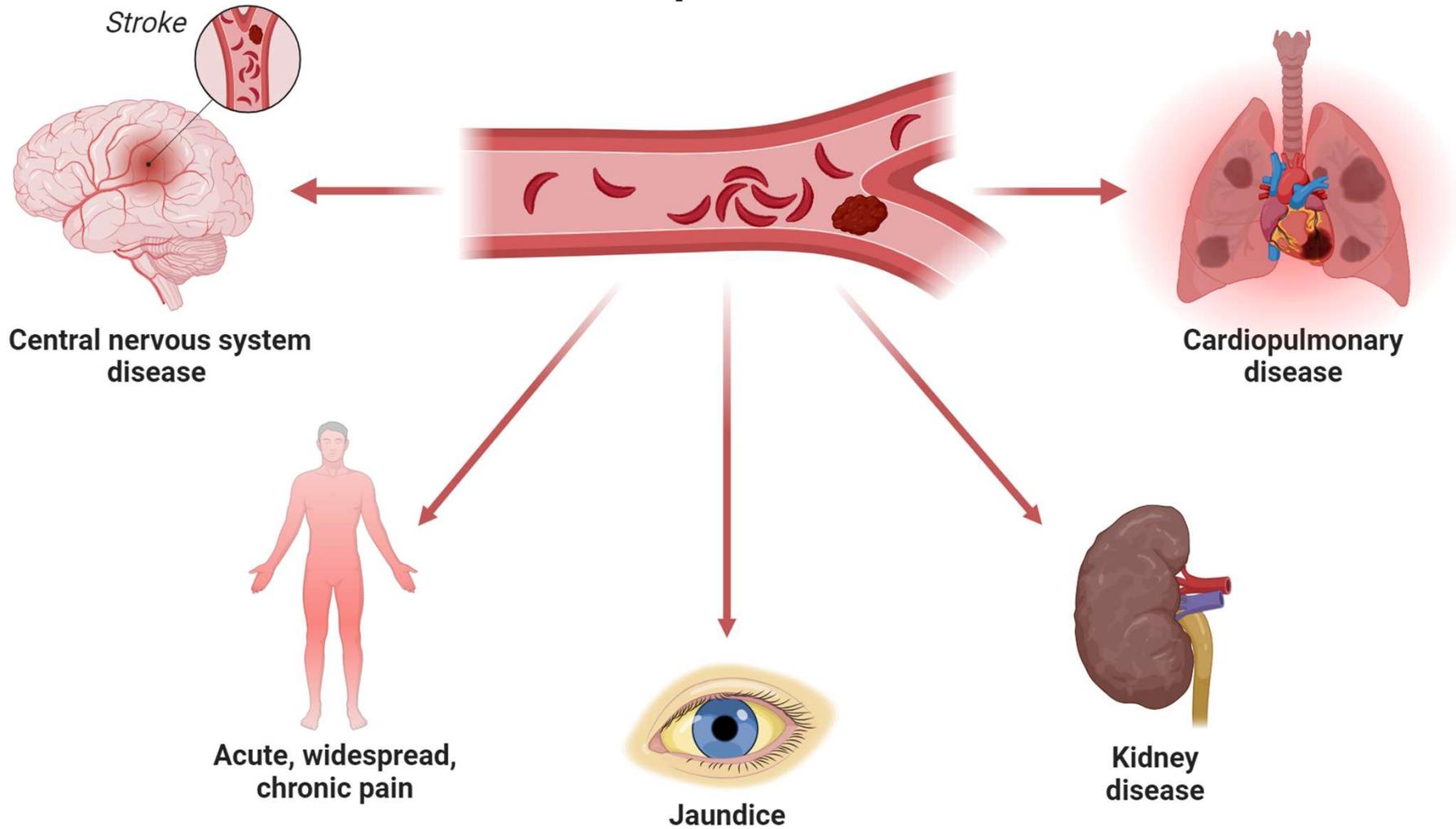
Sichelzellkrise



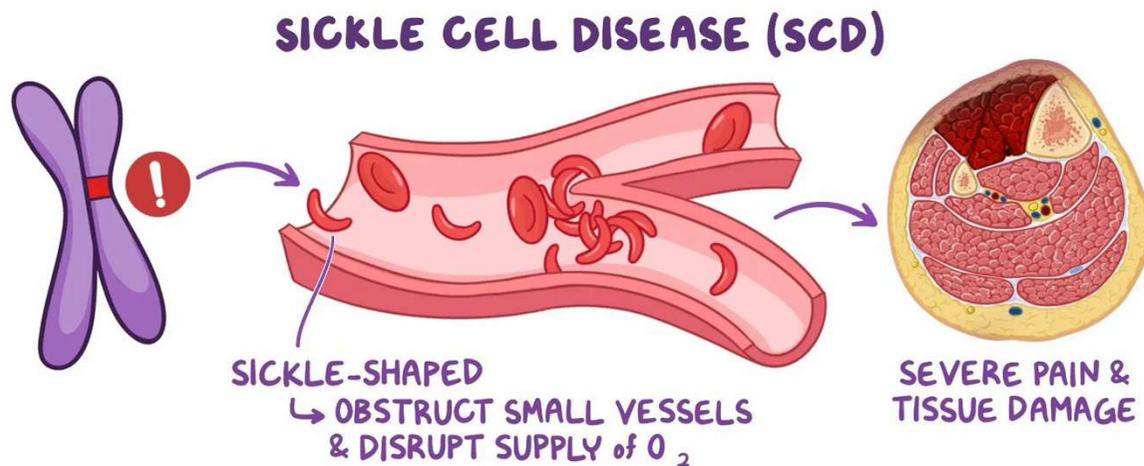
- Mutation β -Hämoglobin-Kette
- **Erythrozyten in Desoxy-Form**
 - Verformung, erhöhte Steifigkeit, vermehrte Lyse
- → verminderter Blutfluss, Hypoxie, Gefäßschädigung
- → Schädigung der Organe



Sickle Cell Disease Complications



Schmerzkrise oder Veno-occlusive Event



PATIENTS should be MONITORED for COMPLICATIONS

Frequent pain episodes.



Pain affects your child's chest, back, legs and arms most often.

Swelling and inflammation of their joints.

Painful swelling of their hands and feet.

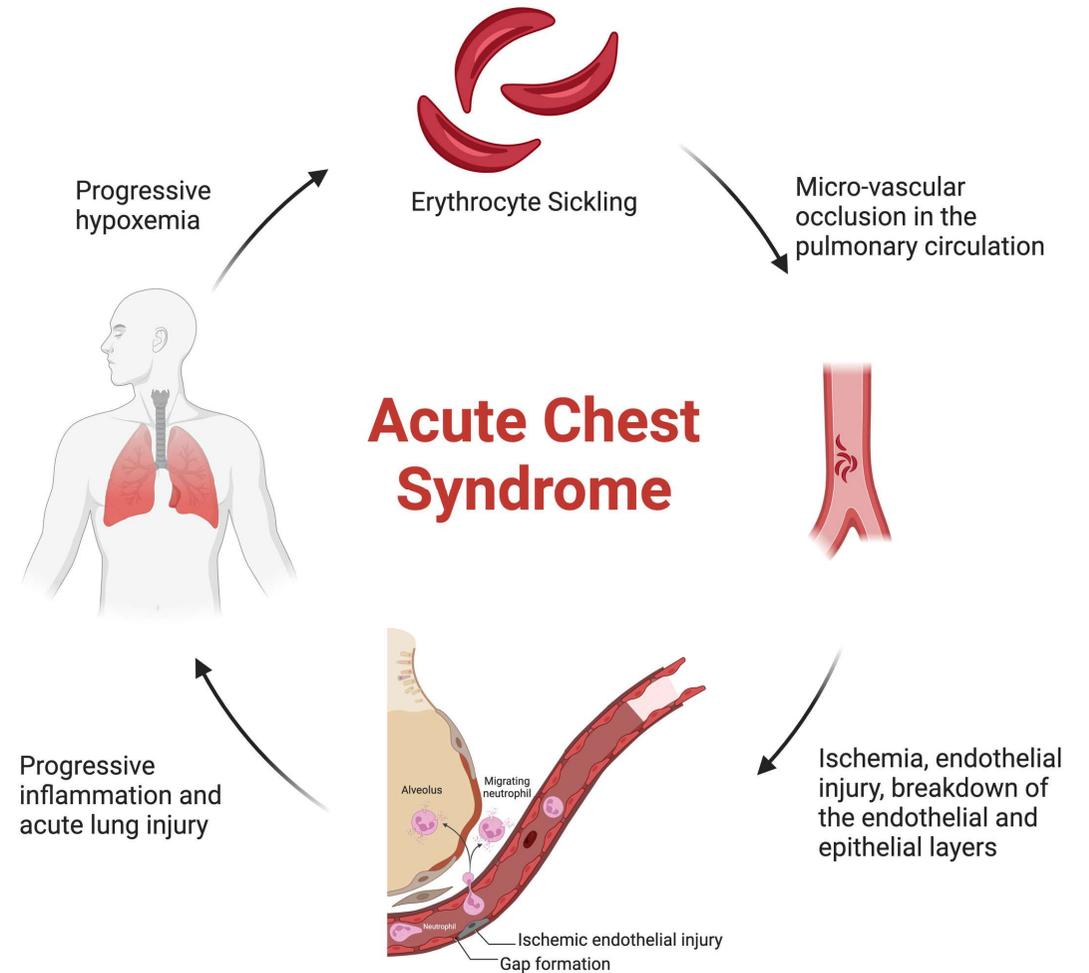
Therapie der Schmerzkrise



- IV-Flüssigkeitszufuhr
- eventuell Bluttransfusion

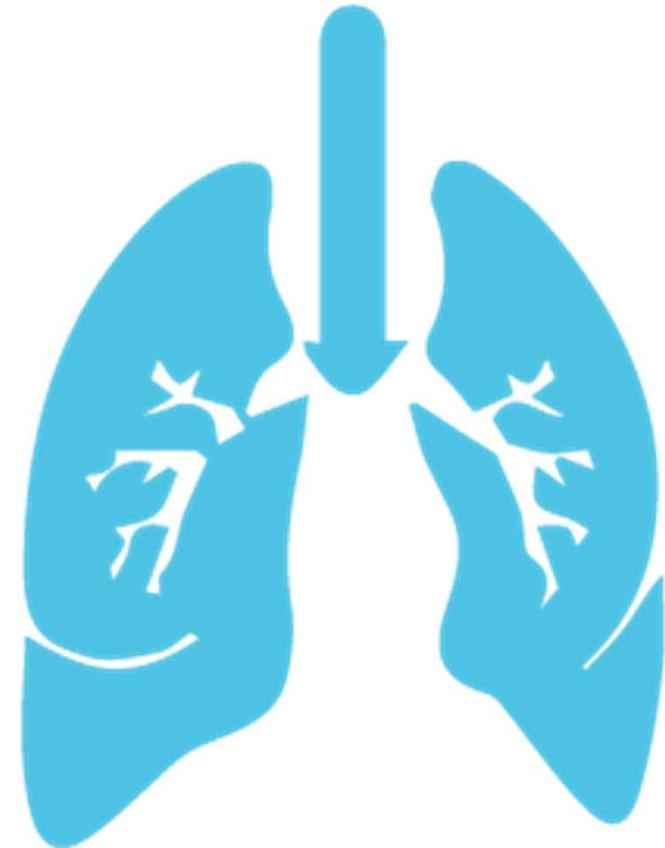
- inadäquates Schmerzmanagement
 - → Exazerbation anderer Komplikationen
 - v.a. Akutes Thoraxsyndrom

Akutes Thoraxsyndrom



Therapie des akuten Thoraxsyndroms

- **Sauerstoffgabe** (bzw. Intubation)
 - Hypoxie beseitigen
- **IV-Flüssigkeitsgabe**
 - Viskosität reduzieren
- **EK-Transfusion**
 - Sauerstoffversorgung verbessern
- **Antibiotika**
 - Therapie der Infektion (Trigger)
- **Bronchodilatator, orale Steroide**
- **Austauschtransfusion**
 - Sauerstoffversorgung verbessern
 - HbS auf <30% reduzieren



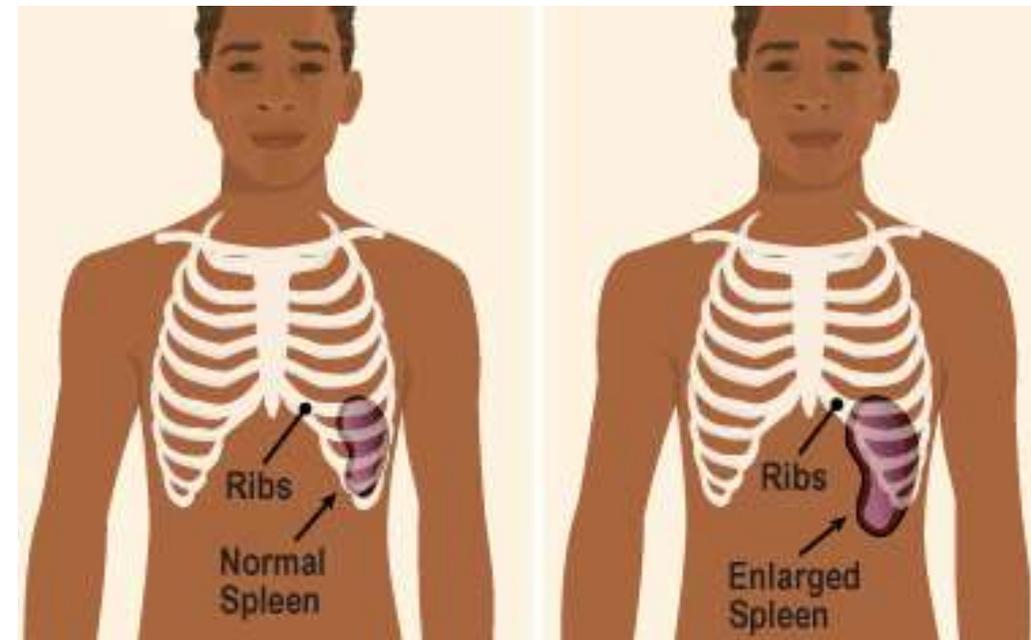
Akute Milzsequestration

- **NOTFALL!!! -lebensbedrohlich!!!**

innerhalb von 30 Minuten möglich!!!



- mögliche Symptome
 - Dyspnoe, Lethargie
 - linksseitiger Bauchschmerz, Erbrechen
 - moderate Thrombopenie



time is survival

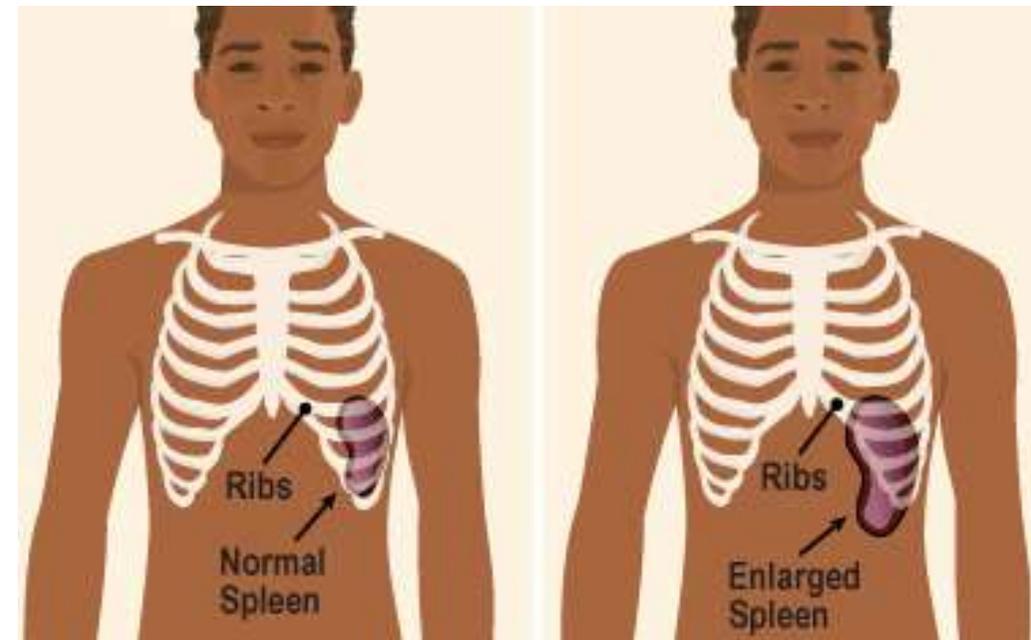
frühzeitiges Erkennen und **frühzeitige Therapie**

verbessern das Outcome

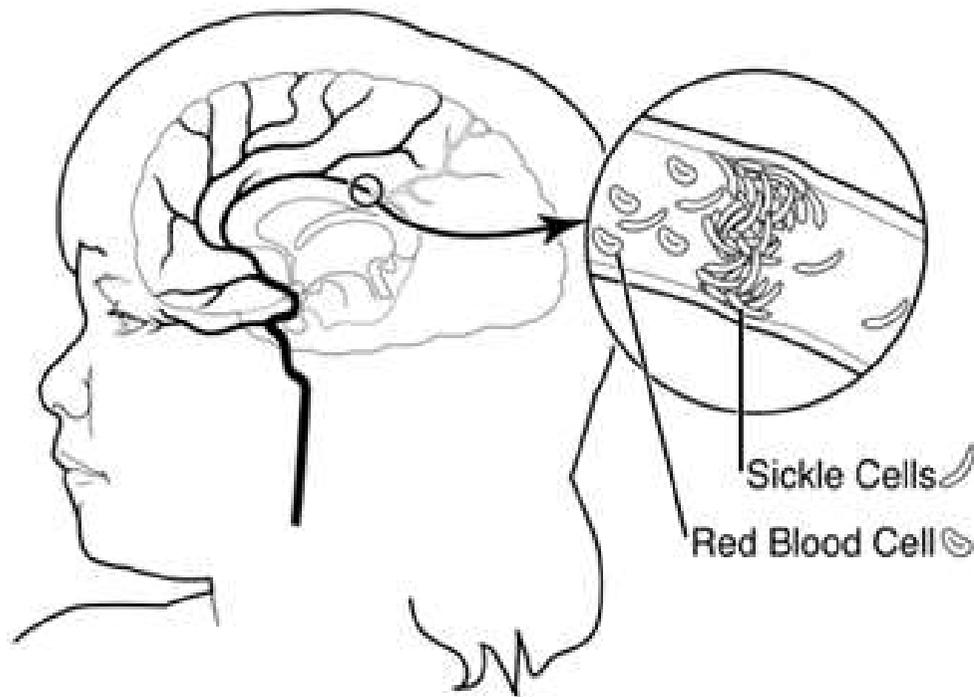


Therapie der akuten Milzsequestration

- Rasche Bluttransfusion
 - das zirkulierende intravaskuläre Volumen wiederherzustellen
 - Small-volume Transfusion 5-10 mL/kg
- Indikation für Splenektomie



Stroke – akute neurologische Events

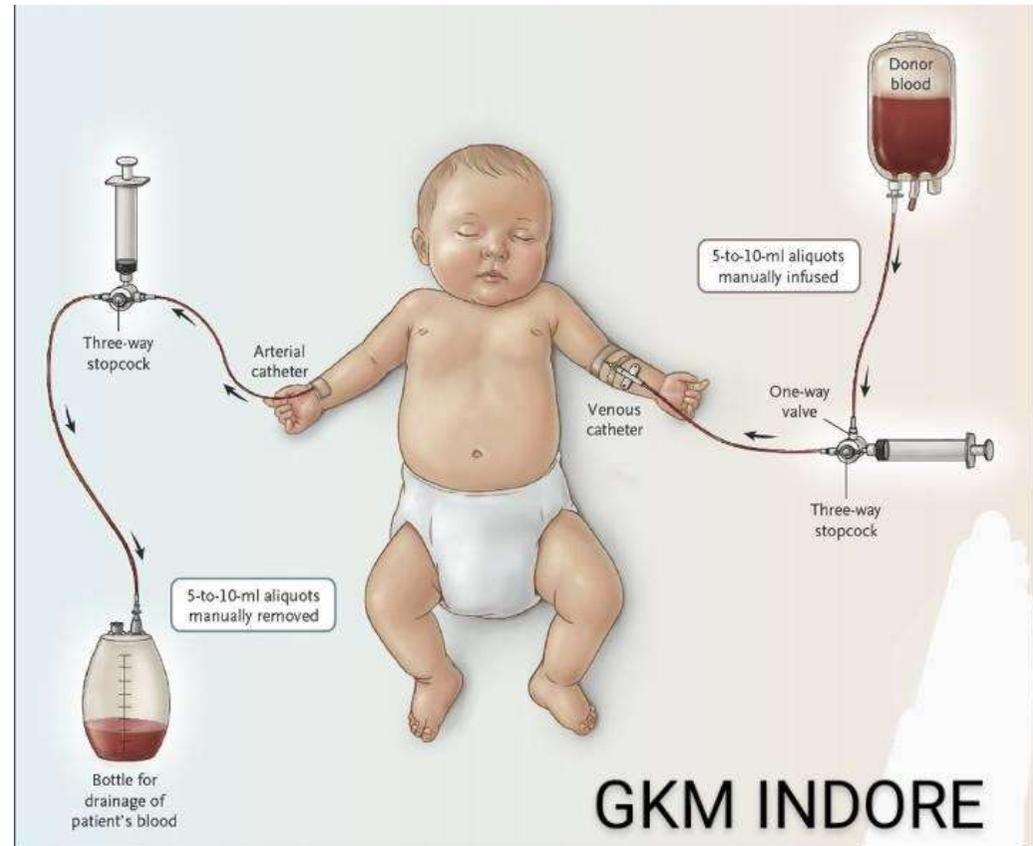
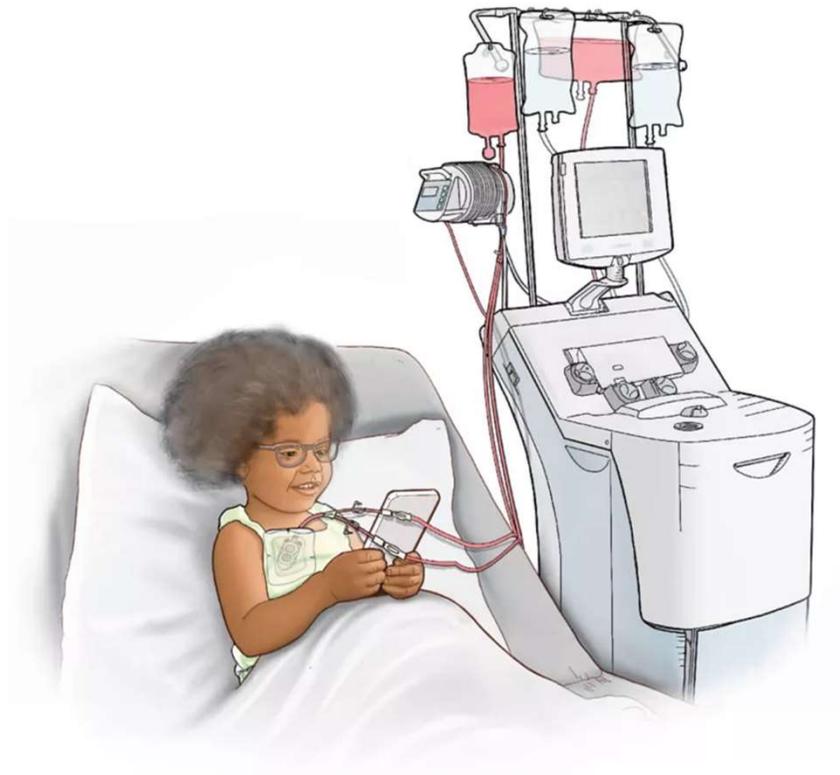


Picture 1 Sickle cells are blocking blood flow in the brain.

Therapie:

Sofortige Austauschtransfusion,
um HbS-Konzentration $<30\%$

Red Blood Cell Exchange





Learning **to** care



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Pathways

PAEDIATRIC haemato-oncology emergencies

VERSION N. 2     

 [Start the pathway](#)



Take Home Message

- Kontaktaufnahme mit Hämato-Onkologischen Zentrum!!!!
 - St. Anna Kinderspital
- Daran denken - frühzeitig Erkennen
- Frühzeitig Therapie
- Lebensbedrohlich!!!



A microscopic view of a blood vessel showing several red blood cells (erythrocytes) in cross-section, appearing as biconcave discs. The vessel walls are visible as a textured, reddish structure. The overall color palette is dominated by various shades of red.

**Vielen Dank für Ihre
Aufmerksamkeit**

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