Histiozytosen:
Definition und Klassifikation

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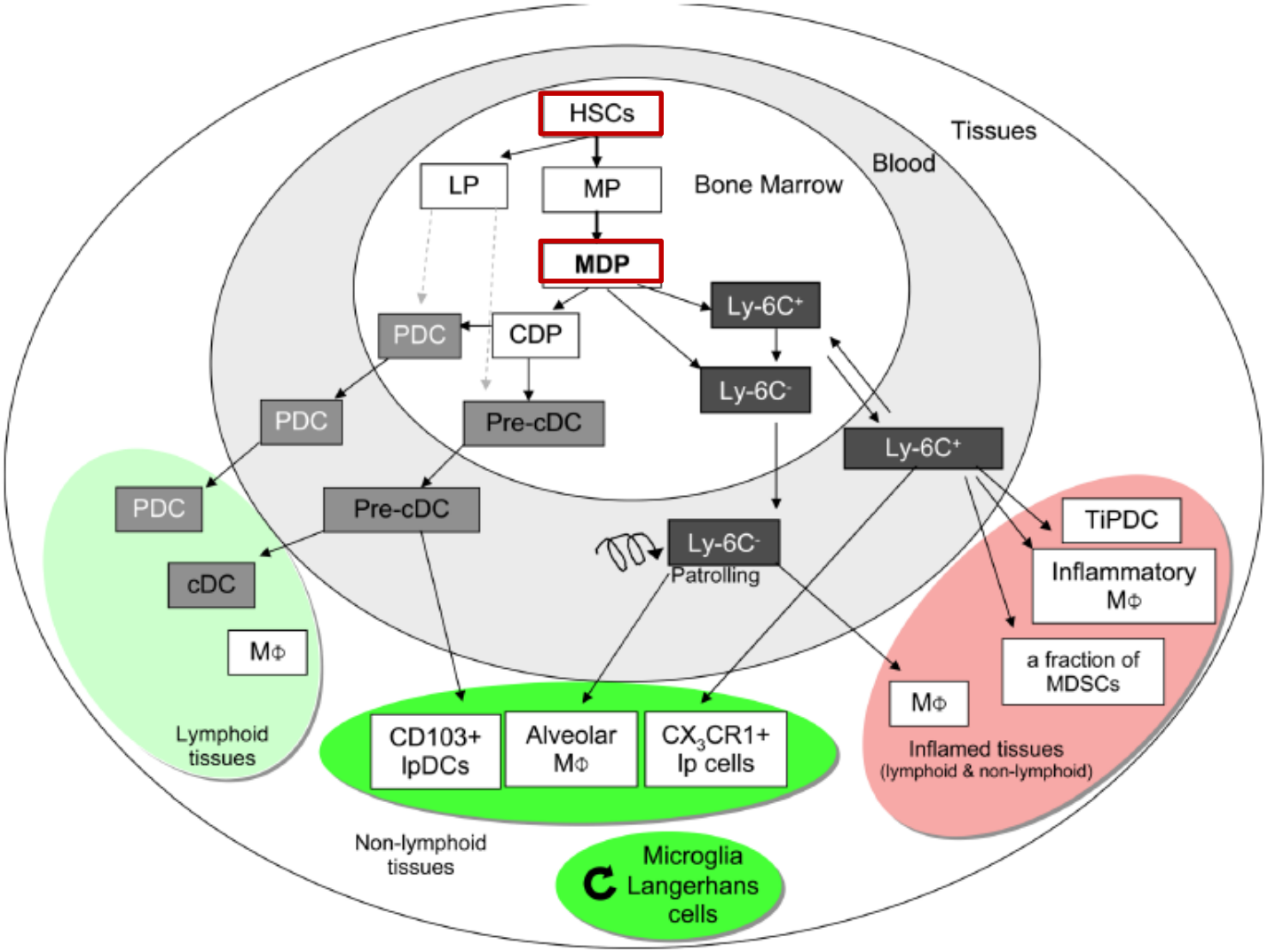
Definition

“HISTIOZYT” = Gewebsmakrophag

“HISTIOZYTOSEN”

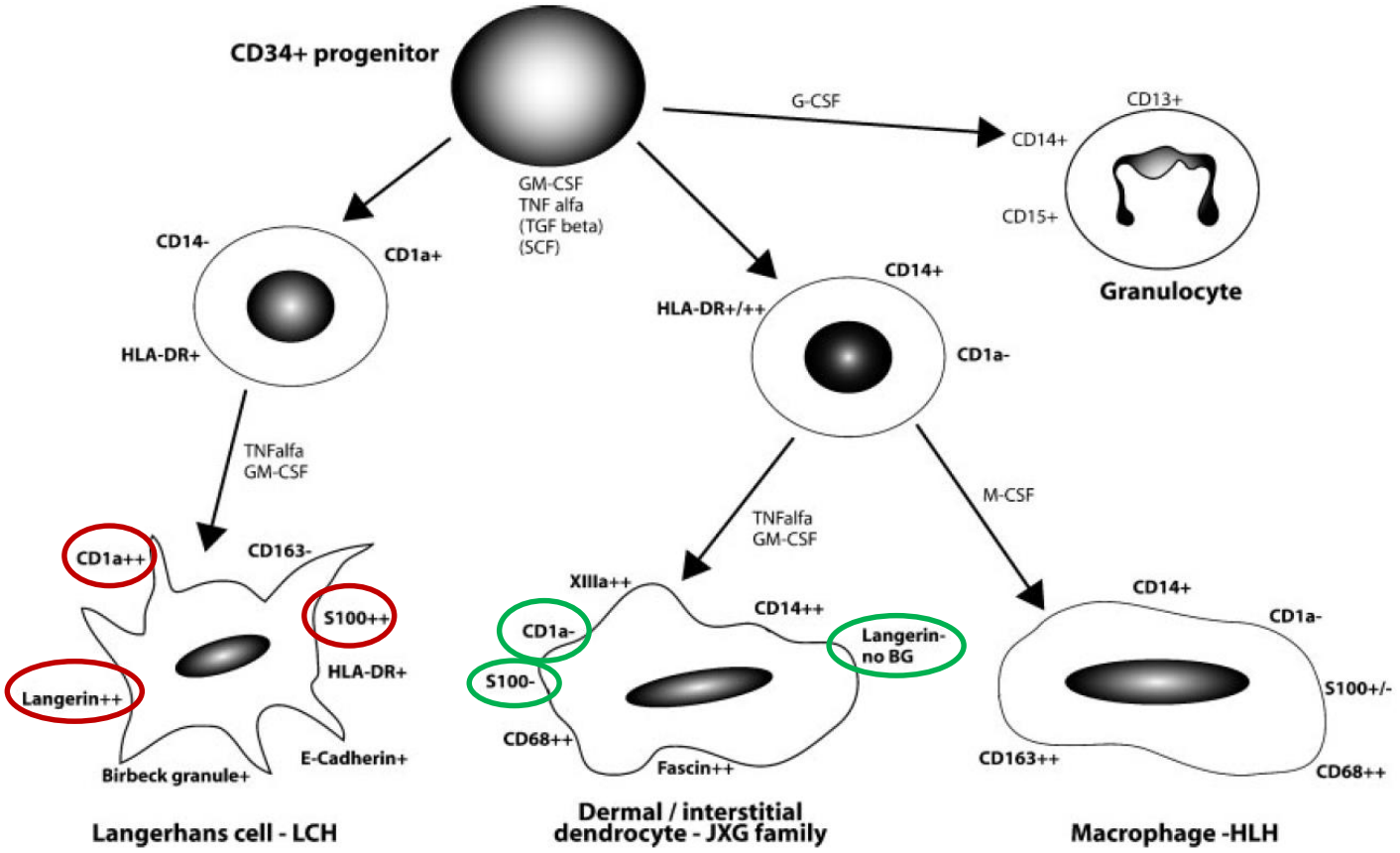
Krankheiten der Monozyten-Makrophagen-Reihe, die durch eine erhöhte Proliferation bzw. Akkumulation von Zellen dieser Reihe in verschiedenen Geweben und Organen hervorgerufen werden.

Das Monozyten-Makrophagen-System



Geissmann F et al., Science, 2010, 327: 656-661

Differenzierung der Histiozyten



LCH
ICH

Seltene Histiozytosen
(Non-LCH, non-HLH)

HLH
Seltene Histiozytosen
(Non-LCH, non-HLH)

Weitzman S. et al., PBC, 2005, 44: 1-9

Klassifikation der Histiozytosen

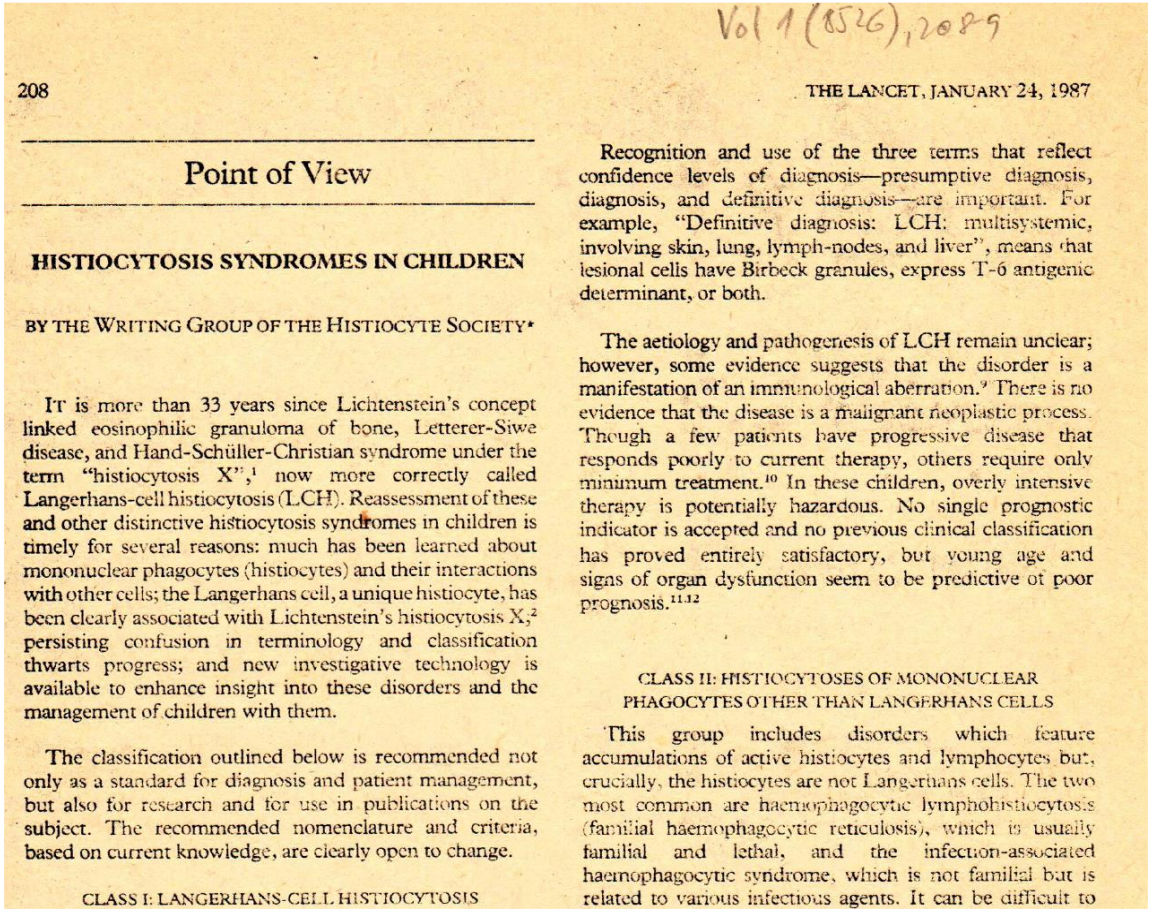
1987 ➡ 1997 ➡ 2016

Grundprinzipien der Einteilung:

- Identifikation des morphologisch dominierenden Zelltyps:
  - konventionelle Morphologie
  - immunohistochemische Charakterisierung
- Zuordnung der Makrophagenreihe bzw. der Reihe der dendritischen Zellen
  - Histiozytosen aus den dendritischen Zellen
  - Histiozytosen aus den Makrophagen
- Erfassung von „Malignitätskriterien“ und entsprechende Einordnung als gutartig oder bösartig

- Benennung nach dem phenotypisch ähnlichen Zelltyp aus der normalen Reihe des Monozyten-Makrophagen-Systems, unter Berücksichtigung des gesamten morphologischen Bildes und der klinischen Präsentation

Klassifikation der Histiozytosen



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Point of View

HISTIOCYTOSIS SYNDROMES IN CHILDREN

BY THE WRITING GROUP OF THE HISTIOCYTE SOCIETY*

It is more than 33 years since Lichtenstein's concept linked eosinophilic granuloma of bone, Letterer-Siwe disease, and Hand-Schüller-Christian syndrome under the term "histiocytosis X",[1] now more correctly called Langerhans-cell histiocytosis (LCH). Reassessment of these and other distinctive histiocytosis syndromes in children is timely for several reasons: much has been learned about mononuclear phagocytes (histiocytes) and their interactions with other cells; the Langerhans cell, a unique histiocyte, has been clearly associated with Lichtenstein's histiocytosis X,[2] persisting confusion in terminology and classification thwarts progress; and new investigative technology is available to enhance insight into these disorders and the management of children with them.

The classification outlined below is recommended not only as a standard for diagnosis and patient management, but also for research and for use in publications on the subject. The recommended nomenclature and criteria, based on current knowledge, are clearly open to change.

CLASS I: LANGERHANS-CELL HISTIOCYTOSIS

Recognition and use of the three terms that reflect confidence levels of diagnosis—presumptive diagnosis, diagnosis, and definitive diagnosis—are important. For example, "Definitive diagnosis: LCH: multisystemic, involving skin, lung, lymph-nodes, and liver", means that lesional cells have Birbeck granules, express T-6 antigenic determinant, or both.

The aetiology and pathogenesis of LCH remain unclear; however, some evidence suggests that the disorder is a manifestation of an immunological aberration.[9] There is no evidence that the disease is a malignant neoplastic process. Though a few patients have progressive disease that responds poorly to current therapy, others require only minimum treatment.[10] In these children, overly intensive therapy is potentially hazardous. No single prognostic indicator is accepted and no previous clinical classification has proved entirely satisfactory, but young age and signs of organ dysfunction seem to be predictive of poor prognosis.[11,12]

CLASS II: HISTIOCYTOSES OF MONONUCLEAR PHAGOCYTES OTHER THAN LANGERHANS CELLS

This group includes disorders which feature accumulations of active histiocytes and lymphocytes but, crucially, the histiocytes are not Langerhans cells. The two most common are haemophagocytic lymphohistiocytosis (familial haemophagocytic reticulosis), which is usually familial and lethal, and the infection-associated haemophagocytic syndrome, which is not familial but is related to various infectious agents. It can be difficult to

Class I: Langerhans-cell histiocytosis

Class II: Histiocytoses of mononuclear phagocytes, other than Langerhans cells

Class III: Malignant histiocytic Disorders

Klassifikation der Histiozytosen

Medical and Pediatric Oncology 29:157–166 (1997)

Contemporary Classification of Histiocytic Disorders

Blaise E. Favara, MD,* and Alfred C. Feller, MD, with members of the WHO Committee on Histiocytic/Reticulum Cell Proliferations: Macro Pauli, MD, Elaine S. Jaffe, MD, and Lawrence M. Weiss, MD, and for the Reclassification Working Group of the Histiocyte Society: Maurizio Arico, MD, Peter Bucsky, MD, R. Maarten Egeler, MD, Goran Elinder, MD, Helmut Gadner, MD, Mary Gresik, MD, Jan-Inge Henter, MD, Shinsaku Imashuku, MD, Gritta Janka-Schaub, MD, Ron Jaffe, MD, Stephan Ladisch, MD, Christian Nezelof, MD, and Jon Pritchard, MD

Pathologists and pediatric hematologist/oncologists of the World Health Organization's Committee on Histiocytic/Reticulum Cell Proliferations and the Reclassification Working Group of the Histiocyte Society present a classification of the histiocytic disorders that primarily affect children. Nosology, based on the lineage of lesional cells and biological behavior, is related to the ontogeny of histiocytes (macrophages and dendritic cells of the immune system).

Dendritic cell-related disorders of varied biological behavior are dominated by Langerhans cell histiocytosis, but separate secondary proliferations of dendritic cells must be differentiated. Juvenile xanthogranuloma represents a disorder of dermal dendrocytes, another dendritic cell of skin. The hemophagocytic syndromes are the most common of the macrophage-related disorders of varied biological behavior.

Guidelines for distinguishing the exceedingly rare malignant diseases of histiocytes from large cell lymphomas through the use of a battery of special studies are provided. Med. Pediatr. Oncol. 29:157–166, 1997.

Key words: histiocytosis; histiocytic neoplasms; Langerhans cell histiocytosis; hemophagocytic syndrome; histiocytes

Klassifikation der Histiozytosen

Nicht-maligne Krankheiten mit variablem klinischem Verlauf:

aus dendritischen Zellen

Langerhanszell-Histiozytose (LCH) — LCH

Erdheim-Chester Krankheit — Non-LCH

Juveniles Xanthogranulom und verwandte Formen — Non-LCH

Solitäre Histiozytome mit dendritischem Phenotyp — Non-LCH

aus Makrophagen

Hämophagozytische Syndrome (HLH)

primäre HLH (familiär oder sporadisch) — HLH

sekundäre HLH (MAS etc.) — HLH

Rosai-Dorfman‘sche Krankheit (SHML) — Non-LCH

Solitäres Histiozytom mit makrophagealen Phenotyp — Non-LCH

Maligne Krankheiten:

aus den Monozyten (Leukämien; monozytäres Sarkom)

aus dendritischen Zellen (lokalis. oder dissemin. histiozytäres Sarkom)

aus Makrophagen (lokalis. oder dissemin. histiozytäres Sarkom)

Klassifikation der Histiozytosen

Blood, Epub ahead of print, 2016

Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages

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Histiocytoses

L Group (Langerhans group)

LCH (Langerhans cell histiocytosis)	CD1a, CD207, S100
ICH	CD1a, CD207-
ECD (Erdheim-Chester disease)	CD68, CD163, FXIIIa, Fascin, CD1a-, CD207-, S100-/low
Extra-cutaneous JXG	

C Group (Cutaneous and mucocutaneous)

Xanthogranuloma family	CD68, CD163, FXIIIa, Fascin, CD1a-, CD207-, S100-/low

R Group (**Rosai-Dorfman** and other Non-L, Non-C) — CD68, CD163, FXIIIa, Fascin, S100, CD1a-, CD207-

M Group (Malignant histiocytoses)

H Group (**HLH** and MAS)