Thomas Hodgkin – The Man, The Legend , The Lecture and his Grave by

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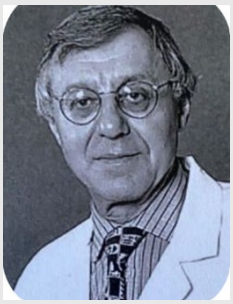
When we were in our third year at U.C.T, we had a host of lecturers in pathology who taught us a subject that for me was fascinating, intriguing and mysterious at once.

In 1972, lecture note taking was pretty standard. Foolscap paper, pen and disciplined listening for the course of what was often a long 45 minutes.

Len Kahn, a young pathologist who had studied in Wits and relocated to Cape Town where he joined the staff of U.C.T Medical School , was our lecturer. As a fairly conscientious student I was impressed by his dynamic and serious approach to teaching

He opened before us the fascinating world of lymphomas. It felt like we were really learning disease from the very bottom up. The histopathological classification, the clinical



PROF LEN KAHN

presentation which were all well-known and systematically described. The treatment approach wasn't tackled , but it felt like it was really important to grasp the various presentations and patterns of lymphomas. After all at 20, we felt ready to deal with anything!

I remember so well the pages Len handed out in the lecture. The first one was blank with headings and we were told to fill it in as the story of lymphoma unfolded. This meant we had to concentrate and notate the pathology accurately.

And then Len came to Hodgkin's Lymphoma. In actual fact, I'd heard of Hodgkin's since a good friend of mine's boyfriend suffered and succumbed to it, so my interest was even more aroused. I simply had to understand this complex but actually well defined tumour.

Len chronicled Thomas Hodgkin's life to us, how , as a pathologist in England he was the first to describe lymphoma which later bore his name, how he fought slavery as a Quaker and that he was a friend of Moses Montefiore, a British banker and philanthropist. After Montefiore's wife died, he travelled with him to Palestine in 1866 and it was in Jaffa that he met his untimely death from dysentery. It was Yom Kippur and medical treatment was unavailable! How sad and unfortunate.

Len went on to tell us how in the early 70's he spent a sabbatical at Tel Hashomer , a hospital in the centre of Israel. He spent his time in Prof Golda Selzer's (ex UCT) pathology department where he had a most enjoyable stay. One of the highlights of his time there was taking it upon himself and a friend to find Hodgkin's grave in Jaffa.

This they did, walking the streets of the town and eventually learning that the grave was tucked away in the back garden of a residential home. To actually enter the small cemetery they needed to climb a fence and then, holy Moses, they found the grave!

So, if we fast forward to 2015, I was based in the centre of Israel , had a busy career in family Practice, and finally decided to try and find Hodgkin's Grave. I had an easier time of this than Len, since I'd read that a group of hematologists from Jerusalem had taken upon themselves to renovate the tomb stone which had become neglected, having lain in the garden for more than one hundred years. I had an inkling where to go and walked the streets of Jaffa until I found the correct address, knocked on the door and was shown through the house, to the back door which led to the garden.

An exciting moment when I saw the tombstone standing quietly in the walled off garden!

HODGKIN'S GRAVE IN JAFFA- GAIL 2015

Not all that long after, I decided to try and find Len Kahn and communicate the amazing effect his lecture had on me, a story that I carried with me throughout my career and would often relate to colleagues and students as an anecdote of my training in faraway Cape Town.

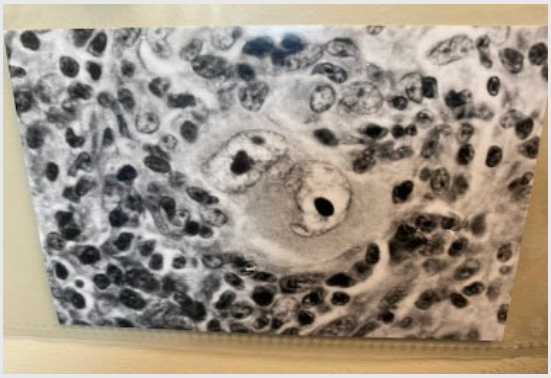
Indeed, I did find Len. We corresponded a few times. He was touched and thrilled that I had remembered his lecture all those years before, told me he'd look for a copy of it in his attic , which he did! Believe it or not, he actually found it.

And so here it is for all those of you who might just be interested in glancing at it. (See the original lecture at end of text)

Len also told me that for many years he was Chairman of Pathology at the Long Island Jewish Medical Center He is still working and recently wrote after a break and told me how touched he was that I remembered his lecture, his tale about Hodgkin's grave and lymphomas in general.

For my part, I felt the need to document this piece of personal history that has threaded its way into my consciousness for so many years.

And so below, an image that Len attached to his letter. He described the cell seen in the centre of the photo as having the ‘eyes of an owl’. Detecting it on the slide of tissue on examination confirms the diagnosis of Hodgkin’s Disease.



THE REED STERNBERG CELL -LEN’S FAVOURITE IMAGE OF IT!

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Thomas Hodgkin – The Man, The Legend, The Lecture and his Grave by Gail Loon Lustig

Written in 2025

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- responsible for humoral antibody production
- form rosettes with SRBC + IgM + complement - "EAC" rosettes

B - Cell lymphomas(and leukaemias) :

1. Most of the non-Hodgkin's lymphomas :
   (a) follicular - predominantly cleaved cell types, low mitotic rate and a better prognosis;
   (b) diffuse - predominantly non-cleaved cell types, high mitotic rate and poorer prognosis.
2. Chronic lymphatic leukaemia and well differentiated lymphocytic lymphoma.
3. Burkitt's lymphoma, non-cleaved cell type.
4. Waldenström's macroglobulinaemia.
5. Myeloma.
6. Immunoblastic sarcoma.

Lukes' hypothesis of a block in transformation of the follicle cell lymphocyte.

(a) at level of dendritic reticular cell ⟶ chronic lymphocytic leukaemia;
(b) at level of cleaved cell ⟶ follicular lymphoma and mixed follicular and diffuse lymphomas;
(c) at level of non-cleaved cell ⟶ diffuse lymphoma and Burkitt's lymphoma.

B - Cell hyperplasia :

? also in infectious mononucleosis, post-vaccination, and following some drugs;

reactive follicular hyperplasia.

M - Cell System

- blood : monocytes
- tissue : macrophages, histiocytes, Kupffer cells
- lymph node : germinal centre and medullary cord macrophages
- spleen : in red and white pulp
- form rosettes with - SRBC + IgM + C ("EAC")
  - SRBC + IgG ("EA")
- contain esterases and can be detected by the α-naphthol acetate reaction.

M-Cell lymphomas (and leukaemias) :

1. Histiocytic lymphoma
2. Histiocytic medullary reticulosis
3. Leukaemic reticulo-endotheliosis

REFERENCES

1. Lukes, R.J., and Collins, R.D. : Immunologic characterisation of human malignant lymphomas. Cancer 34 : 1488 - 1503, 1974.
2. Hansen, J.A., and Good, R.A. : Malignant disease of the lymphoid system in immunologic perspective. Human Path. 5 : 567 - 599, 1974.

LYMPHOMAS

1. The two component concept of the lymphoid system.
2. Structure of an immunologically active lymph node.
3. Structure of the lymphoid follicle (germinal centre).

   Four cell types present :

   - dendritic reticular cell - antigen receptor cell
   - cleaved lymphocytes (small and large)
   - non-cleaved lymphocytes (small and large)
   - macrophages

4. Lymphocyte transformation :

   (a) Change from a dormant (lymphocyte) to a metabolically active state (lymphoblast, reticular lymphoblast, immunoblast).

   (b) The latter is characterised by increase in size, prominent eosinophilic nucleolus, large vesicular nucleus, abundant pyroninophilic cytoplasm and increased mitotic activity.

   (c) Change may be initiated by specific antigenic stimulation, non specific mitogens (phytohaemagglutinin) and allogeneic lymphocytes as in mixed lymphocyte culture.

T-Cell System

- 65 - 80% of peripheral blood lymphocytes
- paracortical region of nodes; perivascular region of white pulp of spleen
- responsible for delayed hypersensivity, allograft rejection and graft - versus - host reactions
- form rosettes with sheep red blood cells (SRBC) - "E" rosettes

T - cell lymphomas (and leukaemias) :

1. ? Hodgkin's disease
   - defect in delayed hypersensivity, normal humoral responses;
   - tendency to lymphocyte depletion with progression of the disease;
   - mediastinal origin of the nodular sclerosing form;
   - focal (early) disease tends to be interfollicular.

   In this disease neoplastic T-cells are considered to be aligned against reactive T-cells.

2. Mycosis fungoides and Sézary's syndrome.
3. Acute lymphatic leukaemia in adolescent with a mediastinal mass.
4. ? Immunoblastic sarcoma.

T-Cell hyperplasia probably occurs in infectious mononucleosis, post vaccination, following some drugs, e.g. hydantionates.

B - Cell System

- 15 - 25% of peripheral blood lymphocytes
- follicles of lymph nodes and spleen; secretory lymphocytes and plasma cells of the medullary cords of the nodes and red pulp cords of the spleen.

CLASSIFICATION OF LYMPHOMAS

A. HODGKIN'S DISEASE

1. Lymphocytic predominant
2. Nodular sclerosing
3. Mixed cellularity
4. Lymphocytic depleted

B. NON-HODGKIN'S LYMPHOMAS

1. Follicular lymphomas
   - Small (atypical) lymphocytic
   - Mixed small (atypical) and large lymphocytic
   - Large lymphocytic

2. Diffuse lymphomas
   - Small lymphocytic → chronic lymphatic leukaemia
   - Atypical small lymphocytic → lymphosarcoma cell leukaemia
   - Mixed small and large lymphocytic ± Reed-Sternberg-like cells
   - Large lymphocytic (pyroninophilic)
   - ? Histiocytic (reticulum cell)
   - Undefined (undifferentiated)
   - Special category*

* Burkitt's lymphoma
Convoluted lymphocytic (thymic)
Mycosis fungoides
Sézary's syndrome
Leukaemic reticuloendotheliosis
Histiocytic medullary reticulosis

Non-specific features associated with lymphomas :

Plasmacytoid differentiation
Immunoglobulin production
  IgG, IgA, IgM (Waldenström)
  Heavy chain (Franklin; α-heavy chain)
Epithelioid cell reaction

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1. Lukes, R.J. and Collins, R.D. : Immunologic characterization of human malignant lymphomas. Cancer 34 : 1488-1503, 1974.

2. Hansen, J.A. and Good, R.A. : Malignant disease of the lymphoid system in immunological perspective. Human Path. 5 : 567-599, 1974.

3. Braylan, R.C., Jaffe, E.S. and Berard, C.W. : Malignant lymphomas. Current classification and new observations. In Pathology Annual, 1975, ed. Sommers, S.C. p 213-270.

HODGKIN'S DISEASE

TYPE	CELL OF ORIGIN	CLINICALLY	PATHOLOGY
HODGKIN'S - FOUR TYPES (Lukes and Butler)	? Lymphocyte (T-type) ? Histiocytic (Reticulum cell)	Probably disease of "unifocal" origin. ? contiguous lymphatic spread ? haematogenous spread	Replacement of node by mixed cell population : 1. Atypical "reticulum-type" cells, including Reed-Sternberg cells - the neoplastic cells in this lymphoma. Reed-Sternberg cells essential for a diagnosis of Hodgkin's : large cells; more than one nuclear lobe ("mirror-image" cell"); large red nucleoli in each lobe with a smooth contour, peri-nucleolar clear area in nucleus. 2. Lymphocytes, plasma cells, eosinophils, reactive histiocytes, fibroblasts - probably inflammatory cells in this lymphoma.
A. Lymphocytic predominant (L.P.) (Hodgkin's paragranuloma)		Very good prognosis	Numerous lymphocytes and/or reactive histiocytes and scanty Reed-Sternberg cells.
B. Nodular sclerosing (N.S.) (Hodgkin's granuloma)		Frequent in females in second and third decade; often involves mediastinal or cervical glands. Very good prognosis.	Cellular areas form nodules separated by encircling fibrous bands. These areas contain atypical Reed-Sternberg cells ("lacunar cells") in addition to cell types enumerated above.
C. Mixed (M) (Hodgkin's granuloma)		Poor prognosis	All cell types as enumerated above in varying proportions but atypical "reticulum-type" cells and Reed-Sternberg cells easy to find.
D. Lymphocytic depletion (L.D.) (Hodgkin's sarcoma)		Very poor prognosis	Very few lymphocytes; numerous atypical "reticulum-type" cells and Reed-Sternberg cells OR extensive diffuse fibrosis with moderate numbers of atypical "reticulum-type" cells or Reed Sternberg cells.

NON-HODGKIN'S LYMPHOMAS

TYPE	CELL OF ORIGIN	CLINICALLY	PATHOLOGY
LYMPHOCYTIC (Lymphosarcoma)	Lymphocyte	Multifocal in origin : lymph nodes, spleen, bone marrow, viscera. Blood - leukaemia.	Replacement of node by sheets of lymphocytic cells - well differentiated or poorly differentiated (lymphocytic or lymphoblastic); increased mitotic activity.
HISTIOCYTIC (RETICULUM CELL) (Reticulum cell sarcoma)	Histiocytic cell	Multifocal in origin : lymph nodes, spleen, bone marrow, viscera.	Replacement of node by sheets of histiocytic cells - oval vesicular nuclei with folded nuclear membranes; prominent nucleoli; increased mitotic activity; each tumour cell is surrounded by reticulin fibres (Cf.reticulin pattern in metastatic carcinoma where reticulin surrounds groups of cells. When histiocytic cells are very pleomorphic, the lesion may resemble Hodgkin's disease (L.D.).
FOLLICULAR	Germinal centre (follicle centre cells)	As above	Replacement of node by follicular aggregates of cleaved and/or non-cleaved lymphocytes. Follicles in cortical and medullary regions; usually all of similar size; ill-defined margins; may fuse to form abnormally shaped follicles (Cf. reactive node with follicles mainly in cortex, often very large, sharp margins, contain many mitoses and "tingible body" macrophages).
BURKITT'S	Lymphocyte	Usually in children mainly Africans, high incidence in regions of Central Africa (? transmitted by mosquito). Lymphoma predominantly of extranodal origin - jaw bones, gonads, other viscera. Good initial response to chemotherapeutic agents.	Replacement of nodes by sheets of poorly differentiated lymphocytes, scattered throughout individual histiocytes showing cytophagocytosis ("tingible body" macrophages) → "starry-sky" pattern.

MALIGNANT LYMPHOMAS

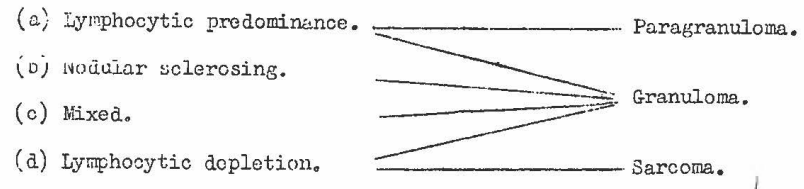
TYPE	CELL OF ORIGIN	CLINICALLY	PATHOLOGY
LYMPHOCYTIC (Lymphosarcoma)	Lymphocyte	Multifocal in origin: lymph nodes, spleen, bone marrow, viscera. Blood - leukaemia.	Replacement of node by sheets of lymphocytic cells - well differentiated or poorly differentiated (lymphocytic or lymphoblastic); increased mitotic activity.
RETICULUM CELL (HISTOCYTIC) (Recticulum cell sarcoma)	Reticulum cell	Multifocal in origin: lymph nodes, spleen, bone marrow, viscera.	Replacement of node by sheets of reticulum cells - oval, vesicular nuclei with folded nuclear membranes; prominent nucleoli; increased mitotic activity; each tumour cell is surrounded by reticulin fibres. (cf. reticulin pattern in metastatic carcinoma where reticulin surrounds groups of cells.) When reticulum cells are very pleomorphic the lesion may resemble Hodgkin's disease (L.D.).
MIXED CELL (some cases of 'giant) (follicular lymphoma')	Lymphocyte + Reticulum cell	As above.	Replacement of node by aggregates of lymphocytes, usually poorly differentiated and atypical histiocytes. These abnormal cells usually form abnormal follicles of varying size throughout the node. Fusion between follicles is common -> bizarre shaped follicles. This condition must be distinguished from reactive lymph nodes.
BURKITT'S	Lymphocyte	Usually in children, mainly Africans, high incidence in regions of Central Africa (? transmitted by mosquito). Lymphoma predominantly of extra-nodal origin - jaw bones, gonads, other viscera. Good initial response to chemotherapeutic agents.	Replacement of nodes by sheets of poorly differentiated lymphocytes, scattered throughout individual histiocytes showing cytophagocytosis --> 'starry-skin' pattern.

All the above may have a follicular pattern or a diffuse pattern.

CLASSIFICATION OF MALIGNANT LYMPHOMAS

	Previous Terms:
1. LYMPHOCYTIC TYPE	
(a) Well differentiated ('lymphocytic')	Lymphosarcoma.
(b) Poorly differentiated ('lymphoblastic')	Some cases of GFL.
2. RETICULUM CELL TYPE (HISTIOCYTIC TYPE).	Reticulum cell sarcoma. / Some cases of GFL.
3. MIXED CELL TYPE (i.e. lymphocytic + histiocytic)	Lymphosarcoma. / Reticulum cell sarcoma. / Some cases of GFL.

4. HODGKIN'S TYPE.



All the above may be NODULAR (FOLLICULAR) OR DIFFUSE.

This classification does not deal with other specialized forms of lymphoma e.g. Burkitt's, Malignant Reticulo-Endotheliosis.

CLASSIFICATION OF MALIGNANT LYMPHOMAS

The purpose of this classification is to attempt to establish some uniformity in the designation of the lympho reticular neoplasms so that pathologists, radiotherapists and clinicians from various centres will be able to communicate intelligently with one another.

The classification is adapted from the Armed Forces Institute of Pathology Tumor Fascide, 'Tumors of the Hematopoietic System', Section III, Fascide 8 by Henry Rappaport. This is a classification based on the cell of origin of the lymphoma.

NOTE:-

(1) The Jackson and Parker classification for Hodgkin's disease has been found to be of limited prognostic value because about 85% of cases fall into the relatively unfavourable 'granuloma' group. A modification of the Lukes-Butler classification separates cases of Hodgkin's into 4 groups. Patients previously diagnosed as Hodgkin's granuloma may fall into any one of these 4 groups:-

JACKSON AND PARKER (1944).	LUKES & BUTLER (MODIFIED) (1966).
PARAGRANULOMA.	LYMPHATIC PREDOMINANCE.
GRANULOMA.	NODULAR SCLEROSING.
	MIXED.
SARCOMA.	LYMPHOCYTIC DEPLETION.

(2) The term giant follicular (GFL) lymphoma does not appear in the new classification as such cases are classified according to the predominant cell type or types present followed by a statement that the lymphoma is of nodular of follicular type.

REFERENCES

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   R.J. Lukes and J.J. Butler,
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