Meeting of the Lymphoma Working Groups
Haematologic Tumours Line

HAEMATOPATHOLOGY
A Leap Forward in Pathology
(a Personal View)

Jerónimo Forteza Vila
One of the first references of Haematopathology in the literature is the description in 1832 entitled "On some morbid appearance of the absorbent glands and spleen" by Thomas Hodgkin, prosector at the Guy hospital in London.

This paper which includes seven autopsy cases with macroscopic description and clinical data clearly emphasizes the clinicopathologic correlation.
Watercolor by Robert Carswell on an autopsy by Thomas Hodgkin
It was Sir Samuel Wilks, Professor of Pathology also from London, who later called these cases Hodgkin’s disease in his treatise “Enlargement of the lymphatic glands and spleen”.

The description by Hodgkin and the later review by Wilks only make reference to macroscopic Pathology and its clinical correlation.
Hodgkin’s disease has been histologically characterized by a proliferation with a minority of neoplastic cells, Hodgkin cells and Reed-Sternberg cells with its variants, in a variable background formed by lymphocytes, eosinophils, histiocytes and plasma cells.

These tumor cells account for 0.1 to 10% of all the cells.
Reed-Sternberg cell in Hodgkin’s lymphoma (HE; 100X)
Paraffin-embedded tissue of one of the original cases by Thomas Hodgkin immunostained with CD15 (David Mason)
Laser microdissector
It is nowadays clear that Hodgkin’s disease is a lymphoma and -more specifically- a predominently B-cell lymphoid proliferation, as evidenced from its immunophenotype and its molecular make-up, the latter determined by single cell PCR studies.

Consequently, the current WHO classification has appropriately and unequivocally chosen the term Hodgkin lymphoma.

B-cell mature, molecular studies (single-cell PCR)

One cell analysis

- Ig gene rearrangements > 90%
  - B-cell origin
- Ig gene somatic mutations
  - Germinal center origin

Loss of B-cell identity
Evolution of the clinical management of the Hodgkin’s Lymphoma

Kaplan stage

Current stage
Hodgkin’s Lymphoma
A Paradigm in Oncohaematology

• Hodgkin’s disease was the first condition described from a cytological base of the neoplastic cells characteristics (Reed-Sternberg cell).

• This was the first neoplasia where the clinical course correlated with affected anatomical regions.

• The development of Oncology is understood through the chronology of Hodgkin’s disease treatment.
  – Gilbert (1925), treated the destruction of the lesion with radiotherapy.

• This was one of the first neoplasias treated with chemotherapy and radiotherapy.
Haematopathology

Basis for the development of new technologies in Surgical Pathology

Philadelphia Chromosome in Chronic Myeloid Leukemia
Philadelphia Chromosome t(9;22) translocation

Inhibitor of the BCR-ABL Tyrosin-Kinase in Chronic Myeloid Leukemia
Targeting the BCR-ABL tyrosine kinase in chronic myeloid leukaemia


Dr. Brian J. Druker
OHSU Cancer Institute, Leukemia Center
(Portland, Oregon, USA)
Numerical aberrations in cariotyping can be detected by FISH using Color Species Banding (RxFISH)

*Courtesy of Francesc Solé (Barcelona)*
(A) Burkitt’s Lymphoma (HE) (B) t(8;14) translocation in Burkitt’s lymphoma (FISH)
Immunostaining for CD30 in a Reed-Sternberg cell in membrane and Golgi
César Milsten (Cambridge)
Nobel Prize in Medicine, 1984

David Mason (Oxford)
Reed-Sternberg and Hodgkin cells, detected by double immunostaining: CD15 (Golgi) in red and MiB-1 (nucleus) in brown.

Ignacio Solas in La Coruña (1982), explaining the method of double labelling published that year in the *Journal of Histochemistry* by Bruno Falini and coworkers.
T-cell with E rosette of sheep erythrocytes, courtesy of Juan Rosai (1974)

“Helped to transform hematopathology from a difficult morphologic exercise into a functionally oriented biologic science” (Berard)
Schrödinger wrote that the first half of the 20th century was the age of the Physics and the second half was the age of Biology.
Molecular Structure of Nucleic Acids

A Structure for Deoxyribonucleic Acid

We wish to suggest a structure for the salt of deoxyribonucleic acid (DNA). This structure has novel features which are of considerable biological interest.

In the deoxynucleic acid, there are two phosphates separated by a glycosidic bond. The deoxynucleic acid is a polymer of deoxyribose and phosphate groups. The deoxynucleic acid is composed of two helical chains, each consisting of deoxyribose and phosphate groups.

One of the chains is made up of deoxyribose units, and the other is made up of phosphate units. The two chains are wound around each other, forming a double helix. The deoxynucleic acid is held together by hydrogen bonds.

The structure is described in terms of the positions and orientations of the deoxyribose and phosphate units. The deoxynucleic acid is a left-handed helix, and the deoxyribose and phosphate units are arranged in a right-handed helix.

The deoxynucleic acid is held together by hydrogen bonds between the nitrogenous bases. The deoxynucleic acid is a double helix, and the two strands are antiparallel.

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Mantle cell lymphoma genotypes identified with CGH to BAC microarrays define a leukemic subgroup of disease and predict patient outcome. Courtesy of Dr. Jose Angel Climent, CIMA (Navarra)
Pathology Case Reviews

Soft Tissue Tumors: The Role of Ancillary Techniques

John R. Goldblum, MD and Torsten O. Nielsen, MD, PhD, FRCP
Guest Editors
Haematopathology

A team work effort and consensus

(Paradigm of the globalisation of Pathology)
Pathologists, radiation oncologists, clinical oncologists, epidemiologists and statisticians who participated in the final meeting held at Palo Alto, California in 1980 and which generated the Working Formulation of Non-Hodgkin’s Lymphomas for Clinical Usage.
Experts of the Working Formulation Group at Palo Alto (California, 1980). From left to right: G. O’Connor (WHO Classification), R. Dorfman (Dorfman Classification), K. Lennert (Kiel Classification), K. Henry (British National Lymphoma Investigation Classification), R. Lukes (Lukes and Collins Classification), H. Rappaport (Rappaport Classification)
(A) Airlie House Meeting (1997); Clinical Advisory Committee for the Lymphoma Classification, previous WHO 2001.

(D) Airlie House Meeting (2007); Clinical Advisory Committee for Nature Lymphoid Neoplasms
World Health Organization Classification of Tumours

Pathology & Genetics

Tumours of Haematopoietic and Lymphoid Tissues

Edited by Elaine S. Jaffe, Nancy Lee Harris, Harald Stein, James W. Vardiman
Introduction to the History of Spanish Haematopathology

(Data from Horacio Oliva)
History of Spanish Haematopathology (1)

- JOSE EZARQUÍ (1827)
- MANUEL HURTADO DE MENDOZA (1830)
- CARDENAL (1877)
- RAFAEL ARIZA Y ESPEJO (1877)
- GUSTAVO PITITALUGA (1876-1956)
History of Spanish Haematopathology (2)

- PEDRO FARRERAS VALENTI (1915-1968)
History of Spanish Haematopathology (3)

• MANUEL MORALES PLEGUEZUELO (1898-1967)

• GERÓNIMO FORTEZA BOVER (1911-1975)

Only two haematopathologists, Morales and Forteza, appear in the book by Karl Lennert, in the handbook of Lubarsch and Henke.
LOS GANGLIOS LINFÁTICOS EN CORTES E IMPROMPTAS

Estudio de 164 casos
con especial referencia al adenograma normal y en las
hiperplasias benignas

Volumen I

Tesis para aspirar al
GRADO DE DOCTOR

MANUEL MORALES PLEGUEZUELO
1954
Dr. Gerónimo Forteza Bover in 1942 at his first private Laboratory in Conde de Montornés street, no. 2 (Valencia)
G. Forteza Bover

EL DIAGNOSTICO
POR LA
PUNCIÓN GANGLIONAR

1947. Editorial SABER - Valencia

DR. G. FORTEZA BOVER
Jefe de Laboratorio de Patología Médica de la Facultad de Medicina de Valencia. Del Instituto de Medicina Experimental. Académico correspondiente de la Real Academia de Medicina y Cirugía de Valencia. Miembro Honorario del Instituto Médico Valenciano

EL DIAGNOSTICO
POR LA
PUNCIÓN GANGLIONAR

CON 55 FIGURAS EN NEGRO Y COLOR

PROLOGO
DE
ALFRED PINEY, M. D.
Member of the Royal College of Physicians of London,
Physician, St. Mary's Hospital, E. 13. Foreign Member
Société de Medicin de Paris

LIBRERIA de F. GARCIA MUÑOZ
Hospital, 14 VALENCIA Teléfono 13425
(España)
G. FORTEZA BOVER

ATLAS DE HISTOPATOLOGIA
DE LAS
ENFERMEDADES DE LA SANGRE

EL DIAGNÓSTICO A TRAVÉS DE LAS PUNCIONES BIOPSIAAS ASPIRATIVAS DE LOS ÓRGANOS HEMOLINFOPOYÉTICOS

EDITORIAL SABER
VALENCIA ESPAÑA
1956

Fig. 100.—KALA-azar de adulto (Medula ósea). Numerosas células reticulares con abundantes parásitos. Manifesta plasmocitosis. Corte histológico a inmersión. Col.: Giemsa
Fig. 57.—FIEBRE TIFOIDEA (Medula ósea esternal). 2.ª semana. A) Se percibe con toda nitidez un nodulillo tífico del resto del tejido mieloide. B) A mayor aumento se ve en el centro de la agrupación celular reticular un vaso y por fuera de aquélla una franja de linfocitos.
Clinical Laboratory of the School of Medicine (Valencia, 1965)
From left to right: Dr. José Esquerdo (Pathologist), Prof. Manuel Beltrán Báguena (full professor of Internal Medicine) and Prof. Gerónimo Forteza Bover (haematopathologist)
(A) W. Dameshek (1900-1969). “Lacking only are electron micrographs” (1964) (B) Periferal blood smear stained with May-Grümwald-Giemsa in Chronic Myeloid Leukemia (C) Cariotype of Myeloid Chronic Leukemia with Philadelphia Chromosome (D) Atlas of Blood Cytology (1964)
Dr. Gerónimo Forteza Bover (1965 and 1969) with an electron microscope at his Laboratory in Jorge Juan 15, Valencia. This laboratory was the basis of the Cytologic Investigations Institute (1974).
Histoautoradiography in Electron Microscopy
Dr. Gerónimo Forteza Bover at the Cytologic Investigations Institute, in a seminar meeting (1974)
Cytologic Investigations Institute at Valencia
(founded in 1970, Caja de Ahorros de Valencia)
Dr. Gerónimo Forteza Bover was the first director
CRONOLOGIA

DIRECTORES

1965-1966  Dr. Gerónimo Forteza Bover
            Director del Laboratorio de Citogenética

1966-1975  Dr. Gerónimo Forteza Bover
            Director del IIC

1976-1977  Dr. Rafael Báguena Candela
            Director en funciones del IIC

1977-1991  Dr. Santiago Grisolia García
            Director del IIC

1991-1993  Dr. Antonio Duato Gómez-Novella
            Director Interino del IIC

1993-1995  Dr. Rafael Sentandreu Ramón
            Director de la FVIB

1995-2000  Dr. Maria Eugenia Armengod Gonzalez
            Directora en funciones de la FVIB

2000-2002  Dr. Vicente Felipe Orts
            Directora en funciones de la FVIB

2002-actual Dr. Ruben Moreno Palanques
            Director General de la FVIB, CSAT, y CIPF

HISTORIA

1940

El Profesor Gerónimo Forteza Bover (1911-1975) inicia la actividad investigadora en el campo de la citología. Su inquietud científica se pone de relieve en numerosas publicaciones, en revistas nacionales y extranjeras, libros y ponencias en congresos nacionales e internacionales.

1961-63

Premio “Cerdà Reig” de Ciencias de la Excma. Diputación Provincial de Valencia. Este galardón se otorga a los resultados obtenidos en los estudios de Citogenética realizados por el Profesor Gerónimo Forteza con la colaboración del Prof. Báguena Candela.
Haematopathology and Spanish Histological School
During time lymphomas were called microgliomas.
Fernando de Castro

Glomus caroticum
Electron microscopy of the bone marrow innervation

Bone marrow innervation with silver stain
(Fernando de Castro’s technique)

Haematopathology and the Spanish University

(Honoris Causa)
Karl Lennert (Universidad Autónoma de Madrid, 1995)
Horacio Oliva and Francisco Nogales in the Honoris Causa Ceremony of Dr. H. Oliva (Granada, 1998)
J. Rosai (Santiago de Compostela, 1999)
Honoris Causa speech “Apología de la Hematoxilina-Eosina”
Elaine Jaffe (Universidad de Barcelona, 2008)
Honoris Causa speech “The Microscope as a Tool for Disease Discovery”
History of Spanish Haematopathology

Spanish Lymphoma Club
Lymphoma Symposiums (1975-1978)
Hospital Juan Canalejo (La Coruña)

Dr. Carmen Rivas
I Lymphoma Symposium (La Coruña, 1975)
II Lymphoma Symposium (La Coruña, 1978)
Augusto Moragas (Santiago de Compostela, 1985)
LINFADENOPATIAS BENIGNAS.
BASES MORFOLOGICAS DE SU
INTERPRETACION CLINICA

Augusto Moragas

Quisiera hoy, con devoción, dedicar el presente trabajo a la memoria del insigne maestro.

Augusto Moragas
Short Course E3a. DIAGNOSTIC QUANTITATIVE PATHOLOGY

MATHEMATICAL MORPHOLOGY. APPLICATIONS IN PATHOLOGY

Augusto Moragas, M.D.
Haematopathology
(Bench to Bedside – Bedside to Bench)

• The knowledge in Haematopathology has gone beyond classical morphological diagnoses to gain a better understanding of diseases and prognosis.

• It has strengthened Surgical Pathology and provided Haematology with firm and secure diagnoses, thus spearheading the advance of current Oncology.

• Cytogenetics and biologic knowledge has taken targeted therapies to other fields in Oncology.

• Its advance and knowledge is the result of the incorporation of immunological and biological advances in diagnosis and therapeutics, and to a teamwork effort of interdisciplinary groups.
“Lecture of Anatomy of Dr. Nicolaes Tulp” – Rembrandt, 1632 (modified)
Courtesy of Carlos Cordón (New York, USA)