THE DEVELOPMENT OF THE KNOWLEDGE OF THE LEUKOCYTE

An Exhibit Prepared for the 26th Annual Graduate Fortnight of The New York Academy of Medicine, on "Disorders of the Blood and the Blood-Forming Organs," October 19 to 30, 1953, Held in the Library Reading Room from October 19 through November 30, 1953

Little has been published on the development of knowledge of the leukocyte. An early book containing mention of the lmyphatic system is William Hewson's *Experimental inquiries; part the second* . . . London, 1774. The first description of the leukocyte is contained in William Addison's paper on "Colourless globules in the buffy coat of the blood," 1840. In the following decades, Donné, Craigie and Virchow made further contributions to this subject. In 1877 Paul Ehrlich was able to differentiate various forms of leukocytes with the help of his staining methods. These studies became the foundation of our present knowledge of these form elements. Since on search, no comprehensive bibliography on the history of the development of the leukocytes was to our knowledge available, an exhibit on this subject was felt to be desirable. We are listing for further reference the following titles:

HEWSON, WILLIAM (1739-1774). "Experimental inquiries: part the second . . ." London: 1774. First edition of this important work on the lymphatic system.

VELPEAU, ALFRED (1795-1867). "Sur la Résorption du pus et sur l'altération du sang dans les maladies. (Clinique de perfectionnement)," Revue Médicale, 1827, v.2, p.216. In 1827 Velpeau wrote of the peculiar alteration in the color of the blood, suggesting the admixture with it of "pus".

ADDISON, WILLIAM (1802-1881). "Colourless globules in the buffy coat of the blood," London Medical Gazette, 1840-41, v.27, p.479. In 1840 Addison made accurate observations on the white blood cells.

ANDRAL, GABRIEL (1797-1876). "Essai d'hématologie pathologique ou études des altérations principales du sang . . ." Bruxelles: 1843. A treatise on the analysis of the blood. Andral was the first to coin the term "anaemia".

DONNE, ALFRED (1801-1878). "Cours de microscopie complémentaire des études médicales, anatomie microscopique et physiologie des fluides de l'économie." Paris: 1844. The earliest microscopic recognition of leukemia. Donné attributed to the spleen the function of converting the white corpuscles into red corpuscles as William Hewson had done in the preceding century.

CRAIGIE, DAVID (1793-1866). "Case of disease of the spleen, in which death took place in consequence of the presence of purulent matter in the blood," Edin-

burgh Medical Journal, 1845, v.64, p.400. Description of an early case of leukemia.

VIRCHOW, RUDOLPH LUDWIG KARL (1821-1902). "Weisses Blut und Milztumoren," Medicinische Zeitung, 1846, v.14, no.34, p.157. In 1846 Virchow brought forward new evidence to support his contention that the abnormal cells of the blood in leukemia were really white blood cells and not pus cells as had been maintained by Craigie and John Hughes Bennett.

JONES, THOMAS WHARTON (1808-1891). "The blood-corpuscle considered in its different phases of development in the animal series." London: 1846. A description of the different types of blood cells in the blood of various animals and man.

VOGEL, JULIUS (1814-1880). "Ein fall von Leukämie mit Vergrösserung der Milz und Leber," Archiv für pathologische Anatomie und Physiologie und für klinische Medicin, 1851, v.3, p.570. In 1851, Vogel was the first German clinician to observe during life that there was a large proportion of abnormal colorless corpuscles in the blood of a patient in whom the liver and spleen were greatly enlarged.

WELCKER, HERMANN (1822-1897). "Blutkörperchenzählung und farbeprüfende Methode," Vierteljahrschrift für praktische Heilkunde, 1854, v.44, p.63. The earliest recorded leukocyte count was that performed by Hermann Welcker on Margaret Mueller on April 25, 1853.

FRIEDREICH, NIKOLAUS (1825-1882). "Ein neuer Fall von Leukämie," Archiv für pathologische Anatomie und Physiologie und für klinische Medicin, 1857, v.12, p.37. An early paper describing the existence of leukemia running an acute course.

VIRCHOW, RUDOLPH LUDWIG KARL (1821-1902). "Die Cellularpathologie in ihrer Begrundung auf Physiologische und Pathologische Gewebelehre," Berlin: 1858. The first use of the word "leukocytosis"' to describe the condition in which the increased proportion of colorless corpuscles in the blood was dependent upon an affection of the lymphatic glands.

SCHULTZE, MAX (1825-1874). "Ein heizbarer Objecttische und seine Verwendung bei Untersuchungen des Blutes," Archiv für mikroskopische Anatomie, 1865, v.1, pl.2. In this work Schultze describes four forms of colorless corpuscles in human blood and recognized those which were finely and those which were coarsely granular. Number 7 is a polymorphonuclear cell, though some of the granules are large for those of a neutrophil.

NEUMANN, ERNST (1834-1918). "Ein Fall von Leukämie mit Erkrankung des Knochenmarkes," Archiv der Heilkunde, 1870, v.11, p.1. Neumann discovered the characteristic changes in the bone-marrow in leukemia and proposed the term myelogenous leukemia to distinguish it from the "splenic or lymphatic forms."

EHRLICH, PAUL (1854-1915). "Beiträge zur Kenntniss der Anilinfärbungen und ihrer Verwendung in der mikroskopischen Technik," Archiv für mikroskopische Anatomie, 1877, v.13, p.263. Erhlich's first paper on the staining of specific granulations in white blood corpuscles by means of aniline dyes was written while he was still a student.

GOWERS, (SIR) WILLIAM RICHARD (1845-1915). "On the numeration of blood-corpuscles," Lancet, 1877, v.2, p.797. "The method [of counting corpuscles]

although it has been largely employed in France, and also in Germany, is almost unknown in clinical work in this country."

EHRLICH, PAUL (1854-1915). "Methodologische Beiträge zur Physiologie und Pathologie der verschiedenen Formen der Leukocyten," Zeitschrift für klinische Medicin, 1880, v.1, p.553. One of the greatest advances in modern hematology was the introduction of staining methods by Ehrlich whereby the various white blood cells could be readily recognized as belonging to the five varieties. An early paper on this subject.

METCHNIKOFF, ELIE (1845-1916). "Ueber die Beziehung der Phagocyten zu Milzbrandbacillen," Archiv für pathologische Anatomie, 1884, v.97, p.502. A paper written by Elie Metchnikoff in 1884 on his discovery of the phagocytes and phagocytosis.

EBSTEIN, WILHELM (1836-1912). "Ueber die acute Leukamie und Pseudoleukamie," Deutsches Archiv für klinische Medicin, 1888-89, v.44, p.343. A clinical description of the outstanding symptoms of acute leukemia.

MUELLER, HERMANN (1866-1898) und HERMANN RIEDER. "Ueber Vorkommen und klinische Bedeutung der oesinophilen Zellen (Ehrlich) im circulirenden Blute des Menschen," Deutsches Archiv für klinische Medicin, 1891, v.48, p.96. First reference to eosinophilia in helminthiasis.

EHRLICH, PAUL (1854-1915). "Ueber schwere anämische Zustände," Verhandlungen des Congresses für innere Medicin, 1892, v.33, p.33. An amplification of Ehrlich's original article on the differential count.

HIRSCHFELD, HANS (1873-). "Beiträge zur vergleichenden Morphologie der Leucocyten." Berlin: 1897. Hans Hirschfeld, the Berlin physician, in 1897 wrote this thesis on his discovery that coarse acidophil granules were characteristically present in the leukocytes of all mammalian species examined by him.

THAYER, WILLIAM SIDNEY (1864-1932). "On the increase of the eosinophilic cells in the circulating blood in trichinosis," Lancet, 1897, v.2, p.788. Summary of two cases observed by Thayer and Thomas R. Brown. Brown's preliminary note appeared in the Johns Hopkins Hospital Bulletin, April, 1897.

BROWN, THOMAS RICHARDSON (1872-1950). "Studies on trichinosis, with especial reference to the increase of the eosinophilic cells in the blood and muscle, the origin of these cells and their diagnostic importance," Journal of Experimental Medicine, 1898, v.3, pl.xxv. In 1898 Doctor Brown published a more detailed study.

NAEGELI, OTTO (1871-1938). "Ueber rothes Knochenmark und Myeloblasten," Deutsche medicinische Wochenschrift, 1900, v.26, p.287. This is the first time that myeloblastic leukemia was distinguished cytologically from other types of acute leukemia.

ARNETH, JOSEPH (1873-). "Die neutrophilen weissen Blutkörperchen bei Infektions-krankheiten." Jena: 1904. The Arneth count—a classification of polymorphonuclear leukocytes into five groups, depending on the number of lobes.

SABIN, FLORENCE RENA (1871-1953). "The vitally stainable granules as a specific criterion for erythroblasts and the differentiation of the three strains of white blood cells as seen in the living chick's yolk-sac," Johns Hopkins Hospital Bulletin, 1921, v.28, p.314.

COOKE, WILLIAM EDMUND (1881-) and ERIC PONDER (1898-). "The polynuclear count." London: 1927. This contribution to haematology is a concise description of a new method of classifying the polymorphs by clinical and experimental tests.

SCHILLING, VICTOR THEODOR ADOLF GEORG (1883-). "Das Blutbild und seine klinische Verwertung. . . ." Jena: 1929. Doctor Schilling simplified the older Arneth method of differential counting, and recorded his results on a chart which he called a "hemogram."

FARLEY, DAVID LABOURE, HUSTON ST. CLAIR, and JOHN A. REISINGER (1901-). "The normal filament and nonfilament polymorphonuclear neutrophil count: its practical value as a diagnostic aid," American Journal of Medical Sciences, n.s.1930, v.180, p.336. The filament and nonfilament count described in 1930.

ROLLESTON, (SIR) HUMPHRY DAVY (1826-1944). "The history of haematology," Proceedings of the Royal Society of Medicine, July 1934, p.5, "As Professor William Bulloch told me some years ago, the word 'leucocyte' made its appearance first in 1855 in M. P. Littré and C. Robin's *Dictionnaire de Médecine* (Nysten); it was probably suggested by and derived from, the word 'leucocythémie' employed in 1851 by John Hughes Bennett in a paper read before the Société de biologie in Paris, to describe 'white-cell blood.' "

The portraits shown were:

GABRIEL ANDRAL, 1797-1876. Graduate of the Paris Faculty of Medicine in 1821, he was elected to the professorship of hygiene seven years later. In 1839, at the death of Francois Broussais, Andral succeeded him in the chair of pathology. His researches on the blood were among his more important contributions to medicine. He died in his seventy-ninth year.

PAUL EHRLICH, 1854-1915. Pioneer in the studies of morphology of blood, in tissue staining and immunology. Sir Humphrey Rolleston wrote in 1933: "Accurate knowledge of diseases of the blood-forming organs is an advance of the last fifty years, and is due to the stains introduced by Ehrlich in the seventies which enabled the greatly improved microscopes to show up the minute structure of the blood corpuscles."

SIR WILLIAM RICHARD GOWERS, 1845-1915. Born in London in 1845, he completed his medical training at University College, London, where he was a pupil of Sir William Jenner. Interested in diseases of the nervous system, his early contributions to medical literature dealt with the blood-vascular system. In 1880 he described for the first time the tract of nerve-fibers in the spinal cord, subsequently known as "Gowers's Tract." In 1883 he became physician and later, professor of clinical medicine at University College. He died in London in 1915.

ERNST HEINRICH PHILIPP AUGUST HAECKEL, 1834-1919. Laid the foundations of the theory of phagocytosis in 1882.

WILLIAM HEWSON, 1739-1774. A surgeon and anatomist, his researches on the blood were of great importance in establishing the essential character of the process of coagulation and the forms of the red corpuscles in different animals.

ELIE METCHNIKOFF, 1845-1916. The Russian physiologist whose recognition of the validity of the doctrine of phagocytosis in relation to wounds, disease,

immunity, and normal healthy life was the result of his scientific insight and boundless energy.

PIERRE CARL EDOUARD POTAIN, 1825-1901. Inventor of the blood-diluting pipette in 1867.

SIR HUMPHRY DAVY ROLLESTON, 1862-1944. A well-known pathologist in British medicine in the twentieth century. In 1922, his position as a leader of the medical profession in his country was recognized upon his election as President of the Royal College of Physicians.

FLORENCE RENA SABIN, 1871-1953. Born in Central City, Colorado. A graduate of Smith College and Johns Hopkins Medical School, she later became associate professor of anatomy and professor of histology—the first woman to become full professor at Johns Hopkins. Her studies in blood and blood diseases were among her principal achievements. She died at the age of 81.

WILLIAM SYDNEY THAYER, 1864-1932. "Thayer," said William H. Welch, "was the physician's physician. The world at large may have heard more of others, but to the medical élite—Thayer!" A graduate of Harvard Medical School in 1885, he later became Sir William Osler's assistant at Johns Hopkins Hospital and in 1905 professor of clinical medicine at the University. In 1917 he joined the Red Cross Mission to Russia to study general health conditions in that country. His researches on blood, malarial fever, parasitology, pellagra and cardiac disease were important contributions to the field of medicine. He died in 1932.

ALFRED ARMAND LOUIS MARIE VELPEAU, 1795-1867. A pupil of Bretonneau, he was surgeon to the Hôpital St. Antoine, La Pitié, and the Charité. He was professor of clinical surgery at the Paris Faculty from 1834 till his death in 1867. His great treatise on diseases of the breast was the most important work on the subject in its time.

RUDOLPH LUDWIG KARL VIRCHOW, 1821-1902. Born in Schievelbein in Pomerania, he took his medical degree in Berlin in 1843. From 1849 to 1856 his life was wholly devoted to work which led to the propounding of his theory of cellular pathology. He was director of the Berlin Pathological Institute until his death in 1902.

HERMANN WELCKER, 1822-1897. Born in Giessen, he took his medical degree in 1851 from the University of Bonn; he became assistant physician at the medical clinic in Giessen and later professor of anatomy. In 1876 he became Director of the Anatomical Institute there.

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