Andrzej Grzybowski *

Ludwik Fleck as a medical scientist, microbiologist and immunologist

LUDWIK FLECK WAS BORN IN LWÓW on July 11, 1896. He gained his first experiences in microbiology as an assistant of Prof. Rudolf Weigl — a famous typhus researcher and inventor of anti-typhus vaccine, at the Lwów University of Jan Kazimierz (UJK). After he received the medical degree from the Lwów University in 1922, he specialized in bacteriology in Vienna. Then he became the head of the bacteriological and chemical laboratories of the State Hospital in Lwów. His expertise primarily included the fields of microbiology and immunology. After the Second World War, during which he was imprisoned in the Auschwitz and the Buchenwald concentration camps, he settled in Lublin (since Lwów was 'ethnically cleansed' by the Soviet occupiers), where he headed the Institute of Microbiology of the School of Medicine at the Maria Skłodowska-Curie University, previously directed by the very famous Polish immunologist Prof. Ludwik Hirszfeld (also 'ethnically cleansed' from Lwów by the Soviet occupiers). In 1952 he moved to Warsaw, where he became the Director of the Department of Microbiology and Immunology at the Mother and Child State Institute, and, finally, in 1957 he emigrated to Israel. He died there in 1961, at the age of 64, of a second heart attack.

Although presently Ludwik Fleck is predominantly recognized as a philosopher of medicine and science, he was a very productive researcher in the fields of microbiology, serology and immunology. He published, as an author and co-author, about 170 original and review papers. His main achievements included the discovery of exanthin reaction, the detection of typhus antigenic substances in urine, the first description of the phenomenon of leukergy, and many observations describing the behavior of leucocytes in infectious and stress situations. The aim of this study is to analyze the perception of Fleck's major medical discoveries in the present-day medical science.

In the years 1923–24 Ludwig Fleck conducted research on proteino-therapy in anafilaxy — see Fleck (1923). In 1930 he described the original skin test for early detection of typhus — see Fleck (1930a). One year later he discovered some new Proteus strains of the X type in association with typhus, and introduced a new method of using Proteus extracts in agglutinin tests — see Fleck (1931), Fleck, Balikówna (1931). In 1938 he demonstrated the influence of colloids on serological reactions and described a new method of distinguishing a real reaction from a pseudoreaction — see Fleck (1938). He described the lack or decrease of the fourth subunit of the component in luetic sera and studied the dependence of hematological pictures on rising agglutinin. He also wrote several papers on dermatology, focusing on lupus erythrematosus, pseudophiloma, and pemphigus — see Fleck, Goldschlag (1937), Fleck, Fullenbaum (1931), Fleck (1930b).

In 1941–42 Fleck discovered that typhus could be diagnosed before severe clinical symptoms were visible — see Fleck (1946). As early as the third day after the infection there would appear an antigen in the urine, which could be discovered by means of Fleck's method. This was a valuable discovery, both theoretically and clinically, and it soon became well known in the Lwów medical milieu. Because of this, typhus (spotted fever) was anecdotically called "the Fleck fever", the name it already had in German ("Flecktyphus", *Fleck* meaning *spot* in German).

He also developed a new method of typhus vaccine production, based on the presence of antigen in urine. He investigated the phenomenon of excreting the typhus antigens with urine and developed a method utilizing antigens for the production of the vaccine against this disease — see Fleck (1946).

One of his late microbiological reports concerning latex agglutination test with Brucella antigen was published in *Nature* in 1962. In this paper he described the test which permitted the detection of minute amounts of Brucella antigen — see Fleck, Evenchik (1962).

* Karol Marcinkowski University Medical School, Poznan, Poland; email: andrzej_grzybowski@um.poznan.pl.

However, the description of the leukergy phenomenon became his main achievement in the field of immunology. The name leukergy was derived from two words: leukocyte and ergein (action in Greek), what meant activation of the leukocyte system.

Fleck described changes in the leukocyte properties due to the inflammation process in living organisms. These changes included the aggregation of leukocytes in homological (or homologous) cell groups (an effect of increasing their viscosity), an increase of oxidation turnover, their migration and phagocytic activity. Leukergy was first observed in 1942, and than described as:

> an inflammatory phenomenon, which can be produced in animals by the intravenous administration of killed bacteria. Tests we have done suggest that there was no link between leukergy and leukocytosis, body temperature and erythrocyte sedimentation rate (ESR). It appears several hours after the injection of bacteria, subsequent to the rise of temperature, but before leukocytosis. It lasts about five days, that is much longer than the length of fever, usually longer than leukocytosis and increased ESR. Leukergy is a very sensitive symptom. (...) While ESR is a strictly humoral phenomenon, i.e. the red cells of a sick patient suspended in serum from a healthy person settle normally, and the red cells from a healthy person suspended in a patients' serum settle fast, leukergy is something different. In leukergy, white cells centrifuged from the inflammatory serum, washed with serum from a healthy person and settled in such serum, remain leukergic (Fleck, Borecka (1946) p.342; see also Fleck, Murczyńska (1947) p.198).

Fleck devoted many articles to the investigation of leukergy and the function of leukocytes in health and disease — see Fleck (1956), Fleck, Lille-Szyszkowicz (1957), Fleck, Lille-Szyszkowicz, Ruszczyk (1957), Fleck (1957). He discovered, among others, antibodies against leukocytes in the blood of mammals and assessed their importance in the formation of characteristic haematologic pictures. Moreover, he studied the leukocyte oxygen processes during phagocytosis.

Acknowledgement

The author wish to thank Prof. Wacław Szybalski, McArdle Laboratory for Cancer Research, University of Wisconsin Medical School for his support and guidance, and Prof. Waldemar Marton for his help with proofreading the English text.

Bibliography

Fleck L. (1923): "O stosunku proteinoterapii do anafilaksji", *Pol. Gaz. lek.* 1923; 52, p. 830–832.

Fleck L. (1930a): "O odczynie egzantynowym", *Wiad Lek.* 1930; 10/11, p. 392–409.

Fleck L. (1930b): "Ein Fall von Pseudosyphiloma anorectale mykotischer Aetologie (Kladiosis)", *Dermatologische Wochenschrift* 1930; 90 (11), p. 379–382.

Fleck L. (1931): "Versuche über eine lokale Hautreaktion mit Proteus X19 Extrakten", *Zeitschrift fur Immunitätsforschung und Experimentelle Therapie* 1931; 72, p. 282–300.

Fleck L. (1938): "Űber Reaktionen, Pseudoreaktionen und ein Verfahren, das Komplementpartiell zu inaktivieren", *Zeitschrift für Immunitätsforschung und Experimentelle Therapie* 1938; 94, p. 49–65.

Fleck L. (1946): "Swoiste substancje antygenowe w moczu chorych na dur plamisty", *Pol. Tyg. Lek.* 1946, 1, p. 663–666.

Fleck L. (1956): "Recent investigation on leukergy", *Texas Rep.Biol.Med.* 1956; 14(4), p. 424–31.

Fleck L., Balikówna (1931): "Sprawa aglutynacji odmieńca X19 przez surowicę świnki szczepionej durem plamistym". *Wiad. Lek.* 1931; 10/11, p. 390–392.

Fleck L. (1957): "La leukergie et son role dans l'immunite", *Ann Inst. Pasteur* 1957; 92 (3), p. 380–95.

Fleck L., Borecka D. (1946): "Zachowanie się odczynu leukergicznego w różnych stanach chorobowych", *Ann. UMCS* Sect. D 1946; 1, p. 335–349.

Fleck L, Evenchik Z. (1962): "Latex Agglutination test with Brucella antigen and antiserum", *Nature* 1962; 194, p. 548550.

Fleck L., Fullenbaum L. (1931), "Clinical and experimental contribution on the etiology of lupus erythematosus", *Urologic and Cutaneus Review* 1931; 35, p. 358–361.

Fleck L., Goldschlag F. (1937): "Experimentelle Beitrage zur Pamphigus frage", *Klinische Wochenschrift* 1937; 16, p. 707–708.

Fleck L., Lille-Szyszkowicz I. (1957): "Cytochemie des leucocytes leukergiques", *Vox sang* 1957; 3, p. 196–201.

Fleck L., Lille-Szyszkowicz I., Ruszczyk K. (1957): "Leukergie at leukoagglutination", *Sang* 1957; 28 (7), p. 589–94.

Fleck L., Murczyńska Z. (1947): "Nowy objaw zapalenia: zlepianie się krwinek białych w cytologicznie jednorodne grupy (leukergia)", *Pol. Tyg. Lek.* 1947; 7, p. 196–200.