CC/NUMBER 50
DECEMBER 12, 1983

This Week's Citation Classic

Biozzi G, Benacerraf B & Halpern B N. Quantitative study of the granulopectic activity of the reticulo-endothelial system. II: a study of the kinetics of the granulopectic activity of the R.E.S. in relation to the dose of carbon injected. Relationship between the weight of the organs and their activity. *Brit. J. Exp. Pathol.* 34:441-57, 1953.
[Lab. Exp. Med., Clin. Méd. Propedeutique, Hôp. Broussais & Ctr. Natl. Recherche Scientifique, Paris, France]

This article describes the first quantitative method for measuring the phagocytic function of the reticuloendothelial macrophages in contact with the circulating blood. This activity is measured from the rate of blood clearance of colloidal carbon particles injected intravenously. [The *SCI*® indicates that this paper has been cited in over 630 publications since 1961.]

Guido Biozzi
Service d'Immunogénétique
Section de Biologie
Institut Curie
75231 Paris
France

September 6, 1983

"After graduating from the medical faculty of the University of Rome (Italy) in 1947, I worked in collaboration with Zoltan Ovary (presently at the department of pathology of New York University) on the modification of endothelial cells of skin capillaries produced by locally injected histamine or by local anaphylactic reactions. This research led to the description of passive cutaneous anaphylaxis.[1,2]

"Among other colloidal dyes used in these investigations, we worked with suspension of colloidal carbon particles. These first experiments were actually carried out using the commercial India ink preparations.

"During these studies, I noticed that the carbon particles (diameter about 200 Å) injected intravenously did not filtrate through the capillary membrane and remained in the circulation until they were phagocytized by the reticuloendothelial system (RES) macrophages in contact with the circulating blood.

"In 1949, I obtained a fellowship to spend eight months in the laboratory directed by B.N. Halpern in Paris (France). There I began to speculate on the possibility of measuring the phagocytic activity of the RES macrophages from the rate of blood clearance of intravenously injected colloidal carbon particles. In the autumn of 1949, Baruj Benacerraf (1980 Nobel prizewinner, presently at Harvard Medical School in Boston) was working on histamine metabolism in Halpern's laboratory. He and Halpern were interested in the project of measurement of the phagocytic function of the RES macrophages.

"The first difficulty we encountered in this study was that commercial India ink preparations contained a shellac which produced intravascular fibrinogen clotting when large doses of carbon were injected. To overcome this inconvenience, which altered the rate of carbon particle phagocytosis, we contacted a commercial firm which specialized in India ink production (Pelikan Gunther Wagner, Hannover, Germany) in order to obtain a special colloidal carbon preparation with standardized carbon particle size stabilized with gelatin. This colloidal carbon preparation, designated C11/1431a, was perfectly suited for the study of the phagocytic activity of RES macrophages in mice, rats, guinea pigs, and rabbits.

"In order to express quantitatively this activity, we created a new terminology: the 'phagocytic index K ' which measures the total activity of all the RES macrophages and the 'corrected phagocytic index α ' which expresses this activity per unit of weight of liver and spleen that contains 96 percent of the RES macrophages in contact with the bloodstream.

"The reason why our publication has been so highly cited is that it described the first method of quantitative measurement of the phagocytic activity of the RES macrophages. This method has been very widely used, therefore, by all the authors studying this important function which plays a fundamental role in anti-infectious immunity.

"For a report of recent work in this field, see reference 3."

1. **Biozzi G, Menê G & Ovary Z.** Ricerche sui rapporti tra istamina e granulopessia dell'endotelio vascolare. Nota II. Sulla granulopessia dell'endotelio vascolare nella reazione anafilattica cutanea locale della cavia. *Sperimentale* 99:1-8, 1948.
2. ----------. L'histamine et la granulopexie de l'endothélium vasculaire. *Rev. Immunol.* 12:320-34, 1948.
3. **Stiffel C, Mouton D & Biozzi G.** Kinetics of the phagocytic function of reticuloendothelial macrophages *in vivo*. (van Furth R, ed.) *Mononuclear phagocytes*. Oxford: Blackwell Scientific Publications, 1970. p. 335-81.