

## Remembrance of Professor Marcel Bessis (1917-1994)

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*“From the Italian Campaign to the First Remission of Acute Leukemias,”* such could be the title of this initial chapter of the work of Marcel Bessis. It was during the Italian campaign that the physician-lieutenant Marcel Bessis, Chief of the Recovery Unit of Military Hospital 421, proposed to treat, by exchange of a large volume of blood, exchange transfusion, the wounded victims of serious muscular crush injuries, poisoned by the myoglobin released into their blood.

It was soon after the end of the war that, trailblazer as he would be in many domains, he treated newborn victims of Rh hemolytic disease at the Saint Antoine Hospital by exchange transfusion. The maternal anti-Rh antibodies present in the blood of the newborn were removed. Many previously doomed newborns survived thanks to Marcel Bessis. Previously, Rh incompatibility killed three to four thousand children in France each year. During this time Marcel Bessis carried out penetrating studies of this illness. He recognized the transmission of dangerous antibodies by maternal milk. He reproduced the illness in young rats, injecting them with rabbit antiserum. He found it in young mules from

Poitou, victims of anti-baudet antibodies secreted by the mare, and showed that they too can be saved by exchange transfusion.

It was during the same period, when renal dialysis did not exist, that he treated and cured by exchange transfusion many patients who were in uremic coma and thought to be incurable.

Finally, in November 1947, at the Herold Hospital, for the first time in the history of leukemia, complete remission of an acute leukemia. I can see again the transformation in the condition of little Michel, the first child so treated; return of the blood and bone marrow to normal. This remission was not obtained by destructive drugs, but by the exchange of blood, by changing the "milieu interieur" where the leukemic cells resided. Leukemia was no longer an illness forever irreversible as it had been long believed. Thus began a long and hard struggle.

I knew Marcel Bessis in the cellar of the old St. Antoine Hospital. In 1946, the cellar laboratories had replaced the Mansard Laboratories of Claude Bernard and of Pasteur. At the age of 29, Marcel Bessis had already devoted half of his life to microscopic studies.

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Fortunately, the young high school student Marcel Bessis had inherited, at age 15, many thousands of slides of bat embryos, collected by the histologist Branca, assuring and strengthening a budding vocation.

During the same period, Marcel Bessis was examining motile *Infusoria* as they searched for food and paralyzed their enemies, as well as the bat embryos. Thus the two great motifs of his research, structure and movement were already suggested. There were several studies of structure. Beginning in 1947, Marcel Bessis was the first, or one of the first, to examine blood cells in the electron microscope and had the joy of discovering new structures, a joy like that of the first microscopists who, three centuries earlier, recognized their own blood cells, the joy of describing the forms, the membranes, the bodies, the filaments, appreciated to the limit of a few nanometers, and approaching molecular dimensions. The link was thus established between morphology and chemistry, recalling Raspail's old term of chemical anatomy.

A good model of this cytochemistry at the molecular level is the study by Marcel Bessis of the ferritin cycle in the organism, its incorporation by red blood cells, its fate. Marcel Bessis showed that the form of red blood cells was due to a delicate equilibrium of forces. In particular, he studied the transformation of normal red cells, the discocytes, into spiked, sea urchin, or echinocyte forms, analyzing the role of anionic and cationic substances taking part in this transformation.

Using the scanning electron microscope, Marcel Bessis showed that one can see the cells *en face*, in three-quarters view, in profile, and make them turn beneath one's eyes. He described different aspects of the red cell deformities of sickle cell anemia.

Extending his studies of comparative hematology, he discovered and described the place and mode of formation of hemoglobin in annelid worms.

As Marcel Bessis himself wrote: "The form of blood cells depends on the code inscribed by heredity and the thousand meetings and

accidents that occur in the course of existence. The doctor who knows how to see can recognize in a red cell the subtle alteration of a gene transmitted from time immemorial on the banks of the Congo River or the marks of aggressions of daily life. This form speaks a difficult language but one which can be entirely deciphered."

Improving his techniques over several years, Marcel Bessis recognized novel forms and structures. Then suddenly, he stopped. The discovery of immobility seemed to him absurd. He would leave it to others to recapitulate this static universe, either citing his early work or, more often, not.

Already the study of changes of the form of red cells by a defractometric method had permitted him to elucidate the relations between the deformability of the cells and their functions. But especially from 1948 he was one of the first to use phase contrast microcinematography, which allowed him to speed up motile phenomena from 30,000- to 60,000- fold, trans-forming centuries into minutes, years into seconds. Marcel Bessis is one of the pioneers of the physiology of blood cells, of the organelles which form the cell. He studied the influence of the environment, the compartment of the cells, their life, their death, their exchanges, their struggles. In the interior of the cell, from organelle to organelle, from mitochondria to centriole ran information that he decoded, constantly comparing function and structure, recognizing elements at the same time message and messenger which are our life, recognizing them in the normal condition and during illness.

Thus he distanced himself from purely anatomical methods, from the autopsy of cells, in order to imagine, to focus upon physiologic methods to study living blood cells and the cells of organs which form the blood, specifying their aptitude for taking up their functions, for answering messages received, their relations with other cells. He went on to describe the birth, the development of red cells, their death, their growth, with the first description of the

erythroblast islet, nourishing reticular cells surrounding the dependent erythroblast.

Their death. After having focused upon methods of microsurgery and of microirradiation, after having, with a laser, destroyed a red cell, he described under the name of necrotaxis the different steps of cellular death, the arrival of predatory white cells, drawn not by death but by the agony of the cell.

This occurred in work carried on over a span of forty years. One of the first notes concerning the death of cells by laser irradiation appeared in the *Comptes-Rendus de l'Academie des Sciences* in 1962. Like an ogre, the cell can kill its adversary by devouring it. It can act on it at a distance by the antibodies its secretes. It can stab it. It can overwhelm it, drive it to despair by its wickedness, whispered calumnies from cell to cell.

Not only red cells were studied. The same methods permitted Marcel Bessis to describe the different steps in the formation of the platelets in the cytoplasm of megakaryocytes, and especially to be the first to reveal to us the liberation of platelets, the forms that they invest.

Thus was born, created by Marcel Bessis, a cellular ethology, a cellular ecology. *The Ecology of Normal and Leukemic Blood Cells*, such is the title of the research center that he directed at the Hôpital de la Salpêtrière during the last years of his life.

Throughout this life devoted to research were formed a triple mastery -- mastery of technique, permitting the great exchanges of blood thought dangerous before Marcel Bessis, permitting the admirable cinematography of cellular move-ments; mastery of thought in a direct line from Harvey and Claude Bernard; mastery of concepts orienting medicine towards new pathways.

Marcel Bessis seems to me defined by two alliances--the alliance of a most rigorous precision to a most lively imagination, and the alliance of biology to a philosophy nourished by the reading of philosophers from Plato to Paul Valery.

I have a strong and moving memory--sadly moving today--of our conversations, at his home, at mine, at the center for biology that he directed for many years at Bicetre, or during those far off voyages that left us free time. I see us again, going down the Argentine Tigre together, the river that descends toward Rio de la Plata or talking with our friends from the United States, from Boston or from Stanford. Marcel Bessis, who had many American students, was loved, admired in the United States. Madame Marcel Bessis had brought to him her knowledge of English. He founded the Blood Cell Club, bringing together Americans, English, French. Co-author of *The History of Hematology*, he taught us, and perhaps taught his American friends, the circumstances of the discovery by Pauling during a conversation with Castle on a train of the structure of hemoglobin S, of the birth of the concept of molecular pathology.

Marcel Bessis easily let his thoughts, his reflection, move away from the science of blood. Here he is, in his book, *Corpuscules*, moved, astonished by the beauty of red cells, analyzing the reasons for his emotion, for his marveling.

Here he is at Montpellier in 1982, participating in a colloquium on the functions of the mind. Thirteen wise men will rediscover Paul Valery. He calls to mind a meeting between Paul Valery and Policard, our sorely missed colleague from Lyon. Policard and Valery questioning each other on genetics: "A spermatozoa, a nothing, carries with it the physical and moral likeness of its author."

Here he is in 1977, examining the relations between scientific research, dreams, and poetry. Ten years later, he would direct a colloquium which would be published under the title *Vagabonde Creation*. This was a modest forerunner of the theme he was to come back to on the occasion of the second century of the Institute.

Here he is asking himself during the course of another colloquium *The Self and the Non-Self*, about the definition of a person, about the relationship between blood groups and

genetic characteristics on the one hand, and the brain on the other.

And going further (this was his last line of inquiry), he worked with computer specialists, wondering if artificial intelligence can help us to understand spontaneous remission of leukemias.

Thus developed and bloomed one of the great careers in research of our time. Research which, beyond the necessary cooperation, will always be inspired by the reflection of a single man. "I cannot believe," he wrote one day, "that

the works of the mind can be born other than in an infinite solitude."

The Academy of Sciences, which had welcomed him in 1979, shares the sorrow of Madame Marcel Bessis and of his daughters.

I think of the children whom the methods imagined by Marcel Bessis have saved and continue to save, and of the new ideas brought forward by Marcel Bessis that have inspired, and continue to inspire, so many investigators.