Paul Ehrlich  
(1854–1915)

PAUL EHRLICH was born one hundred years ago—on March 14, 1854 in Strehlin, Silesia. It is fitting that his birthday should be recalled in these pages, since he was in many respects the father of hematology, and of immunology, immunohematology, and chemotherapy as well. Although hematology would doubtless have cast off its colorless casing eventually, it is difficult to conceive how it could have developed so rapidly without the genius of an Ehrlich. Even as a medical student at the University of Strassburg, he was interested in the differential staining of cells and tissues with some of the new aniline dyes that had just been introduced by the burgeoning German chemical industry. He saw clearly that specific tissues and cells had specific affinities for specific dyes. This led to his development of the triacid stain for the staining of films and thus to a complete revolution in the study of the blood. The “colorless” white cells of the blood became endowed, by this stain, with wondrous blues, reds, and violets. Thus hematology could leave the rather unrewarding fresh preparation, where everything was pale and neutral, as well as ephemeral, to enter a brilliant new domain inhabited by eosinophils and basophils and neutrophils, and by lymphocytes and “transitional” cells.

The impact of Ehrlich’s discovery and its widespread effects on many fields cannot of course be assessed, but it was certainly considerable. It is illustrative of the importance of the development of a method—for this simple staining technic made possible the study of many different kinds of blood cell reactions, including those found in infections, in the different types of anemia, and in leukemia. In the blood, he devised differential counting, made sharp distinctions between the various types of leukocytes and their granules, described polychromatophilia and poikilocytosis, and pointed to the close relationships existing between the blood picture and the bone marrow.

For the first time the marrow could be adequately stained and carefully studied. Here, Ehrlich described the myelocyte, which he considered as the precursor of the granulated white cells of the blood; the megaloblast of pernicious anemia, which he distinguished from the normoblast; the mast cell; and the fatty picture of aplastic anemia. The polemic discussions regarding stem cells and their various progeny, which impeded the literature for so many years, may also be said to have originated with Ehrlich, who believed that the nucleated red cells and the granulocytes arose from a single primitive cell.

There can be no question then of Ehrlich’s importance in inaugurating a new era in hematology. That this discipline did not lose its morphologic shackles for many years was certainly not Ehrlich’s fault, because even while he was staining blood cells, he was simultaneously intrigued by the affinities of antibodies to
“antigens”, as he called them. This led to the development of his famous side-chain theory, which, after a lapse of many years, still has considerable validity. Thus his idea of chemoreceptors on the surface of a cell and their union with haptophores, resulting in the production of specific antibody, was the forerunner of Landsteiner’s work on diazoprotein linkage as well as the work of Haurowitz on antibodies as protein replicas of the original antigen. The importance of Ehrlich’s concepts as they apply to immunohematology and to hemotoxic drug reactions is obvious, although it must be said that he denied the possibility of an autoantigenic effect and of autoantibodies (“horror autotoxicus”). Nevertheless, he produced hemolytic antibodies in goats by injecting them with goats’ red cells (isoantibodies). Parenthetically, and again while still a medical student, he observed and described, in 1871, the phenomenon of erythrophagocytosis in paroxysmal cold hemoglobinuria. Donath and Landsteiner later found an autohemolysin in this disease. A good case may therefore be made for the designation of Ehrlich as the father of immunohematology, although Landsteiner has already been nominated (by Wiener) as this important parent. Perhaps Ehrlich’s interests were too wide for him to be firmly attached to one small field such as hematology, but it is to be noted that in 1908 he received, with Metchnikoff, the Nobel Prize for his work in immunology.

Ehrlich’s Leitmotif—that of specific affinity of chemical for cell and vice versa—led him finally to the remarkable discovery, after many fruitless syntheses, of “606” for the treatment of syphilis. That he was the father of chemotherapy goes without saying, although he was doubtless disappointed that he could not develop the field to its fullest. This was of course done later by others. It must be said, however, that Ehrlich’s aniline dyes, which can be fashioned so readily and in so many different ways, have not been an unmixed blessing, for with them have come the varied and numerous hemotoxic reactions: the aplasias, the agranulocytoses, and the thrombocytopenias. To distinguish nowadays between a disease and a reaction to a drug becomes somewhat difficult, especially when arthritis, hyperglobulinemia, and L.E. cells are found, as in apresoline toxicity.

This towering genius, bearded since youth, an inveterate cigar smoker, who straddled several fields so successfully, died in 1915, shortly after the outbreak of the first World War. His work was carried on in a Germany that was then at the apex of cultural and scientific attainment. He was thus fortunately spared the terrible years to come, and particularly the degradations of Hitler’s era. On this, his 100th birthday, BLOOD—The Journal of Hematology salutes Paul Ehrlich’s memory and is ever mindful of his enormous contribution to the advancement of this broadening field.

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