Check for updates

blood® flashback 1946

This paper, by one of the legends of hematology, William Dameshek, and his colleague Edward Miller, is from the inaugural issue of Blood. *By studying bone marrow specimens from controls, patients with acute or chronic immune thrombocytopenia, or patients with other thrombocytopenic disorders, the authors concluded that, in idiopathic thrombocytopenic purpura (ITP), production of platelets from megakaryocytes is defective, even while marrow megakaryocytes are greatly increased in number. This defect resolved after splenectomy. The authors appropriately credit E. Frank with having proposed defective platelet production from megakaryocytes in ITP in 1915. The idea that platelet production was defective in ITP was superseded or ignored for decades, but it has now been validated by the therapeutic effectiveness of the thrombopoietin mimetics in ITP.*

Dameshek W, Miller EB. The megakaryocytes in idiopathic thrombocytopenic purpura, a form of hypersplenism. *Blood*. 1946;1(1):27-50.

THE MEGAKARYOCYTES IN IDIOPATHIC THROMBOCYTOPENIC PURPURA, A FORM OF HYPERSPLENISM

By William Dameshek, M.D., and Captain Edward B. Miller, A.U.S.

IN his book *Opera omnia*, published in 1775, Paul Gottlieb Werlhof[1] devoted a chapter to "Morbus maculosus haemorrhagicus," which he had first described forty years previously. He wrote:

> An adult girl, robust, without manifest cause, was attacked recently, towards the period of her menses, with a sudden severe hemorrhage from the nose, with bright but foul blood escaping together with a bloody vomiting of a very thick extremely black blood. Immediately there appeared about the neck and on the arms, spots partly black, partly violaceous or purple, such as are often seen in malignant smallpox . . . ; moreover the number of the spots increasing and surrounding completely both of the eyes, the back of the nose and the skin around the mouth and chin, with a livid black color, like marked from bruises.

Since the bleeding began simultaneously with the menses and since there was spontaneous recovery, it is indeed probable, as most authorities have agreed since, that this was an example of idiopathic thrombocytopenic purpura. The reasons for the development of sudden, generalized bleeding from all the mucous membranes and into the skin are almost as obscure today as they were in Werlhof's time. In the present paper, an attempt is made to develop a concept of pathogenesis centering about the failure of platelet growth from the megakaryocytes in the bone marrow, and dependent upon an abnormal inhibitory factor in a distant organ, namely, the spleen.

The great diminution in platelets in Werlhof's disease was first recognized by Krauss[2] in 1883 and by Denys[3] in 1887. Hayem[4] later confirmed and amplified these isolated observations. The relationship of the platelets to the giant cells of the bone marrow—the megakaryocytes—became known with the work of J. H. Wright[5] in 1906 and 1910. In 1915, Frank[6] made accurate studies of "essential thrombopenia" and postulated a marked diminution in platelet production by the megakaryocytes.* In the following year, Kaznelson[7] suggested splenectomy as a therapeutic maneuver in a chronic relapsing case of the disease. He assumed, by analogy with hemolytic anemia, that the spleen might have an unusual thrombolytic function. The results of the first operation were brilliant, but in the next two cases[8] only temporary increases in platelets occurred. Since that time the favorable effect of splenectomy in idiopathic thrombocytopenic purpura has been amply confirmed. The quick recovery following splenectomy of many desperately ill patients bleeding spontaneously from all the orifices is one of the most dramatic events in medicine, and must immediately implicate the spleen as of prime pathogenetic importance in the disease. In confirmation of this, the injection of splenic

From the Blood Laboratory of the Boston Dispensary, and the J. H. Pratt Diagnostic Hospital; aided by grants from the Charlton Fund, Tufts College Medical School, and the Upjohn Company.

* Frank is incorrectly quoted by most observers as having suggested a splenic effect on megakaryocyte platelet growth.

▶The articles featured in the *Blood* Flashback series were selected and the commentaries written by the *Blood* Editors. Complete versions of all the articles in the series, commemorating the journal's 70th-anniversary year, can be found on the *Blood* Web site at www.bloodjournal.org/collection/blood-flashback.

DOI 10.1182/blood-2015-11-682948

© 2016 by The American Society of Hematology

Downloaded from http://ashpublications.net/blood/article-pdf/127/1/3/1391513/3.pdf by guest on 08 June 2024