

**Bernard J & Soulier J-P.** Sur une nouvelle variété de dystrophie thrombocytaire-hémorragique congénitale (Concerning a new variety of congenital thrombocytopenic hemorrhagic dystrophy). *Sem. Hôp. Paris* 24:3217-23, 1948.  
[Hôpitaux de Paris, France]

A new type of congenital, heritable (recessive), hemorrhagic disease was reported in two infants (one male, one female) in one family (with no consanguinity among the parents' ancestors). The disease was distinguished clinically from other known hemorrhagic disorders. It is characterized by a considerable increase in bleeding time and remarkable alterations in the size and shape of thrombocytes; prothrombin is not converted at normal rates. [The SC<sup>7</sup>® indicates that this paper has been cited in over 110 publications since 1955.]

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S.P., a girl born on November 24, 1944, died at the age of 31 months in June 1947 from a hemorrhagic illness. Bleeding time was 35 minutes. Platelets were not counted. Blood smears showed large elements that were thought by some cytologists to be lymphocytes, whereas others were not sure how to classify them.

Y.P. was born a few months after the death of his sister on September 20, 1947. At 15 days there were sparse epistaxes. In February 1948 he suffered nose bridge hemorrhages, following a scratch, that lasted 48 hours. The child was examined by us in April 1948. The characteristics of this congenital and familial illness may be summarized as follows: early and serious cutaneous and mucous hemorrhages, coagulation of normal duration, a normal or moderately decreased number of platelets, normal clot retraction but considerably increased bleeding time, very abnormal prothrombin consumption time, and very remarkable alteration of the size and form of platelets (megathrombocytes looking like lymphocytes with chromomeres and hyalomeres).

Thus, we described in 1948 (in the *Citation Classic*) a new thrombopathy initially known

as thrombocytic hemorrhagic dystrophy and later known as Bernard-Soulier syndrome (BSS). This disease is very rare (no more than 100 cases have been reported since 1948). It is ubiquitous and has been observed in Europe, America, and Asia.

The importance of the new disease was evident at the time of the first description: BSS is, after Glanzmann's thrombasthenia, the second well-defined model of thrombopathy, a hemorrhagic disease caused by a disorder of the quality of platelets and not a diminution of their number. BSS showed, as early as 1948, a dissociation of the tests concerning platelet function: abnormal bleeding time, abnormal prothrombin consumption time, and normal clot retraction.

During the last 40 years much progress has occurred, and the importance of the disease has increased. This very rare disease has inspired important discoveries in the fields of platelet physiology, hemostasis, and thrombosis. For example, in BSS the function of platelet aggregation is normal while the function of platelet adhesion to the vessel is seriously disturbed. On the contrary, in Glanzmann's thrombasthenia, aggregation is disturbed, while adhesion is normal. The discovery by J.P. Caen and A.T. Nurden<sup>1</sup> of the role of the glycoproteins of platelet membrane was important because in BSS glycoprotein Ib is absent. Thus, a relationship is established between structure and function. Normally, this glycoprotein is responsible for the adhesion of platelets to the vascular wall.

A broad field of physiology has been transformed in a few years. A very rare platelet disease led to the knowledge of the molecular abnormality by which the illness is defined.

In particular, three consequences of the discovery of BSS are immediately evident: for physiology, the pathophysiology of thromboses and of hemorrhages and the discovery of glycoprotein I, which fastens the platelet to the vessel; also for physiology, the pathophysiology of the megakaryocyte and medullary fibrosis; and a general understanding of the adhesion of cells to each other and to neighboring membranes in the normal state and during disease.

In 1983 an entire issue of *Blood Cells* was devoted to this subject.<sup>2</sup>

1. Caen J P, Nurden A T, Jeanneau C, Michel H, Tobelem G, Levy-Toledano S, Sultan Y, Valensi F & Bernard J. Bernard-Soulier syndrome: a new platelet glycoprotein abnormality. Its relationship with platelet adhesion to subendothelium and with the Factor VIII von Willebrand protein. *J. Lab. Clin. Med.* 87:586-96, 1976.  
(Cited 160 times.)

2. Bernard-Soulier syndrome and cell adhesion pathology. (Whole issue.) *Blood Cells* 9(2). 1983. 231 p.