In the present study by Zhang et al, the numbers of the patient/control groups are small, but ongoing oxygen stress is a significant factor in patients with chronic ITP. Chronic ITP is an autoimmune disorder where isolated low-platelet counts indicate the immune pathogenesis. In chronic ITP, clinical bleedings occur in some patients with very low platelet counts. Many other autoimmune disorders such as Guillain Barré syndrome, Kawasaki syndrome, lupus erythematosus, dermatomyositis, and dermatologic blistering disease have similar pathogeneses and respond to similar therapeutic interventions. 

Zhang and colleagues report here on gene-expression and molecular-oxidative stress results as causative factors for chronic ITP in children. With transcriptome cDNA microarray analysis of peripheral blood, the authors could show differences of clustering profiles among patients with transient, self-limited ITP and chronic, long-term ITP and control individuals. Overexpression of the gene vanin-1 (VNN1)—an oxidative stress sensor—was associated with chronic ITP only (see figure). VNN1 is characterized by its role in oxidative stress response, and it mediates production of inflammatory cytokines by antagonizing peroxisome proliferative-activated receptor γ (PPARγ). VNN1 is the only gene that was detected in chronic ITP. Exposure of human blood mononuclear cells to oxidative stress inducers (LPS, sodium arsenite) up-regulates VNN1. Quantitative real-time PCR measurement of VNN1 expression confirmed the oxidative stress events in peripheral blood cells. In addition, the ratio of reduced to oxidized glutathione—a parameter of the cellular redox state—was significantly down-modulated in children with chronic ITP in comparison to healthy controls.

In the acute phase of thrombocytopenic purpura [review], von Freytag-Loringhoven postulated that platelet aggregation occurred before fibrin polymerization. This concept was further validated by von Willbrand, who hypothesized that the fibrinogen molecule forms a platelet aggregate, which then forms a fibrin meshwork. This concept has been challenged by several investigators, who have demonstrated that fibrin polymerization can occur without platelet aggregation. The concept of pre-assembly of the fibrin meshwork was further developed by the work of Chernysh et al, who demonstrated that the monomeric domain of fibrinogen polymerizes under conditions of high ionic strength and low pH. This work was later extended by the work of Chernysh et al, who demonstrated that the monomeric domain of fibrinogen polymerizes under conditions of high ionic strength and low pH.

In the present study by Zhang et al, the numbers of the patient/control groups are small, but ongoing oxygen stress is a significant factor in patients with chronic ITP. Chronic ITP is an autoimmune disorder where isolated low-platelet counts indicate the immune pathogenesis. In chronic ITP, clinical bleedings occur in some patients with very low platelet counts. Many other autoimmune disorders such as Guillain Barré syndrome, Kawasaki syndrome, lupus erythematosus, dermatomyositis, and dermatologic blistering disease have similar pathogeneses and respond to similar therapeutic interventions. The described triggering pathways of chronic autoimmune phenomena might provide earlier intervention in selected groups of an autoimmune disorder. 

Conflict-of-interest disclosure: The author declares no competing financial interests.

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self-associate laterally via “B”: “b” and αC·αC contacts. Using a rotating disc confocal microscope, Chernysh and colleagues captured images present at progressive time intervals during the lag phase that they defined by turbidity measurements. Each image was characterized by its diffusion coefficient and by transmission electron microscopy, illustrated in Figure 4 of their article. What is new is the monomer composition of mobile heterogeneous structures whose progressive growth leads to formation of scaffolds. In addition, the smallest and necessarily most mobile structures continued to attach to the increasingly less mobile and larger structures even at gelation point. Demonstration of growing scaffolds provides a novel view of soluble fibrin, perhaps more complex than previously proposed. The study by Chernysh and colleagues substantially advances our understanding of pregelation events, and of the likely composition of circulating fibrin/fibrinogen complexes.

The lag phase underlies clotting-based coagulation tests and soluble fibrin that reflects limited fibrin levels in high fibrinogen excess (see figure panel C), forming soluble fibrin/fibrinogen complexes. These complexes are cryoprecipitable, are cleared rapidly when containing des-AA fibrin than when containing des-AA/des-BB fibrin (panel A), and are markedly increased ex vivo in donated blood. This increase enables harvest of plasma cryoprecipitate that is widely used in clinical medicine. In addition, it accounts for the cryoprecipitate in stored blood (4°C) that is retained by each blood filter (eg, ~170 μ or smaller average size pore) used invariably during transfusion. Moreover, increased soluble fibrin in some clinical disorders, obtained by cryoprecipitation and termed “cryofibrinogen” or “cryofibrinogenemia,” has long been used as a disease marker.

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To gel or not to gel

Dennis K. Galanakis