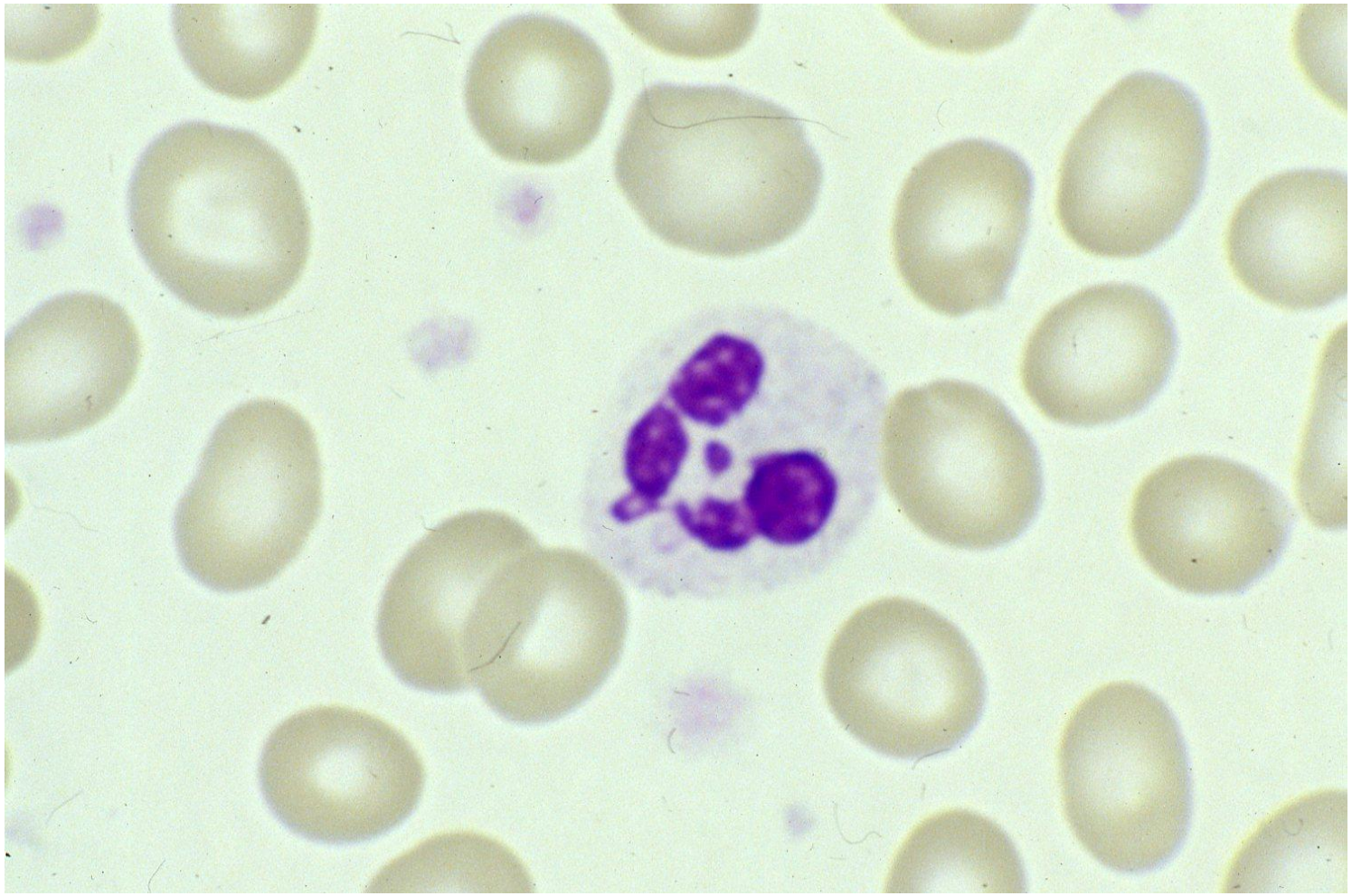
Thrombocyte variations in May-Giemsa-stained smears

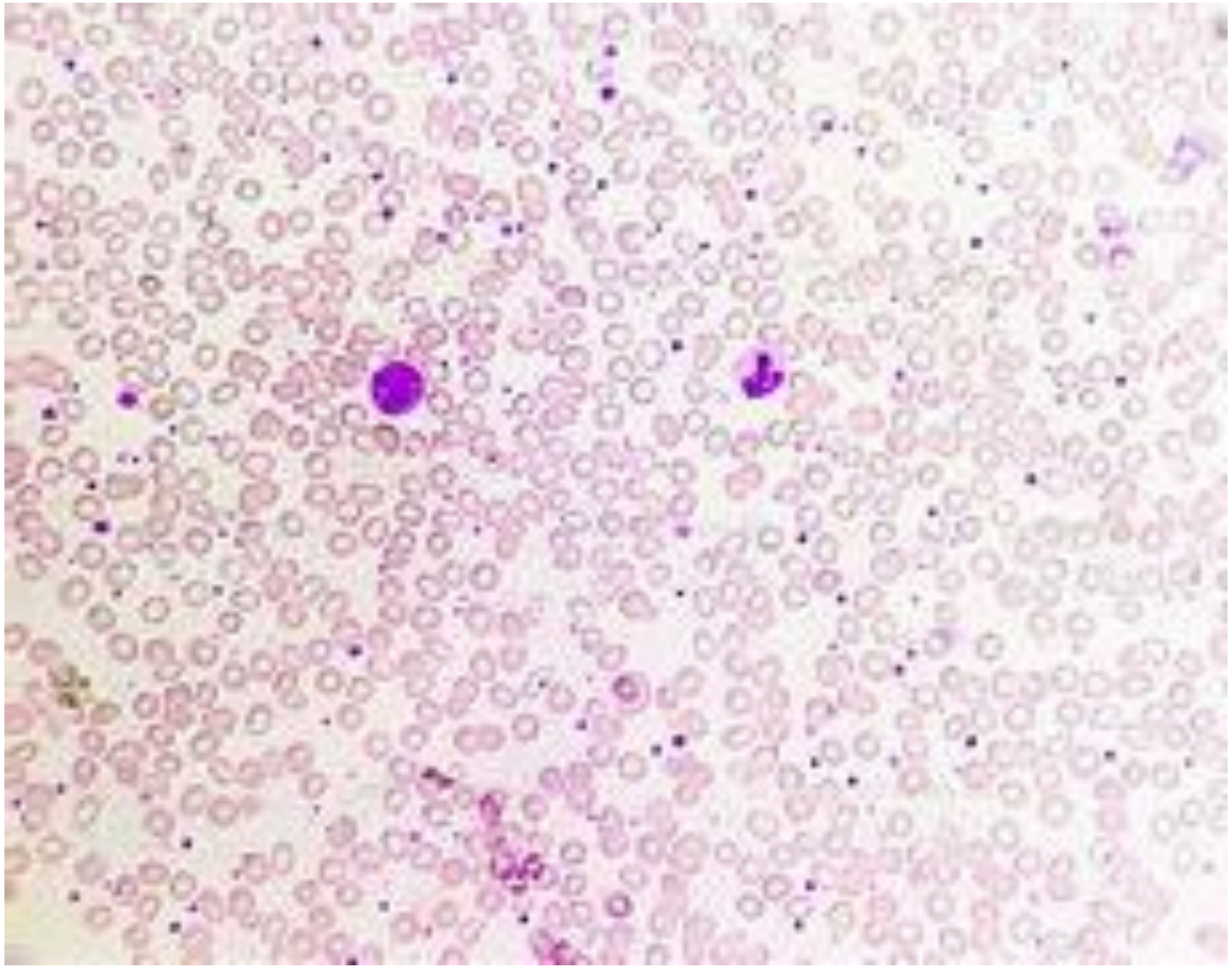
Platelets, small-sized anuclear cells with azurophilic granules, are continuously produced from megakaryocytes in the bone marrow. They are mainly involved in hemostasis and intravascular thrombosis.

The morphologic features of platelets in the peripheral blood and megakaryocytes in the bone marrow are presented.

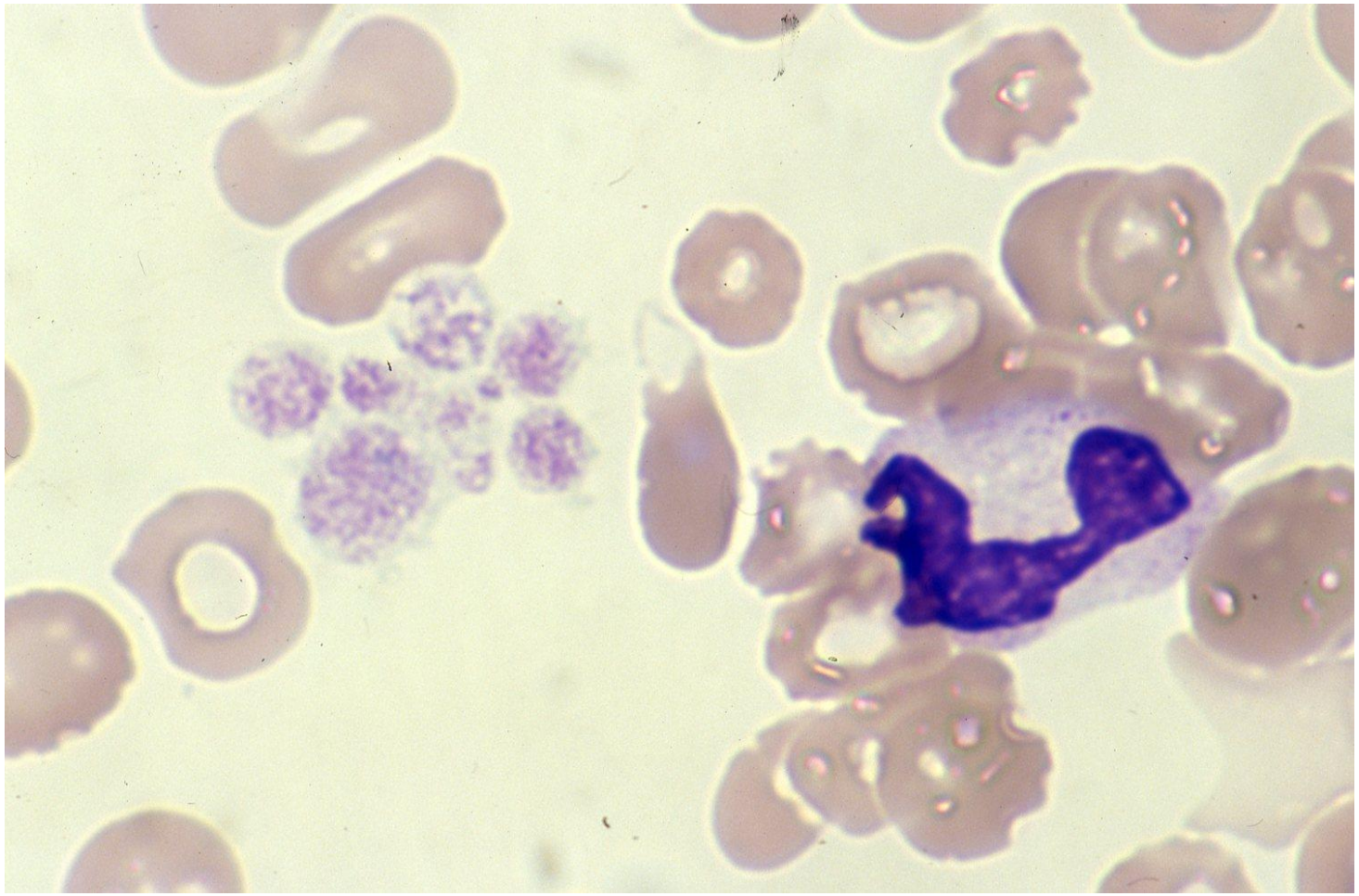
Ref.: van der Meijden PEJ, Heemskerk JWM. Platelet biology and functions: new concepts and clinical perspectives. Nat Rev Cardiol 2019: 16, 166-179. doi: 10.1038/s41569-018-0110-0



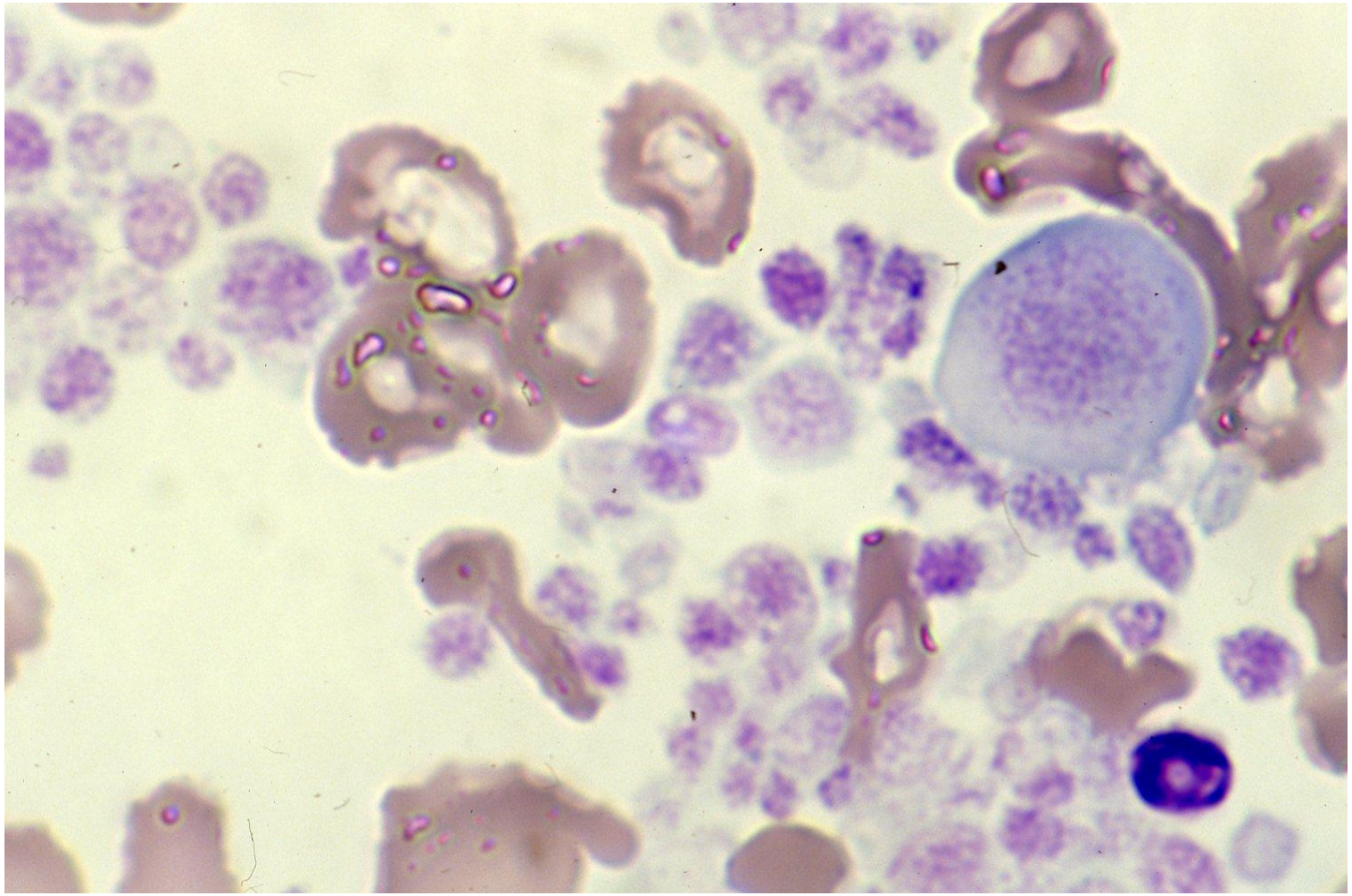
Normal platelets in the peripheral blood. Platelets are the smallest anucleated blood cells, around 2 μm in diameter, derived from the cytoplasm of megakaryocytes in the bone marrow. They contain fine azurophilic granules. The average lifespan is 7 to 10 days.



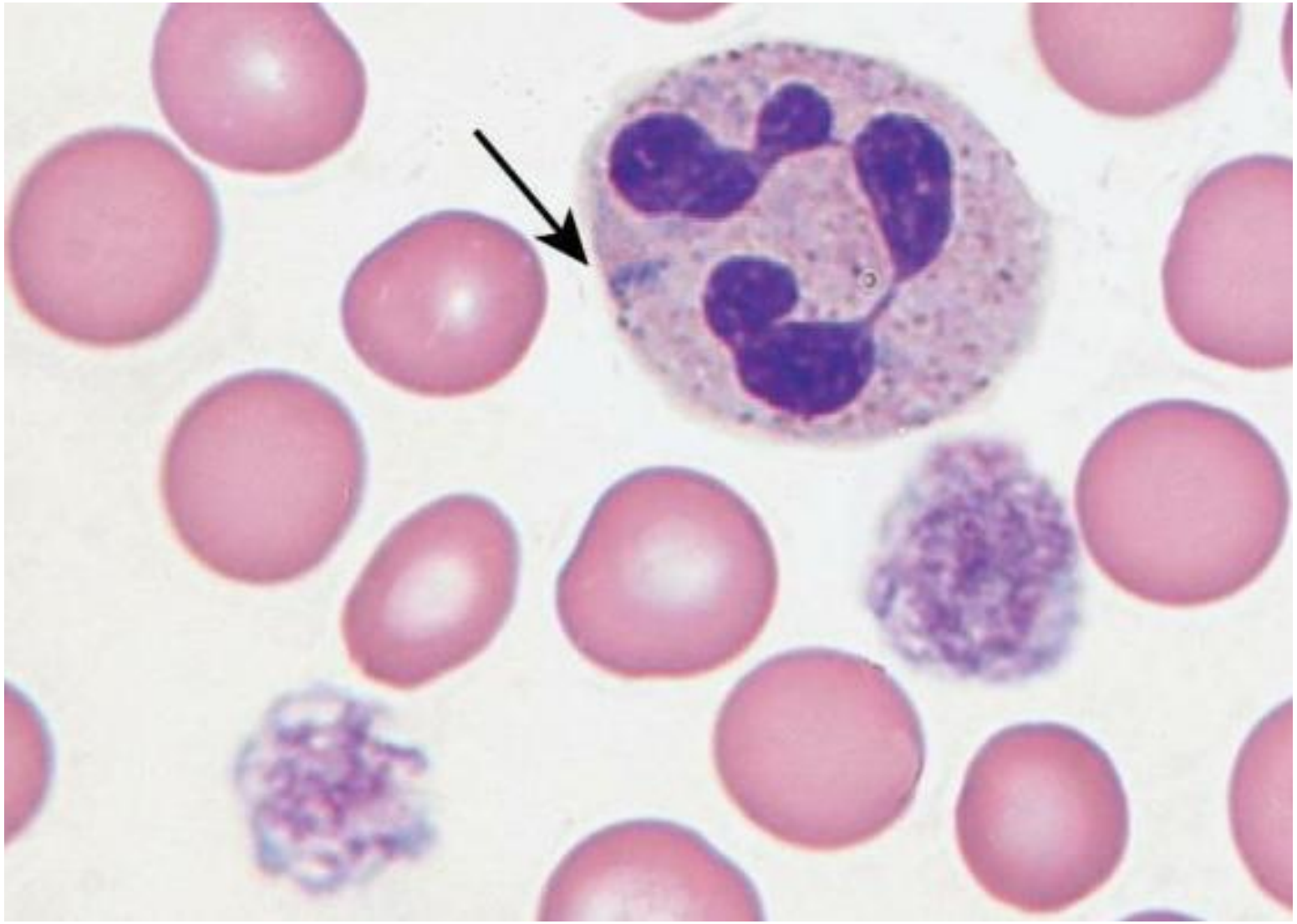
Thrombocytosis (May-Giemsa). In thrombocytosis, the platelet count exceeds 450,000/μL in the peripheral blood. The high counts of platelets are seen in either essential thrombocythemia or secondary (reactive) thrombocytosis in the absence of chronic myeloproliferative disease. Infections, inflammation, hemorrhage or certain medications may cause reactive thrombocytosis usually without any symptoms.



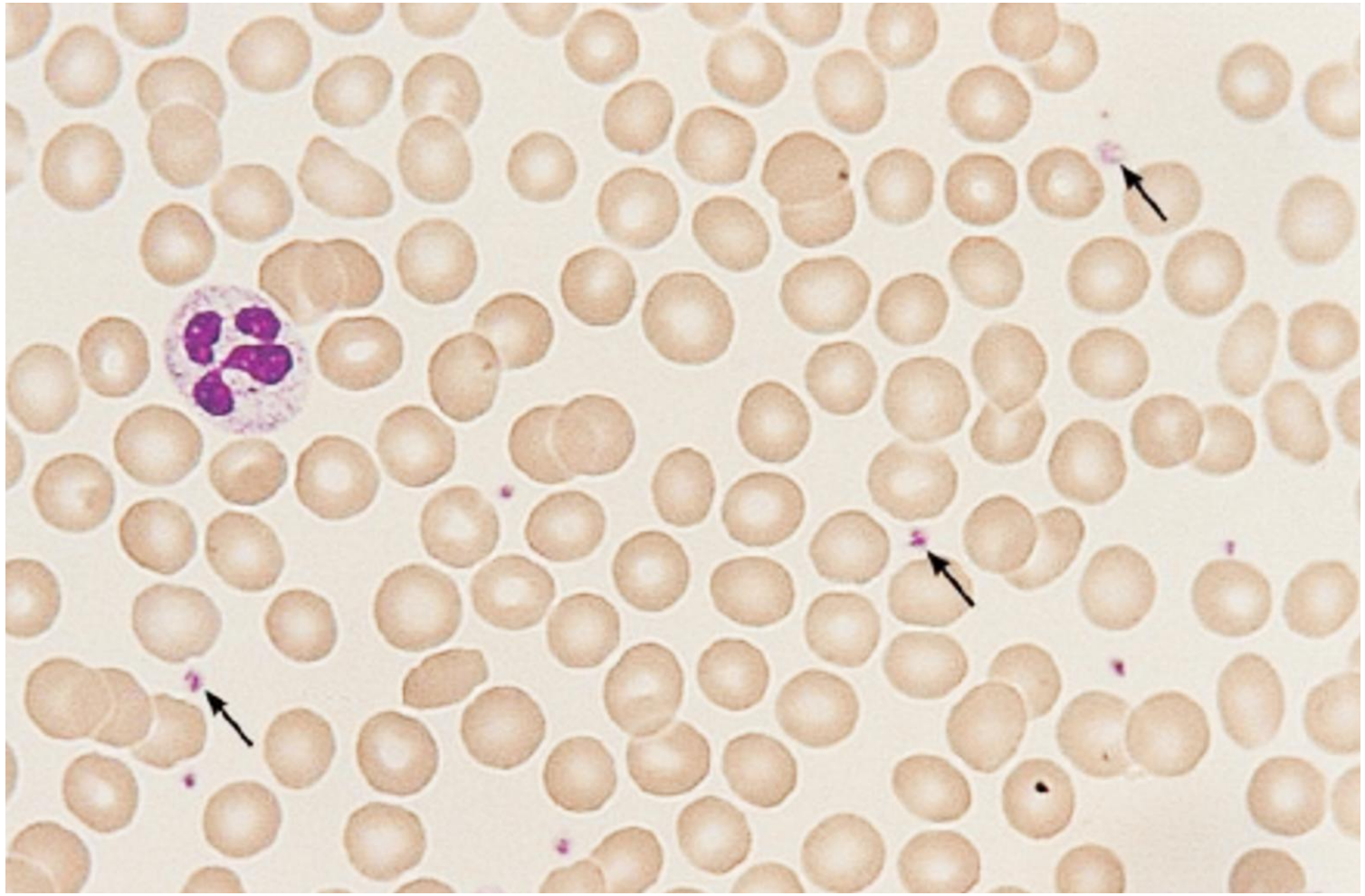
Large platelets in the peripheral blood. Large platelets have a diameter greater than 4 microns. When the size of the platelets exceeds the red blood cells (greater than 7 microns), they are called giant platelets. May-Giemsa



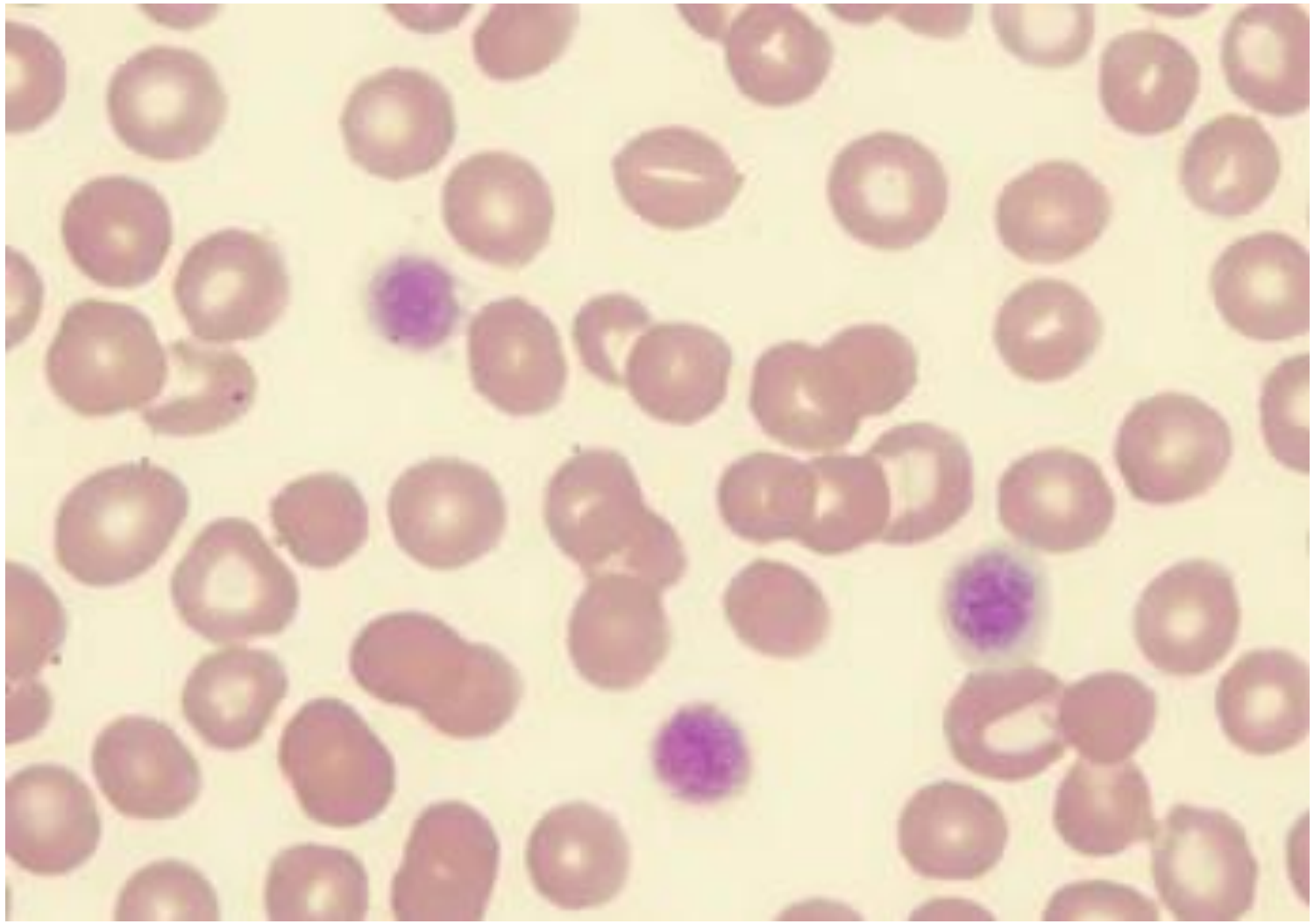
Giant platelets. The largest size of the platelet is greater than red blood cells. Giant platelets are seen in the present case of myelodysplastic syndrome. ITP may also accompany giant platelets. Bernard-Soulier syndrome, gray platelet syndrome and May–Hegglin anomaly are known to be hereditary thrombocytopenia with giant platelets. May-Giemsa



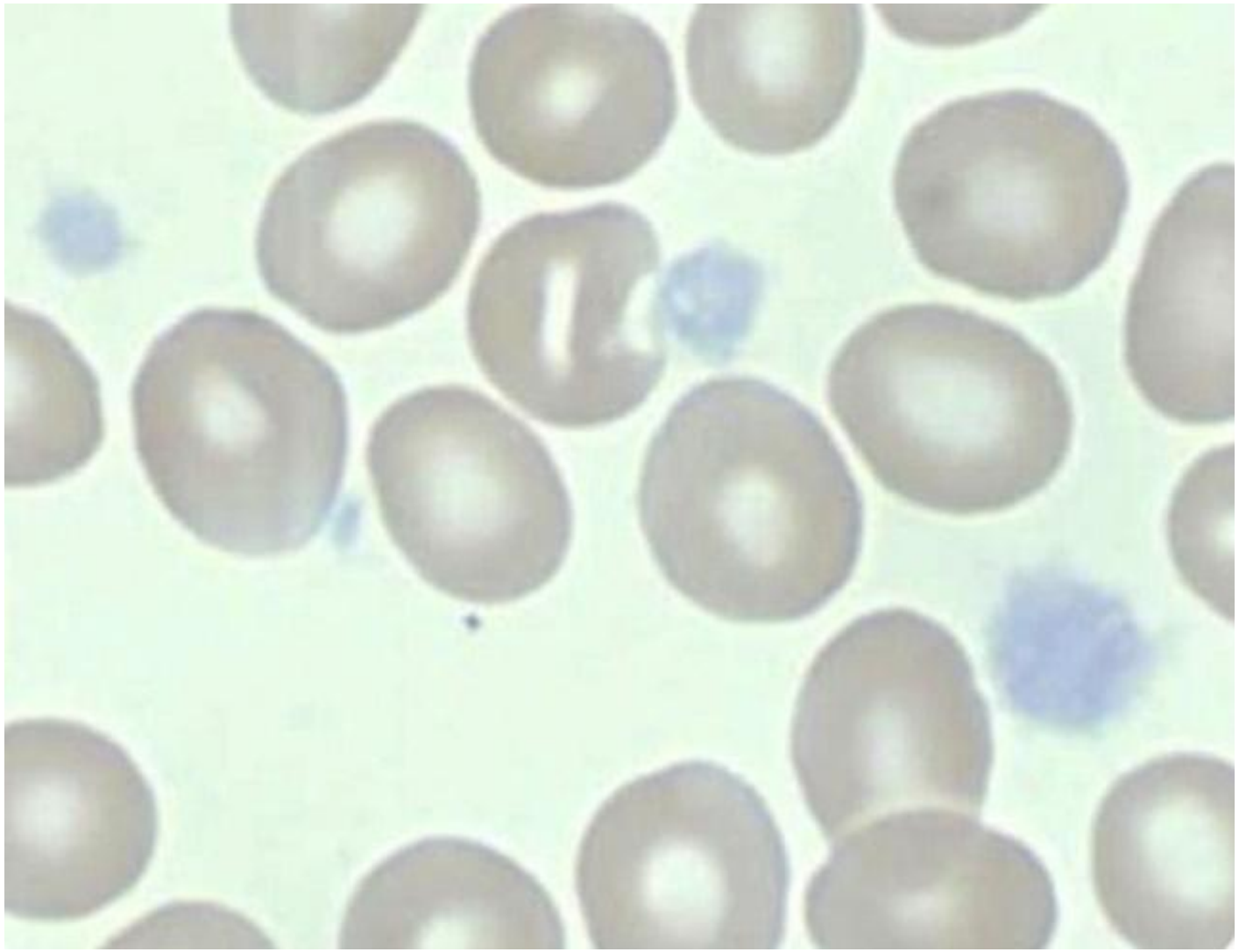
May-Hegglin anomaly is autosomal dominant hereditary disorder with thrombocytopenia and mild bleeding tendency. Giant platelets are observed. Neurophils possess PAS-negative Döhle-like cytoplasmic inclusions, consisting of structural RNA (arrow). Borrowed from SlideServe ID: 2110996



Glanzmann thrombasthenia is an autosomal recessive bleeding disorder caused by mutations of ITGA2B or ITGB3 genes, leading to the deficiency of the platelet integrin alpha IIb beta3 (GPIIb-IIIa). This integrin is the platelet fibrinogen receptor and is thus essential to platelet aggregation and hemostasis. Mucocutaneous bleeding is the main sign. The diagnosis is usually made in early childhood. The morphology and the number of platelets (arrows) in the peripheral blood mostly appear normal in thrombasthenia.



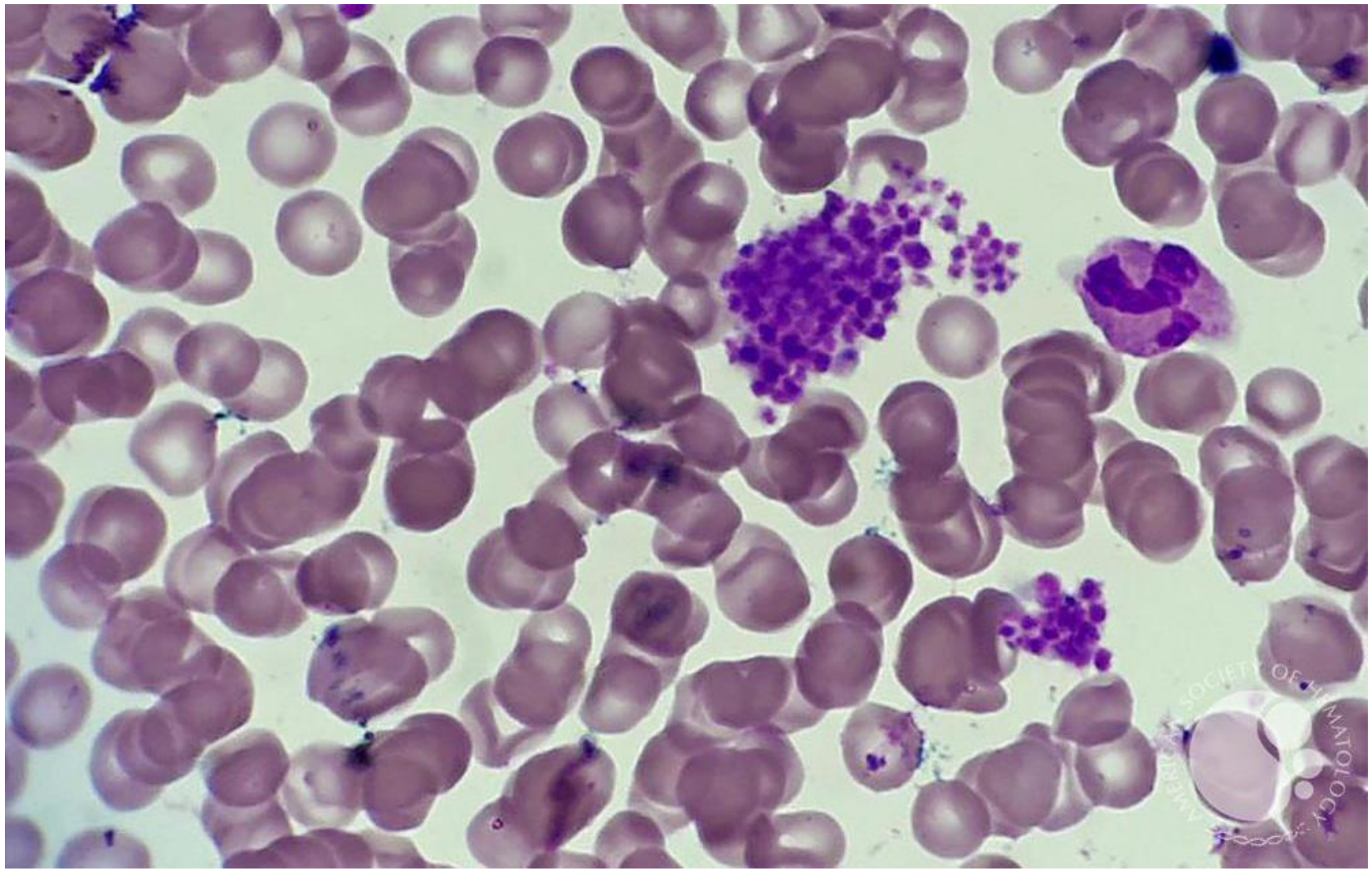
Bernard-Soulier syndrome is a rare autosomal recessive inherited blood-clotting disorder characterized by giant platelet cells, thrombocytopenia and prolonged bleeding time. The disease is caused by the defect in the GPIb-IX-V complex, a critical platelet receptor complex in von Willebrand factor binding necessary for thrombosis, and hemostasis. Borrowed from emedicine/Medscape



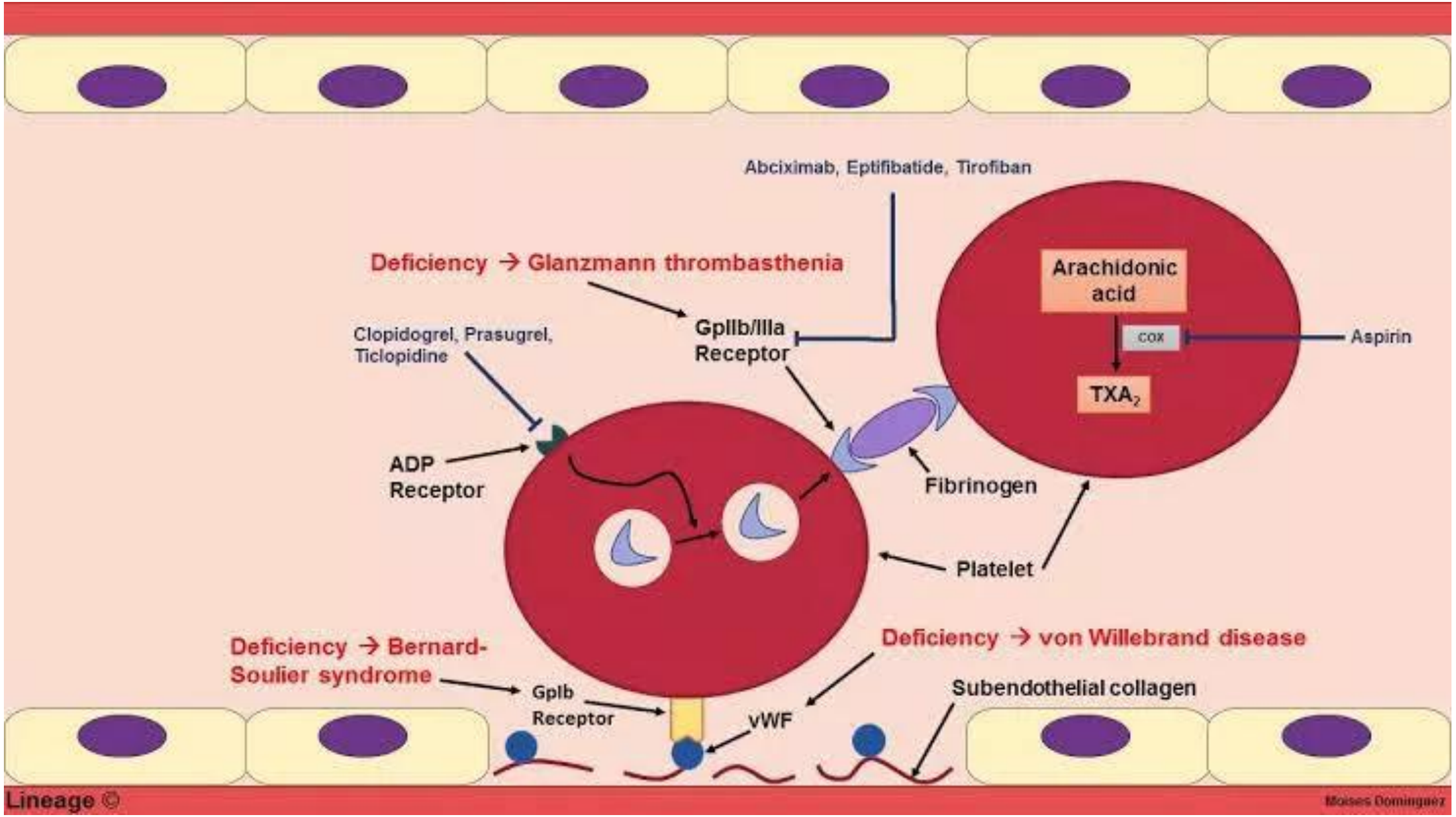
Gray platelet syndrome is a rare congenital autosomal recessive bleeding disorder caused by mutations in the NBEAL2 gene. The platelets lack alpha-granules, and the paucity of granules on blood smears shows gray appearance of the platelets. Thrombocytopenia and large-sized platelets are observed. Myelofibrosis may be associated. Epistaxis and irregular menstrual cycles are common symptoms. Borrowed from ASH Image Bank

von Willebrand disease

von Willebrand disease is a relatively common, autosomal dominant genetic bleeding disorder. The disease is caused by a deficiency or dysfunction of von Willebrand factor (vWF). vWF plays a crucial role in platelet adhesion and aggregation during the clotting process. Platelet morphology is normal-looking. The abnormal vWF shows increased affinity for the platelet receptor glycoprotein Ib-α (GPIb-α), resulting in clumping of platelets, which may lead to false thrombocytopenia. The main reason of the platelet clumping is the use of anticoagulant EDTA. There are three main types of von Willebrand disease. Type 1: a mild deficiency of vWF with mild symptoms (the most common type). Type 2: a qualitative defect of vWF with moderate bleeding symptoms. Type 3: a severe deficiency of vWF causing severe bleeding episodes.



In von Willebrand disease, platelets in the peripheral blood may form clustering. The main reason of this phenomenon is the use of anticoagulant EDTA (May-Giemsa). Borrowed from the Image Bank of the American Society of Hematology.

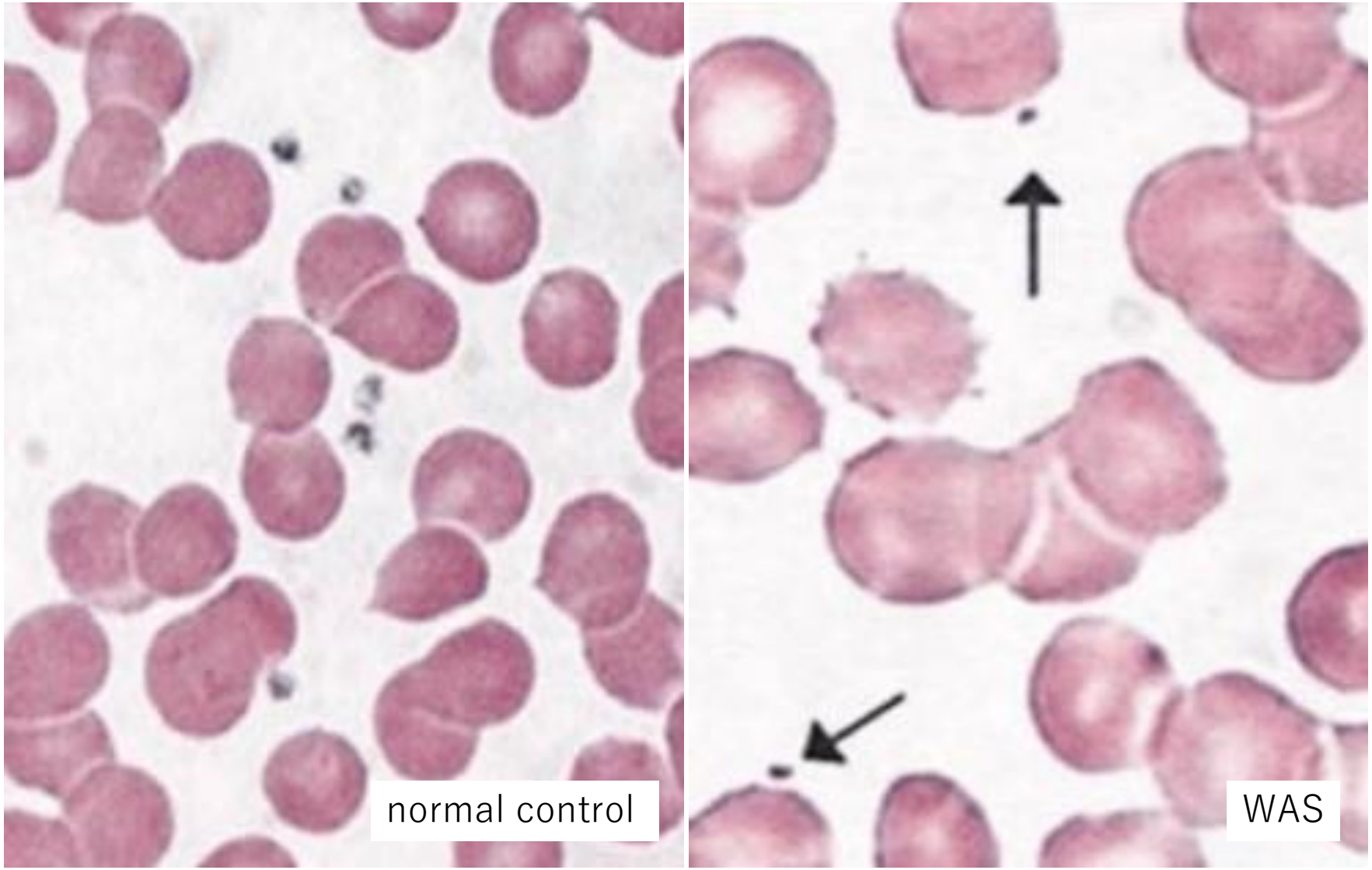


Mechanisms of representative thrombocytopathies: Glanzmann thrombasthenia, Bernard-Soulier syndrome and von Willebrand disease

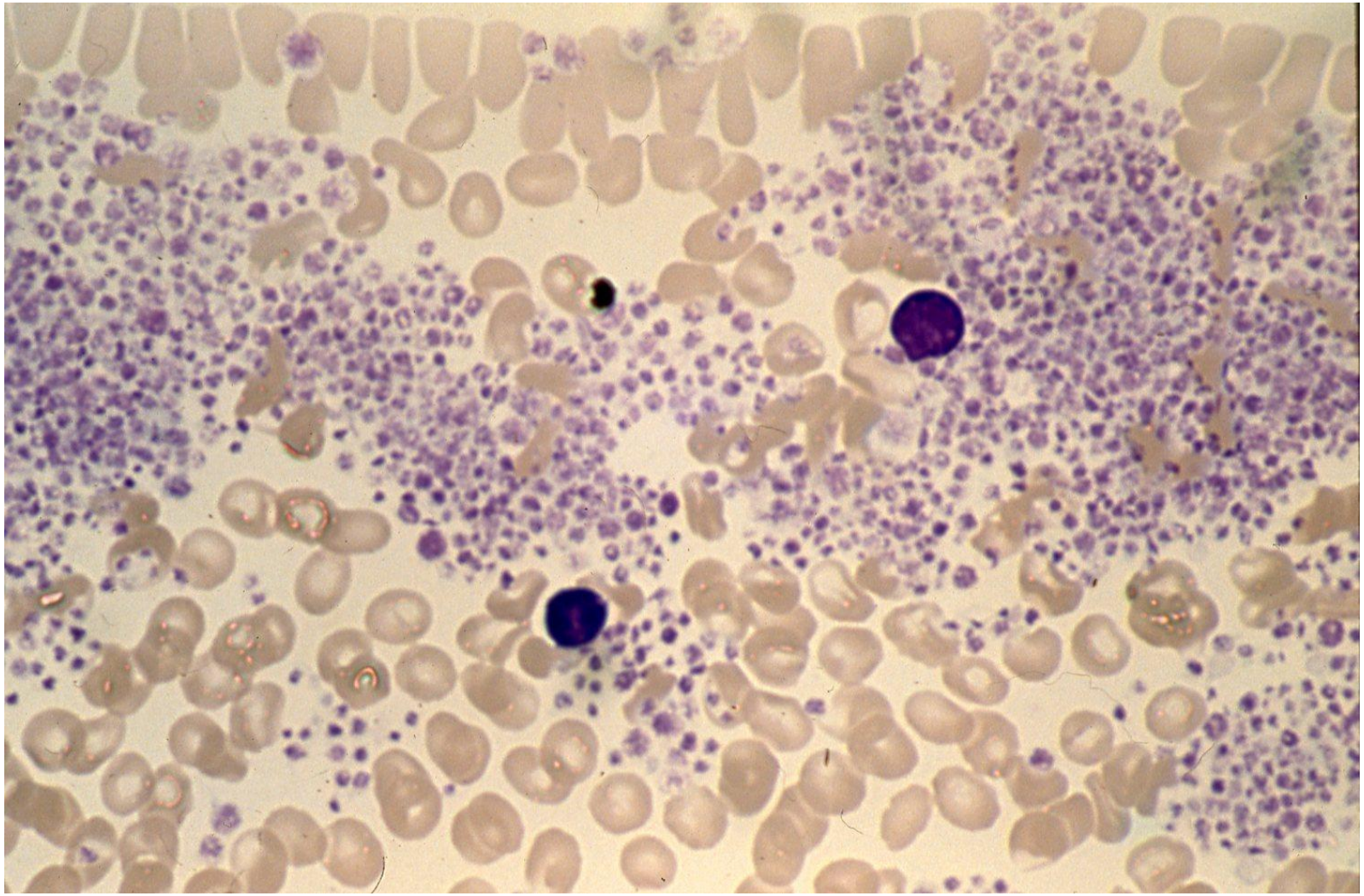
Wiscott-Aldrich syndrome

Wiskott–Aldrich syndrome (WAS), an X-linked hereditary disorder caused by mutations in the WAS gene, is featured by the triad of thrombocytopenia, eczema, and susceptibility to infection. The mutations impair but not abolish the WAS protein expression. The X-linked thrombocytopenia (XLT) is characterized by small-sized platelets. Autoimmune complications, in particular, IgA nephropathy, are common in WAS/XLT, affecting 40–70% of patients. Aberrantly O-glycosylated IgA, showing galactose deficiency in the O-linked glycans in the hinge region of the heavy chain of the alpha chain, may play a pivotal role in the pathogenesis of IgA nephropathy in WAS.

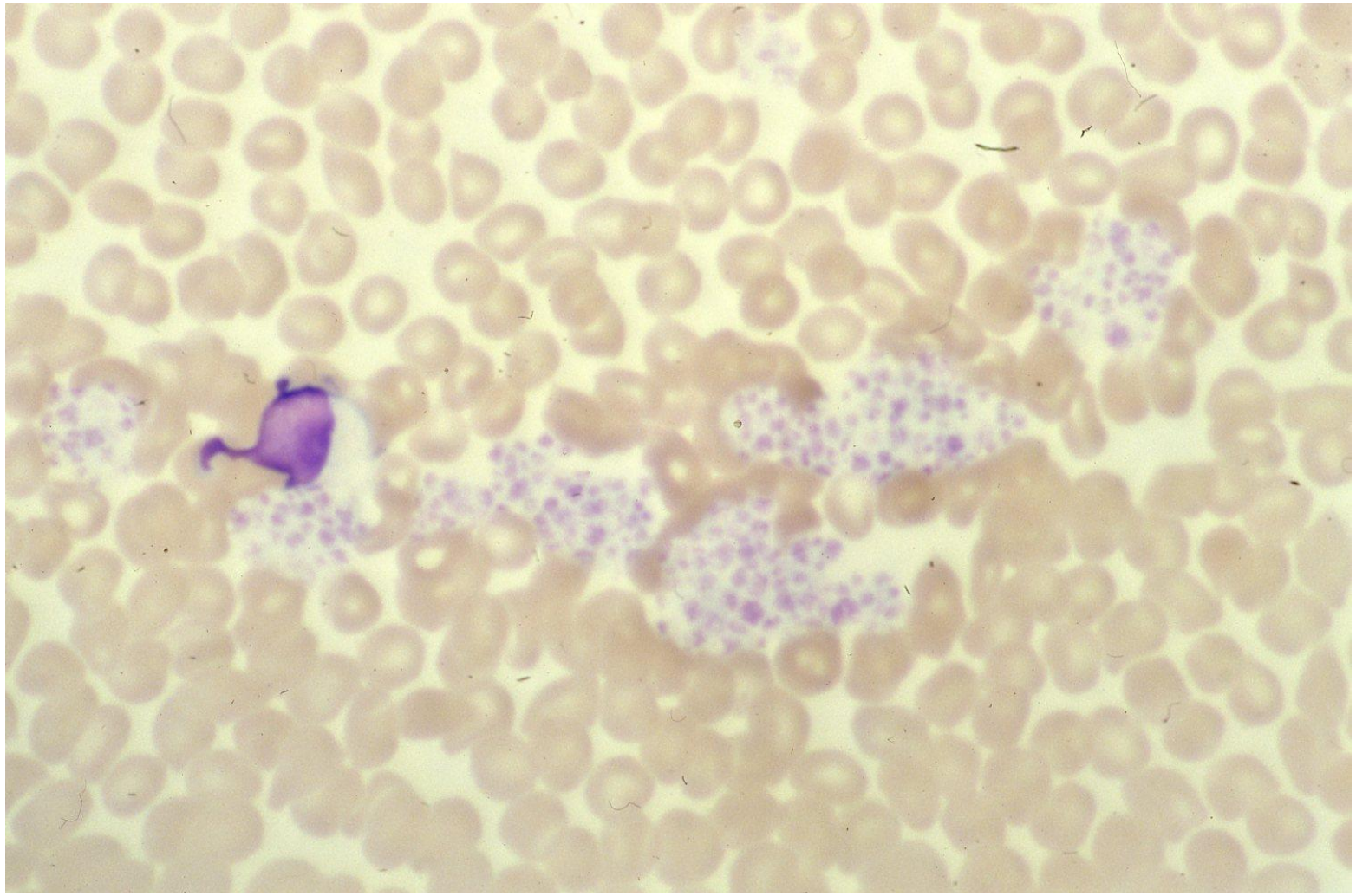
Ref.: Shimizu M, et al. Aberrant glycosylation of IgA in Wiskott-Aldrich syndrome and X-linked thrombocytopenia. J Allergy Clin Immunol 2013; 131(2): 587-590.e1-3. doi: 10.1016/j.jaci.2012.08.040



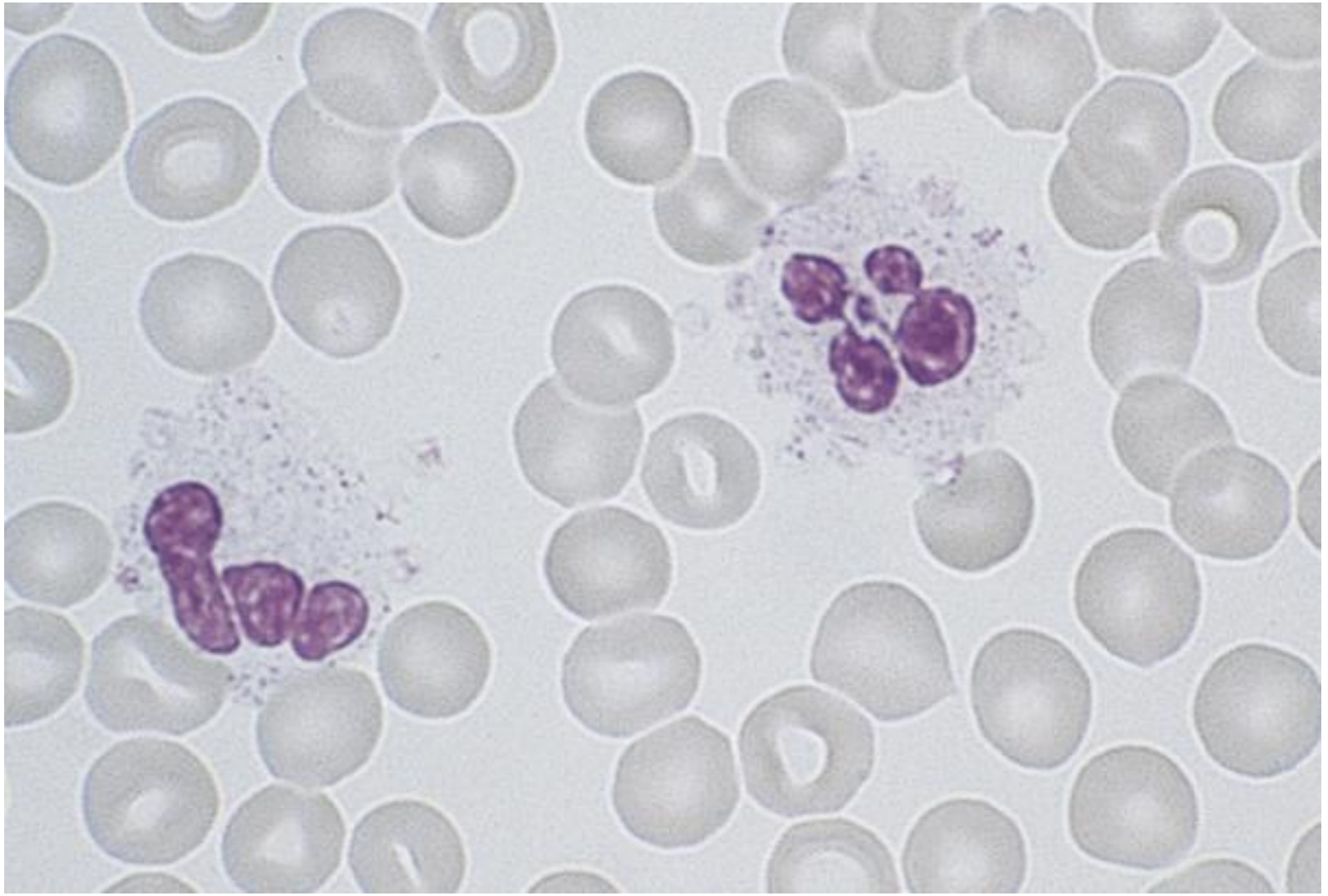
Wiskott-Aldrich syndrome (WAS) is featured by X-linked thrombocytopenia, eczema, and recurrent infections. The platelet size is small (arrows). The platelet production in the bone marrow is ineffective and platelet clearance is more rapid than normal, leading to the lower counts. Borrowed from: https://www.nerdynaut.com/wiskott-aldrich-syndrome-complicated-with-milk-protein-allergy



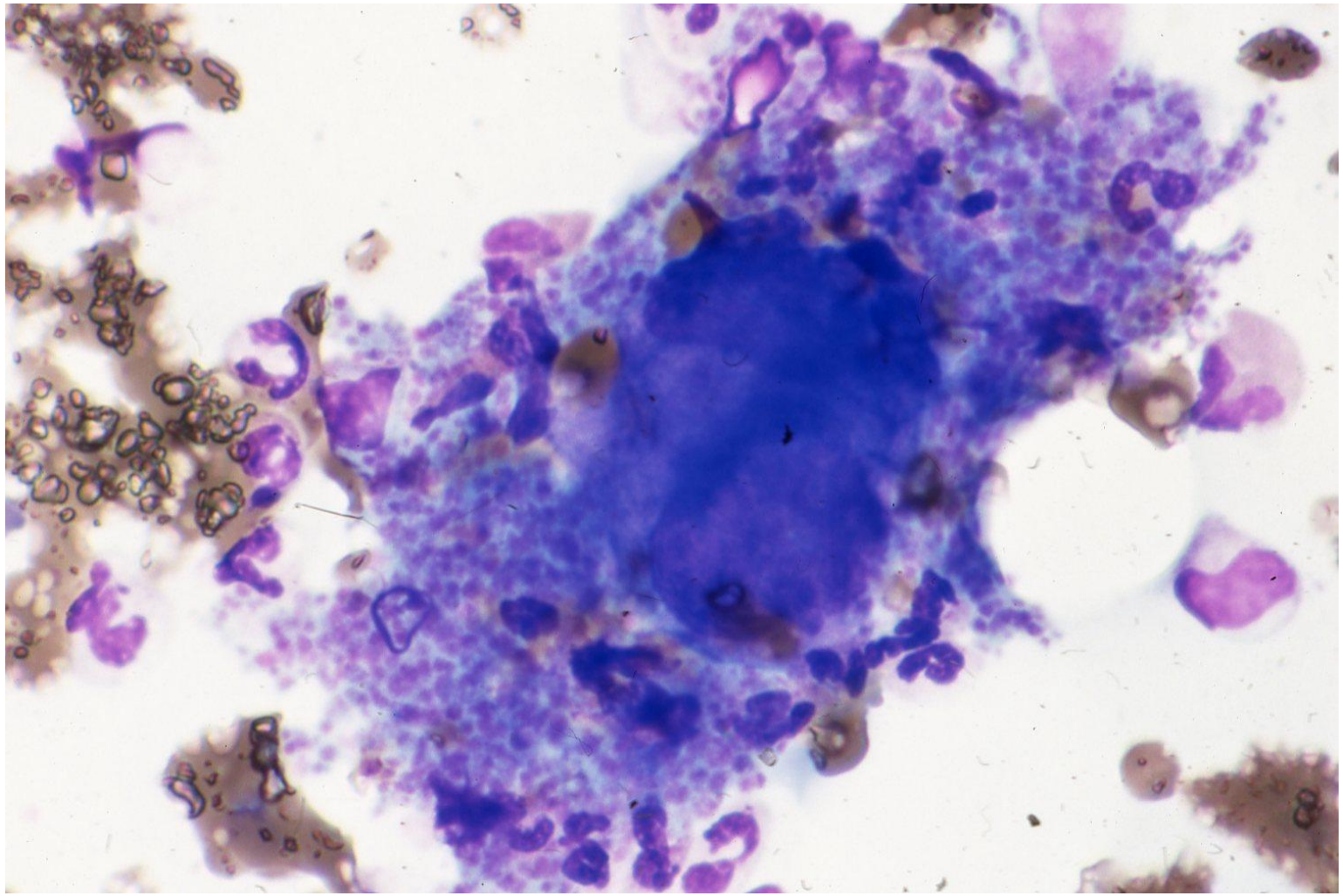
Pseudothrombocytopenia due to EDTA-dependent platelet clumping (1). Agglutination of platelets is caused by IgM/IgG autoantibodies directed against platelet surface glycoprotein (GP) IIb/IIIa. EDTA induces a conformational change in GPIIb/IIIa, exposing the epitopes and resulting in platelet agglutination. The use of an alternate anticoagulant, such as citrate or heparin, may be helpful. May-Giemsa



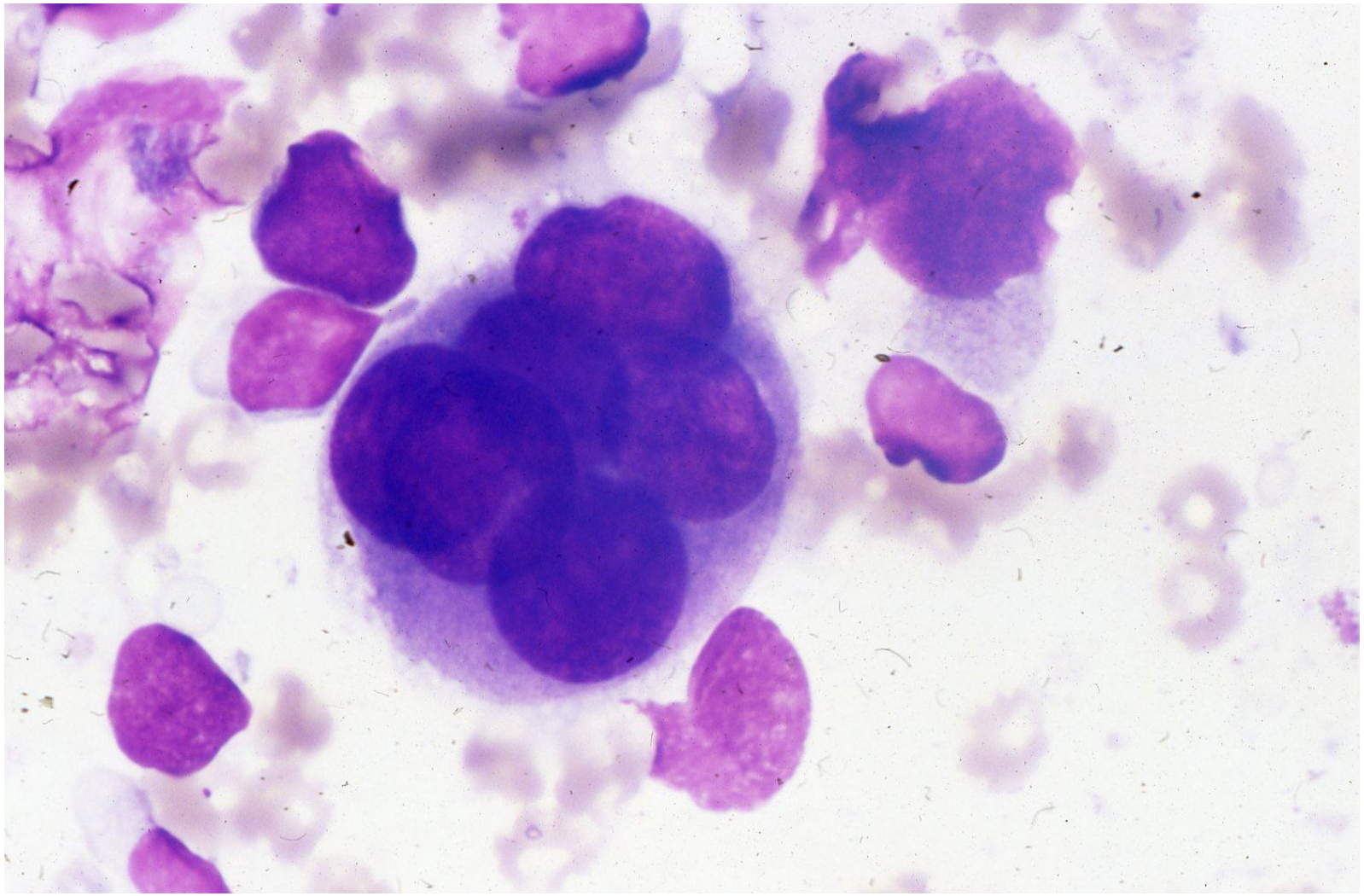
Pseudothrombocytopenia due to EDTA-dependent platelet clumping (2). Agglutination of platelets is caused by IgM/IgG autoantibodies directed against platelet surface glycoprotein (GP) IIb/IIIa. EDTA induces a conformational change in GPIIb/IIIa, exposing the epitopes and resulting in platelet agglutination. The use of an alternate anticoagulant, such as citrate or heparin, may be helpful. May-Giemsa



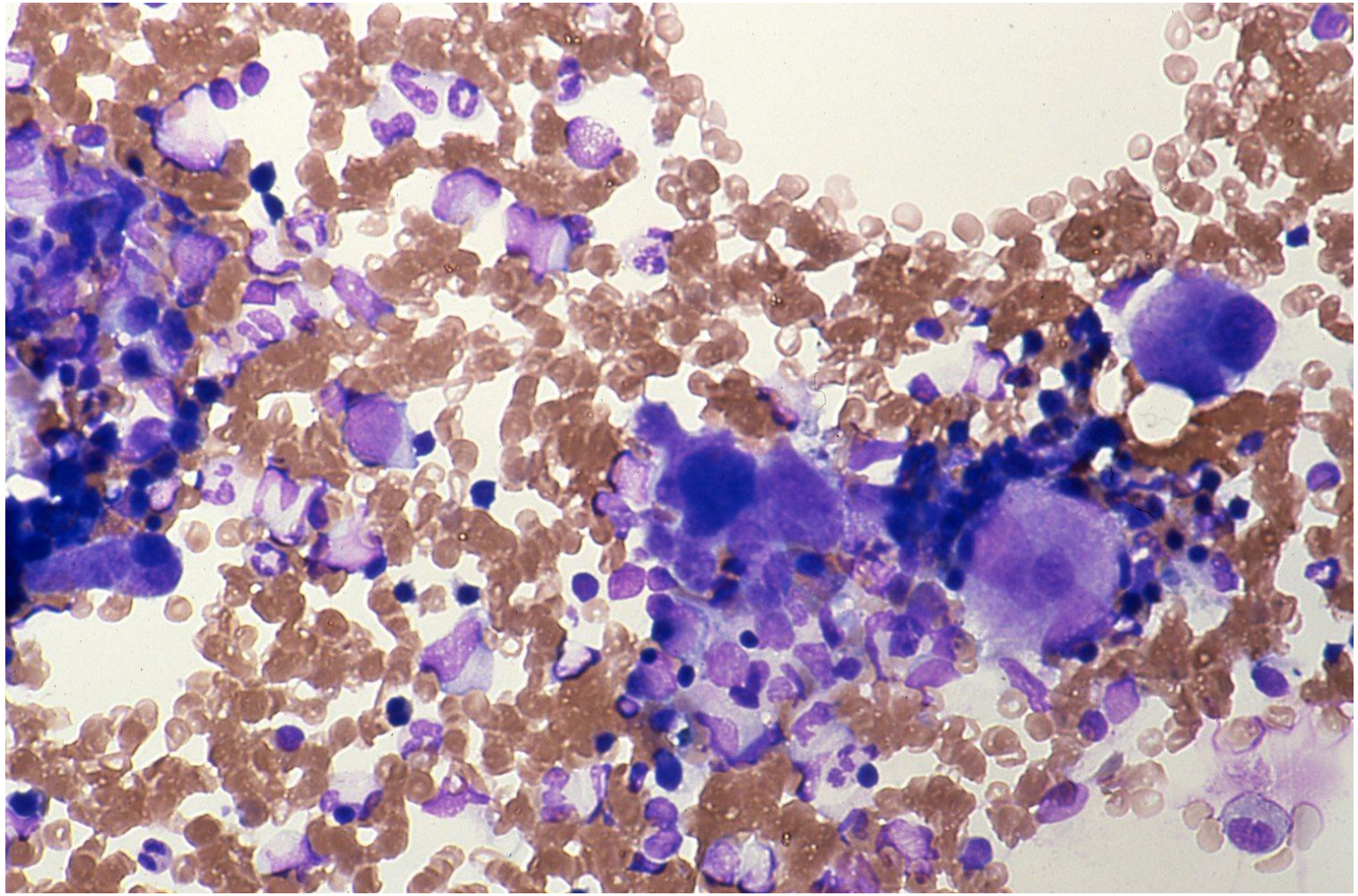
Pseudothrombocytopenia due to EDTA-dependent platelet clumping (3). Platelets satellitism is a phenomenon platelets reset around polymorphonuclear neutrophils as a rosette. The same mechanism as platelet clumping causes rosette formation on the neutrophils. May-Giemsa



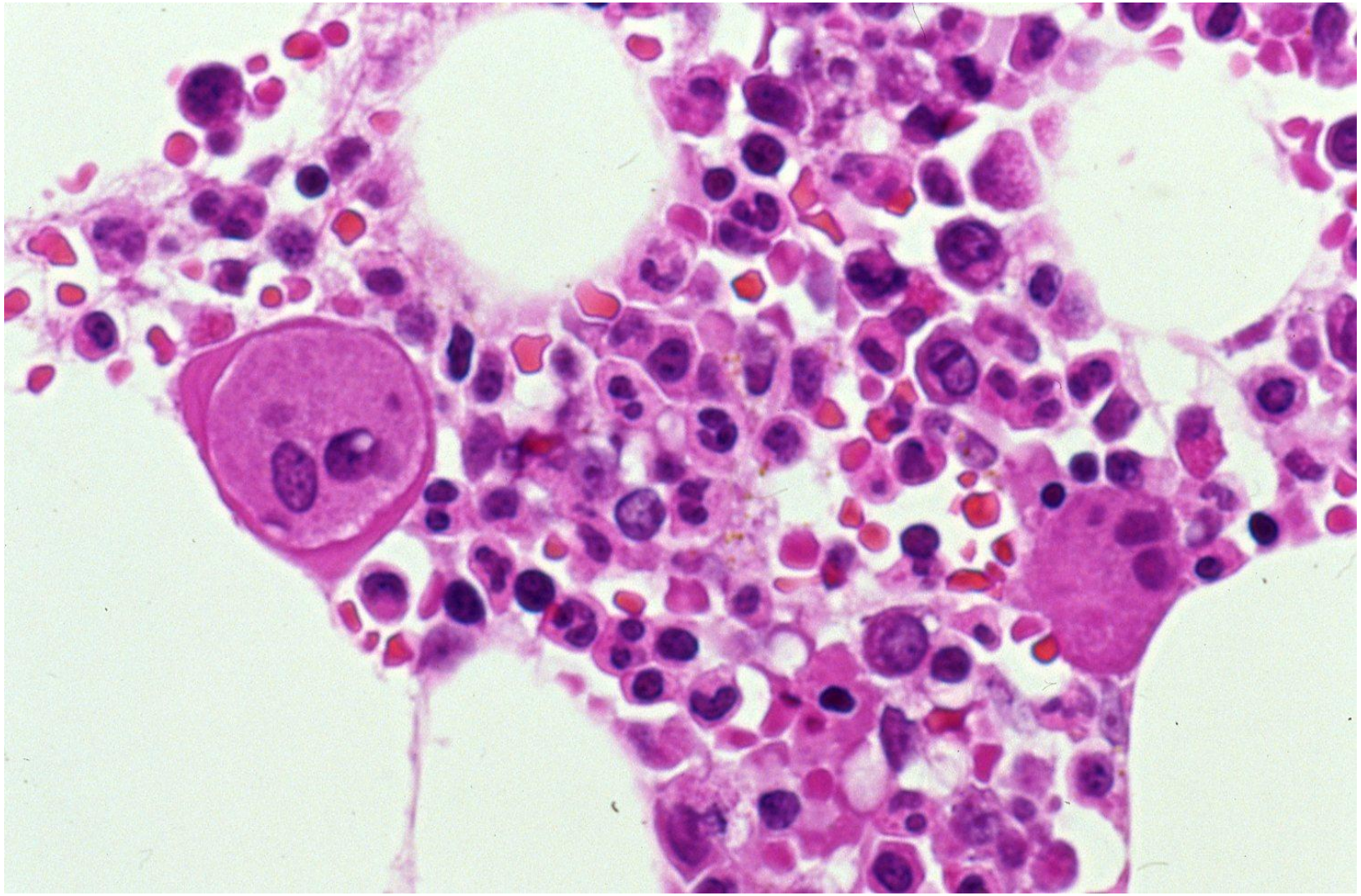
Normal megakaryocyte in the bone marrow smear. Large lobulated nucleus and granular cytoplasm are characteristic. Platelets are released from the periphery of the cytoplasm. May-Giemsa



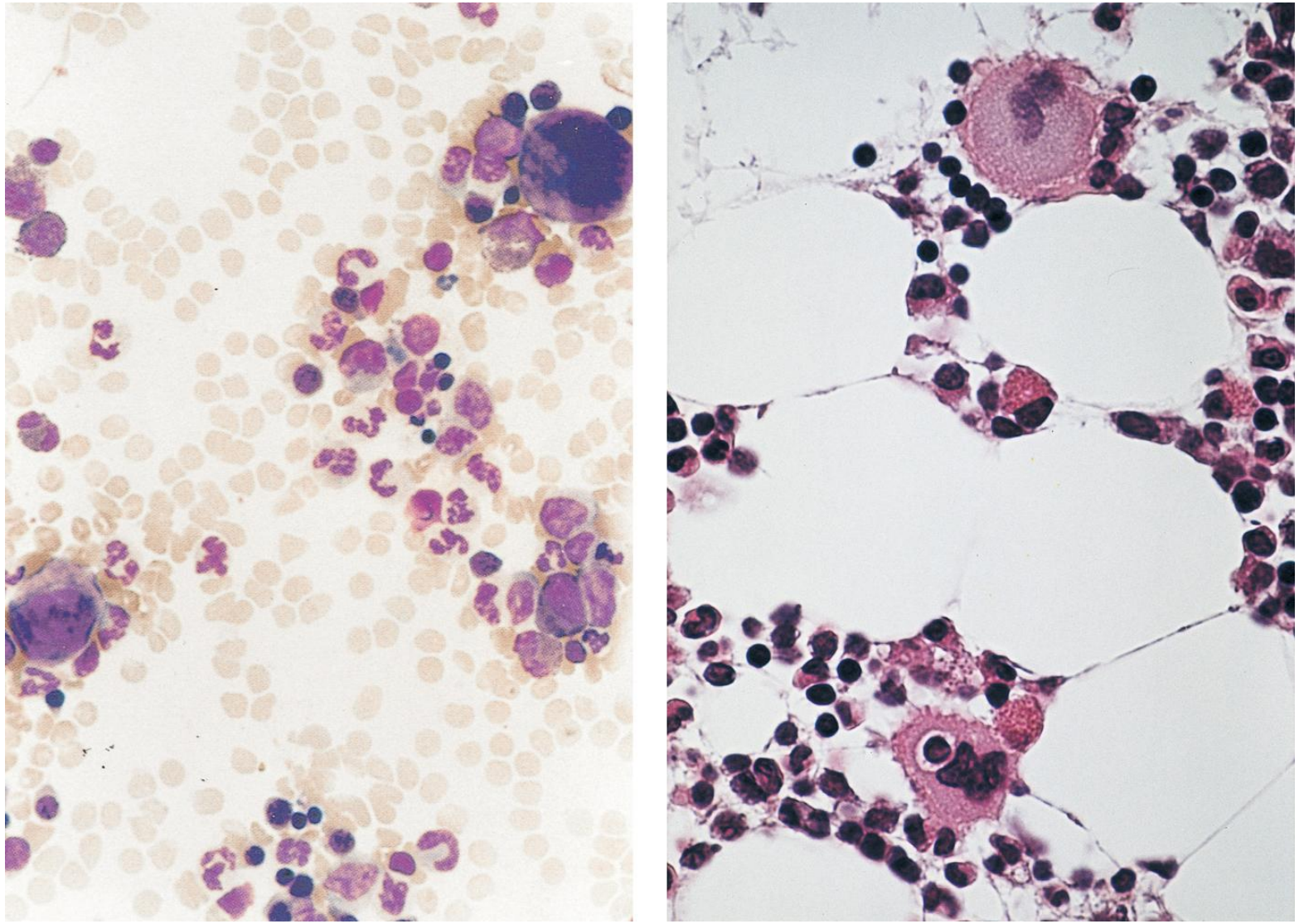
A megakaryocyte in idiopathic thrombocytopenic purpura (ITP). In ITP, the size of megakaryocytes is smaller than normal, and no features of platelet production are recognizable. Azurophilic granules are scarcely seen in the cytoplasm. May-Giemsa



Idiopathic thrombocytopenic purpura (ITP). In ITP, the size of megakaryocytes is smaller than normal, and small megakaryocytes are increased in number. Features of platelet production are scarcely recognizable. May-Giemsa



Idiopathic thrombocytopenic purpura in an adult. The aspirate bone marrow tissue contains an increased number of small-sized megakaryocytes. One megakaryocyte reveals double contour of the cytoplasm: The peripheral cytoplasm is densely eosinophilic, and may represent decreased production of platelets. H&E



Idiopathic thrombocytopenic purpura in a 3-year-old girl. The aspirate bone marrow contains an increased number of small-sized megakaryocytes. Emperipolesis of a lymphocyte is observed in one megakaryocyte (right). Left: May-Giemsa, right: H&E