The causative mechanism underlying the various types of actual erythrocytoses presented varies with the genetic agent active. Different kinds of stimuli may be elicited at the same time by the same agent, and may combine in producing the erythrocytotic response. The following compilation may aid in clarifying this statement.

Causative Mechanisms Present in Actual Erythrocytoses

I. Functional blood anoxemia produced by defective oxygenation of this tissue resulting from
   a. inhalation of air with a lowered oxygen tension (high altitude);
   b. circulatory disturbances of the lung, preventing proper oxygenation of the blood passing through the lungs in the presence of sufficient oxygen in the inhaled air (obliterative pulmonary arteriolosclerosis and fibrosis of the pulmonary tissue);
   respiratory disturbances affecting the lung tissue (pneumothorax);
   c. presence of a pathologic hemoglobin lowering the oxygen carrying power of the blood (carbon monoxide hemoglobin, sulfhemoglobin, and methemoglobin).

Hematogenic anoxemia represents one of the most powerful erythropoietic stimuli of the bone marrow.

II. Anemiogenic agents which exert a cytotoxic effect upon the circulating erythrocytes, the bone marrow and/or the liver. The direct erythrocytotic agents are hemolytic substances such as phenylhydrazine and saponin. Other substances, such as benzol, roentgen-rays, and radioactive materials, act directly upon the proliferative activity of the bone marrow; while phosphorus and arsenic bring about hepatic injury. The appearance of an erythrocytotic effect in response to these agents evidently depends on the possibility of an excessive, regenerative, erythropoietic activity. This, in turn, is dependent upon exposure to small amounts of these anemiogenic agents combined with a proper interval between individual exposures, permitting an adequate regenerative reaction. An erythropoietic stimulation of this kind exerted over too long a period of time may end ultimately in exhaustion of the erythropoietic function with the development of an anemia. The same result may occur if the too prolonged exposure is accompanied by a cumulative effect of the agent, causing a predominance of the injurious action upon the erythropoietic tissue over the regenerative stimulus. Erythrocytoses produced by the various metals mentioned seem to take this course. It is doubtful and controversial, whether any of the erythrocytotic agents included in this group can exert, when acting in minute doses, a direct erythropoietic effect upon the bone marrow without causing an injurious effect upon this tissue.

III. A partial or complete elimination of the spleen, by direct traumatic destruction of the splenic parenchyma or a traumatic thrombosis of the splenic vein, may cause a delay in the normal rate of erythrocytic destruction, and