

The role played by the calcium was eventually cleared up by Hammarsten. He found that calcium was normally present in the blood in two states, (1), either as the free salt, or, (2), in combination with proteids. In oxalated blood it is the free calcium alone, which is precipitated and hence it is this free salt which is important. When this non-coagulable oxalated plasma is cooled to 0°C. a fine precipitate separates out and as this occurs the plasma loses its power of clotting with the addition of calcium. Therefore, this second precipitate is an important factor for coagulation. From the clear supernatant fluid Hammarsten was able to isolate a calcium free fibrinogen which he could clot by the addition of a calcium-free thrombin or ferment. Hence it is proved that the calcium salt is not essential in the conversion of fibrinogen into fibrin. On the other hand, the calcium seems necessary for the formation of fibrin-ferment from the pro-thrombin, that is the calcium converts the zymogen into the enzyme as Pikelharing had stated.

It has been noted by many investigators that certain tissue extracts accelerate the coagulation process. By some it was contended that the disintegrated nuclear material of degenerating cells assisted clotting,—others regarded the cytoplasm as the stimulating substance. Field came to the conclusion that the tissue extracts were a necessary factor for the formation of thrombin. According to him, an element from the plasma unites with a certain element from the tissue cells, and these two agents along with a calcium molecule make up the thrombin or ferment.

Blood which is allowed to flow about in the subcutaneous tissues, or to which a tissue extract is added coagulates more rapidly than that taken directly from the vessels. It seems evident, therefore, that tissue extracts contain an active principle, thrombo-kinase, (Morawitz), which is concerned in the formation of the ferment.

In short, the prothrombin is present in the circulating blood, and is activated in the presence of calcium by a zymoplastic substance obtained from leucocytes or tissue cells, (Schmidt).

Morawitz believes that thrombin or fibrin-ferment has its origin from two sources. On the one hand the zymogen appears in the plasma and is activated by calcium salts alone, the other exists in the serum separated from the coagulated blood and can be activated in the absence of calcium by weak acid or alkalies.

Outside the body the morphological constituents of the blood, and in particular the blood platelets yield thrombo-kinase when brought in contact with non-living matter. As to the origin of the zymogen or thrombogen there is little known.

In these reviews I have drawn extensively from the writings of Minot, Askanazy, Pappenheim, Buckmaster and others.