Imbedded in this mineral and like it derived from some mineral that has disappeared, are spherulites of an undetermined mineral with rather strong birefringence, positive elongation, and a mean index of refraction of about 1.50.

2 Published with permission of the Director of the United States Geological Survey.
3 Unpublished manuscript by Esper S. Larsen.
4 Dana, A System of Mineralogy, sixth edition, p. 181, 1892.

THE PROCESSES TAKING PLACE IN THE BODY BY WHICH THE NUMBER OF ERYTHROCYTES PER UNIT VOLUME OF BLOOD IS increased IN ACUTE EXPERIMENTAL POLYCYTHAEMIA

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In a previous communication to the PROCEEDINGS1 I reviewed the work of the past on polycythaemia, and reported a series of experiments carried out in the hope of determining if possible the process by which the number of erythrocytes per unit volume of blood is increased in acute experimental polycythaemia. Since then further experiments have been undertaken, some of which have already been reported.2 The results of these experiments, and others about to be published, are collected here in a brief summary of this work up to the present time.

This complicated problem may be divided into four main parts:

(1) The causes capable of producing an increase in number of erythrocytes per unit volume of blood.

(2) Localization of these processes.

(3) The manner in which the number of erythrocytes is increased.

(4) The mechanism by which the red corpuscle content of the blood is controlled.

As previously pointed out, the causes of polycythaemia are very numerous, and have received a great deal of attention, but little work has been done concerning the localization and manner in which this increase in number of erythrocytes is brought about.

From experiments previously reported, the present author concluded that the liver is the organ which is responsible for the changes in number of erythrocytes produced by the intravenous injection of epinephrin.3 This conclusion has been confirmed by the following experiments here summarized.
PHYSIOLOGY: P. D. LAMSON

(1) Epinephrin when injected into a dog or cat intravenously in doses of 0.9 mg. per kilo causes an increase in number of erythrocytes of 1.5 to 2.0 millions per cubic millimeter of blood in from five to ten minutes, lasting about one half hour and then gradually returning to normal.

(2) Removal of the stomach, intestine, mesentery, omentum, pancreas, and spleen, either singly or all together has no appreciable effect on this reaction to epinephrin.

(3) A head-thorax animal does not respond to epinephrin.

(4) The addition to the head-thorax animal of the liver, supplied by arterial blood only, gives an animal which responds to epinephrin.

(5) Removal of the liver from the circulation by ligation of the hepatic artery and shunting the portal blood around the liver by means of an Eck fistula, gives an animal in all respects normal except for the absence of the liver. Epinephrin in such an animal causes no increase in number of erythrocytes per unit volume of blood.

(6) In an animal in which all arterial blood supply to the liver is shut off by ligation of the hepatic artery (the portal circulation being left intact), epinephrin causes no increase in number of erythrocytes. But if one half hour or later, after the injection of epinephrin, arterial blood is again allowed to reach the liver by removal of this ligature, the number of erythrocytes is immediately increased as if a fresh dose of epinephrin had been injected into the animal.

(7) In an animal in which the arterial blood supply to the liver is shut off by ligation of the hepatic artery the injection of epinephrin into the portal vein causes an immediate increase in number of erythrocytes.

From these experiments it is evident that it is necessary for the liver to be present in the circulation for polycythaemia to take place. If epinephrin does not reach the liver as is the case when the hepatic artery is ligated (the epinephrin being probably adsorbed to a great extent in its passage through the other portal organs) no polycythaemia takes place. But if in this condition, epinephrin is allowed to reach the liver by injecting it into the portal vein, polycythaemia takes place at once.

As regards the manner in which the number of erythrocytes per unit volume of blood is increased following the injection of epinephrin we know that it must take place in one or more of the following ways.

(1) A decrease in plasma volume.

(2) An absolute increase in number of erythrocytes by (a) a formation of new erythrocytes, (b) a division of erythrocytes (a theoretical consideration), (c) bringing erythrocytes into the circulating blood from a reservoir or reservoirs in the body.

The following facts have been experimentally demonstrated.
(1) The number of erythrocytes per unit volume of blood is increased.
(2) An absolute increase in number of erythrocytes takes place.
(3) Plasma volume is decreased.
(4) Total blood volume is decreased.
(5) The average volume of the individual erythrocyte is decreased.
(6) The haemoglobin content of the average erythrocyte is decreased.
(7) No evidence of newly formed erythrocytes has been obtained.
(8) No evidence of the division of erythrocytes has been obtained.
(9) Proof that erythrocytes temporarily stored somewhere in the body, are brought into the circulation, has been obtained by deduction from the above facts, and a condition in which erythrocytes are stored has been experimentally demonstrated as follows.

If the hepatic artery is ligated and epinephrin intravenously injected, the number of erythrocytes per unit volume of blood remains unchanged, but at the same time the plasma volume is markedly decreased. This is theoretically impossible without a destruction or a storing of erythrocytes somewhere in the body. No evidence of their destruction has been found. There is no haemolysis, and no haemoglobinuria. Furthermore polycythaemia may be repeatedly produced in the same animal.

The localization of this reservoir of erythrocytes was experimentally carried out in the following manner. As shown above, the liver is responsible for the increase in number of erythrocytes which follows the injection of epinephrin, and a certain portion of this increase is due to cells brought forth from some reservoir. In the experiments in which the hepatic artery is ligated and no increase in number of erythrocytes follows the injection of epinephrin, but where a storing of erythrocytes must take place, opening the hepatic artery is immediately followed by an increase in number of erythrocytes in the generally circulating blood. Or if in this same condition where the hepatic artery is ligated, epinephrin is injected into the portal vein, causing a constriction of the liver capillaries, and a decrease in liver volume, an immediate increase in number of erythrocytes occurs.

It has thus been experimentally shown, that the polycythaemia following the intravenous injection of epinephrin is due to some action of the liver. A condition has been brought about by ligation of the arterial blood supply to this organ and the intravenous injection of epinephrin, in which erythrocytes must be stored away. By returning the arterial blood supply to the liver, or by causing a constriction of the liver capillaries by the injection of epinephrin into the portal vein, both of which procedures offers mechanical conditions favorable
for forcing out erythrocytes lying dormant in the capillaries of this organ, the red blood corpuscles known to have left the general circulation immediately appear in the blood stream causing an increase in number of erythrocytes per unit volume of blood. From these experiments it is concluded that the liver acts as a reservoir for erythrocytes.

The process by which the liver increases the number of erythrocytes is thought to be a loss of plasma from the liver capillaries, together with a constriction of these vessels driving the erythrocytes on into the blood stream. It has been experimentally shown that the liver capillaries constrict with epinephrin, causing a sudden diminution in size of the liver. This does not occur except to a slight extent when the hepatic artery is tied, and epinephrin injected intravenously, in which condition no increase in number of erythrocytes takes place. It is also of interest to note, as more fully described in a previous paper,\textsuperscript{5} that Mautner and Pick\textsuperscript{6} have shown that the livers of cats and dogs constrict very markedly when epinephrin is perfused through them or intravenously injected into these animals. Rabbits however do not respond in this way to epinephrin, the liver capillaries not contracting. They also show no increase in number of erythrocytes per unit volume of blood when epinephrin is intravenously injected. Thus we have two types of animals, one the cat, whose liver responds to epinephrin by constriction of its capillaries and gives a polycythaemia, the other the rabbit, whose liver does not respond to epinephrin and in which this substance produces no polycythaemia.

Concerning the mechanism which normally controls the red corpuscle content of the blood, my view was previously expressed that the adrenal glands play an important part in this process. Certain experiments were carried out in which the polycythaemia occurring in the normal animal did not occur in animals after the removal of the adrenals. Two additional experiments have been made which have strengthened the belief in this view.

As previously shown, certain nervous phenomena are capable of producing a polycythaemia. This increase in number of erythrocytes must occur either by some entirely different process from that caused by the injection of epinephrin, or by some nervous influence directly or indirectly affecting the liver. Experiments in which the nerves going to the liver were stimulated, showed no increase in number of erythrocytes. Furthermore in the experiments above reported, in which epinephrin is shown to have no effect on the number of erythrocytes per unit volume of blood in the rabbit, nervous phenomena known to cause polycythaemia in cats (which respond to epinephrin) caused no
increase in number of erythrocytes in these animals. If polycythemia is due to some direct nervous influence it might be expected that in these animals in which the nervous condition is intact, nervous stimuli as fright, would cause an increase in number of red corpuscles.

As the direct stimulation of the nerves to the liver causes no increase in number of erythrocytes, and as in animals in which epinephrin causes no polycythemia nervous stimuli also cause no increase in number of red corpuscles, it appears probable that the polycythemia following the stimulation of certain nerves is not due to a direct nervous influence, but to a reflex stimulation of the adrenals and a secondary action of epinephrin on the liver.

Lamson, P. D., These PROCEEDINGS, 1, 521-525 (1915).
The terms red count, number of red corpuscles, etc., will be used occasionally for the sake of brevity, instead of the more exact term, number of erythrocytes per unit volume of blood.

THE INFLUENCE OF MORPHIN UPON THE ELIMINATION OF INTRAVENOUSLY INJECTED DEXTROSE IN DOGS

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The sugar content of the circulating blood is practically constant. This constancy is upheld by some stable mechanism which controls the supply of sugar to and its elimination from the circulation. Some time ago we communicated the instructive fact that after the intravenous injection of four grams of sugar per kilo of body weight the sugar content of the blood returns to nearly normal again in about 90 minutes. These animals had ether anesthesia during the operation and afterwards a subcutaneous injection of morphin. The question presented itself, whether the anesthetics which were used influenced the rate of elimination of the added sugar through the kidneys and the blood capillaries, or, to express it in the terms of the hypothesis which was uppermost in our minds, whether the anesthetics affected the physiological permeability of the endothelia and epithelia which are concerned in the process of elimination.

We tested first the action of morphin alone. Two series of experi-