

toxins for man and for the goat, and since repeated injections of toxin do not appear to interfere with the reaction, these animals should prove of value in the preliminary standardization of the toxin—tests which up to the present have been made on persons.

On the other hand, in attempts to use these animals for standardizing antitoxic horse serums, it was found that after repeated intracutaneous injections, the goats had become so hypersensitive to the foreign protein that further injections resulted in marked local swelling and oedema. Hence, it would probably be impossible to use the same animal for this purpose more than once or twice.

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The cyanosis of peripheral venous engorgement.

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When the arm is hung down at the side of the body the veins become markedly engorged. Also, there develops a dusky bluish color of the skin of the hand and wrist, extending for a distance up the forearm. Such a state of affairs has usually been assumed to be due to stasis of the blood in the arm.

If the volume flow of blood through the arm is decreased, after a sufficient interval of time, assuming that metabolism progresses normally, there must be a point where the venous oxygen unsaturation is increased above the normal.

In studies using blood taken from the veins on the dorsal surface of the hand, we have found that there is usually a significant decrease of oxygen unsaturation of this blood, when the arm is hung down and immobilized. In eleven experiments, there is a significant decrease of the oxygen unsaturation in six. Of the five remaining, the unsaturation is the same in two cases and decreased in three. In addition, the oxygen capacity of the blood, under these conditions, is usually either increased or remains the same. Of thirteen experiments the capacity is increased in four cases, remains the same in seven and is decreased in two.

It is obvious that such results cannot be explained on the assumption of a simple stasis. The engorgement of the veins suggests that this engorgement extends for some distance towards the arterial side of the vascular bed, at least, into those vessels, venules and capillaries, which are responsible for skin color. Once these vessels have dilated to their maximum degree, there would be a larger volume of blood available for gaseous interchange, which with a normally progressing metabolism would result in less oxygen extracted from each unit volume of blood to meet tissue requirements. However, if there is a decrease in volume flow, the condition in respect to oxygen would be but a temporary one. We have found a decreased oxygen unsaturation after the arm has been held down for an hour or longer. This suggests that the volume flow of blood is not decreased. Only one explanation can be offered, namely, that there is an increase of arterial inflow of a sufficient degree to overcome the lack of the venous pump mechanism and the increased hydrostatic pressure which must be overcome in returning the blood to the heart.

The bluish dusky appearance of the skin is thus not associated with increased oxygen unsaturation of the blood. We have evidence against the assumption that the blood in the superficial skin vessels is different from that which we obtain from the veins. It would seem then that when the vessels of the skin, which give it color, are engorged in large number with blood of normal or even higher than normal blood oxygen, the skin takes on a bluish tinge. The blood coursing through the skin vessels does not appear blue under ordinary conditions, because the vessels are in a relative state of constriction. When, however, they become dilated and the blood is distributed more uniformly over a wide area, the blood imparts a dusky bluish color to the skin. This color appears well below the threshold value for oxygen unsaturation at which cyanosis has been said to appear. The increased amount of hemoglobin, when it occurs, may contribute to this phenomenon. On the other hand, we have noted marked blueness of the skin in the absence of increased hemoglobin.

The concentration of the blood can be explained by capillary and venule dilatation. This brings about an increased area for filtration of fluid from the blood, which is aided by an increase in filtration pressure. The latter is due to a general increase of pressure in these vessels. In the experiments in which concentra-

tion does not occur, or when blood shows a tendency to dilution, we may postulate variations of balance between blood flow and the increased pressure in the vessels.

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Cinematography of skin capillaries in the living human subject.

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Lombard¹ in 1911 showed that by illuminating the skin, the capillaries could be seen under the microscope. Many observations have since been carried out on the changes which take place in various diseased conditions. The possibility of studying alterations in the capillaries by means of cinematography first suggested itself to Krogh and Rehberg.² They developed a method of taking pictures of the circulation in the capillaries in the tissues of *Rana temporaria*. It is naturally simpler to obtain records from the tissues of frogs than from human tissues since for this purpose a technique resembling that used in histological photomicrography suffices. In the human case transmitted light cannot be used. The method of illumination from above has therefore been universally adopted. This method is difficult because, by it, contrast and intensity of light are much reduced as compared to these qualities obtained by transmitted light. Weiss,³ in 1916, devised an apparatus for photographing human capillaries, and published photographs obtained by his method in various diseased conditions. He used indirect illumination and required an exposure of one-quarter to three-quarters of a second to obtain pictures. Siedentopf (Zeiss) likewise has devised an apparatus for the instantaneous photography of skin capillaries under normal

¹ Lombard, *Am. J. Physiol.*, 1911-12, xxix, 335.

² Krogh and Rehberg, *Am. J. Physiol.*, 1924, lxxviii, 153.

³ Weiss, E., *Deutsch. Arch. f. klin. Med.*, 1916, cxix, 1.