

showed that anoxemia in rabbits increased the oxalic acid content of blood by as much as 60%. Kamiya⁶ and Marcolongo¹² showed that it rose in high blood pressure, uremia, tuberculosis, syphilis, beri beri, neuralgia, rheumatism, cirrhosis, and in acute and chronic nephritis. Melocchi¹³ observed a rise of oxalic acid in the blood during intestinal fermentation of carbohydrates. Olson also made the comment in a letter quoted by Schumann² that on the basis of the amount of oxalic acid normally in the blood, it would not seem logical that a small increase could have any effect on the clotting time. The experimental evidence bears out Olson's view.

Conclusions. Oxalic acid injected into animals over a wide range of dosage was found to have no effect on coagulation until a sufficiently high dose level was reached, at which point clotting was delayed. Included in this study were suitable controls, normal and heparinized rabbits and normal and vitamin K-deficient chicks.

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Direct Observations on the Circulation of Blood in Transilluminated Mammalian Spleens.*

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The spleens of living mice, rats, rabbits, guinea pigs and cats were transilluminated¹ and observed at several magnifications, as high as 600 \times (water immersion). Each type of spleen was completely delivered through a long paracostal incision and placed in a suitable celluloid chamber, on a light table, above the abdominal wall. By this means, respiratory motions were eliminated in some, and greatly reduced in all specimens. The spleen, thus supported, was totally immersed in rapidly flowing Ringer-Locke solution at 37°-38°C. Anesthesia hypodermoclyses of sodium iso-amyl ethyl barbiturate

¹² Marcolongo, F., *Clin. med. ital.*, 1934, **65**, 1068.

¹³ Melocchi, W., *Giorn. clin. med.*, 1934, **15**, 1669.

* The cooperation of the Department of Pathology, greatly facilitated this work.

¹ Knisely, M. H., *Anat. Rec.*, 1938, **71**, 503.

(sodium amytal, Lilly) provided adequate narcosis without disturbing the animal's position. Methods were devised for variously stimulating the spleen during the period of observation. The albino mouse was studied in greatest detail. It was noted, however, that the circulatory mechanisms of all species investigated presented fundamental similarities, which seemed to justify the following generalizations.

The afferent capillaries of the pulp communicate with naked pulp spaces at the point where their terminations are marked by ampullary dilatations and diminished mural refractility. No preformed, intactly lined connections between the arterial and venous systems in the spleen have been as yet conclusively demonstrated in our preparations. The break in vascular continuity is obvious in a relaxed or distended spleen, where the walls of the pulp channels are seen to be composed of spherical, oval or polyhedral cells and vague, linear shadows, suggestive of reticulum fibers; but, when the spleen is contracted, it is difficult to detect, because the residual channels, surrounded by compressed pulp cells, then assume the appearance of completely walled vessels, connecting arterial capillaries with venous sinuses and intralobular veins.

The capacity of the pulp is a function of capsular contraction, which takes place rhythmically as well as in response to specific stimulation. The behavior of the individual pulp spaces is additionally governed by arterial and venous blood-pressure variations, relationships to neighboring channels, the obstructing action of migrating leucocytes, derived either from the pulp cords or from associated arterial capillaries, and by swelling or shrinkage of the reticular stroma.

The pulp space is the most variable structure in the transilluminated spleen. It may convey, at different times, plasma almost devoid of red cells, rapidly flowing blood of normal cellular content, or slowly oozing, highly concentrated red cells. When the narrower, efferent end of the pulp channel is blocked by transient leucocytes, or by some other factor, blood accumulates within it. If, at this time, the adjacent pulp cells happen to be compressed, the channel becomes distended, and the blood within it acquires such concentration that the contours of individual erythrocytes are scarcely visible. In the absence of pulp compression and concomitant arterial constriction, the column of blood is obstructed momentarily, but rapidly alters its course and penetrates alternative passages to the nearest venous tributary. In our experience, this intermittency of circulation in the pulp most closely resembles, on a much smaller

scale, the cyclical blood flow observed by Knisely^{2, 3, 4} in the venous sinuses.

The venous sinuses and intralobular veins are passive recipients of blood. Their walls reveal innumerable stigmata, offering little or no obstruction to the influx of erythrocytes, and permitting the passage of lymphocytes and larger white cells with varying degree of distortion. In the absence of extrinsic interference with venous drainage, the sinuses swiftly transmit to the larger venous tributaries the blood which enters them from the pulp spaces. The only vascular sphincteric action that we have observed in the spleen pulp is exhibited by the arterioles and arterial capillaries, which are intermittently constricted, either individually or in groups.

Agonal vascular disintegration, as described by Knisely,⁴ has not been apparent in our preparations. Because of extreme capsular contraction, in the absence of positive arterial blood-pressure, the pulp of the dying spleen pales to a degree that is never otherwise attained. Having seen intracellular erythrocytes in living, normal splenic pulp, we are not satisfied with Knisely's assumption that phagocytosis of red cells is, in this situation, a purely agonal phenomenon. In effect, the spleen pulp acts as a filter, separating red cells from plasma, and removing foreign particulate matter, including certain erythrocytes, from the circulating blood. We have watched the appearance of India ink particles, inside pulp phagocytes, less than 20 seconds following their peripheral intravenous injection.

From the standpoint of reservoir function, the reaction which might be termed the 'emergency response' of the spleen, as classically demonstrated in the gross by Barcroft^{5, 6} and his colleagues, was consistently reproduced in our experiments by such factors as electrical stimulation of the pedicle nerves, adrenalin, exercise, anoxemia, hemorrhage and temperature changes. Microscopically, the response consisted of pulp compression and arterial constriction, leading to obliteration of the extravascular spaces and consequent mobilization of a quantity of relatively concentrated red cells.

Because of the pitfalls inherent in the technic of living tissue transillumination, our conclusions are necessarily tentative. We are reasonably convinced, however, that the circulatory systems of the spleens we have examined are 'open'; that, in other words, they lack

² Knisely, M. H., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 212.

³ Knisely, M. H., *Anat. Rec.*, 1936, **65**, 23

⁴ Knisely, M. H., *Anat. Rec.*, 1936, **65**, 131.

⁵ Barcroft, J., *Lancet*, 1925, **1**, 319.

⁶ Barcroft, J., *Lancet*, 1926, **1**, 544.

the type of connection which commonly links arterial and venous capillary networks; that the pulp space—not the venous sinus—is the primary physiological unit of the splenic vascular mechanism; and that contraction of the capsule and trabeculae may convert the structurally 'open' circulation of a relaxed or distended spleen into a functionally 'closed' circuit.

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Electrical Method for Studying Water Metabolism and Translocation in Body Segments.

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Although the electrical resistance of a mummified arm would, obviously, be very much greater than that of a fresh cadaver, no serious attempt has ever been made to measure the water content of a body segment in terms of its electrical resistance. One of the reasons for this would appear to have been the lack, until comparatively recently, of technics which would permit resistance measurements to be made. Using alternating current, it has now become possible to measure, with a fair degree of accuracy, not only the resistance of various parts of the arm-to-arm segment in man (the upper arm, the chest segment alone or the arm and chest segments together) but also changes in their dielectric properties.^{1, 2, 3}

Hydration. In order to test out the possibility of measuring body water changes electrically, a liter of isotonic saline solution was injected intravenously into a normal individual weighing 50 kg who had been deprived of fluids for 3 hours previously and the electrical resistance of the arm-to-arm segment was measured before and 30 minutes after the injection. Resistance measurements were made by the immersion method at room temperature. The subject stood before a table 32 inches high and immersed the forearms in 9 liters of normal saline (11 cm deep) contained in a pair of arm baths supported on the table so that (1) the elbows rested on the arm-bath bottoms and (2) the upper arms were in a substantially

¹ Horton, J. W., and Van Ravenswaay, A. C., *J. Frank. Inst.*, 1935, **220**, 557.

² Barnett, A., and Bagno, S., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 543.

³ Barnett, A., *West. J. Surg.*, 1937, **45**, 380.