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When Lombard (1) in 1912 introduced the use of the microscope with a few simple adjuvants as a means of examining the capillary blood flow in human beings, he presented investigators with a new field for research. It has become apparent that many branches of medical science will benefit from this access to an all-important but hitherto little-known portion of the circulatory system. Much has been learned concerning the state of the minute blood vessels in health and disease, and we are beginning to understand how important is the part played by the peripheral vascular system in the vital processes of the organism.

Already an imposing bibliography has grown up around the subject of the microscopy of the capillaries. Much of the work done requires confirmation before it can be accepted as authoritative. Krogh, one of the foremost authorities on the subject in Europe, has done notable service in collecting and appraising the value of the newer information. The comprehensive list of references at the end of his book (2) renders any summary of the literature at the present time quite superfluous.

Examination of the capillaries and the state of the blood flow in children and, in particular, infants, has been very inadequate. The conditions governing worth-while study of the living tissues make great demands on time and patience, especially in young subjects. However, the advent of micro- and kinema-photography promises to be of great assistance in certain aspects of the work such as the recording and interpretation of morphological abnormalities. (3) In 1921 Mayer described the normal formation in the nail-bed of infants at birth, and traced its development up

to the sixth month of life. (4) She also gave a summary of previous examinations at this age period. Some years later Roi (5) the Italian pediatricist made observations which do not differ essentially from those of Miss Mayer. Roi states that the adult picture is not reached till the sixth month, and in this he is in accord with the earlier German microscopists. During the past decade certain other Italian pediatricists have studied the capillaries in the young, but not to any extent in infants. Of the Germans, Doxiades has confirmed the earlier work of Holland and Meyer (6) on the morphology of the capillaries in the new-born. This author makes the interesting assertion that in premature infants born with right-sided cardiac enlargement (Foetalists) there is an arrested development of the capillary loop persisting throughout life and quite characteristic of the association. (7) Muller in 1923 gave a fairly comprehensive account of the changes in capillary formation and the blood stream as seen by himself and others in many diseases of children including the so-called vaso-motor diathesis, the exanthems, and following the effect of the sun and ultra-violet radiation; and after the use of digitalis and diuretics in congestive states of the circulation. (8) The German school has paid great attention to the morphology of the capillaries in the feeble-minded and in Mongols and cretins. Some difference of opinion exists among the members of this group of workers as to the significance of the variation in the form of the capillaries found in certain of these conditions. One of them - Pototsky - is probably right when he says that the time has not yet come when conceptions of the type of a disease should be sought and taught from a capillary picture. (9)

My own observations on the development of the capillary formation at the nail-bed confirm in a general way those of Mayer and of Roi. But I agree with the former that there is little change after the fourth month in the normal infant. In dystrophic infants up to the sixth

month of age, however, I have noticed that the capillaries at the nail-bed may be poorly developed and more like those corresponding to an earlier age.

Interest in the subject of dehydration as a cause and effect of profound changes in the circulation leading to grave consequences is perennial amongst those who have to do with the treatment of infants. It has been known for some years that dehydration is associated with a diminished flow of blood. Marriott and Utheim applied the calorimetric method of G.N. Stewart to measure the volume flow in dehydrated infants and found that, in terms of cubic centimetres per 100 grammes of body substance per minute, it was reduced to one seventh of the normal rate in some instances. (10)

A study of the capillaries and the capillary flow was undertaken at the Hospital for Sick Children, Toronto, during the months of August, September, and the first half of October of 1929 and of 1930. The subjects were infants admitted as in-patients who required treatment for the dehydration symptomatic of Acute Intestinal Intoxication (Cholera Infantum) and allied disorders prevalent during this period. Approximately one hundred and fifty were examined. The controls were infants in the ward suffering from a variety of conditions without dehydration. Measurements of the capillaries were made in about one hundred instances; verification is thought necessary and it is proposed to incorporate the results in a later publication. An attempt was made to measure the capillary pressure by the method of direct cannularisation recently invented by Landis. (11) Though his technique was followed to the letter and applied on numerous occasions, success was not obtained. Possibly the smaller size of the capillaries and the short period of time during which the infant could be relied upon to keep still necessitates a prolonged degree of experience, but the method so nearly approaches the ideal that it will be worth while to pursue the endeavour in the future.

In 1929 the apparatus used was that described by Callander in his photo -

-micrographic studies. (12) In 1930 a microscope of German manufacture * specially designed for this type of work proved highly satisfactory and more convenient. The infants were brought into the examining room and examined immediately or left for about fifteen minutes as circumstances warranted. The room temperature was variably between 70 and 75 degrees. The subject was first arranged in a comfortable position so that the hand could be carried to the stage under the eyepiece of the microscope with - -out disturbance and without inducing the least compression on the arm or the shoulder. In this way the maximum advantage could be taken of states of quiet, drowsiness or sleep. The stage bearing the finger was set at the level of the manubrium. No restraining apparatus was used apart from a shallow mold of plasticin to steady the finger, the arm being lightly held in position by sandbags or by the disengaged hand of the examiner. The absence of restraint is imperative if the observations are to be of full value, as it was found that the conditions of flow were easily dis - -turbed by pressure applied to the fingers or arm of the patient. If the infant cried or became restless the observations were perforce abandoned. It is regretted that the skin temperature at the finger was not measured. The co-operation of an additional investigator would facilitate the carrying out of similar experiments in the future. It is to be noted, however, that the infants were subjected to room temperature for some time before the examination. This temperature corresponded as far as possible with that of the cubicles in which the patients were nursed.

The capillary picture in the normal infant: The arterioles into which the smallest arteries break up may be seen forming a plexus in the deepest layer of the cutis vera - the subpapillary arterial plexus. From the oblong meshes so formed, still smaller arterioles spring to end in the

* Supplied by Messrs. Leitz New York.

papillary capillaries, each of these ultimate arterioles supplying a small number of papillae. Each papilla is thus provided with a central papillary loop, which, at the period of greatest development about the fourth or fifth month of extrauterine life, takes the form of an inverted hair-pin. The narrower arterial limb merges into the wider venous limb at the apex of the loop, and the latter returns to enter the subpapillary venous plexus, which ultimately communicates with the smallest veins in the subcutaneous tissues through a series of two or more additional plexuses lying in the deepest layers of the cutis. At birth the capillaries take the form of wide bows and it is impossible to differentiate the arterial from the venous ramus. As it matures the bow elongates, tends to become twisted or spiral and to take on the characters of the typical 'hair-pin' described above.

The normal blood current through the capillaries is seen to be a rapid and continuous flow of red and white corpuscles in the closest formation, the white cells scintillating like so many diamonds at irregular intervals in the ruby stream. In the larger vessels (venules) the flow of the red cells is axial, and the white cells roll along the walls in the surrounding plasma.

The capillary picture in severe degrees of dehydration: The back-ground is pale compared with that of the healthy infant, which is tinted a delicate rose-pink. The blood column itself is often distinctly cyanotic, especially when the skin temperature is low.

The most striking abnormality is the decrease in the rate of the blood flow. Whereas in the normal infant the corpuscles flicker past with an even rapidity that recalls the quick succession of the pictures in a cinema film, in severe dehydration the movement is slow and halting and the progress of the individual corpuscles can be traced with ease from the moment that they enter the capillary loop until they are lost in the venous plexus.

In its severest manifestations the stasis may amount to complete arrest of the blood flow in almost every loop under observation; and in such cases the subpapillary plexus is similarly affected, becoming packed with corpuscles whose movement is at most an irregular mass progression, contrasting with the normal swift return to the larger veins. When the arrest of the flow is complete and the cellular elements of the blood are massed in this way in the loop as well as in the plexus, the difference between the diameters of the arterial and venous limbs of the loop is not apparent. It is impossible to distinguish them apart from any indication that may be given by the direction of the flow; and one gets the impression that the capillaries and smallest veins are in a state of dilatation. The arterioles are not so affected. I have never been able to see this packing of the blood cells in them. They remain narrow. The stasis is maximal when the hand is cold and the skin temperature low. The slowness of the blood current is in itself, doubtless, a cause of the lowered temperature; but it is also true that a low external temperature may lead to capillary stasis in conditions quite apart from dehydration. However, I have seen slowness amounting almost to complete stoppage of the flow where the infant had been exposed for some hours to a temperature of from 70 to 80 degrees, and the hand was warm to the touch.

Another feature is the extreme irregularity of the flow. In the normal infant the rate, while generally rapid and uniform in the majority of the capillary loops, may be comparatively slow and even irregular in a few of them; and very occasionally a loop may remain invisible for long periods when it is presumably impervious to the passage of blood cells, and be revealed only by the intermittent presence of a single corpuscle. But the irregularity under consideration is more than a contrast between the behaviour of one or two loops and that of the

remainder. It is a general irregularity affecting the progression of the current in all parts of the field and evident in the venous plexus as well; and it is associated with a third prominent feature, namely, segmentation of the stream. By this is meant that the blood column is divided up into small groups of cells by clear spaces of variable length. It is likely that these clear spaces are almost devoid of plasma. Although this segmentation of the stream with agglutination of the corpuscles is conspicuous in the capillary loops, it is less usual to find it in the venous plexus, where, as said before, the corpuscles tend to be massed together. But I have seen segmentation in this situation as well.

Capillary pulsation is sometimes visible, showing as a regular irregularity in the flow through the capillaries. It is sometimes transmitted to the subcapillary venous plexus, and it is more often found in extreme than in moderate degrees of dehydration.

Occasionally there is a momentary reversal of the direction of the current - reflux. The reason for this is not very obvious. It is unlikely that it is cardiac in origin. It is probably due to a rise in pressure in a small portion of the plexus due to a temporary blockage at a more central point while blood continues to enter from the distal communications. Such a circumstance would tend to force blood back into those venous rami in which the pressure was lower.

Dehydration of moderate degree: Here the phenomena described above are present to a lesser extent. Features always seen are the slow stream, general irregularity and segmentation. There may be capillary pulsation, seldom reflux. There is no complete stasis. The stream may halt for a matter of several seconds at different times in many of the loops, but there is not the absolute stoppage for half a minute or longer that is characteristic of the more severe dehydration. When dehydration is

slight the flow tends to be continuous. The current in the plexus is fairly rapid, does not exhibit the pronounced stasis of more serious cases, and slowing of the rate of flow may be the only abnormal sign.

Recovery: As the infant becomes less dehydrated the blood stream increases in rate and the other abnormalities gradually disappear - the features of a severe case becoming those of a mild one until there is a return to the uniformly rapid flow of the healthy infant.

Effect of transfusions: There was little difference in the capillary picture in the cases observed before and immediately after the transfusion of whole blood. In some cases there appeared to be a slight increase in rate. Where the stasis had been very noticeable before the operation there was usually a general increase in movement throughout the field after it. Capillary pulsation was present after the transfusion where it had been remarked upon previously.

Effect of intravenous injection of dextrose solution: There was usually a striking change in the capillary picture in cases of severe dehydration examined immediately before and after the injection. Where there had been complete stasis, the whole blood stream was now in motion. The slow irregular flow became quite rapid and regular, and in many instances approached the normal. Segmentation and agglutination were dispelled. Differentiation of the limbs of the loop became easy where it had been formerly difficult. In a few cases the effect was not so dramatic; but in all there was immediate increase in the rate of flow and definite decrease in the degree of stasis. The sluggishness of the circulation returned after an interval of from one half to one hour.

Comment

The above observations establish the fact that there is a disturbance

of the peripheral circulation roughly proportional to the degree of dehydration. It may be questioned whether the capillary circulation in the viscera is affected in a manner similar to that in cutaneous tissues. Krogh suggests that, as a measure of economy, the capillaries in one region may open or close in order to alter the distribution of blood in the body according to local needs at the moment; (2) but it is apparent that the fall in blood volume associated with dehydration is too great to allow of adequate compensation by such physiological means, and so one is justified in assuming that the capillary circulation in the deeper structures does not differ from that visible at the surface. The great diminution in the secretory functions notably of the kidney, stomach and salivary glands of these dehydrated infants is, in fact, material evidence of the generalised nature of the capillary disturbance.

As has already been mentioned, Marriott and Uthelm demonstrated some years ago that the volume flow of blood per unit of time is diminished in dehydration. (10) This is accounted for by the reduction of the blood volume which takes place in dehydration, and also by the increase in blood concentration and consequent increase in blood viscosity. These facts, along with the contracted state of the arterioles, are sufficient to explain the slow rate of capillary flow which has been seen to be so characteristic of dehydration.

With increasing dehydration the relationship of plasma to corpuscular volume becomes more and more disproportionate, and in consequence there is a tendency for the blood cells to adhere to each other and to the wall of the vessels, producing the stasis and segmentation described. In the normal subject there is a clear zone surrounding the axial layer of red cells. The existence of this space is made manifest by the presence of white corpuscles which roll along intermittently between the vessel wall and the column of red cells. No such zone

can be made out in conditions of dehydration. All the cells are massed together and seem to occupy the whole cross-section of the vessel.

One of the most important consequences of the disorganisation affecting the peripheral circulation is alteration of capillary pressure. As visible evidence of this, attention may be directed towards the stasis, the occasional capillary pulsation, and the temporary reversal of the direction of the flow. It is likely that the capillary pressure as a whole is lowered as a result of the constriction of the arterioles and the slow rate of blood flow. The shock-like appearance of these patients is characteristic, and analogous to that which follows burns or the circulatory failure induced by the injection of poisonous doses of histamine in animals. (13)

The temporary approach to normal conditions of flow secured by the introduction of suitable fluids into the blood point to plasma deficiency as being chiefly instrumental in producing capillary stasis. The effect wears off as the additional fluid is excreted by the kidney or leaves the body by the intestinal tract. But used in conjunction with subcutaneous injections of saline, the measure would seem to be rational and valuable, if only for the promotion of more efficient circulation. While the transfusion of blood serves other useful purposes, its failure on the contrary to have any visible effect on the rate of flow may be attributed to the fact that only about 60 per cent of the volume transfused represents additional fluid as plasma.

SUMMARY

- (1) A short synopsis is given of previous investigation of the capillaries of children and infants in health and disease as seen under the microscope.
- (2) A satisfactory method of examination of the capillaries of infants is described, and also the normal capillary formation and blood flow in these subjects.
- (3) Observations on the abnormal state of the capillary circulation in dehydrated infants are set down in detail, and in addition the effect of the intravenous injection of whole blood and of dextrose solution.
- (3) A discussion follows on the significance of the observations.

Grateful acknowledgment is made to Dr. F.F.Tisdall for his very helpful encouragement and assistance.

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