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Progrès en Ophtalmologie

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Editors:
M. J. Roper-Hall, Birmingham
H. Sautter, Hamburg
E. B. Streiff, Lausanne

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Reviews – Sammelreferate – Analyses

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The Blood Circulation of the Retina and the Uvea[1]

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Contents

1. Introduction

The improvement in methods of investigation and the refinement of experimental technique dealing with retinal and uveal blood circulation, with the closely related problem of fluid and gaseous exchange in ocular tissues, have made it possible today to answer certain questions with data, instead of with the descriptive or qualitative statements that were possible before.

In spite of this satisfactory growth of information the vascular system of the eye still holds a few problems: the significant deviations in the anatomical structure of the uveal and retinal capillaries from capillary

1 Respectfully dedicated to Professor Böck on the occasion of his 70th birthday.

systems of other organs in the body is most certainly related to the specific physiological function of this vascular region, namely the nutrition of avascular ocular tissues i. e. the outer layers of the retina, the vitreous, the lens, and probably a large part of the cornea.

In the following report an attempt will be made to understand the function of the uveal and retinal vascular systems, especially concerning fluid exchange between blood, tissue, and aqueous humour respectively. It should be possible to construct, at least in approximation, a model of the ocular circulation based on the anatomical structure, the determination of perfusion volumes and various other physical and physico-chemical factors which have been verified experimentally in the last few years. This must first demonstrate the possibilities of a balanced fluid exchange in steady state, as Starling's model does for the fluid exchange between capillaries and tissues in most other regions of the body, before the more complicated regulative processes can be investigated successfully.

Apart from the well-known classical experiments, our work was based on research carried out during the last two decades, especially that closely related to our problems. Recently this has been summarised and impressively interpreted by BILL [1970]. To a small extent new results from research in the Bonn Institute of Experimental Ophthalmology have added to the resulting conception of the model [KASKEL, 1970; FINK, 1970].

Several interpretations remain hypothetical. We shall attempt to verify these hypotheses experimentally ourselves in the next few years. However, we hope that other departments of research will bear in mind the possible mode of function of the uveal and retinal circulation formulated here, when discussing their results.

2. Physical and Physico-Chemical Principles

As for all other parts of the body perfusion of the eye with blood is achieved by energy from pressure produced by the pumping action of the heart. The further away the blood stream travels from the left cardiac ventricle, the lower the blood pressure. This is a sign of the energy loss which must take place in every circulatory system with internal forces of friction.

According to Hagen-Poiseuille's law, valid for blood circulation only with certain limitations, the loss of pressure ΔP in a known vessel system,

is directly proportional to the volume of flow V in a unit of time t, and to the resistance of flow R.

$$\triangle P = V_t \cdot R$$

The resistance of flow is determined by the length of the vessel, the viscosity of the fluid involved, and as a reciprocal value by the radius of the vessel. When these factors are taken into account the equation of flow for Newton's fluids is as follows:

$$\triangle P = V_t \cdot \frac{8 \eta l}{\pi r^4} \cdot$$

η = viscosity of fluid
l = length of vessel
r = radius of vessel

Although blood is not a Newton fluid, and although an additional energy loss occurs due to the pulsating flow, the elasticity of the vessel wall, and the vascular ramifications, this law applies approximately to the blood circulation with the exception of the capillary system. (In the latter an additional relationship exists between viscosity and radius.)

It suffices, however, in our case for a qualitative observation: Blood pressure at the point of entry of smaller arteries into the eye (anterior and posterior ciliary arteries, central retinal artery) must be relatively high, because of the short length of the vessels compared with other circulatory sections and because of the short distance from larger arteries of supply, in which the loss of pressure is only slight.

A similar situation is found in the kidney. The high arterial pressure here is due to the brevity of the renal arteries, which originate directly from the descending aorta. This high pressure is necessary, because contrary to the usual tissue circulation two capillary systems (glomeruli and actual renal capillaries) must be perfused.

According to STARLING's hypothesis [1904] for fluid exchange between blood and tissues, the hydrostatic pressure of the fluid and the colloid osmotic pressure of the blood act antagonistically. The hydrostatic pressure exceeds the colloid osmotic pressure in the arterial part of each capillary. This results in leakage of fluid from the vascular system into the surrounding tissues. In the venous part, the suctional forces of the colloid osmotic pressure exceeds the hydrostatic pressure, so that a return

of fluid into the blood stream takes place. Under conditions of steady state the leakage of fluid out of the blood into the tissues equals that returning from the tissues into the blood, so that the pressure in the tissues thus supplied remains constant. Should leakage occur solely within the capillary system, then there would be a point in the middle of each capillary at which the mechanical difference in pressure to tissue pressure exactly equals the colloid osmotic pressure. Here neither leakage out of nor resorption of tissue fluid back into the capillary would occur.

Let us name this point the 'turning point', as it marks the boundary between outflow and inflow of fluid in the capillary system. This turning point cannot be defined anatomically. Its position and the mechanical pressure at this point vary. For example, if the resistance in the area of influx decreases due to dilation of arterioles during muscle action, the turning point shifts in the direction of flow into the previously venous section of the capillary. Here the outflow of fluid surpasses the inflow until a new steady state has been attained, on the basis of the increased tissue pressure. The turning point then moves back to its original anatomical position (fig. 1). The anatomical position of the turning point in most animal and human tissues lies in the venous section of the capillary system, because some removal of tissue fluid occurs via the lymphatic system, so that the outflow from the capillaries must be greater than the inflow. An increase in resistance of flow in the regions of drainage, to which the boundary between tissue and vascular system belongs, also moves the fluid balance in a direction encouraging outflow of fluid from the vessels. Oedema accompaning venous thrombosis or heart failure is known to form in this way. Finally changes in colloid osmotic pressure will also cause a shifting of the turning point: If this pressure increases in the presence of a constant blood pressure, the turning point will move against the direction of flow into the previously arterial capillary section. Tissue pressure will then decrease because of excess return flow into the vascular system, until a new relationship to the blood pressure is attained, which corresponds to the new colloid osmotic pressure. The reverse case – decrease in colloid osmotic pressure – is known to cause the oedema in nephrosis.

In recent years modifications of STARLING's hypothesis have been necessary especially under the influence of electron microscopical research on microcirculation, without a change of its basic validity. BILL [1964a, b, 1968a, b] was able to show, that in the eye the tissue fluid of the ciliary processes and of the choroid contains a high concentration of protein, so

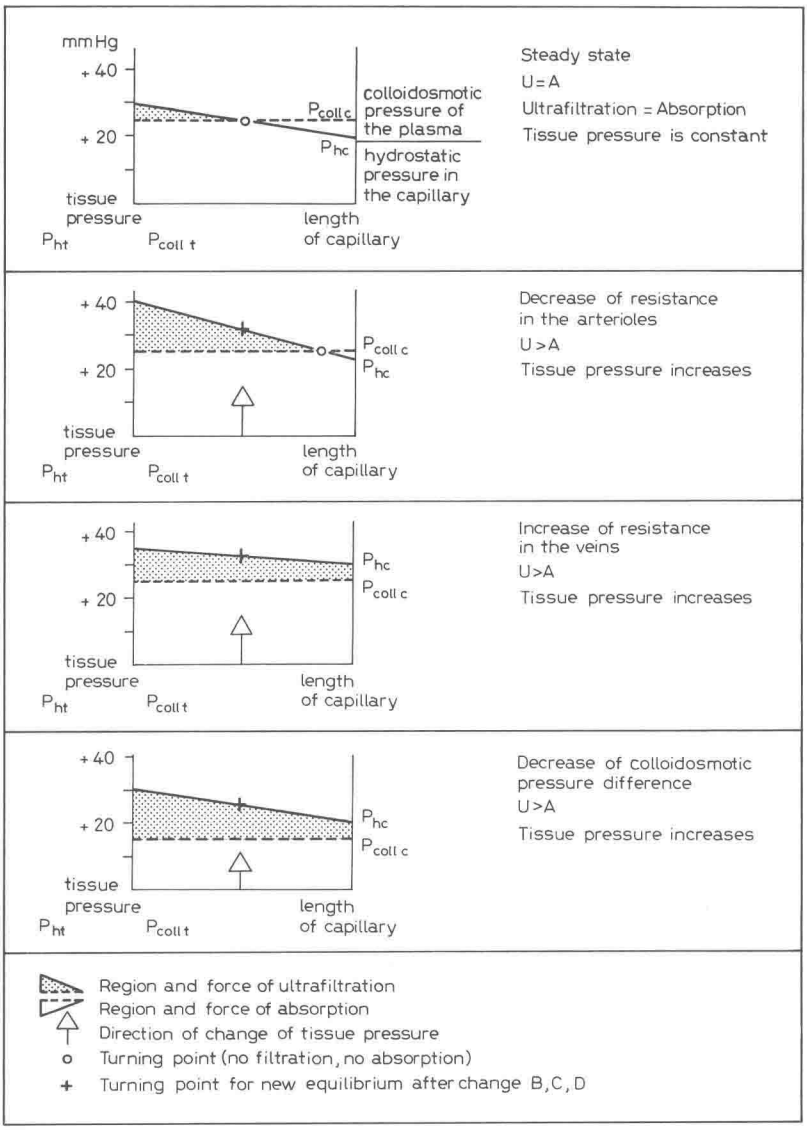

Fig. 1. Starling's model for fluid exchange between blood and tissue. A = Steady state, B = active hyperaemia, C = edema by an obstacle in the venous flow, D = edema by decreased colloid osmotic pressure. Formula for flow [after BILL, 1970]:

$$F = c \times [(P_{hc} - P_{ht}) + (P_{coll\ t} - P_{coll\ c})].$$

that its colloid osmotic pressure is about 50 % that of plasma. On the other hand, the protein concentration of tissue fluid in the iris is very low. This shows that the power of absorption of tissue fluid in the vascular bed by the colloid osmotic pressure of blood plasma should not be regarded as constant, but rather as being variable from tissue to tissue even within a small area. The tendency for protein leakage into tissue fluid is in itself dependent on anatomical characteristics of the capillaries, especially on the number of large pores present in their walls.

It has been known for a long time, that STARLING's hypothesis can be applied to conditions in the eye. KASKEL [1970] and FINK [1970] set up multivariant regressions, and were thus able to show how closely the hydrostatic and colloid osmotic pressures were related to intraocular tension, i. e. the factor which significantly determines tissue pressure in the eye. They have also referred in detail to the literature involved. We mention only the work done by WESSELY [1908], HERTEL [1913, 1915], DUKE-ELDER [1926a, b, 1929], and STARLING and HENDERSON [1904].

3. Choroid

In order to comprehend the mode of action of any technical system, one would first divide it into individual parts, and then attempt an explanation of their separate functions.

We would like to proceed similarly, but attempt to avoid a repetition of well-known facts. To the latter belongs the fact that the choroid has to supply the non-capillarised portion of the retina and the whole retina in some animals and in the human embryo. For this purpose it receives an extremely high blood volume, considering the absolute weight of the tissues involved. In different animal experiments the uveal-retinal system has been found to receive a circulatory blood volume of approximately 10 ml/min/g [LINNÉR 1952; BILL, 1962; TROKEL, 1964; FRIEDMAN *et al.* 1964a]; almost double that of the renal cortex, and 20 times as much as that of the brain (0.56 ml/min/g according to KETY and SMITH, 1948). This value increases considerably for the uvea, when it is isolated from the retina. A higher energy expenditure is required for fluid exchange between the choroid and the avascular section of the retina, than in parts of the body with a capillary system where each cell lies within the proximity of a capillary. The avascular portion of the human retina has a thickness of 130 μm. In animals with an anangiotic or paurangiotic retina even larger

distances have to be bridged. Added to this is the resistance offered by Bruch's membrane and the pigment epithelium. Moreover, an explanation for the extraordinarily high minute volume of this section of the circulation must be found.

The extra energy necessary for the large fluid volume, and the bridging of great distances within the tissue, is supplied with the choroidal circulation in two ways:

(1) That part of the blood circulation in which elsewhere in the body the highest expenditure of energy occurs – namely the arterioles –, is cut down to a minimal remnant, short stumps between the choroidal arteries and the capillaries [ULLERICH and PODESTA, 1957].

(2) The diameter of individual capillaries is approximately 3 times that of the usual.

We have already mentioned that due to their anatomical position, the arteries supplying the eye have a relatively high blood pressure. Blood pressure within the ophthalmic artery between its point of origin and termination was found to be approximately 75 to 85 % that of central pressure, by direct measurements on cats [DUKE-ELDER, 1926c] and by ophthalmodynamometric measurements on man [WEIGELIN and LOBSTEIN, 1963]. BILL [1970] found even higher pressures by direct measurement in the long posterior ciliary artery of the cat, in spite of the more peripheral situation of the area under measurement.

Even more impressive is the situation in the choroid at the transition between the short arteriolar stumps and the capillaries. Due to the practically complete absence of arterioles, which in other circulatory systems expend the main energy, the blood pressure at the beginning of the choroidal capillary system is higher than that at the beginning of normal capillary systems (for instance in muscle, mucous membrane, skin etc.) [DUKE-ELDER and WYBAR, 1961; WEIGELIN, 1957]. One can almost compare it to that which normally exists at the beginning of an arteriolar system. However, one must bear in mind that the slight resistance of flow present until the beginning of the choroidal capillary system, would according to Poiseuille's law lead to a large fluid volume, if no corresponding resistance exists in the capillary and venous drainage areas respectively. But fluid volume is directly proportional to the difference in pressures. We will see later how in spite of this, a high influx pressure into the capillary system must result.

Applying STARLING's hypothesis to the circulation of the choriocapillaris, and ignoring for the time being the influence of the intraocular