The Relation between Secretory and Capillary Pressure. I.—The Salivary Secretion.

By Leonard Hill, F.R.S., and Martin Flack (Eliza Ann Alston Research Scholar).

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Since Ludwig made the discovery that the secretory pressure of a gland may double that of the arterial pressure when the outflow of saliva is obstructed, no one, so far as we know, has investigated the circulatory conditions in the gland under these circumstances. This has been the object of the present research.* Our method is as follows:—We place a cannula in the duct of the submaxillary gland of the cat or dog and prepare the chorda tympani nerve for excitation. A second cannula is placed in the carotid artery of the opposite side of the neck. Each cannula is connected, either with a mercurial manometer or, as in our latest experiments, with two Leonard Hill pocket sphygmometer gauges. This gauge consists of a thick-walled glass tube with a fine capillary lumen closed at one end where the lumen expands into a small air chamber. Half an inch from the open end there is a side hole. On placing this end in a solution of potash a fluid meniscus rises to the side hole, which marks the zero of the instrument. (Potash is used to keep the tube free from grease.) One end of a piece of rubber is slipped over the open end of the gauge so as to cover the side hole, and the other end then connected with the cannula. The pressure of the saliva or blood forces the meniscus up the gauge, which is graduated in millimetres of mercury and acts as a spring manometer. We find these gauges very convenient to use as they can be placed side by side and the readings compared at a glance. Before making the connections with the gauges we expose the veins which course over the submaxillary gland and contribute to the formation of the external jugular vein. Having found the vein which issues from the gland we tie all the other veins, leaving this one free so that at the right moment we can clip the external jugular and open it so as to observe the outflow of blood from the gland. When all is thus prepared we excite the chorda tympani nerve. As soon as the secretory pressure rises above the arterial pressure we open the vein and observe the flow of blood. We find that under

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Table I.

	Salivary pressure.	Arterial pressure.	Venous outflow.
Dog. Morphine, chloroform	140	88	Blood flowing.
„ „ „	190	98	„
„ „ „	164	80	„
„ „ „	157	93	„
Cat. A.C.E.	125	110	„
„ Ether	179	140	„
	160	125	„
	170	125	„
„ „	130	110	„
„ „	160	135	„
„ „	135	110	„
Dog. Morphine, ether	240	130	„

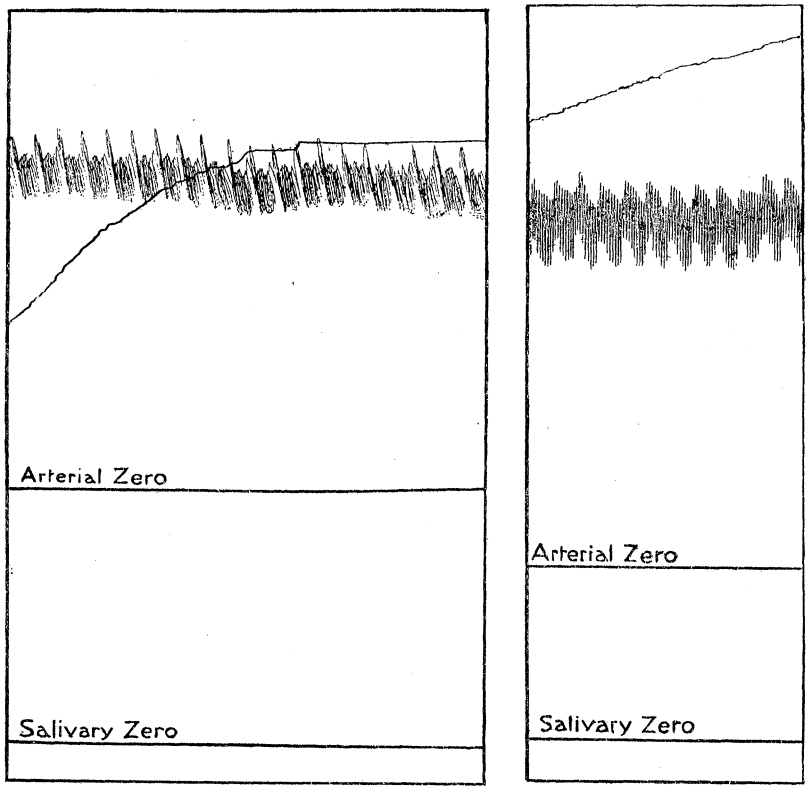

Fig. 1.—Tracings from two different dogs, anæsthetised by morphine and chloroform, showing the arterial (carotid) pressures and the secretory pressures of saliva during excitation of the chorda tympani nerve.

these conditions the blood continues to flow and issues from the vein in a fairly ample stream of a colour more arterial than venous. The gland itself

feels tense to the touch. By squeezing the gland we find that we can further raise the pressure of the secretion, while at the same time we impede the outflow of blood. On allowing the secretory pressure to fall to atmospheric pressure we find that the outflow from the vein becomes much ampler; in one experiment it was approximately doubled, *e.g.* 40 drops in 15 seconds as compared with 27 drops in 20 seconds at the highest secretory pressure (240 mm. Hg.). In some experiments we observed the venous outflow from the time we began to excite the chorda tympani. Under these circumstances we find that the outflow from the gland at rest is very slow and the blood venous in colour. On stimulating the chorda, the outflow becomes very ample, the blood arterial in colour, and remains so during the rise of secretory pressure until this pressure rises higher than the arterial, when the outflow becomes lessened and the blood less arterial in colour.

Our results show clearly that there exists in the salivary gland a structural mechanism which protects the capillaries from the maximum secretory pressure which may exist within the alveoli and ducts of the gland. The gland is of the compound racemose type, and composed of alveoli around which a dense network of capillaries is spun. The alveolar cells, 2–3 μ in diameter, are formed of bioplasm, which probably contains some 80 per cent. of water. The wall of the capillaries is formed of a single layer of exceedingly thin cells, less than 1 μ in thickness. It does not seem possible to us that either the alveolar or the capillary cells can support any difference of fluid pressure. The blood, tissue, lymph and cell protoplasm must all be at one and the same fluid pressure, unless there exists some rigid supporting structure, which surrounds the alveoli and limits their expansion. On seeking for histological evidence, we find that Kölliker* and other histologists describe the alveoli as surrounded by a thin structureless membrane, the membrana propria. This can be easily demonstrated in glands which have been treated with strong potash. The membrana propria is thus shown to be a structureless membrane less than 1 μ thick, and wonderfully strong. Kölliker states that, upon injecting the ducts of the glands under high pressures, the secretory cells may be destroyed or separated from the membrana propria, but that this membrane seldom becomes torn. Before this happens, extravasations will take place through the walls of the ductules. We ourselves have seen such extravasations in glands which have been kept secreting for a considerable time at a high pressure. The so-called basket cells also surround the gland cells, there anastomosing by their branches to form a kind of protoplasmic framework, which contains the secreting cells. It has been suggested that the basket

* Kölliker, 'Handb. der Gewebelehre des Menschen,' Leipzig, 1899, vol. 3, p. 46.

cells are contractile. The membrana propria clearly acts to the secreting cells as does the sarcolemma to the muscle fibre. The cells stimulated to secretory activity imbibe water from the capillaries and extrude the salivary secretion into the ductules at a pressure which may double that of the arterial pressure. Meanwhile the capillaries are protected from occlusion by the membranæ propriæ of the alveoli, which, acting like the leather case of a football or the pericardium of the heart, limit the expansion of the alveolar cells. When the secretion is obstructed, the whole gland becomes tense, the veins are diminished in volume, the circulatory pressure in them is raised until the vessels, arteries, capillaries, and veins approximate to a rigid system at arterial pressure, with a fast rate of flow. As the alveoli swell, this favourable condition of the circulation is at first established; finally, however, the vessels may be so far narrowed that the flow becomes lessened, but not stopped, owing to the restraining action of the membranæ propriæ. It seems to us probable that the slackening of the circulation may be due to the leakage of saliva into the intra-alveolar connective tissue. If we cease to excite the chorda, the secretory pressure drops slowly, owing to such leakage. The basket cells may possibly, by their contractile power, help to squeeze the saliva into the ducts. We have no evidence to offer as to such a function. No doubt the membranæ propriæ may be supported by the strands of connective tissue which surround and knit together the alveoli.

We believe that we are here dealing with a fundamental principle in the construction of many parts of the body. The cells in the secreting glands are enclosed on one side by a cuticular membrane which permits their imbibition of fluid but checks their power to swell, thus enabling them to do work and at the same time receive an ample supply of blood. The mechanism reminds us of Pfeiffer's semi-permeable membrane, with this difference, that the living membrane can vary its permeability. The muscle fibres are enclosed by a sarcolemma, the nerve-fibres by a neurilemma, the secreting alveoli by a membrana propria. In each case the membrane may limit the swelling of the protoplasmic content, and so permit a high imbibition pressure within. Turning to the kidney, we find a similar membrana propria enclosing the secreting cells, both of the capsules and of the tubules. The secretory pressure in the obstructed ureter, however, does not rise so high as the arterial pressure. Starling gives the following readings :—*

* Starling, 'The Fluids of the Body,' 1909, p. 110. Constable, London.

Carotid artery.	Obstructed ureter.
mm. Hg.	mm. Hg.
140	72
138	92
133	88

The structural mechanisms visible in the kidney seem to us altogether opposed to the doctrine that fluid is filtered from the blood into the capsule by the force of the blood-pressure. There are membranæ propriæ which confine the tubules, but no rigid structures which can sustain the capillary wall and convert it into a membrane capable of sustaining a difference of hydrostatic pressure. The glomerulus is a lobulated structure the lobules of which hang in the capsule, just as the ciliary processes hang in a bath of aqueous within the posterior chamber of the eye. We believe that the passage of fluids is determined in both cases by a secretory force acting from the cells which line the vascular processes. The pressure of the fluid within the capsule and of the blood within the glomerular vessels must be the same. In the case of the brain the choroidal fringes secrete the cerebro-spinal fluid; the venous pressure and that of this fluid correspond and are always one and the same. The pressure of the brain against the wall of the skull is also the same; the slightest increase of pressure exerted on the brain squeezes the blood out of the capillaries. If the pressure be made to rise in the cerebral veins, that of the cerebro-spinal fluid rises to the same extent. Suppose fluid be injected, or in some inflammatory state cerebro-spinal fluid be secreted at a higher pressure, then the venous pressure rises concomitantly, since the veins are narrowed by the injected or secreted fluid. We shall show in a subsequent paper that in the eye the same conditions hold good. The ciliary processes are held to secrete the aqueous, and the circulatory pressure in the veins within the eyeball is adjusted to the secretory pressure of the aqueous. The aqueous takes up so much of the total volume and the veins are narrowed to such an extent that the intra-ocular pressure is raised to a considerable figure, some 30–40 mm. Hg. The pressure, both intra-ocular and intra-cranial, depends on the circulation, and ceases with the circulation, but its height is regulated by the secretory action of the cells. In the eye and brain we have the delicate secreting fringes lying in a bath of the secreted fluid, and there exists no supporting structure which can bear off any part of the pressure. We cannot imagine that the fringes are held open as it were by wire springs. The pressure of the secretion outside and of the blood within the capillaries and veins must be

the same. In the case of the brain, the cerebro-spinal pressure, the cerebro-capillary pressure, and the cerebro-venous pressure are one and the same, a fundamental fact which has been proved.* In the secreting glands, confined by a capsule, the same conditions must hold good. The capillary, venous, and tissue fluid pressures must be the same, adjusted one to the other, excepting where, as in the salivary gland, membranæ propriæ are drawn taut by the height of the secretory pressure when the duct is obstructed. In the case of the salivary gland, the capacity to produce so high a pressure may be correlated with the need which arises, under certain circumstances, for a very rapid secretion of saliva, *e.g.* to wash out an irritant. The same high secretory pressure is produced by the sweat glands. A rapid secretion of sweat may be required to prevent heatstroke. Here, again, the membranæ propriæ play the same part as in the salivary glands, the secretory force possibly being increased by the layer outside the secreting cells, which is supposed to be contractile. Both the flow of sweat and of saliva may be temporarily obstructed by pressure applied to the ducts.

In the case of the kidneys a lower secretory pressure suffices. The pelvis and the bladder act as reservoirs, the abdominal wall and the diaphragm regulate the intra-abdominal pressure. The whole kidney, just as the salivary gland, is confined by a capsule which allows a certain expansion and no more. Within the capsule, from time to time, there may be more blood and less kidney substance (including tissue, fluid and secretion), or more kidney substance and less blood. Suppose the arterioles of the kidney dilate, the volume of the blood increases and the whole kidney expands. Suppose, moreover, the renal tubules are inactive, not swollen, and the membranæ propriæ are slackened, then there will be within the capsule less kidney substance and more blood. The whole kidney substance will be at the lowest fluid pressure, namely, that of the veins. The same holds good for the salivary gland. Suppose, on the other hand, the tubules are swollen, actively secreting, with the membranæ propriæ expanded, there will be less room within the capsule for blood, the veins will be narrowed, the renal venous-capillary pressure raised, the vascular system approximated to a rigid system, the velocity of the flow increased. The whole kidney will still be at the lowest fluid pressure, viz. that in the veins, but now it will feel tense, for the venous-capillary pressure, under these conditions, is so much higher. It is clear that the salivary or renal cells, swollen and in an active state of secretion, not only produce a secretory pressure in the tubules, but by narrowing the veins influence the height of the blood pressure within and the rate of blood flow through the capillaries and

* Leonard Hill, 'The Cerebral Circulation,' 1896. J. and A. Churchill, London.

veins. The quality of the blood influences the secretory activity; this, in its turn, influences the blood flow within the kidney. When the ureter is obstructed and the kidney secretes against pressure, the tubules must swell until the membranæ propriæ are drawn taut. In the case of the salivary gland, the swelling of the alveoli is limited by the membranæ propriæ, so that the blood-vessels remain patent in spite of the higher secretory pressure. In the kidney, however, the secretion ceases before the secretory pressure rises to the arterial pressure. Our next point of enquiry must be to determine whether the cells of the tubules are able to swell to such an extent as to impede the circulation. Further experiments will show us what happens to the flow in the renal vein at the moment when the secretory pressure of the urine reaches its highest point.

In states of inflammation, as their osmotic pressure increases, the poisoned tissues swell, the arteries dilate, the blood-pressure rises as the swollen tissues press upon and narrow the veins. The vessels approximate to a rigid system, hence the high tension and the pulsatile throb of the inflamed part. As the tissue pressure rises in the part, so does the circulatory pressure, since the tension depends on the arterial pressure; its height, however, being regulated by the metabolism of the tissues and their imbibition pressure. Finally, stasis is produced in the swollen tissues. The surgeon's knife by cutting, or the hot fomentation by softening, relieve the tension and allow an ample flow of blood to and the escape of immunising plasma in the part. It is a question here whether stasis results from inflammatory changes in the blood or from strangulation of the circulation by the increased imbibition and swelling of the tissues. The tissue cells in the skin are confined by strong frameworks of connective tissue, which limit expansion and act in a similar manner as does the capsule to a gland, the sclerotic to the eye, or the skull wall to the brain.

Summary.

(1) When the pressure of the salivary secretion is raised above the arterial pressure the venous flow of blood from the gland continues.

(2) Under these conditions the gland feels very tense; by squeezing it the secretory pressure is raised but the flow of blood from the vein is stopped.

(3) The view is advanced that the membranæ propriæ (aided possibly by the strands of connective tissue which surround the alveoli) limit the expansion of the alveoli and thus protect the circulation from strangulation by the high secretory pressure. It is suggested that limiting membranes in other parts of the body, *e.g.* the kidney, have a similar function.

(4) By the expansion of the alveoli up to the limitation point set by the

membranæ propriæ the veins are so far narrowed as to raise the pressure in the capillaries and veins; this, coupled with the dilatation of the arteries, gives a greatly increased rate of blood flow. The circulatory conditions which pertain in these encapsulated glands resemble those which pertain in the brain and the skull cavity.

The Effects of Ultra-violet Rays upon the Eye.

(Report of experiments carried out for the Glassworkers' Cataract Committee of the Royal Society.)

By Dr. E. K. Martin.

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(From the Research Laboratories, University College Hospital Medical School.)

[Plates 4—7.]

In 1909 Messrs. J. Herbert Parsons and E. E. Henderson commenced some experiments on the action of short wave-length light on the lens and ciliary body, using Uviol glass mercury-vapour tubes and examining the lens and its capsule after exposure. To test for damage to the ciliary body too slight to be appreciable microscopically use was made of an observation of Römer's, that in animals sensitised to the blood of another species, hæmolysins were not transmitted from the blood to the aqueous unless the constitution of the latter were altered by a previous paracentesis or an inflammatory lesion of the iris and ciliary body. Positive results were obtained, but the experiments were not sufficiently extensive to be conclusive. I have, therefore, on behalf of the Committee of the Royal Society on Glassworkers' Cataract, repeated and extended the experiments along lines suggested by Mr. Parsons.

In the attempt to determine the effect of rays of various wave-lengths on the media of the eye, attention has been paid to three possible ætiological factors:—(1) The intensity of the light. (2) The part of the spectrum mainly represented in the source of light. (3) The possibility of the inclusion of electrolytic and mechanical as well as of radiant energy.

1. *Intensity.*—It has been customary among investigators of the subject to express the intensity roughly by naming the source of light, the quantity of energy (usually electrical) consumed in its production, and the distance of