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From the Practitioner 1884. XXXII.

# ON THE ACTION AND USE OF DIURETICS.

BY T. LAUDER BRUNTON, M.D., F.R.S.

THE part which water plays in the animal body is a very important one. Not merely does it form by far the greatest part of the body itself, constituting no less than 59 per cent. of its weight, but the life of all the tissues is essentially dependent on its presence in them. Without water no vital function can go on. In the dry climate of Egypt wheat has been preserved unchanged since the days of the Pharaohs, without the slightest tendency to growth having occurred until it was moistened ; and when rotifer animalculæ are dried up they will fly about as dust devoid of any appearance of life, until they are again put into the water. In the complicated organisms of the human body the same thing occurs, though to a much less extent. We cannot have any one of the tissues completely desiccated, otherwise it would, like the rotifer, lose all its vital functions, but, unlike it, would not regain them when a fresh supply of water was brought to it. Diminution of water, however, may be endured by the tissues without injury, but diminution will diminish tissue change in them, while increase of water will augment it. When much water is drunk, as certain experiments have shown, the tissue change is increased to such an extent that the body must rapidly waste, and the necessity for more food to supply them is indicated by the ravenous appetite which is induced, as well as by the loss of body weight which occurs when the appetite is not gratified. While water not only increases tissue change, it removes the waste products produced more rapidly than usual, and, indeed, the effect of water-drinking upon the body, in increasing tissue change and removing the waste products, may be compared to raking out the ashes from a fire, and at the same time making it burn more brightly. All the water drunk must find its way out of the body again by one channel or another. Some of it passes off through the lungs, and a little by the bowels, but the greater proportion passes through the skin and kidneys. The action of these is compensatory.

It is difficult to estimate precisely how much is excreted by the skin, but probably it may be taken at about two-thirds of the quantity eliminated by the kidneys. When the skin is active the kidneys have, consequently, less work to do, and when the secretion from the skin is sluggish, the kidneys must secrete all the more. Some years ago, while making experiments upon the urinary secretion, I found that on the sudden occurrence of a cold day after a succession of warm ones, the amount of urine secreted was very nearly doubled. One reason of this compensatory function of the skin and kidneys probably is that the secretion in both, like the secretion in other glands, depends to a great extent on the supply of blood going to them. When the supply of blood is greater, the secretion is also increased. On a warm day, or when the body is exposed to external warmth, the vessels of the skin dilate, and the cutaneous glands are freely supplied with blood. The application of cold to the surface of the body, on the contrary, causes the cutaneous vessels to contract, and thus more blood is driven to the internal organs—the kidney amongst the rest.

The utility of this arrangement is obvious, for although the skin has an excreting function complementary to that of the kidneys, its chief function is that of regulating the temperature of the body. When the temperature rises either in consequence of active muscular exercise or from any other cause, the vessels of the skin dilate, and if the temperature of the external air be lower than that of the body, heat is lost by radiation. The blood returns cooled from the cutaneous capillaries to the internal organs, and thus the temperature is again brought down to the normal. But even when the temperature of the external air, instead of being lower, is higher than that of the body, the skin still acts as a cooling apparatus by means of the evaporation of sweat. The quantity of heat which is changed into potential energy in the process of converting liquid water into gaseous steam is very great. Five and a half times as much heat are required to convert boiling water into steam as to raise the same amount of water from the freezing to the boiling point. The immense loss of heat occasioned by the evaporation of the perspiration is so great that in negroes on the west coast of Africa it has been noticed that the skin, while perspiring profusely, is as cold as marble, and Sir Charles Blagdon observed that in a room with a temperature of 128° F. his side felt quite cold to the touch. The skin cooled by perspiration therefore acts even with a high external temperature as a refrigerating apparatus to the blood, and prevents the temperature of the body from rising too high. When the external temperature is low the vessels of the skin contract so that little blood circulates through them, and loss of heat by conduction or radiation or by perspiration is, to a great extent, prevented. It is evident that on a hot, dry day, with active exertion the loss of water by the skin must be considerable, and sometimes work must be done with but a limited supply of water to drink. At the same time the products of waste must be removed, and under such circumstances, although the skin excretes a very large quantity of water, it excretes but a small quantity of solids. The kidneys are thus put to a great disadvantage. They have still to excrete the solids: they can only do so when these solids are in a state of solution, and yet if they excrete the usual amount of water while more than usual is being thrown off from the skin, and, perhaps, less than usual is being drunk, the proper proportion of water in the body will rapidly be reduced below the normal, and its functions seriously disturbed. In order to prevent this there seems to be an arrangement in the kidney whereby water is retained after it has served its purpose of washing the solids so far through the kidneys that they can be afterwards eliminated without it. The products of tissue waste must be removed in a state of solution from the part of the kidney where they are excreted, and yet sometimes provision must be made for the water by which they are washed out being retained in the body. The urine in mammals and amphibia is liquid; in birds and reptiles it is semi-fluid or solid, yet the solid constituents are removed in solution from the urinary tubules, and the water in which they are dissolved is afterwards absorbed. In cold weather, on the other hand, the vessels of the skin are contracted, there is little or no perspiration and yet it may so happen that the individual is obliged to live on food containing a large proportion of water. This difficulty must also be met, and so in the kidney we have a provision for the removal of water without solids.

We may say then that the kidney has a threefold function :— 1st, that of excretion of waste products; 2ndly, a provision for the removal of excessive water; and 3rdly, an arrangement for the retention of water in the body by its re-absorption, after it has washed out the waste products. On looking at the kidney we find three structures which seem to be connected with these three functions, viz: (1) convoluted tubules with epithelial cells, which in all probability are the chief structures for excreting waste products; (2) the malpighian corpuscles for excreting water along with some solids; and (3) usually one or more constrictions in the tubule which may serve the purpose of preventing too rapid exit of the water, and thus allow time for its re-absorption in cases where its retention is desirable, as for example on a hot day and when the supply of drinking-water is very limited.

The process of secretion in the kidney was regarded by Bowman as consisting of the filtration of water from the vessels of the glomeruli into the tubule, and the excretion of waste products by the epithelium lining the tubule. Ludwig, however, came to look upon it rather as a process of filtration and re-absorption; a dilute solution of urea and salt being according to him poured out from the malpighian corpuscles and gradually concentrated by the absorption of water in its passage along the tubules. This theory had so many facts in its favour that it was for a good while exclusively adopted, but latterly Heidenhain in an admirable series of experiments has shown that substances like indigo are certainly excreted by the epithelium of the tubules. At the same time Hüfner has shown by a comparison of the structure of the kidney in fishes, frogs, tortoises, birds, and mammals, that the form of the tubules closely agrees with that required for the re-absorption of water in each case. Fishes have a low blood-pressure, and so the resistance in the kidney requires to be small in order to allow of the secretion of urine. Living as they do in water, they do not require any apparatus for its retention in the body. In them therefore the tubule is short and wide, and destitute of any constriction which would retard the outflow of fluid. In frogs there must be ample provision for the retention of water in the body, as evaporation takes place freely from their skin. In them we find, as we might expect, that the tubule, and


IG. 1.—Diagram showing the form of the urinary tubules in different classes of animals, after Hüfner. 1. Fish. 2. Frog. 3. Tortoise. 4. Bird. 5. Mammal. The letters have the same significance in each. *a*. Capsule of the glomerulus. *b*. Convoluted tubule. *c*. Loop. *d*. Collecting tube. *u* in 2 indicates the transverse section of the ureter.

especially the contracted part of it, is very long. In tortoises no evaporation from the skin can take place, and in them the contracted part of the tubule is short. This renders it probable that, while the ideas advanced by Bowman and supported by Heidenhain are in the main true, the re-absorption of water on which Ludwig lays so much stress is also an important facter in the secretion of urine under different circumstances.

But it is not only rendered probable by the facts of comparative anatomy; it appears to be proved by direct experiment.

Ribbert[1] has extirpated the medullary substance of the kidney in the rabbit while leaving the cortical substance. He has thus succeeded in collecting the urine as it is excreted by the malpighian corpuscles before it has passed through Henle's loops, and has found that the urine secreted by the cortical substance alone is much more watery than that which is secreted by the entire kidney, a fact which appears conclusively to prove that water is actually re-absorbed, and the urine rendered more concentrated, during its passage through the tubules in the medullary substance.

In the frog and triton the arrangement of the kidney is such as to allow of a much more complete investigation of the different factors in secretion than in mammals, because in amphibia the glomeruli which separate the water and the tubules which excrete the solids receive their blood supply to a great extent independently. The glomeruli are supplied by branches of the renal artery. The tubules are supplied by a vein which proceeds from the posterior extremities and entering the kidney, breaks up into a capillary plexus bearing a somewhat similar relation to the renal tubules, to that which the portal vein bears to the lobules of the liver. It is therefore called the portal vein of the kidney.

The arterial circulation in the glomeruli and the venous portal circulation round the tubules are, however, not entirely distinct, for the efferent arteries of the glomeruli unite with the portal capillaries, and, moreover, arterial twigs also pass directly from the renal artery into the capillary venous plexus. The two systems are, however, so far distinct that Nussbaum has been able to ascertain with considerable exactitude the part played by each in secretion. By ligaturing the renal artery he destroyed the functional activity of the glomeruli, and by ligaturing the portal vein of the kidney he destroyed that of the tubules. By injecting a substance into the circulation after ligature either of the artery or the vein, and observing whether it is excreted or not, he determines whether it is excreted by the glomeruli or the tubules. In this way he finds that sugar, peptones, and albumen pass out through the glomeruli exclusively, for they are not excreted when the renal arteries are tied. Albumen, however, only passes out through the glomeruli when an

[1] Ribbert, *Virchow's Archiv*, July 1883, p. 189.

abnormal change has already occurred in the vascular wall; as, for example, after the circulation has been arrested for a while by ligature of the renal artery. Indigo-carmine, when injected

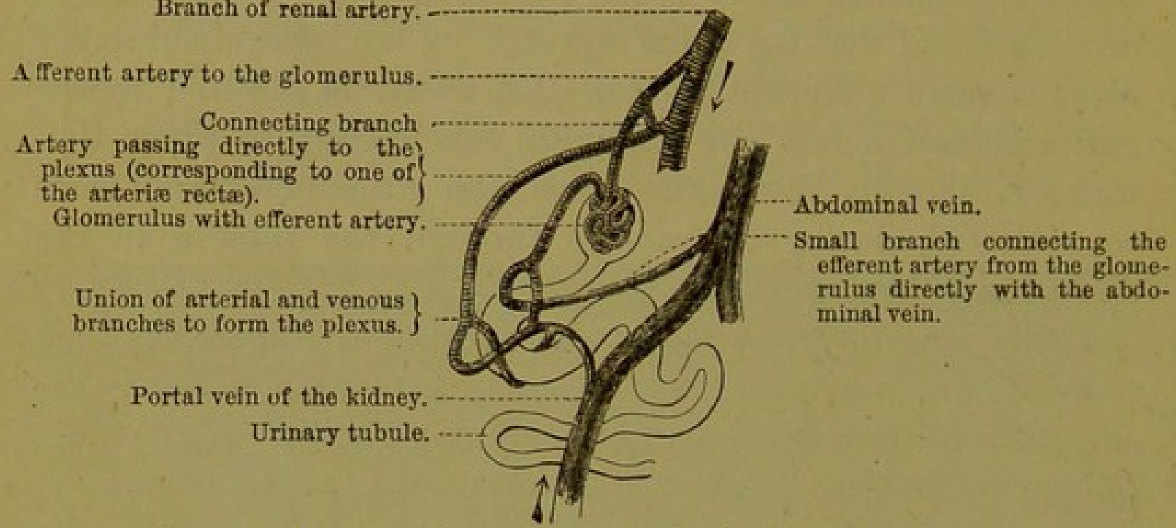


FIG. 2.—Diagram of the circulation in the kidney of the newt. Modified from Nussbaum.

after ligature of the renal arteries, passes into the epithelium of the tubules, but it does not give rise to any secretion of water, so that the bladder is found empty. Urea, on the contrary, is not only excreted by the tubules after ligature of the renal

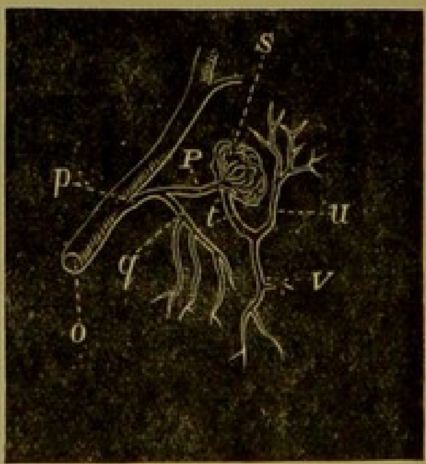


FIG. 3.—Diagrammatic sketch of the blood-vessels in a mammalian kidney. From Schweigger-Seidel, *Die Nieren*, Halle, 1865. *o* is an artery ascending into the cortical substance of the kidney. *p* is a branch from it which divides into two branches, *q* and *P*. *q* breaks up at once into a number of twigs. *P* is the afferent artery to a glomerulus (*s*) of the lowest row. *t* is the afferent vessel of the glomerulus; it divides into two branches, one of which (*u*) ascends towards the cortex, whilst the other (*v*) descends towards the medulla.

artery, but carries with it, in the process of secretion, from the venous plexus a considerable quantity of water, so that the bladder becomes partially filled.

The excretion of water, therefore, takes place in a double manner: it passes out through the glomeruli when the renal arteries are free, and it passes out from the venous plexus along with urea, even although the renal arteries are tied.

In the kidneys of the higher animals and of man the glomeruli and the tubules do not receive blood from two entirely different sources, but there is an arrangement somewhat similar; for the plexus surrounding the tubules does not receive blood only from the efferent vessels of the malpighian corpuscles, but gets it also directly from the renal arteries. There are three channels by which the blood may pass from the renal arteries into the venous plexus without going through the glomeruli. The first is the inosculation which takes place between the terminal twigs of the renal artery and the venous plexus on the surface of the kidney directly under the capsule. The second channel is formed by small branches given off directly by the interlobular arteries or by the afferent arteries before they reach the glomeruli.[1] The former of these may be regarded as corresponding to the artery which passes directly to the plexus in the newt, and the latter to the branch connecting it with the afferent artery (Fig. 3). These arterial twigs are found not only near the surface of the kidney, but also in the deeper layers of the cortical substance.[2] The third and most important channel is afforded by the arteriæ rectæ, which spring from the branches of the renal artery at the boundary between the cortical and medullary substance and pass into the medulla, where they form a plexus with elongated meshes surrounding Henle's loops and the collecting tubules. Near their origin the arteriæ rectæ inosculate with the venous plexus surrounding the convoluted tubules.

Through these three channels it is possible for blood to reach the secreting structures of the kidney and there get rid of urea, salts, &c., without losing water by its passage through the glomeruli. On the other hand, if these vessels contract, while the size of the renal artery and the pressure of the blood within it remain unaltered, more blood will be forced into the malpighian

[1] Ludwig, *Handwörterbuch d. Physiol.* v. R. Wagner, Bd. 2.

[2] Schweigger-Seidel, *Die Nieren*, p. 67; Heidenhain, *Hermann's Handbuch d. Physiologie*, vol. v. Th. I. p. 293.

corpuscles, and thus the quantity of water excreted will be increased. At the same time the contraction of the arteriæ

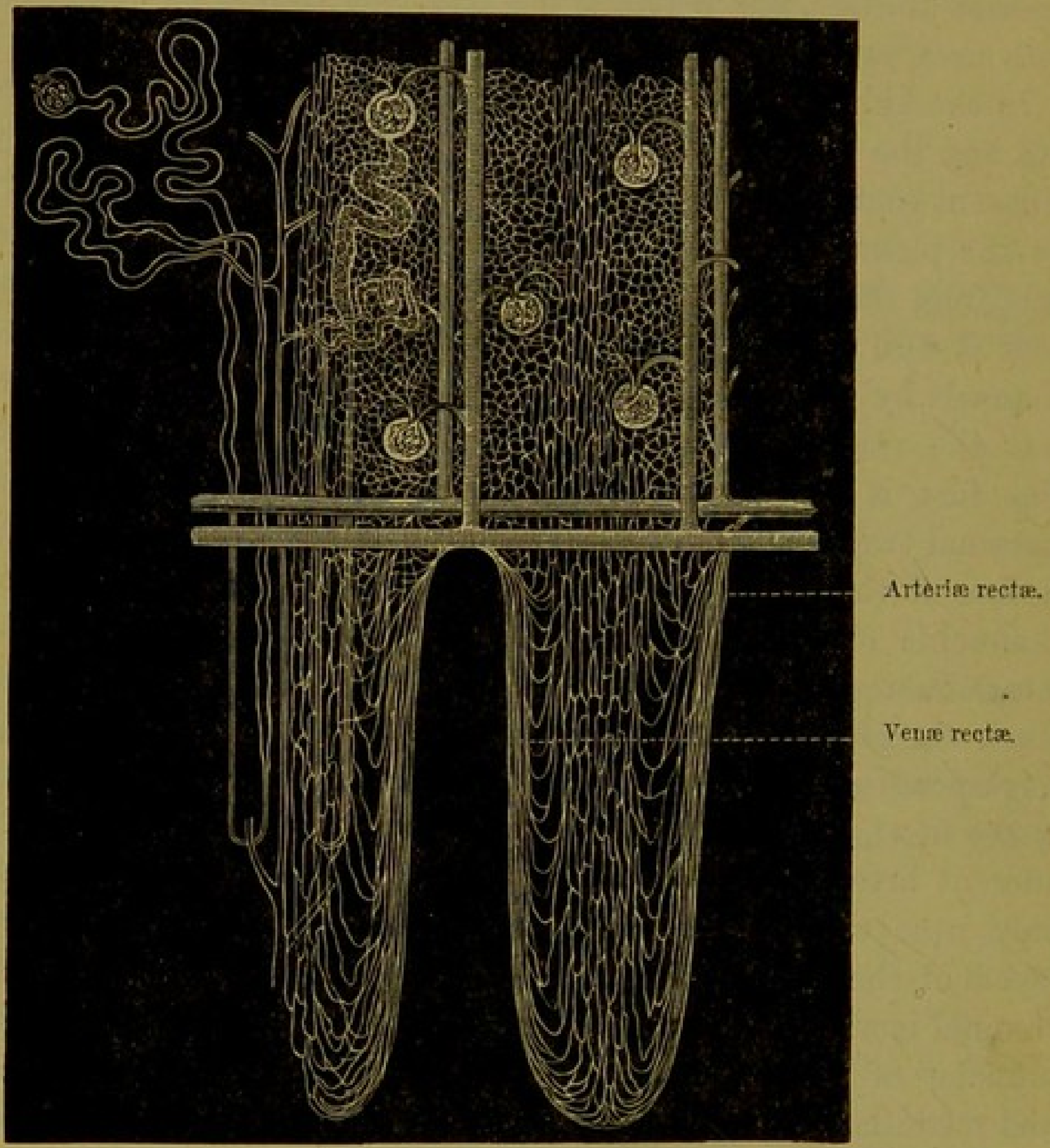


Fig. 4.—Diagram of the tubules and vascular supply of the kidney. On the left is a tubule alone, in the middle is a tubule along with the blood vessels, on the right are blood vessels only.

rectæ will probably diminish absorption from the tubules, and thus the quantity of water excreted will be increased in a two-fold manner.

*(To be continued.)*

# ON THE ACTION AND USE OF DIURETICS.

BY T. LAUDER BRUNTON, M.D., F.R.S.

(*Continued from* p. 282.)

*Circumstances modifying the Secretion of Urine.*—The experiments of Ludwig and his pupils have shown that the amount of urine secreted depends very closely upon the pressure of blood in the malpighian corpuscles, or, to put it more exactly, on the difference of pressure between the blood in these corpuscles and the pressure within the tubules. For if the ureter be tied so that the pressure of urine in the tubules is increased, the secretion is greatly diminished, and even arrested, even though the pressure of blood in the renal artery be high.

A somewhat similar effect to that of ligature of the ureter is produced by ligature of the renal vein, for the blood accumulating in the venous plexus surrounding the tubules compresses them so as to prevent the flow of urine through them. A similar condition may occur from cardiac or pulmonary disease obstructing the venous circulation.

But unless in exceptional circumstances which alter the pressure within the tubules, such as compression of the tubules by congestion of the venous plexus, as in cardiac disease, impaction of a calculus in the ureter, or pressure on the ureters by dropsical accumulations or tumours, the rapidity of the secretion of urine depends on two factors:—(1) arterial pressure in the glomeruli; and (2) the composition of the blood.

The pressure of blood in the glomeruli may be raised—

(1) by increase of the arterial tension generally,

(2) by increased tension locally.

Thus the effect of cold wind and cold baths is probably due chiefly to their power of contracting the vessels in other parts of the body, and thus driving more blood into the renal artery, and increasing the pressure in the glomeruli. In some pathological conditions also we find the blood pressure high, and the secretion of urine abundant. This occurs, as a general rule, in persons suffering from cirrhotic or contracting kidney, in whom the pulse is generally tense, and the blood pressure high, although in these cases also the high blood pressure is probably not the only factor in the increased secretion.

Such a general increase may be brought about by greater action of the heart, or by contraction of the blood vessels in other vascular areas, such as the intestines, muscles, or skin, by nervous stimulation, exposure to cold, or the action of drugs.

The pressure may be increased locally by dilatation of the renal arteries, *e.g.* from section of the vaso-motor nerves, or possibly stimulation of vaso-dilating nerves.

In addition to such increase of pressure in the glomeruli by increase of blood supply to them, we must not, however, forget the possibility of increased pressure in them by contraction of the efferent vessels leading from them, as well as of those arterial twigs (arteriæ rectæ) which pass directly to the venous plexus surrounding the tubules, and which form no inconsiderable part of the vascular supply of the kidney.

Alteration in the size of the renal vessels were formerly ascertained simply by exposing the kidney and observing its colour, contraction of the arteries being associated with paleness, and dilatation with redness of the organ. A much more exact method has been introduced by Roy, who incloses the kidney in a capsule filled with oil and connected with a registering apparatus. When the vessels dilate, the kidney increases in size, and diminishes when it contracts, so that the alterations can be readily recorded on the same revolving cylinder on which the general blood pressure is registered by the manometer.

The pressure of blood in the glomeruli may be diminished generally—

(1) by failure of the heart's action, or

(2) by dilatation of vessels in larger areas, as the intestines, muscles, and skin.

The pressure of blood in the glomeruli may be diminished locally by contraction of the renal arteries, or of the afferent branches to the glomeruli.

The heart's action may fail from many causes, which have already been discussed more particularly.

Dilatation of the vessels in the skin, intestines, &c., may be caused by exposure to warmth, by the action of drugs, or by paralysis due to nervous injury.

Section of the splanchnics or of the spinal cord causes paralysis of the renal arteries, and ought, therefore, to increase the secretion of urine. This does occur, though not invariably, when the splanchnics are divided; but section of the spinal cord, by paralysing the intestinal and other vessels, lowers the blood pressure so much that the supply of blood to the kidney is not only much below the normal, but is so small that the secretion of urine is generally almost completely arrested.

The nerves of the kidney consist of a number of small branches running along the renal artery and containing a number of ganglia. When these nerves are cut the vessels of the kidney dilate; when they are stimulated the vessels contract. A number of these fibres pass to the kidney from the spinal cord through the splanchnics, so that when the splanchnics are cut the vessels of the kidney usually dilate, and when they are irritated, they contract.

The whole of the nerves, however, do not pass through the splanchnics, for stimulation of a sensory nerve, of the medulla oblongata, or of the spinal cord in the neck will cause contraction of the renal vessels after both splanchnics have been cut, and section of the splanchnics does not always cause the renal vessels to dilate.

The nervous centre for the renal arteries is probably, like the chief vaso-motor centre for the body generally, in the medulla oblongata; but in all probability there are also subsidiary centres in the spinal cord and in the solar and mesenteric plexuses.

The reason for supposing these latter centres to exist is, that stimulation of the peripheral end of the splanchnic, divided at its passage through the diaphragm, causes contraction of both kidneys, and the vessels of the kidney of the side opposite to the stimulated nerve commence to contract later than that on the same side. A delay like this in the action of the stimulus means that it has not acted directly, but through the medium of ganglia.

When the splanchnics are divided, the vessels of the kidney sometimes dilate and the kidney increases in size; a profuse secretion of urine may take place, which quickly increases to a maximum and remains for a considerable time. This, however, is not a constant effect, and not infrequently the vessels do not dilate, and the kidney, instead of increasing, diminishes in size. This is what to a certain extent might be expected, inasmuch as a section of the splanchnics causes dilatation of the intestinal vessels and lowers the blood pressure, and thus diminishes the supply of blood to the kidney.

When a puncture is made in the medulla oblongata in the floor of the fourth ventricle, profuse secretion also occurs, but this differs from that caused by section of the splanchnics, in being preceded by slight diminution, in rising rapidly to a maximum, and then rapidly falling. These characters seem to show that it is due to irritation of some vaso-dilating mechanism [1] rather than to any paralysis.

Stimulation of the vaso-motor centre in the medulla oblongata by venous blood, or by drugs such as strychnine or digitalis has a twofold action on the kidney, for it tends to cause contraction not only in the vessels of the kidney, but in those of other parts of the body. The effect on the kidney is thus a complicated one, for the contraction of the intestinal and other vessels by raising the blood pressure tends to drive blood into the kidneys at the same time that the contraction of the renal arteries tends to keep it out. When the renal nerves are cut, the renal vessels no longer oppose the entrance of blood, and therefore the renal vessels dilate very greatly when the vaso-motor centre is stimulated; but when the renal nerves are intact the result is a varying one, for sometimes contraction of the renal vessels may be so great as to prevent the entrance of blood into the kidney, however high the general blood pressure may rise; at other times the general high blood pressure may be able to dilate the renal arteries in spite of any resistance they

[1] Heidenhain, *Hermann's Handbuch d. Physiologie*, vol. v. Th. 1, p. 366.

may offer. These different conditions may occur subsequently to one another; and this stimulation of the vaso-motor centre may cause contraction of the renal vessels succeeded by dilatation, or *vice versâ*. Thus Mr. Power and I found that on injecting digitalis into the circulation of a dog the blood pressure rose, but the secretion of urine was either greatly diminished or ceased altogether. Here it is evident that the renal vessels had contracted so much as to prevent the circulation through the kidney, notwithstanding the rise which had taken place in the blood pressure. After a while the blood pressure began to fall, and then the secretion of urine rose much above its normal, showing that the general blood pressure was then able again to drive the blood into the kidneys.[1]

Similar observations were made by Mr. Pye and myself with regard to erythrophleum, and the accompanying curves show

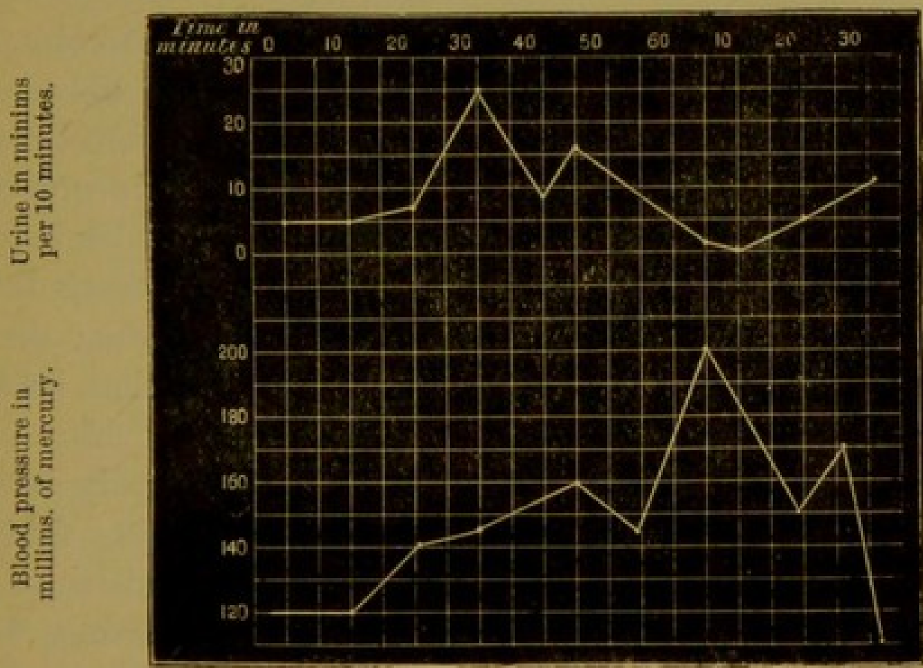


FIG 5.—Curves showing the effect of erythrophleum upon the blood pressure and secretion of urine. From *Phil. Trans.* vol. 167.

well the result upon the urine of the mutual action of the rise in blood pressure and the contraction of the renal arteries upon the secretion of urine. It will be noticed that at first the blood pressure rises more quickly than the secretion of urine, the circulation through the kidney appearing to be opposed by the renal arteries. This opposition is then overcome, and the

[1] *Royal Society's Proceedings*, No. 153, 1874.

secretion of the urine rises more quickly than the general blood pressure. The renal vessels again appear to contract, so that the urine diminishes while the blood pressure rises still further. We have then oscillations due first to one factor and then to the other being predominant; and then, when the blood pressure rises to its maximum, we find that the urine is at its minimum, the secretion of urine again rising as the blood pressure falls.

A good deal of discussion has arisen regarding the mode of action of digitalis, and it has been stated by many to act as a diuretic only in cases of heart disease, and to have no diuretic action in health. In my own experiments, however, I found that it acted as a very marked diuretic even in health, and the explanation of this discrepancy may possibly be that, in my own case, the blood pressure was low, whereas in the others it was probably much higher; but I am uncertain regarding the true explanation, though I am certain of the fact.

By causing increased secretion of water through the kidneys diuretics may increase the concentration of the blood and thus produce thirst, or cause absorption of water from the intercellular tissue or serous cavities in dropsies. In my own experiments on digitalis I weighed all my food and measured all my drink for nearly six months, taking exactly the same quantity every day. After producing profuse diuresis by a large dose of digitaline (sixty milligrammes in two days), such thirst ensued that I was forced to take a quantity of water to allay it.[1]

*Mode of Action of Diuretics.*—From what has already been said, it is evident that diuretics may act in several ways. They may act: (A) on the circulation in the kidney, raising the pressure in the glomeruli, (1) *locally* (*a*) by contracting the efferent vessels, or the arterial twigs which pass directly to the capillary plexus; (*b*) by causing dilatation of the renal arteries, and thus increasing the supply of blood to the kidney. This they may do also in more ways than one, for they may either paralyse the vaso-motor nerves of the kidney, or act on vaso-dilating mechanisms. (2) they may raise the blood pressure *generally* by causing the contraction of vessels in other parts of the body. (B) other diuretics may act on the secreting cells of

[1] The experiments were made in 1865 and published in part in my thesis on *Digitalis, with some Observations on Urine.* London: Churchill and Co. 1868.

the tubules, and may increase both the amount of water and the amount of solids excreted by them.

Diuretics have been by some classified as stimulating and sedative; and the sedative class agrees very closely with the one which we have just indicated as acting on the kidney through the circulation.

From what has been said of the action of diuretics it is evident that we may hope to do much more by combining them, than by using them singly. Thus we see that digitalis, instead of acting as a diuretic, may completely arrest the renal circulation, and stop the secretion altogether. If however, we can combine it with something which will produce dilatation of the renal vessels, while the general blood pressure remains high, we shall greatly increase the circulation through the kidney, and obtain the desired result. Experiments in regard to this were made by Grutzner with nitrite of sodium. He found that this substance increased the secretion of urine when the blood pressure was reduced to a minimum by curara; and he found that it also had this effect when the blood pressure was raised by imperfect respiration. When the vaso-motor centre was greatly stimulated however, by allowing the blood to become very venous, the nitrite of sodium no longer produced any increase of secretion.

All nitrites have an action on the blood-vessels more or less alike. All of them cause the arterioles to dilate either by an action on their muscular walls or on the peripheral terminations of vaso-motor nerves. One of the commonest diuretics is spiritus ætheris nitrosi which contains nitrite of ethyl. Sometimes this is combined with acetate of ammonia as a diaphoretic, sometimes with digitalis, broom, or spirit of juniper as a diuretic. We have already seen that the action of the skin and of the kidneys are complementary, so that if we increase the secretion from the one we tend to diminish that of the other. At first sight then it might appear curious that we should use the same drug to increase the secretion of both. Yet there can be little doubt from clinical experience that nitrous ether is useful for both purposes, and the reason of its utility at once becomes evident when we remember that its action is strictly neither diaphoretic nor diuretic, but simply that of dilating the vessels and consequently allowing the blood to flow freely in whatever direction it may be determined by other conditions. If by combining it with digitalis we can dilate the renal arteries while those of the other parts of the body remain contracted, it is evident that we shall obtain a much freer flow of urine than we could by the administration of digitalis alone.

If instead of a diuretic like digitalis, which acts chiefly through the blood-vessels, we combine spirits of nitrous ether with salts of potassium, which act on the secreting structure, it is evident that we are likely to obtain from the increased circulation in the kidneys caused by the nitrites a much more plentiful secretion than the potassium salts alone would have produced.

The mode of action of diuretics may perhaps be rendered clearer by the following table. At present the data we possess are insufficient to allow us to classify diuretics with absolute certainty according to their mode of action, yet I think the accompanying table may be fairly said to represent our present knowledge of the subject, its imperfections being indicated by the number of notes of interrogation which the table contains:—

TABLE SHOWING THE PROBABLE MODE OF ACTION OF DIURETICS.

| | | | | | |
|---|---|---|---|---|---|
| DIURETICS | Raise arterial pressure... .. | Generally ... | Increased action of the heart by alcohol.<br>Contraction of vessels in intestine and throughout the body. | | Digitalis.<br>Erythrophleu<br>Strophanthus<br>Squill.<br>Convallaria.<br>Strychnia.<br>Cold to surf |
| | | Locally in kidney ... | Contract efferent vessels or arteria recta so as to raise pressure in glomerulus and lessen absorption in tubules, or both. | By action on vaso-motor centres. | ? The same a<br>preceding li |
| | | | | By local action on vessels or nervous structures in the kidney itself. | ? Broom.<br>? Turpentine.<br>? Juniper.<br>? Copaiba.<br>? Cantharides. |
| | | | Dilate afferent vessels | Paralyse vaso-motor nerves or involuntary muscular fibre.<br>Stimulate vaso-dilating nerves | Nitrites.<br>Alcohol.<br>? Urea.* |
| | Act on the secreting nerves. or secreting cells of the kidney itself. | Increase water excreted. | Urea.<br>Caffeine. | | |
| | | Increase solids excreted. | Liquor potassæ.<br>Potassium acetate, &c. | | |

* When a current of blood is passed artificially through an excised kidney, the stream is much accelerated by the addition of urea. Abeles, *Sitz-Ber. d. k. k. Wiener Akad.* Bd. 87, Abt. 3, April, 1883.

It not infrequently happens that one is able to understand a hypothesis more clearly when it is put in a diagrammatic form, and that one can thus perceive more readily the particular points in which it may be erroneous, even if true in the main. I therefore subjoin a diagram of the circulation and secreting apparatus of the kidney to show the parts which are probably affected by different diuretics:—

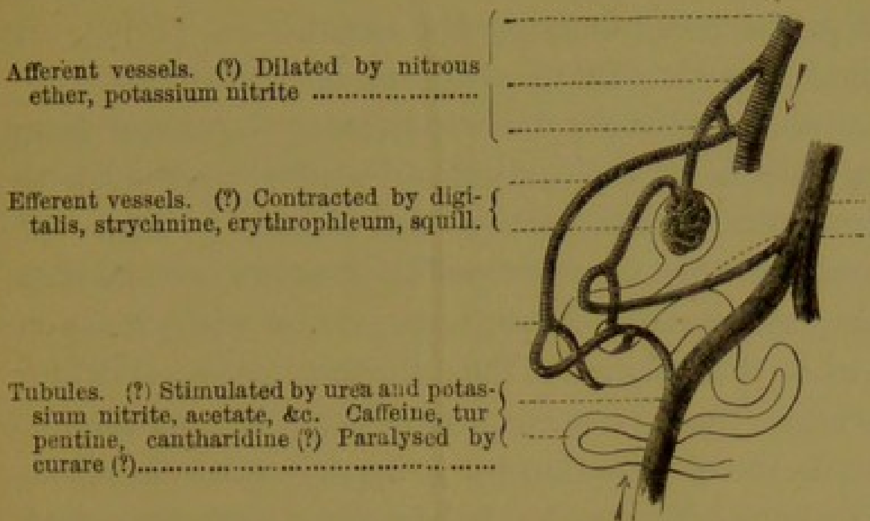


Fig. 6.—Diagram to show the parts of the secreting apparatus of the kidney which are probably affected by different diuretics.

*Uses.*—Diuretics may be employed either for the purpose of removing water or solids from the body. They are used:

1st, to remove the excess of fluid met with in the tissues and serous cavities in cases of dropsy.

2nd, to hasten the removal of injurious waste products and poisonous substances from the blood.

3rd, to dilute the urine.

In cases where the accumulation of fluid depends on venous congestion, as for example in cardiac dropsy, those diuretics which act on the general vascular system, like digitalis, strophanthus, squill, or erythrophleum, are most efficient because they tend to remove the cause of the dropsy, as well as to assist the absorption and excretion of the fluid already effused.

When the dropsy depends on the disease of the kidneys or liver, other diuretics should either be given instead of, or along with, digitalis or squill, even in cases of cardiac disease. Where digitalis or squill are not proving efficacious, the addition of a little blue pill greatly assists their action, though it would be hard to say in what way it does so.

In dropsy depending on kidney disease, decoction of broom, and oil of juniper, and nitrous ether, are amongst the most reliable diuretics, and copaiba in hepatic dropsy.

Diuretics are used to increase the secretion of solids in febrile conditions, and in cases of kidney disease where the excretion of waste products is deficient, and their retention threatens to prove injurious. In such cases, nitrate and bi-tartrate of potassium, turpentine, and juniper, and caffeine are useful.

Diuretics are also used to increase the proportion of water in the urine, and thus to prevent the solids being deposited from it and forming calculi in the kidney or bladder; or even to dissolve again concretions which have been already formed.

Water is perhaps the most powerful diuretic we possess, although fewer experiments have been made with it upon animals than with the others. The diuretic action of water drunk by a healthy man is very marked, and it appears impossible to explain its elimination by a mere increase in blood-pressure, whether general or local. It has, as we have remarked, the power of increasing tissue change, and thus multiplying the products of tissue waste which result from it, but it removes those waste products as fast as they are formed, and thus, by giving rise to increased appetite, provides fresh nutriment for the tissues, and thus acts as a true tonic. In persons who are accustomed to take too little water, the product of tissue waste may be formed faster than they are removed, and thus accumulating may give rise to disease. If water be freely drunk by such persons, the product of waste will be removed, and health maintained or restored. Thus many gouty persons are accustomed to take little or no water except in the form of a small cup of tea or coffee daily, besides what they get in the form of wine or beer. In such people a large tumbler of water drunk every morning, and especially with the addition of some nitrate or carbonate of potassium, will prevent a gouty paroxysm. Still more numerous, possibly, is the class of people who rise in the morning feeling weak and languid, more tired, indeed, than when they went to bed. Now fatigue may be regarded as the imperfect response of muscles and nerves to stimuli, and such an imperfection in their action may be due either to their imperfect nutrition or to the imperfect removal of the products of their waste. Many such people are well fed, they sleep soundly, and it seems almost impossible to believe that the fatigue which they feel in the morning can result from imperfect nutrition, more especially as one finds that after moving about, the languor appears in a great measure to pass off. It seems to me that this languor must depend upon imperfect removal of the waste products from the body, as we know that the secretion of urine in healthy persons is generally much less during the night than during the day. I am therefore in the habit of advising such people to drink a tumbler of water before going to bed in order to aid the secretion of urine and of the waste products during the night. In some cases, though not in all, the result has been satisfactory, and possibly might have been still more so had I added to the water the bi-carbonate and nitrate of potassium which, as I have already mentioned, is so useful in cases of gout.

Lately a plan of treating gout by draughts of water at intervals during the day has been a good deal employed and is in many cases successful. As an example of this I subjoin the diet used along with this treatment by a medical friend of mine who has been a martyr to gout, but who feels himself perfectly well as long as he adheres strictly to this course of diet :—

7.30 A.M. Ten fluid ounces very hot water.

8 A.M. Breakfast : Equal parts of weak tea and milk, a small quantity of white sugar, a slice of fat bacon without a strip of lean, bread and fresh butter.

1 P.M. Milk pudding, rice, sago, tapioca, macaroni, or blanc mange, and small biscuits with butter, ten fluid ounces hot water.

4 to 5 P.M. Ten fluid ounces hot water.

6 P.M. Dinner : White fish or fowl (usually boiled), greens, bread, no potatoes, claret seven fluid ounces.

8 to 9 P.M. Ten fluid ounces hot water.

11 P.M. Ten fluid ounces hot water.

If he indulges either in meat or game, or drinks copiously of claret, or omits one or two glasses of hot water, he feels gouty and gravelly next day. It is obvious that by this plan of treatment, in which the ingestion of nitrogenous food is most strictly limited, at the same time that every facility is given for the elimination of the products of nitrogenous waste by the large quantities of hot water drunk in the course of the day, the accumulation of waste in the tissues ought to be most effectually prevented.

*Adjuvants to Diuretics.*—As the amount of urine secreted depends upon the difference in pressure between the blood in the glomeruli and the urine in the tubules, it is evident that any pressure on the tubules, whether caused by obstruction of the ureter by a calculus, by the mechanical pressure of dropsical accumulations in the abdomen, or by distension of the venous plexus in the kidney itself, will tend to lessen the secretion of urine. Consequently we sometimes find that in such cases diuretics fail to act until the pressure has been relieved by paracentesis in cases of dropsy, or the venous congestion lessened by the use of a brisk purgative, or by cupping over the loins.

If the venous congestion is very great, as in cases of mitral disease or of chronic bronchitis with emphysema and dilated heart, bleeding from the arm may be advantageous or even imperatively necessary. In dilated heart and in mitral incompetence the action of digitalis on the heart itself, strengthening its action and enabling it more effectually to pump the blood out of the venous into the arterial system and thus to reduce venous congestion, will aid its action upon the kidneys.

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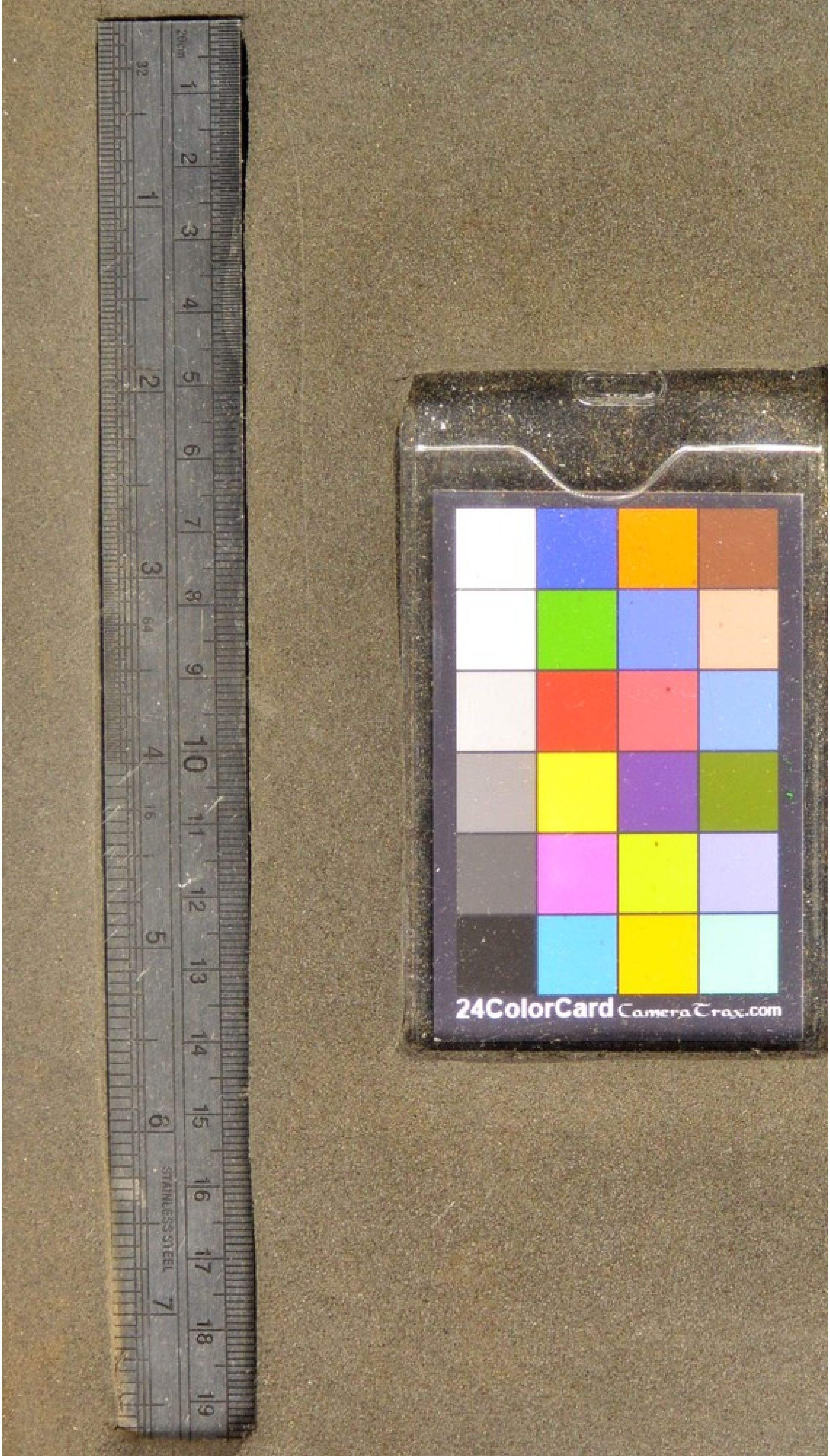
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