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On the action of adrenalin. By T. R. ELLIOTT.

(*Preliminary communication.*)

In further illustration of Langley's generalisation that the effect of adrenalin upon plain muscle is the same as the effect of exciting the sympathetic nerves supplying that particular tissue, it is found that the urethra of the cat is constricted alike by excitation of the hypogastric nerves and by the injection of adrenalin. The sacral visceral nerves, on the other hand, relax the urethra of the cat. But while the hypogastric nerves relax the tension of the bladder wall in the cat, they do not cause any similar change in the dog, monkey, or rabbit: and though, as is well known[1], adrenalin inhibits the cat's bladder, this reaction is the exception in the mammalian bladder, for adrenalin does not produce any change in those of the three animals named above.

I have repeated the experiment of clean excision of the suprarenal glands and find that the animal, when moribund, exhibits symptoms that are referable to a hindrance of the activities of those tissues especially that are innervated by the sympathetic. They lose their tone; and may even fail to respond to electrical stimulation of the sympathetic nerves. The blood-pressure falls progressively, and the heart-beat is greatly weakened. And at the latest stage previous to death, though the nerves of external sensation and those controlling the skeletal muscles are perfectly efficient, the sympathetic nerves exhibit a partial paralysis of such a nature that nicotine, when injected, is unable to effect through them a rise of blood-pressure or to cause dilatation of the pupil.

[1] Lewandowsky. *Centralblatt f. Physiol.* p. 433. 1900.

This marked functional relationship of the suprarenals to the sympathetic nervous system harmonises with the morphological evidence that their medulla and the sympathetic ganglia have a common parentage[1]. And the facts suggest that the sympathetic axons cannot excite the peripheral tissue except in the presence, and perhaps through the agency, of the adrenalin or its immediate precursor secreted by the sympathetic paraganglia.

Adrenalin does not excite sympathetic ganglia when applied to them directly, as does nicotine. Its effective action is localised at the periphery. The existence upon plain muscle of a peripheral nervous network, that degenerates only after section of both the constrictor and inhibitory nerves entering it, and not after section of either alone, has been described[2]. I find that even after such complete denervation, whether of three days' or ten months' duration, the plain muscle of the dilatator pupillæ will respond to adrenalin, and that with greater rapidity and longer persistence than does the iris whose nervous relations are uninjured[3].

Therefore it cannot be that adrenalin excites any structure derived from, and dependent for its persistence on, the peripheral neurone. But since adrenalin does not evoke any reaction from muscle that has at no time of its life been innervated by the sympathetic[4], the point at which the stimulus of the chemical excitant is received, and transformed into what may cause the change of tension of the muscle fibre, is perhaps a mechanism developed out of the muscle cell in response to its union with the synapsing sympathetic fibre, the function of which is to receive and transform the nervous impulse. Adrenalin might then be the chemical stimulant liberated on each occasion when the impulse arrives at the periphery.

The removal of the stellate ganglia. By H. K. ANDERSON, M.D.

(*Preliminary communication.*)

The stellate ganglia have been removed in cats and kittens. To remove them the scapula is drawn downwards and outwards and the 1st

[1] Kohn. *Arch. Mikr. Anat.* LXII. 1903.

[2] Fletcher. *Proc. Physiol. Soc.* This *Journal*, XXII. 1898.

[3] Cp. S. J. Meltzer and Clara Meltzer Auer, who obtained a like result after excising the superior cervical ganglion alone. *Amer. Journ. Physiol.* XI. 1904.

[4] Cp. Brodie and Dixon, this *Journal*, XXX. 1904, regarding its absence of action on the muscle of the bronchioles and of the pulmonary blood vessels; and also experiments quoted above on the bladder.

intercostal space exposed between the levator anguli scapulæ and rhomboideus muscles. A white tendon of the ilio-costalis serves as a good guide to the 1st rib, and the intercostal muscles in the 1st intercostal space are torn through close to the lateral border of this muscle for less than half a centimetre. The stellate ganglion and its branches are seen at the bottom of the hole thus made, and the ganglion can be easily removed, or its branches cut, without damage to the pleura by this method. Both ganglia may be excised almost without loss of blood in half-an-hour. The cats have been observed in some cases for several months afterwards.

In one cat only has a marked fall in the rate of heart-beat occurred under normal conditions either when the ganglia have been excised or the preganglionic branches of the ganglion cut. In several experiments there has been no change in the rate of beat, and in one kitten the heart-beat subsequently to the removal of both stellate and inferior cervical ganglia was more rapid and forcible under corresponding conditions than the heart-beat in a sister kitten of the same age. In this kitten the stellate and inferior cervical ganglia were excised on the 18th day after birth, and the kitten killed 141 days later. The kitten then weighed 1250 grammes and its heart 4·75; the control kitten weighed 1400 grammes and its heart 4·69. The heart of the experimental kitten, therefore, weighed more actually and also more relatively to the body-weight. The forepaws in this kitten were generally a little warmer than the hindpaws, but when the kitten was warmed they were relatively the colder. There was, therefore, no evidence of the passage of vaso-dilatator impulses along the undivided roots of the brachial plexus in response to the increased warmth. There were no signs of atrophy or dystrophy in the lungs or in the areas of skin supplied by the branches of the stellate ganglia. There was no paralytic secretion of sweat, and the forepaws remained very dry even when the kitten was warmed.

The action of eserine and atropine upon the denervated sphincter iridis. By H. K. ANDERSON, M.D.

(*Preliminary communication.*)

The experiments have been performed on cats. The ciliary and accessory ciliary ganglia have been removed on one side: the superior cervical ganglion was also excised on the same side, and in some experiments on both sides. In all the experiments, six in number, the

pupil under normal conditions has remained almost maximal and irresponsive to light, in one case even ten months after the operation. For a period of 3 to 6 weeks there has also been no contraction of the sphincter after the local application of eserine to the eyes, but the excitability of the sphincter by eserine has gradually returned later, and has become even greater than normal, as in the following experiment. In this case 2 months after the removal of the left ciliary and accessory ciliary ganglia an equal drop of 1 % eserine was applied to each eye. The left pupil an hour later was found to be almost a slit, and immobile in dim or bright light. The right pupil on the other hand, though a closer slit than the left in bright light, dilated considerably in dim light, and the left pupil for this reason was considerably the smaller pupil in dim light, though relatively the larger in bright light. The local application of atropine overcame in both eyes the constriction caused by the eserine. The relatively smaller size of the left pupil under the action of eserine in this experiment cannot be attributed to paralysis of the left dilatator since both dilatators had been completely paralysed by removal of the superior cervical ganglia. As in previous experiments with Professor Langley, I obtained in this cat no constriction of the pupil on stimulation of the 3rd or ciliary nerves 3 months after the removal of the ciliary ganglion although there were many medullated fibres in the ciliary nerves close to the eyeball.

On the other hand, I found in another similar experiment that the renewed excitability of the sphincter by eserine disappeared after a second section of the ciliary nerves (together with the optic nerve), but that the excitability reappeared a month later when sufficient time had elapsed to allow regeneration to have occurred a second time.

In another cat two of the malar ciliary branches were cut for the second time 13 weeks after the excision of the left ciliary and superior cervical ganglia. Immediately before this second operation the left pupil contracted regularly and almost to a slit under the action of eserine, but after the operation the left pupil contracted much less on the malar side which is specially supplied by the ciliary branches cut. The left pupil was, therefore, smaller but much bulged on the malar side after the application of eserine, though regular and almost maximal before.

Moreover, excitability has not returned equally to all parts of the sphincter at the same time. In some cases contraction of the sphincter under the action of eserine has at first been confined chiefly to a small patch and the edge of the iris has been protruded at this point.

Later, however, the extent of the contraction has gradually spread over the sphincter.

My observations, therefore, show that the reappearance of contraction in the sphincter under the action of eserine is due not to an independent excitability of the muscle itself but to the regeneration of nerve fibres in the ciliary nerves, although at the same time no contraction of the sphincter can be evoked either by light reflexly or by direct stimulation of the regenerated ciliary nerves.

Products of the distillation of hæmatin with zinc dust. (*A preliminary communication.*) By J. A. MILROY.

(*From the Physiological laboratories of the University of Edinburgh and of Queen's College, Belfast.*)

The facts that Nencki and Zaleski[1] obtained a volatile pyrrol derivative (hæmopyrrol) by the reduction of hæmin with hydriodic acid and phosphonium iodide, and that pyrrol or a substance giving some of its reactions has been obtained by the distillation of hæmatin with zinc dust seem to indicate the need for further investigation of the products of the latter method of reduction.

The following communication gives the preliminary results of an investigation along these lines.

Four and a half gms. of hæmatin, dried in vacuo over sulphuric acid, were mixed with 35 gms. of zinc dust previously dried by heating in a current of dry carbon dioxide. The mixture was then placed in a Jena glass tube. After the air had been displaced from the tube by a current of dry carbon dioxide, the mixture was gradually heated while the current of gas was maintained. The products of the distillation were condensed (1) in a spiral glass worm surrounded by a water jacket, (2) in a coiled tube placed in a mixture of ice and water, and (3) finally the gas passed through a wash bottle containing concentrated hydrochloric acid. A red coloured vapour passed over, which condensed for the most part in the spiral tubes in the form of red oily droplets. The hydrochloric acid in the wash bottle also absorbed some pigment acquiring a faintly red tint, and showing on spectroscopic examination absorption bands apparently identical in position and character with those of acid hæmatoporphyrin. The pigment condensed in the tubes was dissolved in chloroform. The solution thus obtained was reddish brown in colour and showed a faint green fluorescence. Spectroscopic examination of

[1] *Ber. d. d. chem. Gesell.* XXXIV. p. 997 and 1687.

a dilute solution revealed three absorption bands (α) λ578—568, (β) λ540—530, (γ) λ500—482.

The pigment residue remaining after distilling off the chloroform was found to be soluble in most organic solvents, *e.g.* alcohol, ether, chloroform, petroleum ether, glacial acetic acid and benzene. It was insoluble even in concentrated solutions of the caustic alkalies. It dissolved in concentrated hydrochloric acid; but was precipitated by dilution with water.

The greater part of the pigment residue was dissolved in ether. To the filtered ethereal solution hydrochloric acid (1 vol. of the concentrated acid to 1 vol. of water) was added. On shaking up the solutions the greater part of the pigment passed into the acid solution while a brownish pigment passed into the ether. The ethereal solution was separated, and the subjacent aqueous acid solution was repeatedly extracted with fresh quantities of ether until the ether ceased to take up any pigment.

On spectroscopic examination the ethereal solution showed one absorption band, λ506—476. The ethereal solution was separated and washed with water. Dilute ammonia was then added. The supernatural ether which contained all the pigment showed on spectroscopic examination one absorption band, λ520—504. A few drops of an ammoniacal solution of zinc hydrate in alcohol were added to another portion of the ethereal solution. The absorption band appeared to become darker and better defined but remained unaltered in position and extent.

The solution of the pigment which had dissolved in the dilute acid was bright red in colour, and showed on spectroscopic examination (1) a narrow dark absorption band, λ598—588, (2) a faint narrow band, λ578—576, then slightly fainter absorption from λ578—562, and (3) continuous with this shading a dark broad absorption band extending from λ562—538. The positions and characters of these bands correspond closely with those of acid hæmatoporphyrin.

The acid solution was next diluted with water and extracted with chloroform. The latter solvent takes up all the pigment. The chloroform solution was repeatedly washed with water, separated, and filtered. Some 5 per cent. caustic soda was added to part of this solution and the two layers mixed by gentle shaking. When the solution of the pigment in chloroform had completely separated from the aqueous alkali, it was examined spectroscopically and found to show the following four bands: (α) λ617·5—612, (β) shading from λ573·5—567·5, darker absorption from λ567·5—λ561, (γ) λ539—527·5, (δ) λ512·5—492·5.

Dilute hydrochloric acid was added to another portion of the solution of the pigment in chloroform. The subjacent chloroform solution showed the following absorption bands: (α) λ594—582, (β) shading from λ572·5—λ557·5, and a dark absorption band continuous with the shaded area and extending from λ557·5—536·5.

Semmler's modification of the method of zinc dust distillation was also employed as a somewhat less drastic procedure; 1 gm. of dry hæmatin was mixed with 2 gms. of dry zinc dust. The mixture was then placed in a glass tube from which the air was afterwards displaced by a current of dry carbon dioxide. After the ends of the tube had been sealed, it was heated in an oil bath at 180° C. for 8 hours. After cooling the tube was opened and the contents extracted with chloroform. The filtered solution of the pigments in chloroform was reddish brown in colour and showed a distinct green fluorescence. On spectroscopic examination four absorption bands could be made out, apparently corresponding in position and character to those of alkaline hæmatoporphyrin. Part of the pigment residue left after distilling off the chloroform was dissolved in alcohol containing some hydrochloric acid. The green fluorescence disappeared and the solution showed three bands, two resembling those of acid hæmatoporphyrin in position and character, and a band lying between *b* and *F*.

Another portion of the pigment residue was dissolved in ammoniacal alcohol, and mixed with a few drops of an ammoniacal solution of zinc hydrate in alcohol. On standing for a few hours the solution showed three bands, two apparently corresponding to those of metallic hæmatoporphyrin and one lying between *b* and *F*; but situated somewhat nearer the red end of the spectrum than the corresponding band shown by the acid solution.

By a slow distillation of hæmatin with a large excess of zinc dust one obtains more complete reduction. A light yellow oil condenses whose vapour gives the colour reaction for pyrrol with a pine-wood strip dipped in hydrochloric acid; but does not give the colour reactions for pyrrol with isatine or quinone. Its solution in chloroform shows at first no absorption bands; but on standing it darkens to a light red colour, shows a distinct green fluorescence, and a band lying between *B* and *F*.

These results appear to indicate that at least three volatile substances are obtained by the distillation of hæmatin with zinc dust, two resembling in their spectroscopic characters hæmatoporphyrin and urobilin, but differing markedly from the latter in regard to their solubilities, and one probably allied to the hæmopyrrol obtained by Nencki and Zaleski.

Extraction apparatus and their condensers. By HERBERT E. DURHAM. (*Pathological Laboratory, Cambridge.*)

In practice it is an advantage to avoid complicated extraction tubes, especially such as have fine conducting siphons welded on their exterior (*e.g.* Soxhlet tubes).

Extraction of fluids with light or heavy solvents. A simple extraction apparatus, consisting of a wide piece of tube, narrowed below for attachment to the boiling flask, and with a side tube for conducting the vapour, may easily be arranged for the use of solvents which are heavier or lighter than the fluid which is to be extracted. Moreover the apparatus can be adjusted for different quantities of fluid.

In the case of a heavy solvent the aperture of the lower end of the wide extraction chamber is closed by a cork, which is perforated and carries a simple straight piece of glass tube. This tube acts as an overflow and its length may be adjusted to suit the requirements of a given case. The cork should be well softened by steam or by boiling before it is fitted in place, which is done with the help of a wider piece of tube, wherewith the cork is pressed home. Solvent is then poured into the extraction chamber. A piece of glass tube (wider than the overflow) is slipped down over the overflow as a "sleeve"; it may be packed at the lower end to facilitate the passage of fluid from without inwards; its upper end is loosely capped or bent over to prevent the direct entry of drops from the condenser; the upper end of its lumen is open.

The fluid to be extracted is then poured cautiously into the extraction chamber; whilst this proceeds, the previously introduced solvent rises up between the sleeve tube and its contained overflow tube. When all or a sufficiency of the fluid to be extracted has been introduced, there should be enough of a subjacent layer of solvent to "seal" off the lumen of the sleeve tube. The arrangement is perhaps more clearly intelligible by aid of the diagram (Fig. 1).

In the case of a light solvent the small sleeve tube is removed and is replaced by a wide "sleeve" tube (see Fig. 2), which fits the extraction chamber fairly closely for some part of its height; it consists in fact of the cut-off top of a bottle, which fits the extraction chamber. This sleeve is held to the required height by a piece of wire, twisted round its neck of the one part, and hooked into the vapour side tube of the other.

The overflow tube is placed as in the previously described arrangement.

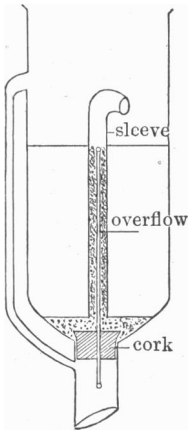

Fig. 1. Diagram of arrangement for heavy solvent.
(Position occupied by solvent dotted)

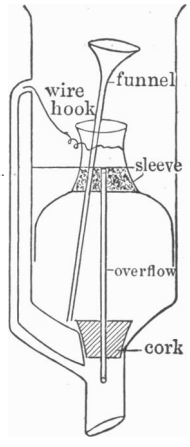

Fig. 2. Diagram of arrangement for light solvent.
(Position occupied by solvent dotted)

In filling the apparatus, some of the fluid to be extracted is first poured in, until the narrow part of the sleeve is nearly reached, solvent is then poured inside the sleeve until there is a sufficiency to make a "seal"; the rest of the fluid to be extracted is then added.

A funnel is passed down to catch the solvent from the condenser and conduct it to the bottom of the extraction chamber.

When at work, as the solvent from the condenser passes up through the fluid, it is retained by the sleeve and prevented from dispersing over the whole surface of the fluid. Consequently the overflow can act with efficiency. In cold weather there may be some condensation of solvent on the surface of the extraction chamber, which consequently trickles down without the sleeve. Should this occur, it is merely necessary to raise the sleeve until its lower edge is completely above the surface and then to lower it again into position; by this means the floating solvent becomes caught and is retained within the sleeve. When very complete exhaustion of a fluid is desired it might be well to perform this raising of the sleeve on one or more occasions, since the portion of fluid without the sleeve does not come into close contact with solvent. Diagram No. 2 shows the arrangement.

This apparatus can be made by any glass blower; the one I have

was made for me by Messrs Müller, Orme & Co. of Holborn. The extraction chamber is about 24 centimetres high and 7½ cm. in diameter; the working capacity is up to about half a litre. Were I to have another made, I should have the height increased so that the entrance point of the vapour tube was not less than 7 or 8 cm. below the upper orifice of the apparatus; the reason for this will be seen later.

Extraction of small quantities of material. The following simple arrangement has worked very well for the extraction of small quantities of material. An ordinary wide test-tube (say 8 × 1½ inches) is taken and into this a support consisting of a section of an ordinary test-tube about 1½ to 2 inches long is dropped. The extraction cup, which is placed on the support, consists of an ordinary specimen tube (3 × 1 inch).

The shorter limb of one or more small capillary siphons is placed within the extraction cup, a pledget of cotton-wool thrust to the bottom tends to hold the siphon in place and to keep it flowing continually. In place of a porous extraction thimble I have used a pottle of thin paper (some Japanese press copy paper I bought in Singapore acts admirably). The boiling tube is fitted with cork and condenser. By varying the height of the lower end of the apparatus above the water bath a variety of ratios of rates of flow from condenser and from siphon may be obtained; thus the substance may be flooded or drained dry. By the introduction of an empty cup the solvent may be distilled off without removing the extract from the apparatus. (This is in fact an adaptation of the extractor of Greiner and Friedrich which is on the market.)

Condensers. The forms of condensers which are ordinarily employed are entirely outside the extraction apparatus. It follows from this that there is a possibility of "idle" vapourisation and condensation in and about the lower end of the condenser. This idle circuit was so great during some extractions, that I was led to arrange my condensers partly inside the extraction chambers. This can be done very simply and gives no chance of idle circuits.

Such a condenser consists of two parts, an outer sleeve into the upper end of which a short piece of tube is welded so that a vacuum pump may be attached, and the condensing surface which consists of a long piece of thin wide glass tube sealed off below and lipped at the top. A doubly bored cork fitted after the manner of a washbottle is fixed in its upper end, by this the tube is kept full of circulating cold water. The condenser may be fixed to the upper end of sleeve, which it fits very loosely, by means of a rubber cork, suitably bored out. I may remark that the use of rubber for this cork is not prevented by the employment

of rubber solvents, for the condensation is so complete that I have had condensers in use with chloroform etc. for very many weeks which still show no sign of destruction of the rubber.

The lower end of the sleeve tube is fitted to the extraction chamber with a rubber or cork bung. The condenser is adjusted so as to project well into the extraction chamber. It will be seen that the vapour passing from the side tube impinges directly on the condenser, thus much of the vapour becomes condensed before it can enter the space between sleeve and condenser.

This has led to a further modification of the extraction chamber, namely, an increase of the length above the point of entry of the side tube. By increasing this a still greater opportunity is offered for con-

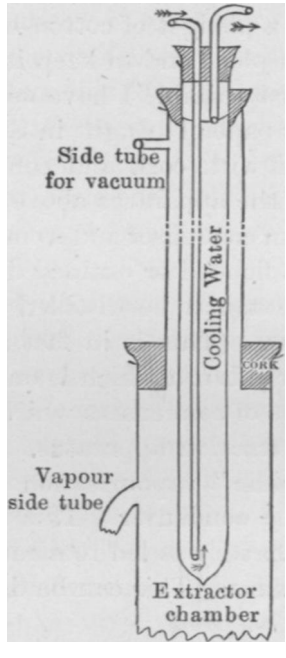

Fig. 3. Diagram of arrangement of "Internal" condenser.

densation to take place before the sleeve is reached. Where rubber corks can be employed this is perhaps of small moment, but when rubber solvents are being used it has some importance. It is well nigh impossible to get corks which are not more or less leaky, but the importance of a leak becomes slight when there is little or no vapour to leak out. In order to rectify leaks, boiling the corks, smearing them with glycerin and then smudging with a paste of bread-crumb and

water has acted fairly well in my hands. Pieces of peritoneal membrane are also of value as wrappings, especially when the extraction is carried out under reduced pressure. The entrance of quite a minute quantity of water, especially when solvents like petroleum ether are used, is very deleterious; water condenses on the outside of the condenser and is apt to find its way through a slightly leaky cork. It appears that a few strands of knitting cotton tied round the lower part of the condenser is enough for the purpose of conducting such water away.

The advantage of using this form of condenser can be shown by putting the apparatus at work; after noting the rate of drip, the condenser is gradually withdrawn up the sleeve; at a certain level, if the rate of boiling off is not too rapid, the drip ceases or slows owing to reevaporation by the hot vapour. In fact the apparatus is turned into the ordinary arrangement, wherein a conducting tube is interposed between the extraction chamber and the condenser.

Reference to the diagram (Fig. 3) will make the arrangement clear. Various sizes of tube have been tried for condensers. An internal diameter for the sleeve tube of about 2 cm. with an external diameter of about 2 or 3 mm. less for the condenser, total height of sleeve tube 45 cm. with a side tube about 7 cm. from its upper end form useful dimensions.

The principle of an internally placed condenser can also be applied to distilling or evaporating apparatus. Such a condenser as has been described above when partly inverted so as to be inclined at an angle of about 50 to 60 degrees with the horizontal will act as a conductor to carry condensed fluid to the sleeve tube, the side small tube of which then acts as a delivery tube. The introduction of the condenser within the evaporating chamber practically makes the connexion between condenser and evaporator "infinitely large," the condenser also tends to catch and lead away vapour which might otherwise condense upon the surface of the evaporating chamber and lastly it tends to keep the vapour motion low in the evaporating chamber and thus promote a circulation or draught; all these factors tend to make such a distillation apparatus more efficient than models ordinarily used. It should be added that it is well to regulate pressure, when reduced pressure is used, and temperature so that spluttering does not occur, if loss is to be avoided.