LECTURES

ON THE

EXPERIMENTAL INVESTIGATION OF THE ACTION OF MEDICINES.

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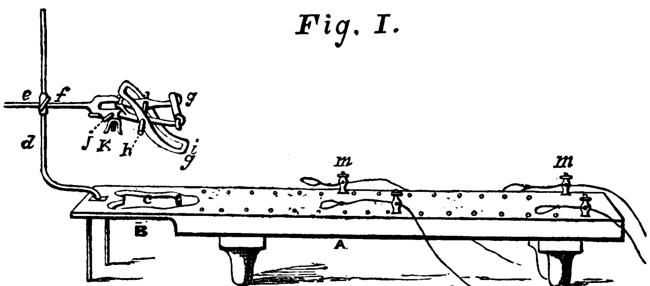
II.—Action of Drugs on Protoplasm: General Directions for Experimental Investigation.

Modes of Experimenting.—Caution.—Action of Drugs on Protoplasm.—Action on Vibriones and Bacteria.—Contagium Vivum.—Action on Fungi; on Fermentation; on Putrefaction; on Oxidation; on White Blood Corpuscles; on Inflammation.—Action of Gases.—Steps of an Investigation.—Administration of Drugs.—Observation of Effects.—Interpretation of Results.—Minimum Fatal Dose.—Various Channels of Administration.—Excretion.—Mode of securing Animals.—Instruments required.—Mode of making Cannulæ, T-tubes, and Pens.—Narcotising Animals.—Action of Narcotics.—Introduction of Cannulæ into Vessels.—Injection of Fluids.—Division and Irritation of Nerves.—Artificial Respiration; in Mammals; in Frogs.—Administration of Gases or Vapours.

Mode of Securing Animals.—In order to determine in an exact manner what organs or parts are affected, we are obliged to make use of apparatus of various kinds; and, before these can be applied to an animal, it must be prevented from moving. Frogs are fastened to a frog-board by a piece of cord with a noose at the end, slipped over each elbow and ankle. The frog-board may consist of a piece of mill-board about nine inches long by three inches broad, with four slits at the sides to keep the cords in position, or of a piece of wood the same size, and from a quarter to half an inch thick, with holes, through which the cords are passed. They may be fastened by simply tying them together or by sticking a small wooden pin into each hole, or by four screws, such as are used by fastening the wires of galvanic batteries, placed in the edges of the board. The last way is, I think, the most convenient. Rabbits are best secured by Czermak's holder and board (shown in fig. 1). The best cord is strong window-

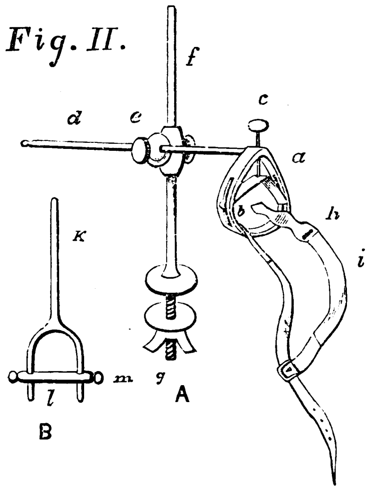
Fig. I.



Czermak's Rabbit Holder and Board. A. The board. B. A bent piece of iron forming the upper part of the board. *c*. An open space through which instruments can be introduced from below to divide the spinal cord. It is generally covered by an iron plate. D is an upright rod fixed by a screw into a slit in B. *f* is a forked rod, which can be moved back or forward, up or down, by the nut *e*. The forks are hollow, so that the ends of the holder can be passed into them and fastened by the screw *j*. *h* is a bar which passes behind the incisor teeth of the rabbit. *g* and *g'* are two bent bars which pass under the chin and over the nose of the animal, and are brought together by the screw *l*. From the upper end of *g'* hangs a screw, which passes between two projections on *g*, and has a mother-screw *k*. The screw *k* works against the projections on *g*, and draws the ends of *g'* and *g* together. These press on the rabbit's nose and under jaw and keep the teeth firmly locked over the rod *h*. *m m* are screws for fixing the cords which confine the legs. They are a remarkably convenient sort, consisting of an outer part with a horizontal hole, and an inner ring with a stalk on which a milled screw plays. When the milled head is at the top of the stalk, the inner ring and outer holes correspond, and the cord can then be easily pushed through; but when the milled head is turned, the stalk and ring are drawn up and the cord nipped between it and the outer part. The cords may either be fastened directly in the screw or passed first through one of the holes in the edge of the board. The board should be covered with a large pad of India-rubber stuffed with horsehair, and there should be another round pillow to put under the animal's neck.

cord. The one end should be flattened with a hammer, and turned over so as to make a small loop, whose two sides are then firmly bound together with waxed thread. Through this loop the other end is passed, and the noose thus made is ready to be drawn tight at any moment. The other end of the cord should be cut to a point and also bound with waxed thread to prevent the strands unravelling. The rabbit is placed on the board, the nooses slipped over the legs and drawn tight, and the ends of each cord passed through the screw which will be nearest it when the animal lies on its back. The rabbit is then turned over, and the cords drawn through the screws and fastened. The bar *h* is then put between its teeth, and the screw *l* turned till *g* and *g'* fit tightly over its muzzle, and the projecting ends of *g* fixed into the ends of *f*. Dogs may be fastened by Bernard's holder (fig. 2A), or by a simple bar of

Fig. II.



A is Bernard's dog-holder. *a* is a metal ring, within which a bent piece of metal, *b*, is moved up and down by the screw *c*. *h* is a straight piece, which is fastened by a screw to *a*, and can be moved nearer to or farther from a corresponding piece at *b*. These two pieces lie under the lower jaw of the dog; the bent piece *b* is screwed down on its nose, and the strap *i* buckled behind its head, which is thus firmly fixed. It may be moved back or forward by sliding the rod *d* through the nut *e*, or up and down by moving *e* on *f*, which is a strong iron rod fastened to a table or board by the screw *g*.

B. Brunton's holder for dogs or rabbits. A loop of cord is tied round the upper jaw, the bar *l* passed behind the canine teeth of the dog or cat or incisors of the rabbit, and the two jaws then tied together to prevent its slipping out. This mode of fastening animals has been long used, and my modication simply consists in the addition of the forked bar *k*. After *l* is fastened in the mouth, the forked ends of *k* are pushed through holes in *l*, and fastened by the screws *m*. *k* may then be fastened to an upright bar by means of a nut in the same way as Bernard's or Czermak's holder.

iron put behind their canine teeth. A piece of cord is first tied round the upper jaw, the bar put into the mouth, and the two jaws tied firmly over it. A split strap may be used instead of the cord. I have had a bar made with a hole at each end, into which a fork of steel passes, and is secured by a screw. The fork may then be fastened by a nut to an upright rod, as in Czermak's holder (fig. 2B). Cats and guinea-pigs may be fastened by Czermak's holder. For guinea-pigs, a little padding must be placed between *g* and *g'* in order to make them catch the head. A simple bar and cord may also be used for rabbits, cats, and guinea-pigs, as well as for dogs.

Instruments Required.—The instruments which we generally require for operations are—sponges, one pair of large scissors and one small pair, cutting well at the points, scalpels, forceps, small bull-dog forceps with smooth points, blunt hooks, a small aneurism-needle, flattened sidewise and with a rounded point (fig. 3 G), ligatures, finder (a kind of probe set in a handle to open up the lumen of a divided vessel), syringe, cannulæ, a piece of card, small whalebone-probe, and one or two swine's bristles. As these are very apt to be mislaid during an operation, I find it convenient to have a small wooden tray about three-quarters of an inch deep, with thin upright sides, and divided into compartments, one for each kind of instrument. It is advisable, also, to have an extra instrument or two of each sort.

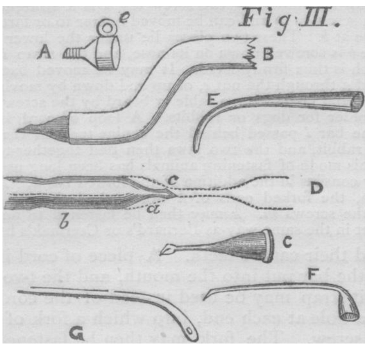
Way of Making Cannulæ.—Cannulæ for injecting into vessels may be made of metal (fig. 3 C) or of glass. Glass ones can be easily made of any size required by heating a piece of glass-tubing over the flame of a blow-pipe, and drawing it out in the middle, as represented by the dotted line (fig. 3 D.) It is then heated at *a* and slightly drawn out, so that a bulging piece is left between *a* and *c*; it may then be heated and very slightly drawn out at *b*, then cut with a three-cornered file at *c*, and the point ground obliquely off on a hone. If the point be at all sharp, its edges may be rounded in a gas-flame. When the cannula is introduced into a vessel, a ligature at *a* prevents it from coming out: it may be connected with a syringe or with any piece of apparatus by a piece of India-rubber slipped over the other end and tied at *b*. A cannula for connecting an artery with a kymographion may either be of this sort, or may be made of metal of the shape shown in fig. 3 A. As it is difficult to hold it with forceps, it should be put on a piece of wood or whalebone of the shape shown at B. This both holds it firmly, and the point entering the vessel allows the cannula to be more readily pushed on into the lumen. A few notches on the side of the cannula prevent the vessel and ligature with which it has been tied from slipping off the end. By means of the little ear at *e*, it can be tied to the tube, on to which it is fitted.

MODE OF MAKING CANNULÆ, T-TUBES, AND PENS.—Cannulæ for the trachea are made by closing one end of a tube, directing a small blow-pipe flame against a point in its side till it is quite soft, and then suddenly blowing into it. The soft part expands into a thin bulb, which is scraped off, and a hole remains in the side of the tube. The object of this hole is to allow the air to escape during expiration. Instead of a hole in the cannula, one may be cut in the side of the India-rubber tube to which it is connected; but this is more apt to be accidentally closed. The tube is then drawn out into the form seen at Fig. 4 A, cut off at both ends, and one end ground obliquely off on a sandstone with some water.

A knob may be made at the ends of other cannulæ for various purposes, by heating the end and striking it against a piece of glass or iron, or by heating the end in a flame, continuing to blow steadily through the tube while you do so.

T-tubes are made by blowing a hole in the side of one tube, in the same way as for a respiration-cannula; and then putting the heated end of another tube over it while the first is still hot, so that the two stick together. The joint must then be annealed by heating it in an ordinary gas-flame, reducing the size of the flame gradually, so that the glass may cool very slowly.

Pens for use with a kymographion are made by drawing tubes to a point, as shown in Fig. 3, E and F; and grinding the point on a fine hone, and rounding it, if necessary, in the flame.



A is a metal cannula with an ear *e*, by which it can be fastened to any tube connected with its large end. B is an instrument for introducing A into a vessel. It consists of a piece of metal tubing, with a pointed piece of wood at one end, over which A is put. The point projects through the smaller opening in A, so as to enter the lumen of the vessel readily. C is a metal cannula which fits on the end of a syringe for injecting fluids into vessels. D is a glass cannula. The dotted line shows the original tube drawn out in the blowpipe-flame; the darker line shows the finished cannula. E and F are two pieces of glass tubing drawn out to make pens. They may be attached by pieces of cork to any writing apparatus. G is an aneurism-needle.

NARCOTISING ANIMALS.—Narcotics cannot be given in all cases to animals on which we experiment, as their action must to a certain extent complicate that of the drug which we wish to investigate. We cannot use them when we are observing what are the general symptoms which a medicine produces. But, when we are investigating its action on particular organs, we may often use them, not only with safety, but with advantage, when they have no action on the particular organ which we are studying, or so little that its disturbing influence is more than compensated by the diminished muscular action, and consequent ease in performing the experiment, which narcotics produce.

It is almost unnecessary to say that, in all cases which admit of it, narcotics should be used, as we have no right to inflict any unnecessary pain, although we may be justified in taking the lives of the lower animals in order to preserve the more valuable life of man, either by supplying him with food by means of those killed in the slaughter-house, or by obtaining the knowledge which shall enable us to cure disease by means of those killed in our experiments. The narcotics which we use are opium and chloral. Chloroform is inadmissible, as its administration generally seems to cause dogs more pain than the experiment itself, and rabbits are very easily killed by it.

A convenient form of giving chloral is a solution containing half a grain in 1 minim or 1 *gramme* in two cubic *centimètres* of water. The dose for a frog is 2 to 5 *centigrammes*, or about 1 to 5 drops. The dose for guinea-pigs is about 12 minims of this solution for an animal half a pound weight; and more or less may be given, according to the weight of the animal, 18 minims being given to one weighing three-quarters of a pound, and 24 to one weighing a pound. About the same proportion of dose to weight may be employed for rabbits.

Opium may be given in the form of laudanum, or of solution of acetate or hydrochlorate of morphia. Much as it is used, the proper dose for different animals has not been exactly determined. We do not often employ it to narcotise guinea-pigs or rabbits, but frequently for dogs. The dose for a medium sized dog is about 40 minims or 2½ cubic *centimètres* of laudanum, or 2 drachms of liquor morphiæ, which is equal to 1 grain or 5 *centigrammes* of morphia. This dose is for injection into a vein: when injected subcutaneously, rather more should be given. If the dog be above or below middle size, the dose must be proportionately increased or diminished. We must be careful not to give too much opium to old dogs, or they will die. Opium is preferred by some to morphia, as producing more certain narcosis, and being less likely to produce the excitement and hyperæsthesia which sometimes follow the administration of morphia.

When we wish to render the animal absolutely motionless, or to observe what effect any drug will produce after the motor nerves have been paralysed, we give curare. Small doses of this remarkable substance paralyse the motor nerves of muscles, but leave the vagi and vaso-motor nerves unaffected. Large doses of it seem also to cause paralysis of the vagi. It affects the blood-pressure to a certain extent, moderate doses contracting the vessels and raising the pressure, while large ones lower it. The dose of curare for a frog is about 1 to 5 drops or more of a solution of 1 part in 1000. The dose varies with the size of the frog and the purpose for which we wish it. If we wish to observe the circulation microscopically, we must not give too large a dose, or the heart may stop. To rabbits, ½ to 1 cubic *centimètre* or 8 to 15 minims, and to dogs, 4 to 6 cubic *centimètres* or 1 to 2 drachms, of such a solution, may be given.*

Definite rules cannot be laid down as to the experiments in which narcotics may or may not be used. The experimenter himself must judge in each case whether their action is likely to disturb that of the drug to be experimented on or not. For this purpose, he must know the action which the narcotics themselves produce; and I will, therefore, mention in a few words what that of each is.

ACTION OF NARCOTICS.—Chloral acts on the brain, producing deep sleep, during which there is no sensation or voluntary motion. The reflex function of the spinal cord is first increased and then diminished in frogs; in guinea-pigs and rabbits, it is diminished for thermal irritations, but not for tactile ones—pinching producing reflex action, but burning or pricking none. It leaves the motor nerves, vagus, and muscles unaffected; but diminishes the activity of the respiratory nervous centre, rendering the breathing slow; and of the cardiac ganglia, somewhat weakening the heart. It lessens the blood-pressure and temperature, probably by dilating the vessels at the surface as the ear of a rabbit becomes hot and its vessels dilated, while the general temperature is falling.

Opium is a mixture of several alkaloids, some of which are purely narcotic, while others produce tetanus, just like strychnia, and others partake of both characters. This is the case with morphia, in which, however, the narcotic qualities predominate. In small doses it first slightly increases, and then diminishes the irritability of motor and sensory nerves, and the reflex action of the cord, the irritability of the vagus (ends and central roots) and the musculo-motor apparatus of the heart, and the temperature. If the dose be large, those functions may be at once lessened. The blood-pressure varies, but is generally raised.

The advantage of giving either a narcotic or the drug to be investigated by injection into a vein rather than subcutaneously is, that the action is immediate, and we know that the whole of the dose has taken effect; whereas, after subcutaneous injection, a part may remain for some time in the cellular tissue before it enters the blood and becomes active. The most convenient vein is the external jugular. In dogs, however, it is sometimes more convenient to inject the narcotic into a vein which runs obliquely across the outside of the hind knee-joint. Before injecting, we must introduce a cannula into the vein; and the introduction of a cannula into a vessel is an operation on

* Curare may be obtained from Messrs. Hopkin and Williams, New Cavendish Street, London; or from Bruckner and Lampe.

the proper performance of which the success of many an experiment depends.

INTRODUCTION OF CANNULÆ INTO VESSELS.—First, the hair must be cleanly clipped or shaved away, and loose hairs removed by a moist sponge. The skin, subcutaneous cellular tissue, and cutaneous muscles, are divided with a scalpel, and any bleeding vessels are twisted or ligatured. If the vessel lie deep, the muscles are separated from each other by the finger of the operator, or by a blunt aneurism-needle, and any unyielding connective tissue may be cut by a pair of scissors. That surrounding the vessel itself should be separated from it by the aneurism needle. A closed pair of forceps may be pushed under the vessel and then opened. This both raises it from its bed, and lays bare a considerable part of its course. A couple of ligatures are now caught between the jaws of the forceps and drawn through. The proximal end of the exposed part of the vessel is now compressed by a pair of smooth-pointed bulldog-forceps, or a ligature laid in a simple slipknot; one ligature is firmly tied round the distal end, and the second ligature is tied in a loop round the middle, but is not drawn tight. A small piece of calling card, about an eighth of an inch broad, is then slipped under the vessel, so that it may rest on it and remain steady; its walls are then snipped by a sharp-pointed pair of scissors just on the distal side of the loop. The finder, or aneurism-needle, may be introduced so as to make the opening more distinct, and, if necessary, this may be enlarged by the points of the forceps being introduced, and then separated. One lip of the divided vessel is seized by the forceps, the cannula introduced, and the loop drawn tight over it so as to tie it firmly into the vessel. The cannula is then filled by a small glass pipette with the fluid to be injected, the syringe is fitted on, the bulldog forceps removed, and the requisite amount injected. The bulldogs are again put on, and the syringe removed.

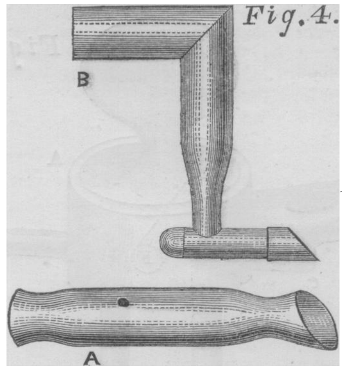
INJECTION OF FLUIDS INTO VESSELS.—First, we prepare the solution to be injected in a test or a watch-glass, and see that the syringe is in working order. The most convenient is one for subcutaneous injection, with a glass barrel and a graduated piston. On the piston-rod a small nut screws up and down, so that it can be set to any figure on the rod, and thus prevents it from being any further pushed in, so as to allow the exact amount required to be given at once, but prevent the accidental injection of more than this amount. The end of the barrel must either fit directly into a cannula of the shape shown in fig. 3 C, or it may be adapted to a glass cannula by tying a small piece of India-rubber tubing to the cannula. The cannula is then introduced into the vessel as already described. A fine pipette must be at hand, made by drawing a piece of glass tubing to a point, and by this the cannula, or cannulæ with the attached India-rubber tubing, must be carefully filled with the fluid, so that no air-bubbles remain. The syringe is then connected to it, the slip-knot of the ligature untied, or the bulldogs compressing the vessel in front of the cannula removed, and the necessary amount injected. The slip-knot is then re-tied, or the bulldogs replaced, if a second dose is to be given. If no more is to be injected, the vessel may be firmly ligatured.

DIVISION AND IRRITATION OF NERVES.—The nerve must be laid bare, and separated from the surrounding connective tissue in the same way as a vessel, especial care being taken never to seize the nerve itself with the forceps. Blood must be removed by a sponge squeezed quite dry, and the nerve must on no account be touched with water. If we wish to remove any adhering clot, or if the nerve happen to get dry through long exposure, it may be moistened with a little saliva or serum. A director is then pushed under the nerve, or we raise it up by a ligature passed below it, so as to secure the adjoining vessels from injury, and we then divide it by a pair of scissors. Very often we wish to have the nerve prepared for section some time before we actually divide it. We then pass the ligature under it and tie the two ends together, so as to prevent the ligature from being pulled from below the nerve, and thus form a loose loop by which we can at any moment raise and divide the nerve.

Nerves may be irritated by pinching, the application of strong saline solutions, or heat; but generally we use Pulvermacher's galvanic forceps, which are made of alternate wires of copper and zinc, and dipped in acetic acid, or, still oftener, the interrupted current from Du Bois Reymond's induction coil. The most convenient electrodes for this purpose consist of two wire points, about a quarter to half an inch long, and an eighth to a quarter of an inch apart. They may either be set in an ivory handle, or they may be simply fixed in a piece of glass tubing by means of cement or sealing-wax, or simply pushed through a piece of cork.

ARTIFICIAL RESPIRATION IN MAMMALS.—Artificial respiration is chiefly used to keep an animal alive after it has been poisoned with curare, for the purpose of rendering it perfectly still during an experiment; or after the thoracic cavity has been opened for observation or experiment on the viscera it contains. It is performed by introducing a cannula into the trachea, and inflating the lungs by means of a bellows connected with it by India-rubber tubing.

Fig. 4.



A is a glass cannula for artificial respiration, large enough for a small dog. A hole for the exit of expired air is seen in the side. B a metal one for a rabbit. The hole for expiration is at the top, and not visible in the figure. The lower part of the cannula can be turned round upon the upper at a joint about one-third of the way from the top, not marked in the figure. The tube which conveys air can thus be brought from the side instead of the front.

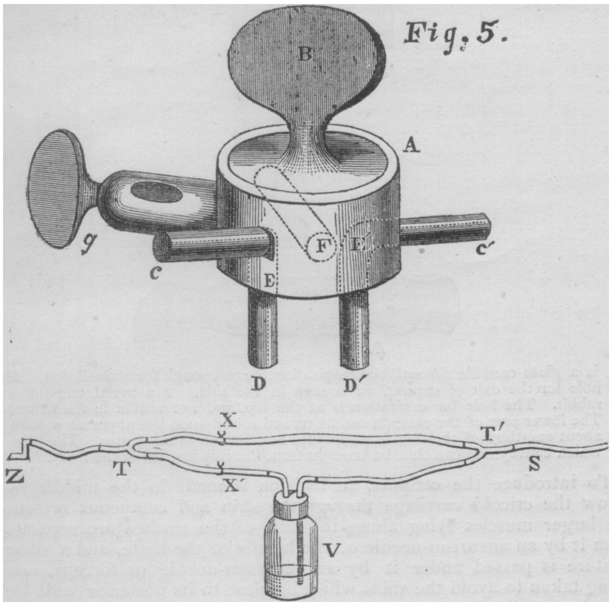
To introduce the cannula, an incision is made in the middle line below the cricoid cartilage through the skin and cutaneous muscles; the larger muscles lying along the side of the trachea are separated from it by an aneurism-needle or the handle of the knife, and a strong ligature is passed under it by an aneurism-needle or forceps, care being taken to avoid the veins which lie close to its posterior wall. A round or oval piece must then be cut out of the front of it by the scissors or knife, and the cannula introduced, and tied firmly in by the ligature.

When the knee-shaped metal cannula is used, it is advisable to push the heel of the cannula into the trachea, so that the tube lies quite in its lumen. After the cannula has been tied into the trachea, the ends of the ligature may be fastened round the upright bend of the knee, to ensure that it do not slip out. The bellows may be simply held in the hand, or fastened to the under side of a table by means of a piece of board screwed to its upper side and larger than the bellows itself, so that there is a rim of board all round. A few screws passed through this projecting rim into the under side of the table hold the bellows fast. A small pulley (one used for window-blinds will do) is then screwed into the under side of the table, and a cord passed over it. One end of the cord is fastened to a piece of board a foot and a half or two feet long, which serves as a treadle; and the other end to the under board of the bellows, so that it may be drawn up when the treadle is pressed down by the foot. A weight must be attached to the under board of the bellows, in order to draw it down again after it has been raised. The respiration is kept regular by depressing the treadle in accordance with the beat of a metronome set to beat the proper number in a minute.

The apparatus may be rendered more complete by the introduction between the bellows and trachea of a valve which will allow the air to pass readily towards the trachea, but hinder its return. Such a valve may be readily made by passing two pieces of glass tubing through the cork of a wide-mouthed bottle, and partially filling it with mercury or water. The tube nearest the bellows must descend nearly to the bottom of the bottle, while the other just passes through the cork. The air from the bellows passes easily through the mercury or water in which the end of one tube dips; but any attempt to return simply raises the mercury in the tube. If water be used, the tube must be longer, so that it may contain a column of water sufficiently high to afford the necessary resistance to the return of the air. This sort of valve is termed Müller's valve. (Fig. 5, V.)

ARTIFICIAL RESPIRATION IN THE FROG.—Although the frog can live perfectly well for some time without breathing, it may be desirable in some experiments to employ artificial respiration. A cannula for this purpose is best made by heating the end of a glass tube about one-eighth of an inch in diameter (more or less, according to the size of the frog), and then suddenly pressing it down on a metal plate, so that a broad rim is formed round the end. The sides of the larynx are seized by two artery forceps, the cannula introduced, and tied firmly in. A Richardson's spray-producer, from which the tubes have been removed, is then connected to it and used as a bellows.

INTRODUCTION OF GASES OR VAPOURS INTO THE LUNGS.—Gases or vapours may be introduced into the lungs either by simple inhalation or by artificial respiration. For the inhalation of a gas, a conical bag of oilskin, India-rubber, or bladder, must be made to fit the snout of the



animal, and connected with a bag, bladder, or gas-holder containing the gas. Or a tube may be put into the trachea and connected with the gas-holder.

For the inhalation of a vapour, a cone of strong paper or cardboard may be used, the wide end being put over the muzzle, and the liquid, the vapour of which is to be inhaled, dropped on a piece of blotting-paper and put on the small end. Or the whole cone may be made of blotting-paper.

Many different kinds of apparatus have been used for the artificial respiration of gases, among which may be mentioned the ingenious instrument of Thiry and the beautiful respiration-pump of Ludwig. The simplest method probably is to have the gas in a bag, connected by means of the bottle or Müller's valve with the tracheal cannula. The gas may then be forced into the lung at intervals, by alternately compressing and relaxing the bag.

Air may be loaded with vapour of any kind of fluid before it is sent into the lungs, by either mixing the fluid with the water in the bottle-valve, or by emptying out the water and putting a little of the fluid alone on the bottom of the bottle. Pure air or air loaded with vapour may be sent into the lungs alternately by the arrangement shown in fig. 5. A stream of air is sent from the bellows through the India-rubber tube S, and divided into two by the T-tube T′. When the clip X is removed, and X′ put on, the air passes straight through to the tracheal cannula Z. If X be now put on, and X′ removed, the air passes through V, and becomes loaded with the vapour of any fluid placed in the bottle.

The alternation may be effected still more rapidly and conveniently by a stopcock which I have had made for this purpose. Two tubes, C and C′, pass from its sides, and two others, D and D′, from its bottom. The interior is perforated with three holes. Two of these, E and E′, are L-shaped, and one (F) passes straight through from side to side. When the handle B is in a line with C and C′, their lumen corresponds with that of the hole F, and air passes straight through. When B is transverse, the hole E corresponds with C and D, and E′ with C or D′, so that air passing in through C′ passes down through D′, and may pass up through D and out at C. When B is neither in a line with C nor yet transverse, but half-way between, the holes in the interior do not correspond with those on the exterior of the stopcock, and no air can pass at all, and it may thus be used for experiments on asphyxia. When such experiments are made, the hole in the tracheal cannula must be carefully stopped with white wax. By means of the screw G the stopcock may be fastened to the rod E of the rabbit-hold in fig. I. The tubes D and D′ may either be attached by pieces of India-rubber tubing to tubes of a bottle such as V, or they may be themselves passed through the cork and a small piece of glass-tubing long enough to reach the bottom of the bottle attached to D′. By then simply turning the stopcock, pure air may be passed direct to the lungs through C′, F, and C, or it may be loaded with vapour by passing it through D′ into the bottle, and then up through D and C to the lungs.

THE PHYSIOLOGY AND PATHOLOGY OF THE CIRCULATION.

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Physician to King's College Hospital, etc.

In an able and interesting leading article on Blood-letting in the BRITISH MEDICAL JOURNAL of March 18th, with the greater part of which I entirely agree, reference is made to some recent observations of Messrs. Legros and Onimus on the influence of the arteries upon the circulation. The writer says: "The part of the circulation the most important to the life of the individual is probably the peristaltic wave, which carries on the blood in an even stream through the muscular arterioles, and which Messrs. Legros and Onimus describe as closely resembling the motions of the alimentary canal." So highly does the writer estimate the doctrines of these physiologists, that, after referring to the observations of Waller, Claude Bernard, and Brown-Séquard, he adds, "but, above all, those of Messrs. Legros and Onimus." The doctrines of Legros and Onimus are also expounded and accepted in an article on the Pathology of the Microscopic Arteries, in the last (April) number of the *British and Foreign Medico-Chirurgical Review*. The papers of the French physiologists are published in Robin's *Journal de l'Anatomie et de la Physiologie*, 1868. I have read them with great care; and not only do I find there no proof that the arteries, by a peristaltic contraction, exert a propulsive influence upon the blood, but I find it impossible to reconcile this hypothesis with the facts regarding the physiology of the circulation which have been established by the observations of Waller, Bernard, Brown-Séquard, Marey, and others.

Messrs. Legros and Onimus are not sufficiently careful to distinguish between the functions of the large elastic arteries and those of the microscopic muscular arterioles. The pulsating wave in the former is obvious and palpable, and it is explained by the action and reaction of the ventricular contraction and the arterial resiliency by which the intermitting rush of blood from the heart is gradually converted into a continuous stream in the small arteries and capillaries. This is the pulsation which Messrs. Legros and Onimus have seen without a lens in branches of the retinal artery and in the ear of the rabbit. The arteries that are large enough to be visible by the unaided eye are mainly elastic, and contain very little muscular tissue. If with a high power we watch the circulation in the web of the frog's foot, we see that the blood-current is equable, and continuous both in the capillaries and in the muscular arterioles. It may sometimes be seen that the impulse from the heart slightly distends the larger microscopic arteries. There is a slight dilatation of the arteries at each contraction of the heart. More commonly, however, the minute arteries remain of uniform size; there is no appearance of dilatation or contraction, and certainly there is no indication of a peristaltic contraction.

It is a well established fact that, in order that a muscular canal may drive on its contents in a definite direction, it must either be provided with valves, or it must contract in the form of a peristaltic wave, like the intestine. We know that the minute arteries have no valves; and we see in the transparent parts of animals that they do not contract peristaltically. It is obvious, therefore, that while, by their contraction, they regulate the blood-supply, they have no power to forcibly drive the blood onwards. This is the generally accepted doctrine, and it is not likely to be more than momentarily disturbed by the inexact observations and loose reasoning of Messrs. Legros and Onimus. These writers maintain that, if the muscular fibres in the arterial walls were intended merely to regulate the current of blood, they would be found most abundantly in the arteries near the heart; whereas, on the contrary, the most minute and distant arteries are notoriously the most muscular. Exactly so: for the obvious reason that the smallest arterioles alone can regulate the blood-supply to the capillaries of each particular tissue and organ.

As an illustration of their unsatisfactory method of dealing with well known phenomena, I will refer to two points. The characteristic pulse of aortic regurgitation—momentarily full, but quickly collapsing —which they inaccurately call "hard and strong", they explain by saying that "the arterial contractions tend to supplement the insufficiency of the cardiac contraction". This explanation is intended to replace that which is generally received, and which seems so simple and satisfactory—namely, that for a brief period the whole arterial system