done myself, in the effort to find such a substance, let me draw your attention to the remarkable fact that no therapeutical agent, no synthetic product of the laboratory, no poison, no drug is known which possesses the property of producing fever. The only liquids which have this endowment are liquids which either contain bacteria or have a marked proneness to their production.

Further, let me remind you that, whatever effort we may make to discover a disease-producing agent, we must take, both as our starting point and as our guide post, the one fact that we know about it, viz., its pathological action. For our problem is this. In a mixed liquid, we have reason to believe that a body exists which has the property of producing fever. Let us suppose that, by the use of appropriate chemical methods, we succeed in separating from it a crystalline principle which forms compounds of definite characters and constitution. To us this is of no value, unless it can be shown that the body so obtained contains the fever-producing property. Or let us suppose that a certain organic form is present, and that, by appropriate methods, we can determine its botanical characteristics, it is of no interest unless it can be proved that the form encloses the property. It was from forgetting this principle that Hallier, whose indefatigable labours as a botanical investigator of the forms of vegetation which he believed to associate themselves with diseased products were referred to in the last lecture, lost his way. He forgot that, in the investigation of morbid agents, pathological experiment and observation are the only safe guides. His results are valueless, not so much because the botanists say they are wrong botanically, but because he went on developing form out of form, without ascertaining as he went along, by repeated experiments, that the clue he was following was the right one.

Let me now return to my own experiments. I will not weary you by detailing the steps by which I was led to adopt my present method, but will content myself with reminding you that the purpose is (assuming that, in all probability, the pyrogenous is separable from what has been called the "phlogogenic" action of the material in question, viz., the septic extract of muscle) to effect this separation by obtaining the "pyrogen" in a convenient form.

The plan is as follows. The liquid is first precipitated by absolute alcohol. The precipitate is separated by decantation, again extracted with boiling alcohol, and then filtered. The residue, after having been freed from alcohol by placing it *in vacuo*, is extracted with distilled water. The water extract is at once filtered. It is a limpid liquid, which, on injection into the circulation, proves to be pyrogenous. It contains 1.2 per cent. of solids. The dose required to produce a characteristic access of fever in a moderate sized dog is five cubic centimetres, that is, three-quarters of a grain of solid matter.

From this experiment, two conclusions suggest themselves—1. That the agent, of whatever nature, is soluble in water, insoluble in strong alcohol; 2. That it cannot consist of bacteria, or have anything to do with them. Both of these conclusions would be erroneous; and this leads me to what I regard as the kernel of the experiment, viz.: We have an apparently homogeneous and transparent solution which is pyrogenous. Are its constituents really in solution? Is it really homogeneous? If I had not from other experiments learnt that no "animal poison" is really soluble, I should have answered the first question unhesitatingly, Yes. To test it, we apply a method first introduced into pathological investigation by Professor Klebs of Prague—namely, filtration under pressure through porous cells. By applying this method, I obtain a second filtrate. I test it physiologically, and find that it is not pyrogenic. Pyrogen, therefore, is a substance which passes through filtering paper, but not through porcelain. Further, I find, on microscopical examination, that the first filtrate, although at first it contains no bacteria, is not entirely free from particles; and, if I repeat the examination after an hour, bacteria are present in considerable numbers. If I examine the second filtrate in the same way, even twenty-four hours later, it remains barren. The porcelain has, therefore, removed from the liquid, along with the pyrogenous agent, that on which the development of bacteria depends.

We can scarcely overlook the bearing of these facts on the question of the mode of origin of bacteria; for, considering that bacteria in their ordinary state are destroyed, as Dr. Bastian and others have shown, at the temperature even of boiling alcohol, and that, without reference to temperature, they are inevitably killed by immersion in absolute alcohol, it is clear that our fever liquid as used contains no active bacteria. It is equally clear that it contains that particulate material out of which bacteria spring, for otherwise it could not be deprived of its fertility by filtration. It must, therefore, contain particles which, although they resist alcohol and heat, yet are endowed with a latent capacity of development. I may add that the existence of such particles has been inferred on other grounds by mycologists, who have compared their condition to that of the winter-spores (*Dauersporen*) of the fungi.

LECTURES

ON THE

EXPERIMENTAL INVESTIGATION OF THE ACTION OF MEDICINES.*

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VI.—RESPIRATION.

Position of the Respiratory Centre; chiefly situated in the Medulla Oblongata, but extends also to the Spinal Cord.—Effect of Strychnia upon it.—Influence of Nerves upon it.—Influence of Vagus.—Vagus contains two sets of Fibres, Accelerating or Inspiratory, and Retarding or Expiratory.—Cause of Rapid Breathing in Pneumonia.—Influence of the Superior and Inferior Laryngeal Nerves.—Nasal and Cutaneous Nerves.—Local Action of Vapours when inhaled.—Action of Ammonia.—Methods of Registering Respiratory Movements.—Acceleration of Respiration by Drugs.—Is it due to (1) Excitement of the Voluntary Nerve-Centres, (2) Increased Temperature, (3) Increased Venosity of the Blood?—Increased Venosity may be due to (A) Prevention of Blood from reaching the Air; (B) Prevention of Air from reaching the Blood. Blood may be prevented from reaching Air—(a) By Stoppage of the Heart: Action of Quinine.—(b) By Embolism of the Pulmonary Vessels; Action of Condurango.—(c) By Contraction of the Pulmonary Capillaries; Action of Muscarine.—Observation of the Pulmonary Capillaries in the Frog under the Microscope.—Effect of Heat and Cold upon them.

It used to be supposed that the respiratory centre was not only situated in the medulla oblongata, but was confined to it. Legallois found that the cerebral hemispheres, cerebellum, and even a part of the medulla itself, could be removed without arresting respiration; and thus showed that the respiratory centre was either in the medulla or in the spinal cord. (*Expériences sur la Principe de la Vie*. Paris, 1830, tome i.) Floreus noticed that injury to a point named by him *neud vital*, at the lower end of the calamus scriptorius, instantly arrested respiration, and thus caused death (*Comptes Rendus*, vol. xxxiii, page 437); and all experimenters have found that division of the cord just below the medulla also arrested breathing. These experiments seem to show most conclusively that the respiratory centre is situated in the medulla, and does not extend to the spinal cord; but the recent researches of Prokop Rokitsky (Stricker's *Medicinische Jahrbücher*, 1874, p. 30) on this subject show how careful we must be in drawing conclusions from experiments. Like all others, he has found that, under normal conditions, breathing ceases as soon as the influence of the medulla is destroyed by division of the cord just below it. But if strychnia be given to the animal, so as greatly to increase the excitability of its respiratory centres as well as of other reflex centres before the cord is divided, respiration will go on after the section has been made; and strychnia injected into the veins after the section will restore the respiratory movements, which the cut had arrested. This shows that the respiratory centre is not confined to the medulla, but extends into the spinal cord. The part contained in the cord is, however, too weak to keep up respiration alone under ordinary circumstances, though it can do so when its power is increased by strychnia. These remarkable effects of this poison give promise of future benefit from its use as a restorative in cases of death from drowning, etc.; but further experiments on animals are necessary before we dare employ such a powerful remedy in man.

Rokitsky's experiments enable us to demonstrate the presence of a respiratory centre in the spinal cord, as well as in the medulla of adult animals; but it is only fair to say that this was shown long ago by Brown-Séquard in the case of young ones. In young mammals and adult birds, he found that the thorax continued to execute rhythmical

* The request of a correspondent for a reference to Hering's experiments has, fortunately, directed my attention to a mistake of some importance in my last lecture. I there stated that Hering found that respiratory movements ceased when arterialised blood was passed through the head and venous blood through the body; while, on the contrary, apyrexial convulsions took place when venous blood was passed through the head and arterial blood through the body. I ought to have said that movements occurred in the blood-vessels such as would have taken place had the same sort of blood which circulated through the brain been passing also through the body. The experiments, however, were made on curarised animals, so that respiratory movements were impossible. Hering had previously ascertained that the arterial movements were synchronous with the respiratory movements, and might, indeed, be regarded as caused by impulses proceeding from the respiratory centre. They might thus serve as indications of the condition of the centre, where respiratory movements had been paralysed by curara. This paper is to be found in the *Wiener Acad. Sitzungs-ber., Math.-naturw. Classe*, vol. ix, Abth. 2, pp. 829-856.

respiratory movements for a short time after the cord had been divided transversely at the level of the first or second pairs of cervical nerves, so that there must needs be a part of the respiratory centre in the cord below that level (*Journal de la Physiologie*, vol. i, 1858, p. 223, and vol. iii, 1860, p. 153). Besides this, he considers that there are what we may term peripheral respiratory centres—viz., ganglia in the substance of the diaphragm itself analogous to those in the heart, which enable it to contract rhythmically after its connections both with the medulla oblongata and with the spinal cord have been destroyed (*op. cit.*, vol. ii, 1859, p. 115).

Although the excitement of the respiratory centre and the amount of work done by the respiratory muscles depend on the venosity of the blood in the medulla oblongata, yet this work may be differently distributed by the respirations becoming quicker but shallower, or slower but deeper, without the quantity of air respired being at all altered. This is effected by the action of various afferent nerves, of which the chief are the vagus, the superior laryngeal, and the nasal nerves; though others, such as the cutaneous nerves generally, have considerable influence.

Irritation of the vagus, or of its central end when divided, lessens the resistance in the respiratory centre, and quickens the respiration, but makes it shallower. Stronger irritation causes prolongation of inspiration. A very strong excitation annihilates the resistance in the centre, and causes inspiration to be almost indefinitely prolonged, so that the breathing is completely arrested.

The ends of the vagi in the lung are normally in a state of constant excitation, and therefore division of these nerves renders the respiration slow.

Irritation of the vagi, on the contrary, causes, as we have said, considerable acceleration of the respiration; and the quick breathing which we observe in pneumonia is probably due to the irritation of the pulmonary branches of the vagus which the inflammation produces. It can hardly be caused by the venous condition of the blood alone, nor yet by increased temperature; for the blood may be very much more venous in bad bronchitis, and the temperature higher in fever, without the respiration becoming anything like so rapid as in a case of pneumonia. But, although I thus speak of the vagus as an inspiratory or

and expiratory fibres, although the former predominate. (Hering and Breuer, *Wiener Acad. Sitzungs-ber. Math.-Naturwiss. Cl.* vol. lvii, Abt. 2, page 672.) The inspiratory fibres are excited by collapse, and the expiratory fibres by distension, of the lung. Thus, these nerves form a sort of regulating mechanism for the respiratory movements. As soon as a deep inspiration is taken, the distension of the lungs excites the expiratory fibres, and leads to the consequent expulsion of the air; as soon as expiration takes place, the collapse of the lungs excites the inspiratory fibres, and thus leads to renewed inspiration.

As the effect of irritating other nerves as well as the vagus is not always alike (Bert, *Leçons sur la Respiration*, page 490), it is probable that the laryngeal, nasal, and cutaneous nerves, may also contain both inspiratory and expiratory fibres. It has already been mentioned, that the accelerating fibres of the vagus in the lungs are probably irritated in pneumonia, but in bronchitis the expiratory ones are chiefly irritated, and give rise to the expiratory efforts in coughing, which serve to expel any irritating substance in the bronchi. When these fibres are exhausted, or the respiratory centre is feeble or irresponsive, the mucus will remain, and consequently strychnia suggests itself as an auxiliary in such cases. If the irritation depend on something which cannot be removed by coughing, such as miliary tubercle, we employ opium, chloral, etc., which lessen the excitability of the respiratory centre.

Moderate irritation of the superior laryngeal nerve renders the respirations slower but deeper; a stronger irritation prolongs expiration; and a very strong one causes the respiration to stop entirely in the state of expiration (Rosenthal, *Athembewegungen*, p. 244) until the increasing venosity of the blood greatly stimulates the respiratory centre, and causes respiration again to commence.

Irritation of the inferior laryngeal nerve (Burkart, *Pflüger's Arch.*, vol. i, p. 107), and of the supramaxillary (Kratschmer, *Sitzungs-ber. der Wien. Acad., Math.-Nat. Cl.* 1870, vol. lxii, Abt. 2, p. 24), and nasal branches of the fifth nerve, acts in a similar way to irritation of the superior laryngeal nerve, as well as irritation of the cutaneous nerves generally, and especially of those of the face and chest. (Schiff, *Compt. rend.*, 1861.)

We have then to find out whether the alteration in respiration produced by any drug is due to its action on the respiratory centre, or on some of the nerves which influence it; and the following table may help us to do so more readily, by showing at a glance the chief ways in which the respirations may be accelerated or retarded.

The respiratory movements may be quickened by	Excitement of nerves.	Increased irritation of the vagus. By action of voluntary centre. Increased temperature of blood. Increased venosity of blood. Action of drugs.
	Greater excitement of resp. centre.	
The respiratory movements may be rendered slow by	Diminished excitement of respiratory centre.	Diminished venosity of blood. Action of drugs.
	Nervous influences	Slight irritation of cutaneous nerves. Action of voluntary centre. Paralysis of vagi. Irritation of superior laryngeal nerves. Irritation of inferior laryngeal nerves. Irritation of nasal nerves.

If the drug to be experimented on be injected subcutaneously or into the veins, the actions on the respiratory centre and on the vagi are the chief points which require attention; but if we are experimenting with a vapour, its local action on the nasal, laryngeal, and possibly, also, on the pharyngeal nerves (Brown-Séquard, *Archives of Scientific and Practical Medicine*, p. 94) must be carefully attended to, as it may greatly modify its general action on the respiratory centres. Thus Kratschmer has found (*op. cit.*) that tobacco-smoke inhaled by a rabbit through its nostrils, or blown upwards into the nasal cavity from an aperture in the trachea, will cause arrest of breathing in a state of expiration from the irritating effect of the vapour on the nasal branches of the fifth, while it has no such effect when blown into the lungs. Ammonia, when inhaled, also arrests the respiratory movements in the same way; but Knoll (*Sitzungs-ber. der Wien. Acad.*, vol. lxviii, Abt. 3, p. 255) has observed that, if it be blown into the lungs, while the nostrils are carefully protected from its influence, it causes accelerated and shallow breathing, alternating with slow and deep respirations, and occasional stoppages in the position of expiration, obviously from its action on the different fibres of the vagi. When injected into the blood, it causes, according to Funke (*Pflüger's Archiv*, vol. ix, p. 436) various alterations in the respiration, which are not easy to analyse, but it

Fig. 1.—Diagram showing the position of respiratory centre, and the afferent nerves which influence it. Inspiratory nerves are indicated by plain, and expiratory by dotted, lines.

A. Inspiratory and Expiratory Fibres for voluntary alterations in Respiration.	F. Larynx.
B. Cutaneous Nerves of Face.	H. Expiratory Fibres of Vagus excited by distension of Lung.
C. Nasal Branch of Fifth Nerve.	I. Inspiratory Fibres of Vagus excited by collapse of Lung.
D. Superior Laryngeal Nerve.	K. Respiratory Centre in Medulla and Cord.
E. Inferior Laryngeal Nerve.	L. Spinal Cord.
G. Cutaneous Nerves of the Chest.	
- } chiefly expiratory.

accelerating nerve alone, I do this only for the sake of simplicity, as this is its chief function. It really contains, however, both inspiratory

certainly seems to excite the respiratory centre; and the use of carbonate of ammonia in bronchitis has long been familiar to the medical profession.

The movements of respiration are not only more easily counted than in any other way, but their depth, and the relation of inspiration to expiration, best noted by causing them to register themselves on a revolving cylinder. Various means of doing this have been suggested by different authors. One of the simplest consists of a needle pushed into the diaphragm, and connected by a thread with one of Marey's levers (see Fig. 2). Marey's pneumograph consists of a cylin-

Fig. 2.—Method of registering respiration. A is the lever of Marey's registering apparatus; B is a hollow drum, with open tube below, and covered at the top with a piece of thin caoutchouc, on which rests a tin plate connected with the lever A. When the air is blown into B, the caoutchouc is lifted, and the lever rises. When air is drawn out, the caoutchouc sinks, and the lever falls. The tube of B may be connected by India-rubber tubing with the respiratory passages in several ways. C is a T-tube, open at one end and connected at the other with a cannula (D), which is placed in the trachea of the animal and brought into communication by its upright limb with B. Instead of D, an India-rubber catheter may be placed in the animal's nostril. E is a caoutchouc-bag, which is tied over the animal's muzzle and used instead of the tracheal cannula. F is a large vessel, from which two tubes (G and H) proceed. G is connected with the lever B, and H with the respiratory passages of the animal. I is a needle, which is simply connected with the lever by a thread: when pushed into the diaphragm, it registers the respirations.

der of soft India-rubber, enclosing a spiral spring, whose extremities are connected with two pieces of metal which form the ends of the cylinder. A band is passed round the thorax of the animal, and attached to the ends of the cylinder. The interior of the cylinder is brought into communication with one of Marey's levers; and as each respiratory movement draws the ends of the cylinders wider apart, or allows them to approach, the air is rarefied or compressed, and a corresponding movement is transmitted to the lever. Bert has modified this, and made it more sensitive by making the cylinder itself of metal, and its ends of India-rubber. Another method—one more ordinarily employed—is to introduce one limb of a T-tube into the nostril or trachea of an animal, or to connect it with a tracheal cannula. The respired air passes through the other end, and the third limb is connected with one of Marey's levers.

IS QUICKENING OF RESPIRATION DUE TO IRRITATION OF THE VAGI?—When the respiratory movements become quickened by the injection of a drug into the circulation, the first cause to which it may be due, mentioned in the preceding table, is irritation of the ends of the vagus in the lung. In order to discover whether this be the cause or not, the vagi must first be divided and the drug injected. If it act only on the ends of the vagus, the respiration which was quickened by injection when the vagi were intact, will not be quickened by it when these nerves are divided.

IS THE QUICKENING DUE TO EXCITEMENT OF THE VOLUNTARY NERVOUS CENTRES?—This cause of quickening is eliminated by narcotising the animal with opium or chloral, or by removing the cerebrum. For the method of doing this, see Sanderson, *Handbook for the Physiological Laboratory*, page 295.

IS IT DUE TO INCREASED TEMPERATURE?—If the temperature of the animal have risen above the normal—the fact can readily be ascertained by the thermometer—it may then be reduced by the application of cold water or ice, or by a stream of cold air directed on the surface of the skin. Unless the cooling be effected very gradually, these applications cause reflex disturbance of the respiratory movements through the cutaneous nerves.

IS IT DUE TO INCREASED VENOSITY OF THE BLOOD?—The drug

may produce this by its action on the blood; and this is to be determined by the means already described. Generally we let a little blood issue from an artery; and if its colour be of normal brightness, we conclude that the gases it contains are also normal.

But external respiration may be arrested or diminished, the blood rendered venous, the respiratory movements consequently increased, and dyspnoea and asphyxia produced by preventing the blood from reaching the air, as well as by preventing the air from reaching the blood. The blood may be prevented from coming into relation with the air: (a) By stoppage of the heart; (b) By embolism of the pulmonary artery; (c) By contraction of the capillaries of the lung.

(a) BY STOPPAGE OF THE HEART.—When respiration is suddenly impeded in any of these ways, the breathing becomes panting; and when it is suddenly stopped altogether, asphyxial convulsions occur. When the jugular vein is chosen for the introduction of drugs into the circulation, they come very quickly and without much previous dilution with blood into contact with the heart and pulmonary vessels, and thus affect them more strongly than they would do if injected subcutaneously, or into one of the veins of the extremities. When a large dose of quinine is thus injected, the heart may be stopped at once, and convulsions ensue. Any alteration of the heart's action produced by a drug is easily noted by means of a needle fixed in the ventricle.

(b) BY EMBOLISM OF THE PULMONARY ARTERY.—This cause of interrupted respiration may easily lead an inexperienced observer to very erroneous conclusions regarding the action of a drug. Supposing him to inject an unfiltered solution of some extract into the jugular vein, he may find the respiration almost immediately afterwards become panting; the eyes start from their orbits, the limbs become convulsed, the head drawn back, and after one or two quivering contractions, life becomes extinct. He at once concludes that the substance he has injected is one of extreme activity, whereas it may be really quite inert; the violent symptoms which followed its injection being due to the extract being imperfectly dissolved, and the suspended particles producing emboli in the pulmonary vessels.

In some experiments which I made on *condurango*, I was at first misled by this circumstance, and believed that the drug had a tetanising action, like that of strychnia, as convulsions came on immediately after injecting a solution of the extract into the jugular vein. The same mistake has probably been made by Giannuzzi,* who attributes a convulsive action to the drug. By injecting the solution into the peritoneal cavity, however, I found that it had no action whatever even when used in large quantities, while a solution of strychnia applied in the same manner would have acted nearly as strongly as when injected into a vein.

(c) BY CONTRACTION OF THE PULMONARY CAPILLARIES.—When contraction of the pulmonary capillaries is produced by a drug injected into the veins, the venous blood is hindered from reaching the left side of the heart, and the left ventricle and arterial system become empty, and the arterial pressure sinks while the right ventricle and venous system become swollen and turgid. The alteration of the blood-pressure in the arterial and venous systems may be measured by manometers connected with them; but while the arterial fall in the pressure is easily observed, there is considerable difficulty in measuring that in the veins, due to the rapid formation of coagula in the tube which is pushed down the jugular vein into the vena cava.

Another method is, to open the thorax and note the colour of the lungs and the comparative fullness of the right and left sides of the heart, and of the venous trunks, before and after injection of the drug. The animal is first narcotised, and a cannula placed in the trachea. The skin and cellular tissue are then divided along the middle of the sternum and reflected on each side. The muscles are then divided along the line of the costal cartilages, and artificial respiration is begun. The abdominal muscles are then separated from their attachment to the sternum and costal cartilages; the latter are cut through, except the first, which is left untouched in order to avoid wounding the internal mammary artery, and the sternum is bent upwards and retained in its position by a hook. In the rabbit, it is generally unnecessary to tie any vessels, as the bleeding stops quickly of itself; but if any one should bleed much, it ought to be laid hold of and ligatured. Artificial respiration being carefully and regularly kept up by means of a metronome, the colour of the lungs, the size of each ventricle, and the number of cardiac pulsations is observed, the drug injected, and the observation repeated. The pulsations must be counted, because slowness of the heart's action, by affording time for the accumulation of venous blood in the right ventricle, would cause it to become distended, although there were no obstruction to the pulmonary circula-

* Giannuzzi and Bufalini, *Ricerche eseguite nel Gabinetto di Fisiologia della Università di Siena*, pp. 71-86; abstracted in the *Centralblatt für die Med. Wiss.*, 1873, p. 824.

tion. When the drug to be experimented on is not a solution but a vapour, it must be passed into the lungs by the method already described (BRITISH MEDICAL JOURNAL, May 20th, 1871).

In this way, I have found that muscarin causes contraction of the pulmonary vessels, and produces dyspnoea (see BRITISH MEDICAL JOURNAL, November 14th, 1874), although the heart continues to beat, and artificial respiration is vigorously kept up. The lungs become pale, the right side of the heart swells up, and the left side and arteries become empty, as represented diagrammatically in Fig. 4.

Fig. 3.

Fig. 3.—Diagram representing the normal condition of the circulation. Both the veins and arteries are moderately full: the two sides of the heart are of much the same size, and the circulation through the lungs is free.

Fig. 4.

Fig. 4.—Diagram representing the condition of the circulation after the administration of muscarine. The veins are distended, the arteries empty; the right side of the heart is much enlarged, the left side collapsed, and the circulation through the lungs almost entirely arrested.

The vapour of chloroform blown into the lungs causes a similar appearance, but it arrests the cardiac pulsations more or less completely at the same time.

The action of drugs on the pulmonary capillaries in the frog may be observed directly by means of the microscope. A frog is curarised, and a glass cannula, to which a short piece of India-rubber tubing is attached, is tied into its larynx. An incision is then made into the side of the frog a little below the arm, care being taken not to injure the lung in dividing the thoracic wall; and, the lungs being inflated through the cannula, one of them protrudes through the opening. The piece of India-rubber at the end of the cannula must then be clamped, so as to prevent the air from escaping and the lung from collapsing (Fig. 5).

Fig. 5.—Form of tube for insertion into the larynx of the frog. It is made by drawing out a piece of tubing to the size marked *a*, heating the end and pressing it against a piece of metal, so that it assumes the shape *b*. *c* is a piece of India-rubber tubing, which must be closed, either by a ligature, as shown in the drawing, or, what is still better, by a clip, so as to prevent the escape of air from the lung.

The whole frog is then placed on a glass plate, which is fixed with a clip to the stage of the microscope. The lung is brought under the objective, and supported, if necessary, by a cork ring fixed to the glass plate with sealing-wax. Any changes in the calibre of the pulmonary vessels are then readily observed by means of a micrometer placed in the eye-piece.

Four years ago, I attempted to ascertain by this method the effect of sudden changes from heat to cold on the lungs; and I have found that, if a stream of warm moist air be first directed on the lung, and immediately afterwards a stream of cold moist air, the capillaries sometimes contract as much as one-third of their diameter under the influence of the cold.

Dr. Sharpey informs me that the lung of the toad, unlike that of the frog, does not collapse even when no obstruction is offered to the escape of air; and therefore, if toads be used, the India-rubber tube and clamp on the cannula are unnecessary.

THE LATE DR. PICKFORD.—At the annual general meeting of the Brighton and Sussex Infirmary for Diseases of the Eye, the following resolution was passed. "That the Governors of this Charity desire to offer to Mrs. Pickford their sincere expression of condolence in the loss of her late husband, Dr. J. H. Pickford, to whose exertions the Charity mainly owes its foundation, and who, during a period of more than forty years, exerted his best interest in its behalf."

REMARKS ON THE LOCAL USE OF LIQUOR FERRI PERCHLORIDI IN CANCEROUS ULCERATIONS OF THE UTERUS.*

By CHARLES J. GIBB, M.D.,

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CANCEROUS diseases of the uterus have generally progressed so far before they come under professional observation, as to pass as incurable from one medical man to another, and it thus happens that I see a large number in my consulting-rooms. It is rare to find the disease so superficial and purely epithelial in character, or, if interstitial, so confined to the mouth and neck of the uterus, that the diagnosis can be made with such certainty as to justify the surgeon in excising it; and, in the advanced stages, the foul discharges make the patient so loathsome, that, in spite of the keenest feelings of pity, the surgeon is inclined to view the case as utterly hopeless, and to leave all manual treatment to the nurse. When we remember how much relief can be given to the worst symptoms of the most incurable cases of external cancer by operation, or by other measures calculated to remove fungoid or sloughing surfaces or masses of the disease; how pain can thus be relieved; bleedings prevented; foul discharge moderated or made less disgusting in character,—it is not surprising that surgeons should strive to give similar relief to the worst cases of cancer of the womb, and be more or less successful in their efforts. From time to time, I have tried the various local applications I have seen recommended; have made use of many caustics; have been taught by painful experience that caustic potash, or caustic potash and lime, are unmanageable, and too dangerous to the surrounding parts to be used with the freedom requisite to be of service; that the actual cautery is too fear-inspiring; that nitric acid or acid nitrate of mercury (which had to be used with great care) are inefficient; and that lunar caustic and powders or points of zinc or alum are useless as caustics.

About two years ago, I had occasion to dilate the uterus in a very obstinate case of menorrhagia proceeding from large vascular granulations in the cavity of the enlarged organ. The strongest pharmacopoeial solution of the perchloride of iron (being in fact iron dissolved in pure acid) was injected into the open uterine cavity, and a piece of sponge soaked in the solution left there for twenty-four hours. This treatment was perfectly successful, and I viewed with surprise the efficient way in which the soft and vascular growths were destroyed, while the normal structures of the uterus and vagina were but little inconvenienced, and certainly not in the least eroded. Since that time, I have been accustomed to use this solution in many cases of cancer of the uterus; and, having promised our secretary to read a few notes at this meeting regarding its usefulness in my hands, I jotted down the histories of the following four cases, being the cases of cancer in which I used it in my consulting-rooms during the week succeeding the day I made that promise.

CASE I.—Mrs. B., aged 36, a shopkeeper, married five years, without children, was a strong powerful woman until fourteen months ago, when she was seized with menorrhagia, followed by the foul sanious discharges and other symptoms of cancerous ulceration. She came to my office six weeks ago, anæmic to the last degree, from almost constant hæmorrhage and putrid discharge. On examination, the mouth and neck of the uterus were found destroyed, and their place occupied by a large, deep, sloughing, cancerous sore. The body of the uterus felt greatly enlarged, and as hard as a cricket-ball, whilst the vagina was quite free from disease. Profuse hæmorrhage attended the examination. The sore was filled with cotton-wool soaked in the solution of the perchloride, and the vagina stuffed with tow. She came from a distance by rail, and was ordered to remove with her fingers, or allow the lady who accompanied her to withdraw, the stuffing of tow next morning, and trust to the injections of zinc and alum to wash away the cotton-wool; and appropriate blood-making and aperient medicines were prescribed. On her second visit, she expressed herself as much stronger, very little bleeding having taken place during the week. The application of the perchloride was repeated; and I did not see her for the next ten days, in consequence of a severe pain compelling her to remain in bed. The sore was much healthier in appearance; there had been very little bleeding, and the discharge had become scanty and semipurulent in appearance, without any of the old putrid smell. She was, however, very feeble, and made the journey with great difficulty. Instead of placing the cotton-wool soaked in the perchloride over the sore, I elevated her breech, half filled the vagina with the solution for a couple of minutes, then sucked it up with a syringe and left a plug of tow in the vagina, to be removed next day. The improvement was

* Read before the Northumberland and Durham Medical Society.