heart and other evidence of obstructed pulmonary circulation, the life of the animal is prolonged for several minutes, and death ultimately results from the influence of venous blood upon the cardiac and nervous tissues.

THE ANÆSTHETIC ACTION OF NITROGEN ALONE OR WITH A SMALL PROPORTION OF OXYGEN.

The phenomena which result from the inhalation of nitrous oxide as an anæsthetic are strictly analogous with those observed in the early stages of asphyxia.*

Some writers maintain that the anæsthetic action of nitrous oxide is due to its preventing access of free oxygen to the system, others believe that it has a specific anæsthetic action. It occurred to me that light might be thrown upon this subject by the administration of pure nitrogen. Accordingly I obtained from the Scotch and Irish Oxygen Company, of Glasgow, a cylinder containing 100 cubic feet of compressed nitrogen in which the proportion of oxygen was only 0.5 per cent. by vol., whilst that of the CO₂ present was 0.3 per cent. As a preliminary trial, Mr. F. W. Braine was good enough to administer this gas in five instances to members of the staff of King's College, who volunteered to inhale it.

The result was, in each case, the production of complete anæsthesia and of general phenomena precisely similar to those observed from the inhalation of nitrous oxide. Encouraged by these results, Mr. Braine felt justified in administering the gas to patients at the Dental Hospital. Nine patients took the gas. In every case, the result was the production of complete anæsthesia, with general phenomena precisely similar to those observed during nitrous oxide inhalation. The pulse was first full and throbbing, then feeble; in the advanced stage respiration was deep and rapid, with lividity of the surface, dilated pupils, and more or less jactitation of the limbs; the only difference, in the opinion of some of those present, being that the anæsthesia was less rapidly produced, and somewhat less durable than that from nitrous oxide, though in each case the tooth was extracted without pain.

On a subsequent occasion, the same gas was administered by Dr. Frederic Hewitt at the Dental Hospital. Nine patients took the gas. The maximum period required to produce anæsthesia was 70 seconds, the minimum 50 seconds, and the mean time 58.3 seconds.

In one case two teeth were extracted without pain; in one only was pain experienced, and in that case, the tooth having been broken and not extracted, the patient said she felt a "smashing up."

I subsequently obtained from the same company a cylinder containing compressed nitrogen with 3 per cent. of oxygen, and a second cylinder containing nitrogen with 5 per cent. of oxygen. These gases were also administered by Dr. Hewitt to patients at the Dental Hospital, with the following results:

Five patients took the 3 per cent. gas. Anæsthesia was complete in 75 seconds (max.) and in 60 seconds (min.), the average time required being 67.5 seconds. In each case the tooth was extracted without pain, the duration of anæsthesia being somewhat longer than with pure nitrogen. In each case there was lividity, dilatation of pupils, and more or less jactitation. Four patients took the nitrogen containing 5 per cent. of oxygen. With this mixture the time required for the production of anæsthesia ranged from 75 to 95 seconds, the average time being 87.5 seconds. In each case there was complete anæsthesia, during which one patient had three molars extracted. Although she said she felt the last two, the sensation appeared to be that of a pull and not of acute pain. In most of these four cases there was slight lividity before the removal of the face piece. In only one case was there slight jactitation of the limbs; the other three patients were perfectly quiescent.

For the information of those who may be disposed to investigate the anæsthetic action of nitrogen with a small proportion of oxygen, I may mention that Brin's Oxygen Company, 69, Horseferry Road, Westminster, are prepared to supply nitrogen containing from 4 to 7 per cent. of oxygen at the same rate as they charge for pure oxygen. Below 4 per cent. of oxygen nitrogen could be supplied only by special arrangement, and probably at increased cost.

* *vide* the author's "Essay on Asphyxia," p. 30.

ON THE CHEMICAL PROPERTIES AND PHYSIOLOGICAL EFFECTS OF THE PRODUCTS OF THE TUBERCLE BACILLUS IN PURE CULTIVATIONS.

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E. F. HERROUN,

Fellow of the Institute of Chemistry.

(*Preliminary Communication to the Physiological Society, February 14th, 1891.*)

DURING the past year one of us has confirmed the experiments of Nocard and Roux with regard to the cultivation of the tubercle bacillus on glycerine agar-agar, and in liquid media both with and without glycerine. Having succeeded in obtaining such cultivations in liquid media in quantity, we were in a position to study the products after removal of the bacilli. We proceeded on a line of research which has been engaging the attention of bacteriologists for some years. In 1886-87, Salmon, in America, produced immunity from hog cholera by the injection of the filtered culture fluids. Later, Charrin, Woodhead and Wood, and Blagovestchensky studied the products of bacillus pyocyaneus. In a similar way Roux and Chamberland investigated malignant oedema; Roux, symptomatic anthrax; Chantemesse and Widal, typhoid fever; and Roux and Yersin, Brieger and Fraenkel, diphtheria. In our own country, Wooldridge, Hankin, and Martin have investigated the products of the growth of the anthrax bacillus.

We filtered our cultures of the tubercle bacillus through porcelain, and obtained on December 5th a clear amber-coloured liquid, which gave important and suggestive chemical reactions. As this filtrate contained the products of the growth of the bacillus, most probably in minute quantities, we evaporated it at a low temperature over sulphuric acid. We obtained after some weeks (January 12th) a viscous residue, which was dissolved in distilled water and tested on the healthy guinea-pig. The result was a marked fall of temperature, staring coat, extreme irregularity of the heart's action, muscular spasms, loss of control over the extremities, and death.

With the cultures in glycerine broth, which we now possessed in considerable bulk, we next proceeded to isolate pure materials, and to determine their chemical properties, their physiological effects, and, if possible, their chemical constitution. We were stimulated in our endeavour to obtain pure substances from the crude extract by Koch's announcement three days after our experimental inoculation of the toxic extract, that the substance or substances which he had found to produce remarkable phenomena in lupus and tuberculosis had been obtained from a glycerine extract of pure cultivations of the tubercle bacillus.

A preliminary examination of our glycerine-broth cultivations having shown the presence of non-coagulable proteid bodies of the nature of albumose and peptone, and a crystallisable precipitate of a remarkable character resulting on the addition of iodine, the idea naturally suggested itself that the tubercle bacillus might form albumoses and an alkaloid or ptomaine similar to the substances isolated by Martin from pure cultivations of the anthrax bacillus.

Koch, after pointing out that the effective substance in his extract could be precipitated by absolute alcohol, states that "for application in practice, however, this purification of the glycerine extract offers no advantage." This seemed to indicate that he regarded the isolation of the active material in a pure state as superfluous. It appeared to us, however, to be a matter of great scientific interest to determine, if possible, the properties and physiological effects of the separated products. We accordingly set to work to isolate the ptomaine, of the existence of which we had some qualitative indication, and at the same time to examine the properties of the albuminous bodies.

In this endeavour the general method we found satisfactory was as follows:—The clear filtrate from the culture was

evaporated at 40° C. to a very small bulk, and the residue thus obtained was mixed with an excess of absolute alcohol, which precipitates the albumoses and peptones. It was found that by adding the alcohol by degrees a partial separation of the albumose from the peptone could be effected, the latter being only precipitated when the alcohol was nearly absolute. The precipitated albumose was collected on a filter, and redissolved in distilled water. In another experiment the albumose underwent a second precipitation, and after washing was again dissolved. The alcoholic filtrate from the precipitated albuminous bodies was then concentrated at a very gentle heat until a viscous residue was left containing the glycerine originally present in the cultivating medium and the extractives and products of the bacillus soluble in alcohol. With the residue definite reactions of an alkaloidal substance or ptomaine were obtained. Careful experiments, however, led us to believe that the whole of the ptomaine was not separated from the albuminous precipitate by simple addition of alcohol, and we have therefore been led to slightly modify the above method.

By Scheibler's method applied to the alcoholic residue it was found possible to separate the ptomaine and to obtain a solution of it free from glycerine and other matters; but the quantity thus treated up to the present time has been so small that only a few qualitative tests could be applied, and as these agreed with those given by the alcoholic residue, they will be described as referring to both.

The ptomaine is soluble in water and alcohol, and sparingly soluble in amyl-alcohol, but insoluble in benzene, ether, or chloroform, which liquids, therefore, fail to extract it from aqueous solutions. In its aqueous solutions it is distinctly but not strongly alkaline to test paper. Phosphotungstic acid gives with it a white flocculent precipitate. Phosphomolybdic acid gives a pale yellow precipitate, soluble in ammonia to a blue solution, which becomes colourless on boiling. In this respect it resembles the vegetable alkaloids, aconitine and atropine. (It must be remembered, however, that albuminous bodies are precipitated by both this and the preceding reagents, and in the case of the latter a reduction of the phosphomolybdate, giving the blue solution with ammonia, is obtained.)

The reducing power of the ptomaine is shown by the conversion after a short time of ferricyanide of potassium to ferrocyanide, giving the prussian blue test with ferric chloride, to which much undue importance was attached by Brouardel and Boutmy. A solution of albumose and a solution of peptone are both capable of giving this reaction as well as many vegetable alkaloids.

A solution of the ptomaine is not precipitated by ferrocyanide of potassium or potassic bichromate. In strong solutions it yields precipitates with platinic chloride (yellow), gold chloride (pale yellow), and mercuric chloride (white). That yielded by the first of these reagents is granular in character and quite insoluble in alcohol, though apparently soluble in water. It is hoped that this compound, if obtained in quantity, might be made to yield quantitative results as to its composition. The precipitation by gold chloride excludes amides and ammonium salts.

With iodine in hydriodic acid or potassic iodide, a precipitate is obtained which is occasionally crystalline, more often granular or amorphous. This precipitate is soluble in alcohol, and is redeposited when the alcohol is evaporated. On heating it is converted into oily drops of a dark colour. With picric acid a granular precipitate is obtained which, under the microscope, is seen to consist of minute crystals. This precipitate on standing is converted into rounded crystalline masses with numerous small crystals admixed.

The ptomaine appears to be easily broken up by heating, especially in the presence of mineral acids or of baryta. The actual quantity obtained from a considerable amount of culture-fluid was very small; and thinking that if the bacillus were grown in a medium richer in albumin, such as the animal body, more of these products might be formed, we examined in a similar manner the liquid obtained by extracting large masses of tuberculous growths from cases of *Perlsucht*. In this extract, after filtration through porcelain, we obtained an albumose, and minute quantities of a ptomaine, which in its reaction was identical with that obtained from the artificial cultivations of the bacillus, but present in even smaller

amount. The probable explanation of this is that in the living animal the ptomaine is constantly being removed; or it may indicate that it is only formed in minute quantity under those conditions.

Reflecting upon the fact that the tubercle bacillus would be destroyed in the process of extraction of its products, we have employed a further modification of the methods which we have described, by dispensing with the tedious process of filtration through porcelain, and thus the copious deposit of the cultivated organism is also submitted to the process of extraction. We are now endeavouring to cultivate the bacillus on media richer in albumin, prepared from white of egg.

Having succeeded in obtaining the albumose and the ptomaine in separate solutions, we next proceeded to ascertain the effects of these substances upon healthy and tuberculous guinea-pigs. Our experiments so far have given the following results:

EXPERIMENT A.—A tuberculous guinea-pig was injected hypodermically with 0.5 gramme solution of the ptomaine obtained from the glycerine-broth cultivations. The temperature before injection was 99.4° F., and subsequently at intervals of an hour, 101°, 102.2°, 102°, 103.2°, 101.8°. While the tuberculous glands were only slightly increased in size, they became distinctly indurated and painful.

EXPERIMENT B.—A second tuberculous guinea-pig was injected with the same dose of ptomaine from another series of broth cultivations. The temperature before injection was 103°, and subsequently 104°, 103.4°, 105.2°, 104.8°, 103.4°. In this case there was distinct enlargement of the tuberculous glands.

EXPERIMENT C.—A tuberculous guinea-pig received 0.5 gramme of the ptomaine isolated from tuberculous tissue (*Perlsucht*). The temperature before inoculation was 102.6°, and, subsequently, 101.6°, 101.8°, 101.8°. Practically the result was negative; there was indication of slight lowering of temperature, but no alteration in the tuberculous glands could be recognised.

Similar experiments were made with the albumose separated from the glycerine extract of tuberculous tissue and the extract of the glycerine-broth cultivations.

EXPERIMENT D.—A tuberculous guinea-pig was injected with 0.5 gramme of a solution of albumose from *Perlsucht*. Temperature before injection was 101.4° F., and afterwards, at intervals of an hour, 104.4°, 104.2°, 103.8°, 102.6°. The glands were distinctly enlarged, and the rise in temperature was in this case very striking.

EXPERIMENT E.—A tuberculous guinea-pig was injected with 1 gramme of the solution of albumose separated from pure cultivations of the bacillus in glycerine broth. The temperature before inoculation was 100.4°, and the subsequent hourly temperature 103.8°, 103.4°, 104.6°, 102.8°, 102.2°.

EXPERIMENT F.—Another tuberculous guinea-pig received the same dose of albumose. The temperature before injection was 102°, and the subsequent hourly temperature 103.2°, 103°, 103.6°, 103.6°, 102.4°. In both this and the previous case there was a visible effect shortly after inoculation, and in guinea-pig E a fatal result was anticipated, but the animal recovered. In both cases the tuberculous glands were distinctly affected.

To sum up, the effect of the ptomaine isolated from different series of cultures was as follows: A rise of temperature occurred in tuberculous animals, and slight indication of depression of temperature or hypothermic effect on healthy animals. The albumose, whether obtained from pure cultivations of the bacillus or from tuberculous tissue, produced a marked rise of temperature in tuberculous guinea-pigs. On the other hand, in an experiment (G) tried on a healthy guinea-pig, there was an equally well-marked fall of temperature. Whether this result is constant can only be determined by repeated experiments.

The effect upon the tuberculous glands in the cases associated with marked rise of temperature, was to render them well-defined, indurated, and painful, rather than to produce any considerable increase in volume.

It is interesting to compare these results with those obtained after the injection of tuberculous guinea-pigs with centigramme doses of Koch's fluid. Until Koch, however, has published the mode of preparation of the substance or

substances used in his anti-tuberculous treatment, it must not be concluded that our researches are necessarily upon exactly the same lines. Koch has stated that his liquid is a "glycerine extract of pure cultivations of the tubercle bacillus," and without further details it is impossible to interpret the exact meaning of this expression, and it does not necessarily follow, however probable it may be, that our extract of glycerine-broth cultivations, or the substances isolated therefrom, would produce exactly similar results to those produced by Koch's fluid.

CASE OF AINHUM.

By H. J. McC. TODD,

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(Communicated by the DIRECTOR-GENERAL OF THE MEDICAL DEPARTMENT OF THE NAVY.)

As cases of this disease are not frequently reported, a short account may interest some of the readers of the *BRITISH MEDICAL JOURNAL*.

King Twala, aged 30, Krooman, was placed on the sick list complaining of pain and swelling of both little toes, which presented the following appearances. The left toe was enlarged to twice its natural size, and was twisted on its axis so that the nail looked outwards, and was so loosely connected to the foot that I feared he would lose the member if it struck against anything. He had no power of moving it in association with the other toes, and its sensation was very deficient. On a level with the web of the toe was a very tight constriction, which on the inner and plantar surface had ulcerated, but on the outer side was represented by a firm band of fibrous tissue; the right little toe was surrounded by a similar tight band, which, however, had not broken down. This man states that his left toe was first affected four years ago, and his right about one year since.

On inquiry into his family and previous history, I can find no cause for this disease, excepting the prevalence of this affection in that part of the West Coast from which he comes, and from his description the disease must be extremely common there, the popular remedy being to tie a piece of string over the seat of the constriction, and to tighten this from time to time until the toe drops off, this occupying about three months. This man is of very good physique, and, excepting his troublesome toes, is in excellent health. As he

wished to have the toe removed on account of the discomfort it caused and his inability to walk, I amputated it at the metatarso-phalangeal joint, previously injecting cocaine. The operation was painless.

On examining the excised portion, I found the constricting band had reduced the structures below it to great thinness. There was a greatly increased development of adipose tissue in the enlarged portion, giving the sensation of fluid before removal.

CASE OF ŒSOPHAGOTOMY.

By THOMAS H. MORSE, F.R.C.S.ENG.

Norwich.

THE operation of œsophagotomy is, I am surprised to find, a very rare one. I hope, therefore, the present case may prove of interest. Mr. Durham, in *Holmes's System of Surgery*, speaks of it as having been performed so long ago as 1738, and that since then as many as forty-five cases have been recorded. On two occasions it was performed at Guy's Hospital by Mr. Cock, for the removal of tooth plates.

The present case occurred on January 11th, 1890. The patient, a woman, aged 32, whilst bolting her dinner and at the same time attending to the impatient indicator of a telegraphic machine, suddenly felt that she had swallowed a foreign body, which gave her considerable pain. The pain, which was increased by pressure, was situated on the left side of the neck just below the cricoid cartilage. An œsophageal bougie when passed was suddenly arrested at a distance of 6½ inches from the teeth, and the passage of both liquid and solid food was obstructed.

With the able assistance of Dr. Hills, Mr. Warlters, and Mr. Cecil Muriel, an attempt was first made with a coin-catcher, but this failing to remove it, the operation was at once proceeded with.

An incision three inches long was made in the left side, on the inner border of the sterno-mastoid muscle, terminating below at the level of the sterno-clavicular joint. After dividing the superficial fascia, the platysma, and the deep fascia with several superficial veins, the omo-hyoid muscle was seen crossing the upper angle of the wound, and, as it interfered with the deeper dissection, it was divided between two ligatures. The dissection was now chiefly carried out with the tips of the two forefingers. The jugular vein and common carotid artery were exposed for about two inches. On the inner side of the wound was the thyroid gland, and deeper down the inferior thyroid artery, running horizontally into the gland was distinctly seen. Next the junction of the larynx and trachea, with corresponding portions of the pharynx and œsophagus, and running upwards between these two tubes, was seen the recurrent laryngeal nerve. A hard substance could now be felt in the œsophagus, and this organ was next separated from the cervical vertebræ and rotated on its long axis, for the purpose of making an opening into its posterior aspect, in order to avoid the recurrent laryngeal nerve. A small opening was made with scissors, and gradually dilated as the foreign body was removed with forceps. The œsophageal wound was not sutured. The skin was closed with silver wire, two drainage tubes being inserted. I need not enter into the details of the after-treatment, except to mention that although no food or drink was given by the mouth at all for three days, yet the pangs of hunger were entirely prevented by nutrient enemata in the form of suppositories. By degrees water, and afterwards milk, were swallowed, small quantities occasionally coming through the wound, and causing the discharge to be offensive, but recovery was practically uninterrupted, and was complete in three weeks.

Should a similar case ever occur to me, I should feel much inclined to suture the œsophageal wound.

The foreign body was a portion of one of the rib bones of a fowl, and measured 1 inch in breadth and nearly 1½ inch in length.

Bone of fowl—natural size.