haps, in communication with those occupied by scarlet fever patients, is one that is specially dwelt upon by Sir George Buchanan, in his introduction to the Report of 1882 on the use and influence of isolation hospitals, where he speaks of the misfortunes within the walls of the institutions themselves. Ten years before the 1892 outbreak at Leicester, there had been experiences in a neighbouring town of the dangers arising from attempting to isolate scarlet fever in a group of huts or sheds arranged on an area of seven acres of ground, when small-pox also at the time of a rising epidemic was being admitted. Small-pox cases took scarlet fever and *vice versa*. Such isolation (so-called) can only be spoken of as quite unpermissible at the present day. It cannot therefore but be recognised that in this respect the Leicester system was especially weak. Taken as a whole, therefore, the lessons taught by Leicester are not nearly so instructive as to the value of isolation as they might have been had the authorities secured a better position for their hospital, and understood the value of true isolation in every respect. In such a case, it is possible they would have still further postponed the occurrence of an outbreak assuming what is termed epidemic proportions. It will of course be understood that I speak of the Leicester experiences strictly from the point of view of isolation, and as illustrating the great influence which was exercised first of all in the provincial towns by precautions other than vaccination, and specially adapted to diseases which are infectious, like small-pox. Elsewhere in the provinces for many years great activity had been displayed in dealing with initial outbreaks of this disease, some towns having acquired not only special powers as to making notification systematic and compulsory, but others having sought for powers which the Sanitary and Police Regulation Committee of the House of Commons were eventually obliged to stop on the ground of undue interference with personal liberty.

SMALL-POX HOSPITALS AND ATMOSPHERIC DISSEMINATION.

I have already expressed the opinion that small-pox hospitals are, under certain circumstances, entitled to be considered a boon. They have, moreover, no appreciable counterbalancing disadvantages. That, at any rate, is the conclusion I arrived at after studying the effects of the extra-urban isolation of small-pox. That also would seem to be the opinion arrived at by Dr. John McVail, who gave a very interesting discourse on the subject of aerial convection of small-pox from hospitals at the Epidemiological Society two years ago.

That discourse contained the following important statement: "No good evidence has yet been adduced of such occurrences in connection with hospitals situated in rural districts." This is true, I believe, in a very wide sense, if we include under the term "rural" institutions which, though not remote from towns, partake of the rural character so far as isolation is concerned. In 1887 I had the opportunity of making a short visit to New York, and of seeing, with the medical officer, some arrangements in that city for the isolation of infectious diseases, for which the public authority was called upon to make accommodation. I was informed at that time by the health officer that no special incidence of small-pox had been noted in the part of the city which would come within the range of distal infection from the island on which the small-pox cases were segregated. Of course the incidence may not have been specially looked for, but it cannot have been marked, or attention would have been drawn to the subject, as was the case round Fulham Hospital in 1880. Within the last few weeks I have received a communication from Surgeon-General J. S. Billings, from which I quote the part relating to small-pox diffusion:

"With regard to your question as to the diffusion from small-pox hospitals, I do not know of any record of anything of the kind in this country, but the small-pox hospitals of our cities are usually located at a distance from any habitations in very thinly settled suburbs. I am familiar with the reports of the Local Government Board on this subject, and think that Mr. Power's argument is a strong one, but I am of the opinion that a collection of small-pox cases may be so managed as to prevent the diffusion of specifically infectious dust therefrom....."

At various times during the last few years I have also had the opportunity of discussing this question with gentlemen officially connected with sanitary administration in Australia and at the Cape Colony, where, so far as my information goes, atmospheric dissemination has not been regarded in any way as a drawback to the hospital isolation of small-pox. Still, as the Royal Commissioners cautiously observed, the utmost care should be taken to guard against it in the event of its becoming necessary, at times of continued fogs or other special circumstances, to retain acute cases of small-pox in towns. It was suggested by Professor Burdon Sanderson, a member of the Royal Commission, that under such circumstances hospitals might be constructed so that the air of the sick wards should be subjected to a high temperature. A small committee, of which I was one, was formed in 1889 to consider the practicability of this suggestion. I believe I am right in saying that Sir Douglas Galton was ready with a plan, but we were unable to persuade the Asylums Board that it was necessary to adopt such a measure. I confess I have been the less disappointed at our failure on learning, as I have done during the last few years, from the reports of medical officers in Surrey that they have been for a long time in the habit of drafting cases of small-pox which occurred in country districts, not, it is true, into the very heart of London, but into a district which, if we take the proportion of persons per square mile, is comparable to a very thickly inhabited town. It is gratifying to note that all the time that process has been going on, we have heard nothing of those dangers which we have been taught to associate with the hospitals for which the Poor-Law Department of the Local Government Board was primarily responsible.

SMALL-POX AN OBJECT LESSON IN THE TREATMENT OF INFECTIOUS DISEASES.

In concluding this lecture I feel that I ought to give some reason for dwelling so long upon the one disease, variola. The proportion of the small-pox death-rate at the present day, since the adoption of vaccination became general, is comparatively insignificant, and if we compare the death-rate from this cause with that of the other principal zymotics, it may be called trifling. On the other hand, this disease affords a most striking proof of the value of preventive measures, such as are administratively possible at the present day. It is from that point of view mainly, I need not remind you, that public health departments have to regard disease prevalence. They must also regard it partly from the view of the lesson which it may possibly afford in the treatment of other infectious diseases. With regard to the prospects held out of a complete riddance of that which a century ago, before the time of our countryman, Edward Jenner, was a terrible plague all over the world, may it not be possible that these lessons we are learning at the end of the century may teach us much which will prove essentially valuable in the preventive treatment of other diseases? The behaviour of small-pox under different conditions, which has been so closely studied, may throw a light on many questions of epidemiology and may eventually enable us in a most practical sense to widen the scope of preventive medicine.

THE PHYSIOLOGY OF THE CARBOHYDRATES.

A REJOINDER TO DR. PATON'S FURTHER CRITICISM.

By F. W. PAVY, M.D., LL.D., F.R.S.,
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(Continued from page 522.)

THE question of the relative state of the blood going to and escaping from the liver is an important one. I dealt with it fully in my *Physiology of the Carbohydrates*, and founded my conclusions on a large amount of experimental evidence. Dr. Paton, in criticising this, brought forward the experimental work of Seegen. I say in my *Epicriticism*, and give the grounds for so saying, that "the experiments of Seegen referred to by Dr. Paton may be unhesitatingly affirmed to constitute experiments from which it is absolutely not permissible to draw a physiological deduction." Seegen's *modus operandi* cannot possibly furnish specimens of blood

which can be accepted as representing truly the physiological state. In his further criticism (p. 727) Dr. Paton says:

I stand by all my objections to Dr. Pavy's method of comparing the portal blood and blood of the right ventricle from different animals and after death. The animals used in his experiments on the portal blood were pithed, then the abdomen was opened, then the portal vein was exposed, then opened, and then the blood procured. I do not know how long this procedure takes, but it appears to me that, whether the process is short or long, such a dead dog is in a far less normal condition than Seegen's animals.

Whether such a dead dog is in a far less normal condition than Seegen's animals is not in reality to the point. The real point is the condition of the blood that is procured for examination, and whether or not it affords a representation of the condition existing normally during life, or, in other words, of the physiological state. The "thens" introduced into the description of my operative procedure suggest that Dr. Paton must have written without having a true conception of the process. But ought he not to have made himself acquainted with it before writing as he has done? In view of the object to be obtained the use of such an expression as "whether the process is short or long" really takes us outside the range of useful discussion. Can it possibly be contended that whether the blood is obtained so speedily after the sudden destruction of the life of the animal as to permit of its being taken as affording a representation of the condition naturally belonging to life, or whether time is permitted for the effects of *post-mortem* change to make themselves manifest, is an immaterial point?

It will not be disputed that, in collecting blood for examination, it is necessary, in order to avoid fallacy, that it should be procured in a condition representative of the physiological state.

To obtain right ventricular blood the plan I adopt is to kill suddenly by pithing, which is an instantaneous mode of destroying the life of the animal, and then without a moment's delay, to thrust a pair of sharp-pointed scissors into the chest, and by frequent snipping to cut freely into the heart and large vessels, so as to secure a full and sudden emptying of their blood into the cavity of the chest, from which it is afterwards collected. In the case of the portal blood the animal is similarly pithed, and instantly afterwards, with the aid of two assistants, quickly turned over on to its back. A free incision at once made through the abdominal walls permits of the finger being quickly introduced, without the aid of sight, into the foramen of Winslow, in front of which the portal vein lies. By drawing the finger forward the vessel is compressed, and the further flow of blood through it immediately stopped. A ligature may now be applied at leisure, and the blood which is subsequently collected by an opening into the vein constitutes blood which may be said to have been on its way to the liver about fifteen or twenty seconds after the sudden destruction of life, for the circumstances admit of the arrest of the circulation through the vessel being accomplished in this time. Such is my method for obtaining blood, and it appears to me that it may be rightly accepted as affording samples of blood representing the physiological state.

Now let us look at Seegen's¹ process. If the wording of Dr. Paton's sentence means anything applicable to the point it is to the effect that blood procured within a few seconds of the sudden destruction of life is representative of a "far less normal condition" than that obtained from the following prolonged and extensive operative procedure.

In order to obtain the portal blood, an abdominal incision was made, the spleen drawn out, its principal vein found, and a cannula introduced and passed along until it reached the portal vein. By another abdominal incision a cannula was introduced into the inferior cava and ligatured into it just above the renal veins. In the order of procedure, blood was now drawn from the portal vein through the cannula passed into it along the splenic vein. Next by an incision through an intercostal space, which rendered the subsequent performance of artificial respiration necessary to keep the animal alive, a ligature was applied around the inferior cava just above the diaphragm. Blood representing hepatic blood was now collected from the cannula ligatured into the inferior cava just above the renal veins.

A second method for collecting the hepatic blood adopted

¹ *Glycogène Animale* (Paris, 1890), p. 68, *et seq.*

in some of Seegen's experiments consisted, after blood had been collected from the portal vein, in opening the abdomen largely and drawing out the liver sufficiently to be able to get hold of one of the hepatic veins into which he introduced a cannula for withdrawing blood. A third process, used only in a few instances, consisted of passing a cannula down through the right jugular vein into the inferior cava, and thence into one of the hepatic veins, its entrance into the vein being determined by feeling for its extremity through the substance of the liver.

In face of the true state of things upon which anyone, from the representation I have set forth, can form an opinion, Dr. Paton boldly argues as he has done. Blood collected after the operative procedures that have been described is to be regarded as in a better position for yielding information as to the physiological state than that derived from the circulation within a few seconds of the sudden destruction of life.

Dr. Paton wishes it to be thought that we cannot get the information that is wanted by taking what is revealed by a large number of observations to be the standard condition of the right ventricular and portal blood. It is from upwards of 100 observations on the right ventricular blood from animals of different kinds that I have made the statement that the sugar has been found to range from 0.6 to 1, or a little over 1 per 1,000. The range met with, it will be noted, is spoken of and not the average. Surely such information may be reasonably accepted as affording a trustworthy basis. In the case of the portal blood the evidence I have supplied is founded upon 38 observations associated with varying conditions as regards food. The results presented to view are of a striking nature, looked at by the side of the condition of right ventricular blood, and, moreover, are consistent with each other and with the collateral circumstances.

In Seegen's experiments it is to be noted that the blood from the two sides of the liver was not in reality collected simultaneously, although a point is made out of the absence of simultaneous collection in my experiments. It is true the blood was derived from the same animal, but an operation of a nature to produce a significant amount of disturbance intervened between the two collections of blood.

Seegen's work is the great resource of Dr. Paton in the endeavours he has made to upset mine. Time will reveal, if it has not already done so, whether what I have said of it is true or not. I have no misgiving upon the point that Dr. Paton will find that he has been resting upon a false foundation. It is impossible for any experienced physiologist to peruse Seegen's *Glycogène Animale* carefully without seeing, as is the case with the work of Schenck, which Dr. Paton has pressed forward so strongly as work upon which reliance should be placed, that, from the nature of the experimental methods of procedure adopted, and the want of consistency in the results obtained, something wholly wrong must exist.

Indeed, apart from all other points which arise for consideration, we have to deal with an assertion which is nothing short of this: That sugar is produced functionally by the liver without glycogen standing as its source; and, further, the impossible position is led up to that there is an ingoing of sugar from the liver, but not an outgoing from the system; for, whilst Seegen differs from me as regards production of sugar by the liver, he agrees with me in finding that there is no loss of sugar in the transit of the blood through the systemic capillaries.

Dr. Paton says in his paper in the *Philosophical Transactions* (vol. clxxxv, p. 233), where my work stands in his way, "the theory of Pavy, repeated in nearly every textbook, that the liver is a 'sugar destroying and not a sugar forming organ,' rests on so unsubstantial a basis, and has been so completely refuted by the work of Seegen and other investigators that it need not be considered." When turned to account for refuting me, Seegen's work is regarded as good and sound. When, on the other hand, as is found to be the case in the paper mentioned, it stands in opposition to what Dr. Paton is endeavouring to maintain, it is spoken of in highly disparaging terms, and, be it observed, the terms apply to work which is mixed up intimately with, and pursued on similar lines to, that which I have been reviewing in connection with the blood.

I would ask: Is knowledge likely to be advanced, is any useful purpose to be served by continuing a discussion upon such grounds? In my *Epicriticism* I dealt with every point that had been advanced against my work, and I showed that its validity remained unaffected. In Dr. Paton's further criticism, whilst much that I have said is allowed to pass unnoticed, certain points are taken up and dealt with again. Neither in his first nor in his second criticism is any attempt made to enter into the question of the soundness of the material which he draws from published literature. I affirm with regard to the second, as I did with regard to the first, that in no respect is the validity of my work shaken.

I have given illustrations of the kind of material to be found in Dr. Paton's reply to my *Epicriticism*, and I consider they render it unnecessary that I should deal *seriatim* with the several points raised. The matter has been sufficiently set forth to be placed in a position to be judged by others, and judgment will with the advance of time inevitably be passed upon it. Science in this department will not stand still any more than in any other, and I for my part am quite ready to leave the matter to the future to decide, and I do so without misgiving as to the result.

It happens, fortunately, that the necessity for prolonging the discussion of collateral points no longer exists in view of what has been admitted by Dr. Paton to constitute the essential point in the question at issue. He says:

The great and central question at issue in Dr. Pavy's work is this: Is there during life a constant production of glucose in the liver? It is upon this point that his theory must stand or fall. If the evidence here is against him, and if he fails to prove that the liver is simply a sugar-stopping and not also a sugar-producing organ, his "system of knowledge" (p. 135) must collapse.—*Edinburgh Medical Journal*, February, 1896, p. 726.

Accept this presentation of the position, and the ground of contention thus becomes narrowed within well defined limits. The question, indeed, may be said to resolve itself into the following simple issue: Can sugar be poured into the general circulation, as is implied by the glycogenic doctrine, without leading to a corresponding appearance of sugar in the urine, which means diabetes? To this, in a decided manner, I say No.

(To be continued.)

THE HYPODERMIC USE OF GUAIACOL IN ACUTE PULMONARY TUBERCULOSIS.¹

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THE more recent and now very general employment of creasote, and more especially its principal constituent guaiacol, in the treatment of pulmonary tuberculosis is another curious instance of therapeutic vicissitude. Creasote was used in phthisis on the Continent quite sixty years ago, but probably owing to crudeness of preparation and insufficient dosage, it gradually fell into disrepute until, restored to favour on the recommendation mainly of Professor Sommerbrodt,² Drs. Paul Guttman³ and Oscar Frantzel⁴ in Germany, and of Bouchard,⁵ Gimbert,⁶ Rodais,⁶ and Bonnefontaine⁷ in France, the last of whom pointed out the greater purity and more agreeable qualities of the creasote distilled from beechwood. In 1877⁸ I published my first paper, describing its efficacy in diminishing the heavy purulent expectoration in phthisical and other lung affections, when used for inhalation, by means of an adaptation of the ordinary respirator. I suggested that it acted as a direct antiseptic on the germs to which the pus formation was due. Latterly, the use of creasote, both internally and by inhalation, has been largely superseded by guaiacol, to which attention was drawn more particularly by Sahli⁹ and afterwards by

Horner.¹⁰ Guaiacol is separated from creasote, a highly complex body, by distillation. It forms from 70 to 90 per cent. of creasote, together with varying proportions of its homologue creosol, the isomeric creosols and phenol, according to the purity of the latter. It is probably the therapeutically active as well as the principal constituent of creasote.

My chief object in this paper, however, is to direct attention more especially to the great value of guaiacol used hypodermically in the treatment of acute pulmonary tuberculosis. Both creasote and guaiacol alone, and combined with iodoform, have been used hypodermically in oily and other sterilised solutions by Gimbert,¹¹ Picot,¹² and Léon Rosenbusch,¹³ the latter of whom injected every three or four days a 3 per cent. solution of guaiacol in sterilised almond oil into the parenchyma of the lung, either through the second intercostal space or the supraspinous fossa. Such preparations are, however, uncleanly, bulky, awkward to manipulate, and comparatively painful. They involve elaborate preparation and great expenditure of time.

It was Dr. Arnold Schetelig,¹⁴ of Nervi, who first showed that a vehicle was quite unnecessary by injecting pure guaiacol in a case of acute advanced pulmonary tuberculosis, which at the moment was in the gravest condition, and which I had subsequently the opportunity of examining during convalescence in this country. The very day—May 5th, 1889—I received Dr. Schetelig's report describing the remarkable results in this case, I happened to have under my care a patient with pneumonic phthisis affecting both bases in a most critical condition. There was extreme prostration, with a nocturnal rise of temperature to 103.8°, which no treatment had been able to affect. Three hypodermic doses of πxv , πx , and πx of pure guaiacol at intervals of four hours brought the temperature down to normal, with rapid amelioration of all the symptoms, followed by complete and permanent recovery.

My subsequent experience in a large number of cases has been very encouraging. I do not, however, for obvious reasons advocate this therapeutic proceeding indiscriminately in every case of pulmonary tuberculosis, without reference to the stage of the disease or consideration of other remedial measures previously exploited or still thought necessary. For instance, if the range of temperature is not extreme, and the other conditions not urgent, it is better to try the effect of guaiacol administered in the usual way by the mouth, either in capsule or dissolved in cod-liver oil. A dose of πv three times a day even may suffice to reduce the temperature, but, on the other hand, it may be necessary to intensify the treatment by raising the dose πv at a time until πxl or even more has been reached. The favourable effect of this exhibition of the remedy *per os* is well illustrated by Chart No. 1 of M. McN., admitted April 1st, 1894.

CASE 1.—This is a case of acute tuberculosis with excavation at both apices, with rapid loss of flesh—9 lbs. the last twenty days—much cough, and heavy nummular purulent expectoration, temperature ranging at night from 100° to 102.4° unaffected by the salicylates and other antipyretics. Under πv of guaiacol in cod-liver oil, commenced May 2nd, the temperature fell steadily to normal, and she left the hospital on July 10th with her disease practically arrested; as stated in the hospital casebook, "no expectoration, very little cough, having gained 13½ lbs." On June 6th, 1895, a letter was received from her uncle, saying: "The late patient now weighs a little over 10 st., and is perfectly well."

In order to understand the indications for employing our remedies in the pyrexia of phthisis, it is necessary we should as far as possible determine the pathological conditions from which they arise. In the light of recent progress in our knowledge of its pathogeny, pulmonary tuberculosis may be defined as an acute infectious disease of bacillary origin, determined by hereditary or acquired proclivity, tending to chronicity, with occasional arrest more or less permanent, and to progressive retrograde changes in the lungs, the seat of characteristic lesion. Regarded thus, we obtain a precision and directness in our therapeutic methods much desiderated, and which permit our basing a rational therapeutics on a sound pathology.

The pyrexia of pulmonary tuberculosis presents two phases, related and consecutive. The first—the primary or initial

¹Read in the Section of Medicine at the Annual Meeting of the British Medical Association, held in London, July-August, 1895.

²Berl. med. Woch., No. 43, 1878, and Therap. Monatschr., July, 1889.

³Zeitschr. für klin. Med., vol. xxii, p. 488.

⁴Berl. klin. Woch., Nos. 8 and 23.

⁵Gazette Hebdomaire, Nos. 31 and 33, 1887.

⁶Union Médicale, No. 66, 1879.

⁷Union Médicale, March 11th, 1879.

⁸Lancet, October 5th, 1877.

⁹Korrespondenzblatt für Schweizer Aerzte, No. 20, 1887.

¹⁰Prager med. Woch., No. 17, 1888.

¹¹Gazette Médicale de Paris, August 8th, 1883.

¹²Bulletin de l'Académie, No. 9, 1890.

¹³Wiener med. Presse, Nos. 24-26, 1888.

¹⁴Deutsche medizin. Zeitung, February 2nd, 1893.