man, who, after treating her for some months for cystitis, sent her into the Royal Hospital, where she is at present a patient. During the three years she has suffered from cystitis she has been troubled with headaches, which she states increase with the pain in the bladder region.

I have been unable to find a record of any case of uncomplicated cystitis from which the typhoid bacillus has been isolated in pure culture. In the exhaustive discussion of genito-urinary infections at the Edinburgh meeting of the British Medical Association this year no such case was mentioned.

This case seems of interest for the following reasons. 1. The history gives no evidence that the patient ever had typhoid fever, and the fact that she spent so much of her time in hospital and was under medical treatment at home may be held to exclude any possibility of mistake in this respect. In cases of typhoid fever the bacillus of Eberth is often found in the urine, even some weeks after the temperature is normal.² This case is one of typhoid infection without the usual symptoms of typhoid fever, and since there is no point in the history subsequent to the commencement of the cystitis three years ago, which suggests the occurrence of a new infection, the probability is that the typhoid bacillus has been present from the beginning. When we consider the fact that typhoid bacilli are so easily destroyed by more vigorous forms, such as Escherich's bacillus, it seems highly improbable that at any time during the course of the cystitis the typhoid bacillus has displaced the coli bacillus in the bladder. The acidity of the urine excludes the probability of other forms commonly found in cystitis ever having been present.

2. The blood serum gave a decided "reaction of infection." This shows that the case is not a simple bacteriuria, but that the bacillus has a nidus somewhere, as for example in the mucous membrane of the bladder, and thereby has such an effect on the blood and tissues as to cause the serum to acquire the agglutinating power.

3. It seems to follow that in this case the bacillus of Eberth was capable of producing a local lesion without the patient suffering from typhoid fever.

4. The fact that the bacillus can grow in the tissues without any symptoms of enteric fever resulting, and produce there a local lesion, is in favour of the view that this fever is a true general infection, and not merely of local origin, in the Peyer's patches of the intestine.

5. It also proves that the bacillus may occur in the tissues, and the blood serum give Widal's reaction, without the infection which we recognise as typhoid fever resulting.

6. To explain the anomalous fact that we have here a lesion, restricted apparently to the urinary organs, produced by the typhoid bacillus, which has persisted for a very considerable time without any symptoms of typhoid fever, three theories seem admissible:

(a) This patient for some reason or other was not very susceptible to infection with Eberth's bacillus, so that when the opportunity for infection occurred a local lesion alone resulted, and no general infection. This agrees with the result obtained when a non-susceptible animal is inoculated with a given bacillus.

(b) We have here a form of typhoid bacillus which differs in its infectious power from the recognised form of Eberth's bacillus.

(c) Typhoid fever is not solely due to the bacillus of Eberth, but other etiological factors must be brought to bear on the patient before the clinical features of typhoid septicæmia result. The researches of Sanarelli,³ which show how the virulence of the typhoid bacillus is increased by the injections of the toxin of the bacillus coli communis, and also those of Sidney Martin,⁴ which confirm his results, make it certain that the bacillus coli communis may be directly concerned in producing a virulent typhoid infection in animals. In the recent report on the Belfast water supply, Dr. Lorrain Smith has shown that the bacillus coli communis had a distinct relation to the etiology of the recent epidemic of typhoid fever in Belfast (1898), and that many of the cases gave evidence of the existence of a mixed infection of the bacillus of Eberth and that of Escherich.

The persistence of the typhoid bacillus in the bladder possibly for three years appears less remarkable when we recall the cases in which abscesses containing typhoid bacilli have been observed six or seven years after the occurrence of typhoid fever in the patient.⁵

I have to express my thanks to Professor Byers for permission to publish the clinical account of this case, and to Dr. Lorrain Smith, in whose laboratory the examination of the urine was conducted, and who not only suggested the line of investigation, but also verified my results.

REFERENCES.

- ¹ Lorrain Smith, *BRITISH MEDICAL JOURNAL*, 1898, vol. ii, p. 1782.
² Petruschky, *Cent. f. Bakt.*, 1892, No. 14; Klein's *Micro-organisms and Disease*, p. 245. ³ *Ann. de l'Inst. Pasteur*, vi, 721, viii, 193, 353. ⁴ Croonian Lectures, *BRITISH MEDICAL JOURNAL*, vol. ii, 1898. ⁵ Flexner, *Journal of Pathology and Bacteriology*, vol. iii, p. 202.

ON THE INFLUENCE OF PATHOLOGICAL STATES UPON THE ELIMINATION OF WATER AND CARBON DIOXIDE BY THE SKIN.*

By J. O. WAKELIN BARRATT, M.D.LOND., F.R.C.S.ENG.

(From the Pathological Chemistry Department, University College, London).

OBJECT OF THE INVESTIGATION.

THE object of this investigation has been to study the nature of the process of elimination of water and carbon dioxide as it occurs locally. To this end it has been necessary, in the first place, to ascertain the normal output of these substances at varying temperatures.¹ This done, attention has been turned to the modification of output induced by abnormal local conditions, it being conjectured that in this way further light would be thrown upon the mode in which these functions of the skin are affected. The surface of the upper limb has been submitted to experiment throughout. The pathological states studied have been those produced (1) by the application of a ligature to the limb,² and (2) by irritating the skin by the application of carbolic acid so as to excite a condition of inflammation.³

The average normal output of water from the skin of the upper limb (up to the level of the insertion of the deltoid) was found to be, at 35° C., about 4 grams per hour, and that of carbon dioxide about 20 mg. The actual output, however, varies from hour to hour, and still more from day to day. The temperature to which the skin is exposed has a marked influence on the discharge of carbon dioxide, and a relatively slighter effect on that of water. Further, the average output varies in different individuals, and also in the same individual at different seasons.

The influence of a ligature applied to the upper limb as close to the shoulder as possible is to cause a diminution of the output of water, amounting, it may be, to as much as 20 per cent., while a still larger variation of the output of carbon dioxide occurs in the opposite direction—namely, that of increased discharge. The extent of the alteration of output corresponds to the degree of tightness of the ligature, and is observed whether the temperature of the water bath surrounding the limb is 35° C. or 25° C.

METHOD OF EXPERIMENT.

In order to study the influence of inflammation, the surface of the limb was irritated by the application of carbolic acid, and it was found that the elimination of carbon dioxide was but little altered, such change as occurs being in the direction of a slight diminution of output at first and a small increase subsequently. On the other hand, there is a marked decrease in the output of water, amounting in the experiments made to more than 50 per cent.

The secretion of water by the skin can also be studied qualitatively, and in this way a valuable illustration is afforded of the mode in which inflammation produces its effect. Thus if an injection of 1/100th to 1/50th of a grain of pilocarpin nitrate is made into the skin of the palm, sensible perspiration is observed over a small circular area whose centre corresponds with the position of the front of the needle. When this area, which presents to the naked eye a finely glistening appearance, is examined with a lens, it is found to be covered with fine droplets of perspiration, situated at the

* Towards the expenses of this research a grant was made by the British Medical Association on the recommendation of the Scientific Grants Committee of the Association.

funnel-like orifices of the sweat glands, some of which may run together (Fig. 1). If an injection of pilocarpin nitrate is made into the palm where this is hard, dry, and parchment

Fig. 1.—Representing the skin of the palm seven minutes after an endodermic injection of $\frac{1}{100}$ gr. of pilocarpin nitrate; the orifices of the sweat ducts exhibit minute droplets of perspiration. $\times 25$.

like as the result of the application of carbolic acid, no droplets are visible as a rule, but should any be present, they are few in number, and appear as excessively fine points (Fig. 2). If a piece of such horny epidermis is peeled off (this cannot be done before about six days from the application of carbolic acid), an opportunity is afforded, when pilocarpin is injected, of contrasting the secretion from the new surface and the old; on the former droplets are seen, which are rather less numerous and somewhat smaller than on the opposite palm, while the latter shows no droplets.

Fig. 3.—Showing the appearance presented by the skin of the forearm when, by enclosing the limb in a glass case kept at 35°C ., the sweat secreted is prevented from evaporating and therefore becomes visible; above and to the left the skin is normal and shows numerous fine beads of perspiration; below and to the right the skin is reddened by the application of carbolic acid and shows very few droplets. Natural size.

Similar observations may be made upon the skin of the arm and forearm without the use of pilocarpin. When an incomplete application of carbolic acid to the skin has been made, so that red and white areas appear side by side, it will be found that if the limb is placed in a glass receiver heated to above 37°C . (to prevent the condensation of moisture on the glass), the air in the receiver being stationary, such perspiration as is produced remains in the visible form. After the expiration of a sufficient period of time the white areas

will be seen to be covered with beads of sweat, while the red areas will be quite free from perspiration, or will merely contain a small number of fine droplets (Fig. 3).

Fig. 2.—Representing the skin of the palm four days after the application of carbolic acid: $\frac{1}{100}$ gr. of pilocarpin nitrate has been injected as in Fig. 1; the number of droplets at the orifices of the sweat ducts is less than in Fig. 1 and the droplets themselves are smaller. $\times 25$.

SIGNIFICANCE OF THE OBSERVATIONS.

We now come to consider the bearing which the experiments above detailed have upon the nature of the processes occurring locally in the skin. Taking first the elimination of carbon dioxide, it is to be observed that the dependence of this upon the temperature of the skin appears to stamp the process as essentially a manifestation of purely local events, and not as an adjustment to general internal or external conditions. The effect of a ligature in causing an increased carbon dioxide output is also significant. The ligature produces compression of nerves and also of blood vessels and lymphatics, but the former is partial in extent and limited in area, not affecting at the most one-fifth of the surface, while the latter is general, and must therefore be regarded as the effective cause of the carbon dioxide increase. Two views of the mode of elimination of carbon dioxide are tenable: one is that it is a respiratory process comparable to that occurring in the lungs, the carbonic acid gas diffusing from the blood through the skin into the external air; the other is that carbon dioxide is produced by the activity of the cells of the skin, in the same way that it is produced elsewhere, and diffuses not only into the blood stream by which it is carried off to be got rid of by the lungs, but also into the external air, the latter being rendered possible by the existence of a free surface. A little consideration will make it clear that these two processes, which are totally dissimilar, would be affected in opposite ways by a ligature. The former would be diminished by diminishing the rate of flow of blood from which the carbon dioxide is derived; the latter would be increased by the arrest of the blood stream by which the carbon dioxide is removed. The increase which actually occurs must be taken to indicate that the formation of carbon

dioxide by the skin is an expression of the general metabolic activity of the skin, and not that of a respiratory function. This view, moreover, is in harmony with the physiology of the tissues generally.

In dry dermatitis produced by carbolic acid, the tendency noted to initial decrease of the carbon dioxide output, followed by increase when desquamation occurs, is presumably related to the thickness of the horny epidermis, which is at first increased owing to the arrest of the normal mode of shedding in fine scales, and subsequently diminished when peeling occurs.

The elimination of water by the skin now remains to be considered. This, unlike the discharge of carbon dioxide, is known to stand in relation to the general needs of the economy, in particular is it associated with heat regulation.

The diminution of the aqueous discharge of the skin caused by the application of a ligature seems to be attributable not to compression of nerves, which is probably too slight in amount and too small in extent to cause such diminution, but to the mechanical obstruction of the blood vessels which presumably in this case, as in that of ligature of the renal artery, tends to throw the secreting epithelium out of action.

The restriction of the output of water caused by the application of carbolic acid to the skin of the upper limb is associated with a remarkable parchment-like hardness of the skin, especially of the palm. That this is due to the horny epidermis becoming abnormally dry is shown by the fact that the stiffness of the skin exactly resembles that which horny epidermis [in the form of shed scales or shavings from a corn] exhibits when dry, and disappears when the skin is soaked in water; and on the other hand when horny epidermis is immersed in liquid carbolic acid it swells up and becomes softened, but on subsequent washing and drying its characters are found to be unchanged, beyond perhaps a slightly greater opacity when soaked in water, and a somewhat increased brittleness when dry. The hard, harsh condition of the epidermis in dry dermatitis is therefore due to the arrest of the secretion of sweat, being not the cause but the effect of the absence of perspiration.

On the other hand, it is quite clear that the epidermis offers a resistance to the passage of perspiration through it, for when the harsh, dry, horny cuticle is pulled off visible perspiration again makes its appearance while, conversely, so long as the hard epidermis remains attached, the surface continues hard and dry.

When vesiculation of the skin or the formation of bullæ occurs the contained fluid does not visibly escape by the ducts of the coil glands, although these may be torn across. The fluid in the cavity of the vesicle or bulla contains coagulated material, part of which is free, while the rest is deposited on the walls of the cavity, some of necessity obstructing the sweat ducts. In dry dermatitis a similar blocking of the sweat ducts occurs, for although there are no macroscopic vesicles, yet the pathological condition which forms a necessary precursor of vesiculation is present—that is to say, there is a moderate degree of spongy transformation of the prickly layer, the prickles themselves are elongated, and the spaces between them distended with coagulable exudation, some of which finds its way into the sweat ducts and is the cause of the arrest of the secretion of sweat which occurs. The dryness of the skin must therefore be regarded as mechanical in its origin.

In conclusion, I must express my great indebtedness to Professor Vaughan Harley for his kind assistance throughout the course of this research.

REFERENCES.

- ¹ On the Normal and Pathological Elimination of Carbonic Acid and Water by the Skin, *Jour. of Physiol.*, xxi, 1897, pp. 192-208. ² *Ibid.* ³ On the Elimination of Water and Carbon Dioxide from Inflamed Skin, *Jour. of Physiol.*, xxii, 1897, pp. 206-214.

ON THE INCUBATORY PERIOD IN VARICELLA OR CHICKEN-POX.

By WILLIAM SYKES, M.D., F.S.A.,

Gosport, Hants.

A CONSIDERABLE difference of statement as to the incubatory period of chicken-pox is to be found in the literature of the subject. Dr. Tannei¹ gives it as no longer than four days:

7

Dr. George Gregory² four to six days; Dr. Heberden³ who in 1761 first differentiated chicken-pox from small-pox, believed it to occupy eight or nine days; Dr. Bristowe⁴ gives it as in some cases exactly a week, but more commonly a fortnight; Dr. Eustace Smith⁵ practically the same, namely, from seven to fourteen days; Dr. Goodhart⁶ eight to sixteen days; the German author, Thomas⁷ who quotes Körber and Hesse as agreeing with him, fixes the period at thirteen to seventeen days, as does Dr. McCombie,⁸ Dr. Liveing⁹ at about thirteen days with eruption on the fourteenth; Dr. S. Gee¹⁰ gives the time as a fortnight; Dr. Clement Dukes, of Rugby (a high authority), fourteen to nineteen days, while Trousseau extends the incubation to so long a period as from fifteen to twenty days¹¹.

With the honourable exception of Dr. Goodhart, all the authors quoted have omitted to supply any details of the cases upon which the statistics of length of incubation were founded, so that it is impossible to compare their statements and reject those which appear untrustworthy. But as their observations differ so widely from each other, it seems worth while recording fresh instances which can be verified, in order to secure some certainty on the subject, and as I have had under observation a limited epidemic of chicken-pox among children of the better classes, in which I have been able to ascertain the incubation period with some approach to accuracy, I venture to bring my observations to the notice of the profession.

M. R., a young lady, aged about 17, was teaching her Sunday-school class of girls in the village school on Sunday, April 17th, 1898, when one of her little scholars complained of feeling ill and asked permission to lean against her teacher, a request good-naturedly granted. The very next day the sick child developed the rash of chicken-pox. M. R. herself exhibited the chicken-pox rash on April 23rd, just six days from this exposure, but as the disease was not recognised by her friends she was not isolated in any way. Seven days later, namely, on April 30th, her youngest brother, O. R., showed a few spots in the evening and was fully out on May 1st.

I am aware that in both these cases there is just the possibility of a fallacy of coincidence. M. R. may not have received the infection from the child who leant against her in school, but from some other source; or, on the other hand, she may have conveyed infection in her clothes from this child directly to her little brother, so lengthening his period of incubation to thirteen or fourteen days, but I do not think either of these errors likely. There were, so far as I can ascertain, no cases of chicken-pox either in class or among M. R.'s friends other than the child mentioned; while, as M. R., who is much attached to her little brother, had both nursed him and played with him frequently while her rash was fully out, it is more probable that he had been infected by her than by any other conveyed infection. It will be noticed that in both these cases when there had been close direct personal contact the incubation period was short, namely, six or seven days. As the nature of the disease was still unrecognised, little O. R. continued to attend a small Kindergarten school for the children of the upper classes. He was there for two hours each day on Monday and Tuesday, May 2nd and 3rd, with the rash fully out upon him. I saw him on the evening of May 3rd for the first time, when he was at once excluded from the school. This little Kindergarten had 16 young scholars meeting in an ordinary sitting-room. Two little boys, elder brothers of O. R., developed rash on May 5th and May 18th respectively. These cases must, however, for the purpose of our inquiry be ignored, since we have no certainty from which relative they contracted the infection. They were, moreover, both too old to attend the Kindergarten. Eleven days after O. R.'s removal from this school, on May 14th, one little pupil, H. C., exhibited a few spots of chicken-pox, and was fully out with the rash on the next day. Three days later, on May 17th, and fourteen days after O. R.'s exclusion, G. C., a brother of H. C.; F. L., T. H., W. G., L. C., and W. C., six pupils of the Kindergarten, all exhibited spots of chicken-pox; while P. L., the little sister of F. L., also an attendant of the school, showed rash the next day, May 18th.

Of one other scholar, who was removed to another town and developed chicken-pox after he arrived there, I have not as yet been able to ascertain the exact date of sickening.

So that of fifteen young children attending the Kindergarten