ON

TEMPORARY GLYCOSURIA AS A SEQUEL TO CHOLERA.

BY

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THE occurrence of choleraic glycosuria has attracted very little notice in this country, although abroad it has received, especially during the last epidemic of cholera, much clinical attention. As yet, however, scarcely any attempt has been made, even by those who have specially studied the subject, to give a physiological explanation of its occurrence during convalescence from this disease, when, apart from any chemical analysis of the urine, it may be observed that a condition of temporary diuresis usually succeeds to a previously more or less complete suppression of the urinary secretion.

The probable discovery of sugar in the urine of cholera patients was, so to speak, foreseen by Reynoso,¹ and he sug-

¹ 'Comptes Rendus Hebd. des Séances de l'Acad. des Sciences,' tom. xxxiii, 1851, p. 606.

gested that it would be desirable for physicians engaged in the study of this disease to seek for sugar in the urine. There was no opportunity of testing the correctness of Reynoso's inference till the occurrence of the epidemic of cholera in 1854-1855, when, as stated by Buhl and Voit,¹ sugar was first distinctly recognised in the urine of cholera patients by Heintz and Samoje, and subsequently Voit himself also found it in two cases of cholera during that epidemic, in no trifling quantity. These observations were confirmed by other observers, and especially by Frederick Lehmann,² who found sugar in some of the forty-eight severe cases of cholera, occurring during the same epidemic, in which he examined the urine; the sugar, according to this observer, being limited to severe cases and never being found later than the third day after return of the urinary secretion. The discovery seems to have attracted at the time scarcely any attention, except among a few Continental observers, and it was almost, if not altogether, overlooked in this country; for Dr. Parkes, in his work 'On the Urine,' published in 1860 (p. 307), states, on the authority of Heintz, Samoje, and Buhl, without reference to any English observer, that in cases of cholera "sugar is occasionally present, sometimes in large quantities, in the first and second day's urine." It was not, indeed, till the epidemic in 1866 that the occurrence of glycosuria as a sequel of cholera can be said to have attracted much attention, and it must be admitted that the information hitherto received on this subject has been derived chiefly from the labours of the medical profession abroad, among which it may be useful to notice the observations of M. Gubler,³ and his pupil M. Bordier,⁴ at the Beaujon Hospital, Paris; of M. Langronne,⁵ aided by M. Bonnefon, at the

¹ 'Zeitsch. für rationn. Medizin,' Neue Folge, vi, p. 25, 1855; cited by Huppert, "Ueber die Glycosurie bei Cholera, &c.," 'Archiv der Heilkunde,' 1867.

² 'Physik. u. Chem. Studien ueber die Cholera,' Inaug. Diss. Zurich, 1857.

³ "Sur la Glycosurie Symptomatique dans la période réactionnelle du Choléra," 'Gaz. des Hôpitaux,' 1866, pp. 410, 411.

⁴ 'Archives Générales de Médecine, Février,' 1867, pp. 176—193.

⁵ "Du Choléra Epidémique," Thèse de Paris, 1866.

Lariboisière Hospital, Paris; of M. Lorain,¹ at the Hôpital St.-Antoine, Paris; of M. Desnos² and his colleague M. Gombault,³ at the Hôpital de Ménages, Paris; the facts collected by this last-named observer being based on 1700 observations. To these may be added the observations of Dr. P. Treibmann⁴ during the epidemic at Leipsic in 1866, both at the cholera station of the Jacob's Hospital and also in the cholera lazaretto which was conducted by himself; and, lastly, the researches of Dr. H. Huppert⁵ during the same epidemic of the disease. Whilst materials for the study of this temporary condition of the urine in cholera have been thus somewhat extensively collected by several able observers abroad, it is necessary to state that almost without exception the best and most distinguished writers on the disease in this country have not even alluded to the occurrence of sugar in the urine, although, as Bouchardat remarks, England is said to be the privileged land of glycosuria. This omission is very noticeable in the ninth report of Mr. Simon, under whose direction cholera was clinically and chemically investigated with much care and skill by Drs. Sutton and Thudichum in 1866. For although, in common with many previous observers, and especially with some of those who watched the first epidemic of the disease in 1832⁶, Dr. Sutton noted the occurrence of choleraic diuresis; yet it does not appear that sugar was in any of his cases suspected to be present; whilst in the report on the elaborate analysis of the urine in cholera by Dr. Thudichum there is no reference to sugar having been sought for on any occa-

¹ 'Études de Médecine Clinique et de Physiologie Pathologique—Le Choléra observé à l'Hôpital Saint-Antoine,' Paris, 1868.

² 'Nouveau Dict. de Méd. et de Chir. Prat.,' tom. vii, 1867, art. "Choléra Asiatique."

³ Unpublished memoir cited by M. Desnos.

⁴ Huppert, loc. cit., 1867.

⁵ Loc. cit., 1867.

⁶ Dr. Lawrie, 'Glasgow Medical Journal,' vol. v, 1832, p. 329; and Dr. Andrew Buchanan, 'Observations on Malignant Cholera,' 1848, pp. 11 and 17—18 (reprint of a paper brought before the Medical Society of Glasgow in November, 1832).

sion, the researches of the last-named observer in this direction having stopped short at the detection of urocyanine, which occurs in the urine during what may, to some extent, be regarded as the preliminary stage of cholera convalescence.

In studying the character of the urine in cases of cholera attention should, in the first instance, be directed to the fact that the first and albuminous urine passed or withdrawn after the usually prolonged suppression of the secretion is, as a rule, deficient in urea and free from sugar; and that the subsequent condition of temporary glycosuria is preceded by the occurrence of a blue colouring matter, which appears to be intimately associated with saccharine transformation. This colouring matter, which is developed by nitric and by hydrochloric acids, and also by simple exposure to the air, in the urine of cholera patients previous to the stage of convalescence, and which has been variously referred to as indigo-blue, indigose, choleraic urocyanine, urocyanose, uroglaucine, cyanurine, &c., was detected in the urine of cholera patients during the epidemic of 1849, by Dr. Parkes,¹ who observed that it was generally developed in large quantity when nitric acid was added to the first urine passed after the cold stage, and also in that drawn from the bladder during the cold stage itself in a case of cholera in which there was no further secretion of urine. The fluid obtained by Dr. Parkes on this last occasion contained, we are informed, "albumen, but no urea; and gave, with nitric acid, a deep violet colour, passing into a blackish purple." Its chief importance in the present inquiry is due to the fact that it is very closely associated with the development of glycosuria, and that the occurrence of sugar in the urine in these cases appears to be simply a somewhat later stage in the series of pathological changes, which, so far as they affect the urinary secretion, admit of being referred to one common origin.

Before attempting, however, to trace the source whence the sugar is derived it will be useful to study the character

¹ 'The Monthly Journal of Medical Science,' vol. ix, October, 1849, pp. 1127—1130.

of the glycosuria which has been observed during convalescence from cholera, together with the various physiological, pathological, and artificially produced states of the system in which sugar may, as in cholera, be present in the urine, without giving rise to confirmed diabetes. For temporary glycosuria, like the previous suppression of urine, has no claim to be regarded as an exceptional phenomenon which is in any way characteristic of this disease; but, on the contrary, it will be found to occur during convalescence from other forms of acute disease, in which it is often associated with the previous development of a blue-colouring principle in the urine; it will be found also to occur, apart from disease, as a physiological condition during certain stages of development and at certain epochs of life; and it will be found, finally, that it admits of being experimentally produced.

Observers have differed, and in some respects very greatly, both with respect to the constancy with which glycosuria occurs, and the importance which should be assigned to this condition of the urine as a sequel of cholera. For whilst some have looked upon it as if it were simply an accidental occurrence and liable therefore to be occasionally, if not frequently, absent, others have been induced to regard the presence of sugar in the urine as an important symptom in the disease. M. Gubler,¹ who has specially studied the subject and who has described glycosuria as "symptomatic in the reactional period of cholera," states that, "in the period of algidity and cyanosis, the urine carries away only albumen and indigose, analogue of the blue of aniline. In an intermediate stage proteic matters may be seen to coexist with the saccharine substance. Finally, in confirmed and advanced reaction sugar passes alone in the urinary secretion," and the sugar thus passed may, we are informed, amount to many grammes per litre of urine. M. Jaccoud² has remarked that "cholera is a frequent cause of passing

¹ 'Gazette des Hôpitaux,' 1866, pp. 410—411.

² 'Nouveau Dict. de Méd. et de Chir. Prat.,' art. "Diabète Sucré," tom. xi, 1869, p. 816.

melituria." M. Lorain,¹ who regards sugar in the urine as a customary phenomenon "in a typical case of cholera," states that its appearance is transient and its amount inconsiderable. M. Desnos² in like manner refers to choleraic glycosuria as a transitory phenomenon developed in proportion to the diminution of the quantity of albumen in the urine; and he cites a passage from the unpublished memoir of M. Gombault, who has gathered a vast amount of information respecting the convalescence of cholera, from which it appears that in a large number of cases there is, during cholera convalescence, a polyuria out of proportion with the quantity of drink taken, that sugar is present in the urine on such occasions in somewhat considerable abundance, and that it may sometimes continue to occur for a fortnight.

Coincidentally with this occurrence of sugar in the urine the amount of urea is considerably increased. According to the observations of M. Bordier³ at the Beaujon Hospital during the epidemic of 1866, which essentially agree with those of other able observers, glycosuria was "a constant phenomenon in the reaction of cholera," and during reaction the amount of urea (analysis made by Dr. Chalvet) was found to be 48 per 1000, or more than double the normal quantity. The increase of this important constituent is the more noticeable from the fact that the albuminous urine which is first passed after a previously more or less prolonged suppression of the secretion in cases of cholera is deficient in urea, and that diminution in the amount of albumen is succeeded by increase in the amount of urea, so that as reaction advances towards convalescence, the albumen, according to the observations of Dr. Parkes,⁴ gradually decreases in quantity and "has, in fact, a course almost inversely that of urea." The well-marked increase of urea which subsequently characterises the urine when, during the progress of cholera convalescence, albumen is not unfrequently replaced by sugar, accords with

¹ Op. cit., 1868, p. 41.

² Loc. cit., 1867, pp. 418 and 426.

³ Loc. cit., 1867.

⁴ Op. cit., 1860, p. 306.

what has been usually observed in cases of confirmed diabetes, in which a permanently saccharine condition of the urine is in like manner associated with an excess of urea : the excess in these cases, as in those of the temporary glycosuria of cholera, sometimes extending to double the normal standard.¹

This occurrence of a large excess of urea in the saccharine urine of confirmed diabetes is associated with a reduction of temperature which is not essentially due to the disease ; for, neither the glycosuria itself nor the relative amount of sugar in the urine can in any way be directly connected with the development of animal heat. In like manner the occurrence of sugar in the urine of cholera patients does not appear to be directly dependent on any change of bodily temperature, for no sugar is found, as a rule, during the algide stage of the disease, nor during the advanced stage of consecutive fever, and no direct connection has been traced between either the previous depression or the previous elevation of temperature in such cases and the subsequent amount of sugar in the urine. This fully accords with the observations of Dr. Balthazar Foster² in cases of confirmed diabetes in which, although the temperature in such patients is on an average reduced 1 to 3 degrees, yet it was found "that the variation in the quantity of sugar passed in the twenty-four hours is not proportional to the rise or fall of the temperature of the body ;" the same temperature having been observed to coincide with widely different quantities of sugar. And it is in accordance also with what might reasonably be expected to occur, for it would be inconsistent with the fact of an increased amount of urea being usually coexistent with the sugar to suppose that there is any direct connection between the glycosuria and the loss of animal heat.

In this brief retrospect of the pathology of the urine in cholera, the chief facts to which attention should be directed,

¹ Dr. Thudichum, 'Appendix to the Eleventh Report of the Medical Officer of the Privy Council,' 1869, p. 130.

² "Note on the Temperature in Diabetes," Humphry and Turner's 'Journal of Anatomy and Physiology,' May, 1869, pp. 377, 378.

with reference to the occurrence of glycosuria, are the suppression of the urinary secretion as a primary result of the disease, with arrested formation of urea; albuminuria with deficiency of urea; the presence of a blue-colouring principle; and, finally, diuresis with excess of urea and sugar in place of albumen. In the sequence of phenomena here indicated urea, as the essential principle of the urine, necessarily occupies the chief position, and the subsequent presence of sugar, during the stage of convalescence, when albumen is no longer present in the urine, suggests that the temporary glycosuria of cholera may be due rather to the progress of reparation than of destruction, and that it is, as it were, the result of an excess of restorative effort on the part of the system to repair loss from previous disease. This suggestion derives support from what occurs in diabetic patients during an attack of fever, when sugar in their urine is apt to be replaced by albumen, and by what occurs in the same class of patients during the last agony, when a similarly retrograde course, with respect to the pathology of the urine is pursued, for in them also the urine becomes albuminous and the sugar disappears; and it is moreover supported by a large amount of collateral evidence which, in the course of the inquiry, will be found to be almost conclusive in its favour.

It would be unnecessary and, indeed, altogether beyond the proposed limits of this paper to enter into any discussion respecting the comparative merit of the several theories which have been advanced to account for the saccharine transformation which precedes the appearance of sugar in the urine. But it is allowable to state that in attempting to explain the temporary glycosuria which occurs as a sequel to cholera, much assistance has been derived from M. Jaccoud's modification of the well-known theory of M. Schiff, and that this modified theory seems to accord best with the facts hitherto observed.¹

¹ With respect to the discovery, if such discovery has been made, of the true principle of glycogenesis, it is interesting to find that on this as on other similar occasions no one is, strictly speaking, entitled to claim any exclusive

In the theory advanced by M. Schiff¹ to account for the occurrence of sugar in the urine it had been assumed that the liver is the passive centre of diabetes, and that when this organ, charged with glycogenic matter, receives, in place of normal blood, blood charged with diastatic ferment, it becomes passively impregnated with sugar, which is carried away in the general circulation and in the urine. The modification of this theory proposed by M. Jaccoud,² and which enables us to account for much which apparently could not otherwise be satisfactorily explained, is founded on an objection to restrict the process of saccharine transformation to the liver; for glycosuria being essentially, a disorder of nutrition, M. Jaccoud not unjustly thinks that it would be unreasonable to limit the process to one organ or tissue; and he therefore argues that "as glycogenic matter and ferment suffice to make sugar, it is very evident that the formation of sugar should take place wherever these two conditions shall be realised, that is to say, wherever the ferment of the blood shall encounter glycogen." There would consequently be a parallelism between the formation of carbonic acid, urea, and sugar, which is obviously in favour of this theory. For in the same way that the formation of carbonic acid, instead of

merit. For even the modification of M. Schiff's theory by M. Jaccoud, referred to above, is simply a reproduction of the theory, unsupported at the time by sufficiently satisfactory evidence in its favour, which was promulgated by Carl Schmidt, of Dorpat, in 1850 ('Charakteristik der Epidemischen Cholera, &c.,' Leipzig and Milan); and which, soon after its publication, was cited and condemned by M. Claude Bernard ('Leçons de Physiologie Expérimentale,' tom. 1, 1855, pp. 444—447). Unconscious of the connection, which has since been established, between glycosuria and cholera, Carl Schmidt appended to his work on the epidemic disease a short notice of diabetes, in which he urged that as both sugar and urea are diffused in the blood of all parts of the body, they have no definite source which can be localised in any special organ, but that these two products are formed everywhere, in consequence of the molecular changes which take place in the blood; and he moreover entertained the opinion that in the course of these changes fat may give rise to sugar.

¹ "Nouvelles Recherches sur la Glycogenie Animale," 'Journal de l'Anatomie et de la Physiologie,' 1866, pp. 354—382.

² "Leçons de Clinique Médicale faites à l'Hôpital de la Charité," 1867, pp. 826—828.

being limited, as was formerly supposed, to the lungs, is now admitted to take place in any part of the system where oxygen has been brought into contact with carbon; and urea, in like manner, having been formed in the general system, is simply eliminated by the kidneys; so the formation of sugar, instead of being restricted, as was at one time thought to be the case, to the liver, may equally take place wherever the materials requisite for such transformation are brought together. Both M. Jaccoud and M. Schiff agree in referring this saccharine transformation to a pathological change, which is essentially dependent on "repose of the blood," or "cessation of its normal movement;" and they are both also of opinion that it is in consequence of this arrest, or "partial or general slackening of the blood," that "experimental lesions of the nervous system lead to glycosuria." It may at the same time be remarked that this modified theory is consistent with the celebrated discovery of Dr. Pavy, which was communicated to the Royal Society in 1858, and which has since been confirmed by many skilful observers, including McDonnell, Meissner, Jæger, Herzen, and Schiff, and fully accepted by M. Jaccoud himself, that the production of sugar in the liver is a *post-mortem* phenomenon. Moreover, the results which have been obtained from clinical observation admit of being most readily accounted for by the modified theory referred to above. For a careful consideration of the conditions which have been observed to favour the development of glycosuria will be found to be in accordance with the supposition that sugar in the urine is consequent on a previous stagnation of blood; and that the cases in which glycosuria may be traced more or less directly to some affection of the alimentary canal admit of being fully accounted for on the same supposition, since the alimentary canal is primarily the source or centre whence the blood or nutritive fluid of the body is supplied. There is no need to assume that the previous stagnation which occurs in these cases involves even temporarily a complete arrest, either general or local, of the circulation, although there are cases in which sugar in the urine has apparently been the result of such a limited arrest

of blood as has been sufficient to cause local death. In cases, for example, of temporary glycosuria consequent on carbuncle, the occurrence of sugar in the urine seems to be the result, not simply of impaired or diminished circulation, but of such a complete arrest of blood as leads to the death of the part affected, a good illustration of which has been published by MM. Philipeaux and Vulpian.¹

Much assistance has been derived in the present inquiry from an examination of the various conditions of the system both in health and in disease during which, apart from cholera, glycosuria is liable to be temporarily developed. For some time it has been known that sugar is physiologically a usual constituent of the urine in certain states of the system and at certain epochs of development, as for example, during lactation, the earlier stages of foetal development, and occasionally also at very advanced periods of life; whilst among those conditions, in which it may pathologically be regarded as a frequent constituent of the urine, are malarious diseases, both intermittent and remittent; the period of convalescence from many acute forms of disease; local arrests of the circulation, such as occur in carbuncle, gangrene, and tubercle; and injuries and diseases of certain parts of the nervous system, the effects of which have often formed the subject of investigation in experimental physiology.

With reference to the occurrence of sugar in the urine during what may be broadly defined as the period of milk formation in women, it may be remarked that although women are usually far less liable than men to suffer from diabetes, yet there is a remarkable exception to this influence of sex in the case of women in the puerperal state, which, taken in connection with what has been observed respecting the continuance of the mammary secretion when the urine is suppressed in choleraic collapse (a condition which has been referred to antagonism between the nutritive and reproductive functions), will be of much use in the present inquiry.

¹ "Note sur un cas de diabète passager survenu pendant le cours du développement d'un anthrax," 'Gazette Hebdomadaire,' tom. viii, 1861, pp. 782—784.

The occurrence of puerperal glycosuria is essentially connected with, and dependent on, the continuance of the lacteal secretion, and it consequently suggests a satisfactory explanation of the presence of sugar in the urine during convalescence from cholera. It was announced by M. Blot,¹ in a communication to the French Academy of Sciences, in 1856, that sugar exists in the urine of all lying-in women, of all suckling women, and in about half the number of pregnant women; the occurrence of sugar in all these cases being essentially connected with the development of the lacteal secretion. In one of the cases recorded by M. Blot (who was assisted in the chemical part of his researches by MM. Reveil and Bertholet), in which a woman had continued to suckle her infant for twenty-two months, he found 8 grammes of sugar in 1000 grammes of urine, whilst, on the contrary, he found that when lactation ceases, the sugar disappears from the urine, "more quickly in women who do not suckle, more slowly in those who, after having suckled, begin to wean." The correctness of his observations was for a time contested, but their accuracy has been fully demonstrated by subsequent inquirers, among whom may be cited M. Lecoq,³

¹ "De la Glycosurie Physiologique chez les femmes en couches, les nourrices, et un certain nombre de femmes enceintes." 'Comptes Rendus de l'Académie des Sciences,' tom. xliii, 1856, pp. 676—678.

Sugar had been detected, previous to M. Blot's observations, in the urine of a puerperal woman on the fifth day after delivery by Lehmann ('Jahresb. d. Physiol. ch.,' 1844, s. 27), in which case the secretion of milk having been suddenly suspended, the sugar only appeared in the urine for four days. The coincidence of lactation and glycosuria had also been referred to by M. Bouchardat ('Répertoire de Pharmacie,' tom. 6, p. 178, and 'Mémoires de l'Académie Nationale de Médecine,' tom. 16, 1852, pp. 69—212), who had specially recorded two cases of puerperal glycosuria, one of them being the case of a healthy young woman, whom he attended conjointly with M. Roche, and in whom during lactation, characterised by a superabundance of milk, temporary glycosuria was developed to so great an extent that the patient passed seven litres of urine containing seven hundred grammes of glucose in the twenty-four hours. Whilst Prof. René (cited by M. Emile Barbier, 'Le Diabète Sucré, Thèse-Montpellier,' 1856, p. 16) had established "the existence of saccharine diabetes in some women arrived at the last period of pregnancy."

³ 'Gazette Hebdomadaire,' tom. x, 1863, pp. 35—39.

who has specially noticed, with respect to the glycosuria of pregnant women, that the quantity of sugar increased towards the end of their pregnancy, when milk begins to be present in the breast, and that sugar is constantly present in the urine during lactation; whilst M. Becquerel,¹ having examined the urine of nine women recently delivered and suckling their infants, has recognised that the facts announced by M. Blot are perfectly correct. The occurrence of this temporary glycosuria in the puerperal state is the more remarkable from the fact that women attacked with true diabetes very rarely become pregnant; whilst, on the other hand, lactation especially when too long continued, appears to be a cause, not only of glycosuria as a temporary phenomenon, but of confirmed saccharine diabetes, three such cases having, for example, occurred in the practice of M. Bouchardat.² The dependence of temporary glycosuria in these cases on a nutrient drain from the system during the puerperal state is well illustrated by a case recorded by Dr. Bennewitz in Osann's 'Clinical Report' for 1823-4-5,³ in which glycosuria was exceptionally developed at a very early period of at least three successive pregnancies, independently of the formation of milk, in consequence of the continuance of a menstrual flux.

There can be no difficulty in perceiving that, owing to the apparent antagonism which prevails between nutrition and reproduction, what has been already suggested to account for the occurrence of puerperal glycosuria is equally applicable to cases of cholera, in which a central arrest of nutrition seems to permit of the continuance, and, as regards lactation, sometimes even of an increase of the functions associated with reproduction, and in which also glycosuria is commonly observed among the sequelæ of the disease, following albuminuria, and apparently preceding the complete re-establishment

¹ 'Bulletin de la Société Médicale des Hôpitaux de Paris,' tom. iii, 1864, pp. 368—369.

² 'Revue des Cours Scient.,' January 9th, 1869, p. 92.

³ Cited in 'Edinburgh Medical and Surgical Journal,' vol. xxx, 1828, pp. 217, 218.

of the nutritive functions. The aid which has been derived from these cases of puerperal glycosuria should moreover lead us to expect that in extending still further the limits of the inquiry by studying the conditions which have been found in other cases and on other occasions to favour or oppose the temporary occurrence of sugar in the urine, we may succeed in obtaining a clearer insight into the nature of this peculiar state of the system. In pursuance therefore of the inquiry in this direction it will be useful to bestow attention on the rarity of the occurrence of glycosuria in infancy, and its comparative frequency in old age; the contrast presented during these two periods being the more remarkable from the fact that at the extreme limits of life there is, as regards the occurrence of sugar in the urine, an inverse relation between the influence of age and the influence of diet, which is opposed to what has been observed respecting the relation of glycosuria to diet during mature life. For the amount of sugar and of sugar-forming material usually contained in the food of infants would, if taken at a later period of life, be capable, at least to some extent, of aiding in the development of glycosuria, and even during lactation, when the mother herself is temporarily diabetic, the urine of the infant which she suckles is free from sugar. Whilst in old age, although the diet is then relatively deficient in saccharine matter, the urine is often found to contain sugar.¹

This temporary glycosuria of the puerperal state, of old age, and of foetal existence, is, strictly speaking, a physiological phenomenon independent of any pathological change in the system, which may, it is true, in some cases be associated with the passage of sugar in the urine, but which may also in other cases intervene to prevent it. In the glycosuria, for example, of suckling women it has been observed that when their health is impaired by disease, sugar sometimes ceases to

¹ Dr. A. Dechambre, "Sur la presence habituelle du sucre dans l'urine des vieillards," 'Gazette Médicale de Paris,' 1852, pp. 220—222; Dr. Bence Jones "On the frequency of Diabetes in Old Age," 'Med.-Chir. Trans.,' vol. xxxvi, 1853, pp. 420 *et seq.*; and Dr. Roberts, 'A Practical Treatise on Urinary and Renal Diseases,' 1865, p. 206.

be passed. The continuance of puerperal glycosuria would therefore have to be regarded as a normal condition, whilst its cessation would be an indication of some abnormal change. Now there is a fact of much significance from its connection with the glycosuria of cholera, to which special attention has lately been directed by M. Burdel,¹ respecting the recurrence, through the influence of intermittent fever, of sugar in the urine of suckling women in whom it had been for a time pathologically suppressed; and he has also directed attention to the very exceptional occurrence, through the same morbid influence of sugar in the urine of infants at the breast. The ordinary occurrence of glycosuria as a result of intermittent or marsh fever, to which M. Claude Bernard, in a communication addressed some time since to the French Academy, directed attention as a new fact, had been noticed many years previously by Dr. Prout,² who, in referring to the connection between saccharine mal-assimilation and malaria, stated that although "diabetes can be hardly pronounced a malarious disease, yet he had seen many cases of diabetes from malarious districts." But it is chiefly to M. Burdell that we are indebted for definite information on this subject, and he has succeeded in showing the extent to which sugar in the urine is liable to occur in the various forms of malarious disease, the greatest quantity being present in cases of the pernicious fever or ague of Algeria. Such observations are interesting and to some extent important from the analogy which can be traced in other directions between the graver manifestations of ague and cholera, of which the culminating point in both, so far as regards the renal secretion, is the complete and prolonged suppression of urine.³

With regard to the occurrence of temporary glycosuria as a result of previous disease, it is instructive to notice that in

¹ "Mémoire sur la Glycosurie dans les Fièvres paludéennes," *L'Union Médicale*, 1859, tom. iv, p. 389.

² 'On the Nature and Treatment of Stomach and Renal Diseases,' 5th edit., 1848, p. 19.

³ Haspel, 'Maladies de l'Algérie,' tom. ii, pp. 292—293; cited by Dr. John Macpherson, 'Cholera in its Home,' 1866, p. 66.

the large group of cases lately referred to in the paper "On some Analogies of Cholera in which Suppression of Urine is not accompanied by symptoms of Uræmic Poisoning,"¹ there is, as regards the urine, essentially the same sequence of phenomena as there is in cholera. The suppression of urine which has been very generally observed in these cases,² being liable to be followed by temporary albuminuria, by the development of a blue-colouring principle in the urine,³ and, finally, by temporary glycosuria. Many of the older writers on diabetes, including Rollo, Cruikshank, Hodgkin, and others, were of opinion that the presence of sugar in the urine was a result of gastro-intestinal disorder, and M. Dezeimeris⁴ has directly referred it to an anterior gastro-enteritis. Dr. Pavy⁵ seems to have been at least willing at one time to have entertained the same opinion, for he writes, "I have often thought that I could trace a connection between diabetes and an irritable state of the alimentary mucous membrane. . . . The idea, in fact, has occurred to me whether a certain state of the digestive canal may not, by reflex action through the sympathetic system, occasion diabetes." Sir Thomas Watson,⁶ Dr. Garrod,⁷ Prof. Griesinger,⁸ and other writers, have referred to the practice

¹ 'Medico-Chirurgical Transactions,' vol. li, 1868, pp. 1—43.

² 'Dict. Encyclop. des Sciences Médicales,' art. "Albuminurie," tom. ii, 1865, pp. 495 *et seq.* See also a paper by Munk and Leyden, "On Albuminuria and Steatosis in poisoning by acids and especially by Sulphuric Acid," cited in 'Gazette Hebdomadaire,' 20 Janvier, 1865, pp. 44, 45.

³ A considerable amount of evidence has been accumulated to illustrate the occurrence of albuminuria, and of a blue-colouring principle in the urine, in gastro-intestinal affections, which, owing to the limited space at the author's disposal, may be more conveniently referred to on another occasion.

⁴ 'Mémoires de la Société Médicale d'Emulation de Paris,' tom. ix, 1826, p. 231.

⁵ 'Researches on the Nature and Treatment of Diabetes,' 2nd edit., 1869, pp. 197, 198.

⁶ 'Lectures on the Principles and Practice of Physic,' 3rd edit., 1848, vol. ii, p. 603.

⁷ 'British Medical Journal,' 1857, p. 321.

⁸ 'Archiv für physiolog. Heilk.,' tom. i, 1859; and 'L'Union Médicale,' 1862.

of drinking a large quantity of cold water when the body has been overheated as a cause of diabetes. Dr. John Grove has informed the author that he has often detected sugar in the urine in cases of typhoid fever, especially in young patients, about the twenty-seventh day of the disease; but it does not appear that his observations have as yet been verified either by Dr. Murchison or by other writers on this disease. Dr. Robinson Hill¹ detected sugar in the urine in a small series of four cases of burns, in which, as is well known, ulceration of the duodenum is liable to occur, and in which, without any special affection of this kind, there may be, as in the case lately observed by Dr. Sutton,² diarrhœa with collapse, and post-mortem appearances very closely resembling those of cholera. M. F. Devay³ (of Lyons) has observed a case of temporary glycosuria, which continued for a year and a half, and which disappeared on the expulsion of a tænia. Dr. Latham⁴ states that in at least two cases of poisoning by arsenic which had come under his own observation there was, as a subsequent result of the poisoning, gradual emaciation and diabetes, and from the observations of Dr. Thudichum⁵ it would appear that in "all cases" of mercurialism, the urine affords indications of the presence both of albumen and of sugar. Dr. Christison⁶ has likewise detected both albumen and sugar in the urine as a result of dyspepsia. M. Becquerel⁷ has found sugar in the urine in a case of chronic diarrhœa and in one of slight enteritis. Sugar has also been found in the urine by Dr. George Harley⁸ after eating cheese or other indigestible food. This last-named observer has remarked that asparagus salad caused saccharine urine in himself; and a case of the same description has come under

¹ Beale's 'Archives of Medicine,' vol. ii, 1861, pp. 172—178.

² 'British Medical Journal,' July 2nd, 1870, p. 7.

³ Cited by M. E. Gueneau, "De la Glycosurie Passagère," 'Thèse de Paris,' 1866, p. 16.

⁴ 'Facts and Opinions concerning Diabetes,' 1811, p. 216.

⁵ 'A Treatise on the Pathology of the Urine,' 1858, p. 408.

⁶ 'Edinburgh Monthly Journal,' vol. xii, 1851, pp. 554, 555.

⁷ 'Bull. de la Soc. Méd. des Hôp. de Paris,' tom. iii, 1864, pp. 368, 369.

⁸ 'L'Union Médicale,' tom. xii, 1858, p. 116.

the author's observation in which asparagus (cooked) invariably caused temporary glycosuria. In pursuance of this subject it may be further remarked that in a case observed by Dr. Cardan,¹ of "Diabetes induced by an overdose of Nitrate of Potash," which was brought before the French Academy of Sciences on January 15th, 1849, the first result of the poisoning, it is stated, was great irritation of the intestinal mucous membrane, and abundant diuresis, followed by a strong desire for eating and drinking, with easy and rapid digestion; notwithstanding which there was gradual emaciation, and the diuresis increased till as much as five quarts of urine containing sugar were passed every night. The strong desire for food and the ability to digest it, which Dr. Cardan refers to in this case, are very suggestive, for when in cases of confirmed diabetes, in which, as is well known, both the appetite and the digestion are apt to be abnormally increased, these conditions, as regards the alimentary canal are reversed, an opposite result as regards the urine, is produced. This was very noticeable in Dr. J. W. Ogle's² case of diabetes associated with disease of the brain, in which, when paralysis "with dysphagia and vomiting" came on "sugar ceased to be found in the urine, even though farinaceous food was permitted," and it fully accords with what has been long since observed by Dr. Budd and Mr. Busk,³ who found that diabetes was completely arrested by an attack of cholera. In like manner Dr. H. Bell⁴ found that in diabetic patients "active purging or abundant diarrhoea has a powerful effect in diminishing the quantity of urine and even of the sugar contained in it. But this effect," he remarked, "is only momentary; as soon as the alvine function is re-established to its normal state the alterations of the urine reappear with the same intensity." It has also been observed by M. Claude Bernard⁵ that when the digestive functions are disturbed

¹ 'Lancet,' 1849, vol. i, p. 155.

² 'St. George's Hospital Reports,' vol. i, 1866, p. 166.

³ 'Med. Chir. Trans.,' vol. xxi, 1838, p. 157.

⁴ 'An Essay on Diabetes,' translated by Alfred Markwick, 1842, p. 40.

⁵ 'Leçons de Physiol. experim.,' tom. i, 1855, pp. 180, 181.

sugar disappears from the urine ; and he mentions the case of a diabetic woman “ who had, at the same time, a chronic affection of the intestines. From time to time this latter affection passed into the acute state, and the patient had attacks of colic and diarrhœa. Immediately these symptoms appeared the sugar ceased to show itself in the urine, but it reappeared as soon as the intestinal affection abated. I saw,” adds M. Bernard, “ these alternations reproduced five or six times.”¹

The temporary occurrence of sugar in the urine, as may be readily inferred from what has been previously said on the subject, is not limited to such cases as the preceding, but may often be recognised during convalescence generally from acute disease, when there is, as in the case of Dr. Cardan and others already described, both a strong desire for food and also the ability to digest it. M. Bordier,² who has lately written a paper on this subject, states “ that glycosuria is a phenomenon nearly normal in the convalescence of acute diseases ;” and he refers to the fact, which is interesting from its connection with the temporary glycosuria of cholera, that in certain cases similar to those in which glycosuria is developed “ the blue coloration appears.”

It would, perhaps, be unnecessary, at this stage of the inquiry, to stay to consider the temporary occurrence of glycosuria in other morbid states of the system, which equally admit of being referred to a restorative effort to repair some previous waste or loss ; but it may be useful to notice, with reference to the coincidence of sugar in the urine with local arrest of the circulation, such more espe-

¹ A paper by the late Dr. William Macintyre on “ Cases of Perforation and other lesions of the Stomach occurring in connection with Diabetes Mellitus, with Observations on the Gastric Origin of that Disease,” was read at the Royal Medical and Chirurgical Society, March 27th, 1849; and was reported in the ‘Lancet,’ 1849, vol. i, p. 376. As the history of the three cases given in this paper is obscure, and as the gastric lesion may not improbably have been a post-mortem occurrence, this paper cannot be referred to with any advantage on the present occasion.

² “ De la Glycosurie dans la Convalescence des Maladies Aigues,” ‘Archives Générales de Médecine,’ 6e. sér., tom. xii, 1868, pp. 183—190.

cially as has been observed in cases of gangrene, carbuncle, and tubercle, that the recent experiments of Prof. Schiff, which have been cited and accepted by M. Jaccoud,¹ tend to establish that gangrene, contrary to the opinion entertained by many observers, may be the primitive accident, and produce, as secondary effect, the diabetic state; "in other terms," adds M. Jaccoud in illustration of M. Schiff's experiments, "the changes produced in the circulation by the local mortification would be sufficient to give rise in the blood to diabetic ferment, which is, according to this eminent observer, the only and constant cause of diabetic glycosogenesis." And this leads to the consideration of the character and the extent of the experimental evidence which can be adduced to show that choleraic glycosuria is the result of a restorative effort consequent on a previous affection of the abdominal sympathetic nervous system, such as would be capable of temporarily producing a central arrest of nutrition and a local stagnation of blood.

It is obvious that, in all experiments on the sympathetic nerve, the primary effect produced must be on the vascular system, to which its branches are distributed; and that any effect produced on other parts of the organism must be secondary to this. When recognising, therefore, vascular paralysis as the primary result of section of the sympathetic nerve in all (or nearly all) parts of the system, it is important to notice that in the secondary results produced, no such constant uniformity has been observed, since these are liable to vary according to the locality in which the experiment has been performed. With reference more especially to the occurrence of temporary glycosuria, all experimental observers are agreed that section of the sympathetic in many parts of the system occasions local hyperæmia and saccharine urine; but it has also been observed that in some parts of the system the primary effect of local hyperæmia consequent on section of vaso-motory nerves has not always been followed by an appearance of sugar in the urine. For example,

¹ Loc. cit., art. "Diabète sucré," p. 279, 1869.

whilst section of the vertebral sympathetic leads to temporary glycosuria, section of the carotid sympathetic is followed by no such result.¹ This difference may possibly be connected with the anatomical fact that the sympathetic nerve at its cephalic extremity divides into two cords, the one vertebral, and the other carotidean;² and it is perfectly consistent with Chossat's³ observation that in death by starvation there is, in the midst of losses sustained by other organs, absolutely no loss of weight sustained by the brain itself; and also with the singular fact observed by M. Claude Bernard,⁴ that in cases of poisoning by curari, in which the urine, after a certain time has elapsed, becomes saccharine, all the nutritive functions are exaggerated, and at the same time the secretions are produced in unequal abundance; the secretion, for example, of the submaxillary gland being much more profuse than that of the parotid gland. But although this part of the inquiry may at present seem to be somewhat obscure, yet it is not unreasonable to expect that such observations will ultimately help to explain why, coincident with a central arrest of nutrition, the cerebral faculties during cholera are unimpaired. Some additional light has very recently been thrown on this part of the inquiry by the observation that not only is section of the splanchnic nerves, like section of the carotid sympathetic, unaccompanied by glycosuria, but that after this operation has been performed, neither irritation of the floor of the fourth ventricle, nor of

¹ It was observed by Dr. Pavy (op. cit., 1869, p. 177) that alkalies injected into the veins before operating on the sympathetic nerve prevent glycosuria; whilst, on the contrary, phosphoric acid (which was selected for the purpose) either swallowed or injected into the veins, causes saccharine urine without any previous nerve-section. The importance of this experimental evidence is illustrated by the fact that the temporary glycosuria which occurs as a sequel of cholera is preceded by diminished alkalinity of the blood. ('On the Nature of Cholera as a Guide to Treatment,' by Wm. Sedgwick, 1866, second issue, pp. 82—84.)

² M. Bourguery, "Extrémité Céphalique du Nerf Grand-Sympathique," Archives Générales de Médecine, 4e sér., tom. viii, 1845, p. 119.

³ 'Recherches Expérimentales sur l'Inanition,' 1843, pp. 90, 91.

⁴ Op. cit., 1855, tom. i, pp. 372, 373.

the distal ends of the cut nerves, is capable of giving rise to sugar in the urine. There is perhaps, with reference to the occurrence of temporary glycosuria as a sequel of cholera, no fact in experimental physiology more significant than this absence of sugar from the urine after section of the splanchnic nerves, which taken in conjunction with the fact just stated, that there is a corresponding absence of sugar from the urine after section of the carotid sympathetic nerves, would lead us to anticipate that the urine during collapse, and for some time afterwards, will, as a rule, be free from sugar, and that the intellectual faculties will at the same time be unimpaired. It appears to have been first pointed out by Eckhard¹ in 1867, that after section of the splanchnic nerves, glycosuria could not be produced. But it was not till the publication of M. Moreau's² experiments in the following year that the connection between these nerves and cholera itself was experimentally demonstrated, when it was shown that section of them was followed by an intestinal flux, possessing essentially the same character as the flux in cholera.³ The evidence afforded by M. Moreau in these experiments of an intestinal flux following section of the abdominal nerves accords with the observations of earlier experimental physiologists, who have noticed that section of the sympathetic nerve in other parts of the body has in like manner been followed by a flux.⁴ But in addition to

¹ 'Beiträge zur Anatomie und Physiologie,' 4ter Band, 1st. heft, 1867.

² 'Comptes Rendus des Séances de l'Académie des Sciences,' tom. lxxvi, 1868, pp. 554—557; and 'Bulletin de l'Académie Impériale de Médecine,' 31 Mai, 1870, pp. 388, 389.

³ Attention may be usefully directed to a paper by M. Demarquay ("Mémoire sur les modifications imprimées à la température animale par la ligature d'une anse intestinale," 'Gazette Hebdomadaire,' tom. vii, 1860, p. 825), in which it was shown that "the phenomenon of coldness which is often observed in man under the influence of hernia or of internal strangulation, and which may simulate cholera in its algide period, is due to a constriction more or less strong of an intestinal fold. The lowering," adds M. Demarquay, "has been so much the more marked the higher the ligature has been placed on the digestive tube."

⁴ M. Pourfour de Petit, 'Histoire de l'Académie Royale des Sciences,' Année 1727. Paris, 1729, p. 14; M. Dupuy, 'Journal de Médecine, Chirurgie, Phar-

increased secretion as a result of sympathetic nerve section, it has been specially observed by M. Schiff¹ that an organ in a state of neuro-paralytic hyperæmia is peculiarly susceptible of local irritation, and in his remarks on "the phenomena consecutive to extirpation of the abdominal portions of the great sympathetic in relation to the stomach," he has helped us to gain an insight into the initial pathology of the flux in cholera, which becomes still clearer when viewed in connection with the fact (of the correctness of which M. Schiff has assured himself by repeated experiments), that after extirpation of the cœliac ganglion there is no interference with the mechanism of vomiting, since animals operated on in this manner are affected exactly as in the normal state by ipecacuanha or antimony; and which, moreover, admits of being subsequently illustrated and confirmed by Pacini's² microscopic observation on the gastro-intestinal mucous membrane after death from choleraic collapse.

When this neuro-paralytic condition of the digestive canal is compared with what occurs after the influence of the central portion of the sympathetic nervous system has been artificially increased by the application of galvanism or electricity to the part during life, it will be found that the results then obtained are essentially opposed to those which follow arrest or diminution of this influence, either from section of the nerves or from cholera. This has been well shown in Messrs. Linati and Caggiati's³ observations on the effects

macie, &c.,' tom. xxxvii, 1816, pp. 340—350; M. Rouget, 'Leçons sur le Diagnostic et le traitement des principales Formes de Paralyse des Membres Inférieurs,' par C.-E. Brown-Séquard; traduit de l'Anglais par le Dr. Richard Gordon; 2e édit., 'revue et annotée par l'auteur, précédée d'une Introduction sur la Physiologie des Actions Réflexes empruntée aux Leçons de M. le Professeur Ch. Rouget,' Paris, 1865, pp. 39, 40; and M. Claude Bernard, 'Journal de la Physiologie,' tom. v, 1862, p. 410.

¹ 'Leçons sur la Physiologie de la Digestion, faites au Muséum d'Histoire Naturelle de Florence,' tom. ii, 1867, pp. 440, 441.

² 'Du Choléra Asiatique,' traduit de l'Italien par le Dr. E. Janssens, Bruxelles, 1865, p. 11.

³ 'Recherches Expérimentales sur les effets du Courant Electrique appliqué au Nerf Grand-Sympathique,' Parme, 1859.

of the electric current applied to the great sympathetic in man, and in some of the lower animals, during an otherwise undisturbed state of the parts. In these experimental investigations the composition and modification of the urine were the principal objects of research, and they will serve to illustrate what occurs during restorative as distinguished from febrile reaction in cholera, when owing to an unduly increased activity consequent on a previous suspension of organic function urea is formed in excess and sugar is passed in the urine. It was noted by these observers that the prolonged application of the electric current to the organs which are supplied by the great sympathetic had the effect of increasing the appetite, of quickening the digestion, of rendering more active the absorption by the stomach and intestines; one of the consequences of which was that the fæcal matters became more solid and united; and, in addition to an increased amount of urea in the urine, it led also to the more rapid diffusion of sugar in the course of circulation and in the urine.

It may be urged against this proposed explanation of the temporary glycosuria, which occurs as a sequel of cholera, that if sugar in the urine be thus due to a restorative reaction from previous arrest, either local or general, of nutrition, and consequent stagnation of blood, that it fails to account for the occurrence of sugar in the urine during lactation and foetal existence, when there appears to be no diminution or arrest, but, on the contrary, and especially in the foetus, increased rapidity in the circulation of the blood. There is, it must be admitted, some difficulty at first sight in replying to this objection, for although alimentation through the medium of the stomach does not occur in the foetus, and nutrition during lactation is insufficient for some at least of the wants of the maternal system, yet many observers would probably be unwilling to allow that the sugar which occurs in the urine at these times can be immediately referred to the previous stagnation of blood.

Notwithstanding the apparent force of this objection, there is no occasion to doubt that the temporary glycosuria which

occurs in such cases is essentially dependent on the same cause as the temporary glycosuria of cholera; and that so far from there being any widely marked distinction between the occurrence of this phenomenon in cholera, in lactation, and in foetal existence, there is, on the contrary, much that is common to them all. In a paper which was lately published "On the continuance of the Mammary Secretion when the Urine is Suppressed in Choleraic Collapse,"¹ it was shown that the continuance of the one secretion and the arrest of the other are to be accounted for by the antagonism which naturally exists between the two great functions of nutrition and reproduction; and that, owing to this antagonism, an interruption of the functions associated with nutrition does not, during the collapse of cholera, lead to any corresponding interruption of the functions associated with reproduction. As a result therefore of this independence, so to speak, of reproductive life, the secretion of milk during collapse is, as a rule, undiminished, if not sometimes even relatively increased; whilst all that belongs to the well-being of the foetus itself, including the integrity of the foetal membranes, and the requisite amount of the amniotic fluid, often remains undisturbed amidst the wreck which, in the maternal system, has followed a central arrest of nutrition. In addition to the evidence cited on that occasion, attention may be directed to Dr. Thudichum's² case of Cæsarian section, in which the bladder of the foetus was found to be full of urine, whilst that of the mother, who had died from cholera, was, as is usual, quite empty. For, apart from any influence which might have affected the general principle of life in the foetus, this presence of urine in its bladder shows, like the undiminished amount of amniotic fluid, that it has essentially an independent existence, which enables it successfully to withhold any contribution to the drainage which is fatal to the maternal system. Moreover, there is, strictly speaking, nothing exceptional in this independent retention of fluid for the well-being or otherwise of foetal existence, since the con-

¹ 'British Medical Journal,' September 19th, 1868, pp. 307—309.

² 'Simon's Ninth Report,' pp. 464, 465.

tinuance of the mammary secretion is an illustration of the same kind of independence, showing that the several functions associated with the maintenance of the species can, during the failure of the life of nutrition, be fully sustained, both directly as regards the life of the fœtus in the womb, and indirectly as regards the life of the infant at the breast.¹

The chief difficulty therefore to be overcome before the occurrence of temporary glycosuria in these cases can be satisfactorily explained in accordance with the theory proposed is to determine the situation and extent of the previous stagnation of blood; for although an arrest of the circulation is very evident in cases of cholera, it cannot be so readily recognised during lactation and fœtal existence, when a stricter investigation is consequently needed to enable us to locate its occurrence. The most satisfactory explanation of the excess of saccharine transformation and of consequent glycosuria occurring in these cases appears to be this: the sympathetic or vaso-motory nervous system is the moderator of secretion in virtue of its action as controller of the circulation, and it occupies a position which is

¹ The antagonism which has been referred to between nutrition and reproduction is in accordance with the observations of M. Legros ('Gazette Médicale de Paris,' 1866, p. 104), that paralysis of the branches of the sympathetic nerve distributed to erectile tissues, not only of the reproductive organs themselves, but also of other parts, instead of causing turgescence produces a less active determination of blood to the part; so that immediately after extirpation of the superior cervical ganglion, for example, in cocks and turkeys, the erectile tissue of the head on the operated side becomes pale and collapsed. The exceptional phenomena in the physiology of erectile tissue are associated with peculiarities of structure to which special attention has lately been directed by M. Legros himself ('Journal de l'Anat. et de la Phys.,' Ch. Robin, tom. v, 1868, pp. 1—24), and by Professor Ercolani, of Bologna (ibid., tom. vi, 1869, pp. 364—389); whilst the fundamental importance of the antagonism on which they depend admits of being very simply illustrated by what naturally occurs in many of the more lowly organised animals, and notably so in certain insects, in which nutrition is strictly limited to the earlier or caterpillar state, and is subsequently rendered impracticable during the later or reproductive period of existence, through a retrograde change having been effected in the organs of alimentation, in consequence of which such animals, more especially belonging to the male sex, cease not only to eat but sometimes even to possess a mouth.

functionally midway between the secretory surface on the one side and the supply of blood on the other. The activity with which consequently a secreting organ exercises its function is, within certain limits, regulated by the amount of blood which passes through the organ in a given time; the effect produced on the circulation being apparently the result of an influence reflected from cell-function; and when, from any cause, the influence emanating from cell-function and transmitted by the vaso-motory nervous system is either temporarily or permanently arrested, the secretion is apt to become immoderate, and at the same time the blood becomes stagnant. It is probable, but not as yet clearly demonstrated, that an excessive or long-continued exercise of secretory function in any organ is of itself sufficient to lead to weakening or exhaustion of the vaso-motory nervous influence of the part; and that the loss of this nervous influence being followed by stagnation of blood is relatively favorable to the continuance of the secretion, but, at the same time, is absolutely unfavorable to the general nutrition of the system, at the expense of which it would, without any equivalent being given in return, continue to be maintained. The fatal character of the flux in cholera may, in accordance with these views, be readily explained, without any necessity for assuming that the flux itself, either with reference to quantity or quality, ought on its own account to be regarded as an essential element of danger, but rather as the expression of such an arrest of vaso-motory nervous influence, and consequent stagnation of blood at the fountain head of organic life, as must, if such arrest of nervous influence be continued, inevitably lead to death. And when, from the consideration of the flux in cholera, attention is transferred to the mammary secretion, the same principle of reasoning is available to account for what must be regarded, so far as the general nutrition of the mother is concerned, as an excessive and exceptional activity of function on the part of the mammary gland, the exercise of function in this case being excessive, as there is no adequate retribution made for the loss thus sustained; and exceptional, as it is not the

customary condition of the gland. In this respect it is obvious that the uninterrupted continuance of the mammary secretion would be indicative of such diminution or arrest of the local circulation of the blood as must be sufficient to account for the temporary glycosuria which has been observed to be coincident with it, and to cease when the mammary gland no longer secretes milk.

The explanation of the temporary glycosuria which has been observed to occur during the earlier stages of foetal development is founded on the same physiological reasoning; for the occurrence of glycosuria during this period of existence is primarily referrible to the placenta, which is at once the most active of the secretory organs of the foetus, and, moreover, is the organ on which it has to depend exclusively for support. It is apparently in consequence of the placenta being thus as it were the central organ of nutrition for the foetus that there is, as regards the anatomical character and distribution of its vessels, special provision for securing a structure favorable to a local delay of blood, and consequently favorable to an excessive activity of function.

The presence moreover, especially during the earlier stages of embryonic life, of an amyloid substance in the cells of the placenta which, according to Dr. McDonnell,¹ "is found in large quantities (in the placentæ of cats and of rabbits) at a time when the growth of the foetus is progressing rapidly," and which, according to the same observer, "has either totally or almost totally disappeared from the placenta, shortly before the birth of the young," seems to show that in addition to the supply of blood there is in these elementary structures a special provision for securing an excessive exercise of cell function. And this supposition is strengthened by an examination of the tissues of the foetus itself; in which, as in the placenta, there is, during embryonic development, a large accumulation of amyloid substance, which is much diminished if it does not altogether disappear before birth. From this examination of its tissues it may conse-

¹ 'Observations on the Functions of the Liver,' 1865.

quently be concluded that as there is in the foetus no such differentiation of the functions of organic life, as is met with after birth—foetal existence representing what is essentially a very low type of organic life—so likewise there is, as regards the formation of sugar, an absence of that localisation of amyloid substance, which, after birth, is normally limited or nearly so to the liver; but which, during embryonic life, is diffused through the foetal tissues in such a way that according to Dr. McDonnell “it would appear to be the formative material from which these tissues are evolved, and would seem related to their growth and development, as starch is to the growth and development of vegetables.” Hence the occurrence of foetal glycosuria which is restricted, as a rule, to the earlier months of intra-uterine life, and which ceases altogether before birth, is an indication that in the series of organic changes in which nutriment is prepared for and applied to the development and growth of the system, the amount supplied is, at some stage of the process, greater than the amount which can be either sufficiently elaborated or employed.

In conclusion it may be urged that the same tendency to increase of fatty matters in the blood which occurs in cases of defective nutrition prevails also in cases of cholera, in which it has been observed that “the fatty matters (of the blood) are nearly doubled (and sometimes trebled) in quantity:”¹ and although there is a want of sufficient

¹ MM. Becquerel and Rodier’s ‘Pathological Chemistry,’ translated by Dr. Speer, 1857, pp. 90 and 131.

The occurrence of diabetes in unusually fat individuals has been noted by many writers on the disease, among whom may be cited Dr. Prout (op. cit., 5th edit., 1848, pp. 30, 31), Dr. Bence Jones (‘Med. Chir. Trans.,’ vol. xxxvi, 1853, pp. 402—419), Dr. J. W. Ogle (loc. cit., 1866, p. 160), M. Jaccoud (loc. cit., 1869, p. 296), and Prof. Seegen, of Carlsbad (‘Contributions à l’étude clinique du Diabète Sucré,’ ‘Archives Générales de Médecine,’ 1867, pp. 295—313; reduced from a series of memoirs in Virchow’s ‘Archiv für Pathologische Anatomie und Physiologie,’ 1861—1866). The last-named observer, who has had great opportunities for studying this subject, states that in more than thirty per cent. of the cases which had come under his own observation an excessive corpulence had preceded the diabetes.

information respecting the relation of fat to sugar which checks for the present any attempt to follow the successive steps of the process, yet, as regards secretion in general, recent discoveries in physiology have afforded some glimpses of the truth respecting the value and use of these ternary compounds, of which it may be said that whatever importance they possess in the work of life they are not essential constituents in organic structure. Further research may possibly establish an antagonistic character in the relation between them, and show that they are respectively the cause and the result both of progressive and of retrogressive change in organic life. But for the present it must suffice to say that the occurrence of sugar in the urine in the cases above referred to, as a consequence of long-continued and immoderate secretion, leads to the inference that all secretion is in like manner associated with saccharine transformation:¹ and that whilst, on the one hand, an excess of secretion is accompanied by a corresponding excess in the formation of sugar, and consequent glycosuria; a moderate exercise of secretory function is, on the other hand, accompanied by a correspondingly moderate formation of sugar, which is not more in amount than can be readily disposed of in the system; and that it is only when the blood contains sugar in excess, from such causes as those already mentioned, that some of it is in consequence eliminated by the kidneys. Consequently, the temporary glycosuria which occurs as a sequel of cholera should serve to show that during reaction from previous collapse there is a temporary excess of restorative effort; and although, as is well known, an abortive attempt at reaction in this disease is a very common cause

¹ This suggestion may be illustrated by what has been observed with reference to the Thymus; for sugar has been found by Friedleben ('Die Physiologie der Thymusdrüse,' 1858) to characterise its functional activity, especially during the early period of infancy, when this organ appears to be especially subservient to the growth of the body; and Schiff ('Journal de l'Anat. et de la Phys.,' 1866, p. 374) in referring to "the very pronounced sugar-forming property," which he has recognised in the Thymus of rabbits, expresses the opinion that it may be due to the chyle which it contains.

of death, yet in those cases of cholera which terminate favorably and in which glycosuria has been observed to occur during convalescence, the subsequent disappearance of sugar from the urine may be accepted as evidence in favour of the normal balance of organic function having been satisfactorily restored, and that the tendency to excess during recovery from a central arrest of nutrition has ceased.