REMARKS ON CODEIA IN THE TREATMENT OF DIABETES.

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IN alluding to the subject of diabetes, one cannot forget what has been done by experimental physiology to place the disease on a true scientific basis: the discovery of glycogen by Bernard, and the demonstration of the connection of glycosuria with vaso-motor paralysis of the liver and with irritation of the vaso-motor centre in the medulla oblongata, are the foundations for a scientific treatment of the disease. The nervous system having been shown to be the agent by which diabetes could be most readily induced, physicians had not long to observe before they found that nature's experiments gave exactly the same results as those on the medulla of the lower animals; and cases of glycosuria associated with disease in the cervical region of the spinal cord are now known to be far from uncommon.

Glycosuria having been shown to depend primarily on disease of the nerve-centres, it is not a little interesting to observe that the drug which most controls it is one which affects nerve-tissues more especially. Opium has, indeed, been used empirically in the treatment of diabetes ever since the time of Aetius. Lecorché observes that since the time of Willis opium has become, so to speak, the panacea of diabetes. Few will agree in the remark of Niemeyer (French edition, vol. ii, p. 761) that "up to the present time, we possess accurate observations on the alkaline carbonates alone which show a positively favourable influence on the course of the disease." The cure at Karlsbad is advocated by Niemeyer as the prescription which merits the greatest confidence in this disease; and he mentions no other treatment. He considers it useless to insist on prescriptions based on purely theoretical ideas; and he argues that opium has been given in this way on the theory that it would diminish the irritability of the kidneys. The experience of our ancestors, who administered opium in the form of Theriaca Mithridatis; the advice given by Willis, Prout, Darwin, Christison, Ormerod, and many other authors; and the more recent, and perhaps more accurate, observations given by Pavy and Thompson, show that the practice is the result of well established experience, and not the result of any temporary fashion or fancy.

Dr. Lauder Brunton says that under the influence of opium the thirst diminishes, the excretion of urine becomes correspondingly less, and the proportion of sugar present in it falls. He might have added that the weight of the patient ceases to diminish, and generally improves. Recent observers have not been content to rest with this knowledge, but have endeavoured to ascertain to which of the alkaloids contained in opium the beneficial effect is due. Morphia has been found to act in a way similar to that of opium; and there appears to be little or no difference of opinion that the one drug, morphia, is equally useful as the other, the watery extract or some other preparation of opium. Codeia was first recommended by Pavy, and was preferred by him, inasmuch as it might be given in large doses without producing drowsiness.

The narcotic action of codeia has been established by various observations on the lower animals; the minor poisonous effects, as noted in human beings, are semi-coma instead of sleep, nausea, vomiting, severe pain in the stomach, sometimes tinnitus aurium, slight salivation, feeling of pressure in the temples, weakness of sight, and a somewhat remarkable retardation of the pulse (Phillips's *Materia Medica*). The potency of codeia as a soporific would appear to have been much exaggerated; the highest dose employed by Krebel was about one grain, and he recommended only one-fifteenth or one-sixteenth of a grain for sensitive subjects. Of late, it has been much employed, as recommended by Dr. Saundby, in the treatment of the cough of phthisis, where one grain dissolved in a drachm of syrup gives very great relief to the cough, and has also an appreciable soporific effect. But it is more particularly in the treatment of diabetes that codeia has proved to be of the greatest service, as the cases to be detailed will tend to prove.

This question of dose is an important one, and is at the root of the use of codeia in diabetes. Some authors recommend small doses; but

Dr. Brunton states that "diabetics bear large and sometimes enormous doses of opium and codeia; and, in administering these remedies, it is well to push the dose until the sugar either disappears from the urine, or until increasing drowsiness obliges us to discontinue it." Dr. Brunton (*Practitioner*, vol. xii) says: "The two remedies which are most serviceable in lessening the excitability of the nervous centres in diabetes are opium and its alkaloid, codeia. The latter may be given in doses of a quarter to half a grain three times a day at first."

Dr. Pavy (*Guy's Hospital Reports*, vol. xv) gives a remarkable series of cases, in which daily records of the composition of the urine were made, and in which careful analysis of the urine showed that the sugar disappeared entirely under the influence of opium, morphia, or codeia, with the aid of restriction in diet. The drugs were given in gradually increasing doses: opium in doses of one grain up to nine grains thrice daily, morphia up to three grains, and codeia up to ten grains three times a day. The great advantage of codeia over opium and morphia was found to be that, whilst equally efficacious in controlling the disease, it does not exert the same narcotic effect. When given in a small dose to begin with, and increased gradually, nothing may be perceived beyond its effect upon the disease.

Dr. Cavafy, in the *St. George's Hospital Reports*, has subsequently reported a case in which he gave fifteen grains thrice daily with a good result.

Dr. Ord has also reported the case of a woman aged 33, with diabetes of four months' standing, who gained seven pounds in one week with one grain of sulphate of codeia twice a day, after diet alone had failed to produce any good effect.

It is remarkable that so experienced a physician as Trousseau should not allude to the use of opium and its alkaloids in the treatment of diabetes. He says that alkalies are unquestionably beneficial; and that other medicines, tonic remedies, such as rhubarb, may be associated with them; and yet he does not mention the fact that opium has ever been given, and he does not discuss its utility. (*Clinical Medicine*, vol. iv.)

It is equally remarkable that Dr. Heineman of New York, in the American edition of Zeimssen's *Cyclopadia*, omits all mention of codeia and of opium in diabetes. He gives details as regards dietary, and states that preparations of ammonia are destined to take an important rank in the treatment of this disease.

On the other hand, Budde states that his observations show that alkalies have no special influence in diminishing the excretion of sugar.

Dr. Kratschmer gives results of a series of observations with a view of testing the value of carbonate and sulphate of soda, and of morphia, upon the excretion of sugar. He finds that neither the carbonate nor the sulphate appeared to exert any influence on the amount of sugar excreted, but he has satisfied himself that in morphia we possess an agent that is not only capable of materially reducing the excretion of sugar, but also of diminishing to a remarkable extent the general tissue-metamorphosis of the body (*Practitioner*, vol. xii).

Carbolic acid and the salicylates have also been much lauded, as also more recently boracic acid. Numerous observations have shown no good result from these drugs; and I submit that time should not be wasted in therapeutical experiments on patients, and that such drugs should only be given when codeia has been found to be either useless or injurious.

Although I cannot claim such satisfactory results as those given by Dr. Pavy, yet the cases to be reported show that the drug employed has a remarkable power of checking the elimination of sugar, and that a corresponding improvement in the health of the patient results. It would appear that alkalies, and all other methods of treatment, are far inferior to the treatment by codeia, which may be considered to have almost a specific action on the disease. The facts before us seem to justify decided language with regard to the use of codeia, which should not be permissive, but imperative, in all cases of advanced diabetes mellitus: whatever else may be given, codeia should first be given, and in fairly large doses, until some physiological effect is produced. Even dieting appears to sink into insignificance by the side of codeia; in one case given by Dr. Pavy, the codeia alone was sufficient, without any restriction of diet, the patient being on a mixed diet the whole time.

It has been supposed that codeia is a dangerous drug. Barnay (*London Medical Record*, October 1877) says: "The tendency of codeine to produce convulsions is so great, that it should be excluded from therapeutics." It has been stated, as a result of Bernard's experiments on the opium-alkaloids, that whilst narceine is the most soporific element, codeine is that which most tends to convulsions. The literature of codeia does not bear out this statement, and I have never observed anything to support it.

I have now endeavoured to show that the utility of codeia is by no means universally recognised, but that it is fully deserving of confidence

—nay, more, is imperatively demanded—in the treatment of diabetes where treatment other than dietetic is required.

CASE I.—Robert C., aged 27, clerk, had been feeling weak and losing weight for four months, as much as 14 lbs. in three weeks. He was admitted October 3rd, 1879, with symptoms of diabetes. The urine was 230 ounces daily, of specific gravity 1032, containing 2 per cent. of sugar, and a trace of albumen. His weight was 7 st. 13 lbs.

Date.	Ounces.	Spec. Grav.	Date.	Ounces.	Spec. Grav.
Oct. 5	Urine 360	1030	Nov. 8	Urine 134	1032 g
" 6	" 250	1031	" 12	" 116	1031
" 7	" 370	1030 a	" 16	" 116	1033 h
" 8	" 255	1031	" 20	" 100	1033 i
" 9	" 274	1030	" 24	" 94	1030
" 10	" 300	1031	" 28	" 86	1028
" 11	" 274	1031	Dec. 3	" 78	1041 k
" 12	" 292	1029 b	" 8	" 120	1040 l
" 13	" 140	1030	" 10	" 86	1037
" 14	" 140	1026 c	" 11	" 70	1039
" 15	" 150	1027	" 23	" 78	1040m
" 16	" 128	1031	1880.		
" 17	" 170	1031	Jan. 27	" 180	1030
" 18	" 144	1029	" 30	" 180	1031 n
" 19	" 180	1031	Feb. 2	" 120	1041 o
" 20	" 250	1033 d	" 4	" 90	1032
" 21	" 194	1030	" 8	" 80	1035 p
" 22	" 170	1030	" 10	" 90	1035
" 23	" 160	1033	" 12	" 84	1037
" 24	" 150	1036	" 13	" 110	1035 q
" 28	" 110	1030 e	" 14	" 80	1037
" 30	" 124	1031	" 16	" 60	1035
Nov. 1	" 110	1030 f	" 18	" 52	1036 r
" 4	" 140	1033	" 27	" 68	— s

a Ordered gluten bread. b Codeia, one grain three times a day. c Weight, 7 st. 12 lbs. d Codeia, three grains three times a day. e Weight, 8 st. 3 lbs. f Morphia, one-sixth of a grain thrice daily. g Morphia, half a grain thrice daily. h Morphia, two-thirds of a grain three times a day. i Morphia, one grain three times a day. k Morphia was discontinued. l Codeia, two grains thrice daily. m Weight, 8 st. 4 lbs.; codeia was discontinued. n Codeia, two grains thrice daily. o Weight, 8 st. 5 lbs. p Codeia, three grains thrice daily. q Codeia, four grains thrice daily. r Weight, 8 st. 7 lbs. s Weight, 8 st. 11 lbs.

He was now made an out-patient.

CASE II.—Albert B., aged 23, clerk, had rheumatic fever four years ago. Before that he had a cough, and was supposed to have disease in the upper lobe of the left lung. His father died of phthisis.

Five months ago he began to notice that he was languid and thirsty; then he found he was losing flesh, and that he passed more urine than usual. Four weeks ago he was hit on the nose with a cricket-ball, and since then symptoms had been worse. He had always had a slight cough, especially in winter; had had a little expectoration and occasional hæmoptysis.

On admission, July 12th, 1880, he was a thin, delicate looking youth, weighing only 7 st. 6 lbs., although of average height. The evening temperature was 98°; pulse 108, small. The skin was dry, the tongue slightly furred. At the left apex some obscure *râles* were heard, but there was no dullness. The heart sounds were normal. The urine was abundant, clear, acid, of specific gravity 1035, containing no albumen, but six to seven per cent of sugar.

From the 12th to the 19th he was put on a diabetic diet with bran-bread, and he took codeia in doses of two grains thrice daily. The fall in the quantity of urine passed was considerable, from 206 ounces on the 12th to 150 on the 19th. Gluten-bread was then given instead of bran-bread, but milk to a pint was continued. On the 21st the codeia was increased to three grains per dose, and on the 24th the urine had fallen to 80 ounces. The milk was then discontinued, and the urine fell still further to 64 ounces on the 25th, and 66 on the 26th. On August 3rd, the patient had gained three pounds in weight; the urine amounted to 64 ounces, of specific gravity 1036. One pint of milk was re-ordered, and also cod-liver oil in drachm doses, three times a day. Four days later the patient had lost two pounds in weight, and the urine had risen to 85 ounces of specific gravity 1040; the milk was therefore left off on the 7th, and the codeia and cod-liver oil continued as before. Two days later the patient took some white bread surreptitiously, as was discovered by the fact that the urine amounted to 100 ounces; but, in spite of this drawback, the urine fell to 64 ounces on the 12th. On the 14th, the weight being now stationary, the codeia was increased to four grains in each dose, and in seven days the weight had increased by three pounds, and the urine on the 21st was 74 ounces, of specific gravity 1037. On the 27th the patient was very drowsy, could sleep at any time, and seemed apathetic from a state of semi-narcotism, the urine being 69 ounces at 1035, the weight being 7 st. 10 lbs. At this stage the codeia was discontinued, and twenty minims of liquor ferri perchloridi, three times a day, ordered instead. One week later, September 4th, the patient had lost two pounds, but passed not more than 68 ounces of specific gravity 1040. He then

left the infirmary, and was lost sight of for two months. At first, after leaving, he spent two weeks at Weston-super-mare, and improved whilst there. On returning home he had an attack of vomiting, and began to be troubled with cough and expectoration. He grew rapidly weaker, and the vomiting recurred occasionally.

On November 6th he was re-admitted to the infirmary, having lost eleven pounds in weight during two months. He now passed 153 ounces of urine of specific gravity 1032, clear, acid, containing a trace of albumen. The tongue was furred; he complained of pain after food and constipation, but his appetite continued good. The sputum was purulent and nummular; there were clicking sounds to be heard at both apices, but no dullness. He was now put on a modified but not rigid diet, brown bread being allowed; and on November 9th, codeia was ordered, with the result that the urine fell from 181 ounces on the 8th to 96 on the 12th. On the 16th, cod-liver oil was ordered, and the codeia was gradually increased from one up to five grains three times a day. On December 14th, the weight had increased to 6 st. 12 lbs. (one pound), and the urine was 96 ounces, of specific gravity 1035; at this time, the albumen had disappeared. On December 28th, there was a loss of three pounds in weight, and the urine was generally about 100 ounces of average gravity 1035. A trace of albumen had reappeared. The expectoration was now profuse, and there was abundant evidence of breaking down at the left apex; but the temperature was always subnormal, ranging from 96° to 97°; the lowest reading was 95.6° on January 1st. On the following day, the temperature rose to 98.8° in the evening; and on the 2nd, it was 100.2° at 8 P.M. This pyrexia was associated with evidences of consolidation at the base of the left lung of inflammatory character, and death took place on January 6th, about ten months after the commencement of his illness. A *post mortem* examination was not permitted.

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CASE III.—Henry B., aged 29, married six years, with three children, a farm-labourer, of good family history, had never heard of diabetes in his family. His father, mother, three brothers, and one sister were all living. Two years ago, he fell with a sack of flour on his back, but was not laid up, and did not appear to have injured himself. For the last twelve months, he had passed a large quantity of urine, and complained of insatiable thirst. During this period, he had been unable to do any work in consequence of weakness. His weight was formerly twelve stone. There was no history of syphilis, of alcoholic habits, or of any previous disease.

On admission, March 21st, 1881, he was found to be rather thin; his weight was 10 stone; he was of average height, and fair complexion. The skin was dry and rough; the pulse 60, regular, and full; temperature 98.4°; tongue white. He had a tendency to constipation. There was no cough. The sounds of the heart and lungs were normal. His sight was good, but the edges of the optic discs were rather ill defined. His urine was abundant, 205 ounces, of specific gravity 1038, acid; it contained no albumen, but much sugar. He was ordered a mixed diet, including meat, eggs, milk, and brown bread, without potatoes or sugar; and treatment by codeia was at once commenced.

On April 11th, after nearly three weeks' treatment, the quantity of urine had come down from over 200 ounces in the twenty-four hours to 170 ounces; the specific gravity remained as before; and the quantity of sugar amounted to about ten ounces daily. Gluten-bread was then ordered, four ounces daily; and the bran-bread was discontinued. The milk was still allowed, two pints each day.

On April 18th, the milk was discontinued; and from this date all saccharine and starchy food was rigidly excluded.

The codeia, at first given in doses of a grain three times daily, had been increased to two grains on March 28th, to three grains on April 2nd, to four grains on April 7th, five grains on April 18th, and six grains on May 7th, when the urine had come down to 144 ounces, of specific gravity 1044. From May 9th to 17th, the pills were omitted, and a saline mixture substituted. The omission of the pills made no apparent difference in the patient's condition; there was no difference in his mental state, no difference in pupils or in pulse; and the quantity of urine ranged from 140 ounces on the 12th to 152 on the 17th. The codeia was then resumed, three grains being given three times in the day on the 17th, and six grains three times in the day on the 18th; on the 20th, six grains were taken four times; and on the 23rd the quantity was increased to nine grains three times daily. The quantity of urine then fell to 80 ounces, of specific gravity 1054, on the 27th; and 70 ounces, of specific gravity 1056, on the 29th. The highest gravity observed was on May 31st, when the quantity was 96 ounces, and the specific gravity 1063. On May 6th, the codeia was discontinued, as the patient complained of drowsiness, and his pulse was 66,

small and weak. This was immediately followed by a considerable increase in the quantity of urine, which rose to 130 ounces on the 13th and 20th. The codeia was resumed on the 21st, in doses of four grains and a half, and on the 30th was increased to nine grains daily, with the same result as before—an immediate fall in the urine from 130 to 90 ounces.

On July 5th, morphia (half a grain three times a day) was substituted for the codeia, and a few days later in grain doses, whereupon he was made an out-patient, and ordered to continue the morphia and cod-liver oil steadily for a month.

These three cases all exhibited marked improvement whilst taking codeia, which improvement ceased when the codeia was withheld, and was renewed on its repetition. Morphia had a good effect in two of the cases; but the improvement was much less marked with it than with the other alkaloids.

NOTE ON UTERINE HÆMOSTATICS.

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As a small contribution to the practical portion of the subject of uterine hæmostatics, I venture to make a few remarks on the mechanical kinds, which we know by the name of plugs or tents. In doing so I must be understood to refer only to those cases where the cavity of the uterus is not sufficiently large to contain blood in quantity, the loss of which from the circulation is likely to produce anything of serious detriment.

If we go back to former practice and to text-books, we find it recommended that, in case of threatened abortion with much hæmorrhage, a vaginal plug should be used.

The vaginal plugs recommended are the tampon, cotton or wool, silk or cambric handkerchief, rags, or sponges passed in till the vagina is filled up. An India-rubber ball also has been suggested, covered with felt or such like material. Now, even with the best management, there is much of distress to the patient in the use of the vaginal plug; and with regard to its hæmostatic effect very much of uncertainty, and generally partial failure; and in the hands of the unskilful and careless there is positively no restraint of bleeding worth the mention. If at any time any good results be produced, it is rather by the reflex irritation that it causes, whereby the uterus expels its contents. It is not so very rare an occurrence that one finds, on removal of the plug, the ovum on the uppermost part of it.

But besides its palpable inefficiency, a vaginal plug, being of a porous texture, absorbs a large quantity of blood and thus conceals it from our sight; it also favours decomposition, and this, as is well known, occurs within a few hours; and thus we have a new element of danger.

Again, in many cases, when called to such a case, we have no speculum at hand; and although we may extemporise one out of card-board, book-covers, or such like material, yet, before we have thoroughly and firmly filled the vagina, we must have given the patient considerable pain and distress, besides having occasion to put such pressure on the urethra as may necessitate subsequent catheterism. For these reasons, namely, the imperfection of action, pain in introduction, and danger if left in long—in other words, its general crudity, it seems to me that as a general rule the vaginal plug should, in the cases I have supposed, be discarded.

And as a substitute I would urge the employment of the cervical plug as being more precise in action, as well as being capable, if we use a dilating kind, of expanding the canal for the purpose of exploration, or for the expulsion or removal of its contents.

If, then, in any case of uterine hæmorrhage, where we have the conditions above alluded to, we desire, besides immediately checking the bleeding, to dilate, we can use the compressed sponge-tent; the best form of which I have found to be those made, after Sir James Simpson's plan, by Duncan, Flockhart, and Co., of Edinburgh. These can be introduced by a long pair of forceps, and retained *in situ* by placing a piece of sponge, with tape attached, in the upper vagina. Of course, even these materials retain some secretions, etc., and tend to facilitate decomposition; but their removal and cleansing can be effected much more readily than the vaginal plug, because it requires but a small portion. The sea-tangle tent, by reason of its slipperiness, is unreliable as a plug in hæmorrhage. If we desire, however, only to plug the cervix, we can very easily extemporise a plug from materials to be found in every house.

For instance: take a stick (say a flower stick) about a foot long, and taper it at one end to about the size of an uterine sound, or rather larger; wind round this end, for about three inches down, strips of cambric

rag, lint, or sponge to the required thickness, judging from the size of the os. Strips of sponge can be readily obtained from cup-shaped sponges of compact texture, and they can be tied on by thread, layer after layer, till the requisite conical form is obtained. The strips of the other materials can be laid on similarly. After the covered end has been well greased, it is passed into the canal, and the stick retained *in situ*, after the manner in which we tie in a catheter; an elastic tape, if obtainable, is to be preferred.

A catheter or bougie, or the end of the long injection-tube, can be treated in the same way. If we require great precision of application, then it is best that the hand should hold the external end till the hæmorrhage has ceased. If the catheter and stilet be used, then I have found it convenient to bend the external portion backwards, between the buttocks, tying the tape round the ring of the stilet—the ends of the tape being carried, as usual, to back and front of the waist-band.

These more homely adaptations I have recommended, rather than the especially made kinds, because they are often wanted at times when we cannot send home for a more showy sort. In any case, a cervical plug, expanding or not, is more precise, less crude and painful in application, than the vaginal, and, in my experience, nearly always successful. In all cases of abortion, where a plug is necessary, I would lay it down as a rule, that the expanding tent should be employed. In cases of flexion with abortion (and it is this complication which so frequently increases the hæmorrhage) it will be found that the covered stick or stemmed plug, above described, is very useful: for, if the fundus be elevated during its introduction, the uterine cavity is straightened, and evacuation of the contents thereby facilitated.

ON STERILITY.

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It is somewhat surprising that more notice has not been taken, in our modern works on gynæcology, of the frequency with which married women miscarry during the first few months of their matrimonial existence, or become mothers within the first twelve months, and yet never afterwards conceive.

The mere fact of conception occurring once, shows that the reproductive organs are in a normal physiological condition to start with. Some new factor must, therefore, have been introduced to explain this sudden cessation of fertility. Can it be that the effort is too great, and the capacity for further child-bearing exhausted? Is it not rather from some of the numerous complications likely to follow the act of parturition? That these latter will explain the occurrence of sterility in many cases, may be readily admitted; but there are a large number of cases where parturition is safely accomplished at full term, where there is no history of subsequent inflammatory mischief, and where, beyond a somewhat tedious convalescence, with possibly prolonged or profuse vaginal discharge, no active symptoms are present, such as to necessitate a local investigation.

A history by no means unfrequently met with is, that the patient was perfectly well up to the time of marriage, menstruation being normal, and unattended by pain or any serious discomfort. The first few periods may be somewhat painful and profuse, and followed by more or less mucous discharge. Cessation of the catamenia and other well recognised symptoms soon warn the patient that pregnancy has commenced. Increased leucorrhœal discharge, pain in the back, inability to stand or walk far, are naturally attributed to her condition, and no steps are taken to relieve them. Miscarriage occurs before the first half of pregnancy has been reached, due really to gradually extending inflammatory mischief of the cervix uteri, aggravated, it may be, by some imprudence in the way of over-fatigue or undue excitement, such as dancing, riding on horseback, travelling, etc. The miscarriage being attributed solely to some apparently preventable cause, no steps are taken to ascertain the exact condition of the uterus. After resting up for a longer or shorter interval, generally the latter, the patient begins again to take her place in society and attend to her domestic duties. Although warned by her own sensations in the form of backache, leucorrhœa, menorrhagia, and other distressing symptoms, that all is not as it should be, the patient imagines that these are but the sequelæ of her miscarriage; and, beyond resting up a little more than usual, simply because she cannot endure fatigue as heretofore, nothing is done to improve the state of the uterus, which meanwhile is in a very unhealthy condition.

Now, what is the interpretation of this? In many of these cases, the patient has become infected with latent gonorrhœa, as pointed out