TOXIC EFFECTS OF COCAINE AND THEIR TREATMENT.

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A VERY few years ago the drug cocaine was comparatively unknown, and the discovery of its effect upon the cornea marks an epoch in therapeutics scarcely less important than that of the discovery of chloroform. Indeed, what chloroform is to the surgeon, cocaine may be said to be to the ophthalmologist. Besides the conjunctival mucous membrane, however, almost all the mucous membranes have been cocaineised for one purpose or another, until the drug has justly been regarded as one of the most valuable in the British Pharmacopœia.

It is hardly to be expected that a powerful drug like this can be applied to the various mucous membranes without some absorption occurring and its physiological effects being manifested. It is to these effects carefully observed that I wish to devote a few words. In the account which follows no single symptom or sign is described that I have not seen and recorded at the moment, time after time. The drug used was the hydrochlorate of cocaine, and the mucous membranes those of the nose and mouth principally. Absorption does not readily occur from the conjunctiva unless an excess of the solution be used and has trickled down into the nose through the lacrymal canals and nasal duct. The Schneiderian membrane, which is almost erectile in structure in some parts, absorbs the drug rapidly. The local effect of cocaine upon this membrane is very marked. A patient presents himself suffering from a watery discharge from the nose, sneezing, lacrymation, and a very unpleasant irritation of his mucous membrane—in fact, all the symptoms of coryza. On examination with the nasal speculum the membrane is seen to be red, injected, and swollen, so that that covering the turbinate bones meets that covering the septum, and nasal breathing is impossible, the patient being obliged to breathe through his mouth. If now a spray be used, and a solution of hydrochlorate of cocaine (2 per cent.) be applied to the membrane, the latter will be seen to shrink, the discharge cease, the surface become pale and dry, and the cavity restored, so that nasal breathing can be accomplished with the greatest possible ease. This I have experienced myself time after time, and I have tried it in other patients with the same result. Does the drug act upon the muscular coats of the smaller vessels either directly or through the terminations of the vaso-motor nerves, or does it, by allaying the irritation caused by various substances such as pollen, remove the cause of the congestion, and thus relieve this very distressing affection? In this affection the relief is so marked that there is a tendency to over-use of the drug, and therefore to the occurrence of the symptoms to be presently enumerated.

I have used solutions of 1 per cent., 2 per cent., 4 per cent., 5 per cent., and 10 per cent., and of these the 2 per cent. would seem to be the best; but it must be applied by means of a spray, as in no other way can the recesses of the nasal cavity be reached. I may say that I have often used the drug for the purpose of observation only, and the symptoms about to be described came on when the drug was used for some time, disappeared on its cessation, and reappeared when the drug was resumed. As to the amount necessary to produce dangerous effects, I may say that I have experienced very unpleasant symptoms after less than one grain, and that the condition produced by six grains sprayed in for experiment was such as to elicit the resolve never to repeat the dose. Weak solutions appeared to be absorbed more quickly than strong ones, and therefore 2 grs. in 1 per cent. solution would seem to be more dangerous than the same quantity in 10 per cent. solution.

The symptoms may come on in a few minutes, and may last three or four hours, or even longer. In small doses a feeling of exhilaration is produced, and the mental faculties are stimulated. If the dose be increased largely, a kind of affective insanity may result. If the *spes phthisica* be regarded as a mild form of phthisical insanity, the condition produced by cocaine must also be regarded as such. It would appear to be a kind of mild mania, in which illusions, hallucinations, and delusions have not yet made their appearance. To say the least of it, the mental con-

dition is not normal. Insomnia is a very important and distressing symptom, as those who have used the drug at bedtime know to their cost. A whole night may be spent without the slightest inclination to sleep; but, strangely enough, there is not so much fatigue next day as might be expected to result from the loss of a night's sleep.

The vascular system is affected by even small doses of cocaine. At first the pulse is strengthened and accelerated, but if larger doses be used it may become very weak and irregular, or even slower than normal. The usual result is a quick pulse, which may be found 120 per minute or more. I have often noticed a pulse of 120 after small doses of the drug. Concurrently with this effect upon the pulse there is commonly a sense of tightness in the chest. One feels as if the heart had contracted and drawn in the chest walls with it. This feeling of oppression is very often present, and is sometimes alarming, as there may also be a feeling of faintness, giddiness, or singing in the ears. One feels almost afraid to sit down, and on lying down there is a feeling of suffocation. The breathing is shallow and quick, often from 20 to 24 in the minute after large doses, and frequent sighing takes place. The whole condition is one of tension, like that produced by suspense. The surface of the body is pale, and often a cold sweat breaks out.

The temperature seems to be raised; I have seen it 99.2° on several occasions. But one of the most interesting effects of cocaine is the effect produced on the pupil. It occurs even when only one grain has been used. I have frequently produced it by a spray of one grain in a 1 per cent. solution. This is, of course, distinct from the local action on the pupil, and is the result of the absorption of the drug. No cocaine is applied locally to the conjunctiva, and yet the pupil dilates and accommodation is relaxed to a moderate degree, if one may judge from the feeling of fatigue produced by reading. If a lighted match be placed before the pupil the latter contracts. Then it oscillates, alternately contracting and dilating, until, as if unable to keep up against its stronger antagonist, the dilating force gets the mastery, and the pupil dilates. After a short rest the pupil can again be made to contract, but the abiding condition is abnormal dilatation. It would seem as if the sympathetic were stimulated, and therefore the third nerve, although not paralysed, must be at a disadvantage. Hence a stronger stimulus than normal is required to produce contraction, and the sphincter iridis becomes fatigued. Other symptoms, such as tremulousness and weakness of the knees, are often present.

With regard to the digestive system, cocaine—at least, when applied to the mucous membrane of the nose or mouth—produces complete anorexia. I have proved this beyond doubt, and have learnt to use no cocaine for at least two hours before a meal. If the use of cocaine be long continued, the tongue gets furred and wasting ensues. The urine is of two kinds. First, when cocaine is being used the urine is pale, limpid, and of a low specific gravity. I have noticed the specific gravity to be as low as 1009, when not an abnormal amount of fluid had been drunk. The urine is therefore similar to that of hysterical patients. On the other hand, after the use of cocaine for a day or two the urine becomes high-coloured and loaded with urates. The urates disappear when the drug is discontinued, and reappear when the drug is again used. In fact, cocaine seems to cause an increased metabolism, as shown by the increased pulse, increased temperature, wasting, and the deposit of urates in the urine.

There is one other symptom caused by the continuous use of cocaine, and that is cocaine craving. This is similar to that for alcohol, opium, tobacco, &c. In fact, after using cocaine for a few days, it may be necessary to exercise some strength of will to overcome the desire. A case of this kind is recorded in THE LANCET of Nov. 1st, 1890, p. 957. I had noticed this before I saw this case recorded, and I was glad to find that it is becoming a recognised symptom.

The treatment of "cocainism," a term which might be used to indicate the group of symptoms produced by cocaine, is very important. The sleeplessness is sure to cause great annoyance, as it is a very constant symptom. I have used opium, bromide of potash and chloral, bromide alone, and chloral alone. Of these, chloral gave the best results, and opium the worst. Of chloral, enormous doses must be given to produce sleep. It is in very mild cases indeed that twenty grains will be of any benefit. I have used forty grains of chloral and forty grains of bromide without producing sleep. The

bromide causes unpleasant symptoms next day, and therefore chloral alone is much preferable. This peculiar resistance to chloral of cocaine insomnia has already been noticed by Dr. Willoughby of London in THE LANCET of Feb. 14th, 1891, p. 365. When sleep is not produced a kind of nightmare may come on—a condition between waking and sleeping in which objects can be recognised and sounds distinguished. The pulse becomes more regular and the cardiac oppression is relieved. A large dose of alcohol in one not accustomed to its use is often very beneficial, and may produce sleep. If the pulse gets weak the best remedies are ether and ammonia, both of which drugs I have used with very good results. The craving can be got rid of by a few days' abstinence from the drug.

Dr. Gluck of Nebraska has discovered that phenol causes a very superficial eschar, and therefore when used with cocaine prevents the absorption of the latter. His observations are published in the *New York Medical Record*, June 21st, 1890, p. 707.

Greenwich-road, S.E.

Clinical Notes:

MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

AN UNUSUAL FORM OF CHANCERE.

By E. D. MAPOTHER, M.D., F.R.C.S.I.

ON Jan. 13th, 1891, a professional man from India, aged forty-nine, and intemperate, consulted me for a chancre which had appeared a week before. About twenty-seven years ago he had chancroids and suppurating buboes, which healed very slowly. The sore was on the dorsum, one-third of an inch behind the corona, and there were hard enlarged glands in each groin. Small doses of blue pill, small inunctions in the groins, and dry lint were ordered. Good progress was made for a fortnight, but then the sore began to extend slowly, and there arose round it, except towards the corona, a thick ridge. This near the frænum was œdematous, but above there was a semi-solid deposit in the areolar tissue of the preputial folds. Many local applications were tried without effect, and iodoform seemed only of little service. On March 9th iodide of potassium was prescribed together with the mercurial treatment. After ten days the skin over the hardest part of the ridge gave way, and matter similar to that in gum-mata came out. Improvement followed, but so slowly that it was April 13th before cicatrisation was complete. It ulcerated again superficially on the 20th, but finally healed in three weeks. The enlargement of the glands has become absorbed, and no secondaries appeared. The peculiar deposit and the extreme slowness of healing, due probably to the age, habits, and former residence of the patient, seem to render the case worth recording. A somewhat similar form was described by Fournier.¹

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A CASE OF CEREBELLAR TUMOUR.

By THOMAS DOBSON POOLE, M.B. EDIN.

THE following case, the notes of which I took on March 30th, may have some physiological interest:—

M. R—, aged four years, was admitted into the Lancaster Infirmary three months ago, the complaint being headache, vomiting, and loss of use of the lower limbs. Her father is healthy, and her mother, who possesses a blue and a grey iris, suffers from occasional convulsive attacks, especially during pregnancy and childbirth. Three of the children died of "fits," and there are three healthy. About nineteen months ago the patient fell into the canal, the cause of this accident being supposed to be due to a "fit." Nine months ago she had two "fits," which were accompanied with bleeding from the mouth, and at this time it was noticed she began to lose the power of walking, which gradually got worse. The temperature is normal. She

is well nourished and muscular, and has a peculiar heavy, sheepish, and expressionless aspect. As regards the alimentary system, it may be noted that the upper incisor teeth are small and placed apart, the canines of the same row appearing as small triangular bodies projecting through the gums. The lower row of front teeth are small, crowded together, and free from notches. Nervous system: The sensations are much impaired. No discomfort is experienced when a hot test-tube is placed in contact with the skin of the legs and arms, and she bears it well on the cheek. Running a pin a moderate depth into the skin of the upper and lower limbs, or the tip of the nose or forehead, is performed without the patient's wincing, or giving other evidence of pain or sensation. But when the pin is thrust into the skin in the same situation so as to cause bleeding, the patient says she feels it, and makes a tolerable good attempt to localise the seat of pain. Pinching the muscles of the calves of the legs causes pain. The pupils are natural and react to light. The senses of taste and smell are affected, she drinks vinegar like a hypnotised person, and the vapour of ammonia when applied to the nostrils is borne well. Touching the conjunctiva causes reflex closure of the eyelids, but apparently with little discomfort. The knee-jerk, if anything, is slightly pronounced. She sits up in bed with the body bent forwards and the knees flexed, but if pushed to one side she falls backwards and to the right or left, and she can just manage, by taking hold of both sides of her cot, especially when requested in a commanding tone of voice, to stand up in bed, though she does this in a very oscillating manner. Closing the eyes affects neither sitting nor standing. She can turn over the leaves of a book and touch the tip of her nose without special effort. With the exception of coldness of the lower limbs there are now no vaso-motor or trophic changes to be detected. Sleep is often prolonged and deep, and her intelligence is good. She stands (with assistance) with the legs separated, feet everted, knee-joints extended, and the spine bent forwards. When assisted to walk, the lower limbs, being abducted and rotated outwards, are thrown forwards and outwards without flexion of the knees, and the plantar aspects of the feet, rather than the heels, come down to the ground with a thud. If any comment on her progress while in the infirmary is needed it is that the attacks of headache diminished in frequency and severity, and the vomiting ceased, while the general anæsthesia and loss of power of the lower limbs gradually increased until the time of her death (April 30th), two hours before which she was unconscious, but previously to the onset of unconsciousness there was nothing whatever to excite suspicion of the sudden termination of the illness. At the post-mortem examination the lateral ventricles were found distended with fluid. Projecting from the under-surface of the cerebellum, and pressing on the medulla oblongata, was a rounded, smooth-surfaced, and hardish (in comparison with the brain substance) tumour about the size of a walnut. Unfortunately I was unable to examine the tumour microscopically, as it had been hopelessly disintegrated by a fluid into which it had been erroneously placed with the intention of hardening.

Poulton-le-Fylde.

CASE OF CHLOROFORM SYNCOPE.

By EDWARD RICE, M.D. LOND.

THE following case may prove of interest during the present discussion as to the existence or non-existence of cardiac syncope during the administration of chloroform.

On Aug. 31st I was asked by Mr. Sankey to give chloroform to a lady about forty years of age for removal of a growth on her tongue. She was a highly nervous but otherwise healthy woman, who had taken an anæsthetic (probably the A.C.E. mixture) without any untoward symptoms on two previous occasions. At 7.30 A.M. on the morning of operation she had some breakfast, the solid portion of which consisted of two meat lozenges and some thin bread and butter. At 11.30 A.M. I proceeded to give her chloroform, using Junker's inhaler with foot bellows attachment, and a new bottle of Duncan and Flockhart's chloroform. All went well for about seven minutes, except that she was at first very excited and talkative, anæsthesia being nearly complete when Mr. Sankey remarked she looked rather pale. My finger on the temporal artery detected nothing

¹ Archives Générales de Médecine, Nov. 1867.