THE PHYSIOLOGICAL ACTION OF COCA.

By ALEXANDER BENNETT, M.D.

IN the recent numbers of the BRITISH MEDICAL JOURNAL, there have appeared several interesting notices on the therapeutical effects of "erythroxyton coca". This substance has been for some years pretty extensively employed at home, but particularly on the continent, as a stimulant and tonic in a variety of diseases, and, it is said, with considerable success. Still, comparatively little is yet known about the action of the plant. The following observations may not be uninteresting to those who are clinically investigating the properties of the drug, which, as our knowledge of it advances, will doubtless prove a valuable addition to the *Pharmacopœia*.

My attention was directed to the action of the coca leaves several years ago; and at different times, and from various sources, I have obtained quantities sufficient for experimental purposes. My object was first to ascertain the effects of the drug upon the healthy human subject, with special reference to its stated stimulant and antitriptic properties; and, with this object, I administered to myself and to others the leaves in doses varying from one to eight drachms in the form of infusion and of extract, and also by chewing them along with different alkalies, after the manner described by travellers as adopted by the natives of Bolivia and Peru. After a series of experiments carefully conducted, I was not able to convince myself that the drug thus administered had any special effects, with the exception of a sensation of slight local tingling of the tongue and mouth when the leaves were masticated for any length of time. Whether this inert action is due to the leaves having lost their active properties by exportation, to their being improperly selected or prepared, to an insufficient quantity having been administered, or to a defective method of application, I am not in a position to decide. After every precaution and variety of treatment with different samples of the leaves, and in as large quantities as could be conveniently administered, I have failed to satisfy myself that there was even any approach to the powerful and somewhat startling results graphically described by many authors as occurring when the leaves are chewed by the inhabitants of the countries where the plant abounds.

I next directed my attention to the neutral principle of the coca leaves, and after great difficulty, with the aid of Messrs. Macfarlane and Co., chemists, Edinburgh, I succeeded in obtaining a small quantity of the crystalline substance cocaine ($C^{16}H^{19}NO^4$). With this I conducted a series of experiments and observations on the lower animals, as far as I am aware, for the first time in this country, and arrived at results which appeared to me of considerable importance, ascertaining that cocaine was a powerful poison with special actions on the nervous system.

As coca is extensively employed in South America as a beverage, and as cocaine bears close chemical relations to the neutral principles of tea, coffee, guarana, chocolate, and other well known stimulants, I proceeded to make a series of experiments also with theine, caffeine, guaranine, and theobromine, with the view of determining the actions of each, and the relations, if any, which existed among them. In the *Edinburgh Medical Journal* for October 1873 will be found a description in detail of these observations. The general results at which I arrived may be given shortly as follows.

1. The physiological actions of coca, tea, coffee, guarana, and cocoa, are mainly, if not entirely, due to their neutral principles.
2. Cocaine, theine, caffeine, guaranine, and theobromine are powerful poisons, inducing a series of symptoms affecting the nervous, respiratory, circulatory, vaso-motor, and glandular systems, which terminate, if the dose be large enough, in death.
3. These five principles are, to all appearances, identical in physiological action.
4. In small doses not ending fatally, these five substances produce—*a.* Cerebral excitement not succeeded by coma, and *b.* Partial loss of sensibility.
5. In large doses they produce—*a.* Cerebral excitement, *b.* Complete paralysis of sensibility, *c.* Tetanic spasms and convulsions, and *d.* Death.
6. They paralyse the entire posterior columns of the spinal cord, also the entire system of peripheral sensory nerves; but the anterior columns of the cord and the peripheral motor nerves are not paralysed.
7. They frequently produce convulsions of a clonic character, but occasionally they cause tetanic spasms, which latter are sometimes so severe as to induce opisthotonus.
8. They do not produce muscular paralysis.
9. They at first increase, then impede, and lastly stop, the respirations.

10. They at first increase, and finally diminish, both the force and frequency of the heart's contractions.

11. They produce at first contraction, and afterwards dilatation, of the capillaries and small blood-vessels, with stasis of the blood, indicating first irritation, and subsequent paralysis, of the vaso-motor nerves.

12. They affect the temperature by first slightly lowering, and secondly increasing, it.

13. They usually produce contraction of the pupil.

14. They produce an increase of the salivary secretion.

15. They induce a peculiar form of tenesmus, accompanied by a copious discharge of clear mucus from the bowels.

These conclusions have been arrived at after a careful series of experiments conducted on more than one hundred animals of different kinds; and it is extremely interesting to learn that those agents, which the different nations of the world have found by experience to produce refreshing and stimulating beverages, although unlike one another and procured from totally different sources, possess in common proximate principles, which not only are almost identical in chemical composition, but also appear similar in physiological action.

According to the above observations, cocaine has the same actions as theine, etc.; so, for clinical purposes, the latter is at present preferable on account of the enormous expense of the former. That the effects of the beverages themselves are mainly, if not entirely, due to the neutral principles they contain, is highly probable; but of their beneficial action in medical practice I am not yet in a position to give an opinion. However, from their stimulant action and effect on the nervous system generally, there is every reason to hope that the concentrated forms of these drugs, or the neutral principles themselves, will prove powerful and useful agents in the hands of the physician for the treatment of disease.

Before the medical man can practise his profession scientifically, he should be acquainted, not only with the natural course of the malady he proposes to alleviate, but also with the physiological effects of the drug by which he hopes to reach this end. By observations upon the lower animals, he may also obtain suggestions and information which will materially assist him in relieving and benefiting the human being.

With this object, the above investigation was undertaken; and, although the research is yet in its infancy, I venture to hope that my conclusions will not be found deficient in interest and importance to those who desire to establish a sound system of therapeutics upon careful physiological experiment.

A CASE OF CHELOID SIMULATING MOLLUSCUM FIBROSUM.*

By H. CUNDELL JULER, M.D.

IN performing a duty imposed upon me by the Academy of Medicine of Cincinnati, I proceed to a description of a very remarkable, although in this country by no means an unique, case of hypertrophic disease of the skin, occurring in a patient in the Cincinnati Hospital, June 24th, 1873. James Bell, a negro, the subject of this sketch, aged 43, unmarried, was born of slave parents, in the State of Tennessee. He appears to be well nourished and well developed, and states that his health has always been excellent. He was raised as a waiting-boy in the service of a family in Penala county, Mississippi, and was always treated by his master with great kindness, being well fed and comfortably bedded. He never received corporeal punishment. He never had any venereal affection. His mother, sister, and two brothers, are still living. He believes that his sister had a swelling in the form of "snakes", that extended from her neck to her face; but he never saw a person affected similarly to himself. He believes that a spell has been put upon him; and states that coloured doctors who had examined him and counted over fifty tumours under his clothes, had told him that somebody had put a turtle upon him. He has suffered from the present disease for thirty years, it having first appeared when about ten years of age, in a cicatrix following an abscess, in front of the lobule of the left ear. As the tumour increased in size, other integumentary sessile growths made their appearance upon different parts of the body, many of which slowly developed into pedunculated excrescences. The tumours are now present in all stages of growth, varying in size from a coriander seed to a mushroom in expansion, measuring several inches in diameter. They are of a lighter colour than the surrounding skin, becoming lighter by age. They are either distinct, grouped together, or several of them have coalesced. Manipulation gives rise to no uneasiness. The maple-tree wart-like excrescences stand out so sharply defined upon the surface of the skin, that an observer might at first sight suppose that the excrescences were

* Read before the Cincinnati Academy of Medicine.

adhering temporarily to the part of the body struck by them. The skin between the elevations is healthy; there are, however, some pigmentary streaks traversing the skin covering the serratus magnus, that may or may not be the result of former floggings with a whip. Usually he is free from pain, but occasionally—especially in the day-time—he experiences pain in these tumours of a darting, cutting, or tearing character. He attributes the pain which he has had in the head to the tumour upon the left side of the face, which has been twice extirpated, and now has its flattened surface covered by leprous scales, to which I shall again allude. The large excrescences upon the jaws and neck give trouble only by their sense of weight. His sleep is disturbed by the uncomfortable interference of the tumours with his rest. He objects to the tumours being pricked, although when a puncture by a needle is allowed it causes scarcely any pain. He complains most dolefully of an intolerable incessant itching of the skin, which, although endurable in cold weather, becomes incessant and exciting in the months of July and August. To use his own expression, “it drives him crazy”. The bath affords him some alleviation. While under examination, he scarcely moves from the position in which he is placed. His mind seems under a cloud; but, when aroused by conversation, questions are answered in an intelligent manner. He has a demure and subdued demeanour; his eyes are downcast, and an expression of melancholy shades his countenance. The deadening conviction that he is under the power of some supernatural agency converts the natural vivacity peculiar to his race to a “death-like silence and a dread repose”.

The hypertrophic disease called cheloid, when of recent formation, has been found in similar instances to consist of numerous bands of connective tissue, arising as spindle-shaped cells along the walls of the blood-vessels of the corium, and developing as wedge-shaped prolongations of parallel fibrous bands, till the whole derma is filled by them. In James Bell, these recent homogeneous prolongations, interweaving in a net-like manner, are peculiar and different in figure. Some of them appear to have grown to a certain extent, and, while new material has been forming toward the circumference, interstitial absorption has given rise to central depression. The new material thus formed around the tumour is arranged in serried lobules directed from the centre to the circumference, similar in arrangement to the divisions in the seed of the marsh-mallow. Thus while the centres are depressed, and the skin shrivelled and puckered, the lobules extending beyond the pedicle are smooth, dense, and resisting to the touch.

Although notes have been taken of the shape, size, appearance, consistence, and position of individual tumours, sixty of which have been counted, it will only be necessary that I should name those that present some special features of interest. It often happens when a skin-disease of long continuance is submitted to a critical inspection, the different observers limit their observations to a partial survey of the case, and thus arrive at opposite conclusions as to the distinctive nature of the disease. The same mistake that occurs when diagnosing cuticular derangements confined to the surface of the skin, also happens when defining the various hypertrophic affections of the derma. In a patient afflicted by one form of the disease, it may not be difficult to detect the existence of a similarity to other dermal affections, indigenous to warm climates. In the malady known as cheloid, dermatologists have specified the disease as consisting of a numerous series of fibrous ridges, springing from the walls of the blood-vessels of the corium, supplanting the derma and imparting to the skin the appearance of a hypertrophic cicatrix, following a burn. Although the case of James Bell but partly accords with this diagnostic description of cheloid, it certainly agrees with those illustrations of the disease figured in American works on surgery. Cheloid is the predominating feature of the affection, and it is, therefore, rightly designated by that name.

It has already been stated that the disease of our patient originated thirty years ago, in the cicatrix following an abscess; and, as diagnostic of the still prevailing cheloid diathesis, there exists upon the inner side of the right thigh, where he was bitten twelve months since by a dog, a small tumour an inch in length and half an inch in width, resembling a curved minnow in shape. I have observed a similar isolated growth upon the face of a negro, arising from the use of a razor. It is most likely with this predisposition to the disease in our patient, the numerous tumours dispersed over the body, reaching from the neck to the ends of the toes, had their origin from mere abrasion of the skin, due to friction or some other accidental cause.

Dr. Fagge of London recently examined, under a low power of the microscope, some molluscous tumours not much larger than a pin's head, and he found that each tumour was originally developed round a hair-follicle, inclosing at the same time the sebaceous glands belonging to the follicle, itself inclosed in a translucent fibrous mass. It is well known that the most trivial damage to the skin may be followed by the appearance of cheloid. It has succeeded the application of a blister,

leeches, and sutures; it has been developed by bleeding, by a scratch, or puncture; in the cicatrices of small-pox, acne indurata, syphilis, burns, and the vaccine scar. If such slight causes be sufficient to produce the disease, I believe it impossible to say whether it be idiopathic or otherwise. As the true and false forms of cheloid are identical in

microscopical structure, as well as in all other particulars, why is it necessary to adhere to the divisions into true and false cheloid arbitrarily created by Alibert?

It is very probable that the peculiar disease affecting the breast of Jas. Bell, which has been eight years in growing, came on, as he states, from friction. (Fig. 1.) The true cheloid nature of the malady, however, is better seen upon the buttocks (Fig. 2), where its presence is of more recent date. Over the gluteal region of the right side, and descending upon the thigh, are nineteen distinct tumours, mostly of a small size. A portion of the diseased structure, which is marked by a tracery of white streaks, and may be pinched up into a fold, commences

Fig. 1.

an inch below the great trochanter of the femur, and extends for a distance of eight inches and three-quarters downwards and inwards, measuring in its widest part four inches. In close proximity to the groin of the left thigh, there exists a peculiar arrangement of small nodules

Fig. 2.

like a cluster of beads of different sizes. Had this morbid condition of the skin invaded the genital organs, it would, as likely as not, have been denominated elephantiasis. The pedunculated tumours have passed through all stages of growth, and, being useless to the economy, are assuming degenerative changes, partly due, perhaps, to the pressure and local irritation. They present more the appearance of molluscum fibrosum than of the cheloid of dermatologists.

The first tumour, already referred to, that made its appearance, and which, after being extirpated, was a year in re-forming, and which, since our war, has undergone another operation, now occupies a very extended surface upon the side of the face, embracing the left ear in the form of a horse-shoe. It measures three inches and a half in front, two and a half above, and three and a half inches below the aural aurifice. Its lobulated inferior border is an inch in thickness, and projects an inch

and a half from its broad pedicle. Its posterior portion includes the lobule and the anterior portion of the ear. Its superficial surface is covered with scales formed from a sero-purulent fluid that exudes from a slightly excoriated surface. A similar appearance is to be found in some forms of lepra. This tumour, in coming into contact with a neighbouring fibrous mass, has the under surface of its overlapping lobule ulcerated. The tumour situated below resembles, in shape and colour, the inferior surface of a liver. When its surface is touched, it shrivels between the fingers, and the touch has the semi-elastic feel of a fungus. Its lower border is sacculated, and discharges a yellowish-white gelatinous fluid from small puckered openings. Situated upon the right side of the jaw is a turtle-shaped tumour; its body rests upon the angle of the inferior maxillary, and its head, having two pea-like bodies in the place of the eyes, includes the lobe of the ear in its substance, and points in front of the aural appendage. Its length is $4\frac{7}{8}$ inches, and its breadth $4\frac{1}{4}$ inches. The hair of the whiskers is disarranged by the tumours. The apposition of the edges of these prominences with the subjacent skin, or with neighbouring protuberances, has given rise to abrasion of their surfaces. A portion of one of the tumours had suppurated, staining the linen with the discharge. When the sacculi, after having excited considerable pain, had given exit to their contents, they closed, as stated, with puckered cicatrices. The tumours have not encroached upon the cavity of the mouth, the mucous membrane of which is entirely healthy.

Upon the nape of the neck a tomato-shaped growth, looking as if it had burst in the centre from over-ripeness, now discharges a yellowish albuminous fluid. Tumours of this nature, according to Virchow, are developed from the corium, or sometimes take their origin from the panniculus adiposus. They may attain to a great size, having been known to weigh forty pounds. When they attain to an inconvenient size around the neck, they are subjected to surgical interference. Dr. Maury of Philadelphia removed from the neck of a coloured man one weighing nine pounds. But in addition to those around the neck, the dorsal surface of the body, as well as the shoulders and arms, presented the singular appearance as if masses of fungi had been attached to the surface of the skin. These excrescences are all of a lobulated or convoluted appearance, possessing a slight degree of mobility and elasticity. The largest of these tumours upon the back is $9\frac{1}{2}$ inches in length and $4\frac{1}{2}$ inches in width; the smallest in size measures $2\frac{3}{4}$ inches in length and 2 inches in width. One of these excrescences, having a depressed centre, and consisting of twenty-three lobules, measures $5\frac{1}{2}$ inches in length, $2\frac{1}{2}$ inches in width, with a thickness of three-quarters of an inch. The tumours situated upon the scapula, on each side of the spine, have a distance from each other of half an inch. These morbid enlargements have a tendency to overlap one another, rather than to root themselves by prolongations in the skin. Upon section, they present a whitish, homogeneous, gristle-like appearance, and the knife is resisted in its passage through the dense, firm, fibro-cartilaginous-like structure. The blood-vessels have an irregular network arrangement upon the surface, and may give rise to severe hæmorrhage when the tumours are removed. Although two or three of these tumours, when irritated, have discharged a yellowish-white albuminous fluid, and resembled fibroma somewhat in appearance, yet the soft purselike appendages are unlike the soft purselike appendages to the skin, having a soft spongy consistence, and composed of young gelatinous connective tissue, characteristic of true molluscum fibrosum; nor can they be easily separated from the pedicle or enucleated from their attachments in the superficial layer of the derma. Besides, James Bell is in perfect health; and, although in such a disease we may suspect some degenerative changes in the substance of the spinal cord, and, as in his case, a greater sensibility on one side than another, that will lead undoubtedly in time to a greater difference in the supply of nervous vigour to the two sides, still he does not manifest those general nutritive disturbances which, in fibroma, often cause death by marasmus or pyæmia. The disease is a localised evidence of disorder of the peripheral nerves, accompanying the blood-vessels of the corium. In the *post mortem* examination of persons who have died of leprosy, the nerves are found to be thickened by a fibrous structure, and their terminal branches atrophied and pearly in aspect, while in the anæsthetic variety the nervous centres in the cranial and vertebral cavities are often found diseased. Yet it is somewhat singular that the microscope seldom reveals the elements of nerve-structure in the tumours attending hypertrophic cutaneous diseases. Even in a case of very painful neuroma, reported by Dr. Dühring of Philadelphia, the microscope failed to discover, in the rounded hard nodules, that were often the seat of the most intolerable pain, the presence of any nerve-fibres. In all similar affections of the skin where peripheral nerves become affected, as in our patient, the morbid nervous condition is conveyed, to a greater or less extent, along the nerves to the central nervous system, and gives rise, not merely in some cases to intercurrent nervous disorders, but to

that characteristic mental condition observed in many cases of hypertrophic disease of the skin.

By the persistent use for several years of small doses of arsenic, not only its sedative influence would be exercised upon the peripheral cutaneous nerves, and, by allaying this extreme sensitiveness to external impressions, remove the causation of the disease, but it might, to some extent, restore healthy nervous functions, by assisting in the reformation of lost nervous structure and the removal of sclerosis of the skin and nervous centres, which seem to form after nervous elements have disappeared. Local measures, as pressure, etc., may at the same time be resorted to for removing these dermal tumours. Mr. George Pollock, of St. George's Hospital, London, has published in the *Lancet*, of March 22nd, 1873, the details of a case of molluscum fibrosum, which appears to have some of the characters distinguishing the case of James Bell.

The woman, aged 33, who had been afflicted since childhood, was in a very low state of health when admitted to the hospital. There were over one hundred tumours of various sizes in different parts of the body. Some were solitary, some were clustered, some with broad base, some pedunculated, whilst others were as small as a split pea. The chief growth extended from the right side of the neck by a pointed extremity to the upper margin of the right mamma. It consisted of a long, thick, and broad pendulous flap of skin about eighteen inches in length. Its anterior surface was thrown into several folds, which give it somewhat the appearance of coils of intestine. One large one, attached to the back of the head, was of the size of a small melon. The microscope, according to Dr. Whipple, showed that the growth was due to excessive hypertrophy of the connective tissue, and partly to abundant cell-growth, occupying interspaces between the bands of fibrous tissue.

The microscopical drawing (Fig. 3) accompanying this essay will show the havoc made by the disease in the dermal tissue. The main feature presented is hypertrophy of the cutis vera, as well as of the deeper pigmentary layer of the epidermis. The connective tissue of which the cutis vera is composed is of a low type, consisting of wavy interlaced bands of fibres, enclosing here and there within its meshes patches of fibroplastic matter, consisting of closely packed, minute, angular, actively growing corpuscles, with faint striæ passing amongst them. The hairs and hair-follicles appear quite normal, though surrounded by a layer of the above mentioned fibro-plastic material. The pigment-layer is very large and abundant, sending in anastomosing processes to the cutis vera.

James Bell's disease is remarkable from the fact that it embraces some of the characters of both cheloid and molluscum fibrosum. If the origin of those cases occurring in England, now called molluscum fibrosum, were minutely investigated, it is possible, from the nature of the microscopical examination of Mr. George Pollock's case, and the fact that molluscum fibrosum is a disease peculiar to warm countries, that they would follow our example, and call their cases cheloid, especially as this disease is more likely to prevail in temperate climates.

Fig. 3.

THE ALLEGED OCCURRENCE OF PURPURA IN CHILDREN.

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REFERRING to Dr. Lewis's communication to this JOURNAL under the title "Notes on Purpura," I had my attention drawn by Dr. Cameron six months ago to the investigations that were being made by Dr. Lewis into the nature of the maculated condition of the skin giving rise to the abnormality of which he treats, and I was induced to devote much time and attention amongst our in- and out-patients to the matter, with a