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THE PROPERTIES AND USES OF THE CALABAR BEAN.

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MESSRS. EDITORS,—As an article in the *Annales d'Oculistique* contains the best statement I have seen of what is known of the Calabar bean (*Physostigma venenosum*), with an account of experiments in which I myself took part at Utrecht, I have made a translation of its important portions, hoping it may interest your readers. Not to occupy too much space in your pages, I omit a long botanical description, and will merely premise, that the bean is the product of a climbing plant found at Calabar, on the Western Coast of Africa, and employed among the natives for the trial by ordeal, being publicly administered to accused persons as a supposed test of their innocence or guilt. It is extremely poisonous; but if the individual escapes, in consequence of the supervention of vomiting, he is considered innocent, and his accuser is submitted to the same criterion. The bean itself is about an inch in length, and covered with a dark, almost horny envelope. The article is by Mons. Warlomont, of Belgium.

The materia medica is composed of a large number of agents, styled therapeutic, which have found a place there, thanks to the results obtained by empirical experiment, but of many of which the value is still contested. Those only which rest upon a well-determined physiological effect have gained a permanent place, for they alone have a firm and solid basis. Opium, belladonna, digitalis, are legitimately in possession of the place which their physiological properties have gained for them, and from which we have educed, without much difficulty, the therapeutic applications from which our science has derived such numerous and important advantages.

It is, then, a fortunate thing for medicine that an agent has been discovered, having well-marked physiological properties which had never before been observed in any known substance, and offering a

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new horizon to therapeutics by filling a void which has long been recognized and deplored, but which will henceforth exist no longer.

Whilst we possessed in belladonna, hyoscyamus, stramonium and their alkaloids, infallible means for dilatation of the pupil, which is so often necessary in the treatment of diseases of the eye, the power of contracting the pupil did not belong to any known product. Opium acted to a certain extent, it is true, in this way; but its action was feeble, irregular and uncertain, and only very limited and doubtful results could be obtained from its use. It is not thus with the *Calabar bean*; its power of contracting the pupil is energetic, prompt and incontestable, and physiology as well as therapeutics has already derived advantages from it.

Dr. Daniell prepared a short paper on the poisonous properties of the *Calabar bean*, in 1846; but it was not till 1862 that its anti-mydriatic qualities were announced by Dr. Frazer, of Edinburgh, who discovered them, and brought specially to notice by Dr. Robertson, who still further investigated them and pointed out to the profession their great practical value.

ACTION OF THE CALABAR BEAN ON THE EYE.

1. *Effect on the Pupil.*—When even a very small amount of the extract of *Calabar bean* has been introduced within the eyelids, the pupil begins to contract considerably in the course of eight or ten minutes—usually without pain or inconvenience. If the dose is larger, or applied to a sensitive individual, it may give rise to palpebral, orbital or frontal pain, sometimes severe and of considerable duration. Sometimes the eye itself feels heavy and painful; but these symptoms are only rarely exhibited. Sometimes the pupillary contraction takes place slowly and by regular progression, sometimes by starts and oscillations.

When an eye has been submitted to strong and repeated doses of extract of *Calabar*, and its full action upon the pupil has been established, the pupil is capable of still further contraction if exposed to concentrated solar rays, and, if the same eye is placed suddenly in a dim light, slight dilatation of the pupil takes place. The *Calabar*, therefore, does not determine the maximum of contraction of which the pupil is capable.

As regards the antagonistic effects of belladonna and the *Calabar bean*, it has been pointed out by all who have experimented that the duration of the effect of the latter is less than that of the former. Thus, when by large or repeated doses of the anti-mydriatic, dilatation of the pupil previously induced by atropia has been overcome, not more than an hour has passed before the atropia has gained the ascendancy and neutralized its antagonist.*

* It is not unlikely that the apparent comparative inefficiency of action of the *Calabar* may be due to the fact that most of the experiments have been made with "Calabar paper," prepared by repeated dippings in a solution of the extract of the bean, or at most with the

2. *Effect upon the Ciliary Muscle and the Power of Accommodation.*
 —Its action upon the pupil is neither the sole nor the most interesting effect produced upon the ocular system by the Calabar bean. At the same that it narrows this aperture it acts also upon the accommodation; but these effects are wholly independent of each other, for the contraction of the pupil often persists for a long time after the disturbance of the function of accommodation has subsided. This action consists in an increase of the refraction of the eye, and consequently in bringing yet closer the near point of distinct vision. This latter phenomenon last longer than the other, but rarely beyond an hour and a half. After this time the muscles of accommodation present a singular condition, resulting from a sort of strabismus in the tensors, so that coöperative action of the two eyes, in binocular vision, becomes difficult.

In the accompanying tables, Dr. Hamer, of Utrecht, has given most accurate observations as to the duration and extent of the modifications of accommodation.

FIRST EXPERIMENT, MADE WITH A SQUARE OF CALABAR PAPER.

Subject of the Experiment.	Age.	Which Eye.	Minutes after the Application.	Far Point.	Near point.	Latitude of Accommodation.		Size of pupil in millimetres.
						Without glasses.	With glasses.	
Mr. Schuurman.	24	Right.	0	6 inches.	3 in. 3 l's.	$\frac{1}{7\frac{11}{11}}$	$\frac{3}{8}$	4.96
			10	5 "		$\frac{1}{9\frac{7}{7}}$		4.05
			35	3 "	2 in. 5 l's.	$\frac{1}{12\frac{3}{3}}$		1.60
			60	4 "		$\frac{1}{6\frac{1}{1}}$		1.56
			155	6 "		$\frac{1}{4\frac{2}{2}}$		

Generally the modifications of the refraction follow immediately upon the production of myosis. The increase of refraction con-

tract itself, and not with the active principle (or Calabarine), which, if hitherto obtained at all, has probably been imperfectly prepared—the extremely small amount of the bean which could be found in Europe not having allowed of experiments on a large scale. Of course, the preparations of the *extract* of the bean could not be expected to compare, in degree of power, with solutions of atropia, the *active principle* of belladonna. W.

tinues some ten minutes from the time it begins to manifest itself; it then decreases, and ordinarily has disappeared at the end of an hour. It is generally equivalent to a lens of eight or ten inches focus.

At the same time, another phenomenon equally remarkable is observed: the near point of distinct vision is brought as much nearer the eye as it would be by a glass of twenty-four inches. If the dose of Calabar has been feeble, the far point remains unchanged, even though the ciliary muscle is very active; the range of accommodation in these cases is therefore increased by the whole extent to which the near point has been approximated. On the contrary, under the influence of a high dose the far point may be brought nearer, by the exercise of the power of accommodation.

In Experiment I., the paper produced irritation of conjunctiva. It was removed at the end of five minutes. Reading, with the book held near the eye, caused a sensation of pain; but not when reading large letters at a distance. After 155 minutes the right eye, with the aid of a concave glass of eight inches, saw much better than the left.

SECOND EXPERIMENT.

Subject.	Age.	Which Eye.	Minutes after Application.	Far Point.	Near Point.	Latitude of Accommodation.		Size of pupil in millimetres.
						Without glasses.	With glasses.	
Dr. Williams.	42	Left.	0	∞ (Infinite distance.)	7 in. 9 l's.	$\frac{1}{7\frac{3}{4}}$	$\frac{1}{8}$	3.40
			10	"		"	"	3.04
			20	36 inches		$\frac{1}{9\frac{7}{8}}$		2.32
			30	24 "	5 " 11 "	$\frac{1}{7\frac{7}{8}}$		1.90
			60	45 "	6 " 3 "	$\frac{1}{7}$		1.90
			72	80 "		$\frac{1}{6\frac{3}{4}}$		1.44
			85	∞		$\frac{1}{6\frac{1}{2}}$		

Ten minutes after the application of the paper, pain was felt in the orbit. The paper was removed after five minutes. Even when the diameter of the pupil was reduced to 1.90 millimetres, it still contracted when exposed to strong light. Objects appeared larger.

THIRD EXPERIMENT.

Subject.	Age.	Which Eye.	Minutes after Application.	Far Point.	Near Point.	Latitude of Accommodation.	Acuteness of vision.		Size of pupil in millimetres.		
							Without glasses.	With glasses.			
Dr. Hamer.	25	Right.	0	80 inches.	4 in. 7 l's.	$\frac{1}{4\frac{1}{2}}$	$\frac{20}{20}$	$\frac{20}{20}$	4.13		
			5	20 "		$\frac{1}{2}$					
			12	7 "		$\frac{1}{9\frac{1}{2}}$				3.24	
			20	7 "	4 " "	$\frac{1}{13\frac{1}{2}}$					
			25	7 "	3 " 9 "	$\frac{1}{8\frac{1}{2}}$				2.53	
			43	7 "		"				1.63	
			50	10 "		$\frac{1}{2}$			$\frac{20}{20}$	1.30	
			55	12 "	3 " 9 "	$\frac{1}{5\frac{1}{2}}$					
			65	18 "		$\frac{1}{4\frac{3}{4}}$					1.10
			70	20 "		$\frac{1}{2}$					
			90	24 "		$\frac{1}{4\frac{1}{2}}$					1.00
			110	36 "		$\frac{1}{4\frac{3}{4}}$					
140	80 "		$\frac{1}{2}$								

Four minutes after the application of the paper to the conjunctiva, painful contractions, like electric shocks, were felt in the lower lid. After fifteen minutes much pain in the globe, which was still further augmented by reading at the distance of a foot. At the end of fifty minutes the iris appeared to bulge forward and to have become insensible to light; the painful sensations persisted; to the right eye distant objects seemed less bright, white paper appearing brown; muscæ volitantes were seen. The spasm of the accommodative power declared itself after twenty minutes, and had not wholly passed off eight hours after. Twenty-four hours after the application of the Calabar, the pupil was still very much smaller than that of the right eye.

In experiments made by Dr. Wecker, of Paris:—in Mr. Pactovan, whose near point was 3 inches, it was brought to $1\frac{1}{2}$; in Dr. Hunt, from 3 to $1\frac{1}{2}$; and in Dr. Salazar, from 4 to 3 inches.

These results perfectly accord, as will be seen, and establish the propositions we have advanced, which are in a great measure borrowed from Dr. Hamer's excellent work, already mentioned.

3. *Effect on Vision.*—At the moment that contraction of the pupil is produced, and that consequently an obstacle is presented to the introduction of a normal amount of light, there is a sensation as if it had become twilight. According to M. de Graefe, there is a moment when the acuteness of vision is diminished one third. This difference, however, is scarcely observed when the light is intense, but is quickly noticed if the light is dim. In some short-sighted persons a sudden and very transient improvement of vision for distant objects has been observed, when a great degree of myosis had been rapidly brought on.

Astigmatism has also been sometimes produced, which Dr. Robertson explains on the supposition that the solution of Calabar had acted unequally on different parts of the ciliary muscle. This same difference of effect would explain the irregular contraction of the pupil which has sometimes been observed.

4. *Mode of Action on the Organ of Vision.*—We know that by irritating the sympathetic nerve we cause dilatation of the pupil; but, section of this nerve increases yet more the contraction caused by large doses of Calabar. The Calabar acts on the sphincter of the iris by irritation, by causing spasmodic action of the third pair; as an antagonist of atropia, which acts by irritation on the radiating fibres of the iris and the tensor choroidæ, through the sympathetic. This is fully demonstrated, first, by the fact that the pupil contracts much more under its influence than it does after paralysis or section of the sympathetic; and, secondly, because the pupil may be acted on even more fully by the Calabar when the sympathetic has been cut. Prof. Donders, of Utrecht, has been able to produce considerable enlargement of the pupil already under the influence of the Calabar, in a rabbit, by exciting the sympathetic;

and having, in another rabbit, cut the sympathetic on one side and applied the Calabar to both eyes, he obtained the greatest amount of contraction on the side where the nerve had been cut.

Like atropine, calabarine acts only on the eye to which it has been applied, and, like it, acts by penetrating to the anterior chamber. It even acts on eyes where the cornea has been perforated, an important fact as regards therapeutics.

THERAPEUTIC USES OF CALABAR BEAN.

1. *In Mydriasis.*—Artificial mydriasis may be corrected, to a certain extent at least, by the use of this remedy. After having dilated the pupil, for an examination of the deep-seated portions of the eye with the ophthalmoscope, we may spare the patient the annoyance caused by a considerable duration of this dilatation, by introducing within the lids a little of one of the preparations of the extract of Calabar bean. The exact amounts requisite to completely neutralize a given strength of a solution of atropia remain to be determined.

Mydriasis, when existing pathologically, may be advantageously modified by the extract of Calabar. Even when the iris has become completely insensible to light, the pupil contracts promptly under its application. To ensure its efficacy, the remedy must be continued for a time. Messrs. de Graefe, Workmann, Hulke and Hart have already reported cases of radical cure of paralysis of the third pair, with mydriasis, where the power of accommodation had been wholly or partially lost. Mr. Soelberg Wells reports an instance of the permanent cure of a patient affected with rheumatic paralysis of the constrictor of the pupil and of the ciliary muscle of the right eye. Vision was so imperfect that the patient could not read, or thread a needle, with both eyes open. She had diplopia and amblyopia in the right eye. The application of the extract to both eyes demonstrated its special action upon the power of accommodation. The pupil of the healthy eye contracted very much, and that of the affected eye, which measured three and a half lines in diameter, was diminished to two thirds of a line within a quarter of an hour after the application. The sight was at once so much improved in this eye that she could read the finest print.

Glaucomatous mydriasis, if the iris has not become completely atrophied, does not prevent the action of the Calabar bean. It has the effect, in this condition of things, to contract the pupil, render the iris tense, and thus offer a larger surface to the instruments with which it is taken hold of in performing iridectomy. The danger of wounding the crystalline is at the same time diminished.

1. *In Paralysis or Fatigue of the Accommodative Power.*—Among the organs which may remain paralyzed after an attack of diphtheria, is to be reckoned the ciliary muscle; the power of accommodation is thus wholly or partly lost. Severe fevers, and especially

typhoid fever, also sometimes leave behind them a general atony, in which the organs of accommodation may share. In both these cases the Calabar bean may be of great service in restoring the contractile power of the ciliary muscle.

3. *In Diseases and Anomalies of the Refractive Power.*—The power possessed by the Calabar bean of bringing the point of distinct vision nearer to the eye, indicates its use in cases where this point is at too great a distance, as, for instance, in hypermetropia. Persons who require spectacles for seeing small objects may replace them, to a certain extent, if they desire it, by the use of a Calabar eye water. It remains, however, to be determined by experience whether the action of this remedy may be indefinitely kept up, as in the case of atropia, or whether its influence will after a time cease to be felt. We know, moreover, that there is a certain degree of diminution of the clearness of vision (independent of what results from the contraction of the pupil) under the influence of the bean: these facts may in a degree counterbalance the advantages to be gained as regards range of vision. Furthermore, the eye sometimes becomes slightly heavy and painful after its application, which should also make us careful in our experiments.

The action of the Calabar may also be useful in myopia, since, by bringing the point of most distinct vision nearer, without approximating the far point, it enlarges the latitude of accommodation; and it may sometimes be of use to the short-sighted to bring their near point yet closer.

4. *In Wounds at the Margin of the Cornea, with Hernia of the Iris.*—As we have in atropia an efficient means of drawing the iris towards its periphery, and preventing it from becoming implicated in an ulceration or a wound of the centre of the cornea, so we have in the Calabar bean a means of averting hernia of the iris, which may threaten to take place through lesions near the corneal circumference.

MODE OF PREPARATION AND USE.

The only active part of the plant is the bean itself, its hard, horny envelope being discarded. Its alcoholic extract, prepared by exhausting the powdered bean with alcohol and evaporating the solution, may be applied by taking a minute quantity of it upon a fine pencil, moistened with water, and applying it to the conjunctiva of the lower lid. The specific action will be observed in five minutes.

Mr. Streatfeild's ingenious invention of a fine tissue paper impregnated with a solution of atropia of given strength, so graduated in squares that one square shall represent a certain quantity of the solution, has also been applied to the preparation of paper impregnated with a solution of the extract of Calabar—and it is in this form, principally, that the remedy can be obtained, the small quantity of the bean to be found in Europe having been entirely insufficient to meet the demand for the extract. A square of this

paper, measuring an eighth of an inch, placed inside the lower lid, begins to act in twenty minutes, and its effects continue several hours.

Another excellent preparation is a solution of the extract in glycerine—two and a half grains of the extract in one hundred minims of pure glycerine.

CASE OF THE LATE DR. DALTON.

[Reported to the Boston Society for Medical Improvement, and communicated for the Boston Medical and Surgical Journal.]

By J. MASON WARREN, M.D.

DR. WARREN gave the following account of the illness and death of the late Dr. John C. Dalton, the valuable and distinguished physician whose case has excited so much interest both among the medical profession and the public generally:—On Saturday evening, Jan. 2d, Dr. Dalton slipped on the ice near his own house, falling upon a piece of iron, the model of a cannon, about six inches long and one inch in diameter, which he had in his pocket, and which was forcibly driven against his left side. He went home and lay upon the sofa until bed-time, complaining of general uneasiness, and expressing the feeling that he had received some ill-defined injury.

In the middle of the night he was attacked with violent pain in the left hypochondriac region, extending thence over the whole abdomen. He sent for Dr. Edward H. Clarke, under whose charge he remained during his illness. At this time he expressed the fear that he was suffering from intussusception of the intestine. Large doses of opium were given without material relief, after which ether was administered by inhalation, and the effect of it was kept up during the greater part of thirty-six hours. He was seen on Sunday afternoon by Dr. Warren, who continued in attendance with Dr. Clarke, from day to day during the remainder of his illness. After a very critical examination, no positive evidence could be discovered of injury to any internal organ. The bowels had been thoroughly evacuated by an enema immediately after the first visit of Dr. Clarke. He had passed no urine, nor was there any sign of any collection in the bladder. At his own request, however, a catheter was passed into the urethra, but it was arrested at the neck of the bladder by spasm, and no farther effort was made. The absence of the secretion was attributed in part to the great quantity of opium which he had taken, together with the ether which he had inhaled during so many hours, and which was attended by profuse perspiration. The stomach having become tranquilized after the etherization was stopped, and some hot drink administered, warm applications being at the same time made over the pubes, micturition took place spontaneously, no abnormal appear-