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ADDRESS.

STRENGTH OF THE DIFFERENT MYDRIATICS AND MYOTICS.

CHAIRMAN'S ADDRESS.

Read in the Section on Ophthalmology, at the Forty-sixth Annual Meeting of the American Medical Association, at Baltimore, Md., May 7-10, 1895.

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It will naturally occur to you that the development of our own Section work, the increase in the number of papers presented here which raise points for our discussion, and the increase in the number of members who can from their own observations add to the value of our discussions, together with the multiplication of ophthalmic journals, has rendered obsolete the Address which the By-laws of the AMERICAN MEDICAL ASSOCIATION say the Chairman shall prepare "on the recent advancements in the branches belonging to his Section." My predecessors for some years seem to have felt this and have chiefly confined their remarks to the other topic allotted them, viz., "suggestions in regard to improvements in methods of work."

Such suggestions as I would make regarding the conduct of our Section have been embodied in the arrangement of our program, or will appear in the course of our proceedings. The most important of them is in the attempt to enforce brevity in the communications that are to be read before us. In this effort I ask your assistance—that as readers of papers or speakers in discussion you will not ask for extension of time—and that as members of the Section you will bear in mind the rights of those who have not yet obtained the floor, as against the natural desire of a speaker to communicate more than a fair share of his ideas.

For a gathering such as this, the elementary principles, the complete and rounded treatise, the historical review, the miscellaneous details of cases, even the professional experiences of the speaker, except as they bear directly on the point under discussion, are all out of place. The office of the written paper here is to awaken and shape the discussion. If you have new facts, even of the highest importance, that will awaken no criticism from our experience, suggest no questions that we want to put to you, do not bring them here. You can communicate them more cheaply and more perfectly through the printed page. The medical society should not be a contrivance for stuffing unwilling victims with even the most valuable information. If we have tried to use it for that purpose, let us stop doing so.

It may often happen that with the papers that are to be printed, as well as read here, we may desire that as they appear in the JOURNAL, or our volume of

Transactions, they should contain matter not essential to the intelligent consideration of the points raised for discussion. Such matter may well be included in the paper, but omitted in the reading.

The absurdity of addressing you on current ophthalmic literature, with the chief additions to which you are already familiar, is too apparent to demand any apology for turning quite aside from such a course. I have chosen, therefore, to speak chiefly on a particular topic, important in itself, but I think especially appropriate, because complete knowledge of it will be best reached through collective investigation.

RELATIVE STRENGTH OF MYDRIATICS AND MYOTICS.

With the first medical use of any drug there arises the question of dosage, so that views, more or less positive, are current with reference to the absolute and relative strength of our various mydriatics and myotics. They are, however, little more than indefinite impressions, such as would not be tolerated among the accumulations of an exact science like chemistry or physics, and it is, I believe, quite within our power to replace them by definite knowledge. The mutual antagonism of these two classes of drugs, and the readiness and exactness with which we can measure the diameter of the pupil and the distance of the near point of accommodation, render this the field in which we can first gain exact quantitative knowledge of the physiologic action of drugs. In other investigations of the kind, we may know exactly the dose applied and the body weight of the animal to which it is applied; but have, commonly, no means of exactly measuring for comparison the result produced. In this matter of the dilatation or contraction of the pupil, the increased or diminished effort of the ciliary muscle, cause and effect, factors and product, can both be estimated with exactness.

The effect of a mydriatic on the eye can be most accurately observed subjectively, the subject of experiment making the observation, and one eye only should be subjected to the influence of the drug at one time, the other being kept normal for control of illumination and for comparison; the size of the pupil is to be measured by the distance apart of pin-hole openings that give tangent circles of diffusion on the retina. I have employed a series of pin-holes punched in a piece of cardboard, the distance between them varying by $\frac{1}{4}$ millimeter intervals from 2 mm. to 9 mm. The effect on accommodation is tested by placing a lens before the eye subjected to the drug, convex for a mydriatic, concave for a myotic, and covering first one eye, then the other, while they are both made to focus fine print at the near point of distinct vision, and changing the lens used until that strength is found which most accurately neutralizes the influence of the drug on the ciliary muscles. Complete absence of accommodative power or pupil-

lary reaction is ascertained by the ordinary methods.

In the experiments now referred to, I have used the various drugs dissolved in distilled water, in proportions varying from 1 to 10 (homatropin) to 1 to 2000000 (hyoscyamin, etc.) and have applied them by dropping on the cornea with a pipette, giving 180 drops of water to a drachm.

As the measure of the strength of a mydriatic we may take the amount required to produce either of several definite physiologic effects. Thus we may take the strength of the solution when carefully applied that will constantly produce the least effect that can be certainly recognized. This I have found to be for pilocarpin (hydrochlorate), 1:2000, or 1-6000 gr.; homatropin (hydrochlorate), 1:10000, or 1-30000 gr.; eserin (sulphate), 1:50000, or 1-150000 gr.; atropin (sulphate), 1:500000, or 1-1500000 gr.; hyoscyamin (hydrochlorate), 1:1000000, or 1-3000000 of a grain.

What will be said of the strength of hyoscyamin applies equally to duboisin and scopolamin, and probably to daturin. In the Transactions of the Medical Society of the State of Pennsylvania for 1882, p.157, I published a study of the subject, and the conclusion reached through it that, "Daturia, duboisia, and hyoscyamia are physiologically identical." Recently I have carefully compared the actions of duboisin and hyoscyamin with that of the newly introduced scopolamin, and have not been able to discover any difference between them.

This relation of the sizes of the minimum dose is a simple one, easily ascertained, and one that each of you may verify or correct without causing yourselves any personal inconvenience. It is to be hoped many will test it, as its general study would almost certainly reveal important facts as to susceptibility and idiosyncrasy.

But in practice we use these drugs in doses enormously greater, and when so used the ratios of their strengths differ markedly from those above indicated. In general it appears that those drugs whose action is more evanescent, require to be used in relatively larger dose to produce the minimum effect; that is, in practical doses they prove relatively stronger. This will appear on comparison of the foregoing with the data to be given presently.

A more practical measure of strength is to be found in the amount of the drug required to produce full dilatation of the pupil or complete paralysis of the accommodation. For purposes of comparison, however, a method which eliminates errors from imperfect instillation and absorption of the drug is to determine the strength of the different mydriatics by observing their power to neutralize a rather strong (1 to 1000, nearly .5 grain to the fluid ounce) solution of eserin sulphate.

The trial has been made by using a single solution containing both the drugs in the desired proportions. When this is resorted to, the myotic effect is first manifest, and as it declines the mydriatic becomes predominant. This is the case to a slight extent even with homatropin, and is much more marked with the slower mydriatics, especially atropin. Still, even with atropin, there is a time at the beginning of its maximum effect when the influence of the eserin has scarcely begun to decline, when they can be made to closely neutralize each other.

Taking this period of most complete neutralization, which is about one and one-half hours after in-

stillation for homatropin, two and one-half hours for hyoscyamin, and three and one-half hours for atropin, I find that to neutralize the influence of the mydriatics requires for 1 part homatropin, 1-6 part eserin; 1 part atropin, 5 parts of eserin; 1 part hyoscyamin, 12½ parts eserin; 1 part homatropin, 4 parts pilocarpin.

Taking homatropin as the unit, the relative strength of the mydriatics and myotics then appears to be: pilocarpin (hydrochlorate), ¼; homatropin (hydrochlorate), 1; eserin (sulphate), 6; atropin (sulphate), 30; hyoscyamin (hydrochlorate), 75.

These proportions hold pretty nearly for either the effects on the pupil or on the accommodation, although in my own eyes (the only ones in which I have been able to note very accurately the changes in the accommodation), the mydriatics have all shown a relatively greater effect on accommodation. That is, in the transition from myosis to mydriasis, there has in each instance been a time when the pupil still remained contracted, although the accommodation had descended below the normal.

The strengths of the mydriatics and myotics that I have thus indicated has been ascertained by experiments first on my own eyes. Nearly all have been confirmed by experiments on the eyes of other persons; but not any large proportion of them on the eyes of any one person. In many respects these observations agree with the recorded observations of others; as with Risley, in his conclusion published in his first account of duboisin, that its influence on the accommodation was more than twice as great as that of atropin, and the chief results obtained by Donders and von Graefe and their students experimenting on atropin and extract of calabar bean.

But in some respects the published conclusions of earlier observers have not been confirmed. This has been especially the case in regard to minimum doses. Thus Loring, for atropin, found the minimum strength that would produce a notable effect on the pupil to be 1:150000, and Jaarsma (quoted by Landolt) concluded that a drop of either of the following solutions was the minimum dose that would affect the pupil: pilocarpin, 1:400; eserin, 1:12800; atropin, 1:80000; daturin, 1:160000; duboisin, 1:1200000. He thought that it required a strength of 1:800 of eserin to affect the accommodation. Graefe speaks of the dilatation produced by a solution of 1:120000 of atropin "long kept in contact" with the eye of a dog. The weakest solution of atropin referred to by Donders in his work was 1:14400, of which he says: "On the following day no trace of mydriasis is perceptible." ("Accommodation and Refraction of the Eye," p. 588.) I have, after the instillation of one-third of a minim of a 1:500000 solution of atropin containing 1-1500000 of a grain of the drug, found a mydriasis amounting to .25 of a mm., greater diameter of the pupil, after twenty-four hours. Subsequently, however, Donders became better acquainted with the mydriatic power of atropin, as is shown by the following letter published in the "Life and Letters of Charles Darwin," vol. II, p. 498:

Down, July 7, 1874.

My dear Professor Donders:—My son George writes to me that he has seen you and that you have been very kind to him, for which I return to you my cordial thanks. He tells me, on your authority, of a fact that interests me in the highest degree, and which I much wish to be allowed to quote. It relates to the action of 1-1000000 of a grain of atropin on the eye. Now, will you be so kind, whenever you can find a little leisure, as to tell me whether you yourself

have observed this fact, or believe it on good authority? I also wish to know what proportion, by weight, the atropin bore to the water solution, and how much of the solution was applied to the eye? The reason why I am so anxious on this head is, that it gives some support to certain facts repeatedly observed by me, with respect to the action of phosphate of ammonia on *Drosera*. The 1-4000000 of a grain absorbed by a gland clearly makes the tentacle which bears this gland become inflected; and I am firmly convinced that the 1-20000000 of a grain of crystallized salt (*i. e.*, containing about one-third of its weight of water of crystallization) does the same. Now I am quite unhappy at the thought of having to publish such a statement. It will be of great value to me to be able to give any analogous facts in support. The case of *Drosera* is all the more interesting as the absorption of the salt or any other stimulant applied to the gland causes it to transmit a motor influence to the base of the tentacle which bears the gland.

Pray forgive me for troubling you, and do not trouble yourself to answer this until your health is fully reestablished.

Pray believe me, yours very sincerely,

CHARLES DARWIN.

The fact here asked for is used in Darwin's "Insectivorous Plants," chap. vii. It is the dilatation of the pupil of the dog by 1-1000000 grain of atropin applied directly to the iris. But I have read this letter, not merely because it supports my observation as to the mydriatic power of atropin, but because in it lies revealed a general fact most worthy of our consideration. Does it appear to any of you that here are two great men in their dotage, pleased with mere trifles? You have then but poorly traced the course of scientific progress. This letter indicates the importance attached by two of the greatest scientists of our century to exactness and definiteness of observation; and all the history of scientific progress testifies that they were right in their estimate.

The observation of the Greek philosopher in his bath-tub, of the loss of weight by displacement of water, with a few similar observations furnished a foundation on which physics grew up, centuries before her sister sciences were imagined. For a thousand years the alchemists distilled and compounded and theorized, until in the eighteenth century, Black took to carefully weighing the products of his experiments. Priestley and Cavendish, Scheele and Lavoisier followed him, and in a single generation the crude theories of alchemy dissipated as mists before the morning sun, revealing the great vistas of modern chemistry. Within the year we have witnessed the proclaiming of a new element in our atmosphere, revealed simply by the minute difference between the weight of supposed nitrogen procured from the air, and nitrogen procured from other sources.

We all look forward to a day when we can speak with more truth of a science of medicine. Let us remember that it will come, and only come, as we bring the balance and the rule, and all other means of minute exactness into our methods of clinical investigation.

ORIGINAL ARTICLES.

THE KRÄG-JORGENSEN RIFLE.

A REPORT OF ITS EFFECTS ON THE SKULL OF THE LIVING, SHOWING THE FALLACY OF THE "HUMANE" THEORY ON GUNSHOT WOUNDS FROM THE MODERN RIFLE.

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The shooting through the head of a military convict attempting to escape from a sentinel at this post,

with the Kräg-Jorgensen, the new rifle adopted for the United States Army—presenting the first instance in the country of its effects on the skull of the living subject, has led to various sensational accounts in the secular press. Based on these, I have received a number of letters of inquiry from physicians interested in the result of the change of caliber. In order to prevent erroneous deductions from newspaper reports, and to give the profession a true description of the injury produced, I have deemed proper to publish this account, with a sketch of the skull as it appeared after removal of the integument.

I saw the man a few minutes after he was shot. His breathing was stertorous; he was, unconscious, and death appeared to be only a question of minutes. A cursory examination revealed two bullet wounds. The entrance wound (he was running away when shot), was located in the upper occipital region of the skull, and that of exit in the forehead a little to the right of the center. (Distance between rifle and victim ninety feet.) After passing through the man's skull, the ball went through a tree eight inches in diameter and buried itself in the ground two feet. The man died in half an hour.

Post-mortem was made the same night. The wound of entrance into the skin presented a round opening, without the appearance of scorching or blackening. The wound of exit in front was larger and more ragged. The integument was carefully dissected off and the bone of the top of the skull found extensively fractured, the parts being connected here and there by fascia.

On the calvarium being removed, the surface of the dura mater presented a state of intense congestion. To the right of the longitudinal fissure it was torn through for a distance of about four inches, about one inch from and parallel to it.

On removal of the coverings, the convolutions of the brain were made prominent by the engorged network of superficial veins. A furrow, corresponding to the injury of the dura was ploughed through the right hemisphere, in the region of the superior frontal convolution, about half an inch deep. The right lateral sinus appeared filled with blood serum; the left was normal. On section, the vessels of the brain were found engorged, but no other macroscopic injury of a prominent nature was apparent.

After removal of the brain, the cribriform plate exhibited comminuted fracture; one or two slight fissures in the petrous and squamous portion of the temporal bone, otherwise the bone was intact.

The skull cap presented the following injuries, viz: at the site of the entrance of the bullet, one-half inch above and to the right of the junction of the occipital and right parietal bones, an oval perforation $1 \times \frac{1}{2}$ inch, the edges shelving inward. From this opening there radiated the following fractures, viz:

1. Downward into the left lambdoid suture, separating it, thence horizontally along the parietal and frontal bones to the left orbital cavity.
2. An oblique into the sagittal suture, opening it for two inches.
3. One parallel with the sagittal suture, bifurcating one inch from its origin into a wedge-shaped piece, which, again fractured, continued to the coronal suture separating it.
4. The left fracture communicated with the horizontal left fracture, described under 1, parallel to the coronal suture and one and a half inches to the rear.
5. A fracture at an acute angle from the former to