the active principle, but I have not yet succeeded in obtaining it in a pure form.

The addition of basic lead acetate produced a copious precipitate, but the active substance was not thrown down, passing over into the filtrate. After freeing the latter from lead by passing through hydrogen sulphid, and evaporating the resultant filtrate there was left behind a mass of thick syrupy consistence, which evidently was largely glucose, since it reduced Fehling's solutions and was also fermentable. In order to get rid of this sugar I took the filtrate resulting from the first precipitation from lead acetate, which still contained an excess of this reagent, and added ammonium hydroxid, with the hope that a portion at least of the glucose might be precipitated as a lead saccharate. Even by this means, however, I failed to get rid of all the glucose, so that I still had left behind a substance which could not be evaporated to dryness. This residue was extracted successively with ether, chloroform, benzol, acetone, amyl alcohol and petroleum ether without yielding any results.

Although I have not succeeded in obtaining the active principle in the pure form, I am, nevertheless, strongly inclined to believe that it is in the nature of a glucosid. This view is supported in the first place by physiologic evidence that all cardiac poisons which resemble digitalis in their action which have as yet been isolated have been glucosids. More important than this, however, is the following chemical evidence: I took 5 c.c. of the fluid extract, which had been freed from resin by precipitation with water, and evaporated off the alcohol, added to it some dilute hydrochloric acid and boiled fifteen minutes. The resulting fluid was neutralized with sodium carbonate and injected into the vein of a dog, with the result that there was neither elevation of the blood pressure nor slowing of the pulse.

DISCUSSION.

DR. CLEMENT B. LOWE, Philadelphia, stated that there is some uncertainty, when apocynum is spoken of, whether we are dealing with *Apocynum cannabinum* or *Apocynum androsaemifolium*, dog's bane. He went to a large drug house for some *cannabinum*, and found that it was *androsaemifolium*. He returned it and was told that they always supplied that preparation when apocynum was ordered. Dr. Lowe said that he is afraid, therefore, that Dr. Wood has been working with *androsaemifolium*. The two are very much alike, but differ microscopically in the arrangement of some of the bark cells, which in dog's bane are thick-walled and arranged in groups in a circle near the middle of the bark. It also responds differently to the phloroglucin test. To distinguish them is also more difficult because of the tendency of dog's bane and Canadian hemp to hybridize. A few years ago, when Dr. Lowe was out botanizing, he came across a plant that he could not understand; on studying it he found that it was a hybrid of these two species. The value of a bitter principle is that it causes an increased flow of gastric juice, just as it increases the saliva. Its bitterness is the important feature, and it is lost when disguised. If patients complain that it is bitter, tell them that is why it is given, and that the effect of the bitter can not be obtained without giving a bitter drug.

PROF. C. S. N. HALLBERG, Chicago, called attention to the fact that the alcoholic concentration has been on the market for twenty or thirty years. This preparation of *Apocynum cannabinum* is called "apocynin," and is prepared by precipitating a concentrated alcoholic tincture of the drug in water, following the usual eclectic method and nomenclature. It would be well to remember the fact that if any physician should prescribe apocynin he would probably get, in the vast majority of instances, the eclectic resinoid, instead of the glucosid recommended by Dr. Wood.

PROF. JOSEPH P. REMINGTON, Philadelphia, said that we are all very apt to believe that the active principles of the various drugs are either alkaloids or glucosids of a crystallizable character. We have been led to this idea from the fact that morphin, strychnin, codein and many others are crystalline. In a great many instances the active principles are not crystallizable. For instance, in cubeb and pepper oleoresins are the important constituents. He thinks that the active principle of the drug would be more likely to be a resinous substance, possibly left in the solution which Dr. Wood threw away, instead of the crystallizable principle. In determining these questions Dr. Wood has a much better opportunity of carrying on an investigation into their physiologic action than a pharmacist would have.

DR. H. C. WOOD, JR., said that he was supplied with fluid extracts of both *cannabinum* and *androsaemifolium*, but he had relied entirely on the statement of the pharmacist as to the identity of the fluid extracts. He stated that he did not throw away the residue after getting the crystals, and on subsequent trial he found that it had some activity. He said that the drug is useful in cases of dropsy, whether associated with cardiac weakness or hepatic cirrhosis. He hopes at a future time to bring some more accurate observations on the clinical uses of the drug.

USE OF DIAPHORESIS AND DIAPHORETIC AGENTS IN OPHTHALMIC THERAPEUTICS.*

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To properly estimate the therapeutic value of an agent, allowance must be made for the natural enthusiasm of those who introduce it and who often record results which later experience fails to confirm, and the tendency of certain things to remedy themselves, the exciting cause having been removed. Disappointment may ensue because too much is expected. Credit may be given when none is due. Truth lies between these extremes, and is to be reached, it seems to me, by finding out what one should look for, basing judgment on the physiologic effects of the remedy, and the teachings of clinical experience. An example of what one may, not illogically, term therapeutic enthusiasm and therapeutic chaos, is found in the statements of books on general therapeutics and those on eye diseases, regarding the use of diaphoretic agents in ocular affections. If we could accept, for instance, all of the following from Potter's "Materia Medica," pilocarpin would be little short of an ocular panacea. Says this writer: "Ophthalmologists employ pilocarpin with most excellent results in the amblyopia of alcoholism, and that from the use of tobacco, in detachment of the retina, chronic iritis, keratitis, glaucoma, hemorrhage into the vitreous, atrophic choroiditis, white atrophy, to promote resolution and absorption in inflammatory conditions with exudation." Bartholow and other writers indicate practically the same scope. The student turning from this general advice to special works will, I think, be disappointed if he expects to find specific and positive information as to what in this list is true and what is not. Most of our special writers indicate that diaphoresis has been recommended or may be tried in these conditions; but in no text-book with which I am familiar is there the positive teaching the subject deserves, and which is justified by our present knowledge. Scattered through current literature are many most interesting and in-

* Read at the Fifty-fifth Annual Session of the American Medical Association. In the Section on Ophthalmology, and approved for publication by the Executive Committee: Drs. Frank Allport, John E. Weeks and R. L. Randolph.

structive articles, but they are so scattered that their usefulness is greatly lessened. The object of this paper and the paper by Dr. Woodruff is to set forth briefly what, in the opinion of the writers, may be theoretically expected in ophthalmic therapeutics from diaphoretic agents, and the extent to which their own and others' clinical observation confirm or contradict claims from time to time put forth for this method of treatment. I regret that my recent illness has prevented such a search of current literature as I wished to make, and confined me to articles at hand or with which I was previously familiar. Still they cover more or less completely the principles involved.

Normal sweating is the result of glandular secretion. Physiologists no longer hold that transudation from the cutaneous blood vessels is its most important element. Says Stewart in his "Manual of Physiology": "Though an actively perspiring skin is in health a flushed skin, the vascular dilatation is a condition and not the chief cause of the secretion." . . . "Even the sweating produced by exposure to high temperature is normally brought about by nervous influence and not by direct action on the secreting cells." How far is the profuse sweating from diaphoretic agents, or high temperature employed in baths or cabinets, to be attributed to secretion from nerve stimulation and how far to transudation from cutaneous blood vessels? That the sweat glands can be stimulated to such an abundant secretion as is observed seems almost incredible. Yet the great salivation, sometimes produced by pilocarpin, shows that glandular activity plays an important if not the main part.

Secretions, however, must ultimately be derived from the blood, and there is doubtless a large element of truth in Hansell's¹ statement: "The efficacy of pilocarpin is, I believe, to be attributed to the inordinate activity of the lymph system induced by its presence. By depriving the peripheral vessels of a large proportion of their fluid content, those of the internal organs meet the deficiency, thus eliminating morbid products together with physiologic excretions."

If the therapeutic efficacy of diaphoresis is due solely to this vascular effect, equally good results should follow similar action on other vascular areas, which, for our purposes, are essentially peripheral. Those of the intestines and the use of salines and hydragogue cathartics illustrate. The copious watery evacuations from these agents are not, however, at least in my experience, followed by anything like the results observed after the use of diaphoretics. Nor does emptying the cutaneous vessels, with compensative filling from internal structures, explain the good results of small doses of diaphoretic agents, which do not produce copious sweats.

There must be something besides this transudation from peripheral vessels, and, I think, we may well consider in this connection the nervous influence which lies behind the diaphoresis. Pilocarpin is the drug in most common use. It acts on the skin by its stimulating effect on the cerebrospinal nerves supplying the sweat glands. Another of its physiologic effects is its inhibitory and paralyzing effect on the vasomotor system. One is surprised—at least I was—to note the similarity between the physiologic effect on the eye of pilocarpin and the results of section of the cervical sympathetic nerve or ganglion, when reading the scholarly paper presented to this Section a year ago by de Schweinitz. If one has occasion to observe cases of bad effects from

diaphoretic agents—the nausea, vesical disturbance, cardiac weakness, etc.—he will find abundant evidence, that in both its stimulating and depressing effect, a diaphoretic has marked nervous influence. By its action on the vasomotor system dilatation of the small arteries, with lessened resistance to blood flow and heightened local temperature, are produced. It seems to me, then, that in estimating the cause of the efficacy of diaphoretic agents, we should count first, as Hansell has said, depletion of cutaneous vessels; and secondly, the action of diaphoretic agents, pilocarpin particularly, on the small arteries.

From this we can draw two theoretical conclusions which clinical experience confirms: 1. Diaphoretic agents should have their greatest efficacy in structures richly supplied by blood vessels. 2. This efficacy should show itself in lessening of hyperemia and removal of exudates.

Of ocular structures the uvea, and hence the vitreous, retina and orbital tissues seem to present most prominently the anatomic and physiologic characteristics. Certain lesions with which the use of diaphoresis has been associated can, I think, be excluded. Atrophy of the optic nerve, no matter what the primary cause nor how clearly it might have come earlier, under this plan of treatment, is out of the question; so is optic neuritis, dependent, as it nearly always is, on extraocular disturbance. An exception must be made here of certain retinal lesions which may be accompanied by more or less papillitis.

It is equally irrational, I think, to apply this treatment to choroidal atrophy, cicatricial changes in the vitreous or uvea following long-standing iridochoroiditis, "chronic iritis" (in the sense of irritative symptoms persisting after an iritis has recovered with synechiæ, and to be distinguished from relapsing iritis), retinal detachment resulting from cicatricial contraction, primary glaucoma. All of these lesions are either essentially incurable or else are better treated in other ways. Whatever good seems to ensue in such patients from the use of diaphoretic agents is probably due to their influence on the choroidal circulation, and hence on the vitreous opacities; but the underlying diseases are not influenced, and in glaucoma time and possibly opportunity is lost.

In another class of cases there is little probability of good, because the tissues involved are not sufficiently vascular to respond. I allude to keratitis and affections of the sclera. In such of these cases as seem to have been helped, I incline to the opinion that a more careful diagnosis would have shown some form of uveitis underlying the superficial disturbance.

Excluding all the above, there are left many lesions which are most satisfactorily treated by diaphoresis. They are acute troubles in the uvea, retina, orbital tissue and toxic blindness. Uveal disturbance will be presented at length in the paper of my friend, Dr. Woodruff. I want, however, to mention in passing three observations made this past winter in cases of iritis. All three were of rheumatic origin, two private cases of my own, and one a hospital patient of my colleague, Dr. F. M. Chisholm. In both of mine, atropia seemed to dilate the pupil a very little, and then, in spite of pushing it to constitutional effects, using an eight-grain solution, and finally the atropia discs, I could not obtain further dilatation. One patient was in intense pain, the other suffered only moderately. The former was given a copious pilocarpin sweat. The latter was sweated, somewhat unintentionally on my part, by taking an unusually large dose of salicylate of sodium. In

1. Philadelphia Polyclinic, Nov. 20, 1897.

each instance, the day after diaphoresis both pupils dilated ad maximum. An interesting thing was then observed, viz., that there were no points on the lens surface indicating synechiæ. Apparently the pupil was kept small through intense iridic hyperemia, and dilated when this was relieved. Chisholm's case was similar in essentials, and had resisted eleven days of strong atropia. There were, however, marks of synechiæ.

A case illustrating the ease with which one can think he has obtained results which he has not is the following:

A young colored man came into my clinic two years ago with a history of defective sight for a fortnight, terminating in pain, which latter symptom led his physician to send him to a hospital. He was almost entirely blind. Pupils were immovable and a little larger than normal. Corneæ were steamy, tension increased, nearly plus 2. I advised immediate iridectomy for glaucoma, which the patient declined. He was put to bed, eserine used locally, and he was given three profuse jaborandi sweats on successive nights. Vision improved, and the case proved to be one of choroidoretinitis with iritis in its later stage, and secondary glaucomatous symptoms. Later I found spots of deposits on the posterior surface of the cornea—so-called descemetitis. Probably I should have found them at first had I looked for them, but it was primary glaucoma, as first supposed.

In leaving the subject of uveitis, I want to urge the systematic study of Descemet's membrane for these spots. As de Schweinitz, Friedenwald and others have pointed out, they are present nearly always in disease of the uveal tract, and when found in connection with such symptoms, as in the case just narrated, or those of keratitis interstitialis or scleral affections, point to the uvea as the seat of the underlying disturbance.

A number of cases of detachment of the retina, cured by diaphoresis, have been recorded. The method employed in most of them has been to confine the patient to bed and administer sweating doses of pilocarpin daily or on alternate days for six to ten times. Some clinicians have advocated the use of small doses as equally efficacious, and have not thought confinement to bed necessary, except for two or three hours when the treatment was given.

An interesting discussion of the subject can be found in the Proceedings of the British Medical Association held at Montreal in 1897. Mittendorf claimed excellent results "in cases of opacity of the vitreous and especially if associated with detachment of the retina" from the administration three times daily "for a long time" of pills containing 1/100 of a grain each of pilocarpin. Holt of Portland and Burnham of Toronto advocated the use of small doses, preferably by hypodermic injection. The most striking report came from Nettleship, who had a man with complete detachment of the retina, high degree of myopia, and no light perception in either eye. He used pilocarpin, and the result was satisfactory. He could read large type, but he could not say he could hold that.²

Many of the reported cases give little data regarding the history and condition of the eye, besides stating that the retina was detached. Alt of St. Louis, however, reported in this discussion the case of a girl with high myopia, in whom the retina had become detached, and had remained so for eleven years after the diaphoretic treatment. Like most oculists who read these reports six to ten years ago, I used the sweating treatment for retinal detachment as opportunity offered. In the class of detachments which is most numerous—in myopic eyes with choroidal atrophies and floating vitreous opac-

ities—my individual experience has been disappointing. It has sometimes occurred to me that maybe a warning given in 1892 by Spalding of Portland might be repeated. In an article in the *Archives of Ophthalmology*, advocating the use of pilocarpin in cases of hemorrhage into the vitreous, he speaks of the possibility of confounding the black appearance of the blood in the vitreous chamber with a detached retina, and insists on confirmation of the ophthalmoscopic diagnosis by field examination and demonstration of a scotoma. Be this as it may, I do not recall ever seeing in my own or the practice of colleagues a permanent cure of retinal detachment in a myopic eye with choroidal atrophy and floating vitreous opacities. Twice I have seen reattachment and improvement—very little—of the field; but they relapsed. Vitreous opacities improve, but this is not cure of the detachment. I have, however, seen three cases of reattachment in eyes which were not myopic and which did not show the chronic degenerative changes observed in the class just under consideration. Acute choroiditis was present in two of these cases, both hypermetropic, and exudate from the choroidal vessels seemed the only explanation of the detachment. Rest in bed with antisyphilitic treatment effected absorption in one. I saw the man several years afterward,

Figure 1.

and the retina was still attached, but that portion of the fundus was blind. Later the eye developed cataract. The patient was first seen in 1889, and disappeared five or six years ago. The other eye remained good. A second case presented, in hypermetropic eyes, double detachment following rapidly the onset of severe choroiditis with floating vitreous opacities. Cause was indeterminable. The case was reported in an analysis of choroidal cases at the Saratoga meeting of this Section in 1902. Pilocarpin was used, with rest in bed. The retinae reattached, but there was no improvement of vision in the affected field. The only case in which I have seen apparent improvement of vision is now under observation:

A woman, 22 years of age, came into my clinic the second of last March. She had a positive central scotoma in the left eye. The right was normal. A detachment of the retina, apparently involving the fovea and upper and inner quadrant, was made out. Her scotoma on admission is shown in Figure 1, and was practically the same eighteen days later. She was kept in bed, with pilocarpin sweats three and four times a week for four weeks. At that time her scotoma was as seen in Figure 2, and central vision 20/30. I last saw her April 19, nearly three weeks after her discharge, and the condition was unchanged.

2. Ophthalmic Record, October, 1897.

I confess to some misgivings of my own diagnosis, based on comparison of the fields at the beginning and end of treatment. While there certainly was a detachment and as certainly the retina became reattached, I am skeptical about the involvement of the fovea in the detachment. Central vision seems to have improved from nothing to nearly normal, with very little change in the periphery. It would be easy for the upper detached retina to overlap the fovea, and so shut off central vision, at the same time giving the appearance of involving the fovea. The cause of this detachment was a mystery. A few fine muscae were in a clear vitreous, but there was no other evidence of choroiditis.

I have had no experience in the use of small doses of pilocarpin in retinal detachment, but in a single case of retinitis seen a few years ago I employed such dosage with good effect. The patient was a boy of 12 who presented in one eye a beautiful example of the exudative retinitis, arranged in radiating spokes about the fovea, described by Marcus Gunn at the Edinburgh Congress in 1894. A few small extravasations and mild papillitis completed the picture. Otherwise the boy was in health. Prolonged exposure to glare from snow was the only possible cause I found. After the mercurials and iodids had failed, the administration of

Figure 2.

pilocarpin in one-thirtieth grain doses cleared the exudates in a month.

The good effects accomplished by diaphoresis in general medicine in the treatment of nephritis, effecting elimination of products which should go off through the kidneys, suggests its usefulness in toxic amblyopia. I think one has to be very careful how he draws conclusions here regarding any remedy. For instance, when we were seeing methyl alcohol and Jamaica ginger cases in Baltimore, it seemed that pilocarpin was the only thing which did good, and that its effects were but temporary. Later we found that these transient clearings and cloudings were part of the toxemia. Again, when a toxic agent is withdrawn, the natural tendency is toward cure. Recently a saloon keeper, with typical alcohol amblyopia, came under my care. I wanted him to go to bed and sweat. He said he could not leave his business, but would let whisky alone. He did so, and with no other treatment than abstinence and epsom salts improved in a week from 2/200 to 20/100. Such observations naturally tax one's faith in the efficacy of drugs reported to have brought about identical results. Still, I had another case this winter, a physician, 33 years of age, with tobacco-alcohol blindness, who did

not improve for three weeks at his home in a neighboring state under abstinence and strychnia. He had 10/200 when I saw him first, and when he returned for hospital treatment. In two weeks under pilocarpin sweats he improved to 20/40. He wrote me recently that he had stayed well. There is, I think, no doubt that diaphoresis is effective in eliminating toxic products, and its employment in toxic amblyopia is not only justifiable but imperative. The fact that some cases do well without it is no argument against its use. It only calls for more exact study of cases before we make up our minds what we have accomplished by treatment and what has gone on without our help.

While orbital lesions logically come under the class of cases apt to be helped by diaphoretic treatment, I do not know of any special reports. Orbital diseases are, I think, among our rare observations, and when they occur usually indicate some other line of treatment.

Last autumn a woman, 41 years of age, came to my clinic with a right subconjunctival ecchymosis of the lower cul-de-sac. It presented an appearance different from that usually seen, in that the blood formed a definite tumor. She had 20/30 vision. The fundus presented evidence of former disseminated choroiditis. There was no doubt of syphilitic infection. She was put on specific treatment, with heat locally, and instructed to return in two days. When she did the blood tumor was nearly double in size, and there was slight exophthalmos. She was now urged to come into the hospital, as I believed the case to be one of syphilitic disease of the orbital vessels. She did so, and the exhibition of mercurials and iodids for a week did no good. The exophthalmos remained about the same, and the blood beneath the conjunctiva was not absorbed. The external rectus became paretic. I now put her on pilocarpin sweats, given alternate days. After three such treatments improvement commenced, and in a short time all traces of trouble, including that in the rectus muscle, had disappeared.

The case illustrates what has frequently been noticed before, that in syphilis diaphoresis, when indicated by the part involved and symptoms present, is a powerful adjuvant to specific treatment.

CONCLUSIONS.

I would offer these conclusions:

1. The greatest utility of diaphoretics is in the acute congestive and exudative lesions of the uveal tract.
2. Diaphoretics are useful in retinal detachment produced by exudate from choroidal vessels during the course of acute choroidoretinitis. Judging from reported cases, they are also useful in the retinal detachment of high myopia. It is doubtful if restoration of function in the detached retina is usual or permanent.
3. Diaphoretics are useful in alcohol-tobacco amblyopia and probably in other forms of toxic blindness.
4. Diaphoretics influence to a slight extent only, if at all, lesions of the cornea and sclera.
5. Diaphoretics are useless in atrophic and cicatricial lesions.

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The Physician as a Business Man.—Dr. C. U. Collins, in the *Medical Standard*, says that the physician must lay sentiment aside and, like the man in business, keep his income equal to or above his expenditure in order to maintain his credit. The business men from whom he buys expect him to be able to pay for what he buys. If he collects a goodly amount each year, it not only enables him to keep his family comfortable, but it also enables him to buy books, instruments and other accessories that make it possible for him to render better service to his patients, and this is a very good argument to give to his patients for collecting promptly.