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PRINCIPLES UNDERLYING THE OPERATIVE TREATMENT OF STRABISMUS *

EDWARD JACKSON, M.D.
DENVER

It seems profitable to discuss here chiefly principles that are but partly recognized, forgotten or ignored, rather than those regarding which there is full recognition and agreement. We never forget that the normal contraction of a muscle brings its origin and insertion closer together. But it often seems to be forgotten that such normal contraction does not arise in the muscle itself, but is absolutely dependent on the nerve impulses coming to the muscle from the motor centers. Functionally the muscle has no existence apart from the nerve supply. Even its anatomic integrity depends on receiving the proper nerve impulses. If these are cut off permanently the muscle atrophies completely. If they are seriously interfered with degenerative changes set in. If they are diminished the muscle shrinks; if they are increased it hypertrophies. No operative readjustment of the ocular muscles can be permanent that is opposed by these nerve impulses; none can be completely successful that is not supplemented by them.

Our so-called "muscle operations," done on tendons of insertion, are attempts to modify the final mechanical results of nerve impulses. The position of an eye at any instant, or its habitual position, depends on nerve impulses. Only when we can not alter such impulses are we justified in attempting to change their mechanical effects by operation. The size, strength and habitual contraction of the different ocular muscles depend as much on the nerve impulses going to them, and as little on congenital peculiarities of the muscles themselves, as do the size, strength and habitual contraction of the muscles that give the soldier his erect carriage or the musician his perfect technic.

Normal binocular vision, as developed in man, rests on highly complex, exact reflex movements. The normal binocular movements are continuously guided by the sense of diplopia and the desire to avoid it. Between the seeing of the two eyes and the movements of the two eyes there is the most minute and comprehensive co-ordination, and the reflex to diplopia, the "fusion sense," dominates every normal ocular movement.

Strabismus is a fault of binocular movement. Somewhere in the co-ordinating mechanism, or the structure it controls, there is a break, a defect. The mechanism of co-ordination is still functionally active, although in some respects crippled and imperfect. The investigation of the particular kind of fault in the co-ordinating

mechanism must, in each individual case of squint, precede the selection or planning of any rational operation for its correction.

TWO CLASSES OF OPERATIVE CASES

The peculiarities of each particular case must be considered, but, in a general way, all cases may be placed in two groups: (A) Those in which the co-ordinated movements of the two eyes are to be guided by the visual impressions made on both, cases capable of true binocular vision, more or less completely developed; (B) cases in which the binocular movements must be guided by the visual impressions of one eye, the eye which "fixes." In the former class the problem is much more complex, the operation is to be an adjuvant, carefully planned to give assistance to the development of and utilization of nerve impulses. In the latter class the nerve impulses have been developed, and, in a sense, fixed, and the operation merely adapts the parts to secure from these impulses the best mechanical results.

In the past, operative success has been most frequently achieved in this latter class, because the nerve impulses to be dealt with, those of fixation with a single eye, were best understood. Normal binocular fixation is still an obscure subject, and of imperfect and abnormal types of binocular vision, such as exist in many cases of squint, we know very little. The nerve impulses connected with such anomalous use of the eyes are pretty certain to overcome and nullify attempts at operative correction, planned without attention to their influence. When, however, we come to understand better the abnormal, but definite and sometimes very persistent co-ordinations that exist between the perceptions and the movements of the two eyes in established strabismus, operative measures more in harmony with the real need of the case may yield good results. In Class A operation can disturb the existing co-ordination, giving opportunity for a new one to be formed under more favorable conditions, as with correcting lenses. With this in view it may well be repeated; its aim should be, not so much exact adjustment, as to establish mechanical relations that nerve impulses will tend to carry forward to complete the cure. In Class B the object of operation is rather the direct, accurate mechanical adjustment of parts, making due allowance for the temporary effects of operation, the modifications produced by cicatrization, and the degenerative and regenerative changes that occur in the muscles.

ASSOCIATED ACTIONS OF OCULAR MUSCLES

Of the infinite number of movements of which each eye is capable, not more than six at most can be brought about by the contraction of single muscles, and only two of these, convergence and divergence in the horizontal plane, are movements frequently performed. Convergence above or below the horizontal plane, like ele-

* Read in the Section on Ophthalmology of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.

vation or depression with the eyes directed forward, require the cooperation of two or more muscles.

While, theoretically, a few movements might be made by single muscles, it is not certain or probable that even these motions are thus produced. For the sake of smoothness, exactness and certainty of movement it is likely that changes of innervation occur in two or more muscles for every movement made. Conversely, each muscle takes part in the execution of many different movements, and even of movements in quite different or opposite directions. To operate on a certain muscle, to increase or diminish its effect on a single movement or group of movements, without any consideration of the effects that will be produced on other movements, is to invite disaster, or to trust to nature for a general readjustment, of muscular actions which the surgeon has never even thought of.

The direction in which the cornea is turned by contraction of a certain extraocular muscle depends on the relation of its point of insertion to the center of rotation of the eyeball. As the eye moves this direction changes, and a corresponding change occurs in the influence of the particular muscle. For instance, the superior rectus, inserted above the cornea and acting on a line passing to the nasal side of the center of rotation, when the eye is in the primary position, tends to turn the cornea upward and inward. When, however, the cornea is turned outward, so that the vertical axis lies in the same vertical plane as the line in which the superior rectus acts, this muscle turns the eye directly upward. If the eye is directed still further toward the temple, so that the line on which the superior rectus acts passes to the temporal side of the center of rotation, this same muscle tends to turn the eye up and out.

Only when the eye is in a certain position can the superior rectus act simply as an elevator. The more the eye turns inward from this position the more it becomes an adductor of the eyeball. The more it turns outward from the same position the more it becomes an abductor. The same is true of the inferior rectus, which in one position may act simply as a depressor, but in all others acts also as an adductor or abductor.

In the adduction of the eye the internal rectus takes part in all positions of the eyeball. It may be called the primary adductor. In most positions it is assisted by the superior and the inferior recti, which may be called secondary adductors. The power of the primary adductor progressively diminishes as the eye turns in and the muscle shortens. The adductive effect of the secondary adductors progressively increases as the eye turns in; that is, the power of these muscles thus becomes more and more devoted to turning the eye in.¹

In abduction the external rectus always takes part. It is the primary abductor. The obliques assist it, but least when the eye is turned in most strongly, so that the visual axis is nearly parallel to the plane of action of the superior and inferior obliques. As the eye turns outward the obliques become more and more effective as secondary abductors, until in extreme divergence they become the more important factor in abduction.

The superior rectus may be called the primary elevator. Such it is when the eye is turned outward, the inferior oblique acting rather to produce torsion. But when the cornea is turned toward the nose the inferior oblique becomes the elevator and the superior rectus has more influence in producing torsion. If, however, the

eye is turned strongly up the internus and externus come to the assistance of the primary elevator and help to turn the cornea up. Their insertions being brought above the center of rotation, they become secondary elevators.

Similarly, the inferior rectus may be called the primary depressor of the eye, its tendency being always to turn the eye down, though least effective in this way when the eye is turned strongly in, and the inferior rectus tends to produce torsion, while the superior oblique becomes a more efficient depressor. But when the eye turns down, so that the insertions of the internus and externus are below the center of rotation, these muscles become secondary depressors. The importance of their function as secondary depressors increases as the eye is turned down.

The obliques may be called the primary muscles of torsion. When the visual axis is turned to the temporal side, and level, so that it makes equal angles with the directions of the four recti muscles, torsion is entirely effected by the obliques. But in other positions the recti muscles take part in torsion; the vertical recti, as the eye turns in from this position; the lateral recti, to a less extent, as the eye is turned up or down.

SECONDARY ROTATORS IN STRABISMUS

In all cases in the execution of a particular movement the further that movement is carried the greater the share that the secondary rotators take in producing it. In strabismus the position of the deviating eye has departed from the normal. The relative importance of the primary and secondary rotators in determining its position correspondingly varies from the normal. The higher the degree of squint the greater this departure, and the greater the share of the secondary muscles in producing and maintaining the deformity.

Consider the bearing of this on particular operations. In a case of high convergent strabismus the eye is held in its abnormal position by the excessive contraction of a whole group of muscles, the internal, superior and inferior recti. Tenotomy of the internal muscle alone is but a partial tenotomy, as regards the muscles concerned. The indication is clear for extending the tenotomy to the superior and inferior tendons, and on them graduating it to the needs of the case. Without such extension tenotomy is absolutely ineffective in high convergent squint.

A superiority of advancement lies in the fact that it changes the position of the eyeball, and so lessens the power of the secondary rotators, whose influence is so large a factor in the maintenance of the squint, and renders more efficient the action of the secondary rotators that oppose the deviation. For example, in convergent strabismus advancement of the internus, actually turning the eye out, diminishes the power of the superior and inferior recti to turn it in, and increases the efficiency of the superior and inferior obliques in turning it out.

There is another difference between the actions of primary and secondary rotators, of great importance with reference to strabismus operations. The primary rotators tend to equilibrium with the eyeball in a median position. The secondary rotators tend indefinitely to increase the deviation. Thus, in convergent strabismus, the greater the squint the less the influence of the internus, and the greater the influence of the externus, tending to turn the eye to a normal position. But the greater the squint the greater the influence of the sec-

1. Trans. Section on Ophthalmology, A. M. A., 1906, p. 237.

ondary adductors in perpetuating it and increasing it, while the influence of the obliques as secondary abductors is correspondingly lessened. Tenotomy, confined to the primary adductor, the internus, lessens the relative power of that muscle, leaves convergence more a function of the secondary adductors, and, therefore, more likely to be extreme. Or, if excessive convergence is overcome, it leaves the eye with a weakened primary adductor to oppose the abductors, and, therefore, especially liable to turn out.

The primary rotators have a peculiar importance in opposing extreme movements in the opposite direction. The secondary muscles have very little value in this direction. Crippling of the primary rotators leaves the eye in a condition of unstable equilibrium, more liable to deviate under slight influences. Nor is this crippling confined to the muscle operated on. Tenotomy of the internus is followed by retraction of that muscle, but it is also followed by retraction of the externus. It is the retraction of the externus and consequent turning of the cornea outward that produces the desired correction of the convergence, for which the tenotomy of the internus is done.² This shortening of the externus diminishes somewhat its power of rotating the eyeball outward. Hence, by the one operation of tenotomy done on the internus, both internus and externus have their power lessened, and the rotation of the eyeball is left more under the control of the secondary adductors, the superior and the inferior recti, and the secondary abductors, the superior and inferior obliques. The eyeball is left in the condition of unstable equilibrium, where the mutually opposing forces that tend to bring it toward a central position are weakened, and those which tend to carry it away from this position and hold it away from the central position are left relatively stronger.

LATERAL DISPLACEMENT OF TENDONS

Another principle that must come to be more generally recognized in the operative treatment of strabismus is that the effect of a muscle on the eyeball can be altered by displacing its insertion laterally. I have previously pointed out that the recti muscles, all having practically the same origin at the apex of the orbit, come to exert different influences on the eyeball through the different positions of their insertions.³

If it were possible to shift the insertion of one rectus to the site of the insertion of one of the others its function would be correspondingly altered. Thus, if we could attach the superior rectus to the eyeball at the nasal side, where the internus is inserted, it would have very much the effect on the ocular movements normally produced by the internus. Such complete shifting of insertion is, of course, impossible, and any shifting brings a bending of the muscle that tends rather to produce torsion. But it is practicable to shift the tendons laterally so as to cause an important change in the effects produced by the muscles acting through them.

One method of producing lateral displacement is by the extended tenotomy, which I described in 1905. This method was probably practiced and its good effects reported, without much theorizing on the subject, by some of the earlier operators for squint. Another method of securing lateral displacement I described as practiced on the superior rectus for paralysis of the superior oblique.³

A third method was brought to the attention of the last Heidelberg Ophthalmological Congress by Hummelsheim. He experimented first on the ape. He removed as much as possible of its internal rectus to destroy the function of that muscle. He then split the tendon of the inferior and superior recti, and transplanted the nasal half of each tendon to where the internus had been inserted. The animal was still able to execute movements of convergence and lateral movements toward the side of the excised muscle. Hummelsheim then performed a similar operation on a case of congenital abducens paralysis, in which the eye was unable to turn beyond the median line. He split the tendons of the superior and inferior recti and transplanted the temporal portions to the point of insertion of the externus. The result, reported five weeks after the operation, was an ability to abduct this eye thirty degrees beyond the median line.

At the French Ophthalmological Congress, in 1907, Dransart presented a case of injury to the superior oblique, in which by grafting its tendon on the upper part of the external rectus he obtained a good result. As to the best method of securing lateral displacement, to enable one muscle to take up the function of another, considerable experience will be required to decide. The point here emphasized is the importance of this principle in the operative treatment of strabismus and the need for its more general recognition.

The question of re-education of nerve centers, so that they can execute desired movements with unaccustomed means, is a large one. Only experience can settle the limits of possible achievement in this direction. But we know that after Motais' operation the patient can learn to close the eyes firmly, without the lifting of the upper lid, that at first occurs from contraction of the superior rectus, and tendon transplantations in other parts of the body seem to show that the possibilities of alteration in the function of muscles are quite extensive. But in the case of the superior and inferior recti we have muscles that normally aid in convergence, and probably to a slight extent in divergence, when convergence and divergence are extreme. There is every reason to expect that they can largely take up these functions in cases of disability of the lateral muscle.

EQUILIBRIUM OF LIMITED MOVEMENT

When extreme and permanent strabismus is brought about by complete loss of power in a certain group of muscles, leaving their physiologic opponents in unresisted control of the position of the eyeball, it should be possible to greatly lessen deformity, either by destroying the influence of the dominant muscles or, better, by neutralizing it through transference. Strabismus of this kind most commonly follows oculo-motor paralysis, because such paralysis acts on a whole group of muscles. Paralysis of the sixth nerve leaves the obliques still able to oppose convergence. Paralysis of the fourth nerve leaves the inferior rectus and the superior rectus and the externus to take up the different functions of the superior oblique. But oculo-motor paralysis destroys all the adductors, and leaves, unopposed, the externus and the superior oblique to turn the eye away from its normal region of fixation.

Some very good results from the operative crippling of unopposed muscles have been reported, notably by Prince.⁴ But I would suggest that it may be possible

2. Trans. Section on Ophthalmology, A. M. A., 1905, p. 73.
3. Ophthal. Rev., March, 1903.

4. THE JOURNAL A. M. A., Oct. 13, 1888, also Am. Jour. Ophthalmol., September, 1902.

to so operate on the superior oblique as to make it something of a substitute for the internal rectus by a readjustment through which most of the belly of this muscle is attached to the tendon of insertion of the internus. Such an operation I have done on the cadaver. Vertical deviation can be prevented by fibrous attachments, and by adding any necessary readjustment of the external rectus it may be possible to bring about equilibrium and limited movement near the center of the field of fixation.

In cases of this kind we may be confronted with the difficulties connected with binocular vision. Where binocular vision is absent readjustment for cosmetic effect may not be very difficult. But with the liability to annoyance from binocular diplopia the difficulties of the case are enormously increased. Even here, however, re-education, with aid by blurring of the sight with lenses, may render relief possible.

SUMMARY

Let us bring together the principles underlying the operative treatment of strabismus that have been here discussed and those that have more commonly received discussion. The ocular movements are executed and controlled by nerve impulses, originated and guided by visual impressions. When these nerve impulses are faulty and can not otherwise be sufficiently modified to produce normal movements, readjustment by operative treatment may be resorted to. This readjustment may be accomplished: (1) By giving greater effect to certain impulses, advancing the insertion of a muscle; (2) by diminishing the effect of certain impulses through tenotomy, setting back the insertion of a muscle; (3) by transferring the impulses so that they will produce results different from those to which they were originally directed, lateral displacement of insertions; (4) by combining two or all of these changes.

Tenotomy allows retraction of the tenotomized muscle and also retraction of its opponent which is no longer resisted. The increase of power secured by muscular advancement may be temporary or illusory. Only modified nerve impulses are required to increase or diminish the power of any muscle. All muscle operations, temporarily suspending function, are followed by degenerative changes in the muscle substance.

Operation on a muscle should be undertaken only after careful consideration of all the movements in which it takes part, either as a primary or secondary rotator of the eyeball. The more important object in the treatment of strabismus is to bring about a muscular equilibrium. Static equilibrium so that muscular rest will leave the two eyes fixing the same point in a central position, and dynamic equilibrium, balanced movements, easy binocular fixation of greatest usefulness around this central point. A less important object is to secure movements, from this central point, of greatest range and with the least expenditure of effort. Where these objects are not attainable by increasing the power of a certain muscle or muscles they are to be sought by diminishing the power of opposing muscles or by transference of muscular power from one movement to another.

ABSTRACT OF DISCUSSION

DR. G. C. SAVAGE, Nashville, Tenn.: The law governing the ocular muscles is this:

The ocular muscles must so relate the two eyes that the two visual axes and the two horizontal retinal meridians shall always lie in the plane of the primary isogonal circle, and

that the two visual axes shall intersect at some point on this circle, in the interest of both binocular single vision and correct orientation. There are just two classes of esotropia (internal strabismus), the curable, including all patients who have ever had binocular single vision, and to whom binocular single vision may be restored, and the incurable, including the many patients who have never had binocular single vision and can never be made to see singly with the two eyes. In the curable patients the crossing has occurred one or more years after birth and the crossed eye becomes amblyopic. Such patients may be cured spontaneously (though rarely) or by art, in the sense that the muscles become obedient to the law of binocular rest and motion. Later by training, the amblyopia may disappear. Operations should always be performed on sinning muscles only. There are two causes of curable esotropia, the one principal (true esophoria, without which there can be no turning in of the eye) and the other accessory (hyperopia), which because of the intimate relationship between the centers of accommodation and convergence, creates a pseudo-esophoria which, added to the true esophoria, increases the work of the externi and the basal centers controlling them, in their effort to prevent crossing. No patient should be operated on without a clear understanding on the part of the operator as to whether the esotropia is simple or complicated. If the condition is simple esotropia, the sinning muscles are the lateral recti, and only those muscles should be subjected to operations. These operations should be done with the view of giving equal tonicity to the four recti, and in the more aggravated cases all four should be operated on. In a case of hyperesotropia, the four lateral recti should be operated on; their tension should be altered but their planes of rotation should not be changed. In the most complicated esotropia—cyclo-hyperesotropia—not only must the tonicity of the muscles be altered but the plane of rotation of one muscle or, maybe, two or three, must be changed.

Whether, in these cases, the esotropia be slight or severe or medium, there is no indication for operating on the superior and inferior recti, as advocated by Dr. Jackson in his paper. Muscles whose tonicity keeps the visual axes in the plane of the primary isogonal circle should not have their tonicity interfered with by any kind of operation; and if their tonicity is not altered it necessarily follows that their planes of action can not be changed. These operations may be safe in Dr. Jackson's hands, but why adopt them when esotropia can be treated on sounder principles? General adoption of this operation, even in the more severe cases, would be attended by frequent disaster. I am sorry that my good friend advocates the punishment of muscles that have not disobeyed the law governing them, which is: The superior and inferior recti must keep the visual axes in the plane of the primary isogonal circle regardless of the point of view.

DR. A. L. DERDIGER, Chicago: I find that sometimes patients present themselves for refractive troubles, headaches or some nervous symptoms. We make an examination both for muscular insufficiency and refractive error and find as much as 3, 4, 5 degrees hyperphoria and 6 to 12 degrees esophoria or exophoria. If we are in a hurry to suggest operation in these cases without going thoroughly into the refractive error we are very liable to fall down. In the last two years I take patients that come in for headache and nervous symptoms, go over the refraction carefully a half a dozen times, and have the patient wear full correction in every instance in which there is hyperopia and astigmatism. If the patient is neurasthenic, I regulate the diet and advise as much out-door exercise as possible. The muscular trouble often disappears after proper correction of the error of refraction and careful regulation of the diet and exercise. I had a patient, a man, aged 39, crossed in both eyes since childhood (convergent squint); right eye turned in more than left eye; vision in right eye, 5/200; vision in left eye, 20/60. Advancement operation was performed on the muscles of the right eye and the opposing muscles were tenotomized. The wounds healed kindly, both eyes being refracted two weeks after the operation with the following results: O. D. V. = 20/200 with + 6.00 V. = 20/60; O. S. = 20/40 with + 4.00 V. = 20/20. Full correction was prescribed to be worn constantly. The eyes being perfectly

straight, the patient can see distant objects and read fine print distinctly. The patient has been under observation for one and a half years and the eyes remain straight, vision being 10 per cent. better than at first. Another case was that of a girl aged 2½ years: V.=5/200; internal squint in both eyes, very high degree. Atropin was used for two weeks and the following correction gave perfect results: Right eye, +4.50 V.=20/20; left eye, +7.50 V.=20/20. Both eyes being perfectly straight with glasses on, I ordered full correction to be worn constantly. This case has been under observation for nearly two years and the eyes are straight with the glasses; they converge slightly without the glasses on.

DR. EDWARD JACKSON, Denver: John Fiske, in his "Myths and Myth-Makers," has written beautifully about the tendency of primitive peoples to find a spirit or indwelling force in all sorts of annoying things. When a man has been killed by a knife, in certain savage tribes, the tribesmen hold an inquest and sentence that knife. Now I think we have something of a survival of that in such phraseology as "innocent, or sinning muscle." Ideas which do not depend on any logical reasoning but are largely a suggestion of the phraseology we use are the chief obstacle to a clear general understanding of this matter of ocular movements and their correction.

TINCTURE OF STROPHANTHUS AND STROPHANTHIN *

ROBERT A. HATCHER, M.D.

Professor of Pharmacology, Cornell University Medical College;
Member of the Council on Pharmacy and Chemistry of
the American Medical Association

AND

HAROLD C. BAILEY, M.D.

Instructor in Pharmacology, Cornell University Medical College
NEW YORK

The pharmacology of strophanthus indicates that it has certain advantages over digitalis, and careful clinical observation has sustained the view of pharmacologists that it has a distinct field of usefulness. It is a fact, however, that the average practitioner either refuses to employ strophanthus at all, or, after a brief trial, dismisses it and returns to digitalis.

We believe that the reasons for this state of affairs can be explained satisfactorily, and that the chief causes militating against the proper use of strophanthus can be removed.

One of the principal causes of the disrepute into which strophanthus fell was the utter unreliability of the tincture because of extreme variability in the strength of the seed, according to the testimony of several German investigators. It has been shown¹ that the tincture of strophanthus made by the large manufacturing houses of the United States is surprisingly uniform in potency—much more nearly uniform than is the tincture of digitalis—but American physicians are so impressed with the weight of German opinion that it is difficult to eradicate a false impression of this nature, and particularly since our friends in Germany are still reiterating the statement that tincture of strophanthus is extraordinarily variable and unreliable, though the standardized tincture is now sold there. Inasmuch as this supposed variability does not exist here, we may dismiss that phase of the difficulty.

Another serious disadvantage common to strophanthus and digitalis has been the want of a pure soluble active principle suitable for hypodermic use. This want, at

least to the extent of the pure and active principle, has been supplied in the crystallized strophanthin of Thoms.

In this connection it may be said that there is the utmost confusion in the minds of many physicians concerning the different strophanthins, and this is not surprising when even the National Standard Dispensatory gives Thoms' formula under the official strophanthin, quoting Thoms as authority. It is probable that the crystallized strophanthin is the only absolutely pure strophanthin obtainable in commerce, but the American house of the manufacturers was unable to supply this direct, but had to import it to our order. They were unable to tell us, before writing to Germany, whether the strophanthin ordinarily supplied is made by the process of Thoms. Though the official strophanthin is not an absolutely pure product, we wish to state distinctly that we do not pretend to say that it may not answer every purpose for which the crystallized strophanthin is used.

A third, and perhaps the most serious, cause of the disfavor into which strophanthus has fallen is the utter confusion concerning the dose. This naturally follows the conflicting statements regarding the toxicity of the different preparations, since the dose is sharply limited by the toxicity.

Potent remedies are almost universally recommended in minimum doses, and in strophanthin we have at once an exceedingly toxic or a comparatively mild remedy dependent on the mode of administration. Less than a milligram of crystallized strophanthin injected into a vein or subcutaneously may give rise to serious symptoms, while 150 milligrams have been given to a man by the mouth in the course of two days.

Table 1 illustrates the confusion existing regarding dosage. The figures in italics are quoted from the several authorities, the others are equivalents calculated from our comparisons of toxicity; while these equivalents are not exact, we have every reason to believe that the limits of error are very narrow. In general, 200 parts of tincture equal in toxicity one part of crystallized strophanthin, or about two parts of Merck's or Boehringer's.

Table 2 affords a comparison of the toxicity according to different investigators, and it will serve to explain the confusion regarding dosage. Digitoxin has been introduced into the table merely for the sake of comparison. It will be observed that ouabain and crystallized strophanthin, which are identical, have been found by several observers to possess the same ratio of toxicity when compared with other substances.

None of the authorities quoted has compared the toxicity of the official and the crystallized strophanthins with digitoxin on the same animal by the same mode of administration. Gley² found crystallized strophanthin, or ouabain (which is identical with the crystallized strophanthin) to be twice as toxic as the common strophanthin (and this agrees very well with our own results on mammals and those of Faust³), and eighty times as toxic as digitoxin, as determined by Koppe.

We found the toxicity of crystallized strophanthin for the guinea-pig to be about three times as great as that of digitoxin as determined by Reed and Vanderkleed.⁴ Fraenkel⁵ found digitoxin to be more than twice as toxic as crystallized strophanthin for the cat by sub-

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.

1. THE JOURNAL A. M. A., 1907, xlviii, 1177.

2. Compt. rend. Acad. sc., Paris, cvii, 348.

3. Arch. Exper. Path. and Pharmacol., xlviii, 272.

4. Am. Jour. Pharm., lxxx, 110.

5. Arch. Exper. Path. and Pharmacol., ii, 84.