SPECIAL REPORT

BUTYN, A NEW SYNTHETIC LOCAL ANESTHETIC: REPORT CONCERNING CLINICAL USE.

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Special reports of the committee on local anesthesia of the section on ophthalmology of the American Medical Association.

Council on Pharmacy and Chemistry of the American Medical Association—

Gentlemen:

At your request the committee secured some samples of butyn, a new local anesthetic, which the manufacturers, the Abbott Laboratories, provided, and submitted it to animal experimentation and clinical trial. These experiments were begun several months ago by the individual members of the committee, and up to the present time seem to have been sufficiently extensive and conclusive to justify the report herewith submitted.

Tho the committee was supplied with samples of powdered butyn, it was thought best to follow the suggestions of the manufacturers and experiment with a 2 per cent. solution, and later, under appropriate precautions, use solutions of great concentration. Accordingly, this report, except where otherwise noted, applies to results as obtained with the 2 per cent. solution.

In accordance with your suggestion, we recorded our observations as follows: anesthesia, including onset, depth, penetration and duration; side actions, including immediate and late irritation, changes in pupil diameter, vascularity, intraocular pressure, desiccation of cornea and other side actions; toxic systemic effects, and comparative value in ophthalmic work, including major as well as minor operations. Under these various headings our observations are as follows:

ANESTHESIA

Repeated trials indicate a striking rapidity of anesthetic action, as indicated by the fact that one minute after one instillation of a 2 per cent, solution of butyn in the eye, surface anesthesia is sufficient to permit of touching the cornea or removing superficially placed foreign bodies without discomfort. This surface anesthesia lasts from fifteen to twenty minutes, when, in the average case, it begins to subside. Occasionally the anesthesia has been noted for from twenty-five to thirty minutes. The depth of anesthesia produced by one instillation is not sufficient for operations, or for even the removal of deeply embedded foreign bodies in the cornea. It is, however, sufficient for the painless extraction of superficially placed foreign bodies, the application of irritating astringents, and the determination of intraocular pressure with the tonometer. When the number of instillations is increased, there is a marked increase in the depth, degree and duration of the anesthesia.

For operative work the committee has followed the plan generally used when cocaine is the anesthetic employed, which consists in four instillations, three minutes apart, the operative work to be begun from five to ten minutes after the last instillation. This method resulted in the production of an anesthesia deep enough and complete enough for all of the commoner major operations on the eye, with the exception of enucleation, which up to the present time has not been performed under butyn anesthesia by any member of the committee. The height of anesthesia appears to be secured at about five to eight minutes after the fourth instillation of the anesthetic, and its duration is from twenty to thirty minutes in the average case, tho
frequently lasting much longer, and in a few instances even the surgical anesthesia has lasted for nearly an hour.

SIDE ACTIONS

One instillation of a 2 per cent. solution of butyn almost invariably produces a mild hyperemia of the conjunctiva. This hyperemia is not noticeably increased by subsequent instillations of the anesthetic. It is controlled readily by epinephrin solution, or may be averted by combining epinephrin with the butyn. When epinephrin is not employed, the hyperemia gradually disappears in from thirty to sixty minutes. The hyperemia seems to be more marked and of longer duration in diseased eyes, even tho the active stage of disease has passed.

Butyn solutions do not affect the pupil diameter in any way, and produce no change in the intraocular pressure. There also is no desiccation or disturbance in the nutrition of the cornea, so far as has been determined. We also are of the opinion that butyn solutions do not deteriorate rapidly, even when exposed to air and light, nor is their anesthetic efficiency impaired by boiling.

TOXIC SYSTEMIC EFFECTS

In beginning the use of butyn, we were confronted with the statement of the Research Committee of your Council to the effect that butyn is two and one-half times more toxic than cocain when injected hypodermically into albino rats, and that the lethal dose of butyn when injected intravenously into cats is about equal to that of cocain. One member of our committee, Dr. H. M. Langdon, in conjunction with Dr. Herbert Fox, director of Pepper Clinical Laboratory of the University of Pennsylvania, has conducted some animal experiments with a view to determining the toxicity of butyn, and the result of those experiments confirmed those of the Research Committee of your Council. The manufacturers state that their animal experiments substantiate these findings.

However, in no instance, including the hundreds of times that butyn has been used by the members of the committee for minor as well as major operations on the eye, as well as in operative work in the nose and throat, have the slightest systemic toxic manifestations been noted. Following the report that surgeons and dentists had freely used butyn for surface and infiltrative anesthesia with no toxic results, some of the members of the committee have used butyn in paste and in concentrated solutions as a topical application for operative work in the nose as well as in the eye, with no evidence of toxic effects. The committee, in comparing the effects on animals and men, is inclined to believe, as suggested by Professor Sollmann of your Research Committee, that there may be (1) differences in absorbability from mucous membranes; (2) different ratio of toxicity in man and animals, and (3) different frequency of idiosyncrasies. It is probable that if butyn is used as extensively as cocain, there will be cases of toxic effects reported, and then it is a question to decide whether the symptoms are due partly to psychic causes, to idiosyncrasy, or to error in using more of the drug than required to produce the desired effect.

COMPARATIVE VALUE IN OPHTHALMIC WORK

In the use of butyn as a local anesthetic, cocain is used as a comparison, and our committee is unanimous in the opinion that butyn for purely surface anesthesia for minor operations is superior to cocain, for the reason that it acts more quickly, fewer applications are required, there are no objectionable side actions, such as dilatation of the pupil or desiccation of the cornea, and the anesthesia is more profound. For producing surface anesthesia for the removal of foreign bodies from the eye, the application of irritating astringents, estimating the intraocular pressure with the tonometer, or for any of the minor opera-
tive procedures, butyn solutions seem to be very useful.

For major operations, particularly those requiring opening of the eyeball, such as iridectomy and cataract extraction, the technic usually employed in obtaining a cocaine anesthesia is employed in obtaining butyn anesthesia. The use of a 2 per cent. solution of butyn results in a more profound anesthesia than is obtained with a 4 per cent. solution of cocaine, and without any objectionable side actions. For operations on the extrinsic muscles of the eyeball, the results are equal to those obtained with cocaine, tho the committee believes that a solution stronger than 2 per cent, may be preferable.

INFILTRATION ANESTHESIA

In view of our understanding that butyn might prove quite toxic, we did not at first use butyn for the production of infiltration anesthesia, and only recently have we undertaken some experimental work, using both 0.5 and 1 per cent. solutions for the purpose. While our experience is limited, up to the present time we have had very satisfactory results. A 0.5 per cent. solution of butyn has been injected rather freely into the tissues for the purpose of doing advancements of the extrinsic muscles of the eyeball, for the opening of abscesses in the orbit and the appendages, and as an adjunct in operations in which the eyeball is opened. In the few cases in which this has been tried, a deep and satisfactory anesthesia has been secured. A more comprehensive report covering infiltration anesthesia with butyn will be made later, and will form a part of the committee report to be presented before the Section on Ophthalmology of the American Medical Association.

BUTYN IN NOSE AND THROAT WORK

The chairman of the committee has used butyn solutions as a routine for several months in nose and throat work, and the results, in brief, are considered worthy of being a part of this report, as they bear directly on the question under consideration.

The recognition of the fact that the nasal mucous membrane possesses greater area and increased absorbing surface, as compared to the conjunctiva, made it advisable to begin with weak solutions and use smaller amounts until the toxicity in the average human being could be determined. Therefore, at first one application of butyn in 1 per cent. solution was made over small areas within the nose, and tests for anesthesia were made subsequently at intervals of from one to three minutes. These tests indicated a mild surface anesthesia produced within one minute. Later these tests were extended to include surface anesthesia sufficient for everything pertaining to an examination, including the use of applicators and eustachian catheters, as also for the allaying of discomfort occasioned by the use of astringents or escharotics. Finally, butyn in 5 per cent. solution was employed as a routine in producing anesthesia for all of the major intranasal operations.

As butyn produces no ischemic effects, there is no shrinking of tissues following its use; hence the condition of the intranasal tissues remains approximately the same except for the anesthesia. This is a valuable feature in those cases in which a portion or all of a turbinate is to be removed. When combined with epinephrin, butyn in 5 per cent. solution produces an anesthesia sufficient for all of the major intranasal operations, including submucous resection of the septum, turbinotomies and intranasal operations on the accessory sinuses. Not only is the anesthesia very satisfactory, but up to the present time not the slightest toxic effects have been noted in the hundreds of operative cases in which the anesthetic has been used. Among these cases are thirty-eight consecutive submucous resections of the septum, and twenty-six consecutive intranasal operations on the nasal accessory sinuses.

The technic employed in obtaining anesthesia has been similar to that employed in obtaining anesthesia from
cocain, except that the butyn has not been used in greater concentration than 5 per cent. solutions. The anesthesia lasts from thirty to forty minutes.

EXCEPTIONS

In comparing butyn anesthesia with cocain anesthesia, the committee has discovered that occasionally a patient seems to be immune to complete local anesthesia from butyn employed in either 2 or 5 per cent. solutions. These cases are relatively few. The failure to secure complete local anesthesia in this very limited number of cases may be due to psychic disturbances or a highly neurotic temperament, or perhaps to a peculiar idiosyncrasy which makes the patient, in a measure, intolerant to the anesthetic effect of the drug.

SUMMARY OF CLINICAL RESULTS

The committee now has a detailed record of clinical experiences with butyn in the performance of several hundred major operations on the eye and the nose and throat. These include cataract extraction, iridectomy (including that done for the relief of glaucoma), trephine operation, magnet extraction of foreign bodies, tenotomy and advancement of the ocular muscles, pterygium operations, removal of cysts and other tumors from the eyeball or lids, grattage, and a few cases of plastic surgery of the lids, including the correction of entropion and ectropion. As yet no enucleations have been performed under butyn anesthesia, but we believe that such an operation may be performed very satisfactorily.

Local anesthesia is put to the best test when used for operations which involve cutting the iris or extrinsic muscles of the eyeball. The committee, December 1, had a record of thirty-nine cataract extractions combined with iridectomy, twenty-three iridectomies for glaucoma or as preliminary to cataract extraction, twenty-one capsulotomies and iridotomies, and eight muscle advancements, all satisfactorily done under butyn anesthesia. Aside from this there were a large number of other eye operations requiring less profound anesthesia, which were performed satisfactorily under butyn.

In nose and throat surgery, butyn anesthesia has been used in practically all of the major intranasal operations, including submucous resection of the septum, turbinotomies, opening of accessory sinuses (including extention of the ethmoid cells), tonsillectomy and adenectomy, in all numbering nearly 200 cases.

In practically all of these cases, including nose and throat as well as the eye, the anesthesia has been very satisfactory, and the few exceptions are considered exceptions such as might occur under any local anesthetic. Two per cent. solutions of butyn were used for nearly all of the eye operations, whereas 5 per cent. solutions were used in most of the nose and throat operations. If more extended experience confirms our present belief that there is little cause for apprehension concerning toxic effects from the judicious use of butyn, then a 5 per cent. solution may be the strength of concentration preferred in some of the major operations in which profound local anesthesia is desirable and has heretofore been sometimes difficult to secure.

A detailed report of each and every one of our cases would extend this report to an unnecessary length, but will be submitted if deemed either advisable or necessary.

CONCLUSIONS

The results of the clinical and experimental use of butyn seem to justify the committee in arriving at the following conclusions:

1. It is more powerful than cocain, a similar quantity being required.
2. It acts more rapidly than cocain.
3. Its action is more prolonged than that of cocain.
4. According to our experience to
Butyn, a new local anesthetic

1. It is a colorless, odorless, and tasteless liquid that is readily soluble in water.
2. It is highly toxic and should be handled with care.
3. It is effective in small quantities.
4. It is not affected by the presence of blood, and therefore, can be used in the presence of hemorrhage.

5. It produces no drying effect on tissues.
6. It produces no change in the size of the pupil.
7. It has no ischemic effect and therefore causes no shrinking of tissues.
8. It can be boiled without impairing its anesthetic efficiency.

Respectfully submitted.

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Chairman.

William Zentmayer, Philadelphia.

Edgar S. Thomson, New York City.

H. Maxwell Langdon, Philadelphia.

Harry S. Gradle, Chicago.

Announcement

Pathologic Exhibit for the International Congress of Ophthalmology.

The Army Medical Museum, in connection with the Section on Pathology of the American Academy of Ophthalmology and Oto-Laryngology is preparing an exhibit of pathologic material for the coming International Congress of Ophthalmology. Owing to the short time that the Section on Pathology has been in existence, the material it already has on hand is of necessity somewhat limited. In order to have a creditable exhibit, all American Ophthalmologists are earnestly urged to send any interesting pathologic specimens they have to the Museum; either as an outright gift, or as a temporary loan during the Congress. Such specimens should be plainly labeled, described fully, and sent to Major G. R. Callender, Army Medical Museum, Washington D. C., Section on Ophthalmic Pathology.