LOCAL ANESTHESIA *

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In 1907 at the meeting of the American Medical Association at Atlantic City, I presented a paper on local anesthesia and in the following year a report through the anesthesia commission on the extent to which it was used in this country. Since that time there have been important developments; the field has been broadened and the popularity of the method has increased both at home and abroad. It has seemed that a general review of this development might be of interest.

Probably the one greatest factor has been the introduction of novocain as a substitute for cocain. First clinically tested by Heinrich Braun in 1905 and extolled by him in several papers,¹ it has been generally adopted and is now recognized as the best and safest substance for the production of local anesthesia. It has the great advantage of being about seven times less toxic than cocain, and its solutions stand boiling. It is conveniently supplied in tablet form in combination with synthetic suprarenin. In preparing solutions these tablets are dissolved in 0.6 per cent. salt solution to which is added a little hydrochloric acid. For infiltration purposes 0.25 to 0.5 per cent. solutions are used and as much as 125 c.c. of the latter strength may be injected with perfect safety. Braun states that he has repeatedly used as much as 250 c.c. (1.25 gms.) of this strength and has never seen trouble therefrom, but cautions that we should in spite of this ever bear in mind that novocain is a poison. We can therefore infiltrate very extensively with no fear of toxic effect, a fact which accounts in large part for the extension of local methods into new fields.

Anesthesia is probably obtained somewhat more quickly with cocain and where small amounts only are necessary I still use it; but, for all larger infiltrations, novocain is the choice.

Urea and quinin hydrochlorid, suggested by Thibault and popularized by Hertzler² and others, is another anesthetizing agent which has proved of value. It has in its favor practically negative toxicity, its control of postoperative bleeding and the fact that anesthesia obtained by it may last for several hours or days, thus eliminating postoperative pain. It is thus well fitted for rectal work and is said to be especially useful in the removal of tonsils. The ordinary strength of the infiltration solution is from 0.5 to 1 per cent. Anesthesia is obtained slowly and one should wait at least fifteen or twenty minutes after the injection before beginning an operation.

In 1908 Bier³ presented an entirely new method of obtaining anesthesia of the limbs through the medium of intravenous injection of novocain. The limb is rendered perfectly ischemic by the application of a rubber bandage from the periphery to a little above the point at which a vein is to be exposed. At the central edge of this expulsion bandage an Esmarch tourniquet is tightly placed over a broad surface. The expulsion bandage is removed and a handbreadth or so below the first tourni-

quet a second is applied. Between these two a vein is exposed, usually the internal saphenous in the leg and the cephalic, median or basilic in the arm. The vein is ligated centrally and a cannula introduced distally and tied in place. Novocain (0.5 per cent.) is then forced into the vein under considerable pressure—from 60 to 100 c.c. in the leg, 40 to 70 c.c. in the arm—the cannula is removed and the vein tied. In one or two minutes there is complete anesthesia in the area between the tourniquets—direct anesthesia—and in ten or fifteen minutes in the parts distal to the second tourniquet—indirect anesthesia. There is also complete motor paralysis; so that there is obtained as thorough relaxation as under general narcosis, rendering this method applicable for any operative procedure. The anesthesia persists as long as the central tourniquet is left in place and disappears quickly after its removal. Bier's longest operation lasted one and three-quarter hours. Hayward⁴ in November, 1912, reports from Bier's clinic 375 operations under vein anesthesia; including amputations, joint resections, fixation of fractures, tendon transplantations, removal of varicose veins, etc. There was complete anesthesia in 93 per cent. and in only 3 per cent. was narcosis necessary. There were no accidents or bad results. Kaerger⁵ from the same clinic reports 150 further cases and gives the details of the method as applied to minor operations on the hand and foot, a most useful procedure in office or dispensary work.

Undoubtedly venous anesthesia furnishes us a useful addition to our means of carrying out operations in non-septic conditions of the extremities, but the discomfort of the tourniquet is often a factor which must be considered.

Goyanes⁶ in 1909 suggested a similar procedure except that he injected the anesthetic by means of a fine needle directly into an exposed artery. Ransohoff⁷ in 1909-10 used a similar method, but did not exsanguinate before injecting. The intra-arterial method seems to show no advantages over the venous and has the disadvantage that arteries are more difficult of access than superficial veins.

A knowledge of sensory nerve-distribution renders easy the anesthetization of distal portions of an arm or leg by perineural or endoneural injection. Crile⁸ in 1902 injected the several cords of the brachial plexus after exposing them. Hirschel⁹ first obtained anesthesia of the whole arm by injecting the plexus in the axilla without incising the skin and Kulenkampff,¹⁰ stimulated by his paper, has worked out a method by which he reaches the plexus above the clavicle. He gives anatomic details and reports twenty-five cases, in fifteen of which total anesthesia was obtained and in only three of which a little ether was needed.

For the leg Læwen¹¹ in 1911 presented the technic of reaching through skin punctures the various nerves so as to anesthetize the whole limb and in 1912 Keppler¹² published an extensive article with further details and

12. Keppler: Arch. f. Chir., 1912, c. 501.

4. Hayward: Arch. f. klin. Chir., 1912, xcix, 993.

5. Kaerger: Arch. f. klin. Chir., 1912, xcix, 983.

6. Goyanes: Rev. clin. de Madrid, 1909, i, 12; Zentralbl. f. Chir., 1909, xxxvi, 791; Zentralbl. f. Chir., 1911, xxxviii, 1900.

7. Ransohoff, J. L.: New Method for Inducing Local Anesthesia, Lancet-Clinic, Aug. 7, 1909; abstr., THE JOURNAL A. M. A., 1909, p. 741; Ann. Surg., 1910, li, 453.

8. Crile, G. W.: An Experimental and Clinical Research into Cocain and Eucain, THE JOURNAL A. M. A., Feb. 22, 1902, p. 401; The Results of Operations, Especially Abdominal, Performed on the Principle of Anoci-Association, ibid., July 13, 1912, p. 114.

9. Hirschel: München. med. Wehnschr., 1912, lix, 1218.

10. Kulenkampff: Zentralbl. f. Chir., 1911, xxxviii, 1337.

11. Læwen: Deutsch. Ztschr. f. Chir., 1911, lli, 252; München. med. Wehnschr., 1911, lyiii, 1300.

* Read in the Section on Surgery of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

1. Braun: Deutsch. med. Wehnschr., 1905, xxxi, 1067; Deutsch. Ztschr. f. Chir., 1911, lli, 321; Lokalanesthetie, Edition 3, 1913.

2. Hertzler, A. E., Brewster, Roger B., and Rogers, Ford B.: Quinin and Urea Hydrochlorid as a Local Anesthetic, THE JOURNAL A. M. A., Oct. 23, 1909, p. 1393.

3. Bier: Arch. f. klin. Chir., 1908, lxxxvi, 1007.

reports of cases. Babitzki¹³ quite recently described a method whereby the sciatic nerve can be reached at the foramen for direct endoneural injection, the needle being introduced through the gluteal muscles and controlled by a finger in the rectum.

Franke and Posner¹⁴ contribute from the Heidelberg clinic in 1912 a study of the sensory nerves of the pelvis and perineum with the technic of reaching them by puncture. They report several perineal prostatectomies and in a footnote ten additional ones, all completed under absolute anesthesia.

Ruge¹⁵ cites numerous vaginal operations and two complete vaginal hysterectomies accomplished painlessly under simple infiltration with novocain, and from Knight Smith¹⁶ comes a report of two successful and painless cesarean sections by the same method. Læwen's method of paravertebral nerve-blocking, reaching the nerves at the spinous processes of the vertebrae, was applied by Finsterer¹⁷ to abdominal work. He obtained perfect anesthesia in four out of six cases and recommends this procedure especially for removal of the appendix. Kappis¹⁸ applying the same method, has removed the kidney in three cases; Schumacher¹⁹ recites thirty-five thoracoplasties and Heidenhain²⁰ four laminectomies. Kappis found that absolute anesthesia could thus be obtained for operations on the gall-bladder and stomach. This is of particular interest in showing that the vagus is not concerned with the sensory innervation of this region.

The head has been a special field of investigation. In the papers of Braun, Offerhaus²¹ and Härtel²² not only are the methods of reaching the individual branches of the fifth nerve accurately mapped out; but even the injection of the gasserian ganglion itself is detailed with mathematical accuracy. All operations in the field of supply of the fifth nerve are done by preference under local anesthesia by these surgeons. Braun states that local anesthesia has made of resection of the upper jaw quite another operation, which may still have its horrors and its difficulties but has quite lost its danger; that patients come through it with absolutely no collapse and quite as fresh as before it began and scarcely need to go to bed. Of ten patients he has lost none and had no pulmonary complications. Härtel reports nine cases in equally glowing terms.

Excision of the tongue or lower jaw comes under the same category. Härtel's brilliant article,²³ published in December, 1912, details the anatomic approach to the gasserian ganglion by needle puncture and its reading would well repay any one interested either in the subject under discussion or the injection treatment of tic douloureux. The ganglion is reached through the foramen ovale and injected with 1 c.c. of 2 per cent. novocain-suprarenin solution. Anesthesia is obtained almost immediately and lasts about an hour and a half. Härtel reports sixteen operations in which he has used this method, in nine of which the ganglion was injected on both sides. The operations included six resections of the upper jaw, three of the lower jaw and two of the tongue. Besides these there were fourteen patients in whom the ganglion was injected with alcohol. In all

there were thirty-nine attempts at puncture of the ganglion, of which he reports twenty-eight as easy, seven difficult and four with no anesthesia obtained, so that the ganglion was probably not reached.

The neck had long been a favorite situation for work under local anesthesia and the accomplishments of Bier, Kocher and others are well known. The progress in this field in the last few years is along old lines, but the possibilities have been greatly increased by the introduction of novocain because of the enormous amount of the solution which can be used. Braun reports, that from 1908 to 1911, his 150 thyroidectomies have without exception been done under local anesthesia.

To one accustomed to the use of cocaine administered as sparingly as possible, it is surprising how simple and painless these operations become with the generous novocain infiltration as recommended by Braun. The third edition of his book on local anesthesia, just published in the last few weeks, is a storehouse of interesting and wonderful descriptions of the conquest of sensation in all parts of the body. The technic of the injections for various operative procedures is given in detail, illustrated by charts and photographs in such a way as to make a practical working guide.

The work of Crile on shock and anesthesia has been of great value. Showing that shock has as its basis a definite injury to nerve cells, he has sought to lessen this by interrupting the conduction paths between the brain and the field of operation, a principle which he has designated "anoci-association." The three factors concerned are hemorrhage, anesthesia and trauma, of which the latter two are the most difficult to control. The influence of trauma, he finds, can be obliterated by blocking the conduction paths by means of a liberal infiltration with 0.25 per cent. novocain. Bloodgood²⁴ indorses and confirms Crile's work and urges surgeons to familiarize themselves with the technic by applying it not only to the handicapped patient, to whom it may be the deciding factor of safety, but in daily routine work. He believes this will also add to the comfort of the ordinary individual who can stand considerable operative trauma and bad anesthesia. Bloodgood states that only by the aid of the sphygmomanometer can the surgeon estimate the real significance of the traumatic factor. He finds that there is no change in blood-pressure in operations under local anesthesia so long as no pain is inflicted; and familiarity with recent methods should enable one to obtain a painless operative field in the vast majority of cases. Braun's description of excision of the upper jaw or tongue is a striking example of the protection against shock which local methods afford. As he says, the patients scarcely need to go to bed.

Nowhere is this better exemplified than in surgery of the aged. How many individuals cannot any one of us recall who have been refused the possible benefits of surgery because of age? We can all remember epitheliomas of the lip, in which the lymph-nodes have not been removed, because it was not thought wise to prolong anesthesia; fractures which have been left to vicious or no union; or hernias doomed to the uncertain protection of a truss and the dangers of strangulation. In these cases a mastery of local methods means safety, and by a judicious combination of local anesthesia with a little nitrous oxid at crucial moments the possibilities are without limit.

The removal of cervical lymph-nodes in epithelioma of the lip is so painless as to cause no disturbance what-

13. Babitzki: *Zentralbl. f. Chir.*, 1913, xl, 227.

14. Franke and Posner: *Arch. f. klin. Chir.*, 1912, xlix, 139.

15. Ruge: *Zentralbl. f. Gynäk.*, 1912, xxxvi, 561.

16. Smith: *Surg., Gynec. and Obst.*, 1910, xl, 423.

17. Finsterer: *Zentralbl. f. Chir.*, 1912, xxxix, 601.

18. Kappis: *Zentralbl. f. Chir.*, 1912, xxxix, 249.

19. Schumacher: *Zentralbl. f. Chir.*, 1912, xxxix, 252.

20. Heidenhain: *Zentralbl. f. Chir.*, 1912, xxxix, 281.

21. Offerhaus: *Arch. f. klin. Chir.*, 1910, xcii, 1.

22. Härtel: *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1911, I, 243.

23. Härtel: *Arch. f. klin. Chir.*, 1912, c, 193.

24. Bloodgood: *Progr. Med.*, 1912, iv, No. 4, p. 207.

ever. My routine is to infiltrate the neck thoroughly with 0.5 per cent. novocain and then proceed with the excision of the growth on the lip. By the time this is finished and the gloves changed, anesthesia in the neck is so well established that the dissection can be carried out at will. I have done this on a man well along in the eighties and had him walking about next day. In a man of 97 I removed a large epithelioma of the cheek involving the zygoma. This was especially interesting in that a section of Steno's duct was removed and an end-to-end suture made with resulting patency of the duct. The operation lasted nearly two hours and was followed by no shock or depression.

In the treatment of fractures the combined method has been found most useful. Thus in a feeble old lady of 85 with a long, oblique fracture of the shaft of the left femur with great displacement, I was able to expose the bone under infiltration anesthesia. She was then given a few whiffs of nitrous oxid and the fragments brought into line. During the drilling of the bone and the application of the plate, she was conscious and talking, but felt no pain. She was gotten up in a chair the next day and left the hospital in six weeks walking and without crutches or cane.

In hernia operations, I do not consider old age a contra-indication. Hernias of all varieties, I believe, are best done under local anesthesia; and, except in very young children, I recall no case in which it has been necessary to resort to narcosis in the last few years. My oldest patient, a man of 98 with a strangulated inguinal hernia, was operated on over a year ago, the bowel in good condition. He made a good recovery and is now pursuing his work as an artist. In a woman of 84 with an eight-day strangulated hernia with gangrenous small intestine, a two-stage operation was done. The bowel was first brought out and opened, and on the following day her condition was so good that a resection and Murphy button anastomosis was made. Her recovery was uneventful.

In presenting this review of the literature of the last few years, I have by no means exhausted or done justice to the material, but have tried to give some idea of the general progress. I have endeavored to point out some of the possibilities and to show the degree of perfection which can be obtained by such skilled masters as Braun, Bier, Härtel and others.

In this busy American life of ours, I cannot believe that many of us will ever take the time or have the patience to attain that degree of skill. I hope, however, that some of us may persevere and be rewarded by finding how much ease comes with experience. As Bloodgood states, in speaking of Crile's work, the technic cannot be mastered by restricting its employment to handicapped patients, who are too few to give sufficient experience. The details should be learned by daily experience where absolute success is not so imperative. Above all, I trust the method will not in the future be condemned, as it has been in the past, because of ignorance of its possibilities and inexperience in its application.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. HERB, SLOAN, PECK, MITCHELL AND BOOTHBY

DR. CARROLL W. ALLEN, New Orleans: As early as 1889 Dr. Matas introduced a method for reaching the second division of the fifth nerve by passing the needle into the orbit, hugging the bone at the lower external angle and directing the needle

slightly inward. It enters the sphenomaxillary fissure, passes backward a distance of 5 cm., in the orbit of an adult, and then is exactly under the foramen rotundum. I have used this method for blocking the second division of the fifth nerve. I have had ten or twelve cases in which the entire jaw was removed. When the needle is passed 0.25 cm. further back, it reaches the third division of the nerve. The methods introduced by Offenhaus and by Härtel exemplify the more notable progress made in this field lately. Härtel produces a small area of anesthesia on the cheek and introduces a needle about 5 cm. in length upward, forward and backward.

DR. KARL CONNELL, New York: I believe that the use of alkaloids before anesthesia is entirely unnecessary unless one is using an anesthetic like nitrous oxid. I do not believe that nitrous-oxid-oxygen anesthesia is preferable to ether. The results, so far as Gwathmey and I have gone, show quite the contrary. The ether blocks shock far better than pure nitrous oxid. Intratracheal anesthesia is one of the most highly advanced methods now in use. It causes beautiful oxygenation, carries the patient without shock and permits positive pressure, if desired, and the highest degree of artificial respiration; but the chief advantage in the average case is that it permits one to carry the anesthesia absolutely on the lowest percentage for that particular person and that particular type of operation. As Dr. Boothby said, one can carry along the anesthesia for hours, possibly days. Ether percentage has come to be an important factor in giving an anesthetic, because it is desired not only to put the patient to sleep promptly, but to keep the patient asleep for as long a time as necessary, even hours, with the use of a minimum amount of ether. The level, as it is called, should be maintained in every case. When the operation is completed, the patient should wake up promptly; in fact, he should be practically out of the anesthesia.

DR. EVARTS GRAHAM, Chicago: We have learned that ether is perhaps indirectly responsible for some of the various post-operative or postanesthetic complications with which we are familiar, such as thrombosis, embolism, various lung complications, shock and acute dilatation of the stomach. It should be further desirable to attempt to devise an arrangement by which the ether will maintain its toxic action on the body the shortest possible time. This concerns also the problem of elimination of ether. Even after a short ether anesthesia the smell of ether may be detected in the breath of the patient for a number of hours afterward, so that even under ordinary circumstances ether is slowly eliminated from the body. Now, if we desire to increase the rapidity of elimination of ether from the body, we must consider first of all the channels by which it is normally eliminated. Ether is eliminated in large quantities through the lungs. It also gains entrance to the alimentary tract. The vomitus even after a short anesthesia smells strongly of ether. The ether also escapes through the skin, and part of it gets back into the alimentary tract and is reabsorbed. A period of hours is necessary to eliminate all of the anesthetic from the body. If we can step in somewhere on this circle and drive out the ether in some other way than occurs naturally, we may prevent some of these distressing postoperative complications. The fact that ether is more soluble in fat than it is in water is evidence that such a process can occur; by placing fat in the alimentary tract we can hold the ether there and prevent its absorption from the intestine. If two dogs of the same weight are given through a stomach-tube the same amount of ether, in one case diluted with the same amount of water, and in the other with an emulsion, the dog which receives the ether and water, if it does not vomit up the mixture, becomes deeply anesthetized, often sufficiently to kill it, whereas the dog which receives the mixture of ether and fat not only does not vomit, but is in no wise affected by the ether. This shows conclusively that the fat has prevented the absorption of the ether. Advantage has been taken of this fact in the clinic. For the last year or two I have administered fat in the form of olive oil after the anesthetic was stopped. I found that not only is the postanesthetic period shortened, but there is also less vomiting, in

spite of the statements to the contrary which one occasionally finds in the literature, based on mere conjecture and not on experimental proof.

DR. HARRY G. SLOAN, Cleveland: The experiments carried out by Crile and Prendergast were as follows: Ten dogs were taken in each of two groups. The first ten were given ether, and shock was produced by rubbing the peritoneum for three hours. The second group were given nitrous oxid, and shock was produced in the same manner as in the first group. Blood-pressure tracings were taken to determine the reaction. The ether dogs showed at the end of three hours an average blood-pressure of 10 mm. of mercury, whereas the nitrous oxid dogs showed a pressure of 110 mm. of mercury. Surely a great difference! The ether was given by the open drop-method, not the intratracheal method. I do not see that there is any great difference in the method of administration, for anesthesia occurs only when the blood-stream contains a certain percentage of ether. In shock, the brain transforms its latent energy into nerve impulse in response to traumatic stimuli; its cells become exhausted. Ether anesthetizes by lipid solution. Nitrous oxid anesthetizes by inhibiting the intracellular use of oxygen, so that we have two directly contrary principles at work. Under nitrous oxid the functional activity of the nerve-cell is curtailed; hence exhaustion is much more slowly reached than under ether when oxidation is normal.

VACCINE THERAPY FOR GENERAL PRACTITIONERS*

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The first record¹ of induction of active immunity for therapy was about two hundred years ago when it was learned that the orientals were practicing immunization against small-pox by means of inoculation of a little small-pox virus under the skin. From this rather hazardous procedure developed the use of the less dangerous and milder virus of cowpox by Jenner² in 1796. The next work of importance was that of Pasteur,³ who developed a mild and at the same time an immunizing attack of anthrax by inoculating animals with anthrax bacilli which had been grown at a temperature of 43 C. (109.4 F.). Since this advancement many different methods of active immunization have been developed. These methods have been well classified by Bolduan⁴ as follows:

1. *Living Cultures of the Virus:* Usually the cultures are attenuated, but there are some exceptions. A number of different methods have been employed for the attenuating of the virus, thus: by drying, as is done with the rabies in the Pasteur⁵ treatment; by growing the virus at a temperature that is unsuited to the development of virulence, as is done in the case of anthrax;³ by passing the virus through a less susceptible animal as is done in small-pox;² by means of chemicals such as the addition of iodine to diphtheria toxin, as was formerly done by von Behring;⁶ or by means of heat as was formerly done with diphtheria toxin.

2. *Dead Cultures of the Virus:*⁷ The cultures can be killed by heat or by the use of chemicals.

* From the Department of Clinical Pathology, Cornell University Medical College.

1. Bolduan: *Immune Sera*, p. 169.

2. Jenner: *An Inquiry into the Cause and Effect of Variola Vaccina*, 1796, iv, 75.

3. Pasteur, *Recherches sur l'étiologie et la prophylaxie de la maladie charbonneuse*, *Rec. de Méd. Vét.*, 1879, No. 6, vi, 193.

4. Bolduan: *Immune Sera*, p. 171.

5. Pasteur, *Le traitement de la rage*, 1886, p. 4.

6. Von Behring: *Die Bluterserumtherapie*, G. Thieme, Leipzig, 1902.

7. Metchnikoff: *L'immunité dans les maladies infectieuses*, Paris, 1901.

3. *The So-Called Combined Method:* This consists of first administering a dose of the specific immune serum and subsequently the virus. This method has been used in typhoid, cholera and plague.

4. *The Products of Autolysis of Cultures:*⁸ These have been used in diplococcus meningitis and in typhoid, and seem to possess certain advantages over native cultures.

5. *Combinations of Preceding Methods:*

CHOICE OF METHOD

The choice of the various methods of immunization depends on the nature of the virus, and has been decided for us by research workers from time to time. For small-pox we use with perfect confidence a virus that has been passed through the less susceptible cow and purified. For diphtheria we also use with perfect confidence an immune serum. For typhoid we use dead cultures of typhoid bacteria, and for anthrax we use living cultures of anthrax bacilli grown at a high temperature. The reasons for a choice arise from certain particular facts of immunity, and their discussion is out of place in a paper of this character.

IMMUNITY BY MEANS OF BACTERIA KILLED BY HEAT

The interest in this work has been much stimulated during the last few years by the work of Wright.⁹ Indeed, it has been activated to such an extent that many drug firms are marketing preparations of uncertain composition and action.¹⁰ These vaccines are all of the stock variety, and are at best inferior preparations. As a rule the instructions for administration are inaccurate or incomplete. For these reasons much negative harm may be done to the patient by the use of too small a dose, or by use of an improper vaccine. Also much positive harm may accrue from the use of too large a dose.¹¹ There is surely necessity of using a vaccine that is beyond question one of the highest efficiency, and it is needful to administer such a vaccine in a proper manner. There is no exaggeration in the statement that more painstaking care is required in the management of a vaccine case than is required in the management of a case of broken cardiac compensation. In both cases the amount of the dosage of vaccine in one case, and of digitalis in the other, must be regulated by the clinical effect on the patient, and it is just as impossible to foretell the dose of a vaccine required as it is to foretell the amount of digitalis necessary to act, and not overact, without knowledge of and experience with vaccines.

PREPARATIONS OF VACCINES¹²

The first rule in the preparation of a vaccine is this: An autogenous vaccine is always more desirable than a stock vaccine. A stock vaccine may be of no value whatever in the production of immunity in any given case. Even when a number of different strains are used in the preparation of the vaccine, it is most often markedly inferior to autogenous vaccines. If there were certainty that the infecting organism were of the same strain as the one used in the preparation of the vaccine, then such a stock vaccine would approach the efficiency of the autogenous vaccine. Unfortunately many of the most common bacteria differ in different strains in the production of immunity as much as the biochemical char-

8. Wright: *Brit. Med. Jour.*, Jan. 30, 1897.

9. Wright: *Lancet*, London, December, 1900; March 2, 1901; Sept. 14, 1901; March 29, 1902.

10. Articles on Vaccine Therapy, editorial, *THE JOURNAL A. M. A.*, April 26, 1913, p. 1306.

11. Allen: *Vaccine Therapy*, p. 112.

12. Wright: *Lancet*, London, March 29, 1902.