

crates with the operator, following with an interest begotten by a sense of responsibility every detail of the procedure. The after-treatment rests largely in his hands. It is the interne who must be on the lookout for complications, and to remedy them in time or notify his chief. Manual dexterity, so essential to the surgeon, can be acquired only by careful observation and long practice. The opportunities for developing the faculty of observation are unlimited during the service of an interne, and it is this essential qualification of the physician that he tries to cultivate. The daily opportunities for educating the special senses by observation and examination of patients results in the acquisition of a diagnostic acumen which can be attained only by an extensive and long clinical experience. The keen eye, the discerning ear, the *tactus eruditus*, the manual dexterity in operating and dressing of wounds, the proper application of splints and other mechanical appliances are the precious fruits and rich rewards of internship.

As the interne penetrates deeper and deeper into the real work of his profession he becomes imbued more and more with the all-important fact that in his, as in any other profession, "practice is the best master," and he soon awakens to a consciousness that with all the splendid opportunities which surround him he is becoming deeply indebted to his profession. He is soon made to see the shortcomings of pure science in the practice of medicine and the great importance of practical training. He is not slow in detecting where our science and art are defective, and soon appreciates that "it is better to create than to be learned."

THE VALUE OF ASSOCIATIONS.

One of the most valuable practical advantages of an internship is the association of his colleagues. A noble spirit of rivalry reigns in the little circle, a healthy stimulus for hard honest work. Books and medical journals are read and their contents discussed. Cases and operations are made the subject of conversation at table and during hours of leisure, and this way each interne receives, to a certain extent, the benefits of the entire service, and such intercourse is the best possible preparation for their future work in medical societies. It is conducive to the development of the gift of debate and a wholesome spirit of criticism. Internes are attracted by medical societies, and often enrich the meetings by the presentation of cases and pathologic specimens, thus filling in many gaps in the program with valuable material. In this way the interne becomes at the very threshold a contributor to medical literature and learns the value of postgraduate education through the medium of medical societies.

The many acquaintances he makes among physicians and the public during his service are most helpful to him when the time comes for him to decide on the location of his future field of practice. This is a very important step in the life of every young physician. Many men of more than average ability have been unsuccessful, not because they were not well prepared and did not make hard efforts, but because they made mistakes in the choice of their locations. The interne owing to his superior qualifications in the practical work, is sought by communities, corporations, hospitals, medical colleges, the Army, Navy and Marine-Hospital Service, and very often steps from the hospital at once into a lucrative practice. In other instances his wide acquaintance with physicians not only in the city in which he has served, but all over the country, is most helpful to him in his

selection of a congenial location, with the necessary opportunities of establishing a growing practice, as opportunities make men as well as men opportunities.

The greatest value of an internship consists, however, in the practical training received. A year and a half in a large, well-equipped hospital, and under the tuition and supervision of a competent staff, is more than equivalent to ten years of active practice. Knowledge begets confidence, while the doubting, faltering, hesitating physician is always a failure. On the other hand, confidence, decision and courage based on knowledge and experience command respect and confidence. It is the confidence in his ability as a diagnostician and his knowledge of and faith in appropriate treatment which makes our internes successful physicians, and their competency in the science and art of surgery safe and successful operators.

At the end of his term of service the interne is fully impressed with the fact that "the road to learning by precept is long, by example short and effectual," and he leaves the institution with a sense of confidence based on the scientific and practical knowledge he has acquired since the day of his graduation.

It is the interne who, during his postgraduate pupilage, has adhered most rigidly to the rules laid down by Platen and has made the best use of his time and opportunities, that will leave the hospital best prepared to battle with disease and to assume the responsibilities imposed on the surgeon.

"Bemerke, höre, schweige, urteile wenig, frage viel."

TUBERCULIN IN PULMONARY TUBERCULOSIS.

WITH PARTICULAR REFERENCE TO THE ADMINISTRATION AND DOSAGE OF DENYS' TUBERCULIN.*

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It is now generally accepted that in tuberculin we possess a most valuable remedy in the treatment of tuberculosis. Koch's tuberculin, introduced in 1890, as a cure for tuberculosis, proved not to be such. Tuberculin was then given in large doses. Violent, dangerous, in some cases fatal reactions were produced; the curative effects were not seen. Error in the conception of the action desired of tuberculin led to misconception as to the proper mode of administration. Reactions were sought; cases were not properly selected; all were subjected to the new remedy. As a result, tuberculin came to be almost universally condemned.

This revulsion of feeling lasted for some years, but about 1898 interest in tuberculin was revived. Infinitesimal doses were given, and an attempt was made to render reactions of minimal occurrence instead of considering them the great desideratum.

In my opinion one of the dangers of tuberculin therapy lies in the fact that patients and physicians place too much trust in tuberculin and slight other elements of treatment. It is natural that the patient should do this, but the physician should insist that the hygienic treatment be carried out faithfully and conscientiously.

The use of tuberculin is based on the principles of artificial immunization. Any poison in the body has the power of stimulating the system to the production of antibodies. It is with the idea of obtaining an over-

* Read before the Tri-State Medical Society of Virginia and the Carolinas, Charlotte, N. C., Feb. 18, 1908.

production of antibodies and a consequent insusceptibility to the disease that use is made of tuberculin. The organism can be immunized by injecting more poison into it, thus forcing it to the increased production of antibodies (active immunization), or we can obtain the antibodies by injecting the blood serum of a previously immunized animal into the infected individual (passive immunization). In the case of an acute disease, running a rapid course, passive immunization should be employed in order to obtain the highest degree of immunity in the shortest time possible. If the disease is characterized by chronicity, active immunization should be employed in order to obtain the more lasting resistance to the poison. Consequently, in tuberculosis active immunization should be produced.

To establish an active immunity it is absolutely necessary that the toxins work with regularly progressive intensity on those groups of cells which manufacture antitoxin. Slight or stationary stimulations are not productive of immunity. It appears from the researches of Roux and von Behring that many small increasing stimulations are of more value than one large stimulation, the aggregate amount of stimulation being the same in both cases, and Trudeau states that "infinitesimal doses, methodically increased, which produce only slight stimulation of the defensive resources of the organism, result in a well-marked toxin immunity, as shown by increased toleration to large doses of toxin, while larger doses or too rapid an increase may bring about hypersusceptibility and an aggravation of all the symptoms of the disease."

VARIETIES OF TUBERCULIN.

Koch's original tuberculin consists of 5 per cent. glycerin bouillon in which human tubercle bacilli have been grown, evaporated by heat to one-tenth of its volume and filtered through a porcelain filter. Denys' tuberculin or bouillon filtrate consists of the bouillon or broth on which human tubercle bacilli of known virulence have been grown, filtered through porcelain and not exposed to heat. It contains, in addition to the toxins manufactured by the living tubercle bacilli, only those soluble proteins which come from the dead tubercle bacilli into the culture fluid. Denys' tuberculin possesses the advantage over Koch's original tuberculin in not having been exposed to heat, so that the chance of the toxins and proteins being affected by thermal influences is eliminated.

Koch's other products, tuberculin new and tuberculin new bacillen emulsion, contain the pulverized bodies of crushed virulent tubercle bacilli, much weakened in virulence by repeated dryings and not capable of reproducing tuberculosis.

From what is known of artificial immunity it would appear that Koch's original tuberculin and Denys' tuberculin would confer the greatest amount of antitoxic immunity; bacillen emulsion would excel in the production of an antibacterial immunity.

DESIRABILITY OF ESTABLISHING ANTITOXIC IMMUNITY.

Tuberculosis is both a bacillary and a toxic disease. The presence of living tubercle bacilli, irrespective of their toxins, does harm to the patient, but also, and we believe to a far greater extent, are the tuberculo-toxins baneful in their influence. While the bacilli are mainly responsible for the local conditions in the lungs, the toxins are the cause of the emaciation, the loss of strength, the febrile temperature, the rapid heart action, the night sweats; in short, the constitutional manifesta-

tions. The origin of this toxemia of tuberculosis can be accounted for only by the assumption that the toxins and soluble proteins manufactured at the site of bacillary invasion are taken into the blood and lymph streams and carried to all parts of the body. By establishing an antitoxic immunity we neutralize the toxin circulating in the blood.

Any direct attack on the bacilli is out of the question. Tuberculin, however, in any form, sets up a hyperemia in the tuberculous and peri-tuberculous tissues, and also excites a localized leucocytosis. Hyperemia is one of the best means at our command with which to combat infection, and leucocytes are considered the principal porters of both elements, amboceptor and complement, of those substances in the blood whose function it is to bring micro-organisms into solution, the bacteriolysins. With the advent of leucocytosis, it may be assumed that phagocytosis sets in, another of Nature's methods of defense against infection. Furthermore, it has always seemed to me that the marked primary increase and subsequent diminution in cough and sputum in many patients being treated with Koch's original tuberculin, or with Denys' tuberculin, was an excellent proof that a local as well as a general beneficial effect was being exercised. Consequently, we see that by establishing an antitoxic immunity we neutralize the tuberculo-toxins, and we also wage war on the bacilli themselves.

Denys' tuberculin appears to be best suited for the production of an antitoxic immunity. Containing, as it does, the soluble toxins and proteins of the tubercle bacillus, not subjected to heat, it would seem to be the most logical tuberculin to use. Furthermore, toxins dissolved in the culture fluid are known to lose their virulence, they become attenuated and are known as toxoids, that is, toxins having lost their virulence but still retaining their combining power with antitoxin. While losing their virulence, however, they do not lose their immunizing power. By injection of toxins thus modified we obtain a considerable increase in the anchorage of specific toxin, but at the same time (while we do not essentially increase the poison production) we obtain a marked increase in the production of antibodies. This occurrence, regularly repeated, must, by the combination of toxin and antitoxin, eventually bring about freedom to the body from the harmful agent.

INDICATIONS.

Tuberculin may be employed in:

1. All incipient cases, cases of closed tuberculosis in which ulceration has not taken place and bacilli are not to be demonstrated in the sputum.
2. Uncomplicated non-febrile, first and second-stage cases.
3. Fibroid cases not running a febrile temperature.
4. Febrile cases in which the temperature does not drop under treatment by rest, and where fever is due to the tuberculo-toxin alone and not to mixed infection. In such cases tuberculin should be administered with the greatest caution, in the most infinitesimal doses, with long intervals between successive doses.
5. Advanced, third stage cases. Tuberculin can here occasionally be used, not as a curative agent, but to aid in relieving distressing symptoms. It will often relieve the tight, harassing cough that is so exhausting, render expectoration easier, do away with thoracic pain, and help to make the patient more comfortable. In such cases its administration should be most guarded and the dosage very minute.

CONTRAINDICATIONS.

1. Greatly emaciated or greatly weakened individuals. The general body strength must first be raised by rest and proper diet before such patients will be able to supply those defensive forces which tuberculin stimulates to action.

2. Third stage cases with mixed infection. Those cases constitute the most absolute contraindications to the use of tuberculosis. In them a hypersusceptibility is easily excited, violent reactions are prone to occur, a general aggravation of the symptoms may set in, and great harm result.

3. Hemorrhage: Hemoptysis occurring during the administration of tuberculin is a signal not for the permanent withdrawal of the drug, but for its cessation at once and until some time after subsidence of all hemorrhagic symptoms.

4. Heart disease: A contraindication only if it is feared that owing to possibility of reactions compensation may be lost.

5. Marked increase in pulse frequency, beginning and persisting during administration of tuberculin.

6. Marked loss of weight, beginning and persisting during the administration of tuberculin.

7. Complications: Diabetes, nephritis, hepatic cirrhosis, hysteria, neurasthenia, epilepsy.

The patient about to take tuberculin should be impressed with the necessity of conscientiously carrying out the physician's orders. Before treatment is begun the physician should acquaint himself with the course of the patient's temperature, a two-hour record being most satisfactory, the temperature being taken preferably on the odd hours to avoid the 2 p. m. temperature coming immediately after a hearty meal, which may, in some individuals, be responsible for a temporary rise of as much as four-fifths of a degree. This preliminary record should be kept at least three days, from four days to a week is better. At the conclusion of the preliminary observation injections can be begun if advisable. They are given preferably in the morning, between 9 and 12 o'clock; injections given in the evening are open to the objection that very mild reactions may set in and pass off during the night, and are thus overlooked. The injection being given in the morning, the patient should be instructed to take very little exercise for the rest of the day (if any be allowed). By very little exercise I mean one-third of a mile, at a slow walk, as a maximum, and, in general, patients taking tuberculin should be allowed less exercise than others. The temperature should be taken every two hours for the rest of the day, the thermometer being left in the mouth five minutes if the weather is warm, ten if cold. In very cold weather it is best for the patient to go into a warm room and remain there ten minutes before taking his temperature.

Two hour temperature records on the day of injection are the best. Occasionally a three hour record may be kept; a four hour record is useless, for mild reactions may come and go in the four hour interval. Except on the day of injection, a three hour record will suffice. A temperature of 100 F. is the minimum reactionary temperature, unless there is headache and general malaise, with a temperature of, let us say, 99.8 degrees, when a reaction can be assumed.

REACTIONS.

We may define a reaction as that clinically demonstrable symptom-complex exhibited by a patient as a

result of too large a dose of tuberculin. Reactions are of all grades; many are so mild as to be overlooked; some have been so severe as to result fatally. Reactions may be divided into three classes: (a) Cutaneous, (b) local or focal, (c) general or systemic.

Too little stress has been laid on the cutaneous and local reactions, the physician generally contenting himself to wait for the onset of a systemic reaction before allowing his dosage to be modified. Reactions are the most important objective phenomena in connection with tuberculin administration, for they serve as the one infallible guide for the regulation of dosage.

CUTANEOUS REACTION.

The cutaneous reaction is seen but seldom. It consists in the appearance at and about the site of injection of a red, tense, slightly edematous, tender, painful swelling, in size usually not over the diameter of a silver dollar. There is no sense of fluctuation. The swelling makes its appearance in from three to ten hours after the injection, lasts a variable time—two days to a week—disappearing gradually. It may be confounded with a hypodermic abscess, but shows no tendency to suppurate, and disappears far sooner than does the other. It has been my good fortune to witness three such reactions, two in the same patient. In each case the mouth temperature failed to reach 99 F. and there were no subjective signs of systemic disturbance.

LOCAL OR FOCAL REACTION.

The local or focal reaction is of far more frequent occurrence and can very often be demonstrated at the height of a systemic reaction, when, of course, its presence from the practical standpoint of dosage loses weight. It consists in an increase in the physical signs in the lungs and occasionally in the appearance of physical signs where formerly none existed. Cough and expectoration become more abundant. These changes are due (1) to hyperemia about the focal process, caused by the administration of tuberculin; (2) to increased bronchial secretion; (3) to increased local leucocytosis.

As I have said, this form of reaction is very frequently found in common with the systemic reaction, but twice within the past two months I have observed its presence in two patients, in one of whom the temperature did not reach 98.6 F., in the other the maximum being 99.4 F.; in neither case was there any subjective discomfort. In one patient, with slight infiltration of the right apex anteriorly and posteriorly, producing tubular expiration and a few subcrepitant râles, slight dulness above the clavicle anteriorly, and in the supraspinous fossa posteriorly, was demonstrable, and the râles were far more moist than they had been at the time of previous examination, ten days before. In the other patient, with very slight involvement of the right apex posteriorly, many moist râles and slight bronchovesicular breathing were noted, previous physical signs having consisted in a few subcrepitant râles. In both cases increased cough and expectoration were noticed within twelve hours after injection of tuberculin, and it was this fact that caused me to examine the chest again, the examination in each case being made within twenty-four hours of the time of injection. The cough and expectoration lessened within a week, and the physical signs were perceptibly receding at the end of that time. Focal reactions, when moderate, are not undesirable; they rid the system of pus and septic material, and we have no better expectorant than tuberculin.

SYSTEMIC REACTION.

The systemic reaction is well known and classical. In from six to thirty hours (the latter being rare) after injection of tuberculin, the temperature rises to anywhere between 100 F. and 106 F. The patient may not complain of any subjective symptoms, but usually there is discomfort, chilliness amounting at times to a definite rigor, headache, nausea, at times vomiting, pains in limbs and body, general malaise, and increase at times in cough and sputum if a focal reaction co-exist. These symptoms are usually proportionate in severity to the height of the temperature. The temperature drops in from two to ten hours (depending on the severity of the reaction) and save for a feeling of weakness, all symptoms except cough and sputum have subsided and the patient is himself again in twenty-four hours in the majority of cases. Sometimes, however, a systemic reaction appears late, thirty hours after injection, and fever persists for two or three days, gradually dropping to normal.

The desirability of reactions has long been a mooted point, but now they are considered to be distinctly undesirable. At the time of his discovery of tuberculin Koch believed that the organism should be subjected to many powerful reactions in order to produce focal necrosis and the elimination of both tubercle tissue and tubercle bacilli. This idea is not practicable and does not now hold good theoretically. It has been abandoned entirely, but many still cling to the idea that occasional reactions are beneficial; morally they may be, but physically they are not. A moderate hyperemia, with serous exudation in the peri-tuberculous tissue, unquestionably has a good curative influence, but this can occur without a systemic reaction appearing, and it is the universal verdict that marked constitutional symptoms are bad.

OBJECT OF TUBERCULIN.

Tuberculin has as its object not so much the effect on tubercle tissue and bacilli as the protection of healthy tissue against the bacilli and tuberculo-toxins. To attain this end, reactions are unnecessary. Were reactions necessary, then the greater the reaction the greater the immunity, but, as a matter of fact, we not only see that we can acquire immunity without reactions, but also that we can get many and repeated reactions without immunity. Moreover, reactions favor the production of hypersusceptibility. To quote Trudeau: "By hypersusceptibility we do not mean the usual susceptibility to an increased dose which shows itself by an ordinary reaction, but an exaggerated and growing sensitiveness to the toxin which follows a reaction without any previous warning. For instance, a patient having reacted in the usual way to 1 mg., and all the symptoms of the reaction having disappeared and the temperature become normal for two days, an injection of 0.5 mg. is followed by a marked, even a more marked disturbance than the one produced by a 1 mg. dose; another interval of rest being given, and the dose reduced to 0.1 mg., another strong fever reaction manifests itself, and this continued and sometimes increasing susceptibility of the organism to a decreasing dose of toxin constitutes tuberculin hypersusceptibility."

If this condition occurs it is not necessary to discontinue tuberculin permanently. All injections should be stopped until the temperature has been normal for ten

days, then a dose of 1/100 of that causing the beginning hypersusceptibility should be given, and the subsequent increase in dosage should be more rapid than before; in fact, more caution is needed. Of course, if marked hypersusceptibility recurs two or three times the case is not a suitable one and tuberculin will have to be abandoned.

ADMINISTRATION OF DENYS' TUBERCULIN.

Diluting the Tuberculin.—As a diluting fluid physiologic salt solution is used, to which 0.5 per cent. carbolic acid has been added to prevent decomposition. A pipette of small caliber, containing 1 c.c. and accurately graduated to tenths of a cubic centimeter, is used. This is sterilized and filled with 1 c.c. of pure bouillon filtrate,² which is then emptied into a sterile bottle. Then, using the same pipette or one exactly similar, 9 c.c. of the diluting fluid are added. This makes a 10 per cent. solution, each cubic centimeter of which contains 100 mg. of tuberculin. Proceeding in like manner, we make from this 10 per cent. solution a 1 per cent. solution, each cubic centimeter of which contains 10 mg. of tuberculin, and in similar fashion we proceed to the weaker solutions.

The solutions should be kept in a cool place, in the dark or in brown bottles, and the weaker ones (0.1 per cent. and under) should be renewed after four weeks. All turbid solutions are worthless and should be discarded.

Eight solutions are used, each one-tenth the strength of the next higher. No. 1 contains 1/10,000 mg. per c.c. and is for febrile cases only; No. 2 contains 1/1,000 mg. per c.c.; No. 3 contains 1/100 mg. per c.c.; No. 4 contains 1/10 mg. per c.c.; No. 5 contains 1 mg. per c.c.; No. 6 contains 10 mg. per c.c.; No. 7 contains 100 mg. per c.c.; No. 8 is pure tuberculin.

A syringe is used holding exactly 1 c.c. and carefully graduated to tenths of a cubic centimeter. Injections (if no reactions occur) are given twice a week. With a febrile patient solution No. 1 is used, and intervals between injections should be four or five days. With a non-febrile patient solution No. 2 is employed, containing 1/1,000 mg. per c.c. and an initial dose of 1/10,000 mg. is given. In other words, as the syringe contains 1 c.c., we give one-tenth of a syringe of solution No. 2. Increase is made at first by 1/10,000 mg., consequently at the subsequent dose we give two-tenths of a syringe, then three-tenths, then four-tenths, and so on, till we have given 9/10,000 mg. or nine-tenths of a syringe.

We then change to solution No. 3, ten times stronger than No. 2, containing 1/100 mg. per c.c. Beginning with 1/1,000 mg., or one-tenth of a syringe, increase is made by one-tenth of a syringe, but we must remember that while with solution No. 2 we were increasing our dosage by 1/10,000, we are now increasing by 1/1,000 mg. When we have reached 9/1,000, or nine-tenths of a syringe of solution No. 3, we use solution No. 4, containing 1/10 mg. per c.c., and proceed as before, bearing in mind that now we are increasing each dose by 1/100 mg. When solution No. 6 is reached the interval between doses should be lengthened to five days, increase still being made by one-tenth of a syringe of the solution used. When the patient is receiving 100 mg. six days should elapse between doses, when 400 mg. are reached, from ten days to two weeks. The maximal dose is 1,000 mg., or 1 c.c.

1. Tuberculin Immunization in the treatment of pulmonary tuberculosis. *Am. Jour. Med. Sc.*, June, 1907.

2. Denys, J.: Le Bouillon Filtré du Bacille de la Tuberculose dans le traitement de la Tuberculose humaine.

of pure tuberculin. This dose may, if reached, be repeated a few times, but, as a rule, tuberculin should then be dispensed with for a time. If no reactions occur the course will consume about a year. Reactions will, of course, greatly lengthen the time; in the majority of cases the maximal dose is never attained.

This is the method of dosage employed by Denys. Naturally the dosage must be suited to each individual case, and in giving such an outline we are, of necessity, forced to generalize. Each physician will learn by experience what tuberculin will do in his own hands and will modify his dosage accordingly. Some patients will withstand rapidly increasing doses, others will have to be dealt with most cautiously.

It is found that patients react most frequently at the second or third dose of a new solution. This is not strange, for with each new solution employed the increase in dosage becomes ten times that of the preceding solution. Consequently, when proceeding to a new solution, it may be well to increase by 5 centigrams instead of by 1 decigram of the solution, for two or three doses, to avoid possible reaction.

With the occurrence of a systemic reaction no further dose should be given until the temperature has returned to normal and has remained so for two days. If cutaneous or focal reactions occur it is well to repeat the offending dose once before proceeding to an increase. After a systemic reaction the offending dose should not be repeated, but a smaller one substituted. Thus if a patient reacts to 1 mg. the subsequent dose should be 1/5 mg., then 0.5 mg., then 1 mg., the interval between doses remaining the same as before the reaction.

If a second reaction occurs before the dose causing the first reaction is reached or surpassed, tuberculin should be stopped until the temperature has been normal for four days, then a still smaller dose should be given. Thus, if 1 mg. causes a second reaction, the next succeeding dose should be 0.1 mg. and progression upward should be made by 0.1 mg. to a dose. If reaction again occurs before the primarily offending dose is reached, tuberculin hypersusceptibility is probably setting in and should be dealt with as stated above.

Schnöller,³ of Davos, advocates the administration of Denys' tuberculin in a slightly different manner. He employs two methods, the conservative and the radical. His conservative method is indicated in: (1) all extensive lesions, (2) patients with slight resisting power, (3) patients with much emaciation, (4) patients with mouth temperature over 99.4 F., (5) patients with inverse temperature, (6) patients with hemoptysis, (7) children, (8) pregnancy.

He advises in these cases the administration of solution No. 2 daily, of Nos. 3 and 4 every other day, of Nos. 5 and 6 twice a week; thus, even in his conservative method, his contention is for more rapid dosage with weaker solutions than are suggested by Denys. I have made a practice of giving solutions Nos. 2 and 3 every other day, if no reactions appear, beginning bi-weekly injections with No. 4, and have not seen any bad results from this procedure.

Schnöller uses the radical method with patients in good physical condition and manifesting strong tolerance in order to establish an active immunity as rapidly as possible. His radical method consists simply in start-

ing with solution No. 4 and following out practically the same schedule of dosage as that outlined by Denys. I have had no experience with this method.

The time necessary for a course of tuberculin can not be estimated in advance, but in every case the patient should be told that it must be administered for several months to be of benefit. We again quote Denys: "The two most important factors in obtaining results are the length of time over which the treatment is extended and the dose of toxin the patient can be made to tolerate. . . . Not much permanent good can be expected from a short treatment extending over a few months, especially if the highest dose reached at the end of that time be a fraction of a milligram. On the other hand, when full doses have been reached they should not be continued indefinitely for fear of exhausting the patient's power to respond, by the formation of antibodies, to the stimulus of the injection of toxin."

RESULTS.

Patients tolerating increasing doses are not so prone to the exacerbations and relapses exhibited by those not so treated. More permanent cures have resulted when tuberculin has been used than where it has been omitted; many patients running a slow but steadily downhill course, in spite of open-air treatment, improve and get well under tuberculin. Tuberculin has a favorable effect on the chronic toxemia of tuberculosis, which disappears under its use to an astonishing degree. Cough and sputum frequently cease, or persist greatly lessened in amount.⁴

CONCLUSIONS.

1. Tuberculin is the most valuable adjuvant to fresh air, rest, good food, we possess in the treatment of pulmonary tuberculosis.

2. Denys' tuberculin appears to be best suited to establish an active antitoxic immunity, the type of immunity capable of doing the greatest good.

3. Tuberculin is indicated in many types of cases, and in the hands of a competent administrator will do no harm.

4. Reactions are often overlooked; they are not to be desired, and when frequent or violent are distinctly harmful to the patient.

5. The dosage should at first be infinitesimal; increase should be very gradual; the word "haste" has no place in tuberculin therapy.

6. Time and tolerance bring success in the treatment by means of tuberculin.

7. Tuberculin should never be used save in conjunction with strict hygienic and dietetic measures.

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4. See also: Brown, L.: The Treatment of Tuberculosis. Osler's Mod. Medicine, vol. iii; Bandler and Roepke: Lehrbuch der Spezifischen Diagnostik und Therapie der Tuberkulose.

Business Methods.—Physicians have the reputation for being very poor business men. It seems almost axiomatic that the physician who succeeds away beyond the rank and file must have in addition to other attainments a keen business mind. The little motto so often seen in the offices of large business firms "Do it now" should be religiously observed by the physician in prompt response to calls, prompt case records, charges, statements and collections. There is no business man who should avoid neglect so strictly as the physician. Someone has said jocosely—it is a transient business; certainly there are many transients. Nothing succeeds like success and the \$50,000 a year man has the confidence of the thousands who have only heard of his success.—*Leucocyte*.

3. Theoretisches und Praktisches Über Immunisierung gegen Tuberkulose nebst Statistik von 211 mit Denys' schem tuberculin behandelten Lungenkranken.