to work the threads. These people have the disease as marked as you see it anywhere, notwithstanding that for twelve months in the year they work in an atmosphere with if anything more than ordinary humidity.

DR. C. M. COBB, Lynn, Mass.—There are several very peculiar things in connection with atrophic conditions of the nose and pharynx. The typical atrophic pharynx is not a pharynx with the crust formation. The atrophy of the nose, if we begin with that part of it, is a very curious formation. The atrophy does not take place where the disease is. The disease and crust formation are around the middle turbinate, which is the last place to get well and the first to become affected. If I understand Dr. Freudenthal, he claimed that the air in the furnace is heated and the moisture is driven off. As I understand it, in the furnace the cold air passes over the hot iron and the temperature of the air is raised, but there is just as much moisture in the atmosphere after it is heated as before, although there is less relative humidity. Another thing is the escape of carbonic oxid from the hot iron, which may be an important point. It may be an irritant to these patients. Furthermore, in regard to irritation, it hardly seems probable that directly, or indirectly for that matter, mechanical irritation produces a disease of that kind. Mechanical irritation does not anywhere else in the body produce atrophy or an atrophic condition. For instance, a man working on the street may get thickened epidermis all over the hand, but the hand will not atrophy. The broadening of the face seems to me as much a result as it is a cause. A person who has atrophic rhinitis from childhood, or in other words, a person who has purulent rhinitis as a child, and this condition follows, may have the broad face because of the nasal disease, and then as it grows older and the bones develop the face is relatively broader. The cases often get well at that time, because the broadening of the face gives them more room to breathe, and better drainage from the sinuses. A very curious case of atrophic rhinitis occurred in my practice the other day. I saw a child 10 years of age, with none of the surroundings in which we would expect a case of atrophic rhinitis to originate. The child had atrophic rhinitis following an infantile vaginitis. The people supposed that the disease had migrated from one place to the other, and I have no doubt that it did so, with assistance, the contagion being carried from one place to the other.

DR. EMIL MAYER, New York City—As germane to the subject under discussion I would like to mention as a therapeutic hint the happy effect I have seen from the application of carbolic acid and glycerin to the pharynx, in a 12 per cent. solution.

DR. HOLMES—I would like to ask Dr. Mayer if he begins with a lower per cent.

DR. MAYER—No. I use a 12 per cent. solution at once.

THE PRESENT STATUS OF OUR KNOWLEDGE CONCERNING THE BACTERIOLOGY AND SERUM TREATMENT OF DIPHTHERIA.*

SAMUEL E. ALLEN, M.D.
CINCINNATI, OHIO.

Although we may not consider this subject as exactly fitting for the deliberations of this Section, still diphtheria is to a certain extent a throat affection, and as such its discussion has a place here. The subject offers something a little different from the ordinary run of topics which engage our attention, and for that reason, on the advice of our Chairman, I take the liberty of introducing it here. It is not my intention to treat the subject from a practical standpoint, but rather to touch on the scientific advances which have been made by the bacteriologists and those engaged in working out the problems connected with serumtherapy. An enormous amount of work has been done and is being done along these lines, and an account of the latest theories advanced, even as imperfectly as given here, can not fail to be of some profit to us. The subject naturally divides itself into two phases: the first concerning diagnosis, and the second including the intensely interesting questions of immunity and serumtherapy. The diagnosis of diphtheria can not be considered as scientifically confirmed without the demonstration of the presence of the Klebs-Loeffler bacillus. No one is now content with a clinical diagnosis alone, because we know that other etiological factors may be concerned in the production of what is pathologically a diphtheritic membrane, for example, the material in crypts of the tonsils in lacunar tonsillitis. Baumgarten, who has studied many true diphtheritic membranes, states that in his opinion streptococci are often the cause of the membrane, and the diphtheria bacillus of the general intoxication.

At the present day, the Klebs-Loeffler bacillus has as distinct a position in the etiology of diphtheria as has the tubercle bacillus in that of tuberculosis. The recognition of the diphtheria germ, however, presents difficulties not met with in the direction of tubercle bacillus. Recognition of the tubercle bacillus is exceedingly easy. An absolutely accurate and positive determination of the diphtheria bacillus is very difficult, requiring time and considerable knowledge of bacterial technique. Under ordinary circumstances the appearance of simply stained specimens from an eight to twenty-four hour culture on Loeffler's blood-serum mixture is sufficiently accurate for practical purposes; but that we are able to recognize the bacillus positively by such simple means is far from the case. Diphtheria bacilli are no doubt definite specific organisms, but with such variations as to shape, size and arrangement, that we are almost justified in speaking of them as the group of diphtheria-producing bacilli. Let any one make fresh blood-serum cultures of the bacilli from different hygienic stations or bacteriological laboratories and he will find marked differences. Again there is a group of organisms often found in the throat and elsewhere that resembles the diphtheria group so closely as to be indistinguishable from them, and differing only in being non-pathogenic. To this group, which now includes the so-called Xerosis bacillus, the name "pseudodiphtheria" bacilli has been given. There is no absolutely reliable quick way of differentiating between them, the test of pathogenesis being the only sure one. In recent years many attempts have been made to devise quick differentiating methods. The most favorably considered is the method of double-staining devised by Neisser. The organisms are first stained with acetic acid methylene blue and then with an aqueous solution of bismarck brown. The bacilli present brown protoplasm and blue polar granules, the so-called Babes-Ernst bodies. Neisser and Fränkel claim the test to be absolutely accurate, if 9 to 24-hour-old cultures on Loeffler's blood-serum mixture, grown at a temperature between 34 C. and 35 C., never above 36 C., are used. That this method is certain is disputed by many competent observers, among them Loeffler. Up to the present day we may say that the variations of neither the true nor pseudo group have been accurately determined. As the disease presents a definite clinical picture while the organisms vary, this variation is probably due to differences in the soil. This much we can at present say of the diphtheria bacillus. It is a bacillus subject to as yet undetermined variations. It can not be absolutely differentiated from the pseudo group,

*Presented to the Section on Laryngology and Otology, at the Fifty-first Annual Meeting of the American Medical Association, held at Atlantic City, N. J., June 5-8, 1900.

except by animal experiment. In practice a reasonably accurate quick diagnosis can be made in nearly all cases. We are more likely to overlook germs when present than to err on the side of an affirmative diagnosis.

We now come to questions of immunity and serum-therapy. It is in the cure of diphtheria that the result of scientific research into these obscure fields has been of the greatest practical worth. Bacteriologists have been trying to work out a theory as to what happens when an animal is made immune by repeated injections of toxins, and as to the real nature and working of the substances—antitoxins—which appear in the blood of an animal so immunized. There has never been any very satisfactory theory offered as to the cause of either natural or artificial immunity until Ehrlich a few years ago formulated his very original theory. According to him, no animal can be inoculated with a bacterial disease unless it has in its body-cells a substance capable of combining with the bacterial toxins. This act of union between this substance in the cells and the toxins gives rise to the fever and other general symptoms of the disease. This substance he considers a sort of side-group in the molecules of the cell and serves to fasten the toxin, altered by the combination, in the cell. Natural immunity, while it may be due partially to phagocytosis or to the germicide properties of the alexins of Buchner, is, according to Ehrlich, in a large measure due to the absence of this side-group or side-chain of molecules, this so-called "Giftbindende Substanz." We can get at the theory best by applying it to the disease diphtheria. The organisms begin development in the throat of the patient; aside from the local inflammatory effect, virulent toxins are produced and absorbed. These toxins combine with the "Giftbindende Substanz" in the cells, and the act of combination causes such a cellular change as to produce the fever and other symptoms of diphtheria intoxication. If the toxins are produced in large amounts the reaction will be such that death results; the cells are too severely damaged to admit of further physiologic function. If, however, the poison is less in amount or the physiologic resistance of the cells relatively greater, further cellular activity is not inhibited, but the cells are stimulated and an effort is made by nature to restore the "Giftbindende Substanz" used up in combining with the toxins. Nature here, as elsewhere, in accordance with known physiologic laws, not only reproduces but overproduces the "Giftbindende Substanz" used up, and the overplus is taken up by the blood. The overplus is then available for immediate combination with the toxins, being produced from the local focus in the throat, and renders them innocuous. The disease becomes in this way self-limited and recovery takes place. The self-limitation of infectious diseases is due, according to this theory, to the overproduction and absorption into the blood of the very same cellular substance which while still in the cell allows of the general reaction of the organism to the infectious toxin. Diphtheria antitoxin is nothing but this "Giftbindende Substanz" produced in overplus and taken up by the blood. The self-limitation of an infectious disease and its cure by the injection of ready-made antitoxin are similar processes. In the first instance the antitoxin which limits the disease is produced within the patient; in the latter, the antitoxin is introduced already formed. Antitoxin is a substance normally present in the animal cells, which allows of the combination of toxin with the cells and the production of the disease, but which, when in superabundance and in the blood, there combines with the toxins, and hence renders them innocuous—a similia similibus theory of the first rank.

Such a principle of cure as this is isopathic. Medicine has invented many so-called principles of cure: the allopathic principle, where the disease is to be cured by the administration of a remedy whose physiological action is opposed to the symptoms of the disease; the etiological principle, where the remedy is directed toward the destruction of the cause of the disease and nature is left to herself after the cause is removed; and, as the latest development of our knowledge, this isopathic curative principle. The various infectious diseases can not be treated on the etiological principle, because we have found that the animal cells are more sensitive to the various disinfectants than are the cells of bacteria; hence the bacterial cells can not be killed by anything short of a quantity which would destroy the animal cell. The isopathic principle is the one from which we are to hope for a solution of the problems of infectious diseases. How often are we forced to recognize the truth that there is nothing new under the sun? Hippocrates said: "That which produces a disease also cures it."

Giftbindende Substanz—antitoxin—is not antitoxin until it gets into solution in the blood; consequently antitoxin has no effect on toxins already combined with the cells, and can do nothing toward remedying the evil effects of such combination when once formed. All antitoxin can do is to neutralize toxins before they get to the cells. Hence, the practical necessity of employing antitoxin early in the course of the disease. The process of immunizing becomes under this theory but a process of cell stimulation; the repeated and ever-increasing doses of toxins injected stimulate the cells to the overproduction of large amounts of antitoxins. For the production of the antitoxin, either that needed to limit the course of the infectious disease, or that which we desire to obtain in large amounts for serum-therapy, it can be readily understood that a nice poise between the amounts of toxins and the cellular resisting power of the animal must be maintained. Let the toxins be relatively too strong and cellular activity is stopped; let them be too slight in amount and the stimulation is not sufficient to produce any overflow into the blood. Take a disease like tuberculosis; here the toxins are so small in amount or slight in toxic effect that no antitoxins are produced, and the disease steadily progresses. Lately, Behring has been able to immunize cattle to tuberculosis by using injections of enormous amounts of tubercular toxins. From the blood of such animals he obtained an antitoxin which prevents tuberculosis in guinea-pigs. This theory of Ehrlich carries with it, of course, the idea of a direct chemical union between toxin and antitoxin. Buchner, Roux and their adherents still cling to a cellular theory of the action of antitoxin upon toxin, claiming that the agency of the living cell is a necessary factor in the action of antitoxin upon toxin.

Ehrlich's well-known experiments with the vegetable poison ricin indicate, at least, that the chemical theory is the correct one. Animals can be immunized to ricin and an antiricin serum obtained. Ricin has the property of precipitating in a peculiar manner the red blood-corpuscles of defibrinated blood. This is purely a chemical phenomenon. When ricin and antiricin are mixed in a test-tube, the mixture loses this coagulating and precipitating property. Ehrlich claims that a sort of double salt is formed by the union of ricin and antiricin, this double salt not having the properties possessed by ricin alone. Just this sort of a combination, it is rea-

soned, takes place when any antitoxin acts upon toxin. If toxin, in producing a disease, combines chemically with a cellular substance, then, in the cells specially affected, we should not be able to find any toxin. This point has been investigated in tetanus. Tetanus toxin affects the cell of the central nervous system. This has been proved by direct examination post-mortem. Now, when the body of an animal dead from tetanus is examined for toxin, it may be found in the blood and various organs, but not in the central nervous system. That portion affected by the poison is the only portion absolutely free from it, showing that a combination of the toxin and cellular substance must have taken place. The above theory is the latest and most generally accepted one concerning diphtheria immunity and serum-therapy.

As far as the practical results of antitoxin treatment are concerned, it is almost universally admitted that the mortality has been reduced nearly two-thirds. Cases still die, as we must expect when we consider the theory on which the action of antitoxin is based. A great point in the therapy is to employ the serum early, before damage is done, because antitoxin does not repair destruction already accomplished. Antitoxin simply neutralizes toxins produced after its introduction; repair and cure are left to nature. We may expect always to find some individuals so sensitive to the diphtheria toxin that the initial amount absorbed during the first day or so of the disease will be sufficient to cause death, and we must therefore expect a certain percentage of deaths. Another cause of failure, is the injection of too little antitoxin. At least 2000 units should be used and repeated every twelve hours if necessary. Any harm done by antitoxic serum is due entirely to outside substances in the serum, and the more carefully this is prepared, the less liability of trouble. Now-a-days we get perfectly reliable serum, and as improvements in its production and preservation are made we hear less and less of the various undesirable complications. Antitoxin as a chemically pure dry substance would be the ideal.

The immunity produced artificially by inoculation with toxins or by injection of antitoxic serum is short-lived. The "Giftbindende Substanz" in the blood, on which the immunity depends, is soon excreted and gotten rid of. Protective inoculation does not last above three or four weeks. When large doses are given, excretion is more rapid and the duration of immunity hardly as long. We are indebted to bacteriology for this new principle of cure, this *isopathic curative principle,* and from its development, if it shall stand, we are to expect great things for the future.

EPITHELIOMA.

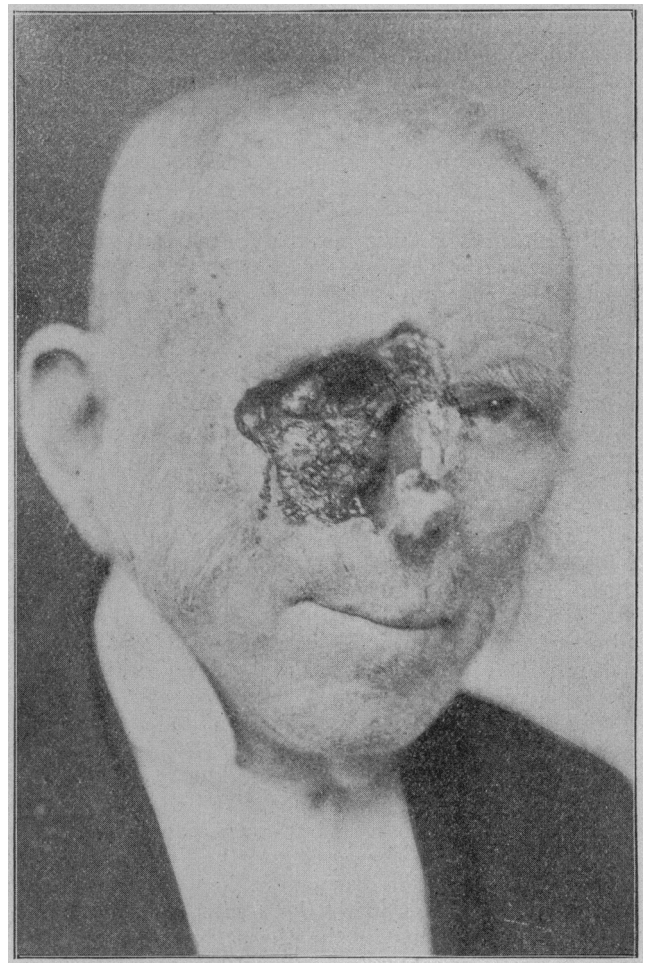
REPORT OF TWO CASES—ONE OF SLOW AND THE OTHER OF RAPID GROWTH.

CHARLES J. WHALEN, M.D., LL.B.
CHICAGO.

The first case represented by the accompanying cuts is of especial interest, as showing how long an epithelioma may remain superficial, and it is also of some interest because of the superficial metastasis which was marked before death.

M. G., 85 years of age, widower, first consulted me May 25, 1897, desiring to be relieved of the severe pain radiating from the extensive ulceration about the right orbit, as represented in Fig. 1. The pain he described as being very severe at times and lasting in the neighborhood of sixty minutes, when it might disappear only to return again some hours later, or it might not reappear again for twenty-four or forty-eight hours.

The trouble on his face is said to have started from a scratch on the nose with a rusty nail twenty years before. The scratch never healed, but it remained very small and seemed to be stationary for a trifle over four years. At the end of that time it began to grow slightly, and up to three years before his first visit to me it had only acquired a size equal to about the diameter of a quarter of a dollar. One year before I saw him it involved the upper part of the lower eyelid. From that time until he first visited me its growth was very rapid. At my first examination, I found it had completely destroyed all the soft parts from the supra-orbital ridge to a horizontal line extending 1¾ inches



from the ala nasi. It had also extended across the bridge of the nose to the inner canthus of the left eye and down the nasal bones and involved all the soft parts of the nose over the right side and to within 1.25 centimeters of the ala of the nose on the left side.

The right ear began to enlarge in January, or four months before his visit to me. At first, there came a little induration directly in front of the tragus; this broke down and discharged. The ear was ulcerated upward, 4 centimeters from its lower extremity, as seen in Fig. 2; there was also considerable swelling and ulceration on the cheek directly in front of the center of the ear. A piece of the swelling of the cheek was excised for microscopic examination. The microscope showed an ill-formed epidermis with no interpapillary cones, but many embryonic ingrowths destined to form hair follicles or sweat-gland. Near the center of the