suggestive of a mild form of infection, or in consequence of an enfeebled circulation. He has not observed it in appendix operations.

J. B. Murphy, Chicago, does not believe that phlebitis is more common following abdominal than operations on other parts of the body. He thinks it is a stasis caused from placing the patient in the recumbent position.

A. J. Ochsner, Chicago, says that two explanations seem somewhat reasonable, though he is entirely unable to state the reasons for the occurrence of the disease. One is given by Witzel, and the other is that the disease usually occurs in patients whose blood is not quite normal.

W. J. Mayo, Rochester, Minn., believes that there are several factors in the etiology. Phlebitis does not occur as a rule unless the peritoneal cavity is opened, thus arousing a process which results in some blood change, and this is instrumental in causing phlebitis. The recumbent position is a factor. While formerly common in interval appendectomies, when patients were in bed two or three weeks, it is now uncommon since patients are allowed to get up in six days, and are instructed to move their limbs freely. On this account the Mayos aim in abdominal cases to get the patients up in ten or twelve days.

Roswell Park, Buffalo, N. Y., in the cases under consideration, thinks that the early condition is one of endophlebitis, which may be of toxic origin, or an indistinct mild form of sepsis. The handling of viscera or clamping of vessels by forceps may commence the thrombotic process. While micro-organisms are more or less at fault, it does not follow that the condition is necessarily other than thrombus produced by chemical rather than biochemical means. He believes that a mild type of thrombophlebitis is the not infrequent sequel of abdominal operations, and that it is due to chemical agencies in the blood rather than to active germ action, and that it is mildly, if at all, infective. The condition, at times, is most difficult of explanation.

Arpad G. Gerster, New York, states that the question is not so simple as many would imagine. Several factors are to be considered. In some faultless cases the thrombosis is due to a ligated pelvic vein, in which the thrombosis extends to the femoral; but the condition of the blood and the endothelium of the vessels has some direct influence on the thrombotic process. Another factor is inaction due to bed rest, and the low blood pressure due to lack of physiologic stimulus to the heart. The coagulability of the blood and the state of the endothelium he thinks are most important.

Joseph G. Blake, New York, believes that the condition is due to an extension of a phlebitis in the neighborhood of the wound across the abdomen through a transverse vein of the abdominal wall which empties directly into the external iliac vein. The original phlebitis he thinks is probably due to injury to the walls of the vein through traction.

A. W. Vander Veer, Albany, N. Y., says that he is not clear as to the pathology. In the plainest cases traumatism is produced which extends to the venous trunk. The clumsy use of retractors will produce injury which is reflected to the veins. Just why a case of appendicitis, complicated with a lesion of right ovary and tube, should cause a phlebitis of the left leg, he is at loss to explain.

CONCLUSION.

My belief is that the cause of phlebitis of the epigastric, iliac, femoral, saphenous and tibial vessels, occurring late after a perfectly aseptic operation, with prompt healing of the wound, is probably not septic.

We do not know the specific cause or causes. The cases, of which a good illustration is reported, with our present knowledge, are very difficult of satisfactory explanation.

In the absence of convincing or pathologic evidence, and in the face of profound surgical skepticism, it is not rational, in the best and cleanest days known to surgery, to assume an infection that is devoid of satisfactory evidence.

The condition which causes the thrombus, before the

inflammation, or of the phlebitis, preceding the thrombus, is the vital question. It is exceedingly difficult, in fact, quite impossible, to reconcile the facts with the recumbent position, the simple ligature or injury of small veins, in a distant field, often on the opposite side of the body, though admitting that infection need not come from the site of operation.

I believe that there is a general condition affecting the composition of the blood, that may, and often does, exist before operation, which is an essential factor in the cause of thrombophlebitis in these cases. A careful scrutiny of patients should be made before operation, and an examination of the blood should be made before and after operation. This on a fairly liberal scale, in my opinion, would reveal interesting and useful information, and shed some light on a puzzling subject.

If the patient is chlorotic and anemic, or if the conditions are not satisfactory, the health should be improved, if delay is permissible, by the administration of iron and acids, and metabolism improved by a suitable food supply, while specific or constitutional affections should, as usual, receive just consideration.

A SERIES OF MEDICAL AND SURGICAL AFFECTIONS TREATED BY ARTIFICIAL AUTOINOCULATION

ACCORDING TO WRIGHT'S THEORY OF OPSONINS.*

A. P. OHLMACHER, M.D.

DETROIT.

It is somewhat surprising, in view of the remarkable character of the results which have been obtained, that an appreciation of the full value of Sir A. E. Wright's theory and practice is not widely disseminated among the medical profession of the United States. Rarely, indeed, in these days of easy publicity, does a scientist effect an accomplishment of far-reaching humanitarian importance without its immediate and extensive proclamation throughout the civilized world. In fact, such proclamation, especially of discoveries in the healing art, is too often premature and over-colored, with the result that disappointment and pessimism are aroused and progress impeded. With Professor Wright, however, the situation is quite the opposite. He has for four or five years patiently worked along a new line in experimental medicine, has evolved an attractive working hypothesis, the application of which has performed veritable miracles in the cure of certain diseases, and all of this with scarcely a ripple of sensation and almost without the knowledge of the medical profession outside of the originator's immediate circle. For Wright is accomplishing results that are the surprise of those who have been so fortunate as to witness them, and the comparatively uncommon worker who is, by previous training, competent to apply Wright's methods in practice, and who has employed them, is also performing therapeutic feats of a most surprising kind. To a large degree this situation has resulted from the principal investigator's natural modesty, and in part has been due to the conservatism of the medical profession, representing the reaction after a number of sensational but unproductive announcements. But the day when Professor Wright's achievements are to remain hidden has passed in England, and in the United States we are on the verge of a similar

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illumination, thanks largely to the visit which Wright recently paid to America and also to the remarkable eulogy accorded his work by our most distinguished medical scientist, Professor William H. Welch. It is, therefore, a pleasure of more than ordinary degree that I feel in bringing to the American medical profession an account of what it has been my lot to effect in applying, in a small way, the methods of Wright to the treatment of certain medical and surgical affections.

It is not my purpose to go into theoretic or technical details, for I am convinced that the appreciation of Wright's conquests has been retarded in the United States by the publication of several papers too severely and too needlessly abstruse, with the result that a comparatively simple theory and the excellent results of its application have been rendered confusing and unattractive to the average medical man. To the physician or surgeon whose interest lies in learning as speedily as possible what can be accomplished by Wright's methods in curing disease it matters not how opsonins may be related to agglutinins, bacteriolysins or precipitins, or whether Ehrlich's side chain hypothesis can be made elastic enough to reconcile opsonins with amboceptors, complements, complementoids, or what not. In fact, because of the industrious quest of Ehrlich's hypothesis by workers in all parts of the civilized world during the last six to eight years, with the voluminous and increasingly complex literature, and the failure to obtain out of all this work an additional remedy for a single infectious disease, the work-a-day physician has lost interest in the theoretic controversies of biologic medicine. But the fashion of theories and standards is on us, and to-day no one proposes a new kind of biologic therapy without formulating some theoretic basis as its foundation, or advocates a biologic remedy without proposing a method of standardizing it. Unfortunately, too, the theory and standard are often as fallacious as the treatment is inefficient. It may or may not have been some such consideration as this which led Wright to propound his theory of opsonins to explain the beneficial results following his use of small, infrequent bacterial inoculations to cure the corresponding subacute or chronic infection, and perhaps he may have laid more stress on the opsonic index and the exact enumeration of the bacteria in a given dose than further experience will warrant. Be that as it may, a most attractive theory has been propounded, an ingenious technic for testing this theory has been perfected, and with what has already been accomplished in successful therapy no intelligent physician will fail to acquaint himself. Accordingly, I shall digress sufficiently to lay before you a brief, and I hope comprehensible, outline of the theory of opsonins and of opsonic therapy.

THE OPSONIC METHOD.

By the ingenious methods of Wright and his associates, Leishman and Douglas, it is possible to study experimentally, outside of the living body, the action of the blood serum called opsonic. If one takes fresh blood of man or any other common mammal and washes the corpuscles free from serum, the polymorphonuclear leucocytes will not ingest such pathogenic bacteria as the pyogenic cocci, colon bacilli, or tubercle bacilli when these are mixed in the form of a fluid suspension with the washed corpuscles and incubated 15 to 30 minutes. If, however, to this mixture of washed corpuscles and bacteria blood serum be added, the phagocytic leucocytes at once begin to take up the bacteria, and, in proportion to the opsonic power of that particular serum against

that particular kind of bacterial parasite, the number of bacteria engulfed by a given number of leucocytes in a certain period of incubation will vary. In virtue of its opsonin, which sensitizes the bacteria so as to allow the white blood cells to take them up by phagocytosis, the blood serum produces the effect just described. Against a given pathogenic microbe, as, for example, the *Staphylococcus aureus*, the serum of one individual tested by a refinement of the method just outlined will permit the leucocytes to take up an average number of the cocci, the number representing this individual phagocytic index for staphylococcus. The relation which exists between the phagocytic index of one individual and that of others presumably normal constitutes the so-called opsonic index. This opsonic index assumes practical importance because it seems to bear a definite relation to an individual's resistance against a given disease-producing microbe. With subacute and chronic infections the opsonic index is usually low for the corresponding bacterial species.

In view of the practical feature of this report which aims to present the actual clinical results which I have obtained in applying Wright's principles to the treatment of certain diseases, it will not be possible to enter further into the matter of technic by which opsonic determinations are actually made. For information on this head and for much enlightenment concerning the treatment of certain infections on the basis of the opsonic theory the full and free publication which Wright and his associates have given, during the last three years, in the Proceedings of the Royal Society, the London *Lancet* and the *British Medical Journal* should be consulted.

I have said that the opsonic theory as a theory may, like other hypotheses in biologic science, be open to question, and it would be unwise to assert that it may not be considerably modified or even overthrown by accumulating experience. Had it been the promulgation of this theory of immunity alone, with its interesting laboratory test, that ended Wright's labors, there would be less excuse for bringing it to the attention of practicing physicians. In reality, however, the *practice* on which the theory of opsonins may be said to rest is the truly valuable contribution which Wright has given to the medical world. While it may still be too early to predict the ultimate bounds which will surround opsonic therapy, there is evidence that we have come into possession of a method of treatment which opens another of the several important eras in the conquest of human disease by medical science.

OPSONIC THERAPY.

Wright has shown that by artificial bacterial autoinoculation one may increase resistance against the corresponding organism to a point at which healing of infectious processes occurs. The bare fact that immunity could be induced or heightened by the use of pathogenic bacteria or their products had been established and extended from the day of Pasteur's epoch-making studies in the bacteriology of infectious diseases; and from Buchner's day it was shown that the blood serum bore an important part in the body's combat against micro-parasites; while the rôle of the living body cell was demonstrated by the brilliant Metchnikoff. But figuratively it remained for Wright to so modify the vaccine of Pasteur as to arouse in the serum of Buchner a substance which prepared the disease-producing microbe for destruction by the phagocyte of Metchnikoff; thus

bringing to practical humanitarian usefulness the laboriously studied theories of three pioneers in biologic therapy.

In practice Wright employs small, infrequent injections of what he calls by the rather unfortunate name "vaccine," to treat the corresponding bacterial disease. His vaccines consist of an ascertained number of a suspension of bacteria which have been heated just sufficiently to kill them, and which are preserved by a chemical germicide. The vaccines are "corresponding," that is, they consist of a germ similar in species to the one exciting the disease, as *Staphylococcus pyogenes aureus* for furuncle; or, better still, they are autogenous, that is, prepared from the patient's own lesion; hence it will be seen that the practice is really a kind of artificial autoinoculation by which the microbe causing the disease is reintroduced by laboratory art. Compared with all similar essays in the direction of artificial bacterial inoculation two features of Wright's methods are prominent—the comparatively small dose and the long interval between inoculations. This may be illustrated in the case of tuberculous affections where the standard vaccine is Koch's new tuberculin (T. R.) consisting of the suspended, triturated bodies of the tubercle bacilli, the average dose 1/1000 mg., and the ordinary interval between treatments 7 days. Compare this with the gigantic dose of previous tuberculin inoculations and their daily or twice daily repetition and you will see the radical and seemingly very fundamental nature of Wright's departure.

Now by following the events subsequent to the introduction of a bacterial vaccine by opsonic evaluations, Wright and his associates show that at first a fall of opsonic index, or so-called "negative phase," ensues; to be followed by a rise, the "positive phase," generally lasting 5 to 7 days; then comes another gradual recession in the opsonic index. Symptomatically these fluctuations are also demonstrable in the constitutional depression and the aggravation of the local lesion during the negative phase, and the improved general tone and healing in the local lesion of the positive phase. An imperative rule in opsonic therapy is to not reinoculate during the negative phase, and the time of election for a new treatment is just after the positive phase begins to fall. The harm of tuberculin injections of previous practice is explained by Wright as the production of a marked negative phase by too large a dose, and its continuous aggravation by too rapid a repetition. One can verify this, and often to his sorrow, in other infectious conditions by giving too large a dose of the bacterial vaccine or by pushing a small dose too rapidly.

With this much by way of imperfect introduction to the principles and technic of opsonic therapy, I shall endeavor to elucidate further points by illustrations in actual cases treated by me or by those with whom I am associated in private or hospital practice.

PERSONAL CLINICAL EXPERIENCE.

A recital of the practical therapeutic results which have followed in various cases that I have personally treated by bacterial inoculation must necessarily take the nature of a summary, as the detailed description of any one of the more interesting cases would make a report of considerable length. Before discussing the groups into which, for convenience, I have assigned the cases, I wish to say that, while the taking of the opsonic index has not been neglected, it has not been carried out in any case with the regularity that would obtain

were my situation more favorable and assistance in this tedious work available. As a matter of fact I have had to rely quite largely on the clinical manifestations as a guide to the repetition and size of dose. With the control afforded by the more systematic opsonic determinations by which a falling of resistance is often shown before symptoms indicate it, I believe the good effects of this treatment could be increased.

STAPHYLOCOCCUS INFECTIONS.

Acne and Furunculosis.—In the first group I shall include the diseases caused by pyogenic staphylococci and mention primarily acne. In my own practice I have treated two aggravated cases of acne vulgaris of one and two years' duration, respectively, in young men. In each the staphylo-opsonic index was low at the outset of treatment and was progressively raised by the injection at intervals of 7 to 10 days of staphylococcus vaccine, in one case being the *Staphylococcus pyogenes albus* from the patient's own lesion, to be followed later by a mixture of the *albus* and *citreus*, and in the other the mixture of *albus* and *citreus* also from the individual's own pustules. In the first patient eight injections have been given and a steady improvement amounting to almost complete cessation of the acne has resulted. All the old brawny, sluggish, indurated nodules have ceased to appear, the seborrhea has given way to a smooth, soft, pliable, non-oily skin, and with these local changes the patient's tone has improved, an excellent appetite has replaced a capricious one, and a gain of five pounds in weight in six weeks has followed, all of this with no other local or general measures. In the second case six treatments have changed a most repulsive case of indurated acne of the face into one with sparing superficial pimples, with a disappearance of black-heads and grease, to be replaced with a soft, clear skin, giving the whole face a new and clean complexion. This patient now seems to have reached Wright's "high tide of immunity," for improvement has been steady since the last injection, three weeks ago, and the previously fluctuating opsonic index now has a high and sustained point. Several patients with acne, including one with an obstinate acne rosacea, have been treated with vaccines of my preparation, and under my direction, by a prominent local dermatologist, with complete recovery or very marked improvement in all. It was this specialist who first called my attention to the simultaneous improvement in the seborrhea during the progress of the acute treatment, a most surprising feature of which is the spontaneous bodily extension of the comedones after an inoculation.

Impetigo.—In one case of obstinate impetigo the *Staphylococcus pyogenes aureus* and a streptococcus were obtained by culture from one of the pustular lesions. The staphylo-opsonic index was low, that for the streptococcus was the same as of a control serum. One dose of the staphylococcus vaccine brought the pustules to a standstill, a dose of streptococcus vaccine was given at the end of a week, with the result that the impetigo absolutely ceased. In a second case of recurring impetigo contagiosa of 14 months' duration, two injections of the autogenous *Staphylococcus pyogenes aureus* have brought the pustules to an end.

Chronic Furunculosis.—My first patient with furunculosis was my 2-year-old baby girl in whom a staphylococcus infection of mosquito bites on the scalp produced a series of large pustules, one after another of which I incised until the procedure became a severe trial for the patient and myself. For six weeks these boils continued to appear on the scalp, and when I finally concluded to

use the vaccine which had been prepared from the *Staphylococcus pyogenes aureus* isolated from one of the early furuncles, one large boil was present on the side of the head, two on the abdomen in sites not previously the seat of mosquito bites, and one very large so-called "blind boil" on the pudendum. All these were incised and the first and only dose of vaccine injected. The incised boils suppurated freely the next day and the child was quite indisposed, but on the second day the supuration ceased. On this day, too, a bright lively revival of spirits and improved appetite appeared and continued, and from that day, last midsummer, to the present the child has had no sign of a furuncle.

Another case of chronic generalized furunculosis of two years' duration has been brought under control by three weekly doses of *Staphylococcus pyogenes aureus* vaccine, the first from a stock vaccine and the two later of autogenous origin. The disappearance of the last boil has now occurred and I predict that one or two more injections will effectually and finally rid this man of his trying affliction. Similarly a case of recurring furunculosis in a physician has been brought to a standstill by two artificial autoinoculations of the *Staphylococcus pyogenes aureus*.

Furunculosis and Axillary Adenitis.—Another of my early staphylococcus cases was one in which a boil appeared on the anterior border of the left armpit, and was fully developed when I first saw the patient, an adult man. Incision and careful antiseptic dressing were practiced, but in two days a second boil appeared in the lower portion of the axilla, accompanied by an enlargement of several contiguous axillary glands. In spite of careful surgical treatment, the infection of the glands progressed until two had suppurated and had been incised; then a well-developed axillary adenitis with the usual mass of tender, indurated, confluent glands, developed, and it was clear that the issue was a total extirpation of the infected mass or intervention with inoculation. The first dose of a stock *Staphylococcus pyogenes aureus* vaccine brought the adenitis to a check and three glands hastened to suppuration, became superficial, fluctuated, and were easily evacuated. A second dose after six days, this time of the autogenous aureus vaccine, promoted the resolution of the infected glands, and at the end of the second week, when the third and last dose was given, the whole indurated mass had melted away and a complete and perfect recovery was effected—all of this with the patient reporting personally for treatment and losing but three days in his employment.

Palmar Abscess.—Closely allied to the foregoing in its surgical significance was a case of palmar abscess in a man who reported to his physician with the hand and forearm greatly swollen; a deep abscess in the center of the palm and much constitutional disturbance. Two injections of antistreptococcic serum had produced no further effect than to lower the temperature, and the attending physician made a small incision in the palm and brought me some of the pus in a sterile syringe. Immediate smears from the pus showed staphylococci, and the first dose of stock *Staphylococcus pyogenes aureus* vaccine was given to the medical attendant who injected it. A halt in the process began in 24 hours, and in three days the improved general condition was accompanied by a reduction in the swelling. From the pus *Staphylococcus pyogenes albus* in pure culture was obtained and a vaccine prepared; on the fourth day a dose of this was injected. The improvement became more pronounced, the suppuration more superficial, and an incision 1½

inches in length, extending the original one, was all that was required. Two more doses of the autogenous vaccine at intervals of a week completed the perfect cure of this infection, with solid closure of the incision, a hand of its original functional perfection, and a splendid gain in general health and spirits. The full significance of this and the preceding result will be best appreciated by the surgeon of large experience who knows palmar abscess and axillary adenitis of the type I have described from the standpoint even of the best aggressive surgery.

Staphylococcic "Psoriasis."—Before dismissing this necessarily hurried account of staphylococcic infections I wish to recount one of my latest experiences which is so unusual in its results as to call for a special and detailed account, although it comes in a group of results all of which are truly astonishing, judged by any previous therapeutic standard. I refer to a case of what was designated by a prominent Detroit dermatologist, who had the woman under treatment twelve of the eighteen months of the disease, as psoriasis, but which I am now prepared to pronounce a most extraordinary staphylococcic dermatosis. At the time I first saw the patient, some five weeks ago, at least one-third of the entire cutaneous surface of the body was involved and of so aggravated a type as to make her a physical and nervous wreck. The immense confluent lesions on the arms, legs, breast, back, sides and buttocks were slightly raised above the unaffected skin, of a dull red color, and covered with large thick scales reminding one of a piece of plate gelatin. Each night, and often twice daily, the woman anointed herself with olive oil and went through the trying operation of pulling off these scales, which, she asserted, would cover a newspaper, and which often left bloody, denuded surfaces exposed. A constant sensation as of a flame against the skin was suffered, and often an intolerable itching, so that sleep of more than an hour's duration had not been possible for months; and with no relief during the day it is little wonder that the victim was on the verge of complete collapse when I first saw her. Movement of the arms or walking were most painful because of the cracking and erosion of the crusted limbs. Besides these confluent areas there were numerous discrete lesions on the limbs, trunk, face, and scalp. The remaining skin was dry and harsh and did not perspire. The hair was coarse, dry and lusterless.

With the evident subacute inflammatory nature of the affection as a ray of hope, I excised completely, with aseptic precautions, one of the discrete lesions on the arm and planted it on glycerin agar. The next day I was rewarded with a pure culture of *Staphylococcus pyogenes aureus* against which I found the patient's opsonic index low. A vaccine from this culture was at once prepared and injected. That same night the patient slept two hours consecutively and the skin broke out in a mild perspiration. The next day the burning abated at intervals and the itching lessened. At the end of the first week a remarkable improvement in the diseased skin was apparent and the physical and mental status of the woman greatly bettered. On the occasion of the last treatment, just six weeks from the time of the first examination and the event of the fifth injection of the staphylococcus vaccine, both the confluent and discrete lesions of the arms and legs had given way to a normal-looking skin covered with delicate fluffy scales, and the only evidence of the original fearful condition were two narrow, slightly elevated, reddened crescents under the breasts. The woman, whose appetite had at once improved, had been placed on a generous mixed diet to

replace the restricted one previously prescribed, she had gained five pounds in weight, her strength and spirits had revived, she slept comfortably all night, her skin had become moist, soft and pliable, and her hair soft and oily and with renewed luster. One additional point of interest was elicited in the previous history—that is, that the forerunners of the dermatosis were a boil on the wrist, one behind the ear, then a crop about the genitals, to be followed first by the discrete and later by the confluent dermatosis.

COLON BACILLUS INFECTION.

Cystitis and Pyelonephrosis.—My primary experience in treating a colon bacillus infection by artificial auto-inoculation has been most satisfactory. The patient was a retired physician afflicted with a chronic tabetic neurosis and consequent palsy of the bladder, followed by infection of the bladder and the usual ascending urinary infection, producing a cystitis and pyelonephrosis of three months' duration. The ordinary lines of medical treatment had failed to bring relief, and the patient was bedridden, emaciated and profoundly septic, with the usual train of anorexia, constipation, vomiting and prostration. The urine was foul in odor and loaded with thick, greenish-yellow, gelatinous pus. Chills, a daily temperature of 103 F. and profuse night sweats were established. The right kidney was plainly palpable and on its ventral surface one could feel a mass as large as a lemon, tender and apparently representing the dilated urinary pelvis. According to precedent, such a case would, of course, be pronounced as incurable, and except from the standpoint of endeavoring to make the remaining existence endurable would be abandoned. From the pus in the urine I obtained abundant bacilli in smears and a pure culture of what was identified as colon bacilli of the usual type. Against this bacillus the patient's phagocytic index was one-third less than that of the phagocytic index of a normal person's serum; that is to say, his opsonic index was about two-thirds the normal. The usual preparation was made from the bacillus obtained from the urine, and artificial autoinoculation at intervals of five to ten days, five doses in all, increasing in size, was practiced. The opsonic index rose in a pronounced manner, but as a strongly agglutinative effect also developed in the patient's serum I am inclined to question the validity of some of the later opsonic determinations, for it was quite impossible to check the rapid clumping of the bacilli by the serum and their consequent ingestion *en masse* in the leucocytes. This, however, is less significant than the improved local and constitutional conditions of the patient. After the first inoculation his temperature never rose above 100 F. After three days his chills and night sweats ceased, not to reappear. The character of the urine changed during these first few days, the pus became less abundant, thinner and not so coherent, and the foul odor disappeared. From the first injection the improvement has been progressive except for several gushes of putrid pus, evidently representing the emptying of pyelonephric abscesses. The right kidney speedily lost its tenderness and the tumor on its surface disappeared. It is now seven weeks since the last treatment. The patient is about the house, his appetite is excellent and he has gained in weight, strength and spirits. The urine at the worst contains but a small amount of thin pus, and ordinarily is clear. Indeed, were it not for his neurosis with its painful crises he would be pronounced as practically recovered. We have stood in readiness to give

additional inoculation, but since the last one the gain has been so steady as to make further treatment superfluous. Evidently what Wright calls the "high tide of immunity" has been established.

Mastoid Fistula.—In a case of mastoid fistula of three months' duration, a single injection of a vaccine from a colon-like bacillus isolated from the pus effected complete and permanent closure of the fistula in a week.

PNEUMOCOCCUS EMPYEMA.

A single example of empyema is all that I have thus far had opportunity of treating, and were it not that the result duplicates those reported by Wright and his followers in a number of similar cases, including some advanced to the chronic unhealing stage, I would not at present report it. The patient was a 7-year-old girl who had a severe atypical pneumonia, with lysis at the end of a week. For ten days after the temperature remained between 99 and 100 F. and then rose to 102 F., accompanied with some dyspnea and pain in the right chest. Three days after this rise in temperature the attending physician found dulness in the right lower chest and on exploratory aspiration obtained a thick pus in a sterile glass syringe. On my suggestion the poor practice of making a very small intercostal incision and inserting a very small drainage tube was at once instituted, with the evacuation of some eight ounces of thick pus, but no expansion of the lung, evidently indicating a sacculated empyema. The next morning the pus was brought to the laboratory, smears showed a diplococcus, and by the following day I had isolated the pneumococcus, from which a vaccine was prepared. Three days after obtaining the pus I visited the patient and gave the first inoculation of the autogenous vaccine. I found her much emaciated, weak, fretful, with a hectic look, a temperature of 100 F., pulse 120, and a profuse discharge of thick pus into the voluminous dressing. Four days later the attending physician reported a pronounced improvement, the appetite had returned, strength increased, the discharge steadily diminished until it was scanty and thin, sero-purulent in character, and the small drainage tube had been pushed out by the expanding lung and could not be re-inserted. On the fifth day only a small quantity of serum oozed from the opening against which the pleura had appeared. A second inoculation was then made. On the seventh day the wound had entirely closed, the little girl was eating splendidly and had gained in flesh and strength, with no pain or fever. That gain has been uninterrupted to the present time, five weeks since the second treatment. In other words, a perfect recovery of a sacculated empyema was effected in seven days by small puncture, evacuation of the bulk of pus, small drainage, and artificial autoinoculation with the infecting pathogenic bacterium. And from what I saw of this case I am of the opinion that the still more unwarrantable practice (according to previous standards) of aspiration of the pus would have been fully effective when reinforced by opsonic therapy.

TUBERCULOSIS.

Because of some delay in obtaining Koch's tuberculin R., which at present forms the standard vaccine for treating tuberculous diseases, my efforts in this direction have not yet progressed to a point at which more than a preliminary report can be made. In fact, it has been impossible, from lack of time and the opportunity of making the proper opsonic tests, for me to go extensively into this very inviting field. In two cases negative results

followed my use of tuberculin injection after Wright's dosage; one of advanced pulmonary tuberculosis and extensive intestinal ulceration where, after a gain in appetite and improvement in the febrile curve following the first injection, the patient progressively declined to the end, with no gain from the following two injections. Another case diagnosed as probable abdominal tuberculosis, but more likely an example of a malignant abdominal neoplasm, was, because of the low tuberculo-opsonic index, tentatively treated with a combination of tuberculin and colon bacillus vaccine. A short and very surprising gain in general and local conditions gave way and death followed in a month.

Urinary Tuberculosis.—A case of urinary tuberculosis in which the pneumococci and tubercle bacilli are present in the pus has been treated with mixed tuberculin and pneumococcus vaccine for some two months, with progressive betterment, a gain in weight and lessened pyuria.

GONORRHEAL AFFECTIONS.

With one class of diseases I believe, from all I can learn, that my experience has been unique, that is, with the affections caused by the gonococcus. If my information is correct Wright has steadily predicted that gonorrheal infection would yield to opsonic therapy, but because of the difficulty in making a suitable vaccine he had not, at least to last midsummer, advanced in this line of work. Perhaps, with some element of chance, it has been my fortune to obtain a strain of gonococcus from which a standard or stock vaccine was prepared which has given some very encouraging results in the treatment of certain forms of gonorrheal infection. I say particular strain because several other strains rendered available to me on account of my special work on the gonococcus, including in two cases the autogenous ones, that is, those from the patients' own secretions, have failed to give the satisfactory results obtained by the one I am using.

Balanoposthitis.—My first test was made early last summer in a case of balanoposthitis and gonorrheal urethritis of eight months' duration, with the usual picture of an immensely swollen and phimosed foreskin and a thick scar-like preputial orifice. On the second day following an injection of the gonococcus preparation the swelling began rapidly to subside and by afternoon the patient reported with the foreskin retreated, the glans clean and free from redness or pus, and the urethral discharge much diminished. He stated that this was the first glimpse of the glans penis that he had had for eight months. Four succeeding injections brought a check to the urethritis and at last account the patient was well.

Double Epididymitis and Perineal Fistula.—Another example of the rapid, specific action of the gonococcus vaccine on the inflammatory complications of gonorrhea was a case of urethritis of six weeks' duration, complicated with a proctitis of three weeks' standing, a double epididymitis for eight days and a forming periurethral abscess. A more miserable individual than the young man with these lesions and a two hours' torture after each urination, a severe backache and general depression would be hard to find. Within twenty-four hours from the first injection of the gonococcus preparation all pain on urination and all backache had left, the swelling in the epididymal tissues had subsided so rapidly as to cause a "crawling sensation" from the retracting dartos, the periurethral abscess had broken, leaving a perineal urinary fistula. Following these events the patient's

appetite returned and became insistent and he began a gain in flesh that has to the present time increased his weight beyond anything heretofore normal, amounting to 9 pounds since the inoculations were begun. Four subsequent injections at weekly intervals have been given, and no other treatment; the proctitis disappeared during the first week, absolutely no induration remains in either epididymis, the perineal induration has disappeared; the urinary fistula has closed, and the urethral discharge has almost completely subsided.

Subacute Epididymitis.—Within the week I have treated by the same method a left-sided gonorrheal epididymitis of a month's duration, as large as a hen's egg, much indurated and exceedingly tender. In twenty-four hours after inoculation the mass had begun to reduce in size, was softer and much less tender. In forty-eight hours all the swelling of the epididymis had subsided except an induration limited to the caput, and by the third day this had departed and the patient's general condition was so excellent that he was discharged from the hospital and will report personally for further inoculation.

As to the significance of these results which I believe are but typical of what can be accomplished in subacute and chronic gonorrheal inflammations by the use of an effective gonococcus vaccine, comment is unnecessary among physicians who have handled these complications by any previous method, including even the use of passive hyperemia or puncture in the treatment of gonorrheal epididymitis.

Gonorrheal Rheumatism.—That a further field of great usefulness is in store for opsonic therapy in gonorrhea is my belief from my experience in treating two cases of gonorrheal polyarthrititis, or so-called gonorrheal rheumatism. In one of these patients the infection had existed four months and involved several joints. Progressive betterment of the arthritis with departure of the swelling, pain and immobility was effected by four injections when the patient considered himself cured and has no longer reported. In another instance the man was almost a helpless cripple with a gonorrheal arthritis of four years' duration involving both wrists, both shoulders, one elbow and one knee, all the affected joints being immovable or of very restricted mobility. The usual symptoms of pain, sleeplessness, cold sensation, cold sweats and physical and mental depression were in evidence. Five injections at weekly intervals have worked a most surprising improvement in this man's condition. Practically all swelling and thickening of the joints have subsided, and all are now freely movable, the range being normal except for the left wrist. Along with the gratifying local improvement there has been a practical cessation of joint pain, good restful sleep undisturbed by chilly sensations or sweats, a progressive improvement in appetite and a steady gain in weight, and with all this a revival of spirits and a physical activity very pleasant to witness.

Gleet.—In one case of long-standing gleet the discharge ceased apparently permanently after three injections; in another after four weekly doses the diffusely purulent urine has cleared, the threads have almost vanished, and in both these patients a greatly improved general tone with increased appetite and weight has followed the treatment. In my only case of subacute uncomplicated urethritis I have not succeeded in entirely checking the discharge, though this patient, too, has gained in flesh to exceed his usual weight in health.

Ophthalmia, Conjunctivitis, and Vaginitis.—In two cases of gonorrheal ophthalmia, two inoculations in each instance sufficed, with the coincident local treatment, to effect a perfect recovery, which was hastened in a manner very surprising to those who witnessed it. So also an example of gonorrheal conjunctivitis of several months' duration has responded with complete disappearance of all conjunctival injection during the positive phase, to reappear as soon as this stage subsides, making the case one of the most striking symptomatic demonstrations of opsonic fluctuation that I have seen. Gonorrheal vaginitis in two little girls yielded to two inoculations each which reinforced the irrigation treatment.

In emphasizing my unusual experience in handling gonorrheal diseases I would lay particular stress on the fact that no other therapeutic measure was used in any of my personally treated cases except the stretching of a stricture in the worst example of gonorrheal arthritis. Because of my inconvenient situation it has not been possible to bring to the aid of the inoculation such other procedures as irrigation, sounding or what not, commonly practiced in the treatment of gonorrhea, and, of course, for the best results, particularly for handling the urethral discharge, such measures probably should be used in conjunction with the gonococcus vaccine. Nor have I been able to make a sufficient number of opsonic indices to furnish this additional guide in opsonic therapy. Still it is clear that therapeutic effects have been obtained entirely beyond anything heretofore possible, and these by the use of small, non-painful, simple subcutaneous injections at weekly intervals.

CONCLUSION.

In dismissing this account of my personal experience with Wright's method of treatment I will say that if the therapeutic results which have been presented were based solely on my own work I would not have the courage to make them public at this time, when but six months have elapsed since my first clinical experiments began. But because they duplicate the published reports made by Wright and his followers in England in connection with the various groups of infections except the gonorrheal, and since they correspond with the reports brought to the United States by those who have visited Wright's laboratory, I am somewhat less diffident.

Moreover, I believe the adoption of opsonic therapy in this country depends on the promulgation among practicing physicians of the actual clinical achievements, and this as speedily as accurate observation shall warrant; and it is my conviction that a method of practice with such vast humanitarian possibilities should be brought into the possession of the medical profession without delay.

Finally, from what I have already seen, which is tempered by a rather extensive experience in private and institutional medical work, I am prepared to assert that with the proper artificial autoinoculation we can obtain constitutional and local improvement in many subacute and chronic infections entirely beyond anything previously possible in medicine. And I am personally assured that in these bacterial inoculations we possess therapeutic agents of a specificity and potency exceeding anything heretofore employed in the treatment of disease except possibly the antitoxin of diphtheria.

ACCURATE MODIFICATION OF MILK, SIMPLE AND PRACTICABLE.*

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Accurate modification of milk involves the calculation of definite percentages of fat, mixed proteids, caseinogen, etc., for mixtures of cream and milk and of cream and milk and whey. The necessary operations are expressed most conveniently in algebraic equations.

Of the merits of percentage modification, the American method of preparing cow's milk for the infant, it is sufficient to say that it provides the instrument of precision; for this reason alone, if there were none others, it is desirable that it should be established on the mathematical principles which it involves and on which it depends. If formulas are employed to determine the required quantities of materials, they should accord with these principles and with the chemical facts; they should be accurate, also, and adequate. None of the published formulas meets these requirements; and generally accepted statements on the subject of the calculation and the preparation of percentage mixtures are, in certain important respects—practically important—misleading: As the formulas to be presented conflict with, or disregarded some of them, their integrity can not be established without reference thereto; moreover, in the absence of error or misconception, there would be no reason—no excuse—for further contribution to this part of the subject.

It is generally understood, for example, that a variety of creams, creams of different strengths, is essential to accurate and adequate modification of milk. What are known, respectively, as 8 per cent., 10 per cent., 12 per cent., 16 per cent. and 20 per cent. cream are commonly employed; directions are given, accordingly, for obtaining these creams by gravity, together with tables that show their proteid and sugar percentages, which are different for each variety of cream, and are differently given by different authors; other tables that show the limitations in the percentages of fat and of proteids that are obtainable by the use of creams of different strengths; others that show the percentages of the food-elements that are reciprocally obtainable, and still others by which the choice of the creams to be employed for particular modifications is directed. Under these conditions, confronted at the outset by these tables, the apparent necessity for the use of a variety of creams, ranging from 8 per cent. to 32 per cent., of which each must be computed by a slightly different equation, it is not surprising that one unfamiliar with the percentage method and mathematical formulas, should find accurate modification impracticable in advance.

But while all these factors may be employed very few of them are essential, either to the statement of the problem, or to its solution. A variety of creams is not only unnecessary, but undesirable, because of the confusion to which it gives rise; and of all the facts recorded in these tables, as factors, knowledge of two only is required, for practical purposes: (1) the analysis (the fat, proteid and sugar percentages) of cow's milk, (2) how to obtain adequate cream, a single variety of adequate cream, by gravity.

Of the published formulas, the series proposed by Dr. Westcott¹ in his admirable monograph are the only ones

[FOR THE DISCUSSION SEE PAGE 639.]

* Read in the Section on Diseases of Children of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.
1. Scientific Milk Modification, Internat. Clinics, Series 10, vol. III.