

company much difficulty was experienced in going to sleep. Therefore, our conclusions are that in this case the motor branch of the fifth nerve was excited in sympathy with sexual excitement; pressure upon the individual teeth was intensified by irregularity in the conformation of the arch, and this irritation was communicated to the sensory portion of the same nerve, with the usual painful result. Instead of grinding I have for some time past tied a piece of rubber dam, over the crown of one of the unaffected teeth so that the jaws can not be brought tightly together. Relief is complete after a few hours, or if applied in the night, next morning the rubber can be removed and the difficulty is completely averted for the time.

Case 4.—Mr. —, much annoyed with slight tinnitus aurium on left side. No evidence of local oral or Eustachian trouble, as testified to by several aurists. Teeth much abraded. Has been much relieved by treatment and grinding off crown surfaces of several teeth.

An occasional slight return of his aural trouble is generally relieved by removal of some occluding portion of the left superior central incisor, which seems to be particularly in sympathy with the ear at this time.

Case 5.—I have under my care at present a woman of about 40, whose incisors are worn almost beyond recognition; tendency to intense mental excitement upon slight provocation, particularly on subjects of politics, dress reform, etc., exists. She suffers from a difficulty of the right inferior extremity, threatening at times loss of sensation and motion.

After typhoid fever or other unusual drain upon the natural forces there seems to be a tendency to develop this habit of the jaws, and in many instances pain in the head and face had been relieved in my practice, by removing the possibility of continued irritation in the manner before described.

The fact that there is seldom soreness on percussion of such teeth, makes diagnosis frequently difficult and doubtless accounts largely for its not having been considered, as it should have been, as a diagnostic indication, but the surfaces of fillings, abraded crowns of teeth, or a dulness of sound on tapping with a metallic instrument will often serve to indicate in the absence of other and more marked symptoms of peridental inflammation.

A frequent complication from this habit, is pyorrhea alveolaris for which condition I have over and over again relieved the discharge about the necks of teeth and have hastened the retightening process of those loose in their sockets, by grinding them down to relieve unusual force in occlusion; its very common association with tenderness and pain following the process of devitalization of pulps, should make its consideration far more frequent than has hitherto been the case. Therefore, in the field of medicine, as a symptom of some neural disturbance of kinetic function or the direct excitant of some pathologic condition, the study of any abnormal activity of the muscles of the jaw is without doubt of far greater importance than is generally realized.

THE LIMITATIONS OF SERUM THERAPY.

BY JOHN MADDEN, M.D.

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A review of the literature of serum therapy of the last two years is likely to produce some confusion. In the light of what has already been shown to be true, much elaborate experimentation seems to have been purposeless and final failure might have been foretold at the beginning. One of the prime causes of much misunderstanding is the failure to discriminate between the production of immunity from a disease and the production of resistance against a disease toxin. There is a wide difference between the two processes and the probable manner by which they are

brought about. In the former some change, the nature of which is not understood, has been produced which makes the body unfit as a culture medium for the growth of a particular bacterium and the consequent development of its special toxin. Ten years ago Buchner showed this substance to be an albuminous body which could be removed from the blood serum by dialyzation, and that it is the product of some unknown chemic reaction brought about by bacterial growth.

More recent investigations tend to show that a bactericidal substance resides in the granular matter of the leucocytes (Kanthook and Horry, Philadelphia Transactions, clxxxv, 1894; Vaughan and Novy, "Pto-maines and Leucomaines," 1896; Hankin, *Centralb. für Bakteriologie*, xii, and Mueller of Vienna, *Centralb. f. Allg., Pathologie und Patholog. Anatomie*, viii, 1896), and that these granules leave the white corpuscles and float free in the blood stream where they have the power of lessening the vitality of bacteria or destroying them altogether. In inflammatory diseases, such as pneumonia, pleurisy, rheumatism and erysipelas, there are an increased number of white corpuscles in the blood stream as well as a marked increase in the fibrinogen and serum-globulin (Halliburton, "Chemical Physiology and Pathology," pp. 306-7). It might therefore be assumed that here is an indication of disease producing its own antitoxin, and that when a sufficient number of white corpuscles are produced to destroy the invading bacteria the disease shall cease.

The problem, however, is by no means as simple as this. If the immunization or cure of a bacterial disease depended alone upon the mustering of an army of leucocytes sufficiently large to overcome and destroy the invading germs, then we should be able to show that the injection of anti-diphtheritic serum really increases the number of white corpuscles and that the subject is immune, not only from the Klebs-Loeffler bacillus but from invasion by all other bacilli as well. We should be able to show that vaccination with the kine pox permanently increases the number of leucocytes in the vaccinated subject and that he is rendered immune against all other bacteria forever.

As a matter of fact, however, when immunity is produced by an attack of bacterial disease or by inoculation in a modified form, that immunity is produced only against a subsequent attack of the same disease. It is clear, therefore, that the problem is a chemic one and that if the immunizing substance resides in the granular matter or if discharged from it, its chemic constituents must depend upon the disease against which the subject has been rendered immune.

If the chemic composition of the antitoxins thus produced were known as well as that of the toxins, the way would be paved for an exact knowledge of what might be expected as a result of applying antitoxin for the purpose of curing bacterial diseases; but so long as this remains unknown antitoxin therapy is liable to be more or less empiric.

It is well established that the changes produced in the blood serum by the development of an antitoxin is either for a time or permanently persistent. It also seems likely that the amount of antitoxin produced in each case is in direct ratio to the amount of toxin. This is well illustrated in vaccination with kine pox, in which the production of several well developed pustules attended with considerable febrile

reaction is usually followed by complete immunity against smallpox or against another vaccination. A very mild attack of scarlatina, measles, smallpox and some other eruptive fevers are sometimes followed by a second invasion. Furthermore, in such diseases as are followed by only temporary immunity against subsequent attack, the more severe the attack the longer the immunity if personal peculiarities are eliminated. If this be true, it may be concluded that the antitoxin results from a reaction between the toxin and some albuminous constituent of the blood serum, not that the toxin makes a definite chemie compound as if it were an acid radical and the serum constituent a base, but the toxin is responsible for bringing the change about.

Granted, then, that the antitoxin is produced, it may act in two ways to effect a cure, by making further bacterial growth impossible or by combining with and neutralizing the toxin as fast as it is produced, until the bacteria cease from lack of pabulum to be virile. Indeed, it may be that the cell protoplasm, constantly bathed in the antitoxin serum, is in some unknown manner changed so that the toxin contact is no longer harmful and is eliminated without disease symptoms.

The next question is: Do all bacterial diseases produce an antitoxin? It is reasonable to conclude that in the self-limited bacterial diseases like diphtheria, typhoid, yellow and other eruptive fevers, a peculiar substance is produced which gradually increases and is persistent in the serum and acts as a remedial agent in some way similar to that indicated above. Is this self-limitation due to the production of the antitoxin? When more is known of the bio-chemistry of bacterial diseases this question will probably be answered in the affirmative. A powerful argument in favor of this answer is that bacteria will develop as long as a suitable culture medium is offered for their growth. Those taken from an old culture medium, the pabulum in which is almost exhausted and which shows very little vitality, become virile when transplanted into a new and favorable culture medium. With the tissue changes constantly going on in the body, even in disease, the blood serum is tolerably constant in its chemie composition; so we may conclude that the self-limitation is not due to the exhaustion of the culture medium in the involved subject. To further support this view, the tubercle bacillus and other bacteria may lose their virility by exhausting the pabulum of an artificial culture medium, while in the body they are virile during the life of the invaded subject, the culture medium showing no change detrimental to their growth.

The question whether an antitoxin may be produced without the intervention of the bacterium is not definitely settled. In 1887 Salmon and Smith succeeded in rendering doves immune against hog cholera by injecting the artificial culture medium freed from bacilli by filtration. Many other similar experiments have been carried out; but what warrant is there for saying that this substance contains the toxin of the disease alone? In the absence of exact chemie knowledge it might be assumed that, even in an artificial culture medium, there are antitoxins as well as toxins generated, and that by injecting the exhausted culture medium, the subject received both the antitoxins and the toxins, retaining the former and eliminating the latter, as is done in the course of disease. Here the presence of an antitoxin might easily escape notice in the overwhelming

symptoms of poisoning produced by the toxin, if equal amounts were injected at the same time. Indeed, the antitoxin might be present in quantities much larger than the toxin, and, as far as its physiologic manifestations are concerned, entirely escape notice. As far as our knowledge is concerned all immunity produced by the injection of toxins may have been produced by the unnoticed antitoxins present.

We will now consider bacterial diseases which are not self-limited: tuberculosis, syphilis, leprosy and the like.

Do they produce an antitoxin? If so, why are they then not self-limited? There is no evidence that any of these diseases produce an antitoxin. The fact that they are not self-limited is a powerful argument against that hypothesis. If an antitoxin is produced by any of them, it is certainly different in all respects from that produced in the self-limited diseases, being insufficient in quantity, potency or persistency to produce any good result. When chemistry has mastered those complicated problems relating to the changes in the blood serum, produced by bacterial growth, we shall know why this is true, but for the present we must assume that the production of antitoxin in those diseases is an impossibility.

Certain animals are partly or wholly immune from particular bacterial diseases. The rat can not be inoculated with anthrax, the cow takes smallpox lightly and the horse is immune from tuberculosis. In some instances the blood serum of the immune animal will destroy the bacillus of the disease against which it possesses immunity, as in the case of the serum of the rat against the anthrax bacillus. In view of this fact, the question arises, whether the blood serum of an animal already naturally immune can be given greater bactericidal powers by injecting into the blood current the toxins of the disease against which it is immune? It can only be said that what evidence we have entirely supports the negative. The sheep and horse are both very susceptible to diphtheria and inoculation with the diphtheria bacillus produces a large amount of antitoxin. Shall we say that in exactly opposite conditions the same result would be had? Shall we say that the horse, immune against tuberculosis, a non-self-limited disease, will therefore yield a valuable anti-tubercular serum when injected with the toxins of tuberculosis? Certainly this is absurd; yet it is just what has been done during the last two or three years, by two or three men who have obtained considerable notoriety and profit. It certainly involves the heights of credulity to believe that the serum of an animal immune against a disease is rendered valuable, as a remedial agent for the same disease, by injecting it with the disease toxin without producing an antitoxin.

After the disastrous experience of a few years ago with Koch's tuberculin, it is not likely that any form or modification of the toxin, produced by the tubercle bacillus, will gain the confidence of the medical profession as a remedy for the disease. Tuberculin never did more than cause the breaking down of certain involved cell groups whose protoplasm was already surcharged with the poison. Under whatsoever modifications it may be used, it can never be of any value beyond an aid in making a diagnosis of tuberculosis.

As to the production of a resistance to a poison, that is quite a different matter from producing immunity, be the poison a disease toxin or something

else. Narcotic and other poisons may be taken in gradually increasing doses until an amount many times a poisonous dose, in the first instance, is readily tolerated. This means nothing more than that a resistance against that special form of poisoning has been established. Experiments of this kind have no value in serum therapy. It is quite likely that one might begin with a very small dose of some disease toxin, like that of tuberculosis or diphtheria, and by gradually increasing the amount exhibited, a resistance would be established which would make the injection of large quantities of the poison possible, but this is not immunity. The resistance would be speedily lost with the withdrawal of the poison, while a true immunity would persist for a longer or shorter time or permanently. The work of Calmette in establishing a resistance to snake poison is classed with serum therapy by some, but as a matter of fact it has nothing to do with serum therapy, unless it can be shown that these inoculations actually produce an antitoxin which renders the subject immune for a considerable time after the inoculations have ceased.

Referring again to the use of immunized horse serum for the treatment of tuberculosis and the favorable results reported, it is quite probable that all the benefits received by the patients subjected to the treatment were due to the serum itself and not to any added value it possessed by reason of the animal having been inoculated with tubercle poison. A Spanish physician, in Barcelona, reports good results from the injection of plain serum in cases of faulty nutrition in children. Indeed, the results reported are quite beyond belief. Its exhibition was followed promptly by an increase of the number of red corpuscles and a gain in weight. He also reported the cure of sixteen cases of chorea in an average of fifteen days, with the serum.

In conclusion it would seem, in the light of our present knowledge, that serum therapy is of value only in those diseases in which it produces an antitoxin and that an antitoxin is produced only in the self-limited diseases.

32 and 33 Sentinel Building.

PROLONGED GESTATION, ACRANIA MONSTROSITY AND APPARENT PLACENTA PREVIA IN ONE OBSTETRICAL CASE.

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The following case, on account of its unique character, will probably be of interest:

About the middle of April, 1897, Mrs. F., 4-para, age 34, engaged me to attend her in confinement which was expected about July 1, 1897. When questioned, she told me her last menstruation occurred September 4, 1896, but did not indulge in sexual intercourse until two days before her next expected menstrual period, or September 30, and that she had not copulated for two months before this period and not at all afterward. Accepting these statements as facts, she should have fallen in labor about July 6, 1897. On June 20, I was summoned to her on account of a "severe period" coming on. Upon arriving at her home and making careful inquiry, I was told that two months before she had passed considerable blood and each time there was very little pain. A vaginal examination showed cervical dilatation to be practically *nil* and hemorrhage decided. Taking everything into consideration, it was decided to be a case of placenta previa. After concluding to dilate and deliver at once, the patient was ordered absolute rest, foot of bed ele-

vated, cool drinks, etc., until an assistant could be procured. The patient when informed of what was proposed to be done strenuously objected and argued that she recovered all right from the attack of bleeding she had two months before and preferred to wait and see if she did not recover from this one. All my persuasion and instructions regarding the dangers of such a course were in vain. The next day when I called the patient was up and walking around the house as though nothing had happened. She was informed that she should send for me at once when the first evidence of her falling in labor occurred as it was then almost due. Nothing more was heard from her until Aug. 5, 1897, when the messenger announced that Mrs. F. had fallen in labor. Upon arriving at the patient's bedside and after thoroughly sterilizing my hands and arms, investigation showed labor well advanced with normal implantation of the placenta. To my surprise and relief, practically no blood was lost before or after delivery, but the child proved to be a monstrosity of the acrania variety. (For an almost exact picture of the monstrosity see cut on page 97 of "J. Lewis Smith's Diseases of Children" 7th Edition.) The vascular exposed mass looked as though it had been bleeding and had been partly covered by a very thin membrane. Probably less than one-half of the brain matter was present. In other words, if a plane had been passed from a point one-half inch above the supra-orbital ridges to the occipital protuberance it would cut off about as much of the brain matter as was absent in the child under consideration. The baby nursed naturally after the first day, but succumbed on the third day.

The first thing to engage our attention is the apparent prolonged period of gestation which, if the woman was not mistaken, was 305 days. We appreciate the fact that all histories regarding time of supposed conception must be accepted with considerable doubt, but, after questioning and requestioning the woman she would invariably tell me she absolutely knew there was no mistake. Inasmuch as several cases have been reported, from perfectly reliable sources, of much longer periods of gestation than this I simply bring out this feature of the case on account of the history seemingly being genuine. In one case, reported by Maur, gestation was believed to have lasted 334 days.

It is quite interesting to read the history of the theories as to the causes of these teratologic objects before the causes were analyzed and considered, from a scientific standpoint. Ambroise Paré,¹ says, "therefore, in times past there have been some, who nothing fearing the Diety, neither Law nor themselves, that is their souls, have so objected and prostrated themselves, that they have thought themselves nothing different from beasts: wherefore atheists, Sodomites, outlaws, forgetful of their own excellency and divinity, and transformed by filthy lust, have not doubted to have filthy and abominable copulation with beasts. This so great, so horrid a crime, for whose expiation all the fires in the world are not sufficient, though they too maliciously crafty have concealed, and the conscious beasts could not utter, yet the generated misshapen issue hath abundantly spoken and declared, by the unspeakable power of God, the revenger and punisher of such impious and horrible actions. For of this various and promiscuous confusion of seeds of different kinds, monsters have been generated and borne, who have been partly men and partly beasts." But it seems the real foundation for the scientific consideration of the subject was laid by Albrecht von Haller. His intelligent and scientific mind enabled him to analyze all the previous theories and make logical deductions. It appears that Bichat, the originator of the science of histology took up the subject where Haller left off. Through his efforts the subject of the study of monstrosities became identified with embryology. We believe now, as was

¹ Ambroise Paré: Surgery, 1579. Johnson's Trans., London, 1634, Book xxv, "Monstrosities and Prodigies."