EXPERIMENTAL DIPHTHERIA

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[IMPERIAL PRIZE ESSAY.]

EXPERIMENTAL

DIPHTHERIA.

—BY—

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PREFACE.

The work which I am about to present to the medical profession in the following pages, has achieved the great honor of being awarded the prize offered by her majesty, the Empress-Queen Augusta, for the best research on diphtheria.

No one can be more fully aware than the author that he has fallen short of the end sought by the giver of the prize, viz., the discovery of a remedy for diphtheria. But in seeking for such a remedy, the following investigations had their origin.

Having lost many a battle with this disease so terribly destructive to infants, I have frequently asked myself if the received opinions upon which our present treatment is based are correct, and here I encountered grave doubts. I was at last moved to make the attempt of looking deeper into the nature of diphtheria.

But few are the steps, and limited are the results, which can be taken by a single individual, in a pursuit like this. It must be left to the judgment of the reader whether or no my researches have brought us nearer the truth, or have expanded our views of it. What I here present is merely the result of my experimental research. My views upon the nature and treatment of human diphtheria—partly the result of these experiments, partly the result of clinical thought aroused by them—I do not give here because I have not yet had an opportunity to put them into practice with that accuracy which necessarily applies to all experimental research. I reported them in brief in the Transactions of the Second Medical Congress, at Weisbaden, and refer those who are interested in them to the reports of this congress, which will shortly appear in print.*

Before one attempts by artificial means to produce in an animal, a disease which is calculated to throw light upon analogous processes in the human subject, it is necessary, above all, to first have as clear and definite a conception as possible of the human disease itself. This necessity becomes particularly apparent when we reflect on the manifold views and varying importance which have been attached to the terms diphtheritis and diphtheria, by individual medical authors in the last few decades.

This denomination, which, since Bretonneau's time, has been given by all physicians to an acute general disease, did not primarily originate in a desire to express the nature of the disease through which the entire organism

* See Appendix.

is involved in a feverish condition, in which the heart, the kidneys, the spleen and nervous system take part, but in the fact that a peculiar local process, the formation of fibrinous membrane on mucous and granulation surfaces, became very characteristic, and the presence of which in certain localities is alone sufficient, in a mechanical way, to terminate life.

In the course of time, however, cases occurred, in which the formation of false membranes did not constitute so prominent a character of the disease, and was not in itself dangerous to life, but in which everything pointed rather to the existence of a grave constitutional infection, involving the entire human organism in a condition of blood-poisoning; when in addition to this a number of experiments, which were made, seemed to prove that by inoculation of certain matters from a diseased human being, diseases, including diphtheria, could be transferred to animals, the importance of the term diphtheria gradually lessened, and began to be more and more restricted to the constitutional condition which always obtains in Bretonneau's disease. And when anyone now speaks of diphtheria of the cornea, for instance, no thought at all is given to Bretonneau's membrane.

It is, however, evident that both elements, the disturbance of the entire organism as well as the local process of the formation of a false membrane, must be taken into consideration as essential factors in our disease. The problem of producing an analogous disease in animals cannot be considered as solved, if the artificially produced disease in animals is only one of general infection, and in which, only exceptionally, a false membrane makes its appearance, which latter is only rarely wanting in the disease as it occurs in the human subject.

But in view of the difficulty of tracing out the causes of diphtheria we must still go a step further in the analysis of our conception of the disease. If Bretonneau's disease is—according to the views of the majority of physicians—a specific one caused invariably by the same poison, we must also take into consideration the fact that Bretonneau's diphtheria, that is, the formation of fibrinous exudation in and upon mucous membranes, does not exclusively belong to Bretonneau's disease. On the contrary, we find it accompanying a great number of diseases, which according to our clinical and etiological views, have nothing in common with genuine diphtheria. Prominent among these stands dysentery, which offers a condition of things in the large intestine, which, anatomically, represents diphtheria. We find, furthermore, genuine diphtheria of the throat in scarlet fever, fibrinous exudation in different membranes in cases of small pox, measles, in the typhoid stage of cholera, in typhoid fever, on granulating surfaces, on the mucous membranes of the bladder, in certain cases of cystitis, even on the mucous membranes of the gall bladder, etc.

From these anatomo-pathological facts we may draw the conclusion that the formation of a false membrane is not peculiar to genuine diphtheria, but that its poison, in common with different other poisons, possesses the property of producing the peculiar disease of the mucous membrane. It is, therefore, to be regarded as highly probable that the immediate causes of

the diphtheritic diseases of mucous membranes are everywhere the same, but that very different morbific agents are capable of calling into existence these immediate causes, in perhaps very many different ways.

It thus follows that the problem of experimentally tracing out the causes of diphtheritis must necessarily be along two different lines of investigation, the one of which must be directed to the conditions necessary for the production of the diphtheritic membrane, the other, to the conditions of the general diphtheritic infection; in other words, to the diphtheritic poison and its relations to the local process of the formation of false membranes. This is the method of research which has been followed out in these investigations.

THE AUTHOR.

LEIPZIG, MAY 11th, 1883.

I. The Experimental Production of Diphtheritic Disease in Mucous Membranes.

The attempt to produce the anatomical changes peculiar to diphtheria by artificial means, has, as is well known, been frequently made. After Treitz, it was particularly Oertel and Weigert, who undertook a most careful investigation of the croupous exudation which follows the application of caustics to the trachea of the rabbit, and they have shown that this artificially produced tracheal croup presents the anatomical and chemical characteristics which are found in the exudations upon the surface of mucous membranes in diphtheria. After this was done Weigert proceeded to study the processes which lead to the formation of an artificial croupous membrane, and he succeeded in clearly tracing out the various steps which are necessary to the production of this fibrinous membrane, thus creating the term coagulation-necrosis, meaning thereby a process of dying under coagulation. Although, doubtless, this was a step in the right direction, it was also true, notwithstanding the identity of the product in the animal with that of man, that the method of the artificial production of this membrane was in no wise analogous to the pathological processes as they occur in the human subject. Apart from accidental cauterizations of the epithelium of mucous membranes, by which, of course, croupous membranes may also arise in the human subject, the process of the formation of croupous membranes in man is not called forth by such injuries as the action of caustics, which may be compared to a poison possessing the property of destroying the epithelium; and the idea that perhaps bacteria exercise an analogous influence over the epithelium, remains for the present a mere hypothesis.

Thus, even after Weigert's work, there remained to be discovered a method for producing the diphtheritic process in the mucous membrane of an animal, which one might well imagine to resemble the process obtaining in the human organism. In this I was successful upon the following grounds: