

## THE ETIOLOGY OF DIPHTHERIA.

*Read in the Section of Practice of Medicine and Physiology, at the Forty-second Annual Meeting of the American Medical Association, held at Washington, D. C., May 3-8, 1891.*

BY J. LEWIS SMITH, M.D.,

OF NEW YORK CITY.

No other infectious disease of childhood has been so much investigated in recent years as diphtheria. It has been the subject of full and accurate study by the most distinguished clinical instructors in both hemispheres, and numerous microscopic examinations and experiments with cultures of its specific principle have thrown light on its nature. Nevertheless, it has continued to extend and destroy its victims. It has encircled the globe, occurring with a heavy mortality in every country reached by commerce or travel. We read in medical journals of its prevalence, with the usual death rate, in Brazil, Algiers, and in distant Australia. It has occurred for ages in Eastern Asia, where it probably originated, and the complex prescriptions of the Chinese doctors, which have descended as an inheritance with little variation from their ancestors, and which are frequently employed by European residents of China, have lately been added to the literature of this disease.

Notwithstanding the many discussions of the treatment of diphtheria in medical societies, the many remedies which have been employed, and the additional light thrown upon its nature by the discovery of its cause, the percentage of deaths from this disease continues large. A recent French writer on diphtheria states that the deaths in France are in numerical excess of the births, and largely on account of the prevalence of this disease. In London the mortality from diphtheria has been steadily increasing. Within the metropolitan registration area it caused 952 deaths in 1887, 1,311 deaths in 1888, and 1,588 deaths in 1889. These numbers would be greatly increased if the deaths reported from croup, which, wherever diphtheria is prevailing, is known to be, with few exceptions, a manifestation of this disease, were added to them. (*London Lancet*, May 17, 1890.) In New York City the deaths from diphtheria were 1,914, and from croup 639, aggregate 2,553 in 1888; from diphtheria 1,686, and from croup 605, aggregate 2,291 in 1889. In Brooklyn the deaths from diphtheria were 984, and from croup 391 in 1889; from diphtheria 1,101, and from croup 366 in 1890. These are probably the average statistics of the mortality from diphtheria in the cities where it prevails.

The presence of a great evil always leads to strenuous efforts to determine the exact nature and the most effectual mode of combatting it. It is now known that diphtheria is produced by a linear or rod-shape microorganism, having about the length of the one which causes tuber-

culosis, but considerably thicker. A rod-shape microbe is termed a bacillus, and that which causes diphtheria, is designated the Klebs-Löffler bacillus in honor of Klebs, who announced his discovery of it in 1883, and of Löffler, who subsequently more thoroughly investigated its nature. Löffler cultivated it in appropriate media, and after a succession of cultivations, which removed it several generations from its source in the child, inoculated pigeons, rabbits and guinea pigs, with the last culture, and produced in them typical diphtheritic inflammation. Many others have repeated and varied these experiments with results similar to those obtained by Löffler, so that the theory that diphtheria is caused by the Klebs-Löffler bacillus is accepted. This bacillus presents aspects which to the experienced eye are characteristic. It often has a granular appearance and is stained in two minutes by the violet of methyle; it often exhibits a more intense coloration of its extremities than of its central parts, and its extremities are sometimes swollen so as to present a dumb bell appearance, or only one extremity is swollen, so that it has the shape of a pear or gourd; occasionally it is curved like an arc. (*Le Bulletin Med.*, June 15, 1890.)

The Klebs-Löffler bacillus alighting upon the faucial or other mucous surface, or the skin denuded of its epidermis, obtains a nidus favorable for its development and propagation, but it does not enter the interior of the system; it is not taken up by the lymph ducts or blood vessels and conveyed to the internal organs; it remains localized upon the surface and produces there the characteristic inflammation; acting solely upon superficial parts, it cannot in itself produce systemic infection, or blood-poisoning, but like as the venomous reptile or the bee secretes its poison, which it communicates by its fang or its sting, it produces a chemical poison, which is readily taken up by the vessels and conveyed to the internal and vital organs.

This substance, which is the poisonous agent in diphtheria, and which produces systemic infection and death of the multitudes who perish from diphtheritic blood-poisoning, has been carefully examined and experimented with by L. Brieger and K. Fraenkel (*Berliner Klinische Wochen.*, March 17th and 24th, 1890). They say that it may be evaporated at 122°, but is destroyed by a heat above 140°. It is soluble in water, but is insoluble in alcohol. It is not precipitated by ebullition, nor by the following medicinal agents: sulphate of sodium, sulphate of magnesium, chloride of sodium, nitric acid and acetate of lead. On the other hand, it is precipitated by concentrated carbonic acid, the ferro-cyanide of potassium, acetic acid, carbolic acid and nitrate of silver. It has, say Brieger and Fraenkel, the following composition: Carbon, 45.35; hydro-

gen, 7.13; azote, 16.33; sulphur, 1.39; oxygen, 29.80.

When it was separated from the bacillus by passing through the porcelain filter, and inoculated in rabbits and guinea pigs, it caused death in the small quantity of two and a half milligrams to each kilogram in the weight of the animal. Sometimes death did not occur until after weeks or months, while the bacillus itself inoculated upon one of the surfaces, caused inflammation with the exudation of fibrin, producing the diphtheritic pseudo-membrane, this chemical product of the bacillus, freed from the bacillus by the filter, did not, when inoculated, cause any fibrinous exudation or diphtheritic pellicle, though its action was so highly poisonous. According to Brieger and Fraenkel it is allied in its composition to the proteids or albuminoids, and it bears considerable resemblance to ichthyotoxinon, the poison secreted by sea eels. Many years ago Trousseau noticed this resemblance and related an instance in which seamen became paralyzed, some of them for three months, by eating a cooked eel. He saw the resemblance in these cases to diphtheritic paralysis. In a vacuum the poison produced by the Klebs-Löffler bacillus retains its virulence for weeks or months. MM. Roux and Yersin state in the records of the Pasteur Institute, Paris, that their investigations have strengthened the belief that the Klebs-Löffler bacillus is in itself comparatively innocuous, the chemical substance produced by it, described above, being the poisonous principle. These bacteriologists also separated this substance from the bacillus by filtration through a porcelain filter, and by inoculating dogs and sheep with it, produced in them a paralysis apparently identical with that occurring in children from diphtheria. Roux and Yersin also state that while the filtered liquid freed from the bacillus, and containing only the chemical substance, if infected under the skin of rabbits and guinea pigs, was very fatal, it caused little inconvenience, if introduced into the stomach.

Experiments similar to those related above, and clinical observations confirmatory of the views expressed by Klebs-Löffler, Roux and Yersin, have been made by many others, which, since they are in the main corroborative, need not be related here.

*Pseudo-diphtheria.*—This term is employed through want of a better one. It is proper to state in this connection that clinical observations and experiments, carefully made, have demonstrated the fact that certain other microbes besides the Klebs-Löffler bacillus, sometimes produce a pseudo-membranous inflammation upon the faucial or other surface, which as regards its anatomical characters, appears to be identical with that in true diphtheria. The only differ-

ence thus far discovered has been the absence of the Klebs-Löffler bacillus, and the presence of other microbes. Whether these other microbes produce poisonous albuminoids by which the system becomes infected must be determined by future research, but if they do, these products seem to be different from that generated by the Klebs-Löffler bacillus, for the peculiar paralysis which is so common in true diphtheria does not appear to occur, or is infrequent in pseudo-diphtheria. If the systemic infection be different in true diphtheria and pseudo-diphtheria, as appears to be the case, we see the propriety of recognizing two distinct diseases, just as our ancestors differentiated measles and scarlet fever, which, since both had a cutaneous efflorescence and redness of the fauces, were formerly considered identical.

M. Talamon states that not only other microbes, besides the Klebs-Löffler bacillus, but also certain irritating medicinal and chemical agents, have the power to excite an inflammation with fibrinous exudation upon the faucial, or other surface, to which they are applied, which cannot be distinguished by its appearance and anatomical characters from that of true diphtheria except by the absence of the cause of the latter disease, to wit, the Klebs-Löffler bacillus. The inflammation produced by non-microbial irritating agents, as steam, boiling water, chlorine, cantharides, and ammonia, though attended by an exudation of fibrin, is obviously entirely distinct in nature, from that caused by microbial agency. Like any inflammation from traumatism, it always remains a local disease, and must not be confounded with diphtheria or pseudo-diphtheria.

Pseudo-diphtheria, according to my observations in the institutions and in family practice, occurs most frequently in the course of the eruptive fevers, and especially in scarlet fever. We must not mistake the necrosis or gangrene which is not uncommon upon the swollen fauces, in severe anginose scarlet fever, for a fibrinous exudation. It is difficult, perhaps in some cases impossible, to distinguish the one from the other on inspecting the fauces. Necrosis occurs upon the most swollen part, as over the tonsils or in their vicinity. A fibrinous exudation due to microbial agency is likely to extend to the velum or uvula. Diphtheria or pseudo-diphtheria complicating scarlet fever usually occurs when there is not sufficient tumefaction to cause necrosis, but it may supervene upon, and complicate a necrosis.

M. Sevestre, of Paris, says that the pseudo-membranous sore-throat, which occasionally occurs in scarlet fever, is generally considered in France as having a diphtheritic origin, and patients who are suffering from it are placed in the diphtheritic ward. It is, however, says he, a variety of sore throat, which ought to be dis-

tinguished from the diphtheritic. It is an early manifestation developing in the first days of scarlet fever. It is characterized by the production of white patches, which frequently are exactly similar to those of diphtheria, and which may occur upon the uvula and soft palate, so that its diagnosis from diphtheritic inflammation is often very difficult, but the pseudo-membrane does not extend to the larynx, and the general condition of the patients remains, in most cases, satisfactory. These sore-throats, adds Sevestre, commonly end in recovery, and they do not communicate diphtheria to neighboring children. Some of the patients alluded to by Sevestre, evidently had what we have designated pseudo-diphtheria, an inflammation with fibrinous exudation produced by other microbes than the Klebs-Löffler bacillus, probably mainly by cocci, which are found in abundance in these cases. Some of the patients referred to by Sevestre, perhaps had scarlatinal necrosis. MM. Wartz and Bourges made microscopic examinations in nine cases of supposed diphtheria, complicating scarlet fever. In two of the cases in which the pseudo-membranous inflammation occurred at a late stage of scarlet fever, the Klebs-Löffler bacillus was found in the exudate, but in the other cases, in which the pseudo-membrane appeared early, this bacillus was not present, but streptococci were abundant. In six of the cases the pyogenic staphylococcus was also observed (*Arch. de Med.*, May, 1890). The fact that the Klebs-Löffler bacillus did not occur in cases in which a pseudo-membranous exudate appeared at an early stage of scarlet fever, justifies the belief, the writers say, that the appearance upon the faucial surface, which so closely resembled that in diphtheria, was due to the intensity of the scarlatinal inflammation. But in the two cases, in which the pseudo-membrane appeared at an advanced stage (the sixth and ninth days), the Klebs-Löffler bacillus was present, and it is evident that true diphtheria had supervened.

We might quote the observations of Prof. Henoch, of Berlin, and Dr. McWerney, of the Royal Academy of Medicine of Ireland, showing that in scarlet fever the faucial inflammation, accompanied by the formation of a pellicle, so closely resembles that of diphtheria that it is difficult to make the differential diagnosis. But this inflammation is not followed by paralysis except when true diphtheria supervenes. It is caused by the agency of the scarlatinal, and other microbes than the Klebs-Löffler bacillus.

The *American Journal of Medical Sciences* for May, 1889, contains an elaborate paper by Prof. T. M. Prudden, relating the microscopic examinations of the pseudo-membrane underlying tissues and the viscera, removed from the bodies of 24 children, who were supposed to have perished from diphtheria. But these cases, with two

exceptions, were treated in institutions, where epidemics of the other infectious diseases are frequent, and sixteen of them had scarlet fever, measles, whooping cough, or an erysipelatous or phlegmonous inflammation, in parts at a distance from the fauces at the time of death. In no one of these specimens sent to Dr. Prudden by curators or reputable physicians, in the belief that they were removed from the bodies of those who had died of true diphtheria, could he find the Klebs-Löffler bacillus, but instead he discovered the streptococcus and staphylococcus. These specimens for a time misled Dr. Prudden and the entire medical profession in this country, for the absence of the Klebs-Löffler bacillus in the specimens of twenty-four consecutive cases seemed to show that this bacillus could not be the cause of diphtheria. But in no one of these cases so far as their histories show, did paralysis, which is so characteristic of true diphtheria, occur. These twenty-four patients died from a disease produced by the agency of other microbes than the Klebs-Löffler bacillus, or what we, through want of a better term, have designated pseudo-diphtheria. Prof. Prudden has since discovered the Klebs-Löffler bacillus in a dozen or more cases of true diphtheria. Prof. Welch, of Johns Hopkins University, also finds the Klebs-Löffler bacillus in diphtheria, has obtained cultures of it, and by inoculating animals with these cultures has apparently produced the genuine disease in them; therefore he believes that the theory that this organism causes diphtheria is fully established.

From the facts as stated above we repeat that the disease heretofore designated diphtheria we must now regard as two diseases, to wit: diphtheria resulting from the action of the Klebs-Löffler bacillus, and pseudo-diphtheria, resulting from the agency of other microbes, or else we must recognize two varieties, or rather forms, of diphtheria, the one caused by the Klebs-Löffler bacillus and the other by other microbes. I may add that there is no evidence, so far as I have been able to ascertain, that the poisonous albuminoid generated by the Klebs-Löffler bacillus, which albuminoid causes the systemic affection, or blood-poisoning in true diphtheria, is produced by any other microbe. If the streptococcus, staphylococcus or any other form of coccus produces a poisonous albuminoid similar to that generated by the Klebs-Löffler bacillus, I am not aware that it has been discovered or isolated.

In the light of our present knowledge are we able to state whether diphtheria is primarily a local or primarily a constitutional disease? It seems that we must regard the disease produced by the Klebs-Löffler bacillus as primarily local; but in reference to the disease produced by other microbes the question is still an open one, for in fatal cases the micrococcus is found in internal organs, as well as at the seat of the inflammation

upon the mucous surface. The length of this paper prevents our discussing the very important subject of the modes of propagation of diphtheria, which must be reserved for some other occasion.

## PREMENSTRUAL PAIN AND CONVOLUTED TUBES.

BY FRED B. ROBINSON, B. S., M.D.,

OF TOLEDO, OHIO.

PROF. OF ANATOMY AND CLINICAL SURGERY TOLEDO MEDICAL COLLEGE.

The views in this article occurred to me from the examination of about 700 ova ducts of man, cow, pig, sheep and dog. The substance of the views is that the main premenstrual pain and the pain which women have who are afflicted with tubal disease is essentially due to peristalsis or vermicular motion of the tubes themselves. It is, in short, tubal colic. The method of arriving at this idea was the following:

Four years ago I wished to acquire a practical knowledge of the heart and its diseases, so I dissected and examined a large number of the hearts of all animals within range of acquisition. Considerable vivisection was done. It does not require but few vivisections to demonstrate that the essential motive power of the heart is situated in its base. That the main ganglia which control and initiate regular movements to the heart reside in the auricles and not the ventricles. The nerve ganglia which give the heart its *rhythm* belong to its basal portion. These ganglia are called Remak's, Ludwig's, Bidder's and Schmidt's, and are well termed automatic cardiac ganglia. It is easy to observe the heart die out from apex to base. If the vivisection is carefully done the auricles (in the dog) will beat regular considerable time after the ventricles have ceased their rhythmical action, so I saw that the heart (which is one of the viscera) had some nerve apparatus within itself which gave it a rhythmical, periodical, cyclical motion. The heart waxed to a maximum and waned to a minimum in its continual motion. In short, it exploded about 75 times a minute.

Three years ago I wished to acquire a similar practical knowledge of the intestines and their pathology. So we included in the examination and dissection the above mentioned animals, but especially the dog, on which the main vivisection was done. To demonstrate the point, the dogs were chloroformed and the abdomen opened. The intestines were generally found still and quietly at rest until the exposure to air stimulated them to move slightly. The dog was nearly always chloroformed to death inside of twenty minutes. But after the dog was dead the intestines, by simply tapping them, would go through their peristalsis, their vericula, periodical *rhythmical*

*cal* motion for at least an hour. If the temperature was 80 degrees the cyclical movements could be kept up an hour and a half. In such experiments alone can be realized what is known as the "invagination of death." Now the same phenomenon which was seen in the action of the heart, is again witnessed in the intestines. It is *rhythmical* motion and must be caused by the same kind of an apparatus known as a ganglion. In fact the ganglia which do the motive work of the intestines are situated in the plexus of Auerbach and the plexus of Meissner. These plexuses reside in the gut wall. The same form of work can be done with the kidney and bladder and the same kind of ganglia found. They are *rhythmical* ganglia. It may be remembered that a nerve ganglion is a little brain. It is an automatic center. It is a sensorium of independent action. A ganglion is possessed with the powers of secretion and nutrition. It is a physiological center endowed with plenipotentiary power to initiate, continue and prohibit action. The function of a ganglion is to produce a rhythm. It is a nerve apparatus which wanes and waxes and explodes. It lives a periodic, cyclical life and the circle of its action is defined by its maximum and minimum points—in time.

Now, this same kind of experimental work was applied to the Fallopian tubes of man, cow, dog, sheep, and pigs. Many hundred ova ducts of the higher animals were carefully examined and lately, while studying with Mr. Lawson Tait, I have had plenty of opportunity to confirm the experiments on fresh human tubes, a few minutes after Mr. Tait had removed them from the patient. Some of the tubes were absolutely healthy, as they were removed for bleeding myoma and other causes. It may be remarked that the Fallopian tubes do not differ from other hollow viscera. They are governed by similar nervous apparatus. The tubes live a rhythmical life. They have a periodic function, and while useful to woman go through cyclical action. After considerable investigation and microscopical work I came to the conclusion that the tubes (and uterus) were governed in their rhythm by ganglia situated along their walls, and along the blood vessels which supply them. In order that these ganglia should be appropriately named, I styled them *automatic menstrual ganglia*.

Until some two years ago, when I began to investigate this subject, I had no idea of the importance of the tubes in the process of menstruation. But now I am becoming convinced that the tubes overshadow every other organ in menstruation. It seems to me that menstruation starts in the tubes and begins with tubal motion. The girl's puberty is heralded by tubal activity, and she is a woman when her tubes begin to move. (I am unable to find any difference in the ovaries at puberty except increased vascularity, and hence