Am Ende (C. G.)

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BY

CHARLES G. AM ENDE, M.D.
New York

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TREATMENT OF DIPHTHERIA UPON ANTISEPTIC PRINCIPLES.[1]

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CHARLES G. AM ENDE, M.D.,

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IT is somewhat singular that, after the achievements of external antisepsis within the last twenty years, application of the simple principle—no infectious organisms, no disease—to *internal* diseases has made so little progress, in spite of the fact that, if properly carried out, the results are no less satisfactory.[2]

At the time when the first article[3] on the use of boracic acid for local, and quinine for internal, antisepsis was published, the results for two years had been uniform and reliable. They have been confirmed by the experiences of nearly two years more, and it would seem that recent bacteriological and physiological researches also sustain them.

Very extensive experiments made in the seventies gave among other results the following: That while the solid—that is, the non-volatile—acids, boracic, oxalic, and others, *do* prevent the growth of bacteria, including coccobacteria and the bacilli of putrefaction, and further that of infusoria and other lower animalculæ, they do *not* prevent the growth of fungi, such as oidium, torula, penicillium, aspergillus, the mucors, etc.; that the effect of a chemical upon these fungi supplies no criterion as to its effect upon bacteria; that in their chemical reaction bacteria differ essentially from fungi and are not therefore schizomycetæ. They confirmed the statement of Delondre[4] that *all* acids and acidulated liquids antagonize the life of bacteria and lower animalculæ, and are therefore all antiseptics, while

[1] Read before the Medical Association of New York City, December 17th, 1894. With some additional notes.

[2] For the result of thorough internal antisepsis in a case of typhoid fever see Medical Record, April 29th, 1893, p. 540.

[3] Medical Record, February 25th, 1893, p. 251.

[4] Séances de l'Académie des Sciences, 1863, II. semestre.

neutral or slightly alkaline media favor their development. Volatile acids are inimical to both fungoid and animal life.

I have been unable to experiment upon pathogenic bacilli, but numerous statements by others show that their reaction is similar to that of other bacteria, and that their development and destruction depend upon similar conditions. According to Tyndall, however, pathogenic germs possess a higher resistance.

These facts show that boracic acid *is* an antiseptic[1]—weak, to be sure, yet the results are practically the same whether we use weaker antiseptics in more concentrated solutions or the stronger greatly diluted. In addition, the conditions within the living body, and probably, too, the lesser resistance of freshly developing germs, seem to aid materially the antiseptics. Boracic acid has also these advantages, that even in the most concentrated solutions it has no injurious effect upon the most delicate membranes of higher animals, but destroys the microbe. It dissolves some fatty materials, though less than its sodium salt.

The destructive action of quinine upon lower organisms, proven beyond doubt by the earlier observers,[2] has been denied in the case of pathogenic bacteria upon culture experiments. This error, like that concerning iodoform, can only have arisen from overlooking the insolubility of quinine in culture gelatin. However finely divided, the gelatin envelops these substances and thus prevents their action upon the micro-organisms. Modification of the experiment by the use of blood instead of gelatin would have shown that these drugs readily sterilize this physiological fluid, especially at the temperature of the body.

But why shall we use in diphtheria these drugs and internal antisepsis, when the cause of all the systemic disturbances and eventual death are the ptomaines evolved by the bacilli harboring upon and within the tonsil and adjacent structures?

The first step in the diphtheritic drama is the specific bacillar infection. The disease begins with *that*, not with the appearance of the false membrane. Preceding the latter we have the stage of incubation, or, as I should for practical reasons prefer to call it, the premembranous stage.

[1] Turbidity of solutions of boracic acid in common water, due chiefly to the presence of lime salts, is overcome by the addition of from one-eighth to one grain of alum to each pint of solution.

[2] Nothnagel, "Arzneimittellehre," p. 347.

It will often be observed in all stages of progress upon examination of the throats of *all* children in a family where one is encountered with patches.

In the earliest stage we see, in many cases, but one tonsil somewhat acuminated, just beginning to enlarge. A little later one tonsil, more enlarged than its mate, begins to look angry; there is a slight rise of temperature above 99°, and occasionally slight gastric trouble. Ultimately one or both tonsils become very large, highly inflamed, covered with a glairy mucus; temperature now above 100°; pulse about 120; head drooping, often toward one side; eyes listless; the appetite lost entirely within the last six to twelve hours of the premembranous stage. The bacilli should already be easily detected.

This premembranous stage derives its special importance from the ease with which it yields to treatment, so that a second membranous case in the same family may either be entirely prevented, or if at all developed be quickly cured. Even without a full-fledged case in a family these symptoms often alarm parents sufficiently to make them send at once for the family physician, who then can easily abort a case of threatened diphtheria in from thirty-six to forty-eight hours.

Observation of the succession of cases in the same family furthermore suggests that considerable *propagation* of the disease emanates from or during this early stage.

The gastric disturbances of the earlier stage, slight at first, deserve attention on account of their probable origin. It will generally be agreed that ptomaine intoxication can hardly at this time originate from the tonsil, but the infection could, as stated, *not* have occurred without the presence of bacilli in the mouth, and, actually, bacilli floating free in the mouths of healthy children have already been noted by Löffler. Our imagination is much less taxed by the assumption that these derangements are caused by passing food carrying some such free floating bacilli into the stomach, where the freed toxic products could directly give rise to the gastric symptoms, rather than by ascribing to them a reflex or other complicated origin.

Protected, for instance, by milk coagula, both the bacilli and the toxalbumin could easily escape the influence of the first heavy influx of acid gastric juice; and, besides, it has been demonstrated by Gilbert[1] by actual experiment that the hydrochloric

[1] Tribune médicale, 1894, p. 917.

acid of the stomach, either free or combined, is unable to sterilize food completely. After development of the membrane with the simultaneous enormous numerical increase of the bacilli, which in usual microbe fashion aggregate in the layers nearer the air, hardly a swallow can fail to carry some into the stomach, which by this time is thoroughly disordered.

The commonly administered acid chloride of iron seems to destroy the bacilli and their products in some of these cases, in others it does not. The use then of an antiseptic which, unlike the iron salt, does not decompose in the stomach, and which, additionally, is capable of resorption into the portal system and the general circulation, may have the desired effect and account for the usual clinical result of the administration of quinine in sufficient quantity and for sufficient length of time.

But for some curious observations this chapter might well close here.

These are that Oertel, Welch, Flexner, and Abbott—from the latter of whom some sentences will be borrowed—observed in various parts, notably the glandular system and the liver, of bodies of individuals who had died of diphtheria, necrotic foci with intensely stained dots arranged sometimes in clusters of various forms, sometimes in fine just discernible lines, or granular, strewn dust-like through the field of hyaline necrotic tissue. If it were possible to connect these with the equally intensely stainable dots in the bulbar ends of the Klebs-Löffler bacilli, precious revelation would result.

Similar granular and dotted matter occurs in coccobacteria. In the study of the microbe of the horse epidemic of 1873 there were observed by myself dots of all sizes, from the most minute to those of the parent organisms, the largest of which, one-fiftieth of a millimetre in diameter, contained these dots mostly in daughter cells impacted within the parent, and some of these parents could be seen with a resorbing, bursting cell membrane, allowing the daughter cells with their various sized dots to float out.

The pathogenic bacilli, usually believed to multiply by cell division only, are assigned the anomalous position that, unlike every other living organism, they should produce no spores. In contradistinction, if these highly stainable dots in the microbic foci should be derived spore-like from the equally stainable dots in the expansions of the Klebs-Löffler bacilli, this would explain :

How, in spite of only sporadic occurrence of bacilli in the system, others, disintegrated, may leave behind them these traces of their previous existence and their especial accumulation in the lymphatics and liver;

Why complete sterilization deprives bacilli of their microbiotic power;

Why antiseptics diminish and eventually destroy the virulence of bacterial extract;

Why coagulating albumen or a freshly forming insoluble salt precipitates from this extract the necrotic or toxic element (an analogous process to those used for the precipitation of germs in fermentable and putrescible liquids, such as wines, etc., by rapid or slow coagulation of albumen or by certain salts);

Why, furthermore, some bacilli are more virulent than others, the former being the older and further developed;

Why the virulence of cultures diminishes with repetitions, like the fruit-bearing quality of a tropical tree in a hot house.

It might further raise the question, What would be the effect of similar necrotic processes in the brain?

Most important of all, it would urge with emphasis suppression of the disease at the earliest possible opportunity, or, if this be impossible, by efficient antisepsis sufficiently prolonged. Still, all this must remain hypothetical with the present development of our microscopes, and can only be considered, and is only presented, as a suggestion.[1]

Now as to the antiseptics used. The boracic acid is used in the form of boroglyceride. The boroglyceride and alum solu-

[1] That much of the alleged ptomainic action of the Klebs Löffler bacilli should really be functional disturbances depending upon tissue changes by other microbic action would not be a novel supposition. The idea that the ill effects and inflammatory antitoxic sequelæ, cutaneous, pneumonic, and nephritic, depend upon germs introduced with the serum, has been exactly paralleled by Czerny and Moser's demonstration of the effects of bacilli, coli communis and streptococcus, entering the circulation from the intestinal tract in gastro-enteritis. That germs, whatever their origin may be, can be scattered and remain in the system of higher animals, even in the capsular joints, is shown by fetid decomposition upon their development after death, their immediate penetration being impossible after cessation of the life currents. That bacterial development does not always imply generations of toxalbumins is proved by the harmless consumption of carne secca, strong game, living cheese, etc. Incomplete sterilization has in cases led to incorrect ideas concerning bacterial toxines. Roux and Yersin destroyed the toxicity of diphtheritic bacillar extract by acidulation with lactic and tartaric acids.

tion, after Wylie's formula, was first resorted to in a case where previous application of mercuric chloride and then of hydrogen peroxide (both of which decompose upon application) had thoroughly hardened the tonsils, which then softened. The creasote was added later for stronger antisepsis. It is rational to suppose that the boroglyceride, a stronger hydragogue than plain concentrated glycerin, abstracts from the mucosa and submucosa with the fluid a number of bacilli then subjected to the antiseptics.

The formula for the compound is: Add to four drachms of fifty per cent boroglyceride a solution of two drachms of alum in nine drachms of pure concentrated glycerin, made by boiling, then add five drops of creasote. Of this I always carry a two-drachm vial and a camel's-hair brush four inches long. Only two or three drops are used for each application; and parents can be instructed in the proper mode of application, which is a gentle touch. The brush should be well cleaned after using, at least by running water from a hydrant with subsequent flushing of the basin, or better yet by a five per cent carbolic acid solution. It should then be well dried to avoid decomposition of the boroglyceride by water.

These applications are usually made once every hour until complete disappearance of the false membrane; after that, four or five times a day until the tonsil decreases perceptibly in size. Usually two such two-drachm vials suffice for a membranous and one for a premembranous case. In the latter, applications once every two hours are usually sufficient. In a few very threatening cases the applications were made once every half-hour for a number of times. The second or third application is usually followed by dissolution of a large part of the membrane, but a few small specks or a whitish infiltration persist for several days.[1]

Slight laryngeal complications require no other treatment; for more serious, sprays were used of a solution of chlorate of potash and boracic acid[2] in the intervals between the pencilling; once also hot wet packs to the throat, at first frequently repeated.

[1] A further valuable property of this preparation is that, unlike the iron salts, it leaves the tissues and their morbid changes or productions of a natural color.

[2] Spraying with this or the boroglyceride diluted with twice its volume of water cleans the nose.

The quinine is administered best in solution with hydrochloric acid after this formula:

℞ Quininæ sulphatis..... .... ℥ i.
Solutionis acidi muriatici..... .. q. s. for solution.
Syrupi..... ....℥ i. or ℥ ij.
Water..... ....q. s. for ℥ iij.

Dose: A teaspoonful every three hours.

Occasionally the quinine will have to be given in pill form or suppository.

In severer membranous cases a few doses are given during the first one or two nights, in addition to those during the day, until the temperature falls to below 102°, but the full day dosage is continued until it is near 99°; after that, for a few days, a teaspoonful three to two to one times a day. This dosage may seem large for children under 5 years of age, but it is well borne, and in only a few cases did it become necessary to counteract symptoms of depression by the addition of a few drops of sweet spirit of nitre to each dose of the quinine. Premembranous cases receive, according to their gravity, from one-half to two-thirds of the regular dose of the quinine, with the result, as already stated, of recovery in from thirty-six to forty-eight hours.

Membranous cases recover usually in from five to six days. In only one instance did a membranous case last longer than six days. It was a little girl of strumous diathesis, who when the primary diphtheria had nearly subsided developed suddenly a suspicious parotitis, first of the right and a few days later of the left side, with persisting reappearance of small membranous foci. During nearly the entire course of thirteen days the quinine was continued in full dosage, but nitre had to be given additionally.

As to results, during nearly four years of this treatment there were lost, out of a few over one hundred cases, four, under the following interesting circumstances:

The first was a boy, aged 9, who so firmly closed his teeth that medical treatment was absolutely prevented for four days up to within two and one-half hours before death. The result had been predicted.

In the second case I was, after the first inspection at a dispensary, not allowed to see the boy, a 3-year-old, for nine days. An improvement had occurred, then a relapse after this disobedience of instructions, and the child died.

The third was an infant 13 months old. There were in this family five more children from 5 years up, all born in Europe. Three more children born here had died—2 to 7 months old—from cachexia. The infant, nourished artificially, lived under nearly continuous medication, but ultimately developed a capillary bronchitis. On the fourth day of this an elder brother developed diphtheria. The infant followed a few days later in spite of isolation, and then, developing severe apnea, died. Three more children in the family developed diphtheria, but all made good recoveries.

The fourth case, aged 3, had been previously treated by another physician with apparently pure tincture of iron. Everything in the mouth was swollen and partially abraded, so that the application of the boroglyceride was rendered exceedingly painful and it had to be replaced by a milder agent. The quinine, as well as food, could be administered only by the rectum. Intubation was out of the question, tracheotomy was refused, and death supervened.

It would seem that the first two cases cast no blame on the method, nor probably also the third, while in the fourth case tracheotomy might have been successful.

Of other complications a few occurred with scarlatina. These gave the impression that when the patient was already under the influence of quinine for diphtheria the eruption was exceedingly evanescent and localized, with very rapid recovery, but if scarlatina preceded the diphtheria the cases would last nearly fourteen days.

Of sequelæ none have ever been noticed.

The usual course of the disease and the rapid and prompt recovery under this treatment will best be demonstrated by the histories of a few cases, about whose outcome apprehensions would ordinarily be felt by the practitioner taking them in charge.

A. G., æt. 4, when first seen on December 2d, 1892, showed diphtheritic membranes covering the right tonsil completely, the uvula partially, the left tonsil partially, and extending downward behind the posterior pillars into the pharynx. Pulse 146, temperature 103.8°. Treatment, pencilling with the boroglyceride compound every hour, twice during night; a teaspoonful of the quinine solution every three hours during the day and twice during night. December 3d: Pulse 124, tem-

perature 102.2°; night treatment discontinued. December 4th: Pulse 111, temperature 99.6°; hard to keep the boy in bed. December 5th: Pulse 104, temperature 99.1°; all parts free from membrane, but tonsils yet enlarged; appetite good. A 3-year-old sister had, on the 3d, premembranous symptoms which under milder treatment disappeared on the 5th.

L. K., æt. 6, diphtheritic croup. Bacteriological examination "mixed." First seen on January 5th, 1895. Previous throat troubles. The three rooms occupied by the family heated by one small cooking stove; strong cold draughts at three feet from the window on the blizzard days; water pipes frozen throughout the house. February 9th: Found with scarlet fever, complicated on February 11th by a very severe croupous laryngitis, persisting till the 15th. On the 13th diphtheritic membranes, receding till the 17th to a whitish induration which disappearing on the 19th left a circular erosion with sharp, partially pointed edge. Desquamation began on the 20th. Faint albuminuria. Treatment as before.

J. L., male, æt. 17; first seen on January 31st; greatly swollen tongue, covered with thick, firmly adhering fur; throat filled with a glairy and flaky mucus; tonsils hidden. February 3d: Tonsils now visible, with membranes of true diphtheria. February 7th: Tongue free from fur, with thick, broad longitudinal ridges. The temperature had become normal on the 6th; last visit on the 9th.

While the boroglyceride compound can perhaps be replaced by some other preparation, a substitute for the quinine in doses sufficiently large will hardly be obtainable. With, as stated, never any sequelæ, their use overcomes the deficiencies of antitoxine. With prompt success in every case, barring such exceptional and uncontrollable occurrences as in the four described, the writer would attribute a fatal result in a case thus treated from the beginning to some serious neglect, and thus may well be pardoned the repeated recommendation to the profession of this simple, gentle, and inexpensive treatment.

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