Jacobi (A.)

CONTRIBUTIONS

TO THE

PATHOLOGY AND THERAPEUTICS

OF DIPHTHERIA.

BY

A. JACOBI, M.D.,

CLIN. PROF. DIS. CHILDREN IN THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK, ETC.

(A Paper read before the Medical Society of the County of New York, December 28, 1874.)

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Twice before this evening have I had the privilege to appear in extenso before the medical profession of New York with remarks on the subject of diphtheria. The first time with a paper published in the *American Medical Times*, August 11th and 18th, 1860, to which Dr. Harris, in his recent remarks before the Public Health Association, kindly alluded as the first elaborate essay written since the times of Barth; the second time in a memoir on croup, read before this Society in 1868, and published in the first number of the *Journal of Obstetrics and Diseases of Women and Children*. At this late day I cannot but look upon those two papers as fair exponents of what, if not generally adopted as final, was believed to be based on the numerous facts then known and attested.

In the first paper I described the pseudo-membranes as "differing in size, thickness, color, and consistency; their shape as various. Some are round, some angular, some regular, some irregular; their thickness varies from a film to a quarter of an inch and more. Their color is white, glassy, greenish, gray, yellowish, reddish, brown, according to their thickness, exposure to air, and admixture of blood; unaltered blood adheres, sometimes, to their lower surface. They are either merely adherent to a mucous membrane, without any alteration of its

* From Journal of Obstetrics, Feb. 1875.

tissue; such is usually the case on the mucous membrane of the bronchi and trachea, and mostly on the soft palate; or they are imbedded in its substance, as mostly on the tonsils, and the posterior wall of the pharynx, and frequently in the larynx. It is a very remarkable fact that the same continuous membrane will now be readily removed from the surface of the mucous membrane, and again at a very short distance tear the substance of the mucous membrane at every attempt to separate it. The surrounding parts are hyperæmic, and swelled by œdema during life. At post-mortem examinations the œdematous swelling is sometimes found, but the hyperæmia is no longer met with after the refrigerating and contracting influence of the atmosphere has had time to operate. Pseudo-membranes are found in the pharynx, on tonsils, uvula, and velum, on the gums, lips, and tongue, on the mucous membranes of the mouth and nose, in the larynx, trachea, and bronchi, in the superior part of the œsophagus, in the lower part of the intestinal canal, round the anus, in the vagina, the external ear, the naso-lachrymal duct, on the conjunctiva, and on the cutis, wherever and by whatever cause it has been deprived of its surface; thus on sore nipples, etc. In all of these places the chemical as well as microscopical constitution of the membranous exudation is entirely the same."

With these observations before me I could not but believe in the identity of the croupous and diphtheritic process. Both clinical experience and the study of the histological elements of the membranes, or deposits, as far as then understood, appeared conclusive. Nor did further experience, necessarily large in this great city, change my views in that respect, when, eight years afterwards, I returned to the subject, in this very place. In the paper then read (*Jour. Obst.*, May, 1868, p. 30 *seq.*) after some remarks upon pharyngeal and laryngeal catarrh, I continued: "Another form is the follicular process on the tonsils with its subsequent changes, the formerly so-called herpetic angina, which I have characterized already in a paper on diphtheria, published in August, 1860, in the *Am. Med. Times*. It is exudative, membranous in character, feverless, but will not infrequently be followed by large croupous or diphtheritic deposits. Another form is the membranous deposit proper, a fibrinous exudation, amorphous in character, mixed with mucus and

blood-corpuscles and normal epithelium. It is either deposited upon the mucous membrane, and then can be easily lifted up from it, or into it, and into its subjacent tissue. The first form has frequently been called croupous, the latter diphtheritic. But whatever clinical difference there may be between a simple membranous inflammation and constitutional diphtheria, there is no anatomical difference between the membranes wherever they make their appearance. Another form, and not an infrequent one, is originally confined to the epithelium, which rapidly undergoes fatty degeneration, which may or may not be complicated with fibrinous exudation. The soft, pultaceous, easily macerating diphtheritic masses are of this character; and the fearful cases of diphtheria with rapid necrosis of the tissue are usually of the same nature. The neighborhood may be in various conditions, œdematous or dry, hyperæmic or anæmic. An œdematous and hyperæmic condition is most frequently found; a dry condition is a frequent occurrence in the necrobiotic process of fatty degeneration; anæmia of the surrounding parts, or interspersed portions, depends on compression of capillaries by infiltration, which means: newly formed cells and connective tissue. Anæmia would once have been considered impossible as a lesion of inflammation, but we have fortunately passed by the time when this nutritive disorder was supposed to depend necessarily on previous congestion of the parts.

All those forms of change of tissue are not found uncomplicated in every given case. When large surfaces are attacked at once, you may see in the mouth a catarrhal proliferation or croupous condensation of the epithelium, on the tonsils a diphtheritic deposit imbedded into the tissue, in the larynx and trachea a plain croupous deposit, and in the bronchi a mucopurulent secretion. And again, under the same endemic and epidemic influences you will find a case of catarrh, a case of croup, a case of diphtheria, a case of follicular exudative amygdalitis in the same family, in the same week. Thus it appears, that in the long list of morbid conditions met with, catarrh on one side, the diphtheria on the other, are but the starting and terminating points between which all the different shapes and forms may be registered according to their dignity—their modification depending on individual, local, endemic and epi-

demic influences. The only form which is perhaps, but perhaps only, to be excluded, is the necrotizing diphtheria. And when we compare the clinical characters of the affection, we find similar differences. The affection may be local without fever, or simply febrile, or local and obstructing, or septic, or obstructing and septic. In some cases the process will not even be confined to the respiratory organs, but similar to the Rinderpest of animals, the digestive organs will participate in the process, and skin, kidneys, spleen may follow."

Now, Mr. President, a careful observation of this year's epidemic, as of those of former years, in which the nature of the cases was the same, only their number less, exhibits the following forms of local change in the complex of symptoms called diphtheria.

1st. Inspection of the pharynx yields catarrhal conditions of its whole surface, or part of it. Soft palate, or pillars, or posterior wall, or tonsils, or some or all of them are of a deep-red color, soft, swelled. This catarrh is a precursor of further development of diphtheria, or its complication. It need not necessarily result in diphtheria, for the number of independent cases of pharyngeal catarrh is very great in every epidemic. The Journal of the Dispensary, from which I took the cases on which was based my paper of 1860, exhibited 185 cases of independent pharyngitis to 200 of diphtheria. Not always is the catarrh very extensive. It is useful to know, and in individual cases very important to notice, that not infrequently small territories of blood-vessels and mucous membranes are in the morbid condition mentioned. This change would be an absolutely indifferent matter in normal times; during an epidemic of diphtheria it may usher in or be the first symptom of a regular attack. Sometimes, however, the differential diagnosis is not easy at all. For in many cases where a slight film of what appears to be mucus is seen to cover a portion of a tonsil on a hyperæmic base, we have in reality to deal with diphtheritic changes in the epithelium, and not infrequently are these the cases in which fever is unusually high, and general symptoms prevalent.

2d. In many cases we have to deal with small deposits as described above. They are not inflammatory, for there is no nuclear proliferation and subdivision, no intimate admixture of

leucocytes, a few of which may, however, be found adhering to the lower surface. The superficial epithelia are the principal sufferers; the lower strata are less changed. Their outlines are but feebly marked, sometimes not perceptible, with the exception of a very indistinct network containing an amorphous granular, dark, contoured material. Such granular material is also found outside the network. Part of it is described as consisting of round, oval grains with sharp outlines, of one-tenth or one-twentieth of the size of a blood corpuscle, conglomerated, and is sometimes found in large masses. It is said to be frequently not distinguishable from detritus, fine particles of albumen, and fat globules. Because it has been observed to spread and increase rapidly, and because of its similarity to the botanical parasites in putrefying material, it has been taken as botanical, parasitical; and called either sphæro-bacteria, micrococci, or monades. These elements have been presumed to be the essential matter in diphtheria, and the source and means of contagion. The fungous vegetations develop either in the mucous membrane without previous exudation, or in superjacent exudation, and are believed to infect the system by entering the lymphatics and finally the general circulation. Nutritive disorders are said to result from embolism of such parasitic masses, which increase rapidly. Thus not only results a destruction of the tissue and epithelial cells of kidneys, liver, spleen, and heart, but also large pneumonic infiltrations. Besides, in the opinion of some, new and unexpected changes result from the products of poisonous decomposition lit up by the presence of the immigrant parasites (Orth). The tendency of natural philosophy and its daughter, medicine, to realistic appreciation of natural phenomena, and the apparent facility of explaining some facts which are difficult to understand, have been the cause of the almost general acceptation of this theory, which appears to subvert well-nigh all our experience on the slowness with which, as a rule, all scientific progress is developed. The theory is so enticing, I might say bewitching, that we can hardly help burying everything we knew of pathology, and diving headlong into the new fountain of apparently "exact" knowledge. To what extent the best intellects can be captivated by a brilliant theory, especially when they had something to do with the establishment of the new edifice, we can learn from the following

quotation from Prof. C. Hueter's General Surgery, 1873, p. 269: "The insufficient penetration of the monades"—this is the name proposed and preferred by him—"into the tissue in cases of croup is an obstacle to their entrance into the lymph-ducts and blood-vessels, and therefore no serious general symptoms are found in croup. The progress of diphtheria cannot depend upon the effects of the movements of vibrating epithelia, because of their rapid destruction by the monades of diphtheria. When diphtheria gets down to the smallest bronchi the monades emigrate into the pulmonary tissue, and establish a pneumonia. But if it first establish itself on the tonsils and the mucous membrane of the pharynx, it cannot but descend into the larynx, because its access to the cheek and tongue is retarded by the heavy layers of pavement epithelium, and the immigration into the œsophagus is rendered impossible by the same cause. The nasal cavity appears to be better protected than the larynx; perhaps the secretion of muciparous follicles has something to do with that." I have quoted this passage to show to what extent the very best intellect can err when obnubilated by the influence of a pet theory. Not only shall we hear of better reasons for the absence of general symptoms in membranous croup of the larynx, but the whole theory, founded on the rapid destruction of vibrating epithelium, is also defective, for the reason that this very epithelium resists better than any other a speedy destruction by the diphtheritic process. Finally, not only is laryngeal diphtheria not an absolute necessity, as Prof. Hueter appears to believe, and nasal diphtheria the exception, but, on the contrary, the former is fortunately rare, and nasal diphtheria a common occurrence in protracted epidemics.

Nor is this all. We ought not to forget that histologists do not at all agree about the nature of the corpuscles claimed as bacteria in almost all infectious diseases. The number of investigators is very large, and good names are counted amongst them. But I, who am not a histologist laden with new discoveries, am aware of the fact that the world-wide reputation of some of these names is based almost absolutely and solely on bacteria, and that is too narrow a basis. I cannot but warn to be careful in accepting not facts, but their explanations. The reading with the microscope is relied upon as unimpeachable least by

those who are the acknowledged masters in that field. Panum is positive as to the chemical nature of putrid poison, so is Bergman, and so Verneuil. Billroth has published a series of investigations extending over many years in his great work on Coccobacteria. His conclusions are not identical with the bacteria theory as defined before. He is more inclined to believe that a chemical poison is the source of infectious disease, but that this *may* result from the presence and influence of coccobacteria in the blood. In the No. of Nov. 30th, 1874, of the *Berliner Medicinische Wochenschrift*, Arnold Hiller contends against the alleged characters of the bacteria as pathognomonic. I described, according to the general acceptation, bacteria as possessing well-marked outlines, great brilliancy, and a strong power of reflection. Hiller contends that it requires unacquaintance with botany and bacteria to believe that. According to him, both direct observation and comparison with fat molecules prove that bacteria excel by an opaque dulness rather than by brilliancy and distinct outlines, and for this reason are so remarkably difficult to discover, and that the reflecting power of a micrococcus stands in the same proportion to that of a fat molecule, as the appearance of an yeast-cell to that of a fat globule of equal size. Thus those very alleged characteristics of presumed bacteria would speak for their being products rather of fatty degeneration. Beale, than whom few investigators of bacteria have been more industrious or successful, insists emphatically upon the immense magnifying powers required to properly study these organisms. He also, as is well known, repudiates the idea that bacteria must be causes of the lesions of tissues in which they are found, when bodies precisely similar in appearance are equally abundant in health, "millions of bacteria are normally present in the mouth." However, it cannot be my aim to go beyond my subject; but in connection with our theme, I meant to protest against the dangerous consequences of an exclusive scientific enthusiasm.

3d. The small deposits spoken of under 2d, go on increasing, not only on the surface, but into the substance of the tissue. They have the same appearance, with a tendency to grayish discoloration. Removal of the surface detritus reveals an ulceration of the membrane with a moderate admixture, among the

epithelial remnants, of pus and blood corpuscles.[1] This is the form in which the detritus, bacteria, or whatever either the morbific or nosogenic elements may be, are principally met with. From what has been said of the elementary structure of the two last forms, we may draw inferences which will be found to exist in reality. We may infer that there may be removable and deeply imbedded deposits in close juxtaposition, and that after the removal of a surface deposit, the same process will take possession of the deeper tissues; and such is just the observation which is frequently made.

4th. The last form of diphtherite, as found sometimes on the conjunctiva, and in all cases of diphtherite of the œsophagus, vagina, trachea, and lower portion of the larynx, has been taken to consist of fibrine as principal constituent. The deposit consists of large flaps deposited upon the mucous membrane, lined underneath with mucus corpuscles, and a very few blood, corpuscles and epithelia. Even that, according to E. Wagner, is the result of a metamorphosis of the epithelium. But it has been urged that this is impossible. Only lately Senator has insisted upon the fact that, at the most, the epithelium is found in three or four layers, and that these are insufficient for the formation of thick and coherent membranes. The objection is not well taken, for in cases where the pseudo-membrane covering, for instance, the uvula, or soft palate and tonsils in general attains a thickness of several lines, it must be remembered that epithelium is known to reappear rapidly when thrown off or removed. A cast of the trachea and bifurcation thrown up by vomiting was replaced by another one within six or seven hours, and found at the post-mortem examination. The same happens in the nares, where the same author, not having seen cases, denies the occurrence of croup membranes altogether. In many of these deposits the epithelial structure has been noticed to be still apparent. It is not, however, necessary to deny that genuine exudation may be complicated with the original process of epithelial proliferation and transformation. For in the chamæleon-like changes of a diphtheritic process, irritation

[1] Fair specimens of this form are found on the tonsils and the upper half of the larynx, rarely the soft palate. Still, I have met with complete perforations of the soft palate in two instances.

of the neighboring tissues, and nutritive disorders of an inflammatory character may be expected to take place.

The several forms of diphtheritic disease, the description of which I have given, have a peculiar tendency to develop in certain localities. Where the whole lining membranes of the air-passages from nares to trachea and the mouth are covered with diphtheritic degeneration, the third form, viz., impregnation of the mucous membrane, with its epithelium, and sometimes submucous tissues, is found all over the tongue, edges of the lips, and frequently over mucous membrane of lips and cheeks; also on the tonsils, at the lower portion of nares, and the upper part, particularly anteriorly, of the larynx. The fossæ Morgagni are also, in most cases, in the same condition; seldom the soft palate, on its posterior aspect, more frequently on its oval surface. The first form, deposits in specks of small size, in the tonsils, and isolated portions of the posterior wall of fauces. The last, the so-called croupous form, viz., deposits upon the mucous membrane, easily removed in large flaps, or readily macerating in the copious secretion of the subjacent muciparous glands, in portions of the nares, in the posterior aspect of the soft palate, on trachea and bronchi.

Certain peculiarities of the tissues in general, the mucous membranes in particular, have frequently been assumed to exert a considerable influence on the nature of the diphtheritic process. Eberth, whose histological knowledge is remarkable, though his clinical observation appears to be but limited, refers [1] to the fact that a violent diphtherite of the larynx need not descend to the trachea, though he exaggerates the frequency of such an exclusive occurrence. Trendelenburg infected the trachea of a rabbit with diphtheritic deposits removed from the pharynx and tonsils, where they had been firmly and deeply imbedded into the tissue, and the results of his experiments were deposits loosely attached to the surface of the mucous membrane of the trachea, where he transplanted them. In general the condition of the mucous membrane varies in different organs and locations. Uniformly we find in successive layers: 1st, epithelium; 2d, the so-called basement membrane, thin and deprived of structure; 3d, connective tissue largely mixed with

[1] P. 6 of C. J. Eberth, "Zur Kenntniss der Bakteritischen Mykosen." Leipzig, 1872.

elastic fibres, with blood-vessels, nerves from both the cerebro-spinal and the sympathetic nervous systems, and frequently spindle-shaped nuclei. On the free surface of the mucous membrane we distinguish in addition papillæ, flocci, villi, and the apertures of a number of various glands. *As all of these constituents influence pathological processes in the mucous membranes*, they require a special consideration. I shall first, however, briefly review the parts which are the principal location of the diphtheritic process.

The mucous membrane of the mouth contains a large number of elastic fibres mixed with its connective tissue, and is covered with a thick pavement epithelium in three layers, the upper one flat, the second more polyedric, the lowest oval and perpendicular upon the mucous membrane. Many small papillæ extend from the mucous membrane into the epithelium, thereby resembling the papillæ of the cutis. Acinous mucíparous glands are frequent, most numerous on the anterior surface of the soft palate. The lymphatic ducts are very numerous on lips, tongue, uvula, soft palate, anterior and posterior pillars, and cheeks. The uvula contains so many that their injection doubles or triples its size. They discharge their contents into, and in case of morbid irritation infect the deep facial glands. Those of the tongue are more intimately connected with the upper layer of the deep cervical; those of the floor of the mouth, and many of the tongue, with the submaxillary glands. The vasa efferentia of all of them discharge their contents into the superior jugular glands in the trigonum cervicale superius, and finally into the numerous (15–20) inferior jugular (or supra clavicular) glands which through numerous connections form the jugular lymphatic plexus.

The tonsils are conglomerates of an uncertain number of glandular bodies, each of which has a thick capsule with irregular outlines, consisting of connective tissue, and is lined inside with mucous membrane and pavement epithelium. In the connective tissue there are a large number of closed follicles containing numerous lymphoid corpuscles. These follicles have been taken for identical with, or analogous to lymphatic glands. This assumption is problematic, as neither in-going nor out-going lymphatic ducts have been conclusively proven to exist. It would result, as a practical conclusion, that there

was *no* connection of the tonsils with the lymphatic system, nor is the supply of blood-vessels a large one; it is decidedly small in chronic inflammation and enlargement, with hypertrophy of connective tissue.

The mucous membrane of the nares is of various thickness, consists of connective tissue fibres with numerous nuclei, and has no admixture of elastic fibres, but many nerves and an unusual number of blood-vessels. In fact the Schneiderian belongs to those mucous membranes which are uncommonly supplied with blood. Its submucous tissue is, therefore, very apt to swell, or to bleed, as well in diseases of distant organs resulting in venous stagnation as in slight local provocation. The inner aspect of the cartilages is covered with pavement epithelium. The lower portion of the nasal cavity, the so-called respiratory part, as far as supplied by the fifth pair of cerebral nerves, has cylindrical epithelium, and a large supply of acinous muciparous glands. The upper portion, the so-called olfactory part, has vibrating epithelium, and, according to Todd and Bowman, long and straight tubular glands. Some of the epithelial cells have been found, by M. Schultze, to connect with the terminal ends of the olfactory nerves, particularly a layer of those which are more spherical, branching out in two directions, and have been denominated as olfactory cells. In this portion the lymphatics are but slightly developed, but they are very abundant in the lower part, also in the alæ. They terminate directly into the deep facial, and the posterior submaxillary glands, with all their connections. Thus the mildest provocation, a nasal catarrh in a child, is apt to produce glandular swelling either temporary or permanent.

The epiglottis has on its anterior or upper surface a pavement epithelium of 0.2 mm. in thickness. On its posterior or lower aspect it is but 0.1 or 0.06 mm. The upper stratum is spherical or polygonal, the deeper more cylindrical and joined palisade-like together. Nearer the insertion of the epiglottis the polygonal cells disappear, the cylindrical then rise to the surface and are supplied with cilia of 0.005 mm. in size. Below them round and oval cells are found to such an extent that the whole epithelial covering measures about 0.15 mm. The same form—ciliated epithelia—are found below on false vocal cords and in the ventricles of Morgagni. But along the posterior

aspect of the pharynx, over the ary-epiglottic folds, where moreover the mucous membrane is lined underneath with a very thick and loose submucous tissue, and along the true vocal chords —the *covering is formed of polygonal pavement epithelium ;* in the direction of both the ventricles of Morgagni and the trachea it is replaced by ciliated epithelium in a thin layer. The mucous membrane itself is most loosely attached in the neighborhood of the ventricles of Morgagni, and is very thin, loosely adhering, and often folded upon the true vocal cords. Acinous glands are numerous, from fifteen to twenty on a square centimetre, and longitudinally arranged. They are very frequent about the ventricles, with cylindrical epithelium (rarely ciliated) in the ducts. There are, however, *no acinous glands, no glands of any kind,* in spite of the looseness of the submucous tissue, in *the true vocal cords.*

These acinous glands carry no lymphatic vessels. In other parts of the laryngeal mucous membrane and submucous tissue these are, however, met with. They are, in fact, both numerous and large, with the general character of the lymphatics, viz., endothelium, dilatations, constrictions. In the epiglottis of the newly-born they form but a single layer, in the larynx itself and in the trachea two, in some portions provided with a large amount of submucous tissue, even three. The inner and smaller layer takes a perpendicular, the outer and larger a horizontal course. The posterior aspect of the epiglottis and the true vocal cords (not only during the first year of life) exhibit by far the smallest number and calibre of lymph-vessels.

Agminated glandular substance, that is, lymphatic glands (extensively found in the cat, according to Verson, and always in Morgagni's ventricles in the dog) are rarely found in man. The exceptions found by Luschka, referring to the vestibule of the larynx and the margin of the plica ary-epiglottica, and also upon the posterior aspect of the epiglottis, confirm rather than weaken the rule.

The mucous membrane of the trachea and bronchi contain more elastic than connective-tissue fibres; a fair number of lymphatic vessels, no lymphatic glands; very many acinous glands; and is thickly lined with ciliated epithelium.

The accompanying table will condense some of the above statements.

	NOSE.	MOUTH.	TONSILS.	EPIGLOTTIS.	LARYNX.	TRACHEA.
Elastic fibres.	None.	Many.	Very many.	Many.	Many.	Very many.
Epithelium.	Pavement near cartilage. Cylindrical in resp. part. Vibrating in olfact. part.	Pavement.	Pavement.	Pavement thick ant., thin post. Vibrating at inner insertion.	Vibrating anteriorly, foss. Morg. and false vocal cords. Pavement posteriorly, and true vocal cords.	Vibrating.
Lymph ducts	Very numerous in resp. part. Moderate in olf. part.	Many. Uvula very numerous.	Few, if any.	Moderate ant., few post.	Numerous, usually no lymph glands. None on vocal cords.	Numerous.
Blood-vessels.	Very numerous.		Few.			
Nerves.	Very numerous.		Scarce.			
Acinous glands.	Numerous in respir. part. Tubular glands in olf. part.	Numerous.			Very numerous in vent. Morg., some, however, have no lymph ducts.	Very numerous.
Submucous tissue					None on vocal cords. Very copious in plica ary-epiglottica.	

Of all the tissues and organs mentioned, the elastic tissue, which enters so largely into the fabric of the connective tissue, is least affected by chemical or organic influences. On being boiled it yields no glue; like connective tissue, it is not changed by water, acetic acid, alcohol, gastric juice, or moderate heat. It is firm, dense, has a degree of elasticity never attained, normally, by any other tissue. It has but few blood-vessels, no nerves; few lymphatics, and a slow metamorphosis. In consequence, upon injuries received, it is not reproduced, but the healing process results in the formation of a fibrous cicatrix.

There is no elastic tissue in the mucous membrane of the nose, a large amount in the oral cavity, and particularly in the walls of the lymph follicles of the tonsils; and such an amount in the trachea that the connective tissue fibres are in the minority. The influence of this anatomical condition on the diphtheritic process must be considerable. It will be easily demonstrable, that where elastic tissue abounds it resists the deep diphtheritic impregnation of the tissue for a long time, but when it has taken place resists recovery as well.

The epithelial changes which form the diphtheritic deposit belong principally to pavement epithelium. Where this abounds, the diphtheritic poison is most apt to find a place to rest and develop; thus the tonsils, not only for their prominent location, but also for the structure of their surface, form a fit receptacle and breeding-place. Vibrating epithelium is not so apt to be destroyed. It is higher in the animal scale, and has a more complicated structure function.

Where muciparous follicles abound, their normal secretion, as a rule, prevents deep-seated degeneration of the tissue. Epithelial conglomerations are lifted up from the surface, no tissue takes part in the morbid process to any great extent, the serum of the mucus penetrates the deposit, and disposes it to macerate. Thus the deposits formed in the respiratory part of the Schneiderian membrane are apt to be constantly discharged from the nostrils unless their production is too massive, and the membranes of the trachea are frequently gushing out of the newly-made tracheotomy opening in semi-solid consistency. The frequency of muciparous follicles in the larynx and trachea is also the reason why the numerous

lymph-ducts of the mucous membrane cannot act much on the superjacent, but loosened masses, thus offering a better reason for the merely local character of laryngeal and tracheal diphtheria, and the absence of constitutional symptoms, than that which Hueter offered as an explanation.

The vocal cords are deserving of a special mention. They form the borders of the narrowest entrance into the lungs. Foreign substances, no matter whether of benign or malignant character, will be retained by them. They are supplied with pavement epithelium, which is the principal seat of diphtheritic degeneration. They have no muciparous glands, nor have they lymph-vessels. Thus, if there is any organ predestined for diphtheria, it is the vocal cords. Where there is not poison enough for a thorough infection, there is still enough for a local deposit. Where diphtheria has died out as an epidemic, the stray cases with limited infecting power will be known for years or decennia as so-called sporadic membranous croup, as you would speak for a generation of an occasional case of sporadic cholera, or a stray case of variola. There is not infection enough to poison the throat and larynx and blood, but just sufficient for the most favorable place, the vocal cord. No speedy removal of the diphtheritic mass can be obtained, for there are no acinous glands underneath. No general infection can spread from them, for there are no lymph-ducts to communicate it. Besides, suffocation sets in too soon for the neighboring lymph-vessels to become agents and bearers of infection, in case the deposit would macerate.

Thus, if anatomy and physiology mean anything, I hope the vexed question of "croup," or "diphtheria" in the larynx will be considered as settled.

The distribution of blood-vessels, and more still, of lymph-ducts, is of the greatest importance as far as general symptoms are concerned. Their absence from the tonsils explains the benign character of tonsillar diphtherite; their number and size, and the direct connection with lymphatic glands in the Schneiderian membranes, explain the danger of nasal diphtheria. Sometimes the lymphatics have hardly time or opportunity to act. In the many cases of slight hemorrhage to which I allude at some other place, from the nostrils, absorption appears to take place through blood-vessels directly; in

those cases the usual immense swelling of the glands of the neck is missed, but the effect on the general system is nevertheless developed rapidly.

To the lymphatic ducts and glands I have alluded very frequently. In fact, they are of prominent dignity in a large number of serious or fatal cases. Thus they deserve a few moments' special attention.

The number of lymph-vessels, distributed as they are over bones and fasciæ, blood-vessels and nerves, connective tissue and fat, is almost incredible. The larger ones form a closed system of canals. Their walls consist, like those of blood-vessels, of three layers—an intima, a media, and an adventitia; the first is made up of elastic fibres, with pavement epithelium; the second is muscular and contractile, only thinner than that in the blood-vessels; and the third has a looser connective tissue than the corresponding layer in arteries and veins. The smallest lymph-vessels, like the capillaries of the blood-vessels, claim no constituent to their walls except a pavement endothelium. Whatever connective tissue is lining this simple layer of endothelium, belongs to the surrounding organs, and not the lymph-ducts. Thus they can hardly be thought of, except in the most intimate connection with the fibres and cells of all connective tissue. Thus far, all histologists at the present time agree. The modus of this connection, however, has been explained in the most different manners. Kölliker, for instance, looked for the last distributions of the lymph-ducts in the pointed outgrowths of the connective-tissue cells. Recklinghausen denies the existence of membranes in the finest distributions; according to him the open interstices between the connective tissue or epithelium cells are the first origins of lymph capillaries. Neumann claims the system of lymph capillaries as a closed system of canals, at least as far as concerns the skin, which he has made the subject of a recent monographical study. Its walls, according to him, are lined with pavement epithelium, not interrupted by any stomata, in no way directly connected with open spaces between the connective-tissue cells; their superficial layer consists of the most minute forms. They are just interior to the superficial blood-vessels; their inner layer is larger and sometimes endowed with valves, and they are found in innumerable quantities all through the connective tissue, fat, perspiration

glands, sebaceous follicles, hair follicles—in all of which Teichmann and Sappey were not able to find them—besides the papillæ and the whole tissue of the cutis. Thus it appears, from the discrepancies of observations and opinions alluded to as specimens, that the origins of lymph capillaries may vary in different organs. Recklinghausen is positive in his statement (so different from Sappey's) that the most minute terminations in the peritoneal epithelium and on the pleural covering of the diaphragm are open stomata, thus exhibiting the large thoracic and abdominal cavities, as it were, in their character of immense lymph-sacs. Through these stomata the lymph, viz., nutrient fluid minus what is being used for tissue building, plus what has been excreted from the tissues, would be admitted to the smaller and gradually the larger lymph-ducts (the valves of which are diverted towards the heart) under the influence of three motors, one of which is muscular contraction, the other arterial pressure, unbroken by the slow current of terminal plasmatic circulation, the third, central aspiration.

The liquid contents of the tissues, or such particles or ingredients as can be suspended in them, of a gaseous or chemical, or parasitic character, are swept off to the lymph-glands, the peripheric fascia propria of which forms a first resting-place. For here the lymph-vessels are divided in branches, before perforating it and discharging into the lymph-spaces of the alveoli of the cortical layer, which are filled with lymphoid corpuscles composed of coarsely granulated protoplasm. From it the lymph, in thin canals, is swept into the medullary part of the glands, the nature of which is the same as the cortical, with the exception that it is less compact, inasmuch as the connective-tissue trabeculæ are less developed, and the lymph-spaces more numerous and larger. The lymphoid corpuscles originally formed in them are swept away with the incoming current, thus increasing the amount getting into the outgoing ducts, which are smaller in number, but larger in size than the ingoing ones. Whatever infectious material enters through the vasa efferentia, and is small enough to be swept out with the lymph and the newly-suspended lymphoid corpuscles, will then be introduced into the unimpeded current of the lymph and blood-circulation, those cases excepted in which another obstacle to an uninterrupted flow is found in a second tier of

lymphatic glands. Whatever is of the unirritating character of the lymph, and not larger in its microscopical measurements than it, is swept through the fascia propria and into the reservoirs of the cortical and medullary substances of the gland in an uninterrupted current. But two accidents may happen. The foreign admixture may be too large to pass easily. Then there will be stagnation, irritation, either in the fascia or the trabecles of the substance. The circulation of the blood capillaries will be stopped by pressure, swelling will ensue, proliferation take place, the circulating lymph mix with white corpuscles from the lymph-spaces and the stagnating blood-capillaries, and an abscess, either intra- or peri-glandular, result. Where this is not the end, the foreign material will be retained inside the fascia, in the connective tissue, or the dilated lymph-ducts of the cortical substance. Thus the coloring matter of injected liquids has been found safely stowed away in this external part of the gland, without entering the circulation. Thus the gland, with or without being much disturbed in its own integrity, may form a receptacle for noxæ swimming with the lymph current. Thus syphilitic or other poisons deposited in the gland may be suspended in their injurious consequences, or when their presence results in irritation and speedy suppuration. Thus they may be eliminated by the timely opening of an abscess.

The glands may be engorged even when the foreign material is not excessive in quantity, but only highly irritating in character, by being of a heterogeneous nature; no matter whether chemical or parasitic. In cadaveric infection the axillary glands will swell to fifty times their original size, they and not the cubital glands, forming the first depot for the majority of the lymph-ducts of the fingers. Thus the glands of the neck swell in diphtheria in a few hours to an unseemly extent. To a certain degree this swelling must be expected to take place whenever anything irritating enters the lymph circulation; the irritation of a simple nasal or oral catarrh results in gradual swelling of the neighboring lymph glands, and many a case of presumed scrofula diagnosticated from glandular enlargement finds its ready explanation in the existence of a chronic catarrh of the nose, or protracted uncleanliness of the mouth. But when irritaments are very small, and very numerous, large numbers

may be swept into the general circulation before resulting in local swelling. When they are very small, and not very numerous, they may pass the lymph ducts and glands for days, and perhaps weeks, resulting in general poisoning rather than in local disturbance. Thus the poisonous detritus, whose elements are ten or twenty times smaller (if at all measurable) than lymphoid corpuscles, may fluctuate to and fro through the blood, interfere with general nutrition, stagnate in the slow side circulation of the white corpuscles in the smallest blood-vessels, increase rapidly, emigrate, form deposits, purulent, septic, and gangrenous, and disintegrate tissue to any extent, before local symptoms are diagnosticated. Not infrequently do we find, that the very mildest cases—apparently—result in the most severe attacks. Sudden collapse and death in diphtheria is generally observed in alleged mild cases, such as I have mentioned fourteen years ago, and it has been my experience and that of many observers, that paralysis will occur in the convalescence in the same class.

Thus the question of mildness and severity of local or general affection appears still shrouded in mystery.

Is diphtheria principally a local, or principally a general disease? Or which form of the two is the more dangerous one?

In 1860 (*Am. Med. Times*, Vol. I. p. 95) I used the following words, which express the opinion, I believe, of many of my professional brethren: "Diphtheria is a general disease; it has local deposits, it is true, but in the same manner that scarlatina will localize itself on the skin, mucous membrane of the Bellinian canals, etc.—measles on the skin and the mucous membrane of the respiratory organs, or typhoid fever on the mucous membrane of the intestinal tract." In most of its bearings the question is, in my opinion, an idle one. Any injury to the system has to pass in through a specified locality. The difficulty to decide through which, is perhaps best illustrated by the dispute concerning the typhoid noxa entering the organism through either the lungs or stomach. In some cases there is no dispute; whooping-cough is admitted to prove contagious by entering the lungs. Nor is there much dispute on the admission of diphtheria into the system. With the rare exception of those cases in which the vaginal mucous membrane, or denuded cutis or the intestinal mucous membrane proved the first seat of infection, we meet it first on the respiratory mucous

membranes or where respiratory and digestive mucous membranes cross. In the large majority of cases we find local changes as soon as called to see a new case, together with, or in preference to, general symptoms. Seldom are there the latter, particularly fever, without some of the former, viz., that class, which more than fourteen years ago, I described as "diphtheritic fever." Taken for granted that the latter cases exist, how do they originate? The morbid matter, chemical or parasitic, unless retained before descending so far, enters with respiration into the pulmonary alveoli. Their surface, if spread out, would cover 2,000 square feet, under which the immense lake of blood, amounting to one-fifth of the whole weight of the body, is brought into contact with five thousand quarts of air every twenty-four hours. Gaseous, or chemical, admixtures of a poisonous character find no difficulty in entering the circulation as easily, or nearly so, as air. The only separating line between the atmosphere and its contents on one side, and the blood lake on the other, is a single layer of epithelium (sometimes absent), of the alveoli, of 0.003 to .004 lines in thickness, spread over an elastic basement membrane, behind which capillaries of 0.003 to 0.005 lines in thickness are found. All the epithelia of the respiratory organs are cylindrical and vibrating, and as such not apt to permit of an easy entrance of foreign substances into the smallest ramifications of the bronchi. Their function of and success in removing large masses of mucus from the bronchi, in an upward direction, would alone make us infer that the admission of specific solid poisons into the blood through the respiratory organs was not an easy matter or frequent occurrence. At all events, such elements cannot be swept through epithelia lining alveoli and capillaries with the same facility as through air, and the relative slowness with which changes in the epithelium of visible mucous membranes are apt to take place, renders the rapid absorption of poisons through lung epithelium somewhat doubtful on the hypothesis that these poisonous germs were really bacteria.

Thus we should say that in all cases in which a patient is taken ill suddenly, or pretty suddenly, in the course of a few hours, or a day, after having enjoyed entire health, with a high fever and some diphtheritic deposit; remains sick for half a day or a day, or even two, with the same fever, which then

rapidly diminishes and leaves him fatigued and feeble for a few more days, until in the course of five or seven days he feels perfectly well again, we should say that such a case of sudden attack and sudden elimination of the noxa must positively be the result of a gaseous substance or of one soluble in the fluids of the human organism, and not of a solid body. And these are no hypothetical cases, they are to be found every day. It is true they are not all of the same kind; nor is, for comparison's sake, scarlatina. There are rapid cases, slow cases, high fever, low temperatures, large deposits, minute plaques. There is no case which would exclude the possibility of a sufficient explanation on the theory that we have to deal with a gaseous or liquid substance, whether complicated with or attached to bacteria or not, is indifferent, but there are at all events some —just such as I have mentioned—which cannot be explained by the bacteria theory as well.

Other facts might be explained by it, as by the gaseous poison theory. The facility of deposits on prominent elevations, such as the tonsils, would occur in both. The resistance of the vibrating epithelium of the nose to diphtheria is explainable by both. Inhalation takes place through the nares principally, and still while we have a great many cases of nasal diphtheria in the epidemic of this year, we can almost always prove the case to have originated in the pharynx, and ascended. Primary nasal diphtheria is but rare, for the pavement epithelium of the lower portion of the nose is so near the surface, and so frequently in contact with mucus, etc., that the first deposit will not take place there. Facts like the following will admit either theory.

Two boys in a family were taken with symptoms of diphtheria at the same time. One evening the one had slight fever, and severe headache, the other without fever, a deposit on the left tonsil, which was by far the larger of the two. In him both tonsils had been known to be large, in his brother they were small, hardly visible. Next morning the one had a deposit on his tonsils in addition to his fever and headache, the other fever and headache in addition to his diphtheritic membrane.

Fever is not the only symptom resulting from the direct rapid introduction of an irritating material into the blood. In fact, it is safe to assume that high fever—individual peculiarities always excepted—results from rapid absorption of large quantities

only; provided again, that they are of an irritating character. For even septic processes run their entire course without, in many instances, a serious elevation of temperature. Not in all cases, however, have we to deal with large quantities of poison and rapid introduction into the blood. What, in my mind, points to a slow absorption through the blood, of more or less of the poison, and to its distribution to certain centres or localities, are the cases of gradual or sudden collapse and paralysis. The first case of collapse I ever observed has been published in the first vol. of the *American Medical Times*, p. 95. A healthy and robust boy of four years complained of some pain in swallowing, and appeared languid and sleepy. It was in the autumn of 1857, and no epidemic of any kind prevailed in the city at that time. The child did not appear to be very sick; there were very few local symptoms in the throat, a little tumefaction of the tonsils, no particular œdematous swelling, no unusual degree of local hyperæmia, but several small patches of membrane on either tonsil. Pulse ninety, feeble. Moderate temperature of the skin, extremities not cold, skin rather dry and flabby. The child was listless, indifferent, took some food as a matter of course without longing or asking for it. No local pain anywhere, except a slight uneasiness on pressure exercised on the tonsils; bowels rather constipated. Questions were answered intelligibly, but indifferently and slowly. Pupils reacted to the light. No cerebral symptoms whatever, except the slowness of mental function alluded to. No diagnosis except that of pharyngeal diphtherite, as I had not seen a case of general diphtherite at that time. No particular change next day, nor on the third, with this exception, that the child grew more and more indifferent, listless, and melancholy, cared little for anything that was done to rouse and ease him, and appeared to have no desire for or objection to anything. The pharyngeal membranes extended somewhat, but not over a surface of more than two-thirds of an inch in diameter. No progress downwards, no affection of the respiratory organs, no dyspnœa. No appreciable change had taken place on the morning of the fourth day, except that the general adynamic condition of the child was increasing. Thus it kept on, although the child took some food, uttered a few words now and then, answered questions, and retained apparently the full amount of

his intellectual faculties. The temperature decreased, the patient sank more rapidly, and died in the afternoon; no dyspnœa, no perceptible cause of death. Extinction of life like a fire slowly extinguished from want of fuel. Post-mortem examination yielded but negative results. No organ abnormal; general anæmia. Little blood in the vessels, thin, and of a dark color. No diphtheritic membrane in any part of the body except in the pharynx.

I look upon the result of that post-mortem examination as very incomplete. Changes in the tissue were not examined or noticed. It was seventeen years ago, long before Zenker and his successors had discovered and described the granular degeneration and parenchymatous inflammation taking place in most tissues in all kinds of feverish, and particularly infectious diseases. The only important symptom mentioned is the dark color and thin consistency of the blood. The same condition has since been found by other observers in cases of sepsis and sudden death; also extravasations, fragility and granular degeneration of tissues, sometimes accumulation of cells and nuclei between the fibres. Hiller and Mosler emphasize in such cases the degeneration of the heart muscle; others, coagulations in the heart, resulting either from insufficient contraction of the heart itself, or from floating thrombi which were formed in distant veins suffering from the general circulatory weakness, sometimes from thrombi formed in the small veins of the neck during the efforts of croupous respiration. Others look for the explanation of the sudden death in the interrupted innervation of the heart. Either the pneumogastric or the sympathetic nerve may be affected, and the symptoms may vary accordingly. A paralyzing influence working in the tissue of the former will accelerate the pulse; a degeneration of the sympathetic heart ganglia renders it slower, and death may finally occur in either condition. It is the same apparent incongruity of symptoms, easily explained, however, which we notice is the common form of fatty degeneration of adults.

We must look upon the changes leading to death, in the majority of such cases, as of the same character, although of different degree, as those belonging to diphtheritic paralysis. It is frequently accepted that the poisonous material, parasitic or chemical, exerts a local influence upon a nerve, or a set of

nerves. Oertel, whose article on diphtheria in Ziemssen's Cyclopædia has suddenly obtained amongst us a notoriety which in my eyes it but partially deserves, takes for granted that diphtheritic paralysis is a progressive peripheric paralysis. He claims that every case begins in the pharynx, admits, however, that diphtheritic paralysis exhibits a very unsteady character, can return to a nerve territory which had recovered, and attack distant territories at once, or gradually. I do not believe that every case of diphtheritic paralysis, many of them appearing when convalescence is fully established, can be explained in the same routine manner. Many of them may be, as they appear to be, identical with the cases of paralysis after typhoid fever, variola, dysentery. In some the paralysis has certainly crept away, as it were, from the first attacked mucous membrane, in others it results from fatty or granular degeneration of muscular fibres (Buhl), or from capillary hemorrhage and waxy disintegration. In some the affection is decidedly central. Thus nuclear proliferation and hemorrhage have been found in the spinal ganglia by Buhl, in the gray substance of the spinal chord, even disseminated myelitis by Oertel. In many it may be due to the facility with which nutritive disorders, local effusions and extravasations occur in conditions of general hydræmia, and insufficient restoration of the blood-vessels, when the progressing convalescence invites to undue over-exertions of the heart. In former years I inclined to explain every case of diphtheritic paralysis upon view. But in a large percentage of cases of diphtheritic paralysis I attribute it to the presence of the morbid substances in the blood and nerve, into which they were received through the lungs, slowly, without much feverish excitement, without many local symptoms about the pharynx or nose. The more fever, the more rapid elimination of the poison. This hypothesis is more than merely plausible for several reasons. It is a frequent experience that paralysis will follow a case of diphtheria with pharyngeal or nasal symptoms, when but little developed. Where they are well marked the temporary paralysis of the soft palate, which Oertel takes as the regular starting-point of the affection, is frequently observed. It results partly from œdematous suffusion of the tissue, partly from diphtheritic affection of the motory branches of nerves distributed in them. But serious paralysis of

distant nerves will rarely follow. On the contrary, the paralysis of the superior and inferior laryngeal, the ciliary, facial, the optic, the spinal nerves of both trunk and extremities, are usually met with after cases of diphtheria, which ran their course in a short time and with but few local symptoms. The very fact that the paralyzed nerves need not necessarily belong to the same neighborhood or territory appears also to prove that the circulation is the highroad on which the poison enters nerve-centres, or peripheries, without regard to tonsils or palate. While Oertel, then, assumes that bacteria mine their way through the tissue, I find it easier to believe, and more in accordance with clinical experience, to assume that a slow admittance of the poisonous elements to the blood, in constant succession but relatively small numbers, yields a readier explanation of that much dreaded symptoms.[1]

The questions regarding prognosis are twofold.

1. Which class of persons are apt to be infected with diphtheria?

2. Which class of cases are apt to prove serious or fatal?

1st. Most infectious and contagious diseases are observed amongst infants and children. Scarlatina, measles, hooping-cough, diphtheria, are mostly seen at that period of life. Typhoid fever is not a rare disease; but it is as frequent in adults as in children, and more serious. In the new-born it is exceedingly rare; there are but four doubtless cases on record. The fifth

[1] Let me here illustrate my opinion of Oertel's article, which is by no means his best work, nor even an addition to our knowledge of diphtheria—after his own previous and other elaborate researches—but has done more than anything else to make his name known amongst the profession, and the public who are never satisfied with anything less than a surprise, or a panic. I allude, as an instance of his methods of reasoning and teaching, to his remarks on the treatment of diphtheritic paralysis. He recommends the interrupted and the galvanic current, warm salt-water, sea and sulphur bathing. Of internal remedies he rejects nux vomica, declares it to be positively injurious, and in its subcutaneous administration abominable. And why? Nux vomica acts through the nervous centres only, therefore, "at the best," it injures the patient. May we ask: What does nux at its worst when "at its best" it injures the patient? Besides, the theory of the efficacy of nux is not so safely established that it can subvert general experience. And general experience is in all countries unanimous in the praise of nux in cases of diphtheritic paralysis. This is one of the remarks in which our author's clinical experience is insufficient, and, at all events, inferior to his powers as a histological observer and describer.

was reported by me, and specimen of intestine shown—baby died when sixteen days old—two years ago in the Obstetrical Society. Throughout childhood the cases are mild, getting more severe with advancing age. I believe this is so, because in very early infancy part of the lymph system, particularly Peyer's plaques, are very undeveloped, and because of the superficiality of inhalation, probably also because of the rapid metamorphosis which enables infants to rid themselves, while slow infection is going on, of a large portion of the noxa. Measles, scarlatina, hooping-cough, are rarely met with beyond the age of twelve or fourteen, because of their having occurred before, and their return being but exceptional. Diphtheria is rare under eight or ten months of age, more frequently before the third, than between the third and sixth or seventh month. Childhood is more liable because of their greater softness and moisture of tissue, their larger number and size of lymph-vessels (Sappey emphasizes the fact that in the young the lymph-ducts of the pharynx are easier to inject than in the adult), their greater tendency to nasal, and especially to mouth catarrh—from want of cleanliness, as far as removal of nasal mucus and remnants of food is concerned, and principally because of the excessive relative size of the tonsils. There are few infants and children where the tonsils do not overlap the pillars of the palate; the roominess of the fauces is relatively little; these large tonsils cease to be annoying only when toward puberty, the fauces enlarge without contemporaneous enlargement of the tonsils. Infants from two to eight months are almost exempt from diphtheria because of the large amount of secretion, slightly acid, in their mouths. Even thrush, with its oidium albicans, is rare at that age; transmigration, or rather attachment of immigrating poisoning substances being prevented by this acid.[1] The majority of cases below seven or eight months, which have come under my notice—two cases of pharyngeal and laryngeal diphtherite in the newly-born included—were under two or three months. Liable to be infected are further

[1] It is probable that the diphtheritic poison attacks the conjunctiva so rarely for the same reason, viz., because of the copious lachrymal secretion. It may, however, be merely accidental that I have seen more cases of conjunctival diphtherite twelve or fifteen years ago than at present. It is probable that such patients avail themselves at once of the increased facilities for the treatment of eye diseases.

all those whose mucous membranes, respiratory and digestive, that have been in a condition of chronic catarrh. Catarrh of the mouth, with caries of the teeth, pharyngeal and nasal catarrh, congenital and acquired enlargement of the tonsils, exposure to cold air, to inhalation of dust, excessive screaming, cauterization, are just as many invitations extended to the diphtheritic poison.

Which locality yields the better or worse prognosis? Affection of the tonsils is decidedly favorable; of the larynx, for reasons amply set forth, decidedly grave, almost always fatal; of the nares grave. The narrowness of the infant's and child's larynx induces suffocation; the adult larynx is large enough to permit the diphtheritic deposit to assume a septic character. But once in my life have I been called upon to perform tracheotomy in an adult for membranous croup. The nares have been spoken of as dangerous ground. The large number of lymph-ducts, and neighborhood of lymph glands, the large number of superficial blood-vessels, and the facility of absorption, the liability to putrefaction through exposure to moisture and air of all the contents of the nasal cavity, and the inhalation and of the fetid smells, explain the fact of nasal diphtherite being so grave. But it shows unacquaintance with the facts, as in Oertel's essay alluded to before, when he assumes that it is almost always fatal, and unacquaintance with the proper treatment on the part of a celebrated Paris authority, when he was heard to say in his wards, but a few years ago, that nasal diphtheria was always a fatal malady. It is apt to be so when not properly treated; its mortality is not grave, when timely and regularly attended to; but this attention must be *timely* and *punctual*.

Which form of the disease is the most grave? Next to the attacks involving laryngeal obstruction, ranks the septic and gangrenous form of diphtheria, whose dangers are in proportion to the rapidity of absorption and inhalation. But the mild form may change into the severe, and therefore the prognosis is never a safe one, until the process is fairly near the end of its full course; and then even relapses may take place.

The condition of the general system is of great importance. Large wounds are liable to become diphtheritic. I have lost two patients of wound diphtheria after exsection of the hip-

joint; one was taken while in fair recovery, in the third week after the operation; one was attacked, a day after the operation, with scarlatina and diphtheria. General anæmia is a bad complication, as is also starvation during the course of the disease. In a condition of hunger or abstinence the absorbing lymph-vessels are found full and active, and the chyle-vessels empty. During digestion the latter are full, the former empty.

Low or high temperatures, when observed but once, give no special prognosis. Of low temperatures in dangerous cases I have spoken before. High temperatures and other grave reflex actions, vomiting, convulsions, may occur without meaning much harm unless they last long. A few days ago the first temperature taken by Dr. Conrad in the axilla of an adult and robust patient, who had complained since the previous evening only, was 107°. The local deposit was but small. In eighteen hours the temperature was 102°, in a few days normal; evidently elimination was as prompt as the absorption of the poison. In such cases a vigorous action of the heart is surely as positive a safeguard as is a feeble circulation a danger.

Liability to glandular swelling, or the presence of enlarged glands, with a tendency to press on the jugular vein, tends to increase cerebral symptoms. Complication with measles or scarlatina is frequent, especially with the latter. The course generally taken by diphtheria complicating these diseases illustrates beautifully the tendency arising from previous conditions of the mucous membranes. Diphtheria in measles, with its catarrh of the respiratory organs, is apt to terminate in membranous croup of the larynx; putrid bronchitis, however, is rare because of the very antiseptic character, to a certain extent, of carbonic acid. Scarlet fever, however, with its localization on the digestive mucous membranes, is but rarely followed by laryngeal diphtheria, while the malignant forms of throat diphtheria are numerous.

Hemorrhages from the throat prognosticate badly. They prove destruction to a certain depth, and prophesy a rapid progress of the process, perhaps with absorption. Fortunately the number of such cases is but small, and a goodly number of them even, as long as no general purpura sets in, are not fatal.

Pneumonia is a serious complication. Of its presumed origin from immigrating bacteria I have spoken. Broncho-

pneumonia may result from atelectasis (as œdema from swelled blood-vessels) in the impeded respiration of laryngeal croup. Pneumonia may result from the aspiration downwards of decomposed materials. Embolism results from thrombi in small veins, either near the larynx in croup, or in other parts from debilitated circulation, or by portions of a heart clot torn away.

Nephritis is not an unfrequent complication, although albuminuria is more so. The presence of albumen is frequent enough. It may result from high temperature only, and then contains but few or no tissue elements, or from swelling and fatty degeneration of the kidney epithelium, as in other acute infectious diseases, or from venous stagnation during the course of membranous croup.

If, at the conclusion of this paper, I venture to speak of the therapeutics of diphtheria, I may be permitted to say a few words in my excuse for appearing commonplace and trite. For in truth, the remedies which I use are so simple in character and so few in number, that I should hardly risk to speak before you were it not that I feel that I have always tried to stand on the safe ground of a sound pathology. Many a case of diphtheria I have not attended, because I believe I have prevented it. I do not speak of those members of a family who if exposed would have fallen sick, but who were protected by isolation of a patient under the same roof. I speak principally of the preventive apparatus in the hands of every family practitioner. I look after the mouth and pharynx of the children in my acquaintance as a regular thing. Eruptions on the head must be removed, and glandular swellings around the neck thereby cured or prevented. The same is done for nasal catarrh and catarrh of the pharynx in the good season, where the prognosis of your treatment is more propitious. Hypertrophied tonsils must be exsected at a time when no diphtheria prevails. For at such times every wound is apt to become diphtheritic; and hardly any operation inside of the mouth will heal without turning diphtheritic. For the same reason I postpone any sort of bloody operations during the epidemic of diphtheria, if barely possible. But lately I have seen the wound of an operation for cystocele, performed by one of our most prominent operators, in a house where there was no diphtheria before, to turn diphtheritic and jeopardize the success of the operation.

As a further means of preventing disease I may at this juncture speak of a remedy. I allude to chlorate of potassa and chlorate of soda. I cannot say that I place much reliance on it as a remedy in diphtheria, and still I give it in almost every case. The chlorate is the remedy eminently fit for most sorts of stomatitis. The large number of cases of stomatitis and pharyngitis during a period of diphtheria, and their usual complication with and initiation of the diphtheritic process justify and require its use. I give it, then, for its effect on the inflamed mouth and pharynx, but not for diphtheria. It acts as a preventive by returning the mucous membrane to a normal condition. Nor do I administer much more in cases of mild tonsillar diphtheria. As this is a benign affection, it is of greater importance to prevent it from spreading than to remove it from the tonsils, where its communication with the systems of blood and lymph vessels is so very limited. In order to have the full effect I insist upon frequent administration. Doses ought to follow each other in rapid succession. At least every hour, every half-hour, every quarter of an hour sometimes, ought a small dose to be given to keep up a constant contact of the endangered mucous membrane with the remedy. From half a drachm to a drachm may be given during the twenty-four hours. As many families are acquainted with the remedy, and use it without being bidden, see to it that the dose is not too large. The death of Dr. Fountain, of Davenport, Iowa, and many others from overdoses of chlorate of potassa ought to be heeded.

My views on the treatment of diphtheria have been framed in strict accordance with the opinions I have expressed in regard to its pathology. Although finally a constitutional disease, it is at the beginning nearly always local, or, in other words, infection enters the blood at a limited portal, which is the same in the great majority of cases. From this point of view constitutional diphtheria is analogous to the septicæmia of wounded men and of puerperal women, and the local disinfection, which has been accepted as the sheet anchor in the treatment of these affections, must be also the main reliance in that under consideration. We may congratulate ourselves upon this fact, since we do possess some positive knowledge in regard to the disinfection of accessible putrid fluids, while it is safe to say

that as yet we have no proof of our ability to disinfect the blood of the living body. We seem indeed to be able to some extent to increase its power of resistance to the action of poisons that have been absorbed into it, but we cannot affirm that our remedies act by destroying the poisons themselves. I shall refer to this again in speaking of quinine.

Local remedies may be divided into three classes. 1st, those which dissolve the false membranes, and thus facilitate their removal. 2d, substances modifying the surface from which the membrane has been removed. 3d, disinfectants, equally capable of arresting chemical changes, and of destroying animalcular life, and applicable therefor, whichever theory be finally adopted to explain the infectious properties of the diphtheritic exudation.

1st Class.—The rapid solubility of the false membranes is chiefly important when they occupy the larynx, and thus in my paper on croup I have dwelt especially upon this class of agents. Those which still hold the first place are lime-water, glycerine and moist heat. The latter is claimed to be particularly effective. I admit it softens pseudo-membranes like anything else, furthermore it may increase the secretion of acinous glands, and thereby raise and expel membranous deposits. But the fact that it softens healthy tissue as well as morbid exudations appears to facilitate the penetration of the poison into deeper layers. Both of these theoretical views ought to be remembered to guide the practitioner in an individual case. In the majority of cases the application of ice will be found more in accordance with the requirements of the secondary inflammations and enlargements.

The remedies in the 2d class that have been most largely employed are, with the exception of chlorate of potassa, all more or less astringent. It is a noteworthy fact, however, that the pure astringents, alum, tannin, nitrate of silver, formerly employed in diphtheria, and still retained in the treatment of simple catarrhal pharyngitis, have been generally abandoned as remedies for the exudative disease. Oertel objects to astringent gargles on the theoretical ground that, instead of facilitating the separation of false membranes and the destruction of micrococci, they tend to arrest the formation of pus, and even favor the wandering of the infectious elements into the

submucous tissues. From what has already been said, it is plain that I do not commit myself to this, or to any other theory of Oertel's, but I am willing to admit that experience has pronounced against the efficacy of the pure astringents, and for my own part I never employ them.

But the substance which to day is ranked among the most powerful of all astringents, the perchloride of iron, is, on the contrary, a remedy which, when suitably handled, most decidedly merits confidence. Muriate of iron was first employed in diphtheria from an alleged analogy between this disease and erysipelas, in which this drug had been found to render real service. It was used in France by Velpeau, and in England in 1851 by Hamilton Bell, in the treatment of erysipelas, being applied locally, and also administered internally. In 1858 diphtheria was treated by the perchloride in France by Gigot, and the following year by Dr. Crichton in Scotland. In 1865 a report was made in Melbourne, Australia, by Richardson, of 220 cases of diphtheria, observed during a period of seven years, and treated since 1861 exclusively by full doses of the muriate of iron, together with chlorate of potassa in powder. The number of deaths was 18, or 8.2 per cent., very little in excess of that of measles. Since these first experiments British and American Journals have abounded with reports of success obtained by the perchloride of iron, and in a recent monograph Schaller has asserted that "the dilute muriate of iron is to be preferred to all other remedies in diphtheria."[1] I have extensively used that remedy myself, have, in fact, mentioned it amongst those employed by me, in the first paper of mine alluded to before, after some considerable experience with it extending over the years 1858, 1859 and 1860.

The mode of administration of the muriate is of the utmost importance. To insufficient doses, or careless applications, may be traced many of the cases of failure. Thus Steiner of Prague is believed to have refuted Schaller's assertions by experiments on four children, to whom was administered hourly a teaspoonful of a mixture containing five to eight drops of the tincture to three ounces of water. Local applications were made three and four times a day of a mixture containing thirty drops to two ounces. The two youngest children, one and three

[1] Reviewed in Schmidt's Jahrb. 149, p. 339, 1871.

years old, died by extension of the disease to the larynx, the two others recovered.

To be of any efficacy muriate of iron must be given in large doses frequently repeated. From five to fifteen drops every quarter, half, or every hour, is a dose that alone fairly tests the effective powers of the medicine. Gargles and direct applications to the pharynx may be dispensed with, and their irritating effect avoided, since the throat is sufficiently washed by swallowing. According to the testimony of all observers, and with which my own observations concur, the muriate does not facilitate the separation of membranes, but seems to act upon the surface from which they have been removed, lessening the hyperæmia, reducing the swelling, and seeming to limit the reproduction of the exudation. But how does the action of the perchloride differ from that of any other astringent? Although all astringents coagulate albumen, there is no question but what the albuminate formed differs notably in different cases. In some comparative experiments, made before the class of the Woman's Medical College of the Infirmary of New York by Dr. Mary Putnam Jacobi upon the white of egg, with alum, tannin, creasote, acetate of lead, carbolic acid, and perchloride of iron, marked differences were observed in the density of the coagulums formed. The tannin produced a cloudy, diffused coagulum; carbolic acid also a diffused coagulum, but only after one-half a minute; alum a tenacious clot that sank to the bottom of the test-tube without increasing in size; three drops of creasote instantaneously formed three dense curds, each of which sank separately, increasing in size like a rolling snowball; perchloride of iron gave a layer of coagulum a few lines in thickness that sank very slowly, leaving the fluid clear above it. When subcutaneous veins were exposed on a living rabbit, and touched with a drop of perchloride, no visible effect was produced for over a minute; then they were seen to markedly diminish in calibre; while a drop of creasote formed a coagulum that instantly obliterated the vein by compression. This second effect was mechanical; the first implied that the perchloride acted by exciting the vital contractility of the blood-vessel.

Nitrate of silver, which when applied to a mucous or a serous membrane is reduced and deposited in the albuminous cement

between the epithelial or endothelial cells, cannot be compared in its action to the perchloride of iron, or rather this latter cannot be compared to it. It seems probable that one of the first ways in which the muriate modifies the diseased mucous membrane is by reawakening the contractility of the paralyzed blood-vessels. The restoration of their tonus would itself diminish the rapidity of putrid absorption by the lymphatics, which we have seen to constitute the great danger of the disease.

Has the perchloride of iron any more direct effect upon the lymphatics?

Such an effect, which was clearly or vaguely assumed when the muriate was transported from the therapeutics of erysipelas, with its predominant inflammation of the cutaneous lymphatics, would indeed be a grand desideratum. It must be confessed, however, that we know little about the matter at present, although from analogy we may believe that a local astringent to blood-vessels would not leave the dilated lymphatics uncompressed. Such compression would oppose a powerful obstacle to the free course of the poisonous particles that are streaming onward towards the torrent of the circulation.

The perchloride of iron, like the sulphate, is a tolerably powerful disinfectant. It is well known that all astringents in sufficiently large doses are disinfectants, and some of the best disinfectants, as creasote, are powerfully astringent. It was used in the treatment of wounds by Nunnely, and is strongly recommended by Beale, especially when associated with glycerine, as a most powerful antiseptic. According to this author, it acts by arresting the growth of bioplasm, which constitutes the soft, pulpy, unhealthy masses that cover ulcerated surfaces. It is equally capable of arresting the movements of bacteria and micrococci, or of coagulating albuminous ferments, so that its action is conceivable according to either of the three great reigning theories of local putrefaction.

In experiments on the disinfection of London sewers, 2.27 litres of chloride of iron were found sufficient to deodorize 30,000 litres of foul water; while for the same purpose 1.36 kilograms of chloride of lime and 36.35 pounds of lime were required.[1] The chloride of iron was included long ago in

[1] Schmidt, Vol. 133, p. 122.

Chevallier's list of disinfectants, and is ranked, with other metallic salts, by Herbert Barker, among those substances which chemically destroy the noxious body.[1]

It is unquestionable, however, that the internal administration of the perchloride is of at least equal importance with its local application. The absorption of the muriate of iron into the blood, and its action after absorption involves many problems that are as yet imperfectly solved. Several interesting suggestions have been made, however, that are worth considering in the bearing on our subject.

1st. It has been said that the perchloride was decomposed immediately after injection, and that the hydrochloric acid alone entered the circulation. But the free acid has not been detected in the urine any more than the entire salt. There is reason, on the contrary, to believe that the perchloride *is* absorbed, and with unusual rapidity, directly from the stomach, the subsequent appearance of iron in the fæces being due to the re-elimination of the metal by the intestines.

2d. Quincke[2] found that, by injection of the perchloride of iron directly into the veins of animals, emboli were rapidly formed in the pulmonary vessels by coagulation of the blood.[3] But if the injection was made very gradually, so that the conditions more nearly corresponded to those of absorption from the stomach, only very minute precipitates *were formed and taken up by the white blood corpuscles*, existing in great abundance in them. This observation, if accurate, may be of importance in explaining the effect of the muriate in septic diseases, accompanied by increased activity of the lymphatics, and an excess of white blood corpuscles.

3d. Saase[4] has modified the common opinion in regard to the influence of iron and the oxydation of the blood, by ascribing to iron salts the property of converting oxygen into ozone. In the circulation they share this property exclusively with the blood corpuscles, and hence are able to supply their

[1] On Deodorization and Disinfection, Hastings Prize Essay.

[2] Arch. für Anat., 1868, Schmidt, Bd. 143.

[3] Dr. M. Putnam Jacobi has observed the same thing in fifteen minutes after ingestion of large doses of solution of tannin. Experiments not published.

[4] Schmidt, Bd. 126, 1865.

place to a certain extent. "Until oxygen has been ozonized," observes Saase, "it is as useless for the purposes of respiration as pure nitrogen."[1]

That iron increases the oxydations in the body has been shown by Pokrowsky, who proves that even in health the heat of the body is raised and the amount of urea in the urine increased by its administration.[2] In anæmic subjects these effects *precede* any increase in the number of blood corpuscles, and hence cannot depend on their renewal. The iron does indeed seem to partly supply their place.

That such substitution, if effected, could not fail to be eminently useful in those poisoned conditions of the blood where the red blood corpuscles are incessantly menaced with destruction is evident.

4th. It has finally been affirmed that, among all the preparations of iron, the perchloride is especially distinguished by a capacity for stimulating the nervous system; probably by increasing the arterial tension in the nerve centres. It is said that its remarkable efficacy in nervous chlorosis, as distinguished from true anæmia, is an illustration of this.[3] If this be true, we may perceive another mode of action in diphtheria in assisting to sustain a nervous system incessantly threatened with local paralysis or general collapse.

I pass to the *3rd* class of local remedies, the disinfectants proper, especially carbolic acid.

It would be quite superfluous in this place to relate or to criticize the vast mass of experiments that have been made to test the disinfecting properties of carbolic acid. Probably nothing is better proved in therapeutics to-day than the fact, that suitable solutions of carbolic acid will arrest putrefaction, kill bacteria and microzyma, and immobilize white blood corpuscles. The great value of carbolic acid as a local disinfectant in diphtheria, as in puerperal septicæmia, cannot be adduced as a proof that the local process depends on the presence of animal germs. These indeed abound in the mouth in the absence of any disease whatever.[4] But carbolic acid exercises a powerful action

[1] I have not had opportunities which would be sufficiently conclusive to test inhalation of pure ozone.

[2] Arch. Virch., Bd. xxii.

[3] See Anstie on Neuralgia.

[4] Beale, Disease Germs, p. 290.

on the life of all vital elements, and therefore upon that of the rapidly proliferating epithelium which constitutes the diphtheritic exudation. It has been experimentally proved to destroy the power of vaccine lymph. It is therefore probable that carbolic acid may also destroy the unknown poison of diphtheria.

In regard to the antiseptic effect of quinine I think that, if exerted, it can only be by immediate contact with the false membrane, and not after absorption into the blood. In Binz's experiments a solution of pure quinine was used, containing from 1 per cent. to 1 pt. in 1,000 of the alkaloid, and this sufficed to prevent the development of bacteria in putrescible fluids. But even in this smallest proportion a patient with 18 lbs. of blood would require to carry in his circulation 138 grains of quinine to realize the conditions of Binz's experiment. The author himself insists that only 2 grms.=32 grains a day should be necessary for a man of 120 lbs. weight, but this calculation is based upon experiments on dogs, where injections of quinine have averted septicæmic fever, and not on the experiments with putrid fluids. However, it is important to remember Binz's assertion that, as an antiseptic and antipyretic, the acid sulphate is the worst preparation of quinine that can be used.

In mild cases of tonsillar diphtheria I sometimes try to remove or to destroy the membrane where it is easily accessible. I insist upon this latter clause, because probang and solid stick and mineral acids have, in my opinion, done much more harm than good. Where I cannot reach the diphtheritic deposit and touch it thoroughly, usually with concentrated carbolic acid, I let it alone altogether. The experience is not new that abrasion of the mucous membrane and injury to the epithelia will spread the process in a very short time. The remarks I made in the course of this paper on the vulnerability of the pharyngeal mucous membrane, the tendency to spread on the part of the disease, and the danger of making new wounds, justify that practice. Thus most of my simple cases of tonsillar diphtherite take frequent and small doses of a chlorate, combined with lime-water, or tinct. ferr. mur. ʒ ss.—ʒ ii. a day, and generally mixed with a little glycerine, principally for the purpose of keeping the remedy in longer contact with the diseased surface, if not for its own anti-fermentative effect. There is seldom any fever which requires attending to, and rarely but little swell-

ing of the neighboring glands. Where there is I use cold water or ice applications, for reasons which I need not here explain after having spoken of the secondary process in and round the lymphatic glands.

At the other end of the list of diphtheritic affections we meet with laryngeal diphtherite, membranous croup. I have nothing to add to my remarks made before you more than six years ago, if it is not that my success in former years, if not with internal treatment, at all events with the ultimum refugium, tracheotomy, has not continued to the same extent. Since 1868 I have saved but a very small percentage of suffocating children, and still I cannot but stand by my former indication for the operation. It must not be omitted when obstruction in the larynx threatens to be the cause of death by suffocation. No complication of disease or epidemic influence ought to be a contra-indication. As in former years, I have used ice externally, an occasional emetic when required, lime inhalations, lactic acid spray.

Every individual case ought to be treated on general principles. Thus fever ought to be reduced by washing, bathing, and remedies by no means exclusively adapted to diphtheria, increasing debility obviated, collapse attended to, severe reflex actions, as vomiting or convulsions, relieved. Whether ether, wine, brandy, champagne, camphor, musk, ammonia, and coffee are to be selected, the individual case teaches better than a lecturer. All of these means are frequently unsuccessful, because they are given too late and in too small doses. Whatever is to be done in a severe form of diphtheria must be done early. If I have reason to be satisfied with my success it is because I have lost no time. More than anything I prize attendance to feeding. Remembering the greediness of lymph-vessels when the chyle-vessels are not supplied, I feed as well as the digestive powers of the patient will permit, always, however, recognizing the fact that the stomach of a feverish patient must be carefully looked after. In most cases of high fever meat diet will neither be relished nor tolerated.

I turn to another class of diphtheria, in which everything depends upon doing the right thing at the right, that is, the early time. I shall, for the pathology of nasal diphtheria, refer to my former remarks. I repeat only this one, that most cases

originate in the pharynx, and reach the nose by ascending. Where an occasional case is first established in the nose it shows itself very soon by a peculiar thin flocculent discharge, sometimes not at all copious, and by very early swelling of glands round the neck. In both of these classes of cases the local treatment has to be commenced at once, and in the large majority of cases the treatment will be successful.

What are the dangers of nasal dipththeria? Rapid absorption, putrefaction, inhalation of foul smells. The indications are clear enough. The surface of the nares *must be cleaned and disinfected.* When you begin early, you reach those layers of epithelium which form the original lesion. Then disinfection is successful, and your injection will wash the surface clean. No strong disinfectant is required. Two or four grains of carbolic acid to the ounce of water is sufficient and mild enough not to be abhorred more than lukewarm water would. Injections must be made into each nostril until the current comes free through the other nostril, or through the mouth, every hour, or oftener if necessary. At the same time care must be taken that some of the liquid reaches the fauces.[1] The fear of otitis I have not. Probably the Eustachian tube is closed by catarrhal or diphtheritic swelling. The mouth ought to be kept open. I have never seen any difficulty arising from my injections. A common syringe suffices; but an ear syringe frequently filled is better adapted to the nursing powers of most attendants. A nasal douche, a fountain syringe is much better, the current more uniform. I have now and then seen neglected cases in which an injection would not open the closed-up nares. In such cases I have used probes and pincers to remove the coarsest material, in the same manner as I, although averse to meddling with the infected mucous membranes, have had to remove large and thick membranes from the uvula, or palate, when deglutition was interfered with. Every hour, or every half hour, is not too often. The child, frequently with swelled glands, head thrown back or sideways, is suffering more, and sleeping less, from the obstructed nares and fauces than when the injections are regularly made with certain relief. I have found many children insisting upon their frequent repetition. Often have swelled glands diminished in size within twenty-

[1] For that purpose the nostrils must be momentarily compressed.

four hours after the commencement of the local treatment. If it was objectionable, or a discomfort, the objection would not count. There is but one way to save a case of nasal diphtheria, that is, by disinfection, and washing of the parts.

What disinfectant is preferable? I avoid those which stain, and those which coagulate. For that reason I avoid the local application of the sub-sulphate of iron, and also the permanganate of potassa. I have generally used carbolic acid. Where there is no smell, I have often used lime-water, pure or somewhat diluted, for its solvent effect.

Internal disinfectants, antiseptics, are of no effect unless the source of the sepsis is stopped, no matter whether hyposulphites, or carbolic acid, or quinia. With the local attendance the large majority of cases will recover; without it they will die. The mortality need not be large. I admit it is difficult to procure just that punctual and sometimes apparently cruel attendance which is required. It is more cruel, however, to sacrifice than to save.

The panic, in my opinion, in the city is absolutely unjustified. It is the result, not the cause, of sensational newspaper articles. Let the public understand that, with the exception of a limited class of almost absolutely fatal cases—as far as our knowledge now goes—there is no infectious disease that can be more readily and more successfully managed than diphtheria, and that its mortality ought to be small. Let them understand that, and the panic will be over.

There is one point to which I wish to return. A case of diphtheria, mild or severe, ought to be attended to at once without loss of time. In connection therewith I will admit that a good deal of "stamping out" has been done amongst us, and I understand diphtheria to have been selected as the next victim of our Board of Health. I propose one measure which will be more successful than the disinfecting of infected houses. Let, for the time being, every district be supplied with a physician, who shall be well paid by the city, who is a beginner in practice, and has ample time, whose residence and business shall be advertised in the papers, schools and police-station houses, and let it be understood that he will at once, when called upon, look after the throat of every pauper or tenement-house child with symptoms of either diphtheria or pharyngitis. And we shall hear less and less of the ravages of the scourge.