and Fischer,[122] provoked tuberculosis in animals, the children had all lived with tuberculous parents.

When the nose alone is used in breathing, the air, on reaching the larynx, is practically free of bacteria; breathing through the mouth, however, deprives the larynx of the protection afforded by the nasal passages and tuberculosis of the larynx may be engendered by tubercle bacilli inhaled with the dust. This occurs very rarely, however. The organ is protected, when foreign substances reach it, as are the anterior nasal cavities, by a copious supply of mucus derived mainly from the ventricles of Morgagni, the secretion being directed outward, *i.e.*, towards the œsophagus. In almost all cases, however, tuberculosis of the larynx occurs as a complication of pulmonary tuberculosis.

Whether primary or secondary, the initial cause of tuberculosis of the larynx is deficient nutrition of its tissues which exists throughout the entire organism, owing to depravity of the adrenal system.* The fluids, lymph, blood and secretions of these tissues being deficient in bacteriolytic activity, the tubercle bacilli not only penetrate the lining epithelium, but being met therein by phagocytes inefficient themselves as bacteriolytic agents, they multiply in the laryngeal lymphatics and start a local tubercular process. The lesions caused by inhaled bacilli usually begin in the portions of the larynx most exposed to the inspiratory current, the tissues overlying the arytenoid cartilages and the posterior and upper surface of the epiglottis. When a laryngeal tuberculosis occurs as a complication of pulmonary tuberculosis, the tissues of the interarytenoid space, which extend over the arytenoid cartilages, are usually the first affected, the bacilli under these conditions being derived from the sputum, which the tracheal ciliated epithelium propels upward.

When voided from the larynx by coughing or hawking, the pulmonary discharges are either expectorated or swallowed, thus exposing, in the latter case, the gastro-intestinal tract to infection.

The pallor of the laryngeal tissues and of the adjoining tissues indicates that deficient nutrition prevails here as elsewhere. A curious feature of the treatment of laryngeal tuberculosis points in the same

* *Author's conclusion.*
[122] Pluder and Fischer: Archiv f. Laryn., Bd. iv, S. 372, 1896.

direction, viz., that irritation, mechanical or chemical, is beneficial: Thus the beneficial effects of lactic acid are greatly enhanced if, while applying it, the mucous membrane is rubbed. The hyperæmia produced with its attendant leucocytosis is obviously the main beneficial agent, the lactic acid aiding by destroying what bacilli it reaches.

Cases of primary tuberculosis of the larynx have been reported by E. Fraenkel, Trifiletti,[123] J. Solis Cohen[124] and many other observers since. In some of these instances careful examination of the lungs showed that they were normal. Such instances are rare in comparison to the laryngeal tuberculosis that accompanies pulmonary tuberculosis, and which occurs in about 35 per cent. of all cases. The opinion that infection by the sputum can occur is disputed by some, but as Cornet[125] says, "The theory of certain authors that laryngeal tuberculosis is not due to contact of the mucous membrane with the sputum, but is, as a rule, hematogenous in fact, lacks all foundation in fact."

The human gastric juice does not destroy tubercle bacilli ingested with contaminated milk, meats or other foods. When the germs reach the intestine, however, they are subjected to the proteolytic action of the auto-antitoxin in the succus entericus, before being ingested by the digestive leucocytes.* In vulnerable, *i.e.*, debilitated subjects, the succus entericus is insufficiently active to affect the virulence of the bacilli; they not only penetrate freely the intestinal epithelium to the lymphatics under these conditions, but they are ingested living by the digestive leucocytes.* The proteolytic activity of these cells being also impaired in vulnerable individuals, they are unable to digest all the bacilli ingested by them with food-stuffs in the intestinal canal, and thus distribute living tubercle bacilli germs throughout the entire body, including the lungs. General infection can thus occur, through the intestinal canal, from two directions: (1) direct penetration of the germs through the intestinal walls, (2) through the intermediary of the digestive leucocytes.*

Wesener[126] and others have contended that the gastric juice could destroy tubercle bacilli, but the investigations of Frank,[127] Fischer,[128] Straus and Wurtz,[129] and Cadéac and Bournay[130] have shown that such was not the case, while Lukaszewicz[131] suggested that the activity of the juice had some influence on the result, since the feeding of tuberculous meat from the one animal to dogs and cats would infect the latter, but not the former. The experiments of Carrière[132] showed conclusively,

* *Author's conclusion.*
[123] Trifiletti: Boll. d. mal. dell'Orecchio, etc., No. 5, 1887.
[124] J. Solis Cohen: Archives of Laryn., Apr., 1881.
[125] Cornet: *Loc. cit.*
[126] Wesener: Cited by Cornet: *Loc. cit.*
[127] Frank: Deut. med. Woch., Bd. x, S. 309, 1884.
[128] Fischer: Archiv f. exp. Path. u. Pharm., Bd. xx, S. 446, 1886.
[129] Straus and Wurtz: Arch. de méd. exp., vol. i, p. 370, 1889.
[130] Cadéac and Bournay: La province méd., T. viii, p. 304, 1893.
[131] Lukaszewicz: Thèse de St. Petersbourg, 1893.
[132] Carrière: C. r. de la Soc. de biol., vol. liii, p. 1098, 1901.

however, that human gastric juice sometimes attenuated the bacilli, but failed to kill them. Sabrazès had previously suggested that the greater part of the elements which constitute the tubercle bacillus were not, as in the case of cellulose and *nuclein*, susceptible to digestion. He found that it took 36 hours' immersion in gastric juice to deprive the germs of their vitality.

This accounts for the frequency of infection by way of the intestine, which, according to Macfadyen and MacConkey,[133] is more important in this particular as regards tuberculosis than the tonsils or adenoid growths. Klebs[134] considers it the chief avenue of infection, while Behring[135] has long held that in the young "the origin of epidemic pulmonary tuberculosis in man and the epizootic pulmonary tuberculosis in cattle, is through an intestinal route." A large number of cases in which fatal infection by milk had been clearly traced to tuberculous cows have been reported by Oliver,[136] Stang,[137] Demme,[138] Hills,[139] Ernst,[140] Stalker and Niles,[141] Leonhart,[142] Sontag,[143] Hermsdorf,[144] Rich,[145] Thorne,[146] all selected from literature with the greatest care by Professor Repp,[147] of the veterinary department of the Iowa State College, who holds with Theobald Smith,[148] Pearson[149] and Dinwiddie[150] and others, that the bovine tubercle bacillus is distinctly more virulent for the species of animals thus far experimented upon than is the human bacillus.

Having pointed out[151] that the intestinal food-products are taken up by the digestive leucocytes and converted by them into tissue elements, I held[152] that these cells were the normal agents of infection, and that when they failed to destroy the germ, living tubercle bacilli could be carried from the intestine to the lungs as well as to other organs. Sims Woodhead[153] says that: "When the tubercle bacillus is carried into the alimentary canal by the saliva, by food-stuffs, etc., it is rendered innocuous in more ways than one; but perhaps the most effectual way is by its being taken into the substance of *lymphocytes* which make their way out and in from the lymphoid patches, and which have the power of taking into their substance the tubercle bacilli. These lymphocytes return with their evil burden to the lymph-glands, and the glands assist in the complete destruction of the bacilli." Cornet[154] also says in this connection: "The bacillus has the power to penetrate not only the intact epithelium (Baumgarten, Dokroklouski, and Tschistowitsch), but also the entire wall of the gut, and to find its way along the lymph-channels to the mesenteric glands, where it first begins its actual career (Orth, Wesener and the author). This it accomplishes partly by mechanical means, partly by the aid of the *wandering cells*, and all without leaving behind a recognizable trace of its passage." Petruschky[155] was also led to conclude that it was through *leucocytes* that the bronchial glands were invaded.

[133] Macfadyen and MacConkey: Brit. Med. Jour., July 18, 1903.
[134] Klebs: Congr. für innere Med., Bd. ii, S. 49, 1883.
[135] Behring: Trans. Tuber. Congr., Kassel, 1902.
[136] Oliver: Cited by Oestertag: "Hdb. d. Fleischbeschau."
[137] Stang: Cited by Law: Bull. Cornell Exp. Sta., No. 65, p. 137.
[138] Demme: Cited by Law: *Ibid.*
[139] Hills: Bull. Vt. Exp. Sta., No. 42, p. 55.
[140] Ernst: Rep. Mass. Soc. Prom. Agric., p. 4.
[141] Stalker and Niles: Bull. Ia. Exp. Sta., No. 29, p. 257.
[142] Leonhart: Cited by Watson: Rep. N. Y. Board of Health, 1892.
[143] Sontag: Cited by Watson: *Ibid.*
[144] Hermsdorf: Cited by Watson: *Ibid.*
[145] Rich: Vet. Mag., vol. iii, p. 729.
[146] Thorne: Ohio Vet. Exp. Sta. Bull., No. 108, p. 348.
[147] Repp: Phila. Med. Jour., Aug. 11, 1900.
[148] Theobald Smith: Trans. Assoc. Amer. Phys., vol. xi, p. 75, 1896.
[149] Pearson: Com. to Repp; *Loc. cit.*
[150] Dinwiddie: Bull. Arch. Exp. Sta., No. 57, p. 46.
[151] *Cf.* this volume, chapter fifteenth.
[152] Sajous: Monthly Cyclo. of Pract. Med., Jan., 1903.
[153] Sims Woodhead: Lancet, Oct. 27, 1894.
[154] Cornet: *Loc. cit.*

The importance of the intestinal auto-antitoxin in this connection is self-evident. In other words, the power of the intestinal juices to kill the tubercle bacilli (thus arresting their power to proliferate) is commensurate with the proportion of auto-antitoxin secreted into the intestine. As this depends upon the functional efficiency of the adrenal system, it is evident that hypofunction of this system predisposes the body at large to infection. Such a condition also involves general hyponutrition. As Sims Woodhead[155a] says: "If the tissues be so weakened that their power of resistance can be readily overcome by comparatively few micro-organisms then infection will probably follow." This "power of resistance" means, from my standpoint, sufficiently active auto-antitoxin in all parts of the body to kill germs, *i.e.*, to paralyze their reproductive activity—the great initial danger in tuberculosis.

The lungs are mainly infected by tubercle bacilli which reach them, (1) with the air through the respiratory tract, (2) by phagocytes and lymph derived from the lymphatic supply of the naso-pharyngeal mucous membrane and lymphoid tissue, (3) by phagocytes and lymph derived from the lymphatic supply of the intestine.

(1) The entire bronchial tract is kept free of bacilli when the quantity inhaled is not excessive, by the ciliated epithelium which propels a current of mucus towards the trachea whence it is eliminated by way of the larynx. What organisms fail to come into contact with mucus of the epithelium (owing to their position in the middle of the air-stream) however, may reach not only the terminal bronchioles, but also the alveoli or air-cells which are not provided with ciliated epithelium. Here, they are met by phagocytes and auto-antitoxin, and if these bacteriolytic agents are sufficiently active,* the germs are promptly destroyed; if not,* the bacilli penetrate the alveolar septa, proliferate therein, and initiate the process of tubercle formation previously described.

(2) Infection of the lungs through the lymphatic system may be provoked by tubercle bacilli which have penetrated the epithelium of the nasal mucosa, or invaded the tissues proper of the pharyngeal or faucial tonsils owing to deficient bacteriolytic activity of the phagocytes of these organs. Once in the lymphatics adjoining the latter, the bacilli can proliferate freely since lymph is poor in all three of the constituents of

* *Author's conclusion.*
[155] Petruschky: Münch. med. Woch., Bd. l, S. 364, 1903.
[155a] Sims Woodhead: *Loc. cit.*

auto-antitoxin, and especially in adrenoxidase because of the absence of red corpuscles.* They invade in turn all the lymphatic glands of the neck down to the upper part of the thorax and thence the bronchial glands. As the lymph of these glands ultimately reaches the right and left lymphatic ducts to be poured into the subclavian veins, and thence into the superior vena cava and the right heart, it finally reaches all parts of the lungs. Having multiplied in an excellent culture-fluid, the lymph, the tubercle bacilli are thus transported by venous blood—in which they suffer no injury—to *all* the pulmonary alveoli.*

(3.) Infection of the lungs through lymphatic paths may also occur by tubercle bacilli derived from the intestinal canal, *i.e.*, with the leucocytes and fats that enter the lacteals and soon thereafter the thoracic duct. With the chyle of the latter these tubercle bacilli are also transported to the subclavian vein and thence to the superior vena cava and the right heart, whence they are distributed with the venous blood to all the pulmonary alveoli.*

The view that infection occurs through inhalation is the prevailing one and is urged by Cornet, who adduces the evidence afforded by the access of coal dust (in miners) and kindred substances to the alveoli themselves, though the coal-particles progressively decrease as these cavities are reached. "The ciliated epithelium, which is a powerful aid in removing foreign bodies, is absent in the alveoli," says this author, "so that these latter form a sort of storehouse for the dust particles"—and therefore, for what tubercle bacilli happen to be in the dust.

The opposite doctrine, that the bacilli reach the lungs through the lymphatics, has not gained support because it involved the conclusion that the germs and the phagocytes containing them had to travel against the lymph current from the bronchial glands to the pulmonary tissues,—a dubious proposition. By the *normal* paths I submit in the text, however, the lymphatic channels are not only in direct communication with the alveoli, but the germs or phagocytes containing them follow the direction of the streams to the latter, from begining to end, and land, unharmed, precisely where the tubercles are found, the external aspect of the alveolar walls, and the partitions between the alveolar recesses.

Viewed in this light, infection through the lymphatics, whether the bacilli enter the body by the respiratory or intestinal tracts, assumes a leading position in the pathogenesis of the disease. Cornet overlooks the fact that miners, stone-cutters, etc., work year after year in an atmosphere literally befogged with dust, and that under such conditions the penetration of particles to the alveoli is not surprising. A sound comparison could only be established if dust composed entirely of tubercle bacilli were also inhaled during correspondingly prolonged periods. The first condition is seldom if ever satisfied; the second, therefore, loses

* *Author's conclusion.*

all weight. St. Clair Thomson[156] contends that "all our knowledge of physiology and all the laws of probability are opposed to the possibility of a germ successfully running the gauntlet of the intricacies of the upper air tract, the mucus spread out for it to adhere to, the phagocytes in readiness to slay it and the waving armies of ciliated epithelium in constant action to expel it." Nor are tubercle bacilli ubiquitous hosts of the respiratory tract as is the pneumococcus. Both Beco[157] and Boni[158] found that although the latter and many other organisms were present in normal lungs, the tubercle bacillus was never present. It must, therefore, be wafted directly from the external air to the alveoli to cause infection, without once coming into contact with bronchial walls which when the terminal bronchioles are reached are but three to four-tenths of a millimeter apart! It is self-evident that the number of germs that reach the alveoli directly under such conditions must be *so* small that even the local defenses of a weakling suffice to annihilate them.

The lymphatic path from the naso-pharyngeal mucosa and the pharyngeal and faucial tonsils to the bronchial glands is familiar to every one. The path thence by way of the subclavian, the superior vena cava and the heart, to which I refer, is in accord with elementary anatomical knowledge. This applies likewise to the connection between the intestines and the thoracic duct. It remains to be shown, however, whether tubercle bacilli can occur in the lymph or chyle stream of the latter. This was demonstrated recently by Nicolas and Descos,[159] who found tubercle bacilli in the chyle of the thoracic duct after feeding dogs with soup to which they had added these germs.

Treatment.—The treatment of tuberculosis involves as a general principle the cardinal fact that the endotoxin of the specific pathogenic organism, Koch's bacillus, not only does not provoke (owing to its identity as a normal component part of the tissues, phosphorus) a reaction of the adrenal system, but that it contains also a poison which depresses the latter.* Its ravages proceed unchecked, unmolested, until a secondary infection, exciting the test-organ, counteracts the paresis produced by the tubercular poison and enforces, as it were, a reaction of the adrenal system—but too late, unfortunately, to arrest the lethal trend.* The indications are, therefore, to administer, at the earliest moment, *even though the diagnosis be uncertain,* agents which stimulate the test-organ, *i.e.*, the defensive properties of the adrenal system, with sufficient vigor to destroy the germ and its endotoxin.*

This applies of course only to cases in which, unlike the many instances referred to in the foregoing pages, spontaneous cure does not occur. In these instances (those in which evidence is afforded post-mortem that tuberculous lesions have at some time existed) the curative process is essentially local, *i.e.*, similar to that following burns, injuries, etc., and irrespective of any intervention of the adrenal system.

* *Author's conclusion.*

156 St. Clair Thomson: *Loc. cit.*

157 Beco: Arch. de méd., vol. xi, p. 317, 1899.

158 Boni: Deut. Archiv f. klin. Med., Bd. lxix, S. 542, 1901.

159 Nicolas and Descos: Jour. de physiol. et de path. gén., vol. iv, p. 910, 1902.

AGENTS WHICH CAUSE THE DESTRUCTION OF THE TUBERCLE BACILLUS AND ITS ENDOTOXIN.—The endotoxin of the tubercle bacillus, owing to the phosphorus it contains, supplies an active intermediary for the destruction of the germ itself when it penetrates the arterial blood, owing to the presence of adrenoxidase in the latter.* The affinity of phosphorus for oxygen being very marked, the germ is at once attacked in the blood-stream; its main endotoxin is converted either into phosphoric acid, a benign and eliminable product excreted in the urine; or, the sodium of the plasma aiding, into sodium phosphate.* Tubercle bacilli are not, therefore, found, as a rule, in the blood,* though a protective covering protects them to a certain extent even in this highly oxygenized medium.

Ample evidence to the effect that the tubercle bacillus is rich in nucleo-proteid—a body rich in phosphorus—has been submitted.

The tubercle bacillus is protected, according to Ehrlich, by a resisting cell-membrane which accounts for its resistance to stains. When the blood is poor in oxygen, as in pre-agonal states, or when the "vitality" is very low, as in some general infections, it can also appear in the blood, where it has been found by Wechselbaum, Meisels, Lustig, Rutimeyer, Sticker and others.[160] That they are present only temporarily, however, and only when they suddenly invade the blood in great numbers, has been emphasized by the searching investigations of Lipari and Lodato,[161] who found that the bacillus was in reality present at no stage of the disease in this fluid. Nor did they find it in the blood of animals in which tubercle bacilli had been injected intravenously. This applies likewise to the proliferation of these germs. Cornet,[162] in fact, states that "the tubercle bacillus is not a blood bacterium and does not grow in the blood." This attests also to a radical difference from *extra corpore* or shed blood which, as shown by Koch, is the best of culture media.

The fact that the tubercle bacillus is readily destroyed in the blood-stream proper accounts for its rapid proliferation in the lymphatics, especially in those of the respiratory or intestinal tracts, through which infection occurs, since the lymph contains no red corpuscles and but little adrenoxidase.*

In the treatment of the disease, therefore, an important indication besides destruction of the germs is to prevent their proliferation in lymphatic vessels and glands. These two ends are met by increasing the functional activity of the adrenal system, since the resulting increase of adrenoxidase in the blood by augmenting greatly its oxygenizing power causes (1) a direct

* *Author's conclusion.*
[160] Sticker and others: Cited by Cornet: *Loc. cit.*
[161] Lipari and Lodato: La Tuberculosi, Bd. i, Hft. ii, 1895.
[162] Cornet: Nothnagel's "Encyclo.," vol. on Tuberculosis, 1904.

destruction of the tissue bacilli that are not encapsulated (in tubercles) and hastens local repair; and (2) an increased production of auto-antitoxin, which, owing to the accompanying leucocytosis, augments the phagocytic activity not only of the blood, but of the lymphatic system.*

Iodine is an efficient agent in this connection. Not only does it actively stimulate the test-organ and through it cause an increase of adrenoxidase, auto-antitoxin, and thyroidase in the blood and promote leucocytosis (and therefore phagocytosis), but it likewise increases the vulnerability of the bacilli to the phagocytes of the blood and lymphatic system by increasing the sensitizing power of the plasma and lymph.* The patient should be given 5 grains (0.3 gm.) of *potassium iodide* immediately after meals, in a glassful of water. In some cases, this suffices to develop after a few days a slight febrile reaction, the temperature ranging between 100° and 102° F. (37.8° and 38.9° C.), with an increase of cough, freer expectoration—the sputa showing bacilli in some instances, although these were absent before—and greater distinctness of the physical signs. This indicates that the curative process has begun.* If these signs fail to appear the dose should be gradually increased by 2 grains (0.13 gm.) every other day until 10 grains (0.6 gm.) are reached. If at this time the reaction does not occur (which is seldom the case when no diagnostic error has been made) iodine should in addition be introduced either by inunction or subcutaneous injection, resorting to either of the methods indicated below.

If the remedy is not well borne, or if distinct progress is not made, more vigorous drugs, viz., thyroid extract or mercury, are indicated.*

Joseph Walsh,[163] of the Phipps Institute, states that "the only specific which has stood the test of time in tuberculosis is iodine." The power of this halogen to increase general metabolism has been reviewed at length under "Iodine," to which the reader is referred. That it affects pulmonary morbid processes is emphasized by the fact that in dogs, injections of iodine have been found to increase markedly the bronchial secretion. Indeed, Sticker and subsequently Vetlesen[164] found that small doses of potassium iodide (one tablespoonful of 1½ per cent. solution, *t.i.d.*) caused the appearance of râles strictly limited to the pulmonary areas where tubercular lesions were likely to appear After two or three days the cough is somewhat increased and the expec

* *Author's conclusion.*
[163] Joseph Walsh: The Georgia Practician, June, 1905.
[164] Vetlesen: Norsk Mag. f. Laeger, Oct., 1897.

toration likewise. Out of 27 cases, the 7 that were clearly tubercular gave these signs; while the 20 which failed to react in the same way (and to the tuberculin test likewise) proved not to be tubercular. E. F. Wells[165] confirmed these observations and obtained the reaction in two-thirds of his cases.

The use of iodoform in surgical tuberculosis suggested that it might also be of value in phthisis. Flick,[166] after using this drug and europhen in a large number of cases, concluded: (1) That incipient cases can almost always be cured by europhen or iodoform inunctions. (2) That cases advanced to the breaking down stage may be improved very much by this method of treatment and can sometimes be cured. A tablespoonful of the following mixture is rubbed into the inside of the thighs and arms before retiring at night: ℞ Europhen, 1 drachm (4 gm.); oil of rose, 1 drop; oil of anise, 1 drachm (4 gm.); olive oil, 2½ ounces (75 gm.). Bathing the regions treated with bay-rum on rising eliminates all odor. Iodoform has also been recommended by Daremberg, Ransom, DeRenzi, Knopf, Foxwell, Russell and others. Flick, however, prefers europhen.

Illustrating more pointedly the effects I attribute to the action of iodine upon the adrenal system, however, is a paper by Geo. A. Brown[167] who employed a solution composed of precipitated iodoform (96 per cent. I.) 100 grains (6.6 gm.); 125 minims (7.7 c.c.) of glycerin; carbolic acid 5 minims (0.3 c.c.); boiled distilled water 300 minims (20 c.c.). This solution is sterilized and injected after cleansing the skin and freezing it with ethyl chloride. In pulmonary cases 24 minims (1.4 c.c.) were injected at intervals varying from two to four weeks, or more toward the end, but with ¼ gr. (0.016 gm.) every four hours during the interval and inhalations of iodine. The improvement began from the first dose in all of the 14 cases reported, including cases of glandular, cutaneous and intestinal tuberculosis. The author states that *leucocytosis* is produced, that "the increase corresponds with the iodoform injected," and that it occurs *with a rise of temperature.* In a chart he also shows a marked *rise of urea excretion, which corresponds* with an *increase of appetite,* and *gain of flesh* and *strength.* The curative process in a cutaneous tubercle is described as follows: "There is a rise of temperature in the first twelve hours, and by twenty-four hours one notices a yellow spot in the center of the tubercle, and almost complete depletion of the inflammatory products in the skin around the tubercle. The skin becomes soft and pliable. By the end of four days the yellow spot becomes a crust, is absorbed or falls out and leaves a small ulcer, which soon heals over and eventually bleaches out as scar tissue."

Iodine is now preferred by most clinicians. It was highly recommended by Potain, Durante and other European authorities, and in this country by Ingraham, Knapp, Fleisberg and others. Among the more efficacious methods, those of Mellor Tyson, of Croftan may be mentioned.

T. Mellor Tyson[168] has used, in a large number of cases, at the Rush Hospital, an iodole composed of 20 grains (1.3 gm.) of iodine to the ounce of olive oil, one drachm (4 gms.) of which was rubbed into the skin three times a day, the dose being gradually increased to one-half ounce *t.i.d.* The patients also received $^1/_{25}$ grain (0.0026 gm.) strychnine *t.i.d.*, nourishing food and were out-of-doors considerably. In the advanced cases the improvement was only temporary, but in the incipient ones it continued as long as the patients were under observation. The improvement covered general conditions, strength, weight, cough, expectoration, dyspnœa, appetite, and even physical signs. In some of the incipient cases the cough and expectoration disappeared entirely, while in others they diminished gradually; the greatest change in the physical signs was a diminution in intensity in the abnormal breathing sounds. The previously harsh bronchial or broncho-vesicular sound became soft and the expiratory sound seemed to be less marked. Râles that were heard over the affected area seemed to be markedly diminished and in some cases to disappear altogether.

As Croftan[169] states, accurate dosage is essential, as large doses aggravate while too small doses prove inefficient. In a report of 27 selected cases, 19 of which had circumscribed areas of infection, treated by means of iodipin injections and which gave results "sufficiently striking to warrant an optimistic view"—though not conclusive—profuse sweats, some pyrexia, acceleration of the pulse; hypochondria were observed in some instances. Beginning with one drop of iodipin dissolved in one-half drachm (2 c.c.) of sterilized oil, one drop was added to the dose each day, the dosage being regulated by the effect. As soon as improvement became apparent the dose was continued 30 to 60 days. If insufficient it was increased drop by drop, not exceeding 60 minims (4 c.c.). Croftan regards incipient tuberculosis one of the most easily cured of bacterial diseases.

Certain cases, those in which there is marked pallor of the mucous membranes, especially of the soft palate above the uvula, patients with auburn hair, or in a word, cases in which the vital process is markedly hypoactive, are rapidly benefited by *thyroid extract* in 3-grain (0.2 gm.) doses after meals, gradually increased to 5 grains (0.3 gm.).* Such doses increase the general nutrition, and activate the defensive process more vigorously than the preparations of iodine.* Thyroid extract is also indicated when iodine or the iodides are not well borne by the patient.*

The treatment of tuberculosis by thyroid extract was employed first by myself. In the dose mentioned in the text its use has never given rise to untoward effects. In incipient cases, in which the physical signs are clearly marked, the benefit is sometimes obtained very rapidly. In one of my cases, a tall man weighing 170 pounds, the loss of weight, 45 pounds in eight months, was at once checked, and in three weeks he had regained 10 pounds. He is now in perfect health and his cough has completely disappeared. Thyroid extract is quite as effective in tuberculosis of organs other than the lungs—provided the doses used be not too large. It is not indicated in the third stage.

Klebs[170] used thyroid extract to counteract the achylia gastrica of tuberculosis. Not only did it prove effective, but the author cites two cases in which "the weight increased markedly as a result of the thyroid." The evidence is all the stronger in that the author did not realize that he was benefiting the general disease proper. We have seen that Morin (1895) noted atrophy of the thyroid in a large proportion of consumptives—a fact which in itself accounts for the beneficial effects I have observed.

[165] E. F. Wells: Jour. Amer. Med. Assoc., Feb. 4, 1899.
[166] Flick: *Ibid.*, July 31, 1897.
[167] Geo. A. Brown: Montreal Med. Jour., Apr., 1906.
[168] T. Mellor Tyson: Jour. of Tuberculosis, Jan., 1901.

* *Author's conclusion.*
[169] Croftan: Jour. Amer. Med. Assoc., Nov. 17, 1900.
[170] Klebs: Berl. klin. Woch., Bd. xxxvi, S. 1100, 1899.

Mercurials, we have seen, are powerful stimulants of the adrenal system, the efficacy in syphilis being due to this property.* *Calomel* has been considered by some quite as efficacious in tuberculosis as mercurials are in syphilis. Small tonic doses should alone be used and mercurialism be strictly avoided. The *biniodide of mercury,* $^1/_{16}$ grain (0.004 gm.) three times daily is a safer preparation than calomel in this connection and is equally effective.*

Stuart, Shattuck and Bowditch[171] coincide in the view that if every case of pulmonary tuberculosis were treated with mercury and potassium iodide more might be cured. Edelheit[172] obtained very favorable results from the use of calomel both in tuberculosis and bronchopneumonia and attributes his results mainly "to the property calomel possesses of stimulating organic changes and the vitality of all mucous membranes, including those of the respiratory tract." The beneficial results were especially marked in the chronic type, and much less so in acute and subacute cases. He administers it in pill form: ℞ Calomel, 0.6 gm. (10 grs.); beechwood creosote, 2 gms. (30 grs.); balsam tolu, 6 gms. (90 grs.); extract of calamus and powdered calamus, of each enough to make 60 pills, 6 of which are to be taken daily. Giampietro[173] also reported a number of cases cured by calomel, which he considers as much of a specific in tuberculosis as it is in syphilis. Other clinicians have found mercury of great value in tuberculosis. Miquel and Rueff,[174] Martell[175] and others who obtained favorable results by using it in the form of spray, ascribe the benefit to antisepsis; but sprays only reach bacteria that are being eliminated. It was the result —interpreted from my standpoint— of stimulation of the adrenal system after a sufficient quantity had been absorbed.

Agents Which Enhance the Nutrition and the Protective Efficiency of the Lungs.—*Creosote* is a valuable remedy in the first and second stages of tuberculosis, excepting those cases in which the asthenia is to any degree marked.* In therapeutic doses it excites the test-organ, thus increasing the volume of auto-antitoxin in the blood, and simultaneously depresses the sympathetic centers.* The arterioles being dilated, an excess of blood rich in auto-antitoxin is admitted into all capillaries, including those of the diseased area, and the curative process is hastened.* The most satisfactory preparation is the *creosote carbonate,* which does not disturb the stomach even in large doses, when given during meals—half way between soup and dessert—and in capsules, which carry the drug safely,

* *Author's conclusion.*
[171] Bowditch: Boston Med. and Surg. Jour., Dec. 20, 1889.
[172] Edelheit: Wiener Klinik, Bd. xxii, S. 259, 1895.
[173] Giampietro: Gazz. degli Osped., vol. xvi, p. 1467, 1895.
[174] Miquel and Rueff: Lancet, Nov. 3, 1888.
[175] Martell: Wiener med. Woch., Bd. xxxix, S. 55, 1889.

though it is a thick, oily liquid. Beginning with 5 drops three times a day, the dose can be increased gradually to 40 drops.

The beneficial effect of creosote carbonate is increased and any tendency to depress is counteracted by giving with each dose and in separate capsules, 2 grains (0.13 gm.) of *thyroid gland.** The two agents can also be given to asthenic cases.* The addition of the thyroid gland, by increasing the proportion of thyroidase in the blood, also enhances its sensitizing action upon the bacteria (as opsonin)—a property which creosote only procures when given in very large doses.*

I showed in the section on creosote that it could markedly depress both the sympathetic and vasomotor centers. This, and the fact that the preparations available are not always pure, accounts for the cases in which untoward effects have been noted. Stoerk[176] taught that when it caused nausea or vomiting, it would do harm. This is an excellent guiding symptom, since it indicates gastric dilation and asthenia; but from my viewpoint this condition indicates that the use of creosote should be preceded for a time by a course of thyroid extract or iodine, to overcome the general asthenia. After two or three weeks the creosote is well borne. Since I have used creosote carbonate in the manner indicated above, even the largest dose mentioned has never caused the least gastric disturbance. Chaumier[177] gave from 10 to 20 gms. (150 to 300 minims) daily without causing the least gastric disturbance. The true contraindications are marked fever or tendency to repeated hæmoptysis.

The great rôle that creosote plays in the treatment of tuberculosis since it was first introduced by Bouchard, in 1877, needs no emphasis.

Strychnine causes effects somewhat similar to those of creosote, but through a different mechanism. It stimulates the test-organ and increases the proportion of auto-antitoxin in the blood; but it excites also the vasomotor center and by provoking constriction of all arteries, causes a larger volume of blood rich in auto-antitoxin to circulate in the capillaries, including those of the diseased area.* Beginning with $^1/_{130}$ grain (0.0005 gm.) three times daily, the dose is gradually increased until the physiological effects of the drug are noted, when the dose is no longer increased. Strychnine is now used mainly as a tonic along with other drugs, especially iodine. It should not be given with creosote, however, since it antagonizes its effects on the vascular centers.* *Adrenal gland* 3 grains (0.13 gm.) added to each dose of thyroid and creosote carbonate, in a capsule, may be employed instead.

* *Author's conclusion.*
[176] Stoerk: Archiv f. Laryn. u. Rhin., Bd. i, S. 208, 1893-94.
[177] Chaumier: La médecine moderne, Nov. 16, 1895.