The formation of the tubercles usually begins in the pulmonary structures below the apex of either lung (not necessarily the left, as generally believed), or of both lungs simultaneously, behind the middle of the clavicle. When sufficient area is involved, reliable physical signs may be detected on auscultation immediately below the clavicle, above it, and over the supra-spinous fossa posteriorly, namely, *roughness of the inspiratory murmur,* coupled with *lowering of its pitch,* and, when the respiratory field is greatly reduced in the area examined, *muffling of the vesicular murmur* with prolonged or *blowing expiration.* These modifications are mainly due to the reduction of the caliber of the bronchioles and of the secondary air-passages in the cavity of the alveoli, by the tubercles. The detection of these signs is facilitated by comparing the sounds heard with those of some other part of the lung, especially the other lobes which are seldom involved early in the disease. It is also only when considerable lung tissue is involved that *dullness on percussion,* the pitch of the notes being somewhat raised, and *increased vocal resonance*—the denser tissues being better sound-conductors—become clearly defined. The *cough* in this stage is marked in proportion as the various factors which oppose the elimination of the excrementitious materials pent up in the alveoli, bronchioles and the rest of the bronchial passages—viscidity, mechanical obstruction, etc.—are great. The sputa at this time often contain small grayish-green masses which originate from the diseased area and are composed mainly of tubercles, broken-down leucocytes, and fibrin. Sputum of this kind usually contains *tubercle bacilli.*

*Dyspnœa,* especially marked on exertion, and *increase of the respiratory rate* are prominent symptoms of this stage. They are due not only to the diminution of the respiratory field owing to obliteration of the air-cells by the tubercles, but also to the deficiency of hæmoglobin, the oxygen intake satisfying the needs of the body only when it is in repose. *Lassitude* also becomes more marked, owing to the increased muscular weakness. The latter condition may now cause interrupted or *cog-wheel inspiration,* the muscles being too weak to expand the chest, and doing so by jerks instead of by means of their usual imperceptible contractions. Another result of muscular weakness is



*dyspepsia,* the muscular layers of the stomach being unable adequately to churn its contents and insure its passage through the pylorus.* This symptom is materially aggravated by the deficiency of pepsin—due to the deficiency of oxygen in the blood and the resulting torpor of all cellular functions, including, of course, those of glandular organs. *Diarrhœa,* owing to this morbid condition of the muscular, glandular and epithelial elements of the intestinal canal, may also occur: a prototype, to a certain extent, of the bronchorrhœa so often mistaken for bronchitis.* In young girls, the same general adynamia shows itself by *absence* or *diminution of menses,* and in a large proportion of cases by *anorexia*—an additional source of emaciation and debility.

*Fever* is another important symptom of the second stage. That it is partly due to auto-protective overactivity of the adrenal system excited by the pulmonary lesions, is shown by the fact that although it is of a continued type, it is attended with evening exacerbations, the fever ranging between 99.5° and 100.5° F. (37.50° and 38° C.), until it assumes the hectic type. It is aggravated, as shown under Treatment, by vascular hypertension.* In markedly debilitated individuals the fluctuations may range from a subnormal temperature of 96.5° F. (35.8° C.), for instance, to 99° F. (37.2° C.). The brightness of the patient's eyes is often sufficiently marked to suggest this febrile condition. Profuse *night-sweats* are commonly observed during this stage, but, as in the first stage, they are the result of the nocturnal depression and relaxation of the spiral muscles of the sweat-glands, the temperature being subnormal.

*Hæmorrhage* from the lungs is of frequent occurrence during this stage. It is rarely profuse, being due to involvement in the necrotic process of an area of capillaries or of some small arterial twig. Although it should excite suspicion when no other symptom of tuberculosis is present, it does not necessarily indicate the presence of this disease, since it can also be due to cardiac disorders, vicarious menstruation, naso-pharyngeal ulceration, sarcoma of any portion of the respiratory tract, aneurism, arteriosclerosis and other conditions. Its occurrence with loss of weight, dullness at either apex and increased vocal resonance, however, suggests tuberculosis.

* *Author's conclusion.*

*Hoarseness* is occasionally the initial symptom, but ultimately develops in a large proportion of cases. It points generally to involvement of the larynx in the tubercular process, and entails considerable suffering. The larynx should be examined, and if local tuberculosis is to develop, the tissues overlying the arytenoid cartilages or the epiglottis will appear œdematous and swollen. Spots of ulceration may also be present, but these are more apt to occur in the interarytenoid space. *Pains* in various parts of the chest, changing from one place to the other, but frequently located in the back and in the region of the scapula, are sometimes complained of. *Pleurisy* is a frequent complication owing to contamination through contiguity; it is also characterized at the outset by pain.

In doubtful cases, when all other means of diagnosis have been exhausted, *tuberculin* may be tried. Its mode of action will be reviewed under Treatment.

The *diazo-reaction* of Ehrlich is of but little value, being often obtained in other diseases and only in tuberculosis when the morbid process is sufficiently advanced to be readily recognized by ordinary methods. This latter conclusion is also applicable to the x-ray method.

Concerning the presence of lesions in both apices, singly or jointly, Tyson[53] states that Osler "out of 413 cases found the right apex involved in 172; the left in 130; both, in 111." He also refers to T. G. Davis, who, out of 94 cases, found the lesions markedly worse on the right side in 39, and on the left side in 29, while both sides were affected in 26.

The value of inspiratory roughness pointed out by Grancher has been generally recognized. It is harsh and rasping and is best heard when the patient takes a deep breath, and leans against some support. It is considered by Grancher, Landouzy, Marfan and equally competent clinicians as positively indicating the onset of tuberculosis, especially when emaciation and pallor are also present. Grancher[54] ascribes it to obstruction of the alveolar vestibule by the developing tubercles, and contends that dullness, upon which so much reliance is placed, occurs only when consolidation is advanced. Pye Smith[55] in fact considers it an even more tardy sign. That the cog-wheel, interrupted respiration means atrophy of the muscles was emphasized by Liebermeister[56] and others.

The frequency of laryngeal lesions in pulmonary tuberculosis is shown by the fact that Stein[57] found them in 170 cases out of 474 examined. J. Payson Clark[58] also found the nasal mucous membrane atrophied in 70 cases out of 100 examined and holds that it precedes the

[53] Tyson: "Pract. of Med.," third edition, p. 254, 1903.
[54] Grancher: Le bull. méd., vol. ix, p. 815, 1895.
[55] Pye Smith: Lancet, Apr. 7, 1900.
[56] Liebermeister: Deut. med. Woch., Bd. xiv, S. 789, 1888.
[57] Stein: Hospitalstidende: Bd. xiii, S, 787, 805, 1905.
[58] Payson Clark: Boston Med. and Surg. Jour., Oct. 3, 1895.



pulmonary lesions. Enlarged axillary glands, varying in size from a pea to a hazel-nut, and rolling under the finger, as pointed out by Fernet,[59] are often present very early when progressive emaciation without apparent cause proves to be tuberculosis.

Trudeau[60] found the tuberculin test generally reliable when in suspected cases the diagnosis could be established by no other means. This represents the consensus of opinion of the many clinicians who have used it extensively.

In the *third stage,* that of softening of the tubercles and cavity formation, areas of caseation in the lung tissue varying from the size of a pea to that of a lobe, or even an entire lung, are formed when the necrotic process is too rapid to permit the formation of the fibrin network or outer zone which in the miliary tubercle encloses the necrotic tissues and the disintegrated bacteria. Hence the fact that the caseous masses are found to contain a large number of tubercle bacilli. A caseous mass is a compound of necrosed pulmonary tissue destroyed by the bacilli, and of the constituents of the auto-antitoxin (now minus its oxygen) accumulated in the corresponding area to destroy these germs.* It indicates that the auto-protective process was inadequate to counteract their development, a fact which accounts for the presence of intact bacteria.* When the masses are not too large, they may undergo calcification or fibrous encapsulation, as in the second stage, both of which are curative processes. Such a fortunate result takes place when the auto-protective resources of the body become sufficiently active from one cause or another to carry it on to a finish.* The diseased tissues are thus completely isolated from the normal parenchyma.

When spontaneous cure fails to occur, the caseous masses soften and are more or less perfectly expelled by way of the bronchi, with which they usually communicate, leaving a cavity. The destructive process continuing in the walls of the latter, however, it is gradually enlarged, and as many undergo this process simultaneously they eventually merge, forming larger cavities. As the tubercle bacillus is the source of all this destruction, the process is one of continuous tissue necrosis, the detritus of which represents morphologically the contents of a large abscess—but minus the pus organism. There comes a

* *Author's conclusion.*
[59] Fernet: Bull. de l'Acad. de Méd., Mar. 10, 1903.
[60] Trudeau: Inter. Med. Mag., Mar., 1900.

time, however, when these organisms are likewise present as prominent factors of the suppurative process, which now becomes one of *mixed infection*, with more or less septicæmia as a consequence.

The apex being the starting point of the cavity-formation, a large vomica may be present in this location, while the lower lobe, which the destructive process is gradually invading, is still the seat of smaller cavities. Sometimes the periphery of the lung is reached, and if it happens to be beneath the pleura, pneumothorax occurs.

Around cavities of all dimensions, especially beneath the pleura, there is clear evidence of an effort to protect contiguous structures, connective tissue being developed to limit their extent. An entire apex may thus be isolated, its numerous cavities being enclosed in dense masses of fibrous tissue—evidence to the effect that even at this advanced stage of the disease, much can be done to arrest the lethal trend.*

That calcareous or sclerotic masses are frequently found *post-mortem* in persons who were free from tuberculosis at the time of their death has long been known. Schlenker found that 65 per cent. of 100 autopsies, irrespective of the cause of death, showed evidences of tuberculosis; Biggs found them in 60 per cent., and in another series, 31.5 per cent. of 4000 autopsies; and Naegeli, 97 per cent. of 500 autopsies.[61] Vibert,[62] in looking over the register of necropsies made at the Paris Morgue, was "struck by the fact that in 131 individuals of from 25 to 55 years of age, having all succumbed to violent or sudden deaths, it was noted that the existence of pulmonary tuberculosis was recognized in 25, in 17 of whom the malady was in a cretaceous, or healed state." Rogée and Bondet, in their anatomical studies of the subject at the Salpêtrière and Bicêtre Hospitals in Paris, among aged subjects, found that the proportion of instances in which there was clear evidence of spontaneous arrest of the disease was as high as four-fifths. Aupinel,[63] in the course of 60 autopsies in aged individuals who had died of various diseases, found evidences of cured tuberculosis in *every instance*, and concluded with Cruveilhier, Cornil and Ranvier, Bollinger and others, that few persons escape infection, but that, thanks to calcareous infiltration and fibrous encapsulation, the lesions are spontaneously healed in most instances.

The general phenomena of the third stage are chiefly characterized by their intensity. The *emaciation* has become very marked and the general *weakness* correspondingly so. The *cough* is not only much more severe, but deprives the patient of sleep by its persistence; moreover, the ingestion of food, by

* *Author's conclusion.*
[61] Schlenker: Cited by Hare: "Pract. of Med.," p. 306, 1905.
[62] Vibert: Lancet, Sept. 22, 1888.
[63] Aupinel: Thèse de Paris, 1895.



causing severe accesses of coughing, provokes emesis, at times of an entire meal. The *expectoration* is now profuse. The sputum is purulent and contains irregular, tough, roundish masses that tend to adhere to the edges of the vessel, the "nummular" or coin-like sputa. These are characteristic in that they are similar to the contents of the cavities, containing innumerable bacilli, pus-cells, epithelial cells, elastic tissue from the disintegrated alveoli, broken-down leucocytes, etc., and —an important feature in view of the rôle of phosphorus in the morbid process as I interpret it—an abundance of phosphates.

*Hæmorrhages* during this stage are more dangerous than those that occur earlier in the disease. They are due to erosion of larger vessels which course in the walls between the cavities or to the rupture of small aneurisms that develop along those vessels. They may, therefore, be very profuse—sufficiently so at times to prove fatal.

The *fever* likewise assumes a different character, owing to the insinuation in the process of pyogenic bacilli, and is given an autonomous position in the symptomatology of the disease as *hectic fever*. It is, in fact, due to two distinct factors.* The first is protective. Pyogenic germs and their toxins are able to stimulate actively the adrenal center and thus to provoke high fever,* reaching generally 104° F. (40° C.), the highest point being reached daily late during the afternoon or in the evening. The temperature then falls, gradually, not to normal, as a rule, but considerably below, as low in some cases as 95° F. (35° C.), the minimum being attained during the early hours of the morning. The second factor does not always exist, viz., an artificial and supplementary fever similar to that evoked by tuberculin, and due to the additional heat energy liberated by the interaction of phosphorus derived from dead bacilli (which accumulate in enormous numbers during the third stage) and the excess of oxygen which the increase of adrenoxidase entails —this latter being due to the fever caused by the pyogenic germs. The temperature sometimes reaches 108° F. (42.2° C.) under these conditions. In the absence of mixed infection, however, or when the adrenal center is unable to respond to the stimulus,* the febrile process may be very slight or fail to occur.

* *Author's conclusion.*

*Sweating* is also profuse in most cases, but in this stage it is due, during the presence of fever, to excessive congestion of the peripheral arterioles and to the resulting overactivity of sweat-glands;* but it may also occur as a result of depression, *i.e.,* during the afebrile period when the temperature is low and the pulse rapid and weak. *Diarrhœa,* due to a corresponding condition of the intestinal glandular elements,* is frequently present during the third stage and is an obstinate symptom.

Among the tardy phenomena are often observed patches of *pigmentation* varying from a yellowish tinge to typical bronzing. These indicate that the adrenal system is failing either through asphyxia of its center, owing to the drain of oxygen which the phosphorus of the disintegrated bacteria imposes upon the body at large, or on account of the excess of work of which the hectic fever is the expression.* Again, the adrenals and the thyroid are themselves the seat of tuberculous lesions in some cases; the typical symptoms of Addison's disease, including the bronzing, may then appear.

The physical signs are clearly defined. There is marked restriction of the respiratory movements of the chest. The *dullness* on percussion persists as long as areas of consolidation are present, but gradually, as cavities are being formed, the resonance increases until it assumes the tympanic character over the cavities. When large cavities are present, the *"cracked-pot" resonance* can be obtained (the patient's mouth being open) provided they are situated not too far from the point percussed. Palpation makes it possible in some cases to distinguish the areas of consolidation from the cavities, the *vocal fremitus* being much more marked over the former, owing to their superior sound-conducting power. Auscultation, when the caseous masses are liquefied, elicits *subcrepitant râles,* and if the air, on deep inspiration, passes through one or more cavities more or less filled with fluid, to reach other parts of the lung, *gurgling* or *bubbling* sounds may be heard. The bubbles formed by the air-streams often break and produce a sound resembling *metallic tinkling.* In cavities in which the air merely passes over the fluid, *cavernous* or *tubular breathing* is easily discernible; and if the air-current traverses the edge of a cavity,

* *Author's conclusion.*



the *amphoric* breathing may be obtained—a sound resembling that produced when blowing across the mouth of a bottle. *Pectoriloquy* is a valuable sign to determine the location and size of cavities, when they are near the surface, the speaking or whispering voice being readily transmitted through them. All these signs are best obtained when the chest and back are bare, a light fabric, a handkerchief, for instance, being alone interposed between the examiner's ear and the patient.

Finally the patient reaches the last stages of marasmus. Certain signs are apt to appear when the end is approaching, viz., *thrush*-like areas in the mouth and soft palate, which are in reality patches of tissue that are no longer the seat of active metabolism; *purpura,* due to breaking down of the cutaneous capillaries, and other manifestations of inhibited nutrition.* The disappearance of suffering incident upon this fact causes the patient during the last days of his illness to expect an early recovery, and some pass away cherishing this hope.

The wide fluctuations of fever are especially met in children. Thus Adams[64] states that in some the temperature may reach 108° F. (42.2° C.) and drop in a few hours to 95° F. (35° C.) without apparent effect upon the child. He has seen children eating the evening meal with relish, in spite of a rectal temperature of 106° F. to 107° F. (41.1° C. to 41.6° C.). Strümpell[65] places the average hectic fever fluctuation from 101.3° to 104° F. (38.5° C. to 40°C.). The rôle of pyogenic organisms in its production is generally recognized, and has been emphasized by Karl von Ruck.[66] This would seem to be antagonized by experiments *in vitro,* but Bernheim[67] has shown that the experimental (direct) antagonism between the tubercle bacillus and the pyogenic organisms does not prevail in the body and that the latter complicate the tuberculous process.

The presence of phosphates in the sputum of tuberculosis, especially when, as in the third stage, the tubercle bacilli are present in large quantities, has long been known, although the cause of this phenomenon has remained unexplained. Thus, C. J. B. Williams,[68] twenty years ago, stated, referring to the expectoration during the stage of excavation, that its pus contains "a large proportion of phosphates." Dubief, in Debove and Achard's treatise,[69] also says that the expectoration contains "phosphates in abundance." This may be due to the sodium phosphate of the blood or to the formation of this compound by the cellular nuclein, but it is not characteristic of other diseases in which the expectoration is profuse, catarrhal bronchitis, bronchorrhœa and kindred disorders, while it coincides with the results to be expected from the rapid proliferation of tubercle bacilli, the ashes of which show 60.9 per cent. of phosphorus (de Schweinitz).

* *Author's conclusion.*

[64] Adams: Archives of Pediatrics, Dec., 1901.
[65] Strümpell: Münch. med. Woch., vol. xxxix, S. 905, 932, 1892.
[66] Karl von Ruck: New Orleans Med. and Surg. Jour., July, 1898.
[67] Bernheim: Indépendence médicale, Aug. 15, 1900.
[68] C. J. B. Williams: "Pulmonary Consumption," second edition, p. 93, 1887.
[69] Debove and Achard: "Maladies de l'appareil respiratoire," p. 363, 1896.

The failure of the adrenal system when the disease is advanced is shown by various stages of melanosis. Bronzing, varying from small melanodermic spots to large patches identical with those witnessed in Addison's disease, was found in 7 cases out of 24 by Laffitte and Moncany,[70] and in 12 cases out of 60 by Laignel-Lavastine[71]—all conditions such as freckles, friction stains, pytiriasis, lentigo, acanthosis nigricans, nævi, etc., being carefully eliminated. A similar pigmentation of the liver and spleen and other organs was reported by Weinburg,[72] in a case of tuberculosis. This observation recalls the finding of promiscuously distributed pigment, by Boinet,[73] in all of 20 rats in which he had caused lesions of the adrenals; the pigment had also permeated the subcutaneous cellular tissue, and proved to be identical with that found in Addison's disease. This applies likewise to the thyroid. Macaggi[74] found experimentally that in subacute and chronic tuberculous intoxication, the secretion of colloid was reduced and that the organ's epithelium became atrophied.

**Etiology and Pathogenesis.**—The predisposing cause of tuberculosis is a deficient functional activity of the adrenal system which may be inherited or acquired.* In the latter case, disease or hypofunction of either of the organs of the adrenal system (the thyroid, the anterior pituitary body, including the test-organ, the adreno-thyroid and the adrenals) may be caused by infectious diseases, starvation, overwork, insufficient oxygenation and other factors which either exhaust these organs by imposing excessive activity upon them, or greatly lower their nutrition.*

As Germain Sée says, "predisposition is a word employed to cover our ignorance"—an inevitable conclusion in the absence of an organ or set of organs whose mission is to govern the vital processes of the body at large—the rôle of the adrenal system. Indeed, the stigmata in such subjects clearly point to debilitated respiratory functions—both as to the lungs and tissues—the domain of this system. The flat, narrow chest and drooping shoulders, the winged scapulæ, obviously constitute an inefficient respiratory mechanism as illy nourished as is the rest of the slender figure; the pallor, the cold extremities, the sensitiveness to cold all point to inadequate oxygenation. It is this depravity of the adrenal system which alone, in my opinion, is inherited, and not the disease itself. This is quite in accord with the teachings of modern research; Senator[75] recently wrote, referring to tuberculosis: "In any event, a decisive rôle in determining the march and distribution of the scourge can never be attributed to hereditary predisposition."

The underlying cause of predisposition is disclosed, however, by the mutual relationship of certain diseases and the influence of hypofunction of one of the organs of the adrenal system, the thyroid gland, on infection.

* *Author's conclusion.*

[70] Laffitte and Moncany: Bull. et mém. de la Soc. de méd. de l'hôp. de Paris, 3 série, vol. xx, p. 1238, 1903.
[71] Laignel-Lavastine: Arch. gén. de méd., Oct. 4, 1904.
[72] Weinburg: Rev. gén. de clin. et de thér., vol. x, p. 250, 1895.
[73] Boinet: Marseille médical, Apr. 15, 1896.
[74] Macaggi: Riforma medica, vol. xx, p. 873, 1904.
[75] Senator: Nothnagel's "Encyclo.," vol. on Tuberculosis, Amer. edition, 1904.



The predilection of chronic alcoholics to tuberculosis has been emphasized by Hector Mackenzie,[76] Lancereaux,[77] Monnier[78] and many others. Osler[79] holds that "chronic drinkers are much more liable to both acute and pulmonary tuberculosis." He believes that "it is probably altogether a question of altered tissue-soil, the alcohol lowering the vitality and enabling the bacilli more readily to develop and grow." Sims Woodhead,[80] Abbott and other bacteriologists have, in fact, demonstrated that alcohol predisposes to specific infectious diseases. Mays[81] and Kelynack[82] have shown that this applies as well to the tubercle bacillus. Among the cases reported by the last-named observer were 10 of alcoholic neuritis, 8 of which were subjects of pulmonary tuberculosis. As I have shown, alcohol reduces the adrenoxidase of the blood-stream and correspondingly inhibits the blood's vitalizing properties. The functional activity of the adrenal center being impaired as well as that of all other organs, it fails to respond actively to the stimulating influence of the bacterial toxins, and therefore to protect the organism adequately. That such is the case is shown by the fact that when the thyroid, whose secretion, as I have shown,[83] upholds the activity of the adrenal center, is itself hypoactive, as in myxœdema, a marked predisposition exists. Thus, as stated by Lorand,[84] "in myxœdema (athyroidea) tuberculosis appears frequently," as shown by Greenfield[85] and Byrom Bramwell;[86] "while," according to Pell,[87] "tuberculosis is very frequent in families of myxœdematous persons."

The influence of such a condition of the adrenal system is shown by the readiness with which a patient succumbs to tuberculosis when syphilis, a disease whose debilitating influence is doubted by no one, precedes the tuberculous infection. Niemeyer long ago taught that "the greatest danger for a syphilitic was to become tuberculous." Landouzy likewise emphasized this fact by the statement: "The worst combination I know of is that of pulmonary tuberculosis with primary syphilis." Jacquinet,[88] who refers to these and other authorities, reported 8 cases in which the two diseases were present, in all of which death occurred very rapidly, one patient indeed dying a few weeks after the onset of the tuberculous process. As I interpret these results, the adrenal system, already semi-paralyzed by the syphilitic virus, promptly yields when another depressant is superadded. Herbert,[89] in fact, recognizes a certain analogy between the primary and secondary stages of tuberculosis on the one hand, and syphilis on the other. Lorand states, moreover, that "Perrando[90] has found degeneration of the thyroid in the fœtus from parents with cachectic disease, especially syphilis." Garnier[91] has also found that "the thyroid in hereditary syphilis is degenerated and contains no colloid substance." As I pointed out in the first volume, it is this identical substance which, owing to its iodothyrin, upholds the activity of the adrenal center of the anterior pituitary to its normal level, *i.e.*, physiological standard.

[76] Hector Mackenzie: Brit. Med. Jour., Feb. 27, 1892.
[77] Lancereaux: Revue gén. de clin. et de thér., vol. x, p. 47, 1895.
[78] Monnier: Gaz. médicale de Nantes, Nov. 12, 1895.
[79] Osler: "Pract. of Med.," third edition, p. 382, 1898.
[80] Sims Woodhead: Brit. Med. Jour., July 13, 1901.
[81] Mays: "Pulmonary Consumption," p. 61, 1901.
[82] Kelynack: Edinburgh Med. Jour., Sept., 1901.
[83] *Cf.* vol. i, p. 145 and 165 *et seq.*
[84] Lorand: Trans. Pathol. Soc. of London, vol. lvii, p. 1, 1906.
[85] Greenfield: Cited by Ewald: Nothnagel's "Handbook," p. 159, 1904.
[86] Byrom Bramwell: *Ibid.*
[87] Pell: Volkmann's Sammlung klin. Vorträge (Inn. Med.), Nu. 36, S. 255, 1895.
[88] Jacquinet: Presse médicale, vol. ii, p. 211, 1895.
[89] Herbert: Med. News, Sept. 8, 1900.
[90] Perrando: "Sulla struttura della Teroide," 1900.
[91] Garnier: Thèse de Paris, 1899.

This applies to all agencies that are capable of debilitating the adrenal system: starvation, overwork, insufficient oxygenation, infectious diseases, etc. "It has been found by several authors," writes Lorand, "that animals whose thyroid has been extirpated easily fall victims to infective processes." The great part taken by the thyroid in infections is shown by the researches of Bayon, of Wurzburg, and de Quervain, which establish the fact that in all grave infectious diseases, the thyroid is in the condition termed by them "thyroiditis simplex" without any secretion. Roger and Garnier[93] had found previously to the former authors, "a hypersecretion of colloid in the thyroid in infectious diseases which after some time may be followed by exhaustion of the gland."

All this applies as well to the pituitary body. Garnier and Thaon,[94] in a systematic study of this organ in tuberculosis, based on 18 cases, found invariably areas of sclerosis in the parenchyma in chronic cases, "the gland appearing less active than normally." In a more recent study based on a larger number of cases, Thaon[95] confirmed these observations.

Exhaustion of the gland here means cessation of the stimulus upon which the adrenal center depends for the preservation of its sensitiveness to poisons that appear in the blood. If it fails to receive this stimulus owing to a corresponding defect in the parents, the "predisposition" to tuberculosis—or any other disease—is inherited; if the deficiency of stimulus occurs as a result of diseases which have exhausted the thyroid or caused lesions either in the test-organ or in the posterior pituitary, the seat of the adrenal center, or in the adrenals themselves, we have the "acquired" predisposition. In whichever direction we scrutinize the question, therefore, we are ultimately brought to the conclusion that the predisposing cause of tuberculosis is deficient functional activity of the adrenal system.

In predisposed subjects the fluids of the body at large, including the secretions of the mucous membranes of the respiratory and digestive tracts, are deficient in auto-antitoxin and phagocytic leucocytes, the agents which under normal conditions destroy the tubercle bacilli and other germs that gain access to these fluids.* When tubercle bacilli are inhaled, the body's first line of defense, the anterior nasal cavities are not provided with mucus adequately supplied with these bacteriolytic agents. As these pathogenic germs can, under such circumstances, penetrate the nasal mucosa itself and enter the lymphatic system, infection may occur irrespective of any contamination through the lungs. It does not occur, however, if the adrenal system is fully active.*

The postulate of Koch that tuberculosis is caused by the inhalation of dried sputum, which met its conclusive proof in the studies of Cornet, has stood the test of time, though his opinion that this was the exclusive mode of infection has not. The manner in which dust may convey

* *Author's conclusion.*
[93] Roger and Garnier: Presse médicale, vol. vi, p. 181, 1899.
[94] Garnier and Thaon: *Ibid.*, Oct. 11, 1905.
[95] Thaon: Thèse de Paris, 1907.



the disease may be illustrated by one of Cornet's more recent experiments.[96] Forty-eight guinea-pigs were placed in a room covered by an old carpet over which dried tubercular sputum mixed with dust had been spread, and the carpet was swept on four different occasions. The animals were killed after a time and 47 out of the 48 were found in an advanced state of tuberculosis of the lungs and bronchial glands. The same year (1888) that Cornet conducted his earlier experiments, Flick[97] showed that tuberculosis was especially prevalent in dwellings in which the disease had once occurred, 33 per cent. of the infected houses having had more than one case and some houses showing eight deaths (in one instance, thirteen) in the course of 25 years, though in the great majority of instances different families had dwelt in them. The area of Philadelphia studied included about 50 blocks of houses.

Yet in the human subject, Strauss[98] found purulent tubercle bacilli in the nasal secretions of 9 persons out of 29 examined, 6 of the 9 contaminated being hospital attendants. All were in excellent health. N. W. Jones[99] obtained 3 positive results from inoculations from 31 persons. Pollock[100] conducted a comprehensive study of the effects on the physicians and attendants of Brompton Hospital for Consumptives, covering a period of 34 years. It revealed no noticeable difference from the ratio of the disease among outsiders. There were no deaths from phthisis among the maids who swept and cleaned the floors several hours daily; of 101 nurses, 1 had phthisis in the hospital, 3 after leaving the hospital. Evidently the greater precautions taken in such institutions account partly for this showing, for in barracks, prisons, etc., the incidence of contamination is much larger. Still, why do not all soldiers, prisoners and particularly the hospital attendants whose nasal cavities contain virulent bacilli acquire the disease? It is here that the physiological efficiency of the adrenal system comes in: All functions are performed with adequate energy.

How is this auto-protective function carried on, on the surface of mucous membranes?

If, as I hold, the phosphorus in the tubercle bacillus is the real pathogenic agent, *two* modes of action should be discernible: one by the *living* bacteria, causing no particular local reaction, another by the *dead* germs, causing a local inflammatory reaction. Cornet[101] says: "When tubercle bacilli are gently rubbed into the nasal mucosa, no change occurs if care be taken not to injure the mucosa; in other cases, inflammation, reddening and ulceration shortly make their appearance." Since general infection occurs under these conditions, it can only be ascribed to *living* organisms absorbed, the local lesion being due to *dead* bacteria disintegrated during the procedure. That there is a solid foundation for this conclusion is shown by Cornet's statement[102] that "the dead forms exercise a more rapid and intense action, by means of the diffusion of their chemical matters, than do the live organisms with their slow process of proliferation." It is plain, however, that we cannot ascribe the resulting infection of the cervical and bronchial glands and of the lungs and spleen to which Cornet refers (especially the enormous multiplication of bacteria which this represents), to the chemical constituents of these organisms, which—interpreted from my viewpoint—caused the local inflammation, but to those which did not.

[96] Cornet: Berl. klin. Woch., Bd. xxxv, S. 317, 1898.
[97] Flick: "The Contagiousness of Phthisis," Phila., 1888.
[98] Strauss: Münch. med. Woch., Bd. xli, S. 567, 1894.
[99] N. W. Jones: Med. Rec., Aug. 25, 1900.
[100] Pollock: Practitioner, June, 1898.
[101] Cornet: Nothnagel's "Encyclo.," vol. on Tuberculosis, Amer. edition, p. 101, 1904.
[102] Cornet: *Ibid.*, p. 110.

Indeed, that living tubercle bacilli can penetrate mucous membranes is well known.

The nasal mucous membrane affords considerable protection against infection. According to Wurtz and Lermoyez,[103] the nasal mucus is endowed with antiseptic properties, but researches by Park and Wright,[104] Liaras[105] and others did not substantiate this claim. H. L. Wagner,[106] however, found that, in accord with Buchner, Kossel and others, leucocytes produced a substance in the nasal secretions which possessed germ-destroying power. This substance, an enzyme, according to Wagner, does not necessarily kill the germs, but it diminishes their activity, and they are thus readily swept away by the secretions. This dual action prevents their penetration into the mucous membrane, and infection. The substance referred to is evidently the auto-antitoxin we have met everywhere. Piaget[107] found, moreover, that phagocytes took part in the process, while St. Clair Thomson and Hewlett[108] emphasized the fact that while the viscid mucus prevents the development of the bacilli, the ciliated epithelium promptly secures their expulsion. "The more active the secretion of mucus," writes Cornet, "and the more swift the current, the more rapidly is the bacillus eliminated."

When the tubercle bacilli reach beyond the anterior nasal cavities they are exposed to destruction by the bacteriolytic action of mucus and phagocytes of the pharyngeal tonsil in the naso-pharyngeal vault and the faucial tonsils. They penetrate the crypts of these organs and it is on reaching their epithelial layer to enter the underlying tissues that they are disintegrated. In predisposed, *i.e.*, debilitated subjects, the protective agents—the bacteriolytic phagocytes and endogenous antitoxin—are inefficient, and the tubercle bacilli being allowed to penetrate to the tonsillar lymphatics, infection occurs.

In some cases the quantity of tubercle bacilli destroyed in the pharyngeal and faucial tonsils is so great that the dead bacilli, owing to the quantity of phosphorus liberated,* provoke local tuberculosis.

Behind the nasal cavities, *i.e.*, in the naso-pharynx and pharynx, the defensive mechanism is of another order. St. Clair Thomson,[109] in painstaking studies of the subject, collected 1427 reported cases of naso-pharyngeal adenoids in which the reporters, including Lermoyez, Gottstein, McBride, Moure, Pilliet, Cornil and other authorities had examined the growths microscopically. Histological evidences of a local tuberculous process were present in 75 instances, *i.e.*, in 5.2 per cent. In another series of 435 specimens examined by Gourc, Broca, Hugh Walsham and Jonathan Wright, referred to by St. Clair Thomson, no evidence of local tuberculosis was found. This reduces the average to

* *Author's conclusion.*

[103] Wurtz and Lermoyez: C. r. de la Soc. de biol., 9 série, vol. v, p. 756, 1893.
[104] Park and Wright: Cited by Wagner: N. Y. Med. Jour., Oct. 15, 1898.
[105] Liaras: Thèse de Bordeaux, 1899.
[106] H. L. Wagner: *Loc. cit.*
[107] Piaget: Thèse de Paris, 1896.
[108] St. Clair Thomson and Hewlett: Medico-Chir. Trans., vol. lxxviii, p. 239, 1895.
[109] St. Clair Thomson: Practitioner, Jan., 1898, and July, 1901.



4 per cent., but it does not disprove the fact that these growths are *penetrated* by bacilli. Indeed, Milligan and Dieulafoy found that 18.2 per cent. of adenoids were capable of causing infection when inoculated into animals, while Brieger found histological lesions in 5 out of 78 cases, and obtained one positive inoculation, though no tubercle bacilli could be found either on the surface or in the crypts. This appears paradoxical, but it is readily explained when the numerous phagocytes which such growths contain are taken into account. The successful inoculations are due to the presence of living, *i.e.*, undigested, tubercle bacilli derived from these protective cells, and the lesions—interpreted from my standpoint—to the phosphorus of the dead bacilli. This suggests that infection through the adenoid tissue of the pharyngeal vault is prevented by phagocytes. That such is the case is shown by the rôle of these cells in the tonsils, which are structurally similar. Recent investigations indicate, moreover, that in these lymphoid tissues, the endogenous antitoxin exercises its bacteriolytic action as everywhere else in the organism.

Goodale[110] found experimentally that foreign substances were ingested by polynuclear leucocytes in and adjoining the tonsillar mucous membrane, and that while bacteria are found in the crypts they are absent beyond the mucous layer, thus suggesting that "at the moment of entering," the bacteria "encounter conditions which terminate their existence." Kayser[111] also observed a defensive cellular process between the epithelial layers and the tonsillar tissues and that very little dust reached the trachea. Jonathan Wright[112] discerned an additional feature in the process, however: that pathogenic germs which penetrated the tonsillar crypts could exercise a property, recently defined by Pfeiffer, Bordet and others, viz., that of provoking in the tissues with which they come into contact, and by means of a constituent entering into their own composition or "endotoxin," the formation of a bacteriolysin of which they, the pathogenic bacteria, were themselves the victims. We have here, therefore, as elsewhere, not only phagocytic protection, but a fluid capable of disintegrating the tubercle bacilli.

If this dual protective process prevails in the posterior nasal, or pharyngeal, tonsil as well as in the faucial tonsils, the disintegration of the tubercle bacilli should, at least sometimes, provoke local tuberculosis. Dieulafoy[113] considers that "primary tuberculosis of the pharyngeal tonsil occurs with about double the frequency of that of the faucial tonsils." Cases of primary tuberculosis of the latter have been reported by Schlenker,[114] Kruckmann, Schreibner,[115] Orth,[116] Stewart,[117] and many others. The tonsils are also frequently involved in pulmonary tuberculosis.

The protective rôle carried on by these lymphoid organs is illustrated by the fact that Latham,[118] by inoculating into animals the central portions of hypertrophied tonsils, removed from 45 otherwise normal children, obtained 7 positive results. Again, in 19 instances out of an aggregate of 161 cases, adenoid vegetations, removed from otherwise healthy children by Lermoyez,[119] Gottstein,[120] Brindel,[121] and Pluder

[110] Goodale: Archiv f. Laryn., Bd. vii, S. 90, 1897.
[111] Kayser: Jour. of Laryn., Apr., 1898.
[112] Jonathan Wright: Med. News, Mar. 4, 1905.
[113] Dieulafoy: Cited by St. Clair Thomson: *Loc. cit.*
[114] Schlenker: Wien. med. Blätter, Bd. xvi, S. 630, 1893.
[115] Schreibner: Deut. med. Woch., Bd. xxv, S. 343, 1899.
[116] Orth: Cited by Cornet: *Loc. cit.*
[117] Stewart: Brit. Med. Jour., May 4, 1895.
[118] Latham: Lancet, Dec. 22, 1900.
[119] Lermoyez: Annales des mal. de l'oreille, etc., vol. xx, p. 979, 1894.
[120] Gottstein: Berl. klin. Woch., Bd. xxxiii, S. 689, 714, 1896.
[121] Brindel: Rev. hebd. de laryn., vol. xvi, pp. 881, 913, 1896.