CHAPTER XXVII.

THE INTERNAL SECRETIONS IN THEIR RELATIONS TO PATHOGENESIS AND THERAPEUTICS (*Continued*).

THE ADRENAL SYSTEM IN THE INFECTIOUS DISEASES OF THE LUNGS.

Tuberculosis, unlike cancer and pneumonia, shows a steadily diminishing mortality, thanks mainly to the painstaking labor that has been devoted to its prophylaxis. About one death in seven is still due to this fell disease, however, and when the fact that it assails mainly adolescents and young adults is taken into account, it may, without reserve, still be regarded as the greatest enemy of mankind.

That the adrenal system plays a rôle of the greatest magnitude in the cure of tuberculosis was suggested in the first volume. As to predisposing conditions, I stated (1903) therein:[1] "Insufficiency of the adrenals" . . . . "by reducing the oxidation processes correspondingly reduces the nutrition of the pulmonary tissues: a predominating feature of phthisis;" again:[2] "It is not in the lungs, therefore, that the primary endogenous cause of the disease must be sought, but in the adrenal system." As to the mode of infection, I emphasized the fact[3] that "as soon as the tubercle bacillus is admitted, it becomes an additional source of adrenal insufficiency" through toxins "which react upon the anterior pituitary body precisely as would any other equally virulent poison." As to treatment, I urged that "medication calculated to raise or develop the functional activity of the adrenal system to a high standard must, in the light of the views submitted, not only prevent the development of pulmonary or any other form of tuberculosis, but arrest it in its earlier stages." The rôle of Koch's tuberculin in the diagnosis and cure of the disease was also stated[4] to give rise to a "febrile reaction when a tuberculous process is present, because it adds to the toxic elements incident upon the disease, a new source of adrenal activity." . . . . "Spurred to unusual energy by the tuberculin, the adrenal system excites a correspondingly active metabolism in all cellular structures, including those endowed with leucocytogenesis. Phagocytes and alexins are produced in profusion, the fixed endothelial and the connective-tissue cells contributing their share to the production of the latter, and there is thus constituted a serum which confers upon the treated individual a degree of immunity commensurate with the degree of the reaction produced in the adrenals."

[1] *Cf.* vol. i, p. 478,
[2] *Cf.* vol. i, p. 773,
[3] *Cf.* vol. i, p. 775,
[4] *Cf.* vol. i, p. 635 *et seq.*,
} in the first two editions.

All these statements were published in January, 1903. We have seen how accurately the able researches of Sir A. E. Wright harmonize with and sustain them, though this observer was unaware of the source of the "internal secretion" which he considers as the "bacteriotropic" or immunizing substance, which accumulates in the blood after tuberculin inoculations. We will now see that the views I advanced over four years ago are sustained by the suggestive fact that they account for every phase of the morbid process and for many isolated experimental and clinical observations which have only tended—without the adrenal system—to increase the complexity of the question as a whole.

The evidence submitted in the following pages appears to me to show conclusively that the disease *is not the unconquerable foe that it is generally thought to be,* and that with the adrenal system as the foundation of the curative process, and remedies which, as I have shown, can control the workings of this system, and through it the body's bacteriolytic and antitoxic agents, we can and should curb the disease and finally obliterate it.

PULMONARY TUBERCULOSIS.

SYNONYMS.—*Consumption; Phthisis; Phthisis Pulmonalis.*

Definition.—Tuberculosis is due primarily to the presence and multiplication in the body of Koch's bacillus tuberculosis. Its characteristic phenomena are provoked by two endotoxins which the dead body of this bacillus liberates: (1) a poison

of unknown identity which depresses directly the test-organ and through it the adrenal system, thus inhibiting the protective functions of this system; (2) a nucleo-proteid rich in phosphorus which, when in contact with pulmonary or other living tissues, abstracts their oxygen, thus forming areas of necrosis. The tubercles which characterize this disease are coverings for the necrosed areas and the remnants of the pathogenic organisms, but which, if some of the bacilli be still living, may become centers of infection.**

Symptoms and Pathology.—The early signs usually described are in reality those of a fully developed disease, when local lesions are sufficiently marked to compromise the issue. A more or less purulent expectoration, the hæmorrhages, etc., point to a process of disintegration, *i.e.,* to a period in which infection has made considerable headway.

Notwithstanding the diagnostic value of the tubercle bacillus, to await the demonstration of its presence in the sputum, as is so often done, before establishing a diagnosis, is to compromise the patient's life.

When the symptoms are such as to suggest the need of examining the sputum, they are sufficiently threatening to impose upon the physician the duty of instituting *at once* measures that will tend to arrest the lethal trend. The absence of tubercle bacilli in the sputum does not prove the absence of the disease either in the lungs or elsewhere; the presence of these germs only serves to place the diagnosis on a surer footing.

The *incipient* or *first* stage is due to lowered nutrition of the body at large, as shown by a more or less rapid *emaciation,* general *weakness* and several other early symptoms. There is often marked *pallor* of the skin and mucous membranes, especially those of the palate and larynx; a tendency to *hypothermia* (replaced by fever when the morbid process is more advanced), cold extremities and sensitiveness to cold, particularly in young girls and children, the temperature declining one or two degrees (F.) at various times of the day or remaining low days, or even weeks, at a time; afebrile *tachycardia,* the pulse being from ten to twenty beats higher than normal, associated with *lowered blood-pressure* and, in cases in which the latter symptom is marked, passive *sweating.*

That the deficient nutrition is primarily due in this disease to an inadequate supply of adrenoxidase* is shown by the readi-

* *Author's conclusion.*
** *Author's definition.*

ness with which such a condition accounts for the symptoms. Thus, a deficiency of oxygen, by reducing the functional activity of all organs, must inhibit digestion, leucocytosis, and reduces, therefore, the amount of food taken by the leucocytes from the alimentary canal and carried to the tissues, thus causing emaciation.* The muscular tissues being insufficiently nourished, weakness follows. The muscular coats of the arteries and veins being similarly influenced, they relax, causing lowering of the blood-pressure, while this fall, in turn, causes acceleration of the heart's action (Marey's law), *i.e.,* tachycardia.* When the muscular debility is excessive, relaxation of the spiral muscles of the sweat-glands gives rise to sweating—especially at night, when all the muscular elements are most relaxed.* All these symptoms are also due in part to the recession of blood from the periphery and its accumulation in the large internal vessels, especially those of the splanchnic area, as a result of the general vasodilation.* The capillaries of the skin being thus rendered ischæmic, the pallor, hypothermia, sensitiveness to cold, etc., are markedly aggravated.*

Of all these symptoms, those most frequently met with during the incipient stage are the rapid pulse and tachycardia, emaciation, pallor of the skin and mucous membranes, slight cough and lassitude. When they are encountered in a subject predisposed to the disease through inheritance, or who has been exposed to contamination, the case should be considered as one of tuberculosis as far as treatment is concerned.* The diagnosis becomes positive, however, irrespective of the absence of tubercle bacilli, when in addition to these signs, the muscular atrophy is sufficiently marked to cause cog-wheel inspiration, *drooping of the shoulders,* with diminished expansion especially marked in the infraclavicular space, and abnormal projection of the scapulæ; and if, moreover, one of the *tuberculous stigmata,* a long, narrow, cylindrical or flat thorax, cutaneous tuberculosis, anal or ischio-rectal fistulæ and especially *enlarged axillary glands* in adults and the *tracheo-bronchial* glands in children, is present.*

These various phenomena (those given in italics) constitute collectively an autonomous symptom-complex differing

* *Author's conclusion.*

from the stage next to be described in that every symptom exemplifies organic weakness. The incipient stage, therefore, is essentially one of functional depression.*

The emaciation, weakness, anæmia and pallor are familiar symptoms owing to their persistence throughout the disease. The important feature in this connection, however, is to detect them before the onset of the pulmonary lesions.

That impaired nutrition is closely related with an abnormal state of the blood is shown by the state of the latter. Grawitz[5] found that at the *onset* of the disease, there was diminution of the red corpuscles. Rachford[6] in 41 convent girls exposed to tuberculous contagion averaged 63 per cent. of hæmoglobin; he asserts that pronounced anæmia in young convent girls of tuberculous stock warrants a diagnosis of tuberculosis. Appelbaum[7] found that particularly in tall, rapidly growing youths with a poorly developed chest "anæmia is present in the first stage of tuberculosis; the erythrocytes are diminished in number, the hæmoglobin is reduced, the specific gravity is lessened and *coagulation is delayed.*" Ullom and Craig[8] also found that before the formation of cavities, the decrease of erythrocytes and a relatively greater decrease in hæmoglobin were constant. Hypothermia, cold extremities, etc., are a normal outcome of such a condition; as observed by Weill,[9] Vargas and Négrié[10] and others, it is especially marked in children and adolescents. Holmes[11] regards the "subnormal morning temperature" as an important sign.

The diminution of the general nutrition is made evident not only by emaciation, but often by atrophy of the muscles. Bompard[12] observed diminution of volume, subsidence of prominences of the body, exaggeration of hollows, loss of strength and diminution of electrical contractility, and advises chamber gymnastics "to combat this form of muscular debility, which is common particularly at the outset of the disease." Carcassonne[13] illustrated by a number of cases that atrophy of the scapulo-thoracic muscles was evident before percussion or ausculation revealed any sign of tuberculosis. De Renzi and Coop,[14] by means of Mosso's myotonometer, found the muscular tonicity reduced from the start, even though nutrition appeared normal. Cecconi[15] claims that it announces an early active manifestation of the disease.

The heart is influenced in the same manner, as shown by its diminution in size. This phenomenon, first observed by Laennec, has ever since occupied a prominent place in the pathology of tuberculosis. Louis,[16] who found it in 109 out of 112 cases, Bizot, Rokitansky, Brehmer[17] and other equally prominent clinicians have, in fact, attributed phthisis to its influence. G. W. Norris[18] in an able paper on the subject, referring to post-mortem findings at the Phipps Institute, states that they tended to show that "in uncomplicated cases of pulmonary tuberculosis, the

* *Author's conclusion.*

[5] Grawitz: Deut. med. Woch., Bd. xix, S. 1347, 1893.
[6] Rachford: N. Y. Med. Jour., Aug. 10, 1895.
[7] Appelbaum: Berl. klin. Woch., Bd. xxxix, S. 7, 1902.
[8] Ullom and Craig: Amer. Jour. Med. Sci., Sept., 1905.
[9] Weill: Lyon méd., vol. lxxvi, p. 77, 1894.
[10] Vargas and Négrié: La Semaine méd., vol. xv, p. 387, 1895.
[11] Holmes: Phila. Med. Jour., Aug. 19, 1899.
[12] Bompard: Jour. de méd. de Bordeaux, Nov. 13, 1887.
[13] Carcassonne: Arch. gén. de méd., vol. clxxxv, p. 226, 1900.
[14] De Renzi and Coop: Trans. Tuber. Congr., Naples, 1900.
[15] Cecconi: Trans. Tuber. Congr., 1905.
[16] Louis: "Recherches sur la Phthisie."
[17] Bizot, Rokitansky, Brehmer: Cited by Norris: Amer. Jour. Med. Sci., Oct., 1904.
[18] Norris: *Ibid.*

heart is subnormal in size in quite a considerable number of cases," an observation also strongly sustained by a fluoroscopic study of 90 cases by Bouchard and Balthazard.[19] Norris lays stress, moreover, on the fact that "the heart of tuberculous individuals is often small, not as the result of hyperplasia, but from *atrophy* or *degeneration* of its substance." This fact, he adds, "has long since been sufficiently pointed out by Louis, Andral, Kidd, Bennet, Quain, Strumpell, von Leyden, and has been observed by all who have given attention to the matter." That deficient general nutrition is the underlying cause of this condition has been emphasized by Brehmer, Potain and others.

Interpreted from my standpoint, an additional cause for the smallness of the heart prevails. A prominent symptom of the incipient stage, we have seen, is a low blood-pressure. Thus, Marfan[20] found it subnormal in 97 per cent. of the cases examined. Goodno[21] also states that while "the normal pressure in a healthy man is 15 to 18 c.m., in incipient tuberculosis it falls to 13, 12 or even 10 c.m.,—a fact noted by many investigators. If we recall that this entails accumulation of the blood in the great central trunks, *i.e.*, the splanchnic area, at the expense of the peripheral circulation, it will become apparent that the volume of blood which the heart has to transmit to the periphery each time it contracts, must be correspondingly reduced. As a result its expansion or diastole is diminished (its systole being commensurate with the reduced volume of blood) and it carries on its functions in this semi-contracted state months, and doubtless years in most instances.* That it should be found in this state *post-mortem*, especially when inadequately nourished during a corresponding period, is self-evident.

The rapid pulse or tachycardia, a sign to which many clinicians, including Potain, Leyden, Cornet and Loomis, attach great importance, is closely related to this process. It is a constant accompaniment of low blood-pressure, the two phenomena being related through a nervous mechanism. Thus, Leonard Hill[22] states that "if," as pointed out by Marey,[23] "all the cardiac nerves be intact, a rise of arterial pressure always slows the heart, and a fall accelerates it." The nature of this functional relationship asserts itself when the reduced volume of blood projected by the heart with each systole is taken into account: it is to *compensate* for this reduced quantity that the cardiac pulsations are reflexly increased, the purpose being to raise the quantity of blood passed through the lungs within a given time up to the normal standard.*

The accumulation of blood in the large trunks of the splanchnic area by depleting the peripheral capillaries is, aside from the diminution of red corpuscles and hæmoglobin, an important factor in the production of all symptoms of the incipient stage, *i.e.*, pallor, hypothermia and chilliness, muscular weakness and atrophy—besides the tachycardia in which, we have seen, it plays a leading rôle.*

This general adynamia is the result of two concurrent factors: the first of these is the presence in the tubercle bacillus of a toxin (an endotoxin, since it is active after death of the bacillus) which depresses the sensitiveness of the test-organ.* The functional activity of the adrenal system being inhibited

* *Author's conclusion.*

[19] Bouchard and Balthazard: Revue de la tuberculose, T. x, p. 1, 1903.
[20] Marfan: La semaine méd., vol. xi, p. 213, 1891.
[21] Goodno: Medical Era, July, 1899.
[22] Leonard Hill: Schäfer's "T. B. of Physiol.," vol. ii, p. 56, 1900.
[23] Marey: "La circulation du sang," Paris, p. 334, 1881.

in proportion, general metabolism is inadequate.* This entails also deficient formation of auto-antitoxin and a corresponding fall of the bacteriolytic and antitoxic properties of the blood.*

This is well shown by the preliminary effect of tuberculin, as demonstrated by Sir A. E. Wright, who states,[24] referring to his own observations: "Upon the inoculation of the vaccine there supervened a period of intoxication which is characterized by a *decline* in the antibacterial power of the blood. This negative phase is more or less prolonged according as a larger or smaller dose of the vaccine is inoculated." That this action is due to active depression, by the germ or its endotoxin, of organic functions is made apparent by the fact that, as stated by Professor Lukis[25] in reference to Wright's investigations: "It is found that injection of small doses of Tuberculin T. R. [an emulsion of dead tubercule bacilli] causes first a temporary fall in the opsonic index, lasting from a few hours to as much as 14 days, and that this fall is followed by a prolonged rise. This action is presumably exactly the same as that caused by the products of bacterial activity in the course of phthisis, the characteristic feature of which is that in the early stages you find periods of activity alternating with periods of quiescence, these alternations being associated with corresponding variations in the opsonic index." These alternations are characteristic of the reactions of the adrenal system, as we have seen under Epilepsy. We will see, moreover, that a similar accumulation of wastes, besides detritus incident upon the tuberculous process, accounts also for the reaction stage caused—indirectly—by tuberculin. That the direct action of tuberculin is to depress the test-organ, is shown by the fact that De Vecchi and Bolognesi[26] found that after inoculation with tuberculous material, the chromatophile cells of the pituitary body showed evidence of *hypo*-function.

The second cause of adynamia is due, even in this, the incipient stage, to the presence in the lungs of sufficiently advanced lesions to reduce markedly the intake of oxygen.

Insidiously, or giving rise perhaps to a slight though *stubborn reflex cough,* tubercle bacilli have been, for some time before the symptoms enumerated appear at all, destroying the functional activity of the air-cells or alveoli. Here they caused the formation of tubercles, small nodules varying in size from that of a pin-point to that of a millet-seed. Located from the first in the delicate partitions that separate the minute saccules or air-vesicles of an alveolus, they gradually increase in number until the latter and the terminal bronchiole leading to it are filled with them. As tubercles are being formed simultaneously in many alveoli, entire lobules (which contain several alveoli) are finally rendered useless, the respiratory area of the region involved being reduced in proportion. Hence the presence of

* *Author's conclusion.*
[24] Sir A. E. Wright: Lancet, Dec. 2, 1905.
[25] Lukis: Calcutta Med. Jour., Apr., 1907.
[26] De Vecchi and Bolognesi: Riforma méd., Aug. 19, 1905.

another major symptom, when the breathing area is sufficiently compromised, viz., *dyspnœa,* which occurs at first only during physical exertion.

The development of the tubercle is primarily due to the local irritation which the bacilli excite in the connective tissue and epithelial elements. The irritated spot attracts numerous leucocytes, many of which, the polynuclears (some being phagocytes), supply the trypsin and nucleo-proteid which, with the adrenoxidase and thyroidase secreted by the red corpuscles, form auto-antitoxin.* The evident purpose of this process is to destroy the germs.*

The tuberculous process *per se, i.e.,* the formation of the tubercle, is due to the disintegration of the bacilli in the alveolar walls by the local bacteriolytic elements, and to the liberation of their main endotoxin,—a substance which enters into the composition of these germs, and *the active principle of which is phosphorus.** So great is the proportion of this element in the solids of tubercle bacilli that their ashes contain over 60 per cent. of phosphoric anhydride. The morbid process is aggravated, moreover, by the fact that these bacilli actively reduce the adrenoxidase at the expense of the tissues.*

Maffucci, of Pisa,[27] found that culture preparations of tubercle bacilli contained, when the bacilli were dead, a toxic substance which resists the action of time, heat, desiccation, sunlight and gastric juice. He ascertained, however, that it is not a product of bacillary secretion, nor derived from the nutrient medium, but a *poison* in the substance of the bacillus itself, and liberated when the germ is disintegrated. A minute dose of this poison sufficed to cause "marasmus" and simultaneously inflammation and necrosis of the tissues, and other lesions typical of tuberculosis and anæmia. On the other hand, Hammerschlag showed that the bacilli produced an extract which contained lecithin (a body containing considerable phosphorus) capable of producing death in rabbits and guinea-pigs, while Levene[28] found that the body-substance of the tubercle bacillus not only contained phosphorus, but a body rich in this element: nucleo-proteid. The most valuable of these researches, however, are those of G. E. de Schweinitz and Marion Dorset.[29] They analyzed the ash of tubercle bacilli to the amount of 1453 grammes after the manner prescribed for plants, and found that it contained 55.23 per cent. of phosphoric anhydride (P_2O_5), a proportion which was raised to 60.90 in a subsequent analysis by de Schweinitz. This obviously indicates that pure phosphorus enters for a large share in the composition of these germs. When the rapidity with which they multiply is taken into account, it becomes evident that under conditions that favor their proliferation in the body they constitute a prolific source of phosphorus.

* *Author's conclusion.*
[27] Maffucci: Il Policlinico, vol. ii, p. 1, 1895.
[28] Levene: Med. Record, Dec. 17, 1898.
[29] de Schweinitz and Dorset: National Med. Rev., May, 1898.

That tubercle bacilli are pathogenic owing to their phosphorus (doubtless in loose combination with other constituents) is shown by the similarity of their effects to those of chronic phosphorus poisoning. Phosphorus, as is well known, arrests local nutrition. While Cau[30] and others found that this was due to oxidation of the element, Araki[31] showed that lack of oxygen was a prominent feature of general phosphorus poisoning. This observation, according to Cushny,[32] "confirms the impression of many earlier writers." This author also states that "as soon as it is oxidized, phosphorus loses its specific action"—thus restricting to the element itself the morbid phenomena witnessed. Comparing these phenomena with those of the incipient stage of tuberculosis—due, in my opinion, to the bacterial (a loosely combined) phosphorus—the analogy is striking. The coagulation-necrosis caused by the tubercle bacillus is a counterpart of that caused by phosphorus. As to the anæmia and diminution of red corpuscles and hæmoglobin, Vogel,[33] d'Amore and Falcone[34] and others have recorded similar effects in phosphorus poisoning. The low blood-pressure and rapid heart-beat are like wise present in the latter condition, as observed by Pouchet and Chevalier,[35] who also noted that large doses of phosphorus (orthophosphoric acid being used) more than doubled the heart-beats. Precisely as is the case in tuberculosis, Pal[36] found that the low blood-pressure was due to dilation of the vessels. Magitot[37] includes among the symptoms of chronic poisoning in French match-factories, wasting of the tissues.

That it is the oxygen of the adrenoxidase that is consumed in the process is also evident. We have seen that Appelbaum found that in tuberculosis the coagulation of the blood was delayed—a phenomenon due to deficiency of coagulating ferment, *i.e.*, adrenoxidase; now Cevidalli[38] also found "diminution and disappearance of the coagulating ferment" in slow phosphorus poisoning, while Araki[39] observed that the coagulability of the blood was so reduced in some instances that it remained fluid forty-eight hours or more.

The formation of the tubercle, therefore, requires the death of the bacilli, thus liberating their principal constituent, phosphorus.* This element, owing to its intense affinity for oxygen, becomes oxidized at the expense of what adrenoxidase may be present, but when this source fails, it takes up that of the underlying cellular elements (of the previously irritated area) and provokes a local coagulation necrosis.* Hence the almost invariable absence of even dead bacilli in the necrotic center of the tubercle, though they may be present in large quantities in the immediate neighborhood.* This central area contains, however, granular masses composed of disintegrated cell-nuclei and the

* *Author's conclusion.*

[30] Cau: Thèse de Paris, 1901.
[31] Araki: Zeit. f. physiol. Chem., Bd. xvii, S. 311, 1892-93; Bd. xix, S. 422, 1894.
[32] Cushny: "Pharm. and Therap.," third edition, p. 603, 1899.
[33] Vogel: Arch. inter. de pharm. et de thérap., T. x, fasc. iii et iv, 1902.
[34] d'Amore and Falcone: Arch. de pharm. de Gand, vol. i, p. 247, 1894.
[35] Pouchet and Chevalier: Bull. gén. de thérap., vol. cl, p. 915, 1905.
[36] Pal: Wiener klin. Woch., Bd. ix, S. 999, 1896.
[37] Magitot: Therap. Gaz., Sept. 16, 1895.
[38] Cevidalli: Riforma medica, vol. xviii, Pt. iv, pp. 686, 699, 711, 1902.
[39] Araki: *Loc. cit.*

remains of necrotic tissue. Surrounding it is the so-called "granulation-tissue" zone which in reality is mainly composed of the leucocytes previously referred to and their used products. Thus, the framework of this zone is a network of fibrin, a substance formed, we have seen, when nucleo-proteid and fibrin ferment (adrenoxidase) combine to form a clot.* In this network are imbedded the leucocytes, remnants of fibrous tissue, granulation cells and their nuclei, the whole forming around the necrotic focus a loose capsule which gradually fades into the surrounding normal tissues or, as is usually the case, merges with adjoining tubercles.

This entire process is an inflammatory one from start to finish.* This is further shown by the presence in most instances, of giant-cells, which occur in other conditions as sequels of inflammation. They consist of a large mass of protoplasm containing numerous nuclei, and are similar to the giant-cells of bone (osteoclasts) known to be phagocytic. As they surround the tubercles, and project pseudopodial processes into them, while, moreover, they often contain detritus, bacilli and disintegration products of the latter, their evident function is to act as phagocytes in order to remove, if possible, the tubercular mass.

If this auto-protective process fails to be carried out successfully,* as is often the case in animals, and when the formation of tubercles is rapid, the central necrotic mass becomes caseous, a feature which tends to cause confluence of a group of tubercles. Under these conditions a more active auto-protective process is awakened,* *i.e.*, fibrous encapsulation. This is brought about by the growth, around each tubercle or aggregate of tubercles, of cellular connective tissue which gradually becomes more fibrous as its cells disappear. Connective tissue bands and a thick, fibrous network soon invest the entire tuberculous mass, enclosing necrotic tissues, cell-remnants and even the giant-cells, in their grasp. The caseous material dries and shrinks, and is finally transformed into a calcareous and gritty mass enclosed in a fibrous cicatrix, which sometimes includes considerable of the surrounding tissues.

* *Author's conclusion.*

The large proportion of phosphorus that the tubercle bacilli contain has suggested that their pathogenicity might be due to the need of phosphorus as food. The fact, however, that they are far more pathogenic when dead, conclusively eliminates such a conclusion.

Koch[40] showed that dead tubercle bacilli, when injected subcutaneously in guinea-pigs, produced an abscess. Prudden and Hodenpyl[41] not only confirmed this result, ascribing the action to a "bacterio-protein" liberated when the bacilli were disintegrated in the tissues, but they obtained, after intraperitoneal or pleural injections of an emulsion of bacilli, nodules of various dimensions. The center of these nodules, composed of epithelioid and giant cells, contained tubercle bacilli in abundance, imbedded in creamy material and surrounded by fibrous tissue. This was confirmed by Straus and Gamaleia,[42] by Vissman,[43] who concluded that "tubercle bacilli, though dead and therefore deprived of the power of growth and metabolism, can still originate alterations in the tissues resembling in every detail the structure of a fresh tubercle;" by Alfred Masur,[44] whose experiments showed that "the bodies of dead tubercle bacilli contained toxic substances which are to be regarded as the cause of the changes in the diseased organs;" and finally by Stewart Stockman,[45] who found that the soluble products of the tubercle bacillus produce little effect on the healthy organism and that the dead bacilli are far more active than the soluble products.

Again, if these lesions are due to the phosphorus of the disintegrated bacilli, they should correspond with the local changes produced by this element. Referring to phosphorus, Cushny[46] writes: "Another feature in phosphorus poisoning, which is, however, better seen after *repeated small doses* than after a single large one, is the proliferation of the interstitial connective tissue of the stomach, liver and kidney, which finally induces typical cirrhosis of these organs." Baumgarten,[47] on the other hand, defines a tubercle as "the result of proliferative and exudative changes." Cushny also says, referring to the action of phosphorus *vapor*, that "many pathologists now regard this proliferation as a secondary result of the *necrosis* of parenchyma cells." Abel,[48] on the other hand, "by the injection of dead tubercle bacilli into the tracheas of rabbits, found, after twenty-four hours, white isolated areas in the bronchi and alveoli made up of round cells, among which were the bacilli; twenty-four hours later these were *necrotic* and epithelial proliferation had begun." E. R. Le Count,[49] from whose paper Abel's lines are quoted, remarks: "Thus we find, in marked contrast to one another, a *liquefactive necrosis*, which we recognize under the more common term of suppuration, *formation of fibrous tissue* and a *necrosis without liquefaction*—three distinct processes differing from one another anatomically and histologically, and having for their etiological factor the poisonous substances present in the bodies of the dead tubercle bacilli." These three processes are also peculiar to chronic phosphorus poisoning, the liquefactive necrosis being especially marked in osseous tissues. Le Count also states that fibrin (composed, we have seen, of nucleo-proteid and adrenoxidase) is "constantly present" in the tubercles of guinea-pigs, and that "the frequent presence of fibrin in genuine tubercle nodules in human beings has been demonstrated by Werneck de Aquilar in Baumgarten's laboratory." The presence of fibrin is, in fact, generally mentioned in text-books. Even the fibrous encapsulation of the tubercle finds its counterpart in the fibrous indurations which terminate the curative process in lesions caused by phosphorus.

[40] Koch: Deut. med. Woch., Bd. xvii, p. 101, 1891.
[41] Prudden and Hodenpyl: N. Y. Med. Jour., June 20, 1891.
[42] Straus and Gamaleia: Arch. de méd. expér., vol. iii, p. 705, 1891.
[43] Vissman: Albany Med. Annals, Dec., 1892.
[44] Alfred Masur: Münch. med. Woch., Bd. xlii, S. 249, 1895.
[45] Stewart Stockman: Brit. Med. Jour., Sept. 3, 1898.
[46] Cushny: *Loc. cit.*, fourth edition, p. 593, 1906.
[47] Baumgarten: Cited by Falk: Virchow's Archiv, Bd. xxxix, S. 319, 1895.
[48] Abel: Deut. med. Woch., Bd. xviii, S. 482, 1892.
[49] Le Count: Jour. of Exp. Med., Nov. 1897.

Suggestive in this connection is the predilection of matchworkers to phthisis. J. Ewing Mears[50] states that "in many there is observed a gradual deterioration of physical condition as manifested in loss of flesh and vigor." In the only three fatal cases to which he refers, "the immediate cause of death was phthisis." Ralph Stockman[51] states that the phosphorus fumes to which match-workers are exposed "consist of phosphorous anhydride (P_4O_6) and some phosphoric anhydride (P_2O_5)"—the latter being the form found in the ashes of tubercle bacilli by de Schweinitz and Dorset, as we have seen. After referring to the cases in which necrosis affects only the jaw-bones, and which recover after surgical intervention, he writes: "In other cases, the disease, instead of healing, spreads locally, involving more bone, the patient becomes cachectic, feverish, and wasted, and ultimately dies of pulmonary phthisis, general tuberculosis or some other tuberculous affection." Convinced by this, and by the fact that, as he states, "the condition generally is *exactly similar* to what is seen in *tuberculosis* of the jaw in cattle and in tuberculous disease of other bones in man,"* he concluded that the cause of phosphorus necrosis was the tubercle bacillus, and examined the pus from six cases by the Ziehl-Neelsen method, finding it in each instance. He says, however, that "the organisms were few in number and difficult to find except on the closest and most careful examination;" that even after centrifugalization and utilization of the sediment "sometimes several coverglasses had to be examined before any of the organisms were seen," and finally that "inoculation of guinea-pigs with the pus did not infect these animals with tubercle."

In view of the data I have submitted in the foregoing pages and the fact that, as stated by Abbott,[52] "there is a group of bacilli whose numbers are in many respects so like the genuine bacillus tuberculosis as easily to be mistaken for it," and which are "characterized by the same staining peculiarities," while "not all members of this group are capable of causing disease," the germs observed by Ralph Stockman evidently belong to this benign class. Indeed, it is doubtful whether cases of chronic phosphorism are even as vulnerable to infection as the average individual, owing to the immunizing influence of their febrile state. On the other hand, when we consider (1) that as Stockman says, "the accounts of post-mortem examinations of fatal cases" show that "in *most cases* death occurs from tuberculosis of the lungs" in match-workers, and that the fumes of phosphorus which they inhale months, or years, finally provoke a general disease so similar to pulmonary tuberculosis, that it becomes a question whether the bacillus of this disease is not its true cause, and (2) that the pathogenic agent of the tubercle bacillus, in the light of the evidence adduced, is phosphorus, the conclusion seems warranted that tuberculosis is a phosphorus necrosis of the pulmonary tissues, and that the tubercle is naught else than a capsule for the necrosed area, calculated to isolate it from the surrounding normal tissues.

The *second stage* becomes clearly defined when the deposit of tubercles is sufficiently great to modify the normal sounds obtained from the chest by auscultation and percussion.

* The italics are my own.—S.
[50] J. Ewing Mears: Trans. Amer. Surg. Assoc., vol. iii, p. 357, 1885.
[51] Ralph Stockman: Brit. Med. Jour., Jan. 7, 1899.
[52] Abbott: "Principles of Bacteriology," seventh edition, p. 363, 1905.