THE SEQUENCE OF EVENTS IN THE DEVELOPMENT OF CLINICAL PULMONARY TUBERCULOSIS

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So MUCH has been written about clinical tuberculosis in recent years that it is only now and then that one can offer a new explanation for some previously observed phenomenon, or give expression to well-recognized phases of the disease with any degree of individuality, yet I am going to attempt a discussion of the events and their sequence in the development of clinical tuberculosis in a manner which may differ somewhat from the usual description.

Primary Infection.—It is inconceivable that any one could pass through life without coming in contact with tubercle bacilli. It is further inconceivable that many should escape infection and its consequent specific protection or destruction.

The question whether or not histologic tubercle is necessary in order to awaken specific resistance in the host is almost universally answered in the affirmative, yet one may speculate as to the possibility of bacilli being taken into the body and being destroyed and setting free bacillary substances in quantities sufficient to stimulate and sensitize the cells, and sharpen the defense in the absence of infection. In this connection it is generally recognized that dead bacilli, when injected into an animal, will arouse the mechanism of specific defense; and it is further known that tuberculoprotein is able to increase a specific defense when once established.[1, 2]

This subject has been approached by Zinsser and Mueller[3] who cite the works of Bail,[4] McJunkin,[5] and Lange,[6] and give some inconclusive yet very suggestive experimental data which show that tissue filtrates of tuberculous lesions when injected into guinea-pigs may cause substances to be thrown into the blood which will sensitize a second guinea-pig to tuberculin, the reaction appearing within a few days.

Primary infection is responsible for establishing an increased resistance to bacilli which proves to be deterrent to further success-

ful implantations, yet, in instances in which complete healing fails to take place, this focus furnishes a source of bacilli for future reinfection. All of the phenomena of primary infection may take place without any recognizable signs on the part of the host.

Reinoculation.—It is not until the primary infection has spread from its first localization or until reinoculation from without has taken place that the phenomena of disease present themselves. The body cells react more or less vigorously to reinoculations according to the degree of sensitization which has been brought about by the primary infection, and the numbers and virulence of the bacilli causing the reinfection. In this connection metastases from the primary focus must be looked upon as reinoculations if they occur after specific defense has been established, otherwise as multiple primary foci. The effect of such further infection coming on after the primary focus has been established will differ according to the degree of immunity that has been built up.

It is the local allergic reaction which takes place between sensitized cells and bacilli and bacillary protein at the point of reinfection that starts the chain of symptoms and signs which characterize clinical tuberculosis.

Allergy.—One cannot understand any of the phases of clinical tuberculosis apart from the allergic reaction, for they are all due directly or indirectly to it. Its pathology, both anatomic and physiologic; its symptomatology; the phenomena by which it is detected by physical examination, X-ray and the tuberculin test; its confirmation by bacilli in the sputum; and its treatment, whether successful or unsuccessful, are all connected with allergy. Fig. 1 shows in the lung, accompanied by an allergic exudative reaction of marked an infiltration in the lung, accompanied by an allergic exudative reaction of marked degree. Fig. 2 shows an infiltration of the preponderantly proliferative type, in which there is a maximum of exudation.

Tuberculoallergy may be described as that quickened and heightened inflammatory response which takes place in one who has previously been inoculated by living tubercle bacilli or dead bacillary substance, whenever bacilli or bacillary protein are again brought into contact with his cells.

The intensity of this allergic reaction depends upon factors

associated both with the previous infection and the reinfection. Being sensitized, the cells are rendered hypersusceptible to the presence of tubercle bacilli and bacillary protein; and at first may react quite violently to very small dosage. Repeated reinoculations, however, are responsible up to a certain point in the immunity response for increasing the capacity of the cells to withstand further inoculations of bacilli or bacillary protein without severe reaction; for later in the course of the disease the patient may respond with mild reaction only, to many times the numbers of tubercle bacilli and many times the amount of tuberculoprotein which was required to produce violent inflammatory response and probably destruction of tissue earlier in the course of the infection.

This increased capacity of the cells to withstand larger and larger doses of tuberculoprotein is a fundamental necessity if the host is to be successful in overcoming tuberculosis. Were it not for this fact no pateint could recover from an extensive disease. In fact, if the cells should continue to be as sensitive during the after-course of the disease as they are when they react to the first reinoculation of any considerable numbers of bacilli with severe exudative inflammation with or without cavity formation, no patient could ever hope to live long after the early extensions of the disease had taken place.

The Allergic Reaction and Specific Defense.—There is much confusion in the minds of medical men as to the nature of allergy and as to its relation to immunity.

That allergy is associated with the reaction of the body to a reinoculation of bacilli or bacillary protein is universally admitted; but writers differ greatly in the properties which they assign to it. Some believe it is primarily protective and that its power to do injury is secondary; others believe that it is an injurious reaction to be avoided; and still others look upon it as a defensive reaction, necessary to protect the host until he builds up a high degree of specific defense, after which the allergic response grows less and less necessary. All admit, however, that it has power of doing injury to the tissues when excessive.

One can make no progress in the interpretation of clinical tuberculosis without recognizing as a fundamental characteristic of the allergic reaction that a small number of bacilli or a small amount of tuberculoprotein will produce a much more violent response early

in the disease than greater numbers of bacilli and larger quantities of tuberculoprotein will later. A patient may show symptoms which are more marked when the lesion is comparatively small than when it is more extensive.

The violent reaction of allergy confined as it is to areas of infection and reinfection must be looked upon as the necessary response of the host to the particular amount of infection at the time. I cannot interpret it in any other way. It undoubtedly concentrates the protective phenomena at the place where they are needed; and particularly in the early stages of the disease before the patient's ability to withstand large doses of bacilli have been developed to the degree that they are later, it even goes to the point of destroying the tissues if necessary in order to remove large masses of bacilli from the body and protect the patient from the necessity of destroying them, which he might not be able to do; or in case of failure, of having them scattered through his tissues to produce new infection.

It is one of the first principles in therapy to always keep the requirements of the allergic reaction below the point of tissue destruction if possible. This is done by avoiding those things which tend to cause massive reinoculation and widespread dissemination of the disease.

Each inoculation and reinoculation successfully combated increases the patient's ability to cope with bacilli until finally a very high state of specific resistance is attained. Whereas a few bacilli gaining access to the tissues through the air passages will cause infection in a non-immune individual, as I have frequently pointed out, the patient suffering from advanced tuberculosis will often cast out millions of bacilli per day which pass over his mucous membranes without causing new implantation. This can be interpreted only as showing that there is some change wrought in the cells of the bronchi of infected individuals which makes them resistant to the entrance of bacilli.

Again, I have called attention to the fact that the patient may react with less violence when the lesion is long existent and extensive than when it is recent and small; and further, that cavity may form early in the disease, but that cavitation rarely continues in the sense of one big cavity forming after another, no matter if the lesion keeps on spreading. The cells seem to attain a certain degree of

protection from the destructive allergic response which manifests itself early. It seems to gain this protection, too, as a result of infections which have gone before.

The body's response to these reinoculations is both anatomic and physiologic. The symptoms are physiologic and indicate in what manner the normal workings of the human machine are disturbed. We compare the symptoms with the anatomic changes present and arrive at a diagnosis and also gain understanding of the mildness or seriousness of the disease process.

Chronology of Early Events in Tuberculous Disease.—Something like the following is the chronology of early events in tuberculous disease:

(1) A reinoculation takes place in an individual whose tissues have been sensitized by previous infection.

(2) As a result of the sensitization the tissues react allergically to the new bacilli, producing, according to the numbers and virulence of the infecting bacilli and the degree of sensitization of the cells, a hyperemia; an exudation of a few cells; an exudation of serum, cells and fibrin into the tissues and air spaces; or a destruction of tissue with cavity formation. Tubercle formation is a secondary reaction in cases of reinoculation.

(3) As the bacillary protein and the protein from destroyed tissue cells is set free it is split into various products some of which are toxic. These gain access to the circulation and produce systemic effects which result in a definite group of symptoms which are known as "general," "systemic," or more appropriately "toxic" symptoms.

(4) The effect of allergy is probably primarily to defend against invasion, and secondarily to facilitate repair of injury which might result from the infection. It produces an inflammatory reaction in the lung which irritates sensory neurons which in turn carry the stimuli to the central nervous system and there transfer them to outgoing neurons which produce reactions in other tissues, causing a large group of "reflex symptoms."

(5) The allergic response further causes certain local structural changes which produce effects immediately at the site of the reaction, the so-called "local symptoms," or the "symptoms due to the tuberculous process *per se*."

(6) The local structural changes, that is, the infiltration and exudation in the tissues and the loss of tissue, produce effects which may be detected on inspection, palpation, percussion, and auscultation, and which further may be visualized by an X-ray film.

Method of Onset of the Disease.—Our conception of what occurs in this early phase of the disease when it is assuming clinical proportions is something like the following. Comparatively small reinoculations take place at first and raise the sensitiveness of the cells toward tuberculoprotein so that a larger reinoculation will be opposed by severe reaction. This reaction consists of many factors, some known and others unknown. That the capacity of the body to cope with greater and greater numbers of bacilli is increased as a result of them is generally recognized. Bacillary destruction is stimulated, humoral antibodies are increased according to many workers, the bacilli are checked in their progress through the tissues and if the numbers of bacilli are too great at any one focus, caseation and destruction of the focus take place through which they are eliminated. So, the first phase of specific defense seems to consist of a more energetic response than is required later; in fact, later the defense seems to be much more effective although accompanied by phenomena of milder reaction.

There are several ways in which tuberculosis advances to the point where it assumes the proportions of a disease:

(1) Slowly: the reinoculation being caused by few bacilli, and these probably of low virulence. This type does not put the allergic defense to any severe test, it does not call out any violent response, and results in a preponderantly proliferative process; and, when it eventually produces symptoms, does so either because of the extent of the lesion or because it has finally assumed characteristics of greater acuteness.

(2) More rapidly: the reinoculation being caused by larger numbers of bacilli and probably of greater virulence, and successive reinoculations coming on with greater rapidity. This type shows greater allergic response. A few foci may liberate sufficient bacillary protein to diffuse through and cause exudative phenomena in areas somewhat distant from the areas of infection. It is characterized by a marked activity and causes symptoms with a comparatively small area of involvement.

(3) Acutely: a large reinoculation with relatively virulent bacilli takes place at a time when the cells are highly sensitized. The result is a violent allergic response which causes a more or less widespread inflammation with or without extensive destruction of tissue. Rapid cavitation with elimination of many of the bacilli, and an open pathway to the outside world for those that remain is a common result of this type of onset.

Etiologic Classification of Symptoms.—In the chronology of events which accompany the onset of the disease, three groups of symptoms were mentioned, each being due to a distinct and particular cause:[7, 8, 9, 10, 11] (1) the "toxic group"; (2) the "reflex group"; and (3) "symptoms due to the tuberculous process *per se*."

This classification gives an understanding of what is taking place. There are many symptoms caused by tuberculosis, but they will one and all fall into one or the other of these three groups. The simplicity and value of this classification must appeal to the student of physiologic medicine. Its value is further enhanced by the fact that the same classification may be used for infections in other organs.

1. *Toxic Group of Symptoms.*—Toxins have a widespread action and probably, directly and indirectly, affect all of the cells of the body, lessening the efficiency of their action. The action of all toxins is qualitatively similar, but quantitatively dissimilar. They produce many of the characteristic effects of the major and minor emotions. They result in a widespread nerve imbalance similar to that observed in so-called neurasthenia, or in endocrine disturbances, or those which characterize psychasthenia. Many of the symptoms of toxemia are expressed in tissues and organs in which we are able to study them carefully such as the heart, blood-vessels, respiratory system, gastrointestinal system and dermal structures. From the viscero-neurological standpoint they may be classed predominantly as sympathetic effects. Thus the heart-beat is accelerated; the blood-vessels are constricted; the secretions of the respiratory tract often seem to be reduced; respiration is hastened; the secretion of the gastrointestinal glands is diminished and the contraction of the musculature is inhibited; and the pilomotor, sweat and vasomotors of the skin are activated. The sympathicotropic glands of internal secretion, particularly the adrenals, thyroid and pituitary, seem to

be stimulated to increased activity by acute toxemia; and to hypoactivity in case of long-continued toxic action.

The following are the common toxic symptoms of tuberculosis, together with the suggested manner of their production.

GROUP I

SYMPTOMS OF TOXEMIA

Caused by Harmful Stimulation of	*Symptoms*
I. Body Cells Generally	1. Malaise
II. Nervous System Generally	2. Lack of endurance
III. Endocrine System Generally	3. Loss of strength
	4. Nerve instability
	5. Diminished digestive activity
	6. Increased metabolic rate
IV. Sympathetic Nervous System	7. Loss of weight
V. Sympathicotropic Endocrines	8. Increased pulse rate
particularly adrenals and thyroid	9. Night sweats
	10. Temperature
	11. Anemia
	12. Leukocytosis

2. *The Reflex Group of Symptoms.*—The lung, being innervated by both sympathetic and parasympathetic (vagus) nerves, has the afferent nerves which course with both of these systems as agents for originating reflexes. These two systems furnish afferent components for some forty reflexes, as I have discussed elsewhere.[11, 12, 13]

There are certain irregularities in the reflexes from the lung when compared with those from other important viscera, which should be discussed. This is shown in the somatic reflexes. Instead of joining with spinal nerves to form reflexes in the upper five or six thoracic segments of the cord, in the same levels which the impulses that are carried over the afferents of the sympathetic system of the lung enter, they join with efferent spinal nerves in the third to fifth cervical segments. This can be explained, however, on the basis that the lung arises developmentally, along with the diaphragm, from this portion of the cord.

I have suggested that the impulses which produce the somatic reflexes from the lung enter the upper thoracic portion of the cord over the sympathetic (spinal) afferent system, and are then transferred upward over intracentral paths to join with the midcervical

nerves to form the reflexes. Rasmussen on account of the paucity of sympathetic fibers found in the lung by Larsell, has suggested that these reflexes might be caused by the impulses being carried over the vagus and then transmitted downward to the midcervical segments. Since all other important viscera when inflamed produce somatic reflexes which are formed regularly by the mediation of impulses transferred centrally over the afferents of the sympathetic system and the efferent spinal nerves, and all of these follow the developmental relationships in the cord it seems equally or more probable that the irregularity in expressing the reflex would be in the afferent component of the reflex. All such organs as the heart,

GROUP II

REFLEX SYMPTOMS FROM THE LUNG

Afferent Nerves		*Symptoms*	*Efferent Nerves*
Inflammation of Lung		Hoarseness	Laryngeal nerves.
		Laryngeal irritation	Superior laryngeal nerve.
		Cough	Laryngeal and nerves to all expiratory muscles with inhibition of nerves to inspiratory muscles.
		Cough	
	Afferent through (vagus) parasympathetics	Inhibition of heart	Motor fibers of cardiac vagus.
		Increased muscle tonus and glandular secretion in gastriontestinal canal	Motor fibers of gastric and intestinal parasympathetic.
		Flushing of face	Sensory fibers of Trigeminus.
		Spasm of sternocleidomastoideus and trapezius	Spinal accessorius.
		Deviation of tongue from median line	Hypoglossus.
		Degeneration of facial muscles	Trigeminus and Facialis.
	Afferent through sympathetics	Flushing of ear	Third sensory cervical.
		Dilation of pupil	Motor from Budge's Center (lower cervical and upper dorsal).
		Spasm of muscles of shoulder girdle and diaphragm	Cervical motor nerves, IId to VIIIth.
		Lessened motion of chest wall, partly due to muscle spasm as above	Cervical motor nerves, IId to VIIIth.
		Pain above 2d rib and spine of scapulae (superficial)	Cervical sensory nerves, particularly IIId, IVth, and Vth.
		Pain in muscles of shoulder girdle (deep pain)	Cervical sensory nerves, IId to VIIIth.
		Degeneration of skin and subcutaneous tissue above 2d rib anteriorly and spine of scapulae	Cervical sensory nerves, IIId, IVth and Vth.
		Degeneration of muscles of shoulder girdle	Cervical sensory and motor IId to VIIIth.

liver, pancreas, stomach, intestines and kidney, when inflamed, produce reflexes regularly in skeletal nerves which emerge from the same segments that receive the impulses over the afferent sympathetic system, while the vagal reflex effects are restricted regularly to the cranial nerves.

If the suggestion of Rasmussen is correct, then the lung proves to be an exception to all of the important organs in not having reflexes which originate in the sympathetic afferent system, which seems hardly probable when it has a sympathetic system.

The table on page 135 shows many of the common reflex symptoms which are met in pulmonary tuberculosis, together with the probable afferent and efferent paths through which they are produced.

3. *Symptoms Due to the Tuberculous Process* per se.—There is one syndrome and three symptoms which are caused directly by the tuberculous process, as follows:

GROUP III

SYMPTOMS DUE TO THE TUBERCULOUS PROCESS *Per Se*

"Colds" (tuberculous bronchitis)
Spitting of blood
Pleurisy (tuberculosis of pleura)
Sputum

Marked immunity responses to fairly large reinoculations of bacilli produce a tuberculous bronchitis with toxic symptoms, cough, sputum, and reflexes in the larynx. The same symptoms are apt to follow whether the infection results in infiltration only, or in infiltration and cavitation. The patient usually speaks of this reaction as a "cold." This is strictly a syndrome comprised of symptoms found in all groups, but its local origin may justify its classification in Group III.

When the allergic reaction results in caseation and necrosis it is responsible for the expulsion of tubercle bacilli from the lung, in which case bacilli may be found in the sputum.

Failing necrosis and the rupture of tubercles into the air passages, the inflammation may still be accompanied by sputum due to a local increase in bronchial secretion. This secretion sometimes contains an increased number of lymphocytes when it is of tuberculous origin, even though bacilli are not found.

It is a recognized fact that vessels which participate in inflammation are dilated. Their walls are more permeable than normal and so at times they allow red blood-cells as well as other constituents of the blood to pass through, causing hemoptysis. Hemoptysis may also be caused by direct injury to vessels.

If the inflammation underlies the pleura, close to its surface, then pleural pain or effusion may be present.

These local effects are the most significant of all symptoms caused by pulmonary tuberculosis. They are definitely localized in the lung.

The Allergic Reaction and Physical Signs.—Tuberculous disease makes its presence known both by disturbances in physiologic action, and by anatomical change. This change in structure, too, is a result of the allergic reaction.[2, 14, 15, 16]

Allergic reaction as it manifests itself directly and indirectly in structure alteration is the basis of most of the findings which are revealed by physical examination and the X-ray.

Through *inspection* we are able to determine the physiologic disturbance in respiratory motion which is produced by the reflex contraction of the apical muscles (the sternocleidomastoideus, subclavius and scaleni) which connect the upper ribs and sternum with the cervical vertebrae above; and, the contraction of the crus and central tendon of the diaphragm below. The contraction of these muscles limits the motion of the hemothorax on the side of the involvement causing so-called "lagging of the side," a very important symptom of pulmonary inflammation when properly interpreted.

Aside from this, the changes in the structure of the muscles, particularly the sternocleidomastoideus, scaleni, pectorales, trapezius, levator anguli scapulae and rhomboidei, in the form of increased tension may often be evident to the eye when the disease in the lung is active; and degeneration of these same muscles and the skin and subcutaneous tissue between the second rib and angle of the jaw anteriorly and the spine of the scapulae and the base of the skull posteriorly may be readily seen when a tuberculous lesion has existed for a long time. Likewise, degeneration of the skin and subcutaneous tissue below the second rib and spine of the scapula tells the eye in unmistakable language that the underlying pleura has been long involved in inflammation.

Through *palpation* we are able better to determine the spasm and degeneration of the muscles and the degeneration of the skin and soft tissue than we are by inspection. Through inspection and palpation of these soft tissues one may not only obtain information concerning the presence of pulmonary tuberculosis, but he may judge as to whether or not it is active or healed and obsolete at the time of examination.

Through palpation one may also determine the differences in density which mark different pathologic processes such as infiltration, cavitation, emphysema, pleural effusion and pneumothorax. Even the differences between severe exudative allergic reactions and mild allergic responses may be appreciated.

It is the allergic reaction in the form of exudation in the tissues, or the fibrosis which has been formed in response to it, or the destruction and excavation which has resulted from it, that we are attempting to detect by *percussion.* The major changes, whether infiltration, exudative or proliferative; excavation; or accompanying emphysema, all result directly or indirectly from the body's allergic response to reinfection or inoculations of tuberculoprotein.

So is it, too, with *auscultation.* We are attempting to discover changes in the tissues as they react to the bacilli and bacillary protein. The signs found on auscultation, whether alterations in the respiratory note or rales, vary with the degree of allergic response of the patient. One learns to distinguish the mildness of the dry infiltration of preponderantly proliferative lesions from the moist processes which characterize the proponderantly exudative lesions and which are due to violent allergic response on the part of the host.

The X-ray, too, depends much on allergy. The roentgenologist has learned to translate his shadows in terms of allergy. The soft cottony shadows of exudation are interpreted as meaning the more active lesions and the discrete, well-defined linear shadows are interpreted as being due to fibrosis. So here, too, the ability to determine the character of the active allergic response or the new tissue formed as a result of it are the chief factors in the diagnostic value of this procedure.

SUMMARY

(1) I have attempted to show in this paper how the primary infection sets the immunity mechanism working so that reinoculation is met by an immunity response.

(2) This immunity response is indicated either directly or indirectly by some phase of allergic reaction.

(3) The allergic reaction, being inflammatory in nature, results in both anatomic and physiologic disturbances.

(4) The degree of allergy present varies with the nature of the onset of the disease; being relatively mild when the onset is insidious and relatively marked when the onset is acute. Allergy further determines the course which the disease will follow after it has developed.

(5) The anatomic and physiologic disturbances caused by the immunity response furnish the symptoms and signs upon which the recognition of the disease depends.

(6) The symptoms group themselves about three causes:

(a) *The toxins, which act generally throughout the body.*

(b) *Stimuli which produce reflex effects* in other organs and structures through the sympathetic and vagal pulmonary fibers.

(c) *Local irritating and destructive effects at the site of infection.*

(7) The anatomic changes which result directly and indirectly from the reaction of the patient toward the infecting bacilli and bacillary substances cause the diagnostic phenomena observed on (a) inspection, (b) palpation, (c) percussion, (d) auscultation, (e) through the X-ray, and (f) through the diagnostic application of tuberculin.

(8) Thus the evolution of tuberculosis as a disease is a natural sequence of events based upon the amounts and nature of bacilli and bacillary substances on the one hand, and the nature of the specific defense by which the patient meets them on the other, and the disease picture at any one time represents the patient's immunity response to his disease at that particular time.

REFERENCES

[1] POTTENGER, F. M.: "Healing of Tuberculosis," *Ann. Intern. Med.*, vol. 4, pp. 281–323, 1930.

[2] POTTENGER, F. M.: "Allergy in Clinical Tuberculosis, 'Tubercle'," John Bale, Sons & Danielsson, Ltd., vol. 10, No. 9, p. 409, London, June, 1929.

[3] ZINSSER, HANS, AND MUELLER, J. HOWARD: "On the Nature of Bacterial Allergies," *J. Exp. Med.*, vol. 41, pp. 159–177, 1925.

[4] BAIL, O.: "Immunitätsforsch, Orig.," vol. 4, p. 470, 1909–10.

[5] MCJUNKIN, F. A.: "Tuerculin Hypersensitiveness in Non-tuberculous Guinea-Pigs Induced by Injections of Bacillus-free Filtrates," *J. Exp. Med.*, vol. 33, p. 751, 1921.

[6] LANGE, L. B.: "Cutaneous Hypersensitiveness to Tuberculin in Guinea-Pigs," *J. Med. Research*, vol. 44, p. 293, 1924.

[7] POTTENGER, F. M.: "Some Practical Points in the Diagnosis of Active Tuberculosis," *Northwest Medicine*, January, 1914.

[8] POTTENGER, F. M.: "The Most Dependable Symptoms for Making a Diagnosis of Early Clinical Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, vol. 15, pp. 194–201, 1927.

[9] POTTENGER, F. M.: "The Syndrome of Toxemia, an Expression of General Nervous Discharge Through the Sympathetic System," *J. A. M. A.*, January, 1916.

[10] POTTENGER, F. M.: "Fever, a Part of the Syndrome of Toxemia," *New York Med. Jour.*, August, 1916.

[11] POTTENGER, F. M.: "Symptoms of Visceral Disease," *Fourth Edition*, C. V. Mosby Co., St. Louis, 1930.

[12] POTTENGER, F. M.: "Über Lungenreflexe (Mit einem Vorschlag zu deren Einteilung) Festschrift für Artur Biedl," *Ztschr. f. d. ges. Exp. Med.*, Band 68, 1./4. H., Verlag von Julius Springer, Berlin, 1929.

[13] POTTENGER, F. M.: "Disturbances in the Vegetative System in Diseases of the Lungs and Visceral Pleura," *Trans. of Assn. for Research in Nervous and Mental Diseases*, 1929.

[14] POTTENGER, F. M.: "The Allergic Reaction, the Basis of Tuberculin Therapy," *Ann. Intern. Med.*, vol. 1, pp. 283–291, 1927.

[15] POTTENGER, F. M.: "What is Clinical Tuberculosis?" *Am. Rev. Tuberc.*, vol. 18, p. 570, 1928.

[16] POTTENGER, F. M.: "Exudative and Proliferative Processes not a Basis for Classifying Tuberculosis into Types, but Represent Different Phases of Allergic Reaction," *Am. Rev. Tuberc.*, vol. 18, p. 580, 1928.

Reprinted from

International Clinics

FORTY-FIRST SERIES,
VOLUME III (September 1931)

LEWELLYS F. BARKER FESTSCHRIFT, IN HONOR OF HIS SIXTY-FOURTH BIRTHDAY, SEPTEMBER 16, 1931

CLINICAL PRESENTATION OF CASES AT THE HARVARD MEDICAL SOCIETY

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CLINICAL PAPERS ON DISEASES OF LUNGS

CLINICAL PAPERS ON DISEASES OF BRAIN

CLINICAL PAPERS ON DISEASES CAUSED BY BACTERIA