X-RAY OBSERVATIONS OF THE PATHOGENESIS OF PULMONARY TUBERCULOSIS

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The purpose of this paper is to outline the knowledge necessary to an understanding of the pathegenesis and progress of tuberculosis of which the x-ray chest plate is a record.

The ultimate aim of all medical research is benefit to the patient. Frequently the mass of detail of scientific study submerges this in the immediate problems to be solved. The test tube and the experimental animal are at our command and in them we are tempted to see end results. Our greatest knowledge of the pathogenesis and pathology of pulmonary tuberculosis has come from two sources; post-mortem studies and animal experimentation.

The most instructive study has been the artificial production of the disease in the animal. In our human patients we have been able to study the actual changes wrought in the lungs by the tubercle bacillus only by the indirect signs elicted by the clinical examination of the patient. We have realized our short comings and errors in translating physical signs into pathological changes within the lungs. Therefore we have seized upon animal experimentation to teach us more, since here we can control our material and make direct observations of the lungs at will.

In our zeal to find out more and more we have pushed our studies on the amimal to such a stage as to provoke the following remark from a learned scientific clinician, "It is almost as important to make observations on the human as it is to make them on experimental animals." We have learned and are learning much from the observation of animals; it behooves us as well to view each human patient as a source of scientific knowledge. Armed with the knowledge gained from experimental studies, the pathologist lays bare the dead lungs on the autopsy table and tells us what has happened. Armed with the same knowledge it is possible for the trained

observer to lay bare the living lungs on the x-ray plate and tell us what has happened, what is happening and what probably will happen. The use of the x-ray plate in the diagnosis of pulmonary tuberculosis is firmly established. Its value does not stop there, for it gives us the means of studying the disease, as a scientific problem in its own unfortunate living host. Anatomy was taught us by dissection of the dead; now in our modern progressive anatomic laboratories the x-ray presents to the student that study in the living. Lung pathology was also taught to us by dissection of the dead, but now the progressive investigator is viewing his post-mortem findings largely as confirmation of his observations and predictions made from an x-ray plate. Such mental dissection of lung lesions from the x-ray plate offer much for our further studies of the disease.

The pathogenesis of pulmonary tuberculosis is explained with wide divergence of opinion, inviting discussion from several angles. The portal of entry of the bacillus which produces the disease in the body is a much debated question. Animal experimentation has failed to settle it to the satisfaction of all. In the experimental production of pulmonary tuberculosis a definite limitation must be recognized. The lesions as we recognize them in the infant can readily be produced in the animal, but the adult type of lesions with cavity formation is rarely, if ever, produced by any of the usual methods of animal inoculation. To produce cavernous pulmonary tuberculosis, whether by inhalation or by feeding, it is necessary to adopt a scheme of introduction of the bacilli whereby they are made to gain entrance into the lymph passages in relatively small doses. When live tubercle bacilli are first introduced into an animal, even if the lung is the primary site of inoculation, a lesion is produced which has little resemblance to the lesion of adult pulmonary tuberculosis. With the first or primary injection of live tubercle bacilli in the animal there will immediately result a relatively slight lesion at the point of inoculation, but the nearest regional lymph nodes will enlarge and show marked reaction. No exudation will occur at the point of inoculation unless the dosage be large. The lesion formed at the point of inoculation will differ according to the dosage administered. With small dosage there will be a slow development of the lesion by proliferation and increase of cells of the fixed type

or the so-called epitheloid cells. With large dosage there will be produced an immediate outpouring of polymorphonuclear leucocytes which rapidly disappear and then the proliferation of fixed cells goes on in an orderly slow manner. When the animal is again inoculated with live tubercle bacilli we observe "Kochs phenomena." There is an active reaction with exudation and necrosis at the site of the second inoculation. This lesion does not progress in an orderly sluggish manner; it tends to heal and no tuberculosis of the regional lymph nodes is produced. So too, if live tubercle bacilli are injected into the pleural cavity of an animal which has received no previous inoculations, no fluid will be produced. But if the inoculation is made into the pleural cavity of an animal suffering with tuberculosis a clear fluid will invariably result. An understanding of these simple experimental observations is necessary to our comprehension of the pathogenesis of tuberculosis in the human. The pathology of pulmonary tuberculosis presents the greatest diversity and multiplicity of lesions. In explaining our physical signs and especially in interpreting our x-ray plates many investigators are too apt to think only of the tubercle as the pathological entity of tuberculosis. We must remember that tuberculosis can mean anything from a small nodule made up microscopically of giant cell, caseation, epitheloid and lymphoid cells, to a whole lung which has become solid, or a lobe entirely honey-combed by cavities. The tissue changes of pulmonary tuberculosis involve exudation, proliferation, caseation, degeneration, necrosis, cavitation, liquefaction and repair. In attempting to explain why the pathological changes produced by the tubercle bacillus in different human hosts can be so extremely varied, many theories have been given and conditions pictured. The virulence of different strains of organism has received exaggerated emphasis. Chemists and bacteriologists would have us take the extreme view of the important part played by colloid chemistry and acidosis.

The normal anatomy and physiology of all individuals at the time of infection gives partial explanation of the pathological changes following that infection, and this is added to by the more abstract reactions of immunity, allergy and resistance. The problem of the unstaple lesions probably will be solved by an understanding of the anatomic defenses always present in the host, and of the intrinsic bodily reactions and extrinsic reactions of the organism.

The anatomic factors of defense are absent in each individual, regardless of the presence or absence of infection. The first obstacle met by any foreign material seeking entrance into the body by inhalation is the fine hair at the entrance of the nose. Beyond this lies the mucous membrane, always moist with secretions, possessed of more or less bacteriocidal action. This membrane lines the nose, mouth and pharynx. In the trachea the ciliated epithelium is so active and capable, that it keeps from the lungs a large amount of the dirt inhaled. No doubt this active waving surface prevents to a great extent, the implantation or entrance of inert dirt or bacteria. This ciliated epithelium lines the trachea and bronchii from the larynx until bronchii of about 1 millimeter are reached[5]. At this point, usually the respiratory bronchus, there is a transition from columnar to cuboidal epithelium and the cilia are lost. Beyond in the ductulous alveolaris and atria the cuboidal epithelium is gradually flattened into the flat single layer epithlium which is continuous throughout the air sacs and alveoli. From the very beginning of the mucous membrane in the nose to the lining of the bronchi in the lungs we find a rich supply of lymph vessels and lymphoid tissue. Dirt accidentally drawn onto the nasal mucous membrane or India Ink injected there experimetally is rapidly expelled or carried into the large lymph nodes of the cervical chain. There is normally no direct flow of lymph from the nasal cavity, pharynx, tonsils or trachea, into the lungs. About the bifurcation of the trachea there is located the large mass of tracheo-broncheal lymph nodes which in our autopsies are found to be heavily pigmented.

Within the inner third of the lung actual lymph nodes with germ centers are found in the walls of the bronchi and particularly at the bifurcation of the bronchi. Beyond the inner third of the lung we continue to find collections of lymphoid tissue, but without germ centers along the bronchi, especially at the bifurcation. In the lower lobes however, the larger lymph nodes with germ centers are found within the parenchyma farther out than the inner third. These masses of lymphoid tissue continue to grow smaller in the finer divisions of the bronchi and vessels and finally are found only at the bifurcations. The end of the ductulus alveolaris is the furthest point along the finer bronchi where we find lymphoid tissue. As the masses

of lymphoid tissue are only filters for the lymph we naturally find lymph vessels in the walls of the bronchi out as far as we find lymphoid tissue. Lymphatic vessels are also associated with the arteries and veins. The pleura has an extremely rich supply of lymph vessels. The lymph flow and the lymphoid tissue within the parenchyma of the lung stand as strong barriers of defense to the invasion of inert foreign particles or living organisms. But beyond the end of the ductulus alveolaris there are no lymph vessels, there is no lymph flow, there is no lymphoid tissue. But the atria, air sacs and alveoli are not left without defense against invasion. Here the phagocyte plays the part of the scavenger in picking up dirt and bacteria, which have penetrated to these depths; carrying them over to the collections of lymphoid tissue where they are then within the realm of lymphatic defense. The role of the phagocyte has been shown to be peculiarly that of a passive barrier. The microscopic study of any lung showing anthracosis reveals these wandering cells engorged with pigment, apparently on their way to the depot of refuse in the lymphoid tissue. Just as pigment is handled so too the tubercle bacillus is disposed of. Excellent studies by Dr. Gerald Webb[20] and co-workers have indicated that while the phagocyte does engulf the tubercle bacillus, it is totally unable to combat or destroy it. Apparently the function of the phagocyte is only to seize and carry the bacillus over into the lymphoid tissue, which possesses the inherent ability to combat the invader. The normal lymph flow in the lung is from the parenchyma toward the hilum, except for a narrow strip of lung tissue immediately under the pleura which can drain into the pleura. The flow in the pleura is over the surface of the lung to the lymph nodes at the hilum. The direction of the flow is established and guarded by valves, which near the hilum open toward the hilum and near the junction of the septa and pleura, open toward the pleura. Pigment is not carried from the hilum into the lung, but vice versa; the tubercle bacillus is not carried from the hilum into the lung, but vice versa; disease does not progress from the hilum into the lung, but vice versa.

Lymph flow, like venous blood flow, throughout the body is maintained not so much by differences in pressure at the source and mouth of the channel, as by constant massage of the vessels by sur-

rounding tissues. The lymph flow is directed by valves as is the venous flow. The venous return from the great toe to the heart is not propelled nearly so much by venous pressure as by the constant massage of the veins by muscular tonecity and active muscular movements of the dependent limbs. Lymph flow within the lung is maintained chiefly by the massage of the vessels due to the reguarly repeated movements of inspiration and expiration and the inherent elasticity of the lung tissue. Promote greater expansion and contraction of the lung and you increase lymph flow. The apices of the lung cramped into the cupolas of the pleura cavities and strapped down by the small circle of the horizontal first rib, undergo a very limited movement. The massage of the lymph vessels is poor, the lymph flow is sluggish and the lodgment of invading tubercle bacilli is comparatively little disturbed. But on the other hand the posterior diaphragmatic borders of the lower lobes experience constant great expansion and freedom of movement; the lymph flow is free and lodgment of tuberculous infection is desperately fought. The record of this phenomena is constantly registered on autopsy findings and x-ray chest plates. This is usually the last part of a lung to become infiltrated by tubercles.

Without an accurate understanding of these anatomic defenses it is impossible to conceive the process of infection, the beginning and dissemination of tuberculosis in the lung. In the vast majority of cases of pulmonary tuberculosis the bacillus enters the lungs by inhalation. It is carried into the small bronchi beyond the ciliated epithelium, beyond the lymphatics and lymphoid tissue, out into the divisions of the primary lobule. There it is taken up by the large phagocytes, just as pigment is handled, and carried to the lymphoid tissue. In this mission the phagocyte acts only as a passive carrier. It does not posses the ability to attack or destroy the tubercle bacillus as I have said, but simply bears the invading germ to the lymphoid tissue where resistance is found. Here in the lymphoid tissue destruction of the bacillus is accomplished or pulmonary tuberculosis begins.

It is not our intention to state that a tuberculous lesion can never start in a capillary or within the lumen of the bronchus. Lesions have been proven to exist in each of these locations but all of our

researches tend to show that whether the entrance of the germ into the lung is by the bronchus or by a blood vessel, the common occurrence is that the bacillus is carried outside of the vessel or bronchus to find lodgment in the lymphoid tissue. This is also the observations of Opie[1] and Krause[4]. Obviously an infection within either a vessel or bronchus so great that the local lymphatics are overwhelmed, results in a lesion at that point. Such lesions occur mostly as the result of experimentation or as late secondary lesions such as caseous broncho pneumonia. Aufrecht[6] and Kretz[7] believed that the lesion starts in the blood vessels. Aufredcht studied the larger veins by histological sections and Kretz used injections of tubercle becilli into the circulation of animals. If Aufrecht had studied serial microscopic sections he would have seen that the lesion started in the lymphoid tissue outside of the vein and extended into the vessel rather than starting from the endothelial cells. Kretz injected such large numbers of bacilli into the blood vessels as to cause emboli in the pulmonary capillaries. The mistake of Kretz has been clearly shown by the careful animal injection experiments of Krause.

With the implantation of the tubercle bacillus in the tissues of the body the pathological changes which immediately result vary with every individual. The lesions of pulmonary tuberculosis are extremely varied, and comprehend practically every fundamental pathological process described. But most striking in the difference of reactions are the changes wrought in the adult and the child. At the very beginning of our researches the great differences between the x-ray chest plates of the tuberculous child and the tuberculous adult were observed and described. It was a great satisfaction when in 1917 Opie[1] discussed these differences from the viewpoint of pathology and post-mortem findings, stressing the points of hypersensitiveness and immunity. Since then a mass of evidence has been accumulated to show that the differences observed between the child and adult are but the examples of reactions in a non-sensitized and sensitized animal.

It has been repeatedly proven and generally known that the first subcutaneous injections of the tubercle bacillus in an animal cause only a slight lesion at the point of inoculation. Dissemination occurs by way of the lymphatics and the nearest lymph nodes undergo a

violent reaction which may progress even to the point of suppuration and discharge. With a subsequent inoculation into the same animal, as when an animal suffering with tuberculosis is re-inoculated, there is an active reaction with necrosis at the site of the second inoculation, and frequently a reaction will occur at the point of first inoculation, which is much more severe than that caused by the first injection. This second lesion is not progressive, it tends to heal and no tuberculosis of the regional lymph nodes is produced. This is known as "Kochs phenomena."

Pulmonary tuberculosis of early childhood does not affect one part of the lung oftener than another. In the first years of life there is almost no tendency for the lesion to heal but progressive caseation occurs; cavities are uncommon but do occur; dissemination readily occurs and miliary tuberculosis is a frequent termination[19]. The lymph nodes at the hilum are invariably markedly involved and usually are the earliest and chief center of the disease. Jordan in examining the chests of children roentgenographically, found these earliest lesions at the hilum. By his pathological researches he proved that the nodes are much more extensively involved than the parenchyma of the lungs and that there is a peribronchial inflammation. Jordan believes in infections of the lungs from the hilum. Ghon[9] recognized pathologically all that Jordan had seen on the x-ray plate and conclusively showed that tuberculosis of the tracheo-bronchial lymph nodes does not occur as the primary focus but is so frequently associated with a lesion in the lung substance that we may assume the invariable presence of the parenchymal focus. Our x-ray observations and pathological studies confirm Ghon's conclusions. The primary intra pulmonary lesion plus that produced in the hilum nodes has been termed the "primary complex" by Ranke. Ziegler[11] recognized exactly the primary seat of the tuberculous focus and describes it to be where we know lymphoid tissue normally exists, but he failed to emphasize the importance of the lymphoid tissue.

Hilum tuberculosis in children with the old Ghon in the parenchyma has all the characteristics of first infection. Following the establishment of this primary complex the disease especially in the young, may become generalized by the blood and terminate in menin-

gitis. With increasing age, however, there is a marked tendency for this primary stage to heal. Various stages in the process of healing may be seen in the lungs of children who die from other causes. These lesions may be recognized as: 1. small caseous nodules encapsulated by fibrous tissue; 2. caseation encapsulated by calcium; 3. calcificaiton with fibrosis. Opie[1] has published some most interesting findings in post-mortem studies of St. Louis children. His figures for the presence of these old lesions found in the lungs of patients dying from causes other than tuberculosis are as follows:

2-5 years;	42.8%	18-30 years;	83.3%
5-10 years;	45.5%	30-35 years;	91.3%
10-18 years;	55%	50-70 years;	93.3%

Examination of the lung on post-mortem may disclose only a few calcified nodules whereas x-ray plates of the chest or lungs clearly show their distribution and number. The routine followed in our studies of correlation of x-ray densities and tuberculosis pathological changes in the lung, was to remove the lungs from the body, inflate them to their normal size and make stereoscopic x-ray plates. From the plates we found we could invariably diagnose and localize such healed areas of calcification, caseation and fibrosis, as to enable us to cut down on them with ease. Just as we localized them with accuracy in the lungs removed from the body, so it is possible to recognize them and place them in the chest in relation to the trunks.

The early puerile lesion as seen upon an x-ray plate consists of a small circumscribed area of density connected to the hilum by a heavy trunk. Such parenchymal foci are usually seen within the mid lung zone. They may be distributed anywhere throughout all lobes and only exceptionally are they found at the apices. There is no special susceptibility at the apices for the primary childhood infection of tuberculosis. The hilum shadows are heavy, showing densities suggestive of calcification, caseation or fibrosis. Sometimes enlarged pulmonary or bronchial nodes may be seen.

The clinical significance of such findings on the x-ray plate of a child is a question of such import as to have caused the formation of a special investigating committee[2,1] by the National Tuberculosis Association to prosecute such research as would tend to standardize

our interpretations. We cannot decide from an x-ray plate alone when these densities are of clinical significance. Thickened trunks and enlarged hilum shadows on an x-ray plate may be caused by various other childhood diseases, such as measles, whooping cough or mumps. They can never be considered as being the result of tuberculosis unless calcification or caseation are definitely shown to be present. Even then these markings cannot be interpreted as being evidence of active disease unless a definite parenchymal "fan" is visible. But there is one peculiar density seen in the hilum which has clinical significance. This we term a caseo-calcareous node. Upon the x-ray plate it has the density of calcium. It is usually quite large and can be seen to be made up of many small flakes of calcium rather than one stone. Upon microscopic section we find that such lesions consist of a soft caseous center containing calcium and larger hard flakes of calcium within the periphery. Such lesions we have never found to be healed on post-mortem studies and they should always be considered as potential foci of infection.

The report of the special investigating committee[21] includes the following paragraph: "It was the concensus of opinion that children are probably more apt than adults to show definite x-ray evidences in the hilum and trunk shadows of simple as well as serious respiratory infections. Practically all children of the ages of those examined have had at one time or another, one or more respiratory infections, especially measles and whooping cough, that are likely to produce very apparent changes in the shadows mentioned and which will remain distinctly visible for a variable period of time. These apparent deviations from the normal are not necessarily abnormal when observed, but may be the harmless results of one or more infections. No doubt such appearances have many times been misinterpreted as evidences of tuberculosis."

The report in its conclusion states, "Calcified nodes at the root of the lung, without evidence of lung disease, are of no significance except as evidence of some healed inflammatory condition, possibly, but not necessarily, tuberculous. They are a common finding in normal chests". Opie[1] is of the opinion that calcification in the lung or hilum signifies a previous tuberculous infection. We are inclined to accept his views in our studies. The clinical significance of these

markings at the hilum is a question only to be answered by careful physical examination, x-ray studies, laboratory tests and observation. Calcification as seen in the hilum on an x-ray plate may clinically mean nothing. Lesions due to infections which have healed are probably our best protection against pulmonary tuberculosis. However, in order to protect as fully as possible the young patient in his fight for health and to guard the doctor in his diagnosis, we are appealing for the term "Potentially Tuberculous." Any child showing ill-nourishment and under weight, with a history of possible exposure to tuberculosis, running a persistent unexplained fever, giving a positive tuberculin test and showing an enlarged hilum shadow on the x-ray plate, should be diagnosed "Potentially Tuberculous" and treated with the same care as a case of active incipient pulmonary tuberculosis until the symptoms are relieved and the ill-nourishment corrected or another diagnosis proven. In this way in nearly every such instance a frank case of active pulmonary tuberculosis will be averted without stigmatizing the child. In such cases the child has withstood the primary infection and as a sensitized individual is better armed to meet the repeated infections of adult life. The scars in the lungs and hilum nodes stand as evidence of the old infections and speak for resistance gained. This truth was suggested early in our investigations when the first fifty sets of x-ray chest plates of healthy adults showed much greater amounts of calcification within the hilum and much more thickening and studding of the trunks than did fifty cases of active pulmonary tuberculosis.

Adult apical tuberculosis resembles in all respects the reaction to the second infection in experimental animals. It is the reaction of an infection in a sensitized animal. The great difference of reactions to the infection of tuberculosis in sensitized and non-sensitized animals has been shown clearly by many workers[1,4]. At the very beginning of our x-ray studies of the chest the great difference between the plates of tuberculous children and tuberculous adults was noted. The usual case of active pulmonary tuberculosis in the adult is the result of repeated infections. The immunity and resistance gained by the infections of childhood alter the course and picture of the disease in later life. The focal lesions of early life which have healed are beneficial but they do not always effectively protect.

The patient has relative immunity but a diminution of resistance is brought about by intercurrent disease, fatigue, malnutrition and various other factors. Immunity diminishes when recovery occurs and disappears after the lesion is completely healed, but is increased by re-infection, spread or metastasis of the active disease. Reinfection may occur after long periods of quiescience. This undoubtedly happens in human beings, when immunity is comparatively low. So, too, in the adult human infection we find the prompt response of local reaction at the point of inoculation, and the constitutional changes so charastic of the reaction in the sensitized experimental animal.

Before a child is ten years of age he is usually sensitized and has acquired a degree of immunity. Infection after this age produces the picture of adult tuberculosis with apical localization, tendency to chronicity with fibrosis, cavity formation and noticeable absence of associated tuberculosis in the regional lymph nodes. The tubercle bacillus has gained entrance by inhalation, penetrated the epithelial lining of the lung, gained entrance into the tissues where it has been gathered up by the lymphatics and then incited a local reaction in an allergic soil. The first reaction to the implantation of the tubercle bacillus in an allergic soil is an exudate at the point of inoculation. This phenomena is the most striking difference between adult and puerile types of tuberculosis. Peculiarly the exudation takes place immediately under the pleura. This observation has been made by Gardner[18] in his experimental work which I will cite, "With inhalation well developed tubercles appear in about two weeks in a group of alveoli immediately beneath the pleura. Occasionaly in certain animals a few similar tubercles may be found in the mid zone regions, half way from the pleura to the hilum. From these foci bacilli are carried back by lymphatic vessels to nodes at the hilum." Our x-ray observations show invariably that the adult lesion starts immediately under the pleura. This phenomena is vitally important because it explains why we find physical signs early in adult tuberculosis and answers the question why the x-ray plate lends itself so readily to the study of the pathological changes in this type of the disease. We do not attempt to answer why the exudation appears immediately under the pleura. Certainly the lymph flow must play a great part.

Krause[4] has approached this same subject when he asks the questions, "Does human tuberculosis in early life tend to localize at the roots because then the drainage is more active and open? How much inhalation of foreign bodies and respiratory infections alter the puerile lymphatic structure?" The blocking of the lymph flow toward the hilum is clearly shown in studies of tuberculous lungs. The engorgement of the peripheral lymphatics may be brought about either by a blocking of the central lymphatics or by an overflow of exudate. It is a frequent observation to find dilated pleural lymphatic vessels over a lesion within the lung and on section find that pressure on the lymphatic vessels running toward the hilum has caused the lymph flow to seek out the collateral route toward the pleura. This is made possible because of the position of the valves. The normal lymph flow through the lung, which occurs from the parenchyma toward the hilum, except for a small area which is immediately under the pleura and which may drain into the pleural lymphatics, can be seen to have a vital bearing on the pathology and progress of the disease.

As before stated an exudate is the first reaction to the implantation bacilli in the tissues of a sensitized individual. If a massive dose has gained entrance at any certain point the exudation is of the polymorphonuclear type, due undoubtedly to the reaction of tissue to a foreign protein. But this polymorphonuclear exudate disappears in about forty-eight hours to be replaced by a mononuclear exudate and proliferation of fixed tissue cells. From these elements the characteristic microscopic picture of tubercle formation with giant cells, epitheloid cells and lymphocytes is produced.

From this point the pathology, progresses either to the reparative changes of fibrosis and calcification or the destructive changes of caseation, ulcerataion and cavitation. When an adult individual is in possession of the ordinary amount of allergy and resistance, any lesion of pulmonary tuberculosis always tends toward healing. It is also true that the lesions of an adult type of the disease are the results of repeated infections either from without or within. For instance the first lesion within the lung of an individual case, let us say, is in the right apex. This particular lesion has gone through the pathological changes of exudation, tubercle formation

and is now present only as an old fibrotic scar. But while this oldest lesion has been progressing to repair and healing, let us say a newer lesion is developed at some other point lower down in the lung or in the opposite apex. This newer lesion may be the result of spread from the original lesion or a new infection from without. This second lesion we will say is in the state of exudation. Drawing the picture still farther, we may have developed an area of caseous broncho pneumonia in one of the lower lobes. This lesion is the result of aspiration of infectious material from an apical lesion. Now in this problematical, yet typical case there are three distinct lung lesions, all due to tuberculosis and each one in a different state of pathological change. There is present exudation, caseation and fibrosis.

We must turn again to anatomy to explain these lesions as we find them on physical examination, on the x-ray plate and in post-mortem studies. Septa are prolongations of the connective tissue from the pleura down into the lung. These connective tissue septa, rich in lymphatics act as excellent barriers to the spread by continuity, of any lung pathology characterized by exudation. Inflammatory exudation starting within any one of the small compartments, anatomically known as "secondary lobules" is definitely limited by these barriers. Spread through such a septum will not take place until cavitation occurs. The localization and restriction of the pathological changes by these septa accounts for our localized rales on physical examination and also explains the "Fan"[15] on an x-ray plate.

Let me state, however, that these fans may be present in any lung disease producing exudation. The cellular elements of an acute lobular pneumonia, apical catarrh or an infarct are all held in check by the septa and can consequently give localized signs and a "Fan". The differentiation of these lesions can be made by an understanding of the progressive pathology of tuberculosis just described and the ability to recognize it upon an x-ray plate.

From extensive research it has been established that the densities caused by the pathological changes of pulmonary tuberculosis as shown on an x-ray plate vary in their quality and degree of density, progressing from the least dense to the heaviest as follows:

1. serous exudate, 2. cellular exudate, 3. fibrosis, 4. caseation, 5. calcification. Given then, the problematic case cited above or any case of adult tuberculosis showing two or more lesions, the x-ray picture will be characterized by the densities of different qualities. A thorough study of x-ray chest plates with this understanding will enable you to read the changes in terms of actual pathology. The localized, cone-shaped lesions, walled in by the septa will never be seen in post mortem studies if the pathologist's usual sweeping cut from apex to base is made. But if you will carefully dissect out along the bronchi you will easily lay bare these lesions immediately under the pleura. So, too, if you read your x-ray chest plates with no respect to trunks you will never see the fan. But again if you will follow out along the different trunks, the lesions present will not appear as one continuous mass of pathology but you will be able to mentally dissect the changes and translate them in their actual progressive pathology.

After the apical lesion, the most common lesion of adult pulmonary tuberculosis is caseous broncho pneumonia. It is invariably associated with old apical lesions, usually containing cavities. It invades the lower and middle lobes and lower part of the upper lobes and not infrequently the apex opposite to an old lesion. It is in all probability caused by aspiration of sputum droplets containing large numbers of the bacilli and so can be described as the reaction of massive infection in a highly allergic soil. Upon gross section of the lung and microscopic studies it is recognized as diffusely scattered yellow nodules of caseation, between which lie areas of normal lung tissue. Upon the x-ray plate it is easily recognized as a diffuse heavy mottling, frequently seen scattered along the main trunks suggesting "raisins upon a stem." It may become confluent and produce pseudo-lobar caseous pneumonia. As confluent localized areas it may take on a "Fan" shape. Caseous broncho pneumonia may exist in a large area without causing any signs or symptoms. Its recognition in any case has always led us to a grave prognosis. Recent studies however, have made radical changes in our views relative to the clinical gravity of this complication. The observations which have startled us and made us shift our views is the extent to which caseous broncho pneumonia can be absorbed. Too often has our

grave prognosis, given because of the presence of caseous broncho pneumonia, been mocked by the clinical cure of the patient and evident absorption of the exudate.

The possibility of the absorption of tuberculous exudate was given consideration by early workers. Ziegler[11] states: "It is very doubtful whether complete recovery of the effected tissue by reabsorption of the exudate is in any case possible, and indeed it can only occur in the very smallest patches whose vessels are not yet obliterated. In larger patches, healing can only take place when the inflammatory process issues in fibrous hyperplasis and induration." However, Virchow[10] in 1858 stated.: "These cheesy transformation is the regular termination of the tubercle, but on one hand, it is not the necessary one, in as much as there are rare cases in which tubercles in consequence of their undergoing a complete fatty metamorphosis, become capable of reabsorption; on the other hand the same cheesy metamorphosis befalls other kinds of cellular new formation, for pus may become cheesy and likewise cancer and sarcoma."

Recently Gardner[18] in his excellent studies on the healing by resolution in experimental tuberculosis has shown conclusively that "caseous tubercle can heal by resolution and finally disappear completely." The interest in these experimental studies is manifoldly increased by the work of Dunham and Norton[17] on the x-ray studies of the absorption of tuberculous exudate within the lung. The latter report noticeable absorption of tuberculous exudate in 59 cases of a series of 489 or more than 12 present. In 7 cases the change was slight, in 24 the change was moderate, in 18 the change was marked. In all there was clinical improvement of the patient. Since the report of this series of cases the same observations are constantly being made by us in our office and at the Cincinnati Tuberculosis Sanatorium. Here again the experimental and post-mortem observations of a most vital phase of the disease can readily be followed and studied more fully in the living human. The clinical importance of the scope of this work is tremendous. The observations are startling because the changes noted are neither slight nor infrequent.

In seeking explanation for this phenomena of absorption of tuberculous exudate anatomy may again show us the answer. Miller[5]

in his newest work on reticulum of the lung has shown that reticulum precedes white fibrous tissue in the formation of tubercle and scar. By special stains of very thin microscopic sections the location of tubercle can be detected by the arrangement of reticulum even before the cellular elements of a typical tubercle can be made out. But in sections of caseous pneumonia reticulum is noticeably absent or at least not so prevelant. Reticulum precedes white fibrous tissue. In caseous broncho pneumonia reticulum is comparatively less; therefore may we deduce that it is more possible of absorption?

Lobar or massive caseous pneumonia occurs in both the adult and child. In the adult type old apical lesions are always present. Large areas of the lung may be involved for months without causing severe symptoms. The old apical lesion is seldom found by physical examination and so, although a definite tuberculous lesion may have existed for some time, it is too frequently only recognized when the massive lesion has progressed to cavitation and death is close, thence the name "hasty consumption." Allergy as shown by Krause[4], teaches us that "if a man falls acutely ill with tuberculosis it means that there has been rapid fresh extension of metastasis of infection from pre-existing foci, known or unknown." In x-ray studies the old lung foci are found and the progress of the new massive lesion followed.

Acute miliary tuberculosis deserves special consideration. We believe it is the result of lack or loss of immunity. Krause[4] states "miliary tuberculosis is always the result of re-infection from older foci." Thus we find it associated in the adult with definite old healed lesions as revealed by the x-ray plates. In children the old focus may not be evident, but a Ghon is usually seen or the primary focus found in other parts of the body. Many cases of healed miliary tuberculosis are being found by our more general use of the x-ray chest studies. This diagnosis is only justified when the subject gives no history of work in a dusty trade: Lungs of anthracite miners most nearly simulate miliary tuberculosis. The x-ray picture is that of fine sharp, discrete studdings more or less evenly distributed throughout all lobes. It has been our good fortune to have had two such cases come to autopsy and to be able to definitely prove the diagnosis. Most peculiarly these patients seldom if ever give any

history suggesting serious lung infection. Opie[1] in his pathological studies has noted the same and states, "such extensive calcified tubercles of the lung and its lymph nodes were disclosed, that a grave infection must have existed at some time previous; even though there had been no history of corresponding symptoms, there was doubtless at some period imminent danger of death from tuberculosis. This form of infection has an interest not only for the pathologist, as often assumed but for the clinician and for those interested in the epidemiology of the disease." Such diffuse lesions located by the x-ray chest plate in an individual apparently well, may have no greater clinical significance than that there is definite loss of lung function; even shortness of breath may not result. Furthermore it has been our observation that when a new tuberculous infection is superimposed upon these old healed miliary lesions, the progress of the case is rapid and the prognosis necessarily grave. This was taught us by studies of the living, made with x-ray plates, plus the knowledge given us by the pathologist.

The predominance and significance of caseous pleurisy has been greatly emphasized by x-ray studies. The x-ray picture is that of empyema associated with caseous broncho pneumonia without old apical lesions. At U. S. General Hospital No. 19 we had opportunity to study 17 cases by x-ray plates and careful post-mortems. The pleura shows massive thickening with solid caseation, involving chiefly the parietal pleura. The lesions within the lungs are comparatively slight. Old apical lesions are seldom if ever present. In some cases the solid caseation of the pleura measured 5 c. m. in thickness. The end is invariably rapidly fatal, although the patient neither feels nor looks sick. Literature reveals meagre mention of the condition. Letulle[22] gives a short concise microscopic description with some excellent illustrations. German investigators during the war reported a few cases among the Arabian troops in Turkey. To us caseous pleurisy represents the massive reaction of an individual devoid of resistance. It is comparable to the other massive lesions found in the lymph nodes, or represented by lobar caseous pneumonia as found in the aborigines and other primitive tribes. This has been emphasized by Bushnell[2]. Of our 17 cases studied, 14 were found in young adult negroes coming from rural districts.

The x-ray studies in each case showed the massive changes and absence of old apical lesions. The type of case and progress of the disease was followed in the living, by the x-ray. Our deductions were proven on autopsy.

In conclusion we wish primarily to emphasize the importance of the "fans" or cones which are so constant in and characteristic of the adult apical type of pulmonary tuberculosis, to note their differing densities and their definite location within the lung and to contrast the importance of this finding with the conception of pulmonary tuberculosis as expressed by hilum and per-bronchial tuberculosis.

Hilum and peribronchial tuberculosis are terms born of a false conception of the pathogenesis of pulmonary tuberculosis. It is conceded that the tubercle bacillus enters the system in one of many possible ways, such as passing through the large bronchial walls, to the bronchial nodes or through the intestinal tract without involving the mesentary nodes and in some mysterious way reaching the bronchial nodes. This is supposed to occur usually during childhood. The infection then lies dormant in the bronchial nodes for many years and sometimes after puberty, immunity or resistance is lost and the infection passes backward through lymph strains to the parenchyma of the lung by way of the peribroncheal or perviscular lymphatics. Thus we have first hilum tuberculosis and then paribroncheal tuberculosis and finally parenchymal tuberculosis.

This conception, which seems false to us, received its greatest impetus since the study of x-ray chest plates has become general. It is contrary to our knowledge of anatomy, pathology and to the modern conception of pathogenesis which has been so ably described by Krause under the term of Allergy.

In contrast to this we conceive that the adult and puerile types of pulmonary tuberculosis which are so clearly differentiated by the x-ray chest plates have a firm foundation in anatomy, pathology and allergy. The infection enters the lung by the air passages or the blood stream, is carried from either to the lymphoid tissue which is directly connected with the lymph vessels. In the child we have very little reaction except near the point of inoculation and this is mostly interstitial, but a great reaction of the regional lymph nodes. In the adult we have comparatively little reaction of the lymphnodes but

massive reaction around the infection with extensive exudate which floods a definite part of the lung. Thus in the child which is not sensatized the reaction to the tubercle bacillus is little like an inflammatory reaction, while in the adult the reaction is a severe inflammatory reaction and is seen upon the x-ray plate as a lobular density under the pleura like a fan or cone in shape as it is confined by the lung structure. Pulmonary tuberculosis is a disease of successive infections, therefore of differing ages which causes the fans to have differing densities. These differing densities are easily recognized upon the x-ray plate. The only tuberculous lung lesion which we have observed on the series of x-ray plates of a given patient, that spread from the hilum to the periphery is tuberculosis caseous broncho pneumonia. This spreads by aspiration of droplets from open lesions. This lesion must not be confused with perivascular or peribronchial tuberculosis. It can only originate from the hilum where a tuberculous lymph node ruptures into a bronchus and infectious material is aspirated into the smaller air passages.

We have tried in this paper to review in abstract form the facts and literature which we find necessary to the reading of a chest plate. such readings require more than a knowledge of clinical tuberculosis or roentgenology. They require a knowledge of anatomy, pathology, physiology, pathogenesis of tuberculosis, in addition to clinical tuberculosis and roentgenology. Is it surprising that so many of you depreciated the x-ray readings which you have received and which you have not understood?

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DR. DUNHAM: The greatest trouble in using an x-ray plate is when the reader does not know the normal chest plate of an average individual. It is of the greatest importance to be able to positively state by an x-ray reading of the chest plate that the man has no pulmonary tuberculosis. It is also vitally important to be able to state that although there is tuberculosis present, the symptoms of which the patient complains cannot be accounted for by the condition in the chest. When we find rales on physical examination and the x-ray plate does not show a corresponding lesion let me emphasize the importance of a thorough study of the nasal sinuses as a possible source of infection.

I hope you will clearly understand the big point that in the interpretation of x-ray plates a knowledge of tuberculosis in all its angles is necessary. A thorough knowledge of clinical tuberculosis and an understanding of the significance of physical signs is of great importance. Therefore you men who know tuberculosis will best be able to read your own plates. In answer to Dr. Webb's question as to whether we have seen any of these things develop I may state that we have observed children in which at first there was no evidence of pulmonary tuberculosis. They were classed "Potentially Tuberculous" because they came from tuberculous families, were definitely undernourished, some gave positive Von Pirquet reactions. In a few of these cases by observing serial x-ray plates we have seen fans develop.