Chronic Nontuberculous Pulmonary Infections and Their Sequelae*

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FORWORD

The role of chronic nontuberculous infections as a cause of human misery and disability has not been adequately appreciated. The initial, causative factor, primarily seemingly insignificant and justifying scant consideration, may eventually pass through a series of conditions, leading in the end to invalidism and even death. It is my purpose in this paper briefly to sketch the course of chronic nontuberculous infections from the beginning through their progressive stages to their end results, such as, pulmonary fibrosis, cavitation, and bronchiectasis.

It is impossible to deal separately and fully with each of the etiologic agents involved in these infections, but reference will be made to the role of chronic lobar and chronic bronchopneumonia, aspiration pneumonitis, atelectasis, pneumonoconiosis, bronchial and bronchiolar stenosis, metastatic lung infections, the mycoses and syphilis, as well as the milder, but quite important, chronic infections of the nasopharynx and bronchi. It is necessary to stress the role in the initial development of these chronic infections of such conditions as acute nasosinusitis, subacute bronchitis, and the acute pneumonias. A closer cooperative understanding between the nose and throat specialist and the general practitioner would be helpful in diagnosing and eradicating suppurative conditions of the nasal sinuses. These infections are often given palliative treatment, only to recur each winter, until a chronic bronchitis and eventually a chronic pneumonitis and bronchiectasis may develop. The dreadful end results could be, in many cases, obviated in the beginning by prompt treatment, and by carefully following the patients through to a cure. Patients following attacks of acute pneumonia should be regularly checked for the presence of residual foci of infection in their lungs; small atelectatic areas, single or multiple, small bronchopneumonic areas, and slight abscesses, may be found to reward us for our diligence.

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Bacteriology

The bacteriology of chronic nontuberculous pulmonary infections, is well worth considering. Petroff and Schwartz in an excellent study have stressed that the bacteriology of chronic nontuberculous pulmonary infections has not kept pace with other methods for diagnosis. They discuss the bacteriology of these pulmonary infections by studying three types, namely, lung abscess and gangrene, bronchiectasis, and pulmonary infections which simulate pulmonary tuberculosis or at times may occur in symbiosis with tuberculosis. They state that abscess of the lung is not due to a specific micro-organism but is the result of various types, differing as to the kind of abscess found; anaerobic bacteria, such as vibrios, anaerobic streptococci, and fusospirochetal organisms especially being the main causative factors in producing putrid lung abscess and gangrene; aerobic, nonputrid, lung abscess having the pyogenic bacteria, diplococcus pneumonlae, Hemophilus influenzae, Neisseria catarrhalis, diphtheroids, streptococci and especially staphylococci predominating; mycotic suppurative processes, frequently simulating tuberculosis, may be caused by actinomycetes, monilial, aspergilli, penicillia, and coccidiodes, and to a lesser extent by many other fungi, especially of the fungi imperfecti group. It is understood that tubercle bacilli are always absent in the sputum of these patients.

Etiologic Diseases

Although some of these patients may present an acute, and at times a stormy onset, the process develops more gradually in a large percentage of them. A simple bronchitis, following an acute nasopharyngeal infection, for instance, may lead to an extension of the infection into the wall of the bronchi with areas of pneumonia resulting. The general health of the patient may be practically unimpaired, although there may be a tendency during exacerbations to increased cough and some fever. The majority are in full adult life. The period of increased symptoms is usually during the colder, winter months. Cough and expectoration may be the only symptoms, although fever, pleurisy, and even hemoptysis may occur. The lesions are ordinarily in the lower lobes, especially the left. It is interesting to recall that with the recurring exacerbations the physical findings have a marked tendency to recur in their original location. The similarity of the clinical findings to early pulmonary tuberculosis is striking, but the distinction between the two entities is aided by the basal location of the physical and roentgenologic findings in the nontuberculous individual, in contradistinction to the upper lobar findings in the
tuberculous patient. It is possible the pathology in these cases may be a localized bronchitis with lobar or lobular distribution involving the submucous and peribronchial tissues. This condition may clear up after an attack and recur at a later date, or persist in a latent subacute form. In this latter case, the acute recurrences affect the original site and are probably due to a localized lesion. This may lead into chronic interstitial pneumonia or bronchiectasis. It is my opinion that these recurring episodes are due, not to new acute infections, but to recrudescences of the same infection which has been lying dormant in the lungs during the interium between flare-ups.

It has been indicated heretofore that conditions other than described in the proceeding paragraph may be operative in producing chronic nontuberculous pulmonary infections. Some consideration of these conditions will be mentioned.

**Pulmonary Abscess and Gangrene**

Pulmonary abscess and gangrene\(^5\) may follow aspiration of foreign material after surgical operations, pneumonia, wounds to the lungs, the presence of carcinoma of the bronchus, lung or esophagus, and rarer infections such as mycoses, cysts or the extension of suppuration from beneath the diaphragm, liver or perirenal tissues. They are not specific diseases because they are due to a wide array of bacteria. Bucher\(^5\) in a study of the pus obtained bronchoscopically in 118 cases of pulmonary abscess found 18 different organisms, with the streptococcus (hemolyticus, viridans, nonhemoliticus), micrococcus catarrhalis, pneumococcus, bacillus influenzae, staphylococcus albus and aureus, diphtheroid bacilli, spirochetes, fusiform bacilli and the micrococcus tetragenas predominating. Rona\(^5\) in 1905 first recognized fusiform bacilli in pulmonary gangrene. Oliver and Wherry\(^6\) in 1921 first described the bacterium melaninogenicum, and since that time this strictly anaerobic, non-motile, polymorphic and gram-negative organism in symbiosis with other bacteria has been shown to produce extensive tissue necrosis in the lung. Unless this acute process heals, a chronic abscess associated with bronchiectasis may ensue.

**Chronic Lobar and Bronchopneumonia**

Especially after influenza, measles and whooping cough, an acute broncho-pneumonia may be followed by a chronic progressive pneumonitis, or the development of atelectasis and bronchiectasis. In some cases of lobar pneumonia resolution of the lung tissue may not occur promptly, and rarely abscesses may be followed by cavitation, or another group may develop a chronic course through
many months or years. We have seen a case of acute Friedlander's bacillus pneumonia assume a chronic form which lasted for years, and closely resemble the clinical picture of chronic tuberculosis.

Aspiration Pneumonitis

The aspiration of foreign bodies, especially those of an organic nature, may give rise to bronchial and peribronchial inflammation and suppuration, usually in the hilar or midportions of the lungs. It is clear that these unfortunate conditions may be obviated only by making roentgenograms at once when there is a likelihood of a child aspirating any foreign material.

Atelectasis

Atelectatic areas, occurring in infants at birth, or from massive collapse following operations in any age group, may become infected; at first the bronchial and bronchiolar mucous membranes are involved, later the infection may spread to the peribronchial tissues. A focus for subsequent exacerbations of infection may follow, and be erroneously termed "bronchitis," or, if the recurring attacks of acute pneumonitis be more severe, they may be diagnosed "pneumonia." As time passes on, a chronic recurring, localized pneumonitis develops and may last for many years.

Bronchial and Bronchiolar Stenosis

It is well recognized that the occlusion of the bronchi or bronchioli may precipitate the development of atelectatic areas distal to the obstruction, and that a chronic pneumonitis may develop with either bronchiectasis or pulmonary abscess occurring, singly or together. An inflammatory condition of a bronchus, a benign or malignant bronchiogenic tumor may be the etiologic agent.

Metastatic Lung Infections

A chronic, relatively mild pulmonary infection may follow metastatic pulmonary emboli. The clinical picture will vary according to whether the emboli are large, or small and numerous; a serious localized abscess may follow a large embolus, whereas small, multiple emboli may rarely produce a chronic recurring pneumonitis.

Pneumoconiosis

Workers on sandstone and quartz, or any combination of large amount of silica, frequently suffer from chronic pneumonitis and nodular pulmonary fibrosis often follows.

Syphilis

Many years ago in a study of the incidence of syphilis in the Houston Anti-tuberculosis Clinic, I was impressed with the belief
that pulmonary syphilis is more frequent than is commonly believed to be true. About 1 in 250 cases, previously diagnosed as tuberculosis, was believed to have pulmonary syphilis. The patients were largely drawn from Negro and Mexican admissions. Single or multiple gummas were noted, as well as definite fibrotic streaking and thickening of the bronchial and peribronchial tissues.

**Mycoses**

Meakins\(^8\) lists four mycotic diseases of the lungs, namely, blastomycosis, actinomycosis, streptothricosis, and aspergillosis. The term blastomycosis is used in a general sense, meaning the various fungi reproducing by blastospores; the so-called "yeast-like" fungi—the cryptococcus, monilia, torula and oidium. Actinomycosis and streptothricosis may be classified under the nocardia, and distinguished by the fact that a case of streptothricosis has no granules in the sputum and actinomycosis has. Aspergillosis is a very chronic disease and runs a mild course. We have previously stressed the insidiousness and latency of mycotic infections of the lungs. The clinical course of these invasions may be quite similar to chronic fibrosing pulmonary tuberculosis. The diagnosis may be difficult, and should never be made from the expectorated sputum alone. In a personal study\(^9\) of 301 patients, fungi were isolated from the expectorated sputum in 45 patients; in 18 patients (6 per cent) we isolated fungi from tracheal washings. We considered the other 27 fungi contaminants and pathogenic; the saprophytic fungi were of the following genera: cryptococcus Kützing, monilia Persoon, sporotrichum Link, acremonium Link, saccharomyces Meyen, and aspergillus Micheli. The saccharomyces, constituting 64 per cent of the fungi classed as contaminants, were consistently saprophytic and parasitic. There were 5 cases of pure mycoses, identified as 1 aspergillus fumigatus, 1 cryptococcus hominis Vuillemin, and 3 sporotrichum Schenki; an incidence of 1 to 60 mycotic to tuberculous patients. Although fungous infections, occurring as single entities, usually run a benign, but protracted course, we believe fungi, when associated with tuberculosis, enhances the activity of the tuberculous process.

**Classification**

Chronic nontuberculous pulmonary disease may be classified on an anatomical and pathological basis according to the following table;\(^10\)

I. Bronchial Tube Disease

A. Reactive injury
   1. Mucous membrane—reaction "catarrhal bronchitis"
   2. Bronchial wall—reaction "mural bronchitis"
B. Traumatic injury
   1. Bronchial obstruction
   2. Bronchial dilatation

II. Air Cell Disease
   A. Reactive injury
      1. Pneumonia
         a. Inflammatory
         b. Organized
   B. Traumatic injury
      1. Pulmonary collapse (atelectasis)
      2. Pulmonary over-expansion
         a. Diffuse (emphysema)
         b. Localized (pulmonectasis)

There is a type of bronchitis, which Andrus\textsuperscript{11,12,13} terms idiopathic, occurring in a large group of people, characterized by chronic cough and expectoration, which does not result in a chronic pneumonia, fibrosis, bronchiectasis, etc. This is the so-called “catarrhal bronchitis.” There is a similar group showing in the radiographs some thickening of the bronchial tree, due to reactive changes in the bronchial walls. This is the “mural bronchitis” of the previously listed table, and the bronchial wall reaction is a postpneumonic type of injury. The radiographic shadows in mural bronchitis may be due, however to an arteriosclerotic process. It has been shown from Robinson’s\textsuperscript{14} studies on surgically removed bronchiectatic lobes that the infection probably passes from inside the bronchial wall, rather than from within the lumen of the bronchi, because he found normal mucous membrane and functioning cilia in the bronchi in such cases. We may, then, have two distinct types; catarrhal bronchitis (x-ray negative), mural bronchitis (vascular, infectious) (x-ray positive). Traumatic injury to the bronchi may be due to either, or both, obstruction or dilatation of the tube. The presence of a major area of atelectasis indicates obstruction of one of the larger bronchi; smaller, patchy atelectatic areas the result of a bronchiolar stenosis as may be found in bronchopneumonia.

Chronic disease of the alveolar air cells may be caused by either inflammatory or traumatic injury. There may be a shrinkage or an overexpansion of the pulmonary tissues. Pulmonary shrinkage, caused by contraction of scar tissues, may be extensive or “patchy” in distribution. It should be stressed that postpneumonic lung shrinkage is more likely to be caused by pulmonary collapse than to fibrosis, although fibrosis usually follows atelectatic collapse. The primary underlying factor in the production of chronicity in nontuberculous lung disease is atelectasis. Pulmonary overexpan-
sion is a compensatory mechanism, when the volume of the chest contents is reduced by localized shrinkage, or the capacity of the thoracic cage is increased by outward displacement of the chest walls. The overexpansion may be diffuse or localized. The localized type is due to an infection with a persisting chronic patchy atelectasis, and consists of localized emphysematous air blebs. Andrus calls this latter condition "pulmonectasis," and a chronic infection and overdistension of the pulmonary bases, formerly listed as unresolved pneumonia, chronic basal disease, pneumonitis and bronchiectasis—suspect could fall in this category.

B. End Results

It has been suggested by Miller\textsuperscript{15} that bronchiectasis is of congenital origin, but the wide concensus of opinion is that a congenital origin is doubtful. In my opinion the secondary factors, bronchial obstruction and atelectasis, with an infection following such a mechanical obstruction, seems more plausible as etiologic factors in a preponderant percentage of cases. It must be added, however, that congenital bronchiectasis may occur, although we are not especially concerned with a discussion of the congenital type in this paper. Ballon and Ballon\textsuperscript{16} have classified five types of bronchiectasis, based on iodized oil injections, as follows: grape, clubbing, cylindrical, saccular, and bead formation. The symptomatology may be quite varied, in fact lacking in early cases, and consist only of the subjective and objective signs of the primary causative disease. As time runs on, the clinical picture gradually changes, and new added symptoms come into prominence. Cough and expectoration may be the only distinct symptoms. The cough may be hacking, persistent or severe, dry or productive. The inhalation of substances, such as tobacco smoke or gases, may be very irritating. The sputum\textsuperscript{17} contains a large amount of water and albumin, peptones, amino acid, pus and bacteria; it usually has a foul odor, and may exceed 1000–15000 cc. in 24 hours, being expectorated more or less persistently, or more usually, paroxysmally. The sputum, ordinarily but not regularly, separates after expectoration into three or four layers; a pale greenish-yellow layer of air bubbles, mucus and pus; a mid-layer of pus cells, fat rests, Dittrich's plugs, and detritus. The foul odor of the sputum may be distressing to the patient and as previously stated is due to the presence of anaerobic organisms. More advanced cases of bronchiectasis may have fever, sweats and chills. These episodes are due to attacks of recurring pneumonitis and not to retained intrabronchial secretions. It follows, therefore, that fever may continue, even though the bronchial secretions are expectorated. Especially in cases of numerous smaller bronchial or bronchiolar
dilatations it must be assumed that pneumonitis is present when toxic manifestations, fever and sweats, are present. Hemoptysis is frequently noted. Joint pains may also be associated. The physical findings are not typical, although they are usually basal in location, in contradistinction to the findings in tuberculosis, which are more likely to be apical. There may be increased voice conduction (pectoriloquy) or decreased breath sounds, and most always rales. Signs of localized atelectasis or even cavitation may be present. There is usually a moderate, secondary type of anemia and some polymorphonuclear leucocytosis. The organisms in the sputum consist of the great array previously discussed. The diagnosis, although to be strongly inferred from the history, symptoms and physical findings, is not complete without iodized oil injection. The normal primary and secondary divisions of the bronchi do not cast a radiographic shadow, and although a diseased bronchus does cast a shadow, it is very difficult to decide whether the shadow is due to the bronchus itself, or to a peribronchial pathology. Therefore, for exact diagnosis of bronchiectasis, iodized oil injection is essential. Bronchoscopy is of great help in that obstructive new growths in stenotic conditions may be found, the discharging pus may be localized, the iodized oil injection may be more accurately made, and uncontaminated cultures may be obtained. Singer has stated that a diagnostic pneumothorax may reveal a bronchiectatic, atelectatic lobe, hidden in the cardiac shadow. It is my opinion that advanced bronchiectasis is incurable by the ordinary remedial agents, although they may be definitely palliative. The disease is characterized by remissions, and it is difficult to judge the value of rest, climate, postural drainage, vaccine, drug therapy, or local treatment, such as direct intra-bronchial application of drugs, bronchial lavage and inhalations.

Considerable pulmonary fibrosis, with chronic pneumonia and abscess formation, may be expected to be found in many, if not most, cases of definite bronchiectasis. It has been shown that an exudate in the alveoli of the lungs may become vascularized and fibroblasts and capillaries, with the formation of connective tissue, ensues. Scar tissue will ultimately distort the bronchi and make emptying impossible. The added presence of pneumonic patches and fibrinous pleuritis, resulting in parenchymal fibrosis and adherent pleura, respectively, further distort the bronchi and the pulmonary tissues and the chest cage. Chronic abscesses may form in the resulting atelectatic areas; these may empty periodically through the bronchus, or, when they are numerous and small, may remain as purulent foci within the lung tissues.

The ultimate fate of these patients depends upon the type and prominence of the bronchiectatic process, and the extent of com-
plicating factors, such as pulmonary fibrosis and recurring pneumonia, abscesses, the presence of scar tissue, the degree of intrathoracic distortion of the heart and mediastinal contents, and the associated cardiovascular and toxic phenomena. Severe cases may die in a relatively short time from fulminating hemoptyses, acute pneumonia or abscess, or they may survive many years. Eventually the latter cases die from a severe recrudescence of the bronchiectatic and associated conditions, or from the more gradual development of cardiac failure, amyloidosis, or general nutritional failure from chronic toxemia.

SUMMARY

It should be evident from this review that the early treatment and eradication of acute and subacute disease entities within the respiratory system, is positively necessary if we are to expect to obviate their serious sequelae. The best treatment is, therefore, preventive, and little may be expected from medical measures after these chronic infections have become evident. It is the main and primary object of this discussion of chronic nontuberculous infections of the lungs to stress the urgent necessity of diagnosing the earliest etiologic pathologic states, which lead otherwise to an incurable and serious disease, and, do all in our power to promote, if possible, their prompt and thorough eradication.

RESUMEN

Este repaso debe hacer evidente que el tratamiento temprano y la erradicación de las enfermedades agudas y subagudas del sistema respiratorio son absolutamente necesarios si hemos de abrigar esperanzas de evitar sus graves secuelas. El mejor tratamiento es, por consiguiente, profiláctico, y poco se puede esperar de medidas médicas cuando estas infecciones crónicas han llegado a ser evidentes. El objeto principal y primario de esta discusión de infecciones no tuberculosas crónicas de los pulmones es recalcar la necesidad urgente de diagnosticar los estados patológicos que las anteceden, los que de otra manera conducen a una grave e incurable enfermedad; y de usar todos nuestros esfuerzos para lograr, si es posible, su erradicación pronta y completa.

REFERENCES


