Changing Concepts of the Pathologic Basis for Resection in Pulmonary Tuberculosis*

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The concepts regarding the pathogenesis and evolution of the lesions of pulmonary tuberculosis in man which have hitherto been taught and generally accepted, may have to be revised in the light of recent experimental and clinico-pathologic studies. The most careful and complete appraisal of the behaviour of pulmonary tuberculous lesions, based on animal experimentation, and necropsy and surgical material, is that of Medlar1, which has recently been published in monograph form. This observer had the opportunity of studying the disease in addition, in its non-clinical or pre-clinical state, from autopsy material from a large group of patients who had died accidentally from causes unrelated to their pulmonary infection. This monumental work has revolutionized the thinking of many phthisiologists and chest surgeons. There is no doubt that modern antimicrobial therapy has also influenced this changing attitude.

As a mark of this change, one need only compare present-day indications for resection in pulmonary tuberculosis with those favoured by earlier workers, and present day results with earlier results2. For example, in 1946, Sweet3 reported upon 63 patients who had undergone pulmonary resection for tuberculosis. The indications were thoracoplasty failure, destroyed lung, tension cavities, lower or middle lobe cavities, broncho-stenosis and bronchiectasis, etc. Only two were performed for “tuberculoma” “because of the well-recognized difficulty of management of such lesions”. Four years later4, he reported again on the course of these 63 patients, all of whom had been operated upon prior to the appearance of the effective modern antimicrobial drugs. He found that only 24% of patients who had had lobectomies, and 45% of the patients who had had pneumonectomies, remained continuously well after surgery. The others had died, or developed reactivations, and still had active disease, while some developed reactivations of disease which subsequently became arrested or inactive again. Significantly, a greater per cent of patients who survived pneumonectomy (which, however was associated with a higher operative mortality rate) remained continuously well, than patients who had had a lobectomy only.

On the basis of this rather discouraging study Sweet had concluded that the indications for pulmonary resection should be four in number:

(1) irreversible broncho-stenosis with chronic infection and secondary bronchiectatic dilatation,
(2) lower lobe, or, occasionally, middle lobe cavities.
(3) persistent cavity after adequate thoracoplasty,
(4) possibly *tuberculoma* (italics mine).

Cases suitable for thoracoplasty were no longer considered suitable for extirpation. In many quarters, these are still considered to be the standard indications for extirpative therapy.

Beginning scarcely two years later, however, reports in increasing numbers began to appear in the literature concerned with “simple excisions” for “localized necrotic lesions” by segmental resections, and “wedge resections” in addition to lobectomies.

What has been the rationale behind this enthusiasm for removing localized caseo-necrotic lesions? An examination of the pathological concepts which we were taught in medical school, compared with the concepts which have recently emerged based upon studies of clinicians and pathologists led by Medlar, may help in giving us the answer to this question.

We were taught some ten years ago, that

(i) the first or primary infection was usually an innocent affair. Progressive pulmonary tuberculosis was supposed to result from “re-infection” of endogenous origin, from a break down of apical pulmonary lymphohematogenous seedings.

(ii) Old necrotic lesions represented healed, inactive, tuberculosis which ordinarily inspissated (thickened) and calcified, and did not break down. The presence of epithelioid cells and giant cells represented “active” disease.

(iii) The occasional liquefaction of a caseous focus occurred as a result either of allergic response to tuberculin, or following an acute upper respiratory infection. Such suppuration might then lead to rupture of the fibrous capsule around the old focus, and rupture of a neighbouring bronchus, with emptying of the liquid contents of the focus into the bronchus (sloughing), with consequent open cavity formation. Subsequently, the disease spread by endobronchial dissemination, and this process would continue until the cavity was closed, and the fibrous capsule sealed off again by fibrous tissue.

(iv) The important component in the primary complex was not the parenchymal lesion, but the lymph node component, because this led to the late, lymphohematogenous, post-primary seedings, not only to the apical portions of the lungs, but also to bones, kindneys, etc. Activations of these seedings in later life led to “adult tuberculosis”—which was a disease of the young and poor adult. If no clinical tuberculosis appeared by the age of 35, the individual was probably “immune” to tuberculosis.

(v) Spread was believed to be due to “endogenous” sources—and ordinarily there was no lymph node involvement in “endogenous reinfection” because there was rather prompt localization of the lesion in an allergic soil. “Exogenous reinfection” was believed to be rare indeed.

These concepts, in brief, were the accepted concepts which provided the rationale for treatment for many years, and are still being taught in many medical institutions. They are being seriously challenged by the new school of phthisiopathologists, spear-headed by Medlar.

It is beyond the scope of this paper to describe the details of the twenty-five years of research which formed the basis of Medlar’s concepts of the behaviour of pulmonary tuberculous lesions. These can be best understood by referring to the monograph previously mentioned. However, it is the purpose of this paper to briefly review the salient features of his concepts, and to illustrate some of his points from surgical material from this Sanatorium.

In brief, minute tubercle bacilli-laden particles which are inhaled by man may give rise to multiple widely-scattered minute areas of necrotic lobular pneumonia, scattered by chance in any or all parts of the lung. These ordinarily heal by calcification or hyalinization.

When the air-borne particle lands in the upper or posterior portion of the lobes of the lung (apical or posterior segments of upper lobes, superior segment of lower lobe) the initial small necrotic lesion may undergo liquefaction and sloughing into draining bronchi, and in this manner give rise to progressive pulmonary disease. (Not all lesions in such locations progress, but enough do to prompt Medlar to call these “vulnerable areas” of the lung. There is some experimental evidence to indicate that posture has something to do with these “vulnerable areas”). Endobronchial dispersion of the bacilli-laden slough may slowly or rapidly produce dissemination of disease. The rapidity of the rate of necrosis, liquefaction, sloughing, and spread determine the extent of disease, whether minimal, or moderately advanced, or far advanced. The age of the lesion is not related to its roentgenographic extent. Dead tuberculous tissue is very difficult for the lung to dispose of, and the larger the area, the more difficult of disposal. There is always a communicating bronchus to these necrotic lesions—although sometimes hundreds of serial sections are necessary to demonstrate it. Tubercle bacilli may be harboured in necrotic lesions long after all non-necrotic components of disease have healed under the influence of modern antimicrobial therapy. These features of necrotic lesions, that is:

1. difficulty of disposal,
2. bacillary content,
3. tendency to liquefy and slough, and
4. drainage through connecting bronchi,

Cause the late relapses in the disease. Antimicrobial therapy can eliminate the non-necrotic component of disease—the histologic tubercles, and can cause cavities to shrink or even to disappear roentgenographically, with disappearance of acid fast bacilli from the patients’ sputum—but the residual necrotic lesion is not significantly affected by antimicrobial therapy. Most disturbing of all is the evidence of continuing liquefaction and sloughing of some necrotic lesions even after prolonged uninterrupted combined antimicrobial therapy in adequate dosage. Thus the residual necrotic lesion, especially the sizable one, remains a threat to the patient which antimicrobial therapy has been unable to eliminate.

Since in most cases, at some stage, the pulmonary disease is limited to a relatively small area of lung tissue, it would appear that resection of such areas offers, at the present time, the best chance of eliminating these dangerous residuals.
What *sine* constitutes the dangerous residual? Medlar is quick to state that he does not know—that not *size, per se* but subsequent *behaviour*, is the important item. He can only state that small lesions, 2 to 3 mm. in size, if they are located in “vulnerable” portions of the lung, are more likely to liquefy and slough, than if they were located in the basal portions or in the middle lobe. Ultimately, of course, it is the clinician who must weigh experimentally, and clinically observe facts, and decide for or against surgery for caseo-necrotic residual lesions. Most phthlsiologists feel that residual necrotic lesions over 1.0 cm. in diameter, on the chest x-ray, constitute a dangerous residual focus.

**Clinical Material**

Of our 25 cases of resection for pulmonary tuberculosis, one-third were for thoracoplasty failures, one third for caseo-necrotic residual lesions, and one-third for miscellaneous indications, including destroyed lobes or lungs, bronchiectasis, lower lobe cavity, etc. The eight patients in whom the caseo-necrotic residual lesion was the indication for resection had the following things in common:

1. The sputum of all had been negative for acid fast bacilli for months or years.
2. Previously obvious cavitary lesions had shrunk down to solid-appearing nodules or round dense shadows with less dense centres, often clearly visible only on planigrams.
3. All had had long courses of combined, uninterrupted anti-microbial therapy in adequate doses from eight months to two years.
4. All but one had had months to years of ancillary temporary collapse measures—either pneumoperitoneum, pneumothorax, or phrenic crush—in spite of which the nodule remained roentgenographically obvious.
5. At operation all had more disease in the localized area than suspected, or had an additional unsuspected localized area of residual necrotic disease.
6. Pathologically, *all* had active disease, as evidenced by caseation necrosis or liquefaction.
7. All did well following surgery.

**CASE REPORTS**

**Case 1**

M. B., a 21-year old Indian female, with a two year history of pulmonary tuberculosis classified as far advanced, was admitted with extensive involvement of the right upper lobe in December 1953. After eight months of bed rest, pneumoperitoneum, and combined uninterrupted antimicrobial therapy, the upper lobe shrank to a small solid-looking mass, and sputum, previously positive for acid fast bacilli, became repeatedly negative. The upper lobe was removed in August, 1954. The specimen showed three encapsulated areas of liquid pus, from one to two cm. in diameter, and many smaller confluent caseous nodules. Microscopic sections showed areas of extensive caseation necrosis, with a narrow border of fibrosis surrounding these areas. The patient did well post-operatively, and has been followed for one year after surgery, with negative sputum to smears and cultures, although she is no longer taking any antimicrobial therapy.

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Case 2
A. B. J., a 22-year old Arabian male with far advanced pulmonary tuberculosis since 1953, characterized by a large (4 cm. diameter) cavity in the superior segment of the right lower lobe, was admitted to the Sanatorium in February 1954. On seven months of antibiotic therapy, pneumoperitoneum, and right phrenic crush, the cavity shrank to a small solid nodule over 1 cm. in size. Surprisingly enough, at the time of resection of this lesion, the right middle lobe was also found to be the seat of significant nodular lesion 5x4 cm. in diameter. The middle lobe, and the superior segment of the lower lobe were removed. The patient did quite well post-operatively. Grossly, the older disease appeared to be in the superior segment, which was almost completely replaced by dense scar tissue, containing enlarged, diseased looking bronchi, and occasional caseous nodules. The middle lobe was the site of many caseous nodules, up to 0.5 cm. in diameter, confluent with one another to make the sizable nodule felt at operation. Sections showed multiple caseous nodules surrounded by loose fibrous capsules within which were tuberculous granulation tissue. The patient’s sputum remained negative on smear and culture; drugs were stopped six months after surgery, and he was discharged to the Persian Gulf eight months after surgery, apparently inactive.

Case 3
C.D.K., a 28-year old Indian female, was admitted to the Sanatorium in February 1954 with a huge cavity in the right lower lobe measuring 5 cm. in diameter. She had a right phrenic crush in June 1954, and pneumoperitoneum and uninterrupted combined chemotherapy for eight months. Sputum became negative for acid fast bacilli; and the cavity shrank to a small dense shadow. In November 1954, right lower lobectomy was uneventfully carried out. The superior segment was shrunken and replaced by a 2cm. fibrous area containing caseous material, with a small slit-like cavity in its centre. Multiple small caseous nodules up to 0.5 cm. in size were scattered throughout the basal segments. The patient did well, and has been followed up to 10 months post-operatively, sputum negative to smear and culture, although she has been without drugs for four months.

Case 4
K.G., a 22-year old Indian female, with onset of pulmonary tuberculosis classified as moderately advanced, in 1953, was admitted to the Sanatorium in January, 1955. A cavity in the left upper lobe had shrunk on an inadequate pneumothorax of one year’s duration into a solid-looking nodule which showed up on several levels on planigraphy. After 18 months of uninterrupted combined antimicrobial therapy, sputum having remained negative for many months, segmental resection of the apico-posterior segment of the left upper lobe was carried out, on January 25, 1955. A 4cm. rubbery nodule when opened exuded green cheesy semifluid pus. On microscopic section of this segment, multiple caseous nodules with narrow fibrous capsules were present. The patient did well postoperatively and has been followed for eight months since surgery. All sputa at this institution were negative, as was culture. A single sputum smear done in another laboratory five months after surgery was reported positive. This was unverified by subsequent studies, by cultures, or by roentgenographic findings. After so many years of negativity, with the major focus removed, we believe that this single report was a laboratory error. We are following her closely.

Case 5
A.B.I., a 19-year old Arabian male gave a two year history of moderately advanced pulmonary tuberculosis, confined largely to the right upper
lobe. He had had right pneumothorax, right phrenic crush, and antimicrobial therapy for eight months. A large solid-looking lesion remained on the x-ray films, although sputa were repeatedly negative for acid fast bacilli, and therefore a right upper lobectomy was uneventfully done in February, 1955. A 6x3 cm. area of confluent caseous nodule occupied over one-third of the right upper lobe. Sections showed these to be thin-walled caseous nodules. The patient did well postoperatively, and was followed for seven months after surgery, with negative bacteriologic findings of sputum, and arrested status.

Case 6

Y. K., a 40-year old Indian female nurse, with moderately advanced tuberculosis since 1951, was admitted for surgery to the Sanatorium in June, 1955. For years, three solid-looking nodules had been observed in the upper right lobe, but only a brief period of chemotherapy had ever been tried because of allergy to Streptomycin. In October, 1954, and in subsequent films, it was noted that one of the shadows had begun to enlarge, and to become hazier. She had a low-grade temperature. Consequently, she was put on bed rest, and INH and PAS were started. Her sputum was never positive. She gained considerable weight on this regime. The nodular shadows regressed to the point where they had been for years. An upper lobectomy on the right was done in June 1955. Three large 1.5 to 1.0 cm. caseous nodules occupied the apical and posterior segments of the right upper lobe. Because of a small apical empyema due to incomplete expansion of the remaining lobes on the right, a small tailoring thoracoplasty was done two months after the resection. She has done well, but it is too soon to report on her follow-up.

Case 7

H. M., a 21-year old Arabian female with disease dating back to 1953, moderately advanced in extent, had a small cavity in the left upper lobe. This was treated elsewhere with rest, drugs, and an attempt at artificial pneumothorax, which failed. Subsequently, she had a moderately severe hemoptysis, and reactivation of the lesion was noted on x-rays. She was admitted here in December, 1954, and after seven months of bed rest and combined antimicrobial therapy, the apical posterior segment of the left upper lobe was removed. Multiple caseous nodules up to 7 mm. in diameter, in clusters, were found to occupy about one-third of the volume of this segment, and sections showed multiple young tubercles without fibrous tissue reaction surrounding the caseous nodules. This patient also did quite well following surgery. She is still on bed rest and drugs.

Case 5

H. S. B., a 28-year old Arabian male, the onset of whose disease was in 1953, with moderately advanced tuberculosis, and a cavitary lesion thought to be in the right middle lobe, was treated with combined uninterrupted antimicrobial therapy for two years ; pneumoperitoneum for one year, and a right phrenic crush done in October, 1953. The cavity became a solid-looking nodule 1.5 cm. in diameter, which persisted for two years, and there was some suspicion of a tiny area of diminished density in its centre. After having observed this nodule for one year it was decided to resect it. However, the patient refused to consider surgery for an additional year, during which time it remained unchanged. At operation, to our surprise, in addition to the 1.7cm. nodule in the middle lobe, there was a 1.2 cm. nodule in the superior segment of the lower lobe. Both portions of the lung were resected. Grossly, the lesion in the superior segment appeared to be the older, with more fibrosis and some beginning calcification. The patient is still on bed rest and drugs. We might have saved him a year of hospitalization if he had agreed earlier to our plan of therapy.
DISCUSSION

In all these cases we were struck with the finding of a greater amount of disease than was expected judging from the roentgenograms, including planigrams of the chest. In addition, the presence of caseous nodules, which pathologically denote active or potentially active disease, after adequate antimicrobial therapy, bed rest, and ancillary collapse measures, up to two years in duration, was disturbing. This has been the experience of others as well.\textsuperscript{10,11,12}

We do not have the facilities here for serial sectioning of such caseous lesions as we have described. Medlar sectioned similar lesions studying hundreds of sections in some instances. He was always able to demonstrate a connecting bronchus with such caseous lesions, sometimes plugged with necrotic debris, and sometimes open.

Similarly, we have not been equipped to study these lesions bacteriologically in great detail. Others who have, however, have, found that usually acid fast bacilli are not difficult to demonstrate on smears, but are somewhat difficult to culture, by ordinary methods.\textsuperscript{10,13,18} However, if special methods are used, a much higher per cent of positive cultures is obtained.\textsuperscript{19,20} The significance of the combination of these findings, that is, invariable connecting bronchus, and high per cent of lesions containing culturable bacilli, cannot be over-estimated. If such lesions of significant size are, indeed the source of reactivation of disease, and if they can be safely eliminated, thus removing the major focus of disease, the future of such patients should be much more firmly assured. Whether one accepts or rejects the view that such residual necrotic lesions of significant size should be removed because of the danger of liquefaction and sloughing via the ever-present connecting bronchus, the concepts of Medlar certainly deserve more detailed study and appraisal. What causes liquefaction and sloughing? And how can it be prevented? Or how can it be encouraged to go on to completion, thus allowing the resulting small cavities to completely heal? What will happen to these large necrotic lesions after prolonged antimicrobial therapy and negative sputum, once treatment has stopped?

Informed opinion in many quarters, especially in the Western countries, based on these investigations, is that large necrotic lesions which are well localized and have remained stable for some months on adequate antimicrobial therapy, in patients who are suitable surgical risks, should be resected.\textsuperscript{20}

We feel that these eight patients represent examples of this type of lesion. These people were all young, with presumably many years of active life facing them. They should be followed very carefully for years, and their course compared to similar cases in whom resection has not been done. Occasionally reports of studies become available in which so-called “tuberculomas” or localized rounded lesions have been followed for many years. Some of these are comparable to our cases—that is, they are “closed” or “inspissated” or “filled” cavities. Others have formed by the deposition of concentric layers of fibrous tissue, apparently with later calcification. The pathogenesis of such lesions is in doubt. Without serial roentgenograms from the initial appearance of such lesions, one cannot often distinguish clinically such lamellated “tuberculomas” from closed or inspissated cavities. Grenville-Mathers\textsuperscript{21} in a study of such lesions observed up to 12 years, roentgenographically found that over half showed activity, either by enlarging, excavating, or actually going on to dissemination. In America, such lesions are often indistinguishable from those due to certain fungi, such as coccidioidomycosis, and histoplasmosis.\textsuperscript{22} This type of lesion has not been observed in India, to my knowledge.
Summary and Conclusions

(1) Recent clinico-pathologic investigations extending over a period of 25 years, have brought into question previously accepted concepts of the pathogenesis and behaviour of lesions of pulmonary tuberculosis.

(2) New concepts have arisen which indicate that not only is the open cavity a menace to the patient, but that “closed” or “filled” cavities of significant size are also probably dangerous, in that the contents of such lesions tend to liquefy and to slough out through connecting bronchi which are always present. They occur after the passage of variable periods of time, and apparently in spite of adequate combined antimicrobial therapy.

(3) Eight cases have been presented in which resections for this type of lesions have been done, and the rationale for advocating resection in such of cases is discussed.

REFERENCES


15. STEENKEN, W. JR.; and WOLISNSKY E. (see ref. 13 above) p. 269.


