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Author(s)	NAGASAWA, Naoyuki; YAMASHITA, Masayuki; OKAMOTO, Hiroshi
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## Studies on the Relationship between Pulmonary Tuberculous Cavities and Draining Bronchi, by Injecting Acrylic Resin

Naoyuki NAGASAWA<sup>1</sup>, Masayuki YAMASHITA<sup>2\*</sup>

長沢直幸

山下政行

and Hiroshi OKAMOTO<sup>3</sup>

岡本博史

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We have carried out three-dimensional observations of the relationship between cavities and draining bronchi, by injecting plastic substances into the pulmonary bronchi and blood vessels of lungs of cadavers with pulmonary tuberculosis and into specimens removed by lobectomy, these lungs were studied pathologically and histologically. The results of our studies are reported here.

### Materials and Methods

Materials used in the study consisted of 83 tuberculous lungs removed from cadavers at autopsy or from patients undergone lobectomy or pneumonectomy. Plastic materials were injected into bronchi and blood vessels of 42 of these lungs by means of Method I of T.R.I., Kyoto University (P. 54, No. 1, Vol. 8, Kekkaku Kenkyu), making casts of lungs in order to observe them three-dimensionally. The remaining 41 lungs were fixed with formalin, and studied pathologically and histologically. The results of the above studies were compared with the pre-operative clinical findings, especially bronchography.

\* From the 4th Division, Division of Surgery (Chief: Prof. C. NAGAISHI) of the Tuberculosis Research Institute, Kyoto University and National Shigarakien Sanatorium (Head: E. YOSHIMURA)

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Present address: 1 & 2. Tuberculosis Research Institute, Kyoto University,  
3. National Shigarakien Sanatorium.

At the time of the above investigation, we also investigated by inspection and palpation, cavities in cases of cavernostomy, in order to observe the state of cavities and draining bronchi in living patients.

### Results obtained

#### 1). *Fundamental condition necessary for forming a draining bronchus*

Plastic casts are the casts of vessels; therefore, by proper preparation of the injecting materials and a suitable method of injecting it is possible to observe the whole bronchial systems — from trachea to alveolus — as a prototype, in other words, in the original size. That is to say, the plastic casts make it possible to clarify the relation between the interiors of cavities and draining bronchi as shown in photo 1, and some parts of cavity walls covered with caseous substance are observable as a defect in the plastic. When the plastics are injected into both the bronchial and vascular systems and reach the newly-formed capillaries in the cavity walls, the area of coagulation and necrosis is clearly recognized as the sole defective part, and caseated foci which have not decayed yet are observed as defective areas as seen in photo 2. The same kind of finding is seen at the time of bronchography as in photo 3, that is the medium is intercepted just in front of a tuberculous focus.

When we measure the size of cavities and their draining bronchi in these casts, we find that most of the cavities are more than 2 cm. in diameter with certain exceptions; some larger cavities are 10 cm. in diameter, and it is comparatively rare that the diameter of a cavity is less than 2 cm. An overwhelming majority of draining bronchi are more than 0.3 cm. in diameter.

According to the plastic casts, the pulmonary lobules which are in contact with the pulmonary pleura, in many cases, are coneshaped with their bases on the pleura; and the diameter of their bases is about 2 cm., although there are some differences according to the location.

Some of the lobular bronchi, if we name each lobar branchus as the 1st bronchus, correspond to the 7th to 9th bronchus of 0.2 cm. to 0.3 cm. in diameter.

It is assumed that the inner wall of a lobular bronchus is kept open all the time in order to make use of its canal for gas interchange, (with the exception of greatly collapsed lungs), from the fact that cavities which were just under the pulmonary pleura and less than 2 cm. in diameter, were observed to have usually an opening of one draining bronchus at the time of cavernostomy, and also from the fact that the contrast materials penetrate deep into 7th to 9th bronchi easily with deep breathing in taking bronchograms of moderately of collapsed lungs. In other words, it is probable that any caseated lesion, larger than one lobule in size, may always be subjected to the internal pressure of the trachea. From this, it can be said that bronchi which can become

draining bronchi are the lobular bronchi and those supplying the interior pulmonary parts larger than a lobule.

The above facts, however, are the fundamental conditions to be generally recognized; so that it is not necessary to mention that we cannot stick to the above conditions all the time. For instance, among the various types of tuberculosis, there is one that is rapidly progressive, which is called the "exudative lobular form" pathologically, and causes death within a comparatively short time. When the plastic materials are injected into the lungs of such cases at autopsy, it is observed that most of the caseated lesions have softened and decayed suddenly to become cavities and that the plastic materials penetrate into small cavities 0.5-1.0 cm. diameter, and the pulmonary blood vessels reach the center of the fused cavity groups as in photos 4 and 5. In this type of tuberculosis, it is assumed that the newly-formed small cavities appear as if honeycombed and then fuse together into one large cavity. As is well known, the development of tuberculosis depends on the relationship between the resisting power of the individual and the virulence of the tubercle bacilli.

The former idea that cavities are recognizable only at Ranke's so-called stage III (term of visceral tuberculosis) has been gradually altered as a result of clinical and pathological studies on tuberculosis. It is now recognized that, in not a few cases, a rather large caseated focus can appear and decay to form cavities, not only in secondary pulmonary tuberculosis, but even in primary infections, in accordance with the extent of the disease and its location. Therefore when we understand the pathogenesis of cavities, it is apparent that the patient's body shows a defensive or healing ability and that cavitation is not very different from an ordinary suppuration and natural discharge of purulence in nonpulmonary tissues.

This point of view may have promoted the idea that tuberculous cavities are nothing but non-specific inflammation in cases of surgical treatment; this is due to the fact the recent discoveries of powerful chemotherapeutic agents have made it possible to have a direct intervention against tuberculous lesions and direct surgical treatments have brought about remarkably good results in those cases in which surgery has until now been contraindicated. There are many problems to be solved, however, before the above mentioned interpretation will be accepted literally, which identifies the specific inflammation of tuberculosis with other nonspecific inflammations, because lungs are specific airy organs full of alveoli and thus cavities are cured naturally in only very rare cases as it takes much time for cavities to be cleansed spontaneously.

## *2). The relationship between forms of cavities and the tuberculous lesions of draining bronchi*

Histologically we studied cavities or caseous foci, which were the main foci,

of 41 lungs resected, and we classified them into several types as shown in table 1, comparing histological with clinical findings.

Table 1 Histological classification of main tuberculous foci.

Preparation Stage of cavity (Precavitation)	type I	Capsulated caseous focus which image of tissues is stable, including incomplete membrane formation.	Reposing Stage
	type II	Part of caseous focus softening & decaying.	
Completed Stage (Prime of cavity)	type III	Fibrous obstruction of bronchi not recognizable but inspissated.	Active Stage
	type IV	Not accompanied by mixed infection.	
	type V	Accompanied by mixed infection.	
Cleansing Stage (Declining cavity)	type VI	Interiors of cavity cleansed, granulation exposed, a part of cavity has caseous substance.	Subsiding Stage
Healing Stage of cavity	type VII	Capsulated healing.	
	type VIII	Cicatrized healihg.	
	type IX	Epithelial healing.	

Type 1 is comparatively stable from the histological point of view, and has no signs of softening and decay at present, nor in the past. Some of these will take a better course in future to become type VII which may proceed to a capsulated healing. Some of them are called clinically tuberculoma, and have a comparatively clear membrane; on the other hand however, some have a poorly-formed membrane.

Judging from the histological stand-point, it is assumed that type II comprises those which once had softening or decay in a part of the caseous focus, such as many groups of acid-fast bacilli and round cell infiltration recognizable along the fissure in caseous foci.

The item common to types I and II is that the caseous focus directly adjoins to a bronchial canal without being covered with a membrane at the bronchial opening. This fact accords with Graeff's so-called "unemptied cavities" (geschlossene Kavernen), and these may be regarded in form as a stage previous to the typical cavity. We call this a preparation stage (or pre-cavitation stage) provisionally; they may also be said to be in a reposing stage as a source of discharging bacilli.

It is considered that type III is the unaccomplished form of capsulated healing and no fibrous obstruction is found in the draining bronchi.

It can be assumed that this type includes those type IV cavities whose layer

of caseous substance is thicker and whose interior is small enough to be reduced and inspissated by collapse therapy.

Among those which we call tuberculoma clinically, the cavities in our studies are semi-round in cross-section and surrounded by membrane from comparatively healthy pulmonary tissues; and it is almost impossible for us to classify them into type I or type II, if we observe them only histologically disregarding the clinical symptoms.

Those which belong to type IV are the completed, typical cavities, and both specific and nonspecific membranes are recognizable outside the caseous substance. In this report we treat the cavities with membranes of varying thickness as type IV for the purpose of our studies.

Those accompanied by a mixed infection belong to type V, and all of these had large cavities more than 4 cm. in diameter situated in a lower lobe B<sub>6</sub> near the hilum with comparatively large draining bronchi. In these cases, the inner walls of the cavities are irregular and rough, and there is a small amount of caseous substance within, and the exposed granular layer is observed here and there.

There is large amount of muco-purulent matter within these cavities and Gram-positive cocci were found in our cases.

The above-mentioned types III, IV and V include completed cavities in an active stage and are sources of discharging bacilli, with the exception of some of the cases belonging to type III.

Interiors of type VI cavities are comparatively clean, and the exposed and the exposed granular layer containing many newly formed blood vessels.

In these cases, the caseous substance still exists here and there and round cell infiltration is present here too.

Some cavities of this type, in the most fortunate cases, reach type VIII, a cicatrized closing healing that brings about obliteration of the cavity after the fusion of the granular layers and then the fibrous obstruction of the draining bronchi; on the other hand, some of them become to type IX with epithelial open healing, in which case the inner wall of the cavity is lined with epithelium and the interior remains open. It may be said, in either case, that these cavities are in a declining or subsiding stages.

A comparison of the histologic findings of a main focus with those of bronchi supplying the main focus is shown in table 2.

A mark + in table 2 indicates that a tuberculous lesion is observable only in submucous tissues, ++ means that a lesion extends further to the perichondrium and cartilage, and +++ that the caseated lesion of the bronchial wall penetrates into the interior of the bronchi where granula is exposed, and non-specific lesion means that no tuberculous sign can be observed on histological examination,

Table 2 State of cavity and tuberculous lesion of draining bronchi.

Lesions in Bronchi		Histological findings in draining bronchi				
		Nonspecific lesion		Specific Tuberculous lesion		
State of cavity		-	+	+	++	+++
type I	2		2			
type II	7		4	3		
type III	5		2	3		
type IV	21		2	3	12	4
type V	2				1	1
type VI	4			1	1	2
type VII	0					
type VIII	0					
type IX	0					

i). Tuberculous lesions of draining bronchi are scarcely recognizable in the preparation stage of cavity formation (or pre-cavitation stage), namely type I and type II; the lesion is extremely slight if present at all, and in such cases only a slight inflammation is recognizable in the mucous membrane. Some type III cavities may have a slight bronchial lesion, but this is generally definitely observable in the cavities of completed stages IV, V and VI.

ii). There is a difference in the extent of the diseased state between the "clean cavities" and their draining bronchi. The interiors of the clean cavities are to some extent in the declining stage. Never the less the draining bronchi are at the height of their descend state and getting worse and usually show no sign of healing.

### 3) Opening of draining bronchus

According to the plastic-injected casts, the modes of opening of a cavity into its draining bronchus are roughly classified into the following two patterns.

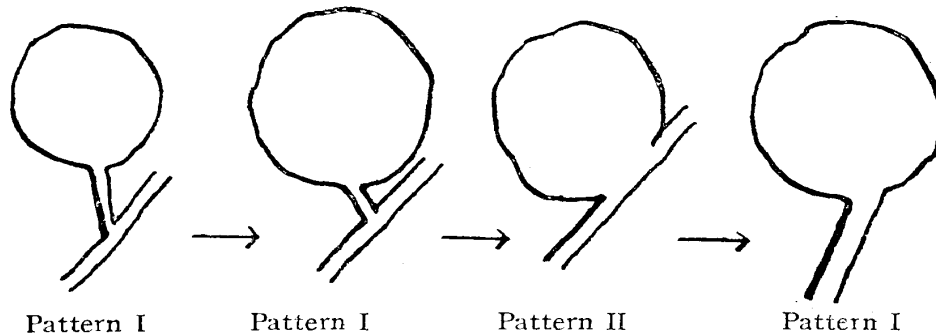
Fig. 1. Opening of draining bronchus.



As illustrated in figure 1, one pattern is that of a cavity opening into the end of a bronchus, and the other is that of a cavity draining into the lateral wall of a bronchus. We call the former pattern I, and the latter pattern II. Pattern II does not always have a cavity into the end of a bronchus, but sometimes accompanies pattern I. Judging from

the cause of cavitation and the function of the draining bronchi, it is assumed that pattern II is of secondary importance. However, when pattern II occurs in large cavities or those in the interiors of complex form in many cases pattern I plays a leading role functionally. At different stages of the developing cavity, the patterns seem to alter as follows — pattern I → pattern II → pattern I (figure 2).

Fig. 2 Cavity and draining bronchi.

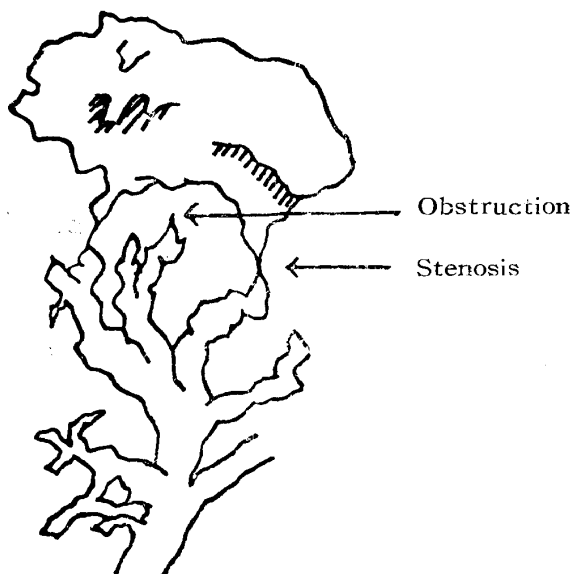


These modes of opening of cavities into a draining bronchus are also recognizable by means of bronchography — namely the bill-shaped and club-shaped types that belong to our pattern II are sometime observable, but in many cases pattern II is not observable by this method.

#### 4). Number of draining bronchi

It was observed, in the plastic-injected casts, that a cavity, which is less than 2.0 cm in diameter, usually had one draining bronchus, while larger cavities had generally two or more bronchi. Sometimes it looks as though the latter had only one bronchus, but actually it has two or more bronchi as shown in figure

Fig. 3 Number of draining bronchi.



3, and only one of them plays a leading role as a communication in the cavity for an airway, the others being sometimes obstructed on the way to a cavity. In other words, it is observable that a cavity, which is more than 2.0 cm in diameter, has two or more bronchi; and cavities 3.0 cm.-5.0 cm or more in diameter have several draining bronchi, but only rarely more than 5. The fact that the draining bronchi to very large cavities 5 cm. or more in diameter are fewer in number but larger in size in many

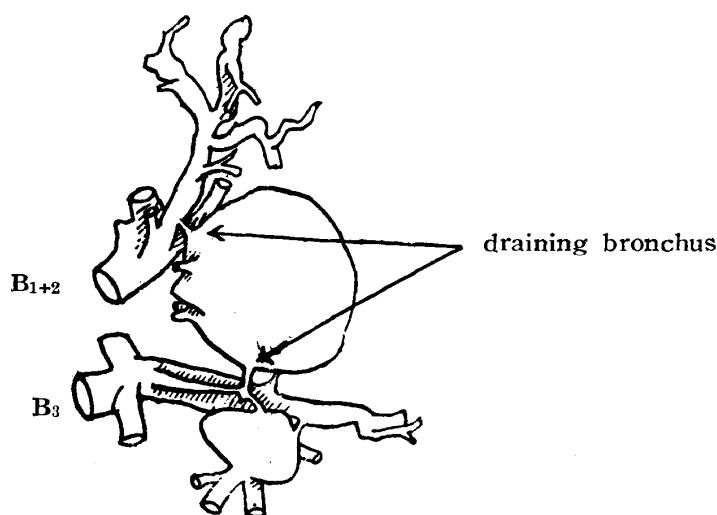


cazes than those to the above cavities, seems to be due to the fact that the other small draining bronchi were obliterated during the course of development of the disease. The draining bronchi of the comparatively large cavities, which belong to S<sub>6</sub>, sometimes are fewer in number but larger in diameter.

#### 5) *The relationship between pulmonary segments and draining bronchi*

In the study of the correlation between draining bronchi and pulmonary segments, it was observed that a cavitation is not necessarily limited to a single pulmonary segment, and the draining bronchus of cavities, of 1.5 cm. in diameter, as shown in figure 4, may communicate with the two neighboring segments.

Fig. 4 The relationship between pulmonary segments and draining bronchi.



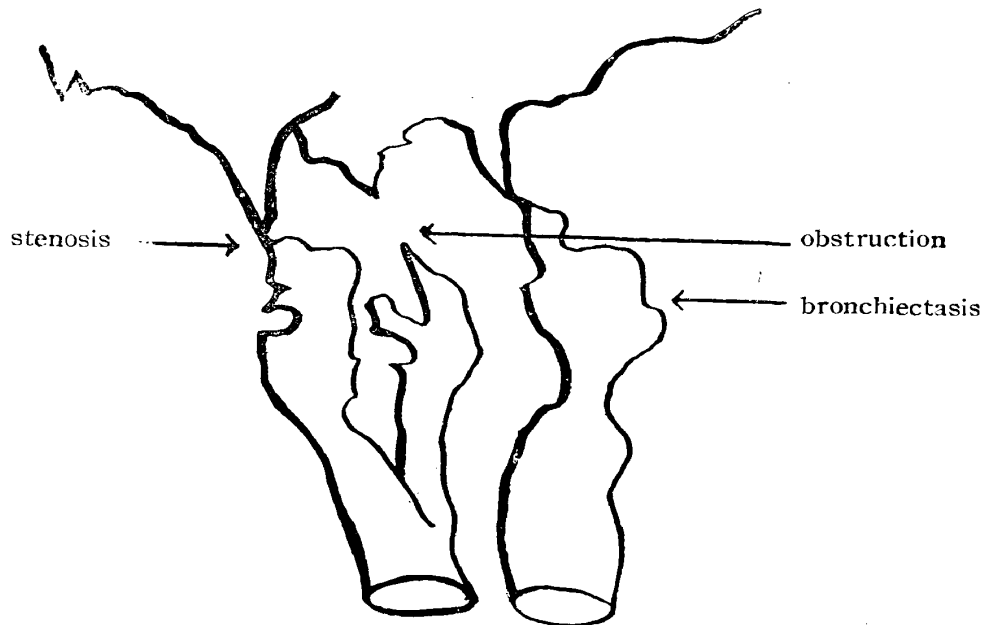
And draining bronchi of very large cavities may communicate with many segments. The intersegmental partitions, which consist of connective tissue and branches or pulmonary veins, are not firm enough to check caseation and cavitation of the intersegmental connective tissue at the time of development and fusion of the tuberculous focus.

#### 6) *Morphology of draining bronchi*

Several morphological changes may occur in draining bronchi such as stenosis, obstruction, partial dilatation, and single or multiple flexions, as shown in figure 5. Partial stenosis was distinctly observable at the opening of the bronchi into cavities, and bronchography shows that an abnormal bronchial course and an abnormal position occurs in the diseased area. According to our precise histological studies however, complete fibrous obstruction of a bronchus has never been recognized, and this indicates how difficult it is for an organized obstruction of a draining bronchus to occur naturally.

As necessary conditions for bringing about bronchial fibrous obstruction, R. Kita enumerated (1) bronchial lesions and (2) organic obstruction, but it is supposed that, in order to bring about fibrous obstruction, the bronchial mucous membrane must be broken and granulation tissue must come out to cause organic obstruction of bronchial interiors. It seems very rare that Kita's so-called conditions for the organic changes may occur in the slow course of healing of cavities. This may be said, because, the plastic casts show that even in the

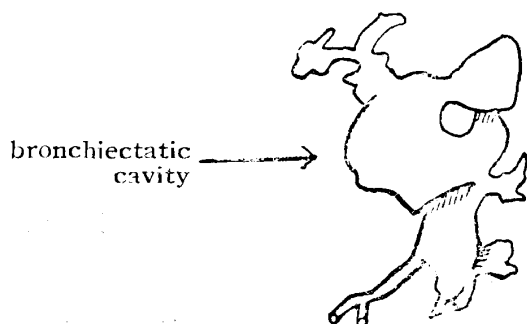
Fig. 5 Morphology of draining bronchi.



healing stage of cavities, their connecting bronchi are at the height of their disease histologically.

Partial stenosis and partial dilatation of draining bronchi occur alternately, and sometimes the partial dilatation is of such an extent that it may look like a bronchiectatic cavity as shown in figure 6. These bronchial tuberculous lesions

Fig. 6 Bronchiectatic cavity.



gradually decrease in degree as the bronchus approaches the hilum.

As mentioned above, in many cases the morphological changes are influenced by the extent of the tuberculous lesion around the cavity or the caseated focus, by the nature of the cavity.

#### 7). Influence of collapse therapy on cavities and draining bronchi

Since various forms of collapse therapy, extrapleural plasticball plombage and artificial pneumothorax etc., cause morphological changes in a cavity and its draining bronchus, we studied lungs removed at autopsy or at operation from patients, who had received pneumothorax, by injecting plastic materials. As a results of this study, it was found that the bronchi showed a stratified arrangement roughly parallel to the axis of a lobe as in Photo 6, and those bronchi which had left the main bronchi at rather wide angle before the operation, were bundled together after the opera-

tion like a folded umbrella and they generally looked like a bundle of brushwooden block.

Anatomical and histological studies of resected lungs, which had been under pneumothorax, showed an inspissation and a capsulation of the cavity. In order to have this kind of good results, certain conditions must be present with regard to the size, form, nature and inner pressure of the cavities. That is to say, if a cavity is smaller than 2 cm. in size, if only a portion of the cavity is softening and fusing, if there is healthy pulmonary tissue around the cavity and the cavity wall is thin and soft, if the inner pressure of the cavity is low, a comparatively good result can be achieved.

Inspissated cavities, that have been under artificial pneumothorax, even when the lung is well collapsed and a diffusing shadow is observable roentgenically, often are shown to contain holes anatomically.

Unlike thoracoplasty and plastic-ball plombage, pneumothorax does not cause the draining bronchi to bend or become obstructed, thus in many cases of bronchography, the contrast medium penetrates deep into the periphery even in moderately collapsed lungs; and even in the highly collapsed lungs of perfect pneumothorax, bronchial obstruction is not visible, but only shortening and narrowing of the bronchi. The value of pneumothorax therapy should be reconsidered in the light of these facts.

8) *The direct therapy of pulmonary tuberculosis in respect to the relation between cavities and draining bronchi*

In considering the relationship between cavities and draining bronchi, as already mentioned, it is very important to notice not only the morphological relations, but also the differences in the stages of disease and the progress of the lesion in both cavities and bronchi. That is, it must be realized that the healing of a cavity cannot be studied completely without also considering including the draining bronchi.

The direct treatment of pulmonary tuberculosis is at present roughly divided into incision and resection. Cavernostomy, Mauer's treatment and Monaldi's treatment, which make use of incision, are all similar in principle in respect to draining pus through the body, not through a draining bronchus, and in respect to promoting the cleansing of the cavity by means of chemotherapy, although there are some differences in the effect of the operation on the body. Incision is performed mainly on those cases in whom thoracoplasty or plombage was unsuccessful, or on those seriously ill patients who cannot stand a very large operation in order to improve their disease or to prevent a lesion from getting worse. This treatment seems to be as complete as a direct treatment when compared with resection. That is to say, considering the relationship between cavity and draining bronchus, it is practical and radical to treat the cavities at

its open scale. However, it is not always easy to treat positively the disease existing in the draining bronchus. As there are many indications, we cannot speak dogmatically, but it is expected that the cavity will undergo cicatrical healing after being cleansed and this secondarily has a good influence on the lesion of the draining bronchi. So it is necessary to continue medical treatment patiently with chemotherapy at the same time.

Most of the cases in our experiment have had satisfactory results. Lobectomy, partial pulmonary resection, and segmental resection, which are included in the latter type of treatment, have as their object the resection of a tuberculous focus through healthy pulmonary tissue. Considering the relationship between cavity and draining bronchus, this is the most thorough method of treatment. However, as the lung is an air-including organ, we have to keep firmly in mind that these operations may be accompanied by definite bronchial dissemination simultaneously with softening of the caseated focus. Especially, when cavities of type IV or type V, have a specific lesion not only in the draining bronchi, but in the bronchi at the pulmonary hilum, it was proved that there are foci which can disseminate disease through several pulmonary segments. So in many cases, we have to resect the main tuberculous focus, removing at least a lobe as the unit of resection, including the draining bronchi and foci of dissemination. However, specific tuberculous lesions seldom occur in the bronchi, in those caseated foci or cavities which belong to types I, II and some of type III; and the disseminating focus will be limited only to a small part around the main focus or within one pulmonary segment, therefore an excision of the main focus only will do in these cases. Even when the tuberculous lesion in the draining bronchus and the disseminating focus are not very significant, they should be partially resected together with their main focus, or if some of them, are limited to the specific segment, they should be resected segmentally. However, caseous foci, which are larger than a certain biggness, decay extremely fast, and the transition types, between type VI and type IV are very temperate and few in number; accordingly, such tuberculous foci should be excised selectively before they start to decay, in order to remove thoroughly the source of bacilli.

Prof. Nagaishi et al, worked out the method of excision of cavities and tuberculoma in Feb., 1951 and advocated that, caseated foci, which look as though they would, should be partially excised at an early stage, before cavitation. This report was made public at the 10th Tuberculosis Surgery Society (Oct., 1952) and No. 12, Vol. 34 of "Chiryō" (Dec., 1952).

In short, if partial or segmental resection is performed when tuberculous bronchia lesions especially the specific bronchial lesion are very slight and when no significant disseminating focus is present, we can expect the maximum effect, in other words, nearly perfect cure by means of minimum resection.

### Summary

We have studied 83 tuberculosis lungs removed at operation or at autopsy, three-dimensionally, pathologically, and histologically by means of the plastic-injected casts, and further investigated the relationship between cavities and draining bronchi and have reached the following conclusions.

1). The 7th to 9th bronchi in each lobe are big enough to play the role of draining bronchi, thus it may be said that the caseated foci larger than a lobule are facing directly to these bronchi. This is why these foci are always threatened by the danger of cavitation.

2). It is extremely difficult for a cavity to be cut off from the trachea by connective tissues obstruction of its draining bronchus; indeed this kind of obstruction has not been found at all in our studies.

3). There is a parallel relation between the state of a cavity and the tuberculous lesion of its draining bronchus, but in many cases there is a difference in the extent of the disease. Accordingly it is necessary to keep in mind the state of the draining bronchus at the time of treatment of the cavity.

4). The modes of opening of a cavity into its draining bronchus are; (1) a cavity opening into the end of a bronchus at its top (pattern I), and (2) a cavity opening into the lateral wall of a bronchus. According to the different stages of the developing cavity, the patterns seem to alter as follows → pattern I → pattern II → pattern I.

5). A cavity, less than 1.5 cm in diameter, has usually one draining bronchus, while a bigger cavity than the above has generally two or more bronchi, and a cavity larger than the above two kinds of cavities has several draining bronchi, but seldom more than four. The draining bronchi from megacavities are fewer in number but manytimes larger in size than those of the above cavities. This is apparently due to the fact that the other small draining bronchi were obliterated during the course of the development of the disease.

6). A cavitation is not necessarily limited to a single pulmonary segment, but the draining bronchus of a cavity, which is 1.5 cm. in diameter, communicates with the two neighboring segments, especially those of megacavities sometimes communicate with many segments. The intersegmental partitions, which consist of connective tissue and branches of pulmonary veins, are not firm enough to check caseation and cavitation of the intersegmental connective tissue during the development and fusion of the tuberculous focus.

7). Morphological changes in draining bronchi such as stenosis, obstruction, partial dilatation, and single or multiple flexions are observable. Partial stenosis is distinctly observable at the opening of the bronchi into cavities, and in other parts, a partial stenosis and a partial dilatation of the draining bronchus occur

Photo 1. Cavity and draining bronchus (plastic cast) 2.5x



Photo 2. Caseated foci (the area of coagulation and necrosis is clearly recognized as the sole defective part in plastic cast) 2.5x



Photo 3. Bronchography (gaint cavity of left upper lobe)

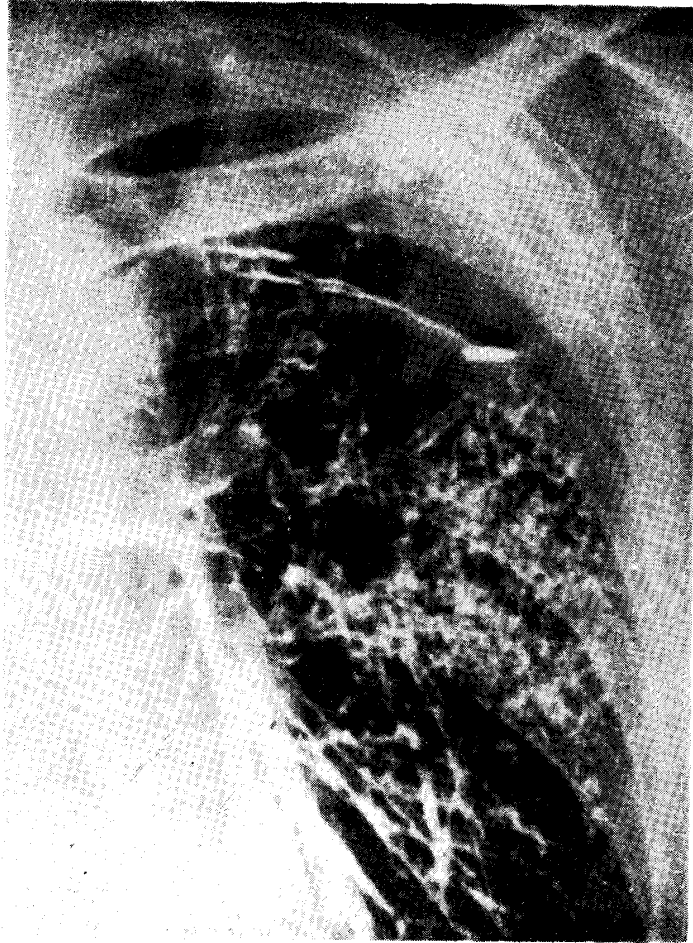


Photo 4. A number of small cavities softened and decayed suddenly

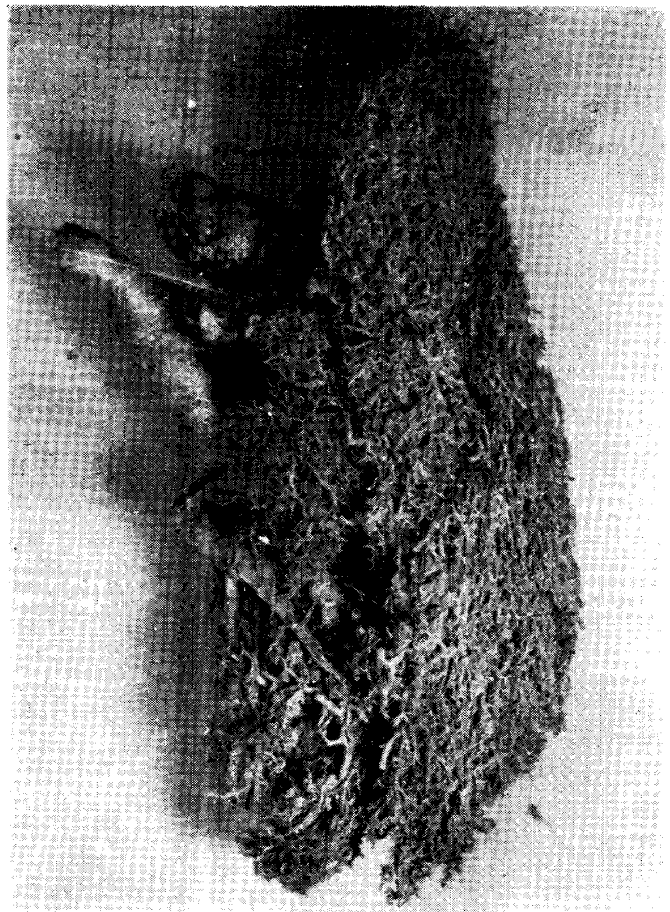
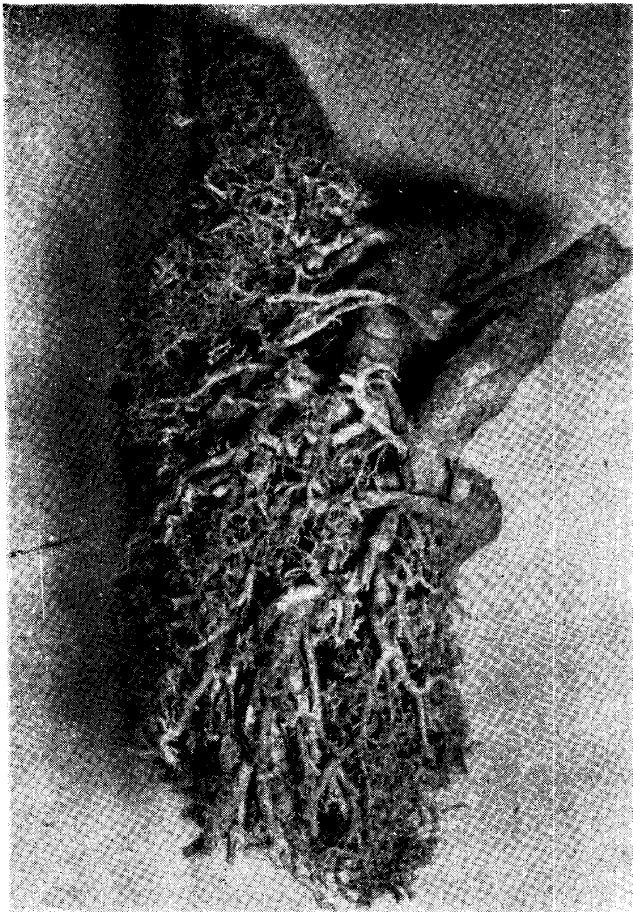




Photo 5. Small cavities and pulmonary blood vessels



Photo 6. Komplete pneumothorax (plastic cast of left lung)  $\frac{1}{3} \times$





alternately and the extent of the lesions gradually decreases in degree towards the pulmonary hilum. The morphological changes of draining bronchi parallel the degree of the tuberculous lesion around the cavity or the caseated focus.

8). With pneumothorax the bronchi take the form of stratification roughly parallel to the axis of a lobe, and the bronchial bending and obstruction are not recognized. Even in highly collapsed lungs of perfect pneumothorax, bronchial obstruction is not recognizable, but only the shortening narrowing of bronchi.

9). One form of direct treatment of tuberculosis, the incision treatment, aims at cleaning the cavity and cicatrized healing by means of draining the contents of cavity through the body wall, and not through a draining bronchus. But unfortunately this treatment is not very thorough when we consider the relationship between a cavity and the bronchial tuberculous lesion. From this point of view, resection seems to be the more thorough treatment, but indications for this treatment are limited to cases in the early stage, if we consider bronchial lesions and disseminated foci.

Therefore, those caseated foci which seems to tend towards softening and decay should be resected selectively as soon as possible in an early stage, namely before they become cavities.

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