

Th. Sect.

THESIS

on

"Primary Carcinoma of the Bronchus, with an Investigation into
its Early X-Ray Diagnosis"

by

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GENERAL CONSIDERATIONS

INTRODUCTORY: The more one delves into medical literature in these days of universal publication, the more is one forced to the conclusion that especially in definitely circumscribed subjects, such as primary lung tumors, the bulk of the literature is purely repetitive, dating back to some one more or less outstanding article or book. The subject of primary lung tumors is an unusually good example of this. In reviewing the literature in preparation for this paper I was immediately struck with the frequency and the consistency with which the writers referred back to a monogram by Adler in 1912. This author, I found, gives a most complete account of all the work done on this subject up to that date, summarizing the previously ill-assorted and ill-collected literature, and apart from the purely radiological side I have found but little really new since his day.

I therefore think as an introduction to the historical, pathological and clinical aspects I can do little better than briefly review Adler's findings, note the extra points of interest in subsequent work, and contrast this with the pathology and symptomatology of my own small group of cases before going on to the strictly x-ray viewpoint.

The group of cases which I desire to discuss consists of cases investigated in the Mayo Clinic in the latter half of 1926. In all I have assembled twenty-three cases, probably bronchial carcinoma,

and fourteen cases of possible primary lung tumor, but for analysis I am using a group of seven cases from all of which a biopsy section was taken from the bronchus through the bronchoscope (by Drs. Vinson and Moersch at this Clinic), and in which the lesion was visualized. One admits that even pathologists are not infallible, but taking pathological diagnosis of carcinoma from a biopsy section along with the visualization of the lesion as a proven case of an early lesion, one has at one's disposal a group of cases such as has never previously been investigated. All work to date where there has been established proof of the identity of the lesion has depended on post-mortem results and in these cases the radiological picture has, except in rarer instances, been of the later case and the so-called "typical" roentgen picture of primary carcinoma of the lung is vastly different from that in this group.

HISTORICAL: Primary cancer of the lungs has only been recognized in relatively modern days as an entity. The first real case was published by Morgagni in the middle of the eighteenth century and cases of this disease were recognized clinically and by gross pathology throughout the whole of the early nineteenth century "Clinical Period" of medicine dominated by Laennec. Throughout this period, however, the differentiation from gross tuberculous lesions was extremely weak.

The ultimate segregation of a group of primary lung tumors really depended on the introduction of the microscope and on the work of the well-named "Histological Period" of medicine of the

late nineteenth century dominated by Rokitansky (2), and later by the great Virchow (2A). Essentially the distinction between cancer and tubercle of the lungs, considering the protean gross pathology of each, depended on the microscope - as it still must.

Up till 1912 a large number of small, incomplete groups of cases had been published and these cases Adler assembled and used to establish a clinical and pathological grouping.

INCIDENCE: Taking the literature all in all, the consensus of opinion is that the disease is following the modern trend of malignant disease and has an incidence on the increase. Besides this, there has been a steady improvement in diagnosis which has isolated and recognized an increasing number of cases.

ETIOLOGY: As elsewhere in the body, it does not seem possible to elicit any hereditary factors.

As regards sex, Adler puts a grouping as follows:

In 374 cases of lung carcinoma,

Men: 269 71.9% of whole group

Women: 93 26.8% of whole group

And a similar grouping for sarcoma.

The largest modern group of cases, that by Eloesser (3) publishing twenty-seven proven post-mortem cases, gives a very similar relation of three male to one female.

The male preponderance in my small group is even more striking, in so far as we find only one female in seven cases. Sherman

(4) would like to relate this to the heavier smoking habits of the male population, but it is difficult to prove such a relationship, though the possibility is interesting.

On this male preponderance hangs the old established theory of chronic irritation as a part basis in the etiology of malignant disease, the male being the more exposed both to chronic irritants of the pneumoconiotic type and to respiratory infections.

Related, too, to the subject of chronic irritation is the relative incidence on the two sides: In all published groups of cancer the right side suffers more frequently. Is this due to the straighter course from the trachea? Adler's group works out to 187 right to 157 left and he decides the results are merely incidental. Subsequent writers, e. g. Fried (5), find their figures more striking except in a group of thirteen cases with eight left-sided reported by Barron (7). My group shows this markedly, with incidence of six right to one left.

Age incidence shows a maximum at 55-64, a rare incidence below 40, but sporadic cases as young as 17. Hall (6). In my seven cases the ages run 39, 40, 41, 48, 58, 58, 63.

Previous Disease: As regards the significance of previous inflammatory disease of the respiratory system and especially that of tuberculosis, Adler believes that he deduces from his tables a weak but definite relationship to tuberculosis and brings forward as contrast points of similarity the incidence of epithelioma in lupus and carcinoma of the tongue in leukoplakia. He admits, how-

ever, that if there is any relationship it may be only that of irritation of the chronic scar tissue, rather than peculiarly tuberculosis. He makes little count of the incidence of other diseases.

Moise (8) and one or two others, discussing the increase in incidence in modern years, wonder if there is any relationship to the recent pandemics of influenza but do not produce any figures.

In the histories of these seven cases I noted particularly any suggestion of previous tuberculosis, influenza, a trade causing pneumoconiosis or excessive smoking.

I had one case of tuberculosis - the radiogram showed the lesion on the other side!

Influenza showed two cases in the seven and ten in the total group of forty-one cases.

Only one man, an old coal miner, was likely to have pneumoconiosis; that he had it very definitely was obvious from the film. But one incidental case can prove nothing.

Two were extreme smokers - one said that he had smoked forty cigarettes a day for forty years - but two in seven is a fair average for the male sex of the present generation, as is also the total incidence of heavy smoking of five cases in forty-one.

CLINICAL ASPECTS

SYMPTOMATOLOGY: While on the subject of pathology both Adler and subsequent writers are fairly definite, there runs throughout all the discussions on the clinical aspects a certain unsatisfying vagueness. That is, I feel, due to two points:

1. That the bulk of the cases quoted or discussed are later cases where secondary effects blur the primary picture.

2. That there is an insufficient appreciation of the two clinically distinct groups of cases which I think can be established:

(a) Bronchial: Giving clean-cut symptoms referable to the respiratory tract.

(b) Parenchymal: Often latent, or at least extremely lacking in any typical syndrome. As will be noted later, this group will include many of the pathologically "bronchial" group - i.e., cases arising from bronchial epithelium of the lesser bronchi.

Throughout the literature these two groups are slumped together.

Briefly, this composite symptom group consists of:

Pain: Is vaguely thoracic, and pleural in origin - i.e., relatively late.

Cough: Is found in well over fifty per cent of the cases. It

is of two types:

- I. Dry, short, constant, unproductive cough
- II. Associated with secondary results such as bronchiec-tasis.

Sputum: Adler gives a rather lengthy dissertation on the possibilities of sputum diagnosis, isolating:

- (a) Blood-tinged group as a common element, and as rarities
- (b) Prune-juice sputum of text-books
- (c) Green sputum of sarcoma
- (d) Tumor-element bearing sputum of later cases

All subsequent writers find the last three elements so inconstant as to be negligible as a diagnostic aid.

Dyspnoea: Is a curiously inconstant accompaniment though present in some fifty per cent of the cases.

Cachexia: Is said to be less noticeable than in other malignant lesions and there are few cases in which the patient died of dyspnoea with negligible weight loss.

Fever: Is a definite associate of only the resultant secondary lesions.

Blood Count: Is of no primary significance but a leucocytosis is of great value in isolating infected cases.

Other Signs such as osteoarthropathy, clubbed fingers, cyanosis, etc., occur as with all respiratory lesions.

CLINICAL GROUPING: It is interesting to note that Osler's short notes on "New Growths of the Lungs" is practically a condensation

of Adler's chapter on the clinical grouping of those lesions.

He groups them as:

A. Acute Pleuro-Pulmonic

B. Chronic Pleuro-Pulmonic

I. Pulmonary or Broncho Pulmonary Form

II. Mediastinal Form

III. Pleuritic Form

C. Latent form is also discussed but not tabulated.

This essentially is a grouping of the later cases based rather on the dominant direction of growth of the lesion than on its earlier focus of origin and I do not think will justify critical discussion in an essay on the earlier lesions, such as this is.

Three points are stressed that are of interest:

1. The frequency of physical findings indicative of a bronchial stenosis and total or partial atelectasis of part of a lung.
2. Absence of mobility on the affected side.
3. The extreme difficulty of disentangling the purely physical examination signs from those of tuberculosis in some form or other.

In the most recent article I can find on this subject (Sherman (4)) there is little advance from this situation, and in none of the intervening publications is there any really crisp determination into those two groups which I suggested above, except perhaps in the article by Elloesser (3), who certainly recognizes the clinical division of the two groups but does not, I think, give this division

the emphasis it merits. He characterises the parenchymal group as the only one recognizable by the x-ray.

Before detailing my cases in full I would present a summary of what I consider to be the salient features.

BRONCHIAL CARCINOMA: - Table I. The group of seven cases forming my major group are essentially "Bronchial Carcinoma." These cases all give reasonably early symptoms - in fact, in all cases comparison of the length of the history with the x-ray findings seems to indicate that symptoms will be present before there is even appreciable radiologic evidence of a lesion - i.e., very early.

Taking those symptoms in series, we find:

Cough: Cough is an invariable accompaniment. This cough has one noticeable characteristic, that, once it has started, it remains constant; it is never periodic. At first merely a dry, unproductive, irritating cough, it usually goes on to the production of some degree of sputum. In the causation of this cough I think the cancer is really only acting as a foreign body to the bronchus, a foreign body which the cough is a reflex effort to void.

Sputum: The amount of sputum is very variable. I feel that the characteristic is a merely mucoid sputum but the histories show all varieties from this to profuse purulent. This last arises not directly from the lesion but is the product of bronchiectasis or other infective processes which form the natural second stage of the life-history of the growth, but which are merely secondary.

Blood: This appears to be the crux of the question. In only two proven cases was there an absence of hemoptysis in some form, varying from a brisk hemorrhage (sometimes the first symptom) as in a case reported recently (9) to a mere constantly blood-tinged sputum.

In many ways carcinoma in this zone reminds one in its symptom grouping of sigmoid carcinoma: Too far down for the simpler methods of inspection, yet not too far for direct symptoms to be produced and proveable merely by taking thought of suggestive signs, to look for it by proctoscope or bronchoscope. Cancer of the sigmoid evidences itself first by irritative phenomena, including ulceration and bleeding, and later by obstruction. So here we have the irritant cough with the bleeding of ulceration, and later, as I think I can show, stenosis giving lung atelectasis.

These two, cough and bleeding, are, I think, almost constant concomitants of a truly bronchial carcinoma. The other symptoms usually given in the literature do not appear to be stressed.

Pain is seldom complained of.

Dyspnoea seems to be rather oftener absent than otherwise.

Weight Loss is nearly always present in some measure; indeed, an absence of, or a slight, weight loss is exceptional.

Fever is comparatively uncommon. To determine whether appearances suggestive of bronchiectasis in the x-ray film are really so or not, I tabulated the blood-counts. In only two cases was there a leucocytosis.

The "Probable" group of bronchial cancers shows largely the same findings (Table II) corroborating especially the constant cough with blood and the rapid weight loss.

PHYSICAL EXAMINATION: As far as physical signs go, there is little to note. I am treating of the earlier lesion only: It is deep in; it is small; and one cannot expect much that is typical. Beyond a tendency to pick up evidence of some degree of stenosis or dullness due to atelectasis, there is nothing of interest. And even these are not good enough to bear contrast with the x-ray. Whatever physical signs will show, the x-ray will show better.

BRONCHOSCOPY: And lastly there is the ultimate diagnostic - the bronchoscope. It is to this that we owe the isolation of this group of cases. It is as nearly definite a diagnostic ^{method} as possible, but - though of itself in expert hands perfectly simple - it cannot be applied sufficiently widely to allow it to be used in all cases with indicative signs. Hence the need for the much simpler radiogram as a means to cut down the list of possibilities to limits capable of being dealt with by the bronchoscope. Of itself the x-ray cannot be absolute, but I feel that a suggestive film along with cough and blood will always justify bronchoscopy. I have not been able to do any bronchoscopy for myself as it is essentially a skilled technique, but Dr. Vinson, who is responsible for the bronchoscopies quoted herein, describes the typical findings as follows:

"While there is what might be considered a 'typical epithelioma' appearance in the bronchus resembling epithelioma of the oesophagus, yet in the majority of cases it would be extremely difficult to feel at all certain of the nature of the condition seen. With the distance at which the lesion is observed, often all that is to be seen is a somewhat granular appearance, with a red bleeding surface, and practically always a certain amount of narrowing of the bronchus: This is an appearance which could not be said to be definitely 'not inflammatory' and in these cases the biopsy section often showed malignancy when least expected. In some cases the lesion was more striking, showing a heaped-up irregular tumor mass with central ulceration and again bronchial stenosis as well as the bronchial obliteration due to the mass."

One might suggest that possibly these appearances represent a papillary type of fungating growth, resembling medullary carcinoma of sigmoid, on the one hand, and, on the other, a primarily submucous growth of a deeply infiltrating nature like malignant ulcer of the floor of the mouth.

PARENCHYMAL CARCINOMA: - Table III. While it is easy, working from a proved group such as the above, to draw justifiable deductions, yet it should also be possible to draw reasonably consistent deductions from a clinical group of cases, radiologically apparently malignant, and clinically diagnosed as malignant cases.

For the sake of contrast, though I do not desire to stress

those cases as I do the others, I collected fourteen cases which appear to be primary lung malignancy but which are either bronchoscopically negative or lack those signs which I have associated above with the bronchial group.

These I take to be malignancy developing in the actual lung parenchyma. They may be the relatively rare alveolar carcinoma of the pathologists or they may be, as are the others, from bronchial epithelium or glands, but of the lesser bronchi and therefore will clinically act as a parenchymal tumor.

The characteristic of this group seems to be a certain element of latency. Hidden away in the substance of the lung, an insensitive organ, they remain symptomless till they become of sufficient dimensions to invade farther. They may

- a. Reach the pleura or mediastinum, or metastasize.
- b. Invade a larger bronchus and act as irritant or stenose it.
- c. Necrose and become secondarily infected.
- d. Fill the bulk of a lobe or lung, remaining still symptom-

less till large enough to put that lung out of commission.

Associated with these different methods of extension we get a varied symptomatology contrasting markedly with the crisp symptomatology of the bronchial growth. This will include one or more of the following:

Fever is due to onset of infective complications, either in necrosis or in bronchiectasis following partial bronchial occlusion.

Pain usually means pleural involvement (probably by permeation)

but tends to occur quite early.

Cough, blood and sputum will occur just as in the other group if the growth invades a bronchus. It is this that makes a sharp line of demarcation between the two difficult. The x-ray appearances in the parenchymal should be of a larger tumor relative to the length of the history.

Dyspnoea comes either by direct blotting out of lung tissue or by compression stenosis of a bronchus or trachea.

Invasive symptoms such as venous tract obstruction or recurrent laryngeal paralysis with aphonia or phrenic paralysis, do occur.

Metastatic nodes are usually seen and are especially frequent in the supraclavicular region, when a biopsy gland section can be taken. Distinct metastasis occurs early - the brain being an unusually common site.

Weight Loss of the whole group of symptoms in this series, is the most constant sign, varying from ~~nil~~ to thirty pounds, averaging about twenty.

If one were to attempt to outline a syndrome at all the nearest approach would be "Loss of ^{Weight} from unknown cause coupled with either unexplained dyspnoea or unexplained chest pain of vague distribution or with the cough-blood syndrome of 'bronchial' carcinoma."

This group of cases is analyzed for the symptomatology in Table III. I do not purpose giving full case histories for these cases as they cannot be considered certain, but desire to discuss

the x-ray appearances of a few of them as a contrast group to the true bronchial carcinoma.

The following are the x-ray appearances of a few of them as a contrast group to the true bronchial carcinoma.

- (a) Solitary
- (b) Multiple
- (c) Diffuse or lobular
- (d) Infiltrating
- (e) Vascular

Solitary - This is the most common type of bronchial carcinoma. It is usually a well-circumscribed, rounded or lobulated mass, usually solitary, though probably the most frequent type. It is usually found in the periphery of the lung and is usually of the peripheral type. It is usually of the peripheral type and is usually of the peripheral type.

Multiple - This type is characterized by the presence of multiple nodules of varying sizes, usually in the periphery of the lung. It is usually of the peripheral type and is usually of the peripheral type.

PATHOLOGICAL ASPECTS

MACROSCOPIC PATHOLOGY: The old Pre-Histologic Period considered two groups

Encephaloid

Infiltrating

and though actually this would still offer quite a reasonable grouping, the more usual gross pathologic subdivision is somewhat along these lines:

I. Nodular

(a) Solitary

(b) Multiple

II. Diffuse or Lobar

III. Infiltrating

IV. Miliary

Nodular: This is the typical earlier parenchymal tumor and tends to local metastasis showing radiologically (or post-mortem) a surrounding group of satellite growths, an appearance which is typically malignant. Although probably the commonest tumor, early, yet it is not so often seen in the post-mortem room as it usually ceases to be nodular before the stage at which it causes death.

Diffuse: This group I have culled from Barron (7) as it fits well into the x-ray grouping. It is probably only a later state of the nodular tumor, but in its marked localization power to single lung lobes it really offers an isolated group, which I consider worth segregating.

Infiltrating: This group will include all my bronchial tumors and as well probably a number of bronchogenetic carcinomas which, though clinically parenchymal, arise near the hilus and infiltrate outwards rather than concentrically expand as do the true nodular.

Miliary: This is invariably included in the literature as a group. I believe that it is always secondary - perhaps occasionally to an undistinguishable single pulmonary tumor. Several writers (e.g. 11) include also a "Mixed" group. I believe that this is merely a large primary with multiple metastasis.

HISTOLOGY: As regards histology, Ewing (10) early laid down the three foci of origin as:

- | | | |
|--|---|----------------|
| I. Bronchial Epithelium |) | Bronchogenetic |
| II. Bronchial Mucous Glands |) | |
| III. Flat Epithelium lining Lung Alveoli | - | Alveolar |

Ewing gives the relative incidence as two bronchial to one parenchymal. Fishberg (16) believes bronchial to be as high as ninety per cent. This grouping has been staunchly repeated to the present day. It is probably right but does not take us far as it is extremely difficult to relate the cell groupings as found to any one of those foci of origin. Grove and Kramer (11) first stressed this point and emphasized rather a tumor cell type classification. They consider the majority of tumors are bronchogenetic - sixteen out of twenty-one in their own reported group. They classify histologically:

I. Cylindrical Celled

- (a) Adenocarcinoma
- (b) Carcinoma Simplex
- (c) Scirrhus
- (d) Alveolar
- (e) Medullary

II. Squamous

III. Mixed Cell

Elloesser in his excellent article (3) subdivides his twenty-three cases as follows:

Bronchial	-	Squamous	10
		Medullary	5
		Adenomatous	2
		Sarcoma	1
Parenchymal	-	Squamous	1
		Medullary	1
		Sarcoma	1

To these groups we might also add:

Colloid Cancer - described by Barron (7)

Columnar Cell Ciliated - as seen in case of Playfair's (12)

As this histology is all post-mortem, there is in no literature any attempt to segregate a pathology for the clinically purely bronchial group.

The Adenocarcinoma seems to have no characteristics peculiar to the lung: It is a simple gland-like type resembling the corresponding breast or prostatic tumor. It is interesting that in

my parenchymal group all but one of those with neck gland metastasis were of this type.

The Medullary group is of rather more interest in that it may be found so highly cellular as to almost resemble a sarcoma.

Scirrhus refers to the amount of fibrous tissue. I think it is now commonly agreed that this probably represents the vigor of the body reaction irrespective of the grade of the tumor. In this relation it is of interest that the two cases in my series showing considerable fibrosis are those of longest duration for the same obvious amount of lesion.

The Squamous Celled group is that which offers material for most reflection. Practically all the writers of other than a few page articles comment on the anomaly of this type of tumor in this situation. There is normally no squamous epithelium present in the bronchus, yet all the reports show a fairly considerable incidence of a definitely squamous celled tumor. Whence does this arise?

The earlier writers tend to put it down to an origin from the flat alveolar epithelium but the alveolar epithelium is not a squamous epithelium but an altered cylindrical celled. Adler discusses rather the incidence of the rare endothelioma of the lung as probably the only true alveolar tumor. Others find a distinct type of pleomorphic celled tumor peculiar to the lungs as the "Alveolar Carcinoma."

Epithelial rests are also discussed but discounted.

The large bias of opinion is that this tumor arises from a true metaplasia. Writers supporting the scar tissue origin in tubercular or influenzal patches would have it that the metaplasia precedes the malignancy. Others rather have it that the metaplasia is a result of the riot action of tumor growth and as evidence of reversion to the earlier type of cell. In this connection one finds it interesting to note the origin of the tracheal and bronchial tree from an invagination of the fore-gut in common with the oesophageal bud - and squamous celled tumors are common in the oesophagus. I discuss this point at length owing to the definite findings in my own group. Of the seven cases six are squamous celled epithelioma.

Dr. Broders, the pathologist at the Clinic to whom I am indebted for the use of these sections, in his excellent article (13) on the grading of tumors from the point of view of what might be called the "virulence of the type of cell" shows how the less the differentiation in the cell type the more the virulence of the type of tumor growth. Using Broders' grading, only one of my group was other than a Grade IV (least differentiated) and that one was a III plus.

We therefore are dealing with a markedly undifferentiated cell and therefore perhaps stretching the situation somewhat in calling some of the growths squamous. Case No. 4 is a case in point. Of themselves the cells look squamous but they have absolutely no arrangement typical of anything. We have merely a cell infiltrated

mass which might quite justifiably be called, simply "Carcinoma Grade IV". On the other hand, there are sections, such as Cases No. 2 and No. 5, which are unmistakably squamous. Case No. 2 especially is living with cell nests.

The only non-squamous type is Case No. 3, which is typical adenocarcinoma - showing in marked contrast to the others.

One can venture nothing from so few cases, but it would be interesting, in view of this very heavy incidence of squamous metaplasia, to see how a larger number of proven, clinically bronchial, cases would work out.

The various sections will be discussed more fully under the individual cases, but the points of note are:

The relatively large number of squamous celled growths.

The virulent type of growth - as measured by Broders' grading.

The relation of the amount of fibrous tissue to the length of the history.

CLINIC NO.	SEX	AGE	ETIOLOGY			SYMPTOMS									SPECIAL EXAMINATIONS				BLOOD				OTHER LESIONS	DIED - MONTHS LATER	REMARKS			
			PROVEN	PATIENT'S OCCUPATION	INFLUENZA	TUBERCULOSIS	SMOKING	COUGH	SPUTUM	T.B. IN SPUTUM	BLOOD	PAIN	DYSPNOEA	WEIGHT LOSS - LBS.	FEVER	LENGTH OF HISTORY - MONTHS	ORIGINAL X-RAY REPORT	BRONCHO-SCOPIC FINDINGS	BIOPSY SECTION	GRADE OF MALIGNANCY	HEMOGLOBIN %	REDS				WHITES	WASSERMANN	
564226	M	40	Farmer	0	0	0	+++	+	0	++H	+	0	20	+	16	Abscess	Epithelioma R.M.B.	S.C.E. IV	77	4.46	7500	0	Pleurisy	-	Well-January 1927			
555012	M	48	Coal miner	0	0	1/2 plug	+++	0	0	0	++	0	30	++	24	Abscess	Epithelioma R.U.B.	S.C.E. III	47	3.94	15300	0			Dec. 1926 - Condition unchanged.			
574429	M	39	Farmer	1918	0	0	+++	+	0	++	+	++	30	0	6	Negative	Bleeding lesion-LMB	A.D.C. IV	80	5.16	8400	-	0 0		Alive Jan. 1927-severe hemorrhage			
573241	M	58	Tailor	0	0	40 cigs. day	+++	++	0	+	0	0	6	0	1 1/2	Bronchiectasis or abscess	Bleeding point R.L.B.	S.C.E. IV	68	3.91	6300	0	Adenomatous goiter		Almost moribund December 1926.			
557157	M	63	Metal worker	0	0	0	+++	++	0	++	+	+	10	++	4	Interlobar fluid plus bronchiectasis	Stenosis bleeding R.B.	S.C.E. IV	74	4.52	1500	4+	Tabes		None			
514638	M	58	Manager	0	0	6 cigars day	++	+++	0	++	0	+	36	+	9	Carcinoma right lobe bronchus beyond	Bleeding R.L.B.	S.C.E. IV	64	3.89	21000	0	0 0	9	Death of pulmonary hemorrhage			
574152	F	41	House-wife	1925	0	0	+	+	0	0	0	0	40	0	12	Abscess	Stenosis R.B.	S.C.E. IV	70	4.81	9100	0	Metastatic neck glands		Jan. 1927 - condition unchanged.			
Table II															PROBABLE BRONCHIAL CARCINOMA													
573607	M	31	Lawyer	0	0	0	+	0	-	+	+	+	50	0	4	Abscess right mid lobe	Bleeding deformity R.B.	neck gland A.D.C.	73	4.81	8300	+	Dysphagia from onset	3				
577866	M	40	Farmer	0	0	0	++	++	0	0	+	+	39	+0	12	Pneumonia with fluid	Stenosis R.L.B. Bleeding	Ca. IV	68	3.84	10700	0	Pleurisy recent		Chest - query metastases Strong abdomen history preceding			
406584	M	40	Cigar merchant	1918	0	0	++	++	0	+	++	0	14	++	4	Malignant	-	Neck gland Ca.	64	4.46	9800	0			Extremely ill on admission.			
585575	M	38	Miner	0	0	++	+++	0	+	0	0	+++	57	0	4	Lymph-blastoma	-	Ca. autopsy	70	4.01	7400		On admission		Autopsy carcinoma bronchus multiple metastases.			
567074	M	56	Railway guard	0	0	0	+++	++	0	++	0	+	30	+0	8	Malignancy	Epithelioma R.U.B.	inflamm. tissue	68	4.09	12700	0	Adenomatous goiter	3				
670	M	57	Merchant	+	0	0	++	+	0	+	+	+	6	-	2	Malignant hilus	Bleeding lesion L.M.B.	inflamm. tissue	70	4.65	8300	0			Bronchoscopic appearance typical epithelioma Alive - December 1926			
460190	M	59	Peddler	0	0	0	+++	0	0	H	+	+	-	0	3	Thick pleura query malignant	No	No	51	3.07	10900	0		3	Brain metastases			
366319	M	56	Merchant	0	0	0	+++	+++	0	-	++	++	28	+	4	Malignant	-	-	56	3.46	22800	0	Laryngeal hoarseness		None			
103523	F	67	House-wife	0	0	0	+++	++	0	+++	0	0	0	0	5	Bronchiectasis	-	-	60	4.04	9000		Hypertension	3	Cerebral metastases			
487186	M	50	Farmer	0	0	0	+++	+	0	++H	0	0	10	0	1	Malignant	Bronchial ulcer R.M.B.	S.C.E. III	54	3.26	9200	-	Bladder tumor 8yrs. ago	-	Different pathology from old tumor but query metastases.			
504254	M	33	Broker	1919	0	0	+++	++	0	+	+	+	25	+	21	Malignant			46	3.41	11200	-	-	3				
511710	F	58	House-wife	1919	0	0	+	+	0	+	0	+	0	+	1	Metastases	Granular lesion R.M.B.		73	4.00	8000	-	Dyspeptic history 18 months	-	No worse 6 months later Possibly metastases			
391474	M	34	Railway switchman	1918	0	0	++	+	0	+++	+	++	29	+	56	Mediastinal tumor			57	4.31	1100	-	-	12	Apparant pleurisy aspirated without success			
357153	F	43	House-wife	0	0	0	+++	++	0	+	0	0	25	0	8	Fluid Hilar.	Neck gland A.D.C.		79	4.51	10300		Glands neck	-	Several aspirations unsuccessful			
402587	M	66	Janitor	0	0	0	+++	+	0	0	0	+	-	-	8	malignancy	-	-					Glands neck		Pt. left before completeing exam.			
507107	M	62	Farmer	0	0	0	++	0	0	0	+	+	query	-	2	Abscess							Epithelioma lip		Possible old pneumonia with abscess			

Table I Proven Bronchial Carcinoma.

Table II Probable Bronchial Carcinoma.

Key to Abbreviations,

+++ Marked or excessive.
++ Definite.
+ Slight.
O Absent.
+O Periodic.
- Not noted.
H Severe Haemoptysis.
R.L.B. Right lower Bronchus. } Etc.
L.M.B. Left main Bronchus. }
S.C.E. Squamous Cell Epithelioma.
A.D.C. Adeno-carcinoma.

CLINIC NO.	SEX	AGE	PATIENT'S OCCUPATION	ETIOLOGY			SYMPTOMS							SPECIAL EXAMINATIONS				BLOOD				DIED - MONTHS LATER	REMARKS				
				INFLUENZA	TUBERCULOSIS	SMOKING	COUGH	SPUTUM	T.B. IN SPUTUM	BLOOD	PAIN	DYSPNOEA	WEIGHT LOSS - LBS.	FEVER	LENGTH OF HISTORY - MONTHS	ORIGINAL X-RAY REPORT	BRONCHOSCOPIC FINDINGS	BIOPSY SECTION	GRADE OF MALIGNANCY	HEMOGLOBIN %	REDS			WHITES	WASSERMANN	OTHER LESIONS	
575007	M	31	Lawyer	0	0	0	+	0	-	+	+	+	50	0	4	Abscess right mid lobe	Bleeding deformity	neck glands	A.D.C.	73	4.31	8300	+	Dysphagia	3 mo. later		
480459	M	67	Painter	1912	0	0	++	+	-	+	0	0	0	0	5	Abscess	Slight infiltration	Inflam. tissue		79	4.32	7400	-	-			
568447	M	43	Farmer	0	0	0	+	0	-	0	++	++	10	0	5	Malignancy	Bulging R.M.B. Lesion	Inflam. tissue Lympho-sarcoma		50	4.1	12800	neg.	Arthritis	4 mo. later condition unchanged.		
571356	M	42	Salesman	1919	0	0	+	+	-	+	+	+++	10	0	3	Thick upper med.	R.L.B. Prob. Ca.							Palpitation Aponia-cord paralysis	Much improved, 1 mo. later after deep therapy,		
481448	M	62	Salesman	1919	-	0	+	+	-	+	++	0	20	0	12	Malignant				74	4.40	8400			Possibly bronchial	Improved with therapy, recently worse	
577893	M	61	Engineer	0	0	0	+	0	-	0	++	0	30	0	2	Malignant	Bleeding R.L.B.	Inflam. tissue		70	4.48	11300					
516648	M	50	Fisherman	0	0	50 cigs. a day	+	0	-	0	+++	+	27	0	10	Metastases	-			65	-	6900				later	
494886	F	54	House-wife	0	0	0	0	0	-	0	++	++	25	0	8	Carcinoma	-			-	3.52	4200				3	
580151	F	44	House-wife	0	0	0	0	0	-	0	+++	0	18	0	6	Basal infiltrat.	-	neck glands Ca.	IV	78	4.40	7900		Neck glands			
462306	M	57	Farmer	0	0	0	++	+	-	+++	+	+	6	++	7	Abscess		neck glands Ca.	IV	68	4.02	9000	neg.	Neck glands	3		
483698	F	48	House-wife	+	0	0	0	0	-	0	0	0	0	0	8	Node left lung query prim.	-	Brain tumor A.D.C.		72	4.60	6100	-	Brain tumor		Brain tumor operated and found metastatic.	
503157	M	52	Oil prod.	0	0	0	0	0	0	0	0	0	0	0	0	50% malign. 50% inflam.	-	Neck glands Ca.	IV	59	5.16	9800		Brain tumor	11	Metastasis to brain.	
579590	M	67	Farmer	0	0	0	++	+	0	0	+	+++	20	+0	5	Fluid Tumor upper left	Bulging in of L.L.B.	Neck glands A.D.C.	II	73	4.40	4300	-	Pleurisy	-	Pleurisy - 1400 cc tapped. Aspiration for fluid?	
409986	M	64	Farmer	0	0	0	+	+	0	0	++	+	15	+0	7	Tumor upper left	-			72	4.55	9700	neg.	-	5	Unsuccessful.	
4313	M	47	Miner	0	0	0	++	0	0	0	0	0	9	0	2	Tumor upper left	-	necks glands Ca. Prob. S.C.C.		-	-	-	4+	Aponia vocal cord paralysis	10	Condition did not react to anti-syphilitic treatment.	

Table III Carcinoma of Lung - Parenchymal Type.

For Key see Previous Table.

CASE NO. 1

Clinic No. 564226, Mr. S. L., aged 40, a farmer, came to the Clinic in August 1926, complaining of chest trouble of sixteen months duration. In the April of the previous year, while in apparently good health, he had a sudden haemoptysis - not severe - followed by a period of coughing, fever and slight weight loss. He recovered rapidly but retained some cough, which later became productive of sputum. In January - i. e., eight months before admission - he took a definite illness diagnosed as "flu" in which he was laid up for three months in bed, raised abundant sputum and had a pleurisy drained. Since April he has almost completely recovered, having only occasional periods of mild fever but with constant cough, often blood-stained and always productive. He is twenty pounds below his normal weight. On physical examination the whole right base was dull. He showed no leucocytosis. The radiologist reported "an infiltration at the third to the fifth spaces, probably old abscess with calcification." On account of the suggestive history the patient was bronchoscoped and the finding was noted as a "typical epitheliomatous lesion of the right main bronchus", the pathological findings being a "Grade IV Epithelioma" in the biopsy section. Patient was advised to have x-ray treatment which he elected to have elsewhere. He wrote in January 1927, saying that he was still keeping apparently as well as on examination.

The x-ray film shows an obvious definite hilar mass centered at the hilus and with radiating prongs into the lung substance. Below this there is an appearance of vague irregular densities that one associates with bronchiectasis. I think that this represents the actual tumor growth with considerable scirrhus effect as one would expect after a sixteen-months history, and causing only partial obstruction and hence a bronchiectasis rather than an atelectasis. This tallies with the history of recurrent fever, even though the present condition shows no leucocytosis.

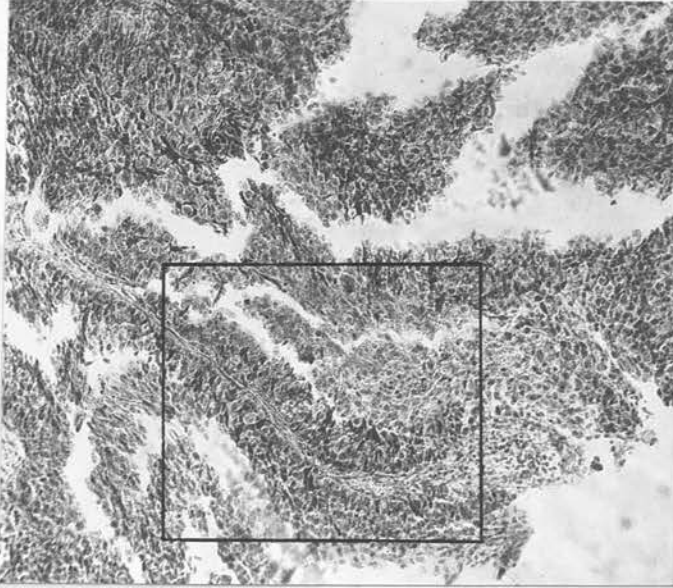
The microscopic section is from a very small fragment, but it shows a fairly extensive infiltration with cancer cells, and in this particular piece not as much fibrosis as one would have expected to fit the history. The malignant cells are in a somewhat "squamous" arrangement but of themselves very squamous like, some even showing prickles - difficult to bring out in the micro-photograph - but no keratinisation. There does not appear to be any great degree of infiltration with inflammatory cells.

Case No. 1

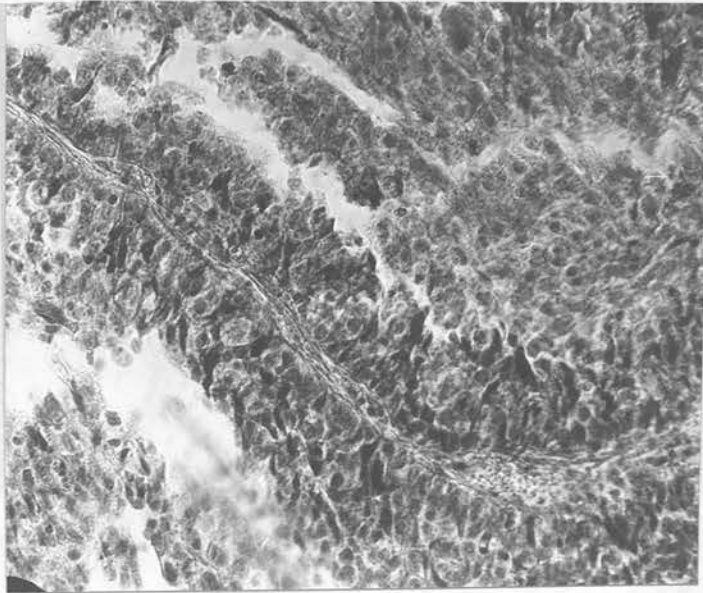
Clinic No. 564226.

Microphotographs from Biopsy Section

Epithelioma Grade IV



A. Low Power: x 60. Note the papillary arrangement of the malignant cells.



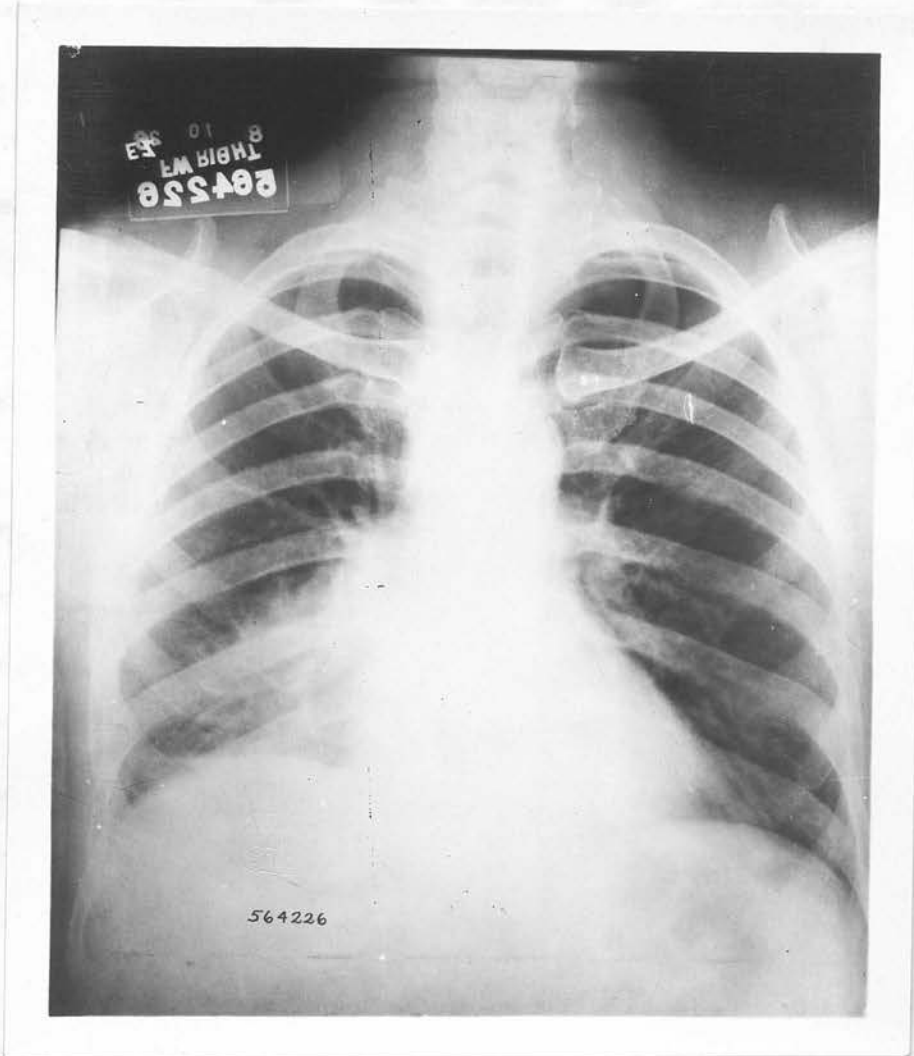
B. High Power: x 120. Section from area marked on low power section.

Case No. 1

Clinic No. 564226

Reduced Print of X-Ray Film

Epithelioma Right Main Bronchus



Case No. 2

Clinic No. 555012. Mr. L. C., aged 48, at present a laborer but up till 8 years ago a miner, first came to the Clinic in June 1926, with a vague complaint of loss of weight and strength and some dyspepsia, and chronic cough of 2 years duration. Physical examination showed a negative chest but a leucocytosis (15,300) and other evidence of a low grade fever. X-ray then showed a pneumoconiosis and a bronchiectasis of the lower left lobe. The clinician suggested a malignancy of lung but considered history too long and patient was not bronchoscoped. He went home as an indeterminate case of low grade fever. There were four T.B.C. negative examinations of the sputum.

Patient returned to the Clinic in August, feeling better, sleeping better, and without fever. He now suffers from attacks of pain in the chest lasting about 4 days at a time. The leucocytosis had disappeared but x-ray of the chest showed "a localized abscess at the hilus" and it was decided to bronchoscope. Bronchoscopy revealed a localized, in appearance typical, epithelioma on posterior wall of right main bronchus. Biopsy from this showed a squamous celled epithelioma, grade III.

The x-ray film of the first examination shows, knowing the subsequent findings, a just perceptible hilar mass with radiating fibrosis throughout the lungs typical of a rather harsh type of pneumoconiosis and in the lower right base the irregularly mottled, fan-shaped density of a bronchiectasis.

The later film shows a dense localized hilar shadow with radiating strands, distinguishable from the pneumoconiotic fibrosis. The bronchiectasis is less prominent.

In considering this from the point of view of abscess differentiation the distinguishing point lies in the marked absence of definite edge and the slight line of separation from the mediastinal shadow. This film I consider as my most typical one in the group. The density is of interest considering the length of the history.

The microscopic section shows a highly cellular tissue with cells arranged in very irregular clusters strongly resembling a typical skin epithelioma. Quite a number of the cells show keratinisation and as will be noted in the micro-photograph, cell nests are frequent. This very decided metaplasia raises the question as to whether it is in any way related to the chronic irritation of the dust disease noted: This is the only pneumoconiosis in the group and the only section showing such decided epithelial differentiation.

Case No. 2.

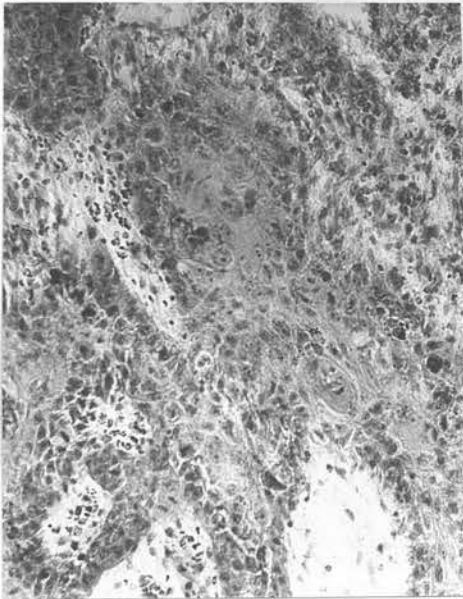
Clinic No. 555012.

Microphotographs from Biopsy Section

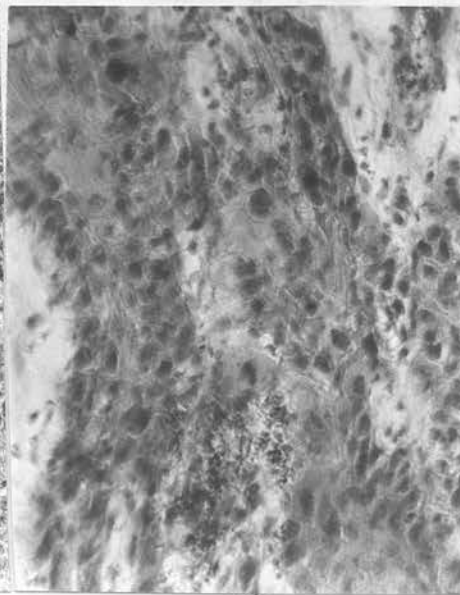
Squamous Celled Epithelioma Grade III



A. Low Power: x 60. Note the extreme cellularity of the tissue and the extraordinary number of epithelial cell-nests.



x 120



x260

B. High Power: These sections bring out the marked cellularity and the squamous type of cell constituting the growth.

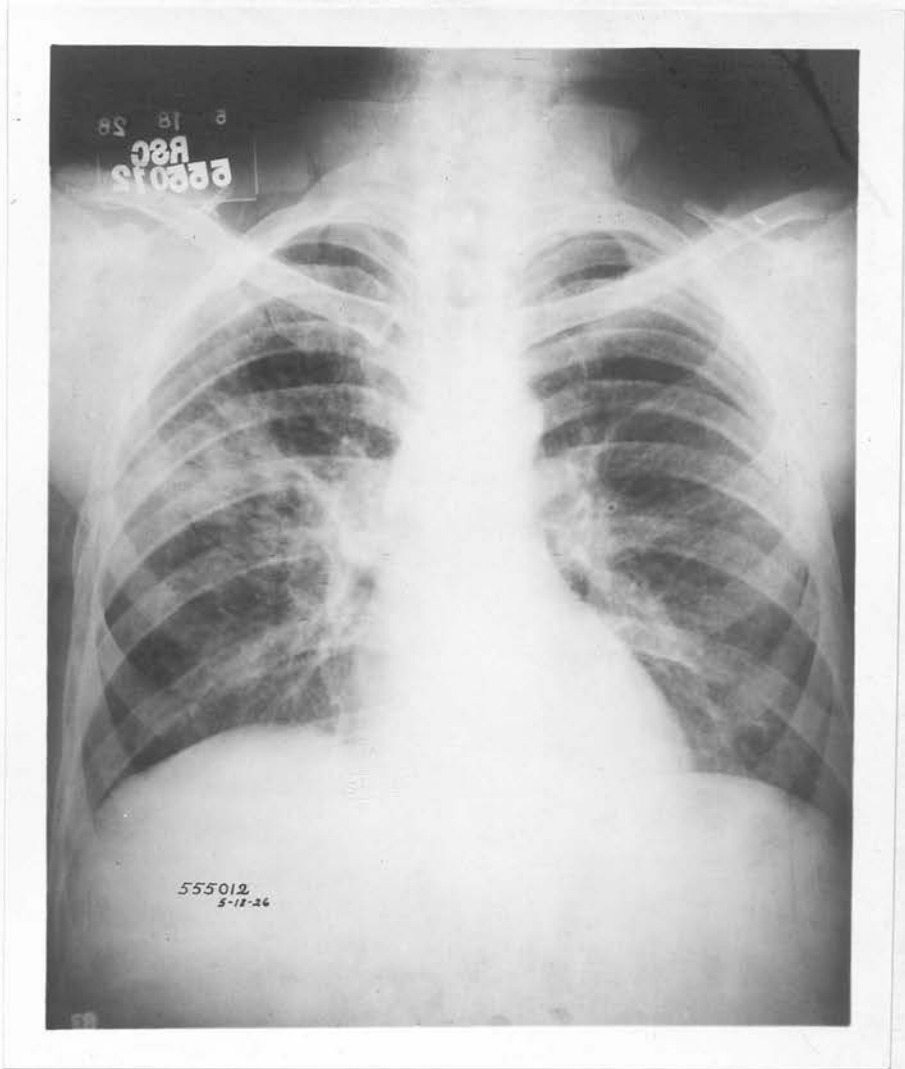
Case No. 2

Clinic No. 555012

Reduced Print of X-Ray Film

No Lesion Noted

Taken June 1926.



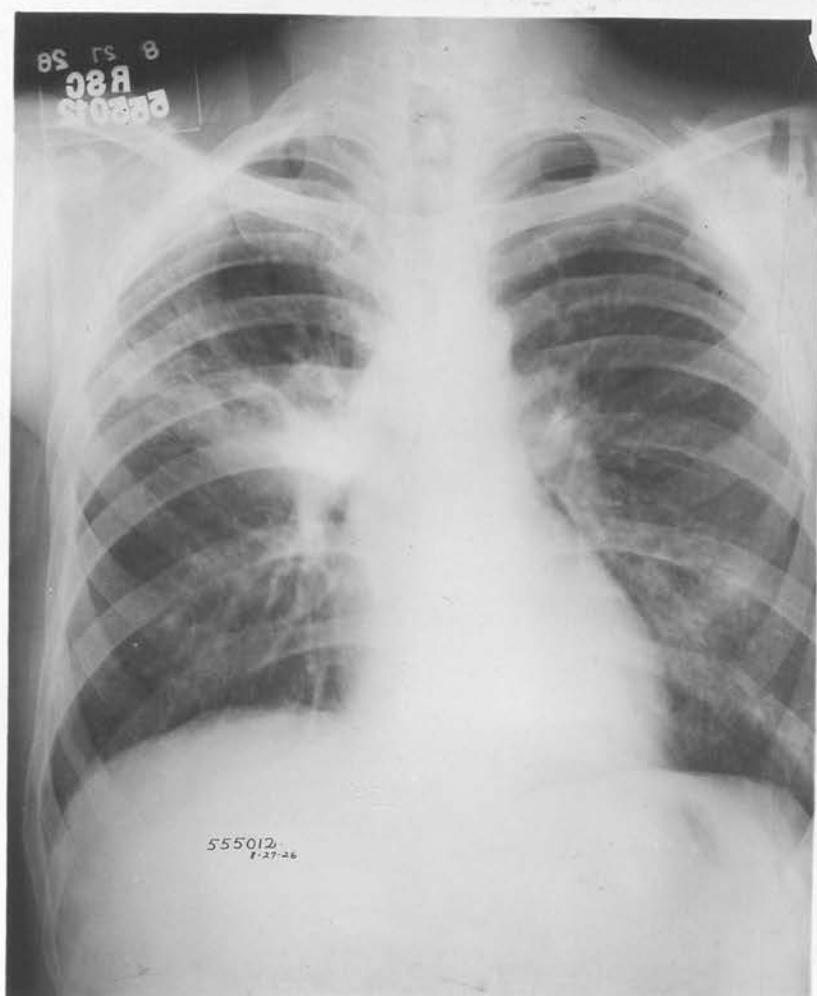
Case No. 2

Clinic No. 555012

Reduced Print of X-Ray Film

Epithelioma Right Main Bronchus

Taken August 1926.



Case No. 3

Clinic No. 574429. Mr. O. L., aged 29, a farmer, came to the Clinic in October 1926. He gave a history of four months of hard, constant cough, with at first traces of blood but very little real sputum. Two months ago he began to bring up definite quantities of blood (teaspoonful to tablespoonful at a time) and ~~now~~ hemoptysis frequently. He had some dyspnoea and vague chest pain but no evidence of fever. An x-ray taken elsewhere was reported negative three months before coming to the Clinic. He had no other complaints. He had lost 30 lbs. weight.

only He was an apparently healthy man and the only abnormal physical findings were diminished sounds over whole left lung interpreted as a bronchostenosis. The x-ray was reported negative except for old T.B. scars in the right apex.

He was bronchoscoped and a soft bleeding granular lesion was found in the mid portion of the left main bronchus. A biopsy section from this showed an Adenocarcinoma, Grade IV.

A blood count of 80% . 5160000 R.B.C. and 8400 W.B.C. would seem to negative both infection and marked blood loss.

X-ray treatment was given and patient was advised to have other courses at home.

On examination of the film there seems to be a definite density of the hilus on the left side only; This is neither larger nor denser than one often sees in a normal hilus but it is not associated with a similar density in the right hilus. The whole left side is less clear than the other side but there is no heart or

tracheal displacement. I think the density is the actual lesion just after it has spread outside the bronchus but before there are any secondary results other than very mild lack of aeration due to partial obstruction of bronchus.

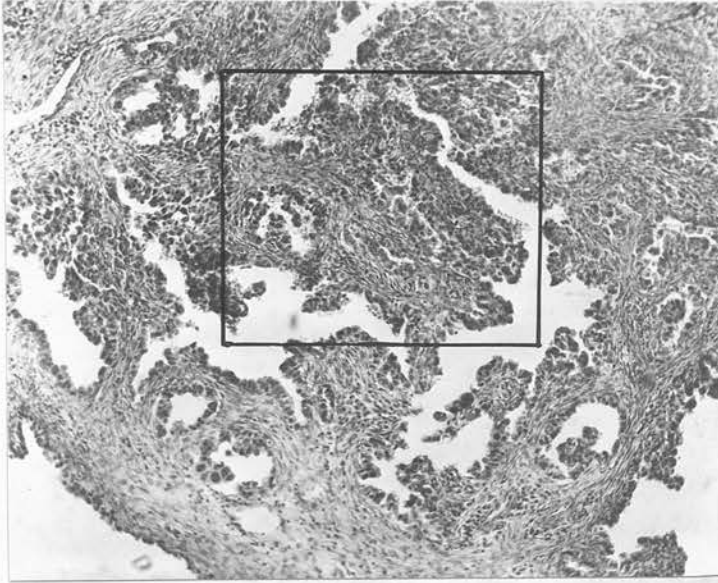
The pathological slide shows a definitely malignant tissue of adenomatous structure, with fair amount of fibrous tissue and large acinus-like spaces into which the growth proliferates in an almost papillary manner. The cells themselves are columnar and the section was extremely rich in mitotic figures. This is the only clear-cut adenomatous lesion in the group.

Case No. 3.

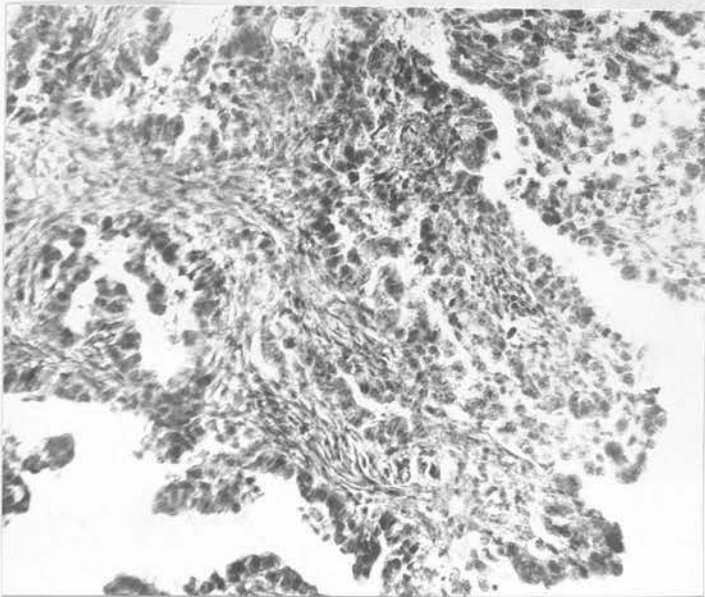
Clinic No. 574429.

Microphotographs from Biopsy Section

Adenocarcinoma Grade IV



A. Low Power; x 60. This section brings out very clearly the adenomatous arrangement and the intra-acinous papillary nature of the proliferation.



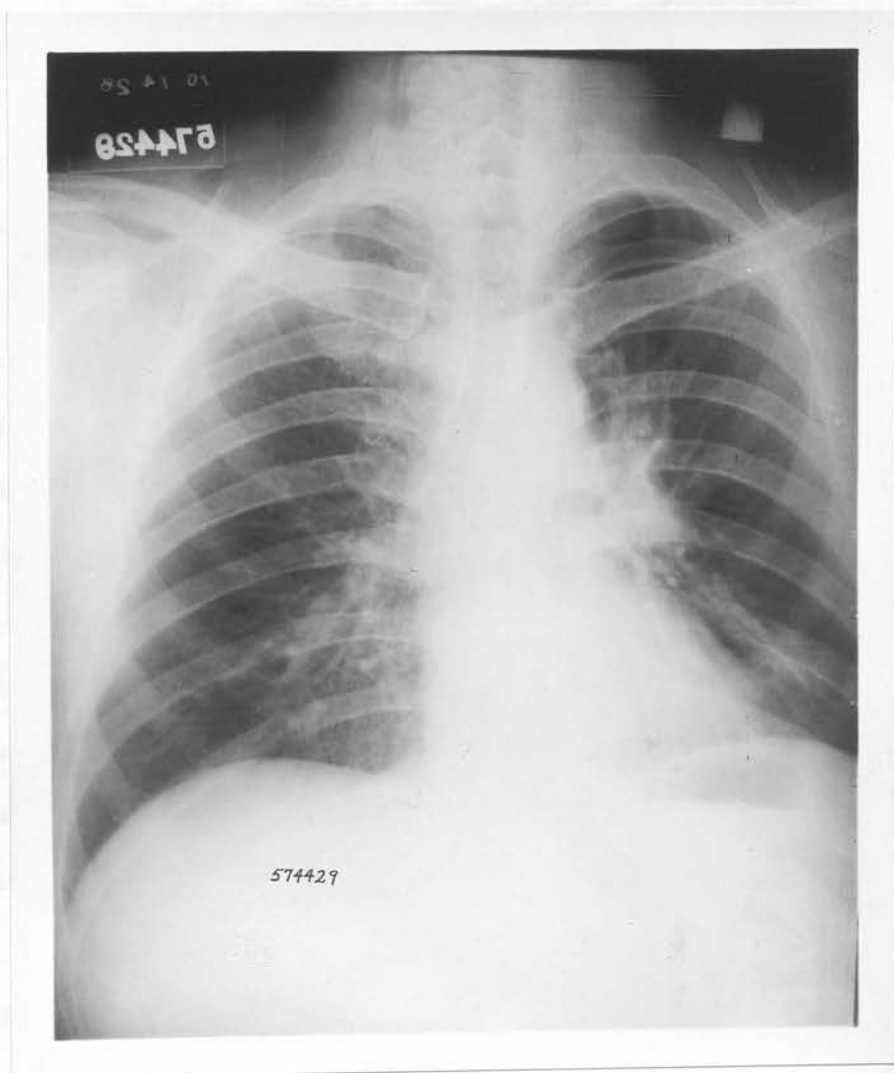
B. High Power; x 120. This is from area marked in the other section and shows the columnar nature of the cells and the moderate amount of fibrous stroma.

Case No. 3

Clinic No. 574429

Reduced Print of X-Ray Film

Adenocarcinoma Middle Left
Main Bronchus



Case No. 4

Case No. 573241. Mr. S. F., Aged 58, a tailor, came to the Clinic in October 1926. He had been in the habit of smoking 40 cigarettes a day for 40 years and when in ordinary health had a dry throat and some hacking cough. Six weeks before admission the cough became suddenly very severe and he developed pain in the chest. Very shortly after he began to cough up red blood, regularly. He ceased smoking and cough became easier and only produced blood in the mornings. Beyond that and a constant dull aching pain patient gave no helpful history. Physical examination showed flatness and diminished breath sounds in the middle area of the right chest. The blood count was not informative. One could also feel an adenoma in the thyroid gland but there were no associated signs indicative of a toxic state. The blood pressure was high 186-96. The x-ray report was "Bronchiectasis right base." The patient was bronchoscopeed on account of the history of free bleeding without apparent cause, and a bleeding point in the mid lobe bronchus, lower side, was seen. Biopsy from this showed epithelioma Grade IV. The patient was given a course of deep x-ray therapy before going home but died in January.

Both the x-ray and the pathological slide of this case, as will be seen, are unusually interesting.

The film shows absolutely no hilar density. In the lower half of the right lung there is a semi-translucent, peculiarly homogeneous area of consolidation with a sharp upper limit but

fading below, with clear lung tissue separating it from the hilus and from the periphery. There is slight increased density of the lung mottling towards the base medially, suggesting, taken alone, a bronchiectasis. The homogeneous mass taken alone seems to me to be best explained as a total atelectasis of the middle lobe due to total obstruction. It is unlike pleural because of the good lung laterally, and unlike abscess because of the sharp upper edge - which is anatomically correct for the horizontal upper surface of the middle lobe: The lower being oblique gives the fading out appearance. The bronchiectatic appearance below may be of that nature but I would rather consider that as an unevenness of density due to some collection of blood by gravity. There is no leucocytosis and no fever. This is a case where the lesion itself does not show: We have only a six week history; we are within rights in assuming that the disease has not burst the bronchial boundary.

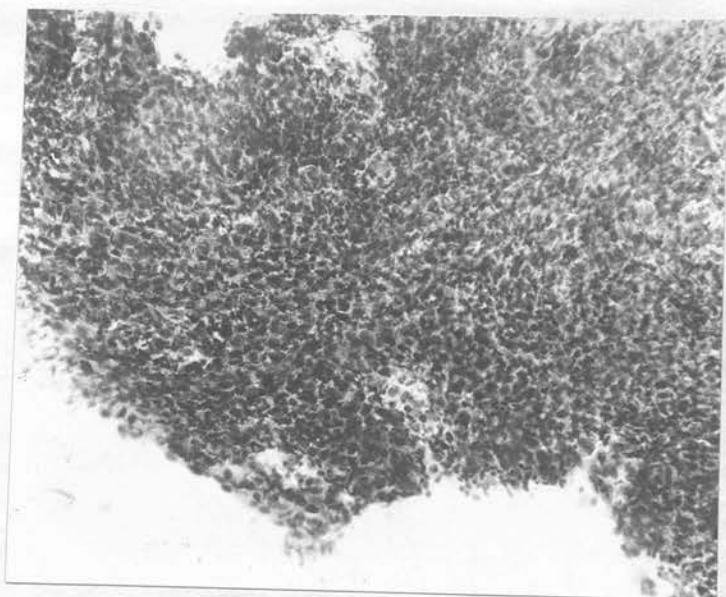
The sections showing tumor as an almost totally cellular mass with some inflammatory cells, ^{and} many lymphocytes, ~~and~~ carcinoma cells of squamous appearance, as far as differentiated at all, infiltrate this tissue in absolutely no definite type of arrangement. This is the true medullary type, which could, with lack of care, easily be taken for a sarcoma. The absence of any schirrus matches up very well with the extremely brief history. In another part of the biopsy fragment one sees an area of normal tissue, which is, apparently, covered with squamous epithelium where one would expect columnar. Is this a metaplasia preceeding cancer - due perhaps to the chronic irritation of over-smoking.

Case No. 4.

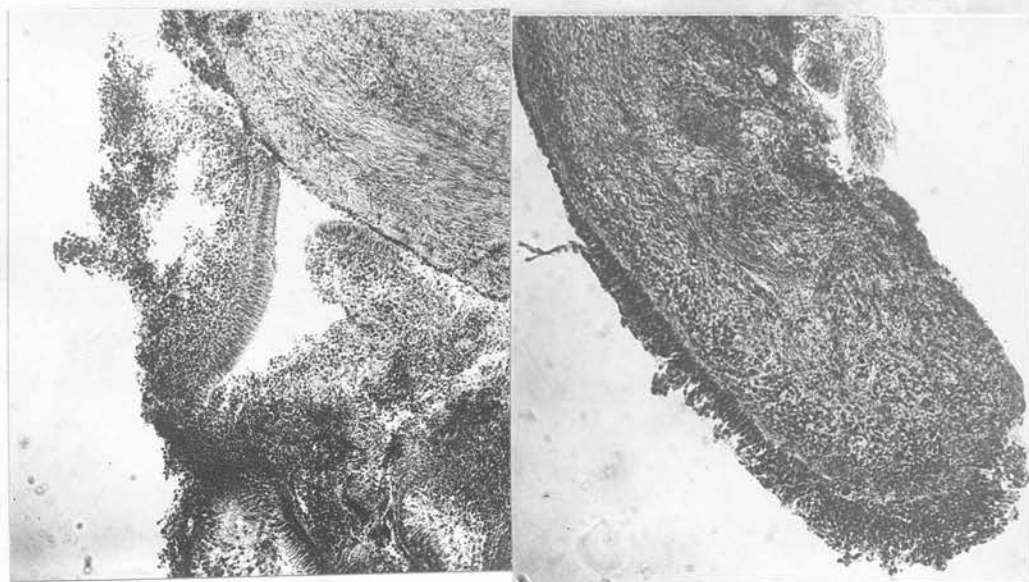
Clinic No. 573241

Microphotographs from Biopsy Sections

Carcinoma Grade IV



A. High Power only: x 120. The section shows the extreme cellularity. The photograph increases the similarity to sarcoma but in the original section the malignant cells show more distinctly.



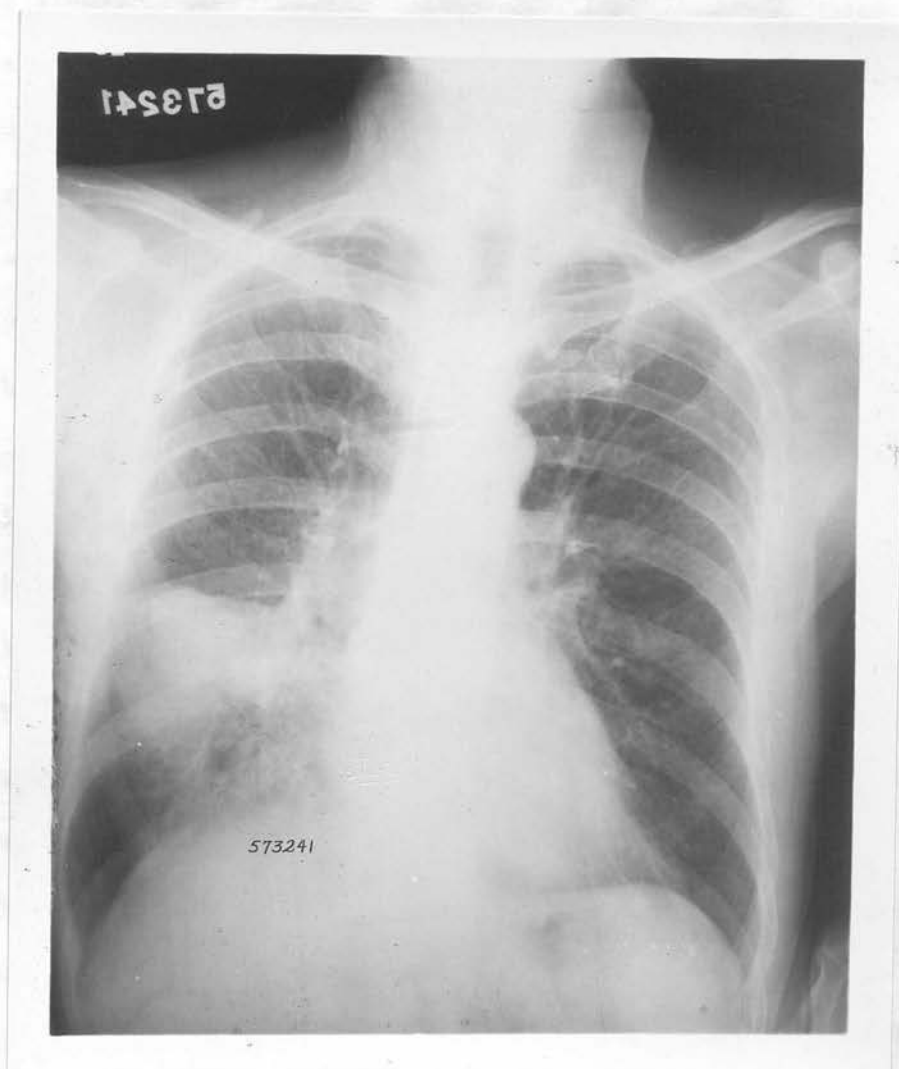
B. Low Power: These two fields are from a normal fragment of the same piece of tissue. The first shows normal columnar epithelium. The second, I think, demonstrates a metaplasia to squamous. Neither shows malignancy.

Case No. 4

Clinic No. 573241

Reduced Print of X-Ray Film

Carcinoma Right Middle
Lobe Bronchus



CASE NO. 5

Mr. L. S., Case.No. 557157, aged 63, a metal worker, came to the Clinic in June 1926. He was a Russian and history had to be taken with the aid of an interpreter. For 25 years the patient had had "winter bronchitis" cough, never bad and never showing blood. Suddenly four months ago cough became much worse, being especially severe at night, producing considerable yellowish sputum - never foul - which was often blood-stained. He had had periods of fever with some night sweats, and some dyspnoea. Occasionally he had pain in the chest after coughing. He had lost 10 lbs. weight in four months.

Physical examination of the chest revealed a definite suppression of the breath sounds to the upper right lung area. General physical examination showed presumptive evidence of Tabes Dorsalis - Argyle-Robertson pupil, absent reflexes and a strongly plus-4 Wasserman. He had a leucocytosis of 15000.

The x-ray report was "Interlobar pleurisy 3rd space right with dense area same location, possibly abscess or localized bronchiectasis."

The patient was bronchoscoped. Dr. Vinson found the right bronchus narrowed to 1/3 with infiltrating lesion, which bled easily, and with ulceration involving the posterior and lateral wall of the bronchus. No apparent opening in the right upper lobe. The biopsy section was reported as squamous-celled carcinoma grade IV.

He was sent home untreated and has not since been heard from.

With the bronchoscopic history of obstruction one would have expected to have had evidence here of an atelectasis, yet this is one of the cases which does not show that to any appreciable extent. One can only suppose that the bronchus is in no branch totally obstructed - total obstruction being required for a true atelectasis. The hilar lump is most evident, is dense and shows the typical infiltrating rays. The most obvious other explanation would be an interlobar-mediastinal empyema, but this would scarcely tend to have its base inwards, apex out, as is this. I take it that this hilar density is the actual lesion. The base here shows evidence of bronchiectasis: This fits with the leucocytosis and the abundant sputum, and confirms the suggestion of partial obstruction

The biopsy section shows malignant tissue that is fairly fibrous but with some inflam^{matory} infiltration. The malignant cells lie in irregular clusters, look of squamous type and show numerous mitotic figures. The amount of fibrous tissue hardly holds with my attempt to co-relate the amount of scirrhous with the length of history, yet it does tally with the density of the lesion as seen in the x-ray. I feel that we have here a moderately scirrhous lesion of an infiltrative type that has spread along the bronchi and into the subjacent tissue but has not fungated into the lumen, and hence has not yet obstructed as do some of the more medullary lesions at the same stage.

Case No. 5.

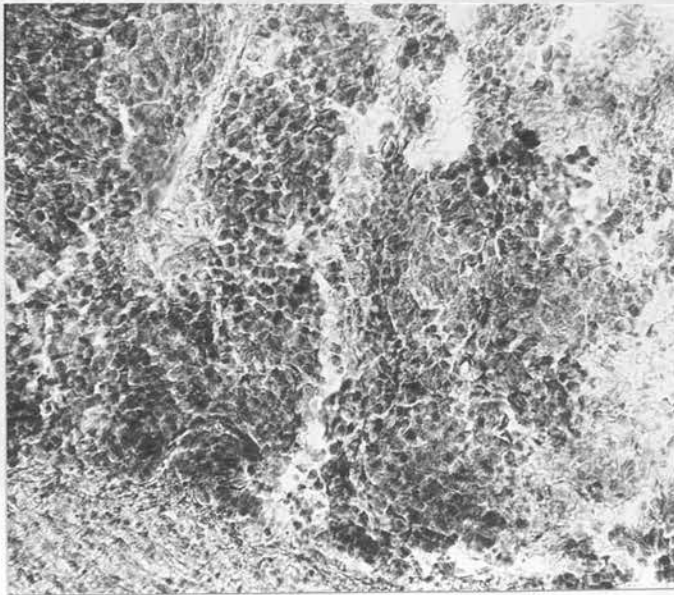
Clinic No. 557157.

Microphotographs from Biopsy Section

Squamous Celled Carcinoma
Grade IV



A. Low Power: x 60. This shows the amount of fibrous tissue and irregularly clustered arrangement of the malignant cells.



B. High Power: x 120. This is from a different field. It shows the squamous type of cell and the irregularly infiltrating arrangement.

Case No. 5

Clinic No. 557157

Reduced Print from X-Ray Film

Carcinoma Distal End
Right Main Bronchus



Case No. 6

Clinic No. 514638 Mr. W.S.D. A gas company manager came to the Clinic on July 20, 1925. He gives no history of tuberculosis or influenza and is moderately heavy smoker (5-6 cigars daily). About the beginning of the previous December he had a sudden hemoptysis in which he brought up $\frac{1}{2}$ pint of blood. This recurred twice in three days: blood loss was so severe that he was transfused. Since that time he constantly spits blood. Just following this he was laid up with acute respiratory trouble diagnosed by his own doctor as influenza and pneumonia. Since recovery from this he has suffered constantly from cough, worse in the mornings, and bringing up considerable sputum, always bloodstained and sometimes of a thick brown slough-like nature. He has no pain, and except for the one episode at onset no fever. His present complaint is of pain in the upper abdomen associated with coughing. He lost 36 pounds during the prodromal illness but has recovered some since. He has some dyspnoea on exertion but not otherwise.

On examination the patient looked definitely emaciated. Other systems were clinically negative but examination of the thorax showed clinical findings suggesting a cavity in the right upper, with some dullness and decreased resonance in the right base.

Blood-count of 64% Hb and 3890000 Reds showed evidence of some anemia. A leucocytosis of 21000 with a differential count of 80% polymorphs to 12% lymphocytes seems to indicate that there is an infective process still present.

The clinician considered Fungus Infection, tuberculosis, and malignancy, in each case with bronchiectasis, as possible diagnosis. The x-ray films were reported "Diffuse infiltration right lower lobe - primary carcinoma. Localized bronchiectasis beyond the lesion."

The patient was therefore bronchoscoped. There was free bleeding from the right bronchus; the bronchi in the right lower lobe were dilated and contained secretion and blood; the walls were granular and firm. A biopsy was taken and was reported squamous celled epithelioma Gd.IV.

The patient had radiotherapy in the Clinic but died ten months later.

Clinically the point of note in this case is the bronchiectasis: Analysis of the history would suggest in sequence small almost latent tumor, haemoptysis from surface ulceration, filling up of the lung below this by gravity, infection in this blood or blood clot, and then with recovery from the acute infection a chronic infective process, showing on physical examination, in the copious sputum, in the leucocytosis, and seen by the bronchoscopist.

The x-ray shows this bronchiectasis and slight relative failure to illuminate on that side (part bronchial stenosis) but of the actual lesion probably very little: The diagnosis must be made by having to find a cause for the bronchiectasis.

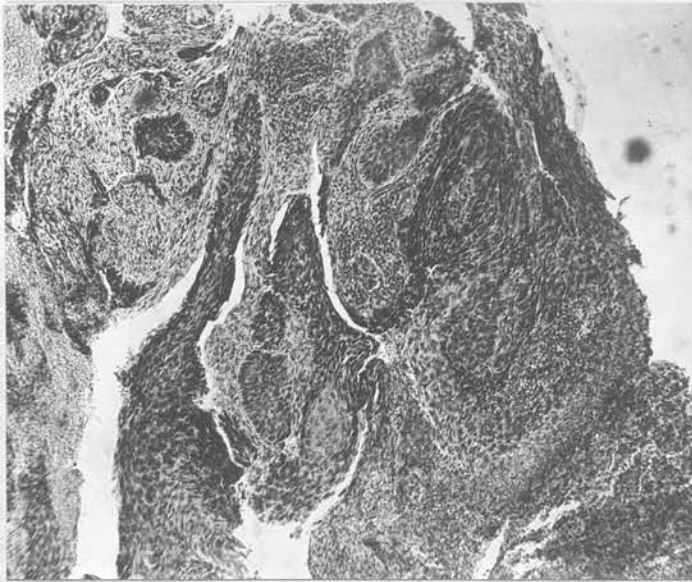
The Hopsy section shows masses of totally undifferentiated cells showing an arrangement like a skin^{Epithelioma.} There is a reasonable amount of fibrous tissue (3 month's history) and matching the history of infection, a considerable infiltration of this stroma with inflammatory cells.

Case No. 6.

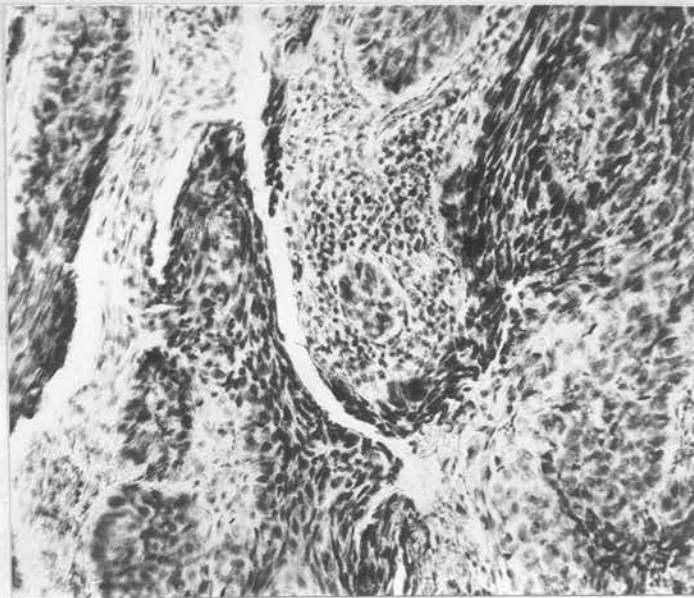
Clinic No. 514638.

Microphotograph from Biopsy Section

Squamous Epithelioma
Grade IV



Low Power Section: x 60. This section shows extremely prettily the marked degree of metaplasia possible. The whole arrangement is very reminiscent of a skin epithelioma, though there are no cell nests. Note the amount of fibrous tissue and how sharply demarcated the fibrous stroma is from the malignant groups - contrasting with Case 5.



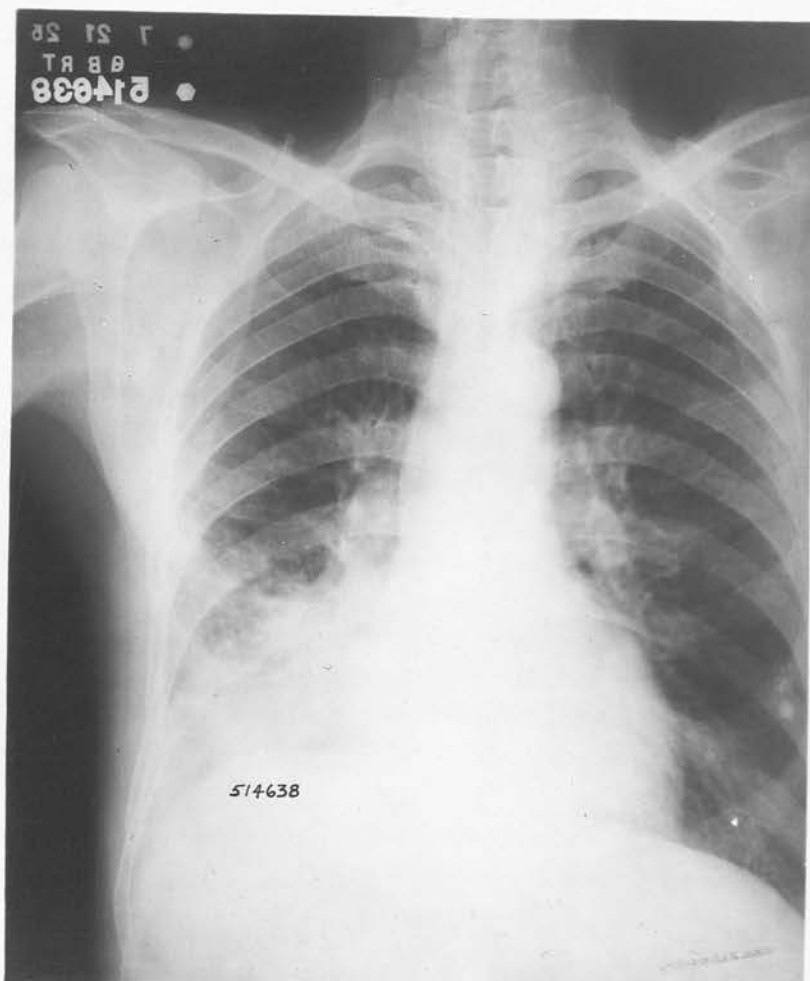
High Power Section: x 120. Further illustrating the same.

Case No. 6

Clinic No. 514638

Reduced Print of X-Ray Films

Epithelioma Right Lower Bronchus



CASE NO. 7

Mrs J. W., Clinic No. 574152, a married woman aged 41, living at home, came to the Clinic first in October 1926. She complained of cough of one year's duration. Twelve months before she took a "cold" which left her with a dry, irritative, persistent cough that has been present since. In February she had a severe attack of "influenza" (?). The cough did not become productive till June, when for three weeks only she produced greenish yellow pus that her home doctor found negative for T. B. She never coughed blood. She has pain only with severe coughing. Never fever recently. On physical examination the right chest was found flatter than the left but moved on respiration. Tubular breathing and some increase in fremitus was also noted. There was a hard gland (walnut size) in the right supraclavicular region. The film was reported as thickened pleura upper and middle lobe, probably abscess. Bronchoscopy was done and the right main bronchus was seen to be very narrowed but not definitely ulcerated. A biopsy section was taken and showed Epithelioma, Grade III. She was sent home. She wrote in January to say that she felt quite well still and had gained three pounds. Her home doctor reports that an x-ray taken at home showed the abscess and base almost clear and antral portion more translucent with apparently an improvement from the previous films!!

The x-ray as here reproduced shows almost complete opacity of the whole lung except for a trace in the costo-phrenic angle. This opacity is moderately homogeneous but does fade out peripherally to some extent and has a definite radiating striature centering at the hilus.

The trachea shows a marked deviation to the right. Reviewing the film in the light of the known history it looks just a little too even for a thickened pleura. A lymphosarcoma would be denser. I do not think that this is tumor at all. I feel that here we have a total lung atelectasis due to a small scirrhous (twelve months history) growth practically occluding the bronchus. I would explain the improvement in the more recent x-ray findings by supposing that some degree of breaking down has occurred, relieving the atelectasis and hence altering the x-ray picture. We occasionally have similar symptom relief when esophageal cancer first ulcerates.

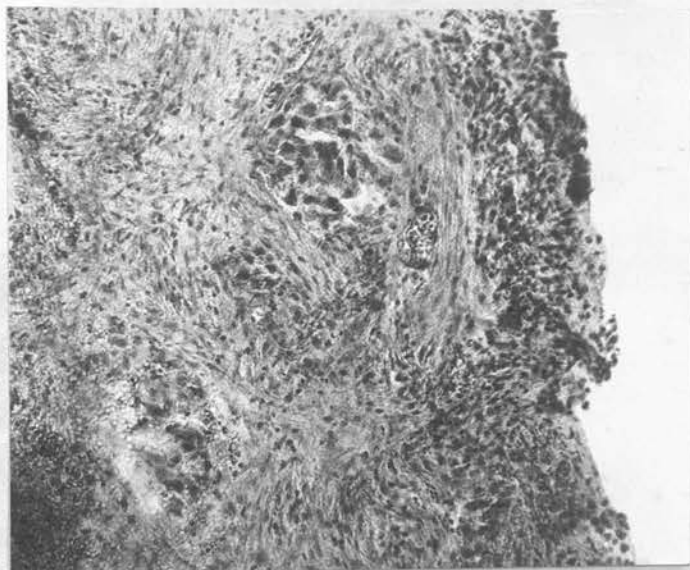
Study of the sections taken at biopsy shows tissue with more fibrous tissue stroma than in the majority. The cells are in irregular clusters and here and there we have small patches of necrosis and of hemorrhage. This fits with the longer history and with the above suggestion of an annular constricting lesion that later ulcerates, and also with the absence of increase in symptoms three months later.

Case No. 7.

Clinic No. 574152.

Microphotograph from Biopsy Section

Squamous Celled
Epithelioma Grade III



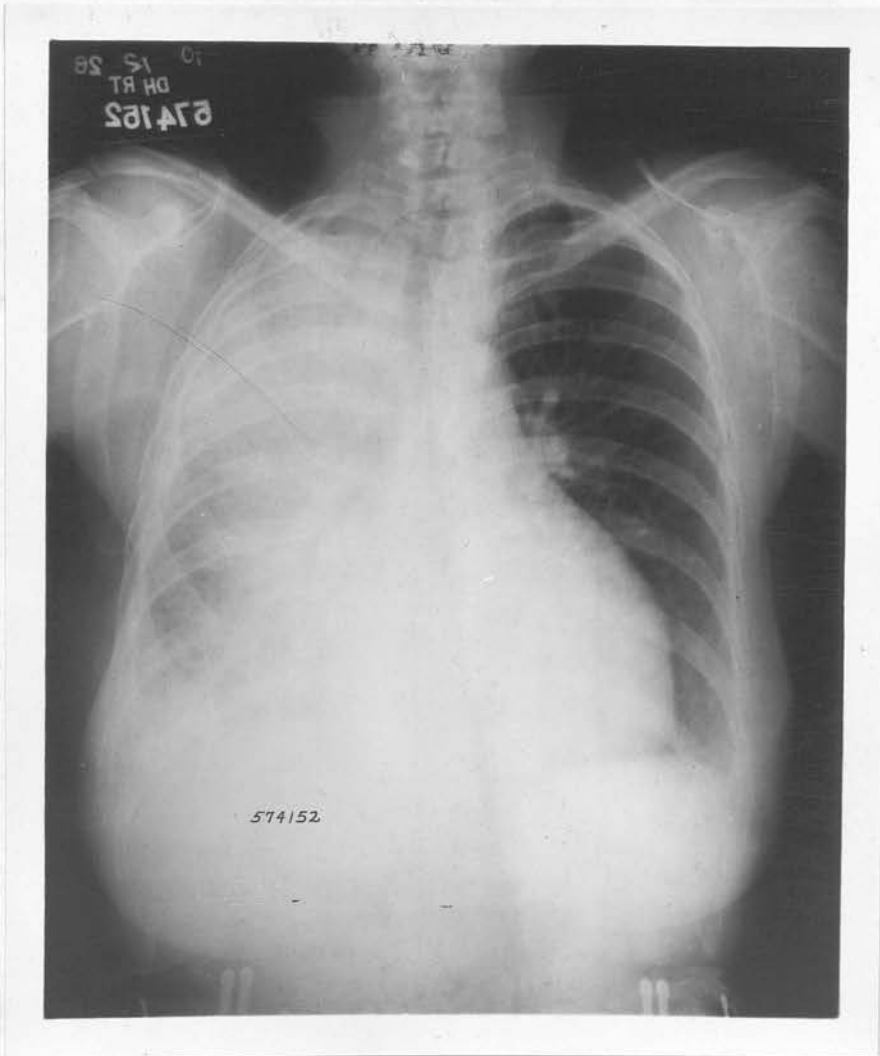
High Power only; x 120. The field shown is quite representative showing the extremely fibrous nature of the tumor with the circumscribed clusters of malignant cells and in the corner a red cell infiltrated area of early necrosis.

Case No. 7

Clinic No. 574152

Reduced Print of X-Ray Film

Malignant Stenosis Right
Main Bronchus



ROENTGENOLOGY

The literature on the subject of the Radiology of Lung Malignancy is more prolific than one would have expected for such a relatively rare lesion. I believe that I have abstracted the whole of the literature bearing on the radiological side of the question. The general impression is that the type of case used for publication is for the most part late or necropsy material with only occasional early cases and no segregated group of early cases. Hence the consensus of opinion and the typical x-ray descriptions worked out from these cases represent a later state than that represented by my group. In presenting this section of the subject I feel that the most suitable arrangement would be:

1. Analysis of the findings of previous literature.
2. Technique.
3. Attempt to establish from my own group of proven cases an earlier picture.
4. Review of a series of "probably bronchial" cases in the light of this.
5. Contrast of these with a small group of parenchymal tumors.
6. Discussion of the problem of differential diagnosis.

SUMMARY OF PREVIOUS LITERATURE: Radiologically, lung carcinoma fall into two major groups:

Hilar

Lobar or Nodular

These do not necessarily correspond to the like clinical groupings. The hilar groups are stated to be the commoner. Clinically a true bronchial carcinoma appears to be less common than a parenchymal tumor. The x-ray preponderance of hilar is first that all tumors rising near the lung roots will give a hilar picture, and secondly because after the early stage is passed the two types tend to blend to a common late picture, which most people have classed as hilar.

The Hilar Tumor shows a consolidation of the lung centered in the hilus, densest at the hilus and shading out into the lung tissue without definite edges, but rather infiltrating in wide strand-like processes into the healthy lung. Assman (3) showed by contrasting immediate ante-mortem rays with post-mortem findings that these processes were a lymphatic channel permeation of the same nature as that worked out by Sampson Handley for the breast.

The hilar density is the tumor itself and it gradually grows out as if to absorb the whole lobe or even lung and become indistinguishable from a lobar growth. Such a complete absorption does occur with sarcoma, but with carcinoma almost invariably secondary changes, as will be noted later, alter the picture before that occurs.

One of the characteristics of the hilar growth that has been noted by several men, e.g. Pfaler (16), is the tendency to invade, in preference, the upper lobe but always sparing the apex. The

lesion most easily confused with this growth is a mediastinal mass but this does not tend to infiltrate to the same extent, but rather to have a definite edge pressing on the lung and displacing it.

This group must inevitably include all my bronchial carcinomata.

The Lobar or Nodular group (called pneumonic by Kerley (6)) has these two main forms.

The Nodular consists, when seen early, of a localized density roughly circular, at times with satellites of much smaller size and lacking the sharply demarcated edge of the nodular type of metastasis.

The Lobar form fills up the whole lobe with a dense growth easily mistaken for a caseous tuberculous pneumonia and sharply limited by the interlobar septa, but, as Barjon (17) points out, the lesion where not infected is confined to whichever lobe it involves and the rest of the lung fields should be entirely clear, while a massive tuberculosis would seldom be so limited.

To these two commoner groups Wessler (5) adds a type which is probably rare. This takes the form of a very increased density of the whole ramification of the bronchial tree markings, as nodular strands like a pneumonitis, but without a central hilar mass at all. Wessler suggests that this is a squamous surface type of growth, spreading superficially along the bronchus and bronchioles but not erupting through their walls.

Other types described

Miliary or carcinosis by Assman (3)

Multiple nodular by Holmes (7) Carman (1)

Cavernous by Kerley (6)

do not appear to me to be justly called "types" of lung malignancy. Both miliary and multiple are local metastatic results, while cavernous is merely a central necrosis.

Unfortunately these two pictures do not make up the usual "typical picture" of lung malignancy as by the stage at which the cases have as yet been discovered and published other processes have taken place. Such secondary processes fall into four groups:

(1) Stenotic

(2) Infective

(3) Pleuritic

(4) Metastatic

Stenosis: This may result from either a bronchial growth obliterating the lumen of the bronchus or from a parenchymal growth so bulging in the wall as to close it or, later, by erosion of the wall and fungation into the lumen. In the absence of infection such stenosis will cause an atelectasis of the lung. The importance of this has recently been stressed by Golden (8) who points out that, unlike other secondary results, this may be an early sign or even a first sign. This I hope to be able to bring out also. With uninfected atelectasis the air is absorbed in the isolated tissue and local collapse occurs. The same appearance has been noted by Manges (9 and 10), in Chevalier Jackson's clinic, from foreign body totally obstructing.

Radiologically one finds an area of "consolidation" following anatomical lung markings, with a peculiar, semi-opaque, very homogeneous appearance, unlike tumor or pneumonia in that one can still just trace the bronchial tree structure through the "consolidation". If a large amount of lung is involved we get associated elevation of the diaphragm, relative collapse of the ribs, and tracheal and cardiac displacement to the side of the lesion. With smaller areas of atelectasis the rest of the lung compensates and no such signs are seen.

Pyogenic Infection: This is the most frequent secondary result. It may appear as a bronchiectasis, a pneumonitis or an abscess.

Bronchiectasis arises from partial obstruction of a bronchus. At first it will give the typical appearances of bronchiectasis with its fan-shaped area of irregular densities and somewhat "bunch-of-grapes"-like masses. (Moore (11)). The infection does not necessarily remain localized, however, and large areas of lung tissue will become infiltrated with a pneumonitis which may give a variety of x-ray appearances and in which the actual lesion is absolutely lost in the inflammatory densities.

Abscess, if single, is probably peculiar to a lobar or parenchymal tumor. In its formation there will be first a true necrosis of tumor tissue (a condition that even at this stage gives the x-ray appearance of abscess) with later opening of this to a bronchus and inevitably infection.

Pleurisy: This is a frequent accompaniment of lung carcinomata. The true malignant effusion is characteristically blood-stained and non-purulent and has a most marked tendency to refill after tapping - so much so that when one taps to allow an x-ray to be taken of the underlying lung this must be done within the next few hours (Thomas, etc. (13)). Radiologically this effusion gives the typical x-ray appearances of a free fluid. It should always be a rule to tap any such fluid before giving any opinion from the x-ray as to the condition of the underlying lung. LeWald (14) even suggests replacing the fluid with air as an aid to a diagnosis.

The origin of the fluid is a moot point. It is seen even in purely hilar lesions. Engelbach (15) has noted that it is always preceded by a simple effusion. Any abdominal cancer associated with ascites is inoperable (except perhaps hepatic obstruction ascites). Does pleurisy in the lung similarly indicate that the lesion is beyond surgery - even when surgery becomes possible? I am inclined to believe that this is mostly so and that, properly speaking, we will have to consider pleural effusion as a lymphatic permeation metastasis, and look on it as indicative that the lesion has ceased to be early. There probably are, however, both true obstructive pleurisies due to occlusion of the bronchial lymphatic system and reversal of the normal lymph flow, and infective pleurisies associated with other infective results of malignancy. But these types on tapping will show their own particular effusions - transudative or purulent - and not the sanguinous pleurisy of malignancy.

Metastasis: In the clinical discussion we noted the supra-clavicular glands as a common site of early metastasis that might often be just what was needed to clinch a diagnosis. So too, here, we often find that the x-ray picture is altered by such glandular extension of the lesion. Pleurisy results from retrograde permeation. The natural drainage is towards the bronchial root glands and thence up the mediastinum. Thus we may, for instance, see an upper mediastinal thickening due to secondary glands, the whole lesion resembling a Hodgkin's. Or we may get bronchial root glands involved from a parenchymal tumor, thus simulating a hilar tumor.

The lungs themselves are a common site of metastasis for most malignancies. And so also here; and the picture of a primary carcinoma of the lung may easily be obscured by multiple metastasis in the other lung or a bronchial carcinoma not noted in the picture of a true miliary carcinosis.

Not only do we have such blood spread, but I think we must suppose from the frequency with which we find local metastasis around a lung lesion that there is an implantation spread of the lesion by aspiration from the ulcerative surface of a primary lesion. This frequency of local metastatic-like spread is extremely frequent and is emphasized by the majority of the writers, or is classed as a separate type - Multiple Nodular - and certainly is one of the characteristics that is simulated by no other lesion, hence the emphasis on this as a diagnostic point. One notes too that such nodules tend to lie peripheral to the primary lesion.

Or, again, the clue evidence as to the nature of a pathological lung picture may be found in metastatic bone involvement of the ribs or spine.

But these are all late effects and must be regarded in the same light as we now regard a cervical carcinoma that has infiltrated the broad ligaments and invaded rectum or bladder or shows palpable sacral glands - in other words, as a case that has been missed.

Can we establish an earlier picture - suggestive even if not pathognomonic?

TECHNIQUE

While scarcely rash enough to say that the technique is unimportant, yet I do not think that one needs to lay undue emphasis on any special method. Any routine method which takes good uniform chests with a reasonably short exposure should be satisfactory. One's object here is not to develop a method of demonstrating suspected lesions most satisfactorily, but to isolate from routine chest examinations a group of possible carcinomas before they are suspected clinically. Two points I would stress as, I think, distinctly advantageous:

Stereodiagnosis

Teleradiography

We are dealing with a hilar lesion, simulated by many conditions. The stereo film pair localizes the lesion to the hilus and cuts from the differential diagnosis all pleural and rib or chest wall densities which on the flat film will give similar appearances to the hilar lesions. So too distance films give one a better balanced view of the hilus and show rather more of it.

The technique one would recommend as satisfactory is that used here:

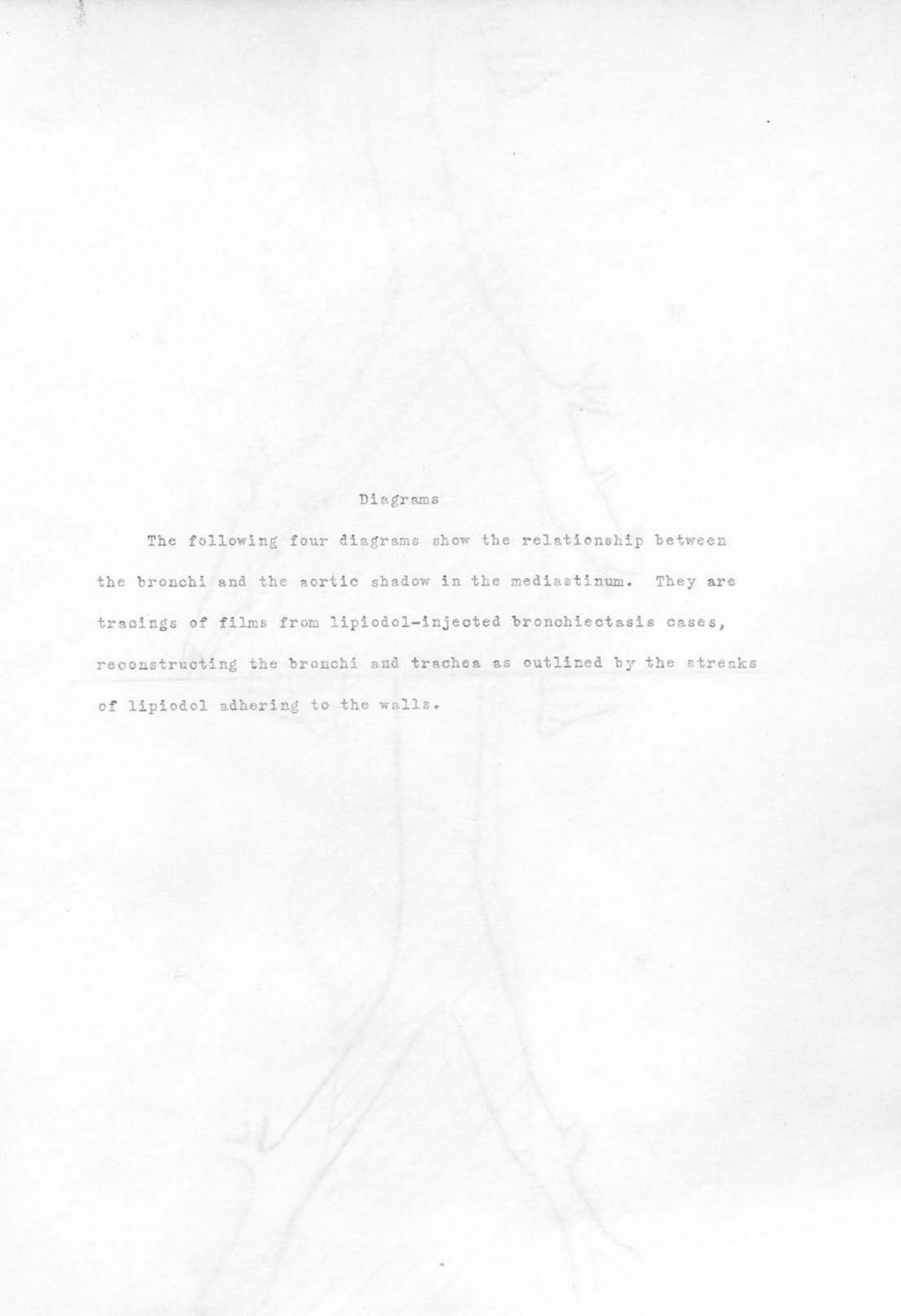
Large films are used (14 x 17) and only postero-anterior films are taken. A point of importance is to have the patient absolutely square on: The least degree of rotation will so upset the hilar balance as to give very false appearances; no diagnosis should be made on films in which the inner ends of the clavicles do not set symmetrically astride the interspinous-process line. A 6-foot (or 2-metre) distance is ample. At that a stereoshift of the tube of 12 inches is required. This is best as a vertical shift as

by moving across the rib lines the ribs are brought out better than by the horizontal shift and hence one gets a better perspective of the "cavity" of the thorax. As regards exposure, where the apparatus will carry it an exposure of $1/5$ second carrying approximately 100 milliamperes suffices. Penetration, contrary to older teaching, is not here of the same importance as in bone radiography and I think a variation of penetration to suit the stoutness or otherwise of the patient gives more consistent pictures than by varying the time for this purpose. One can use a range from about equivalent $3\frac{1}{2}$ " - $5\frac{1}{2}$ " spark gap and only add time for really heavy patients. The breath must be held best at the height of normal, not forced, inspiration. I feel that comparative inspiration-expiration films would help but there is an economic factor and I would rather have a stereo pair than a flat pair of the other nature. Where stereo is not obtainable I think an inspiration-expiration pair should be used.

THE EARLY BRONCHIAL LESION:

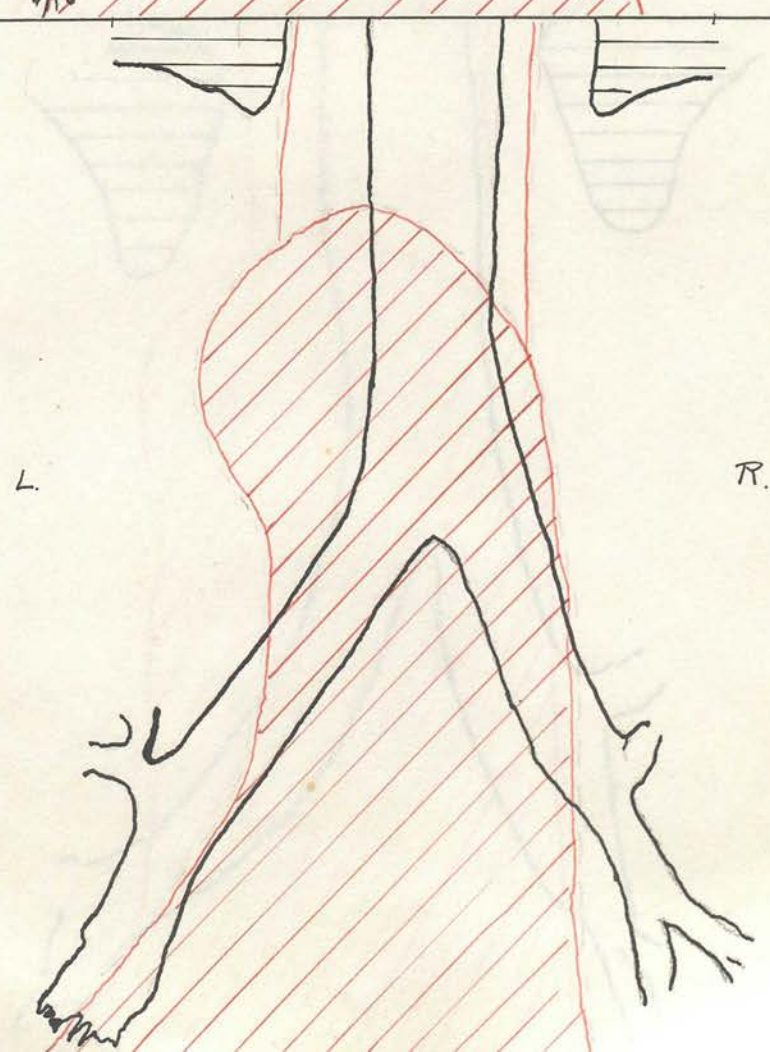
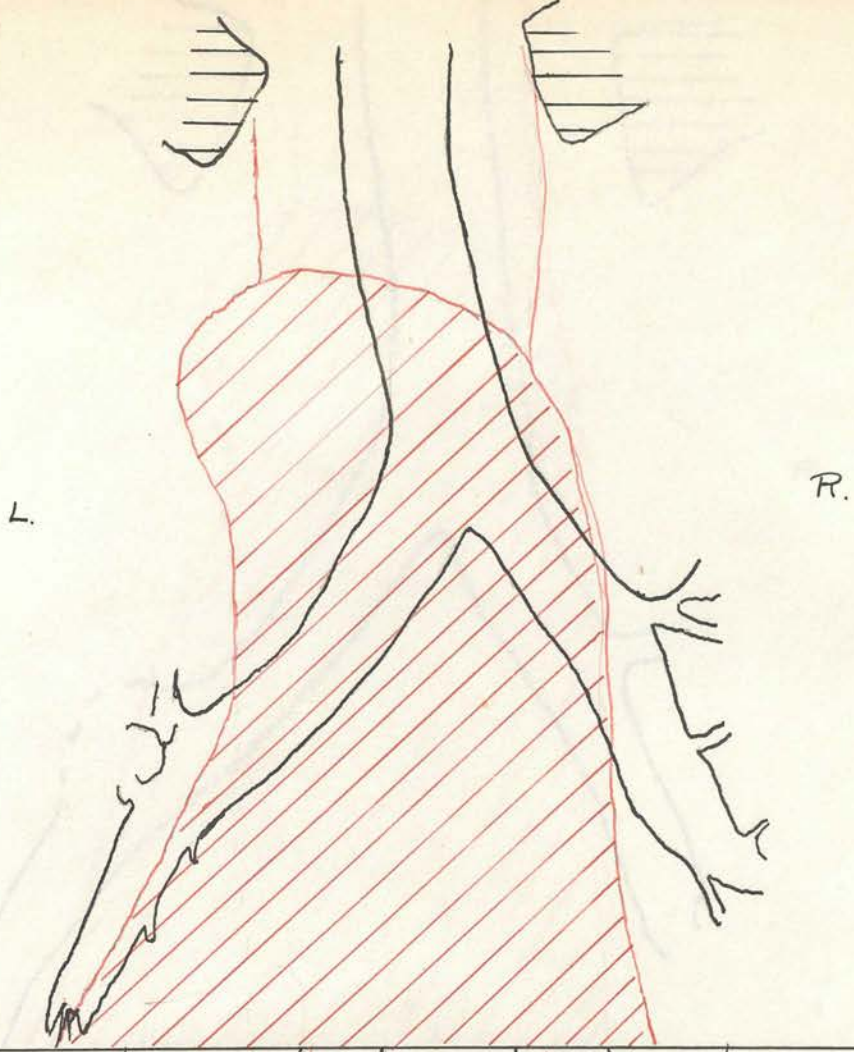
Note on the Anatomy: The grouping "Bronchial" which I have tried to segregate is a clinical entity: It might be defined as a lesion in a bronchus of such dimensions as may be reached by the bronchoscopist. As an anatomical entity this segment varies to a certain extent. Anatomically the upper end maintains a more or less constant position: It lies on the level of the line joining the manubria-sternal junction to the lower edge of the 4th L. V body. With standard technique a spinal landmark would satisfactory but in the consideration of my plates I have found that, where the air filled trachea does not show, the knob formed by the protrusion of the arch of the aorta to the left is the best landmark. In a direct A P film this will always show, and we can safely assume that the level of the bifurcation is just at the level of the lower border of this rounded knob, and being at the same depth this landmark is independent of the line of the central ray—see illustrative diagrams overleaf.

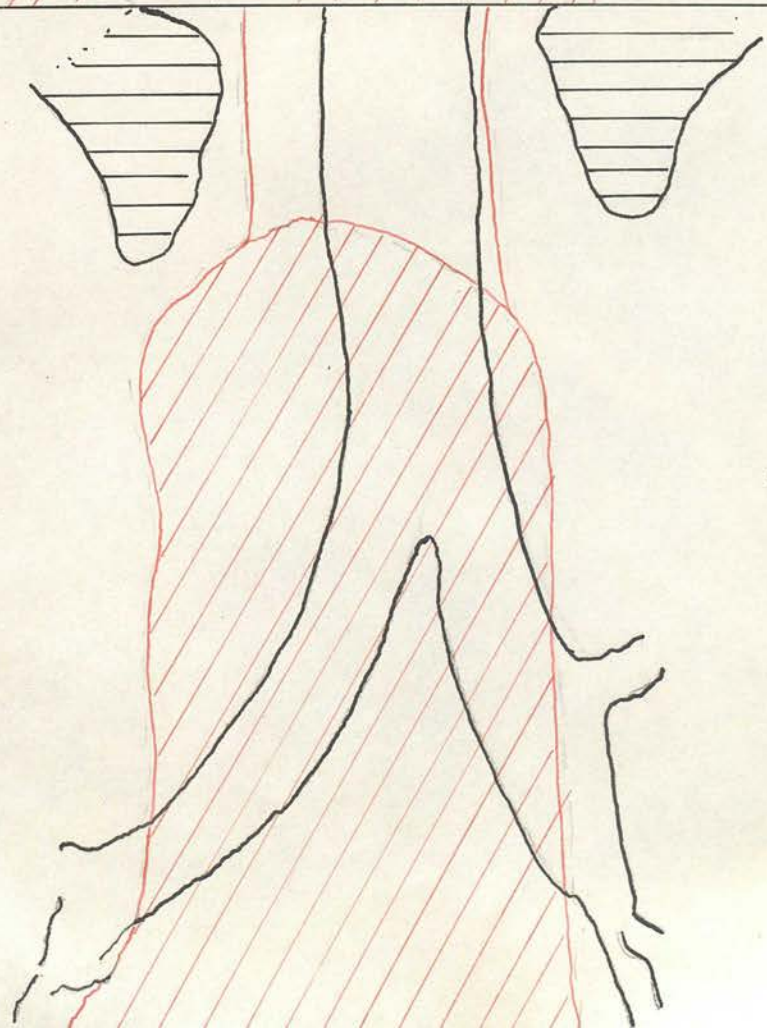
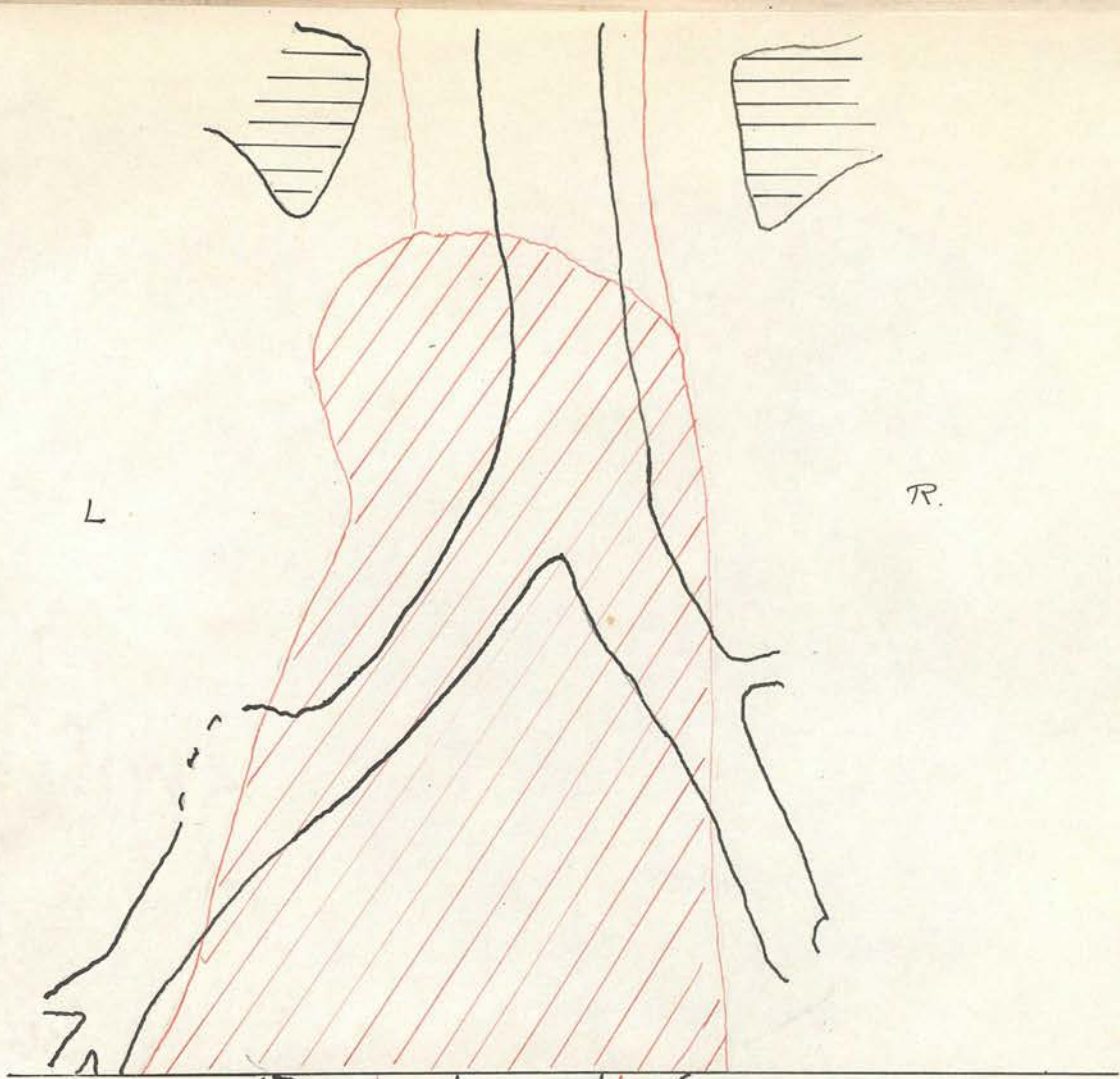
From this the right bronchus passes more directly downwards than the left, the latter, however, having the longer course. The first part of the bronchus V is therefore totally in the mediastinum. The amount of projection into the lung tissue is the variable quantity and I am using the figures on the accompanying plate to show this variation. These were culled from a large number of x-ray films of cadaveric lungs injected with opaque medium.

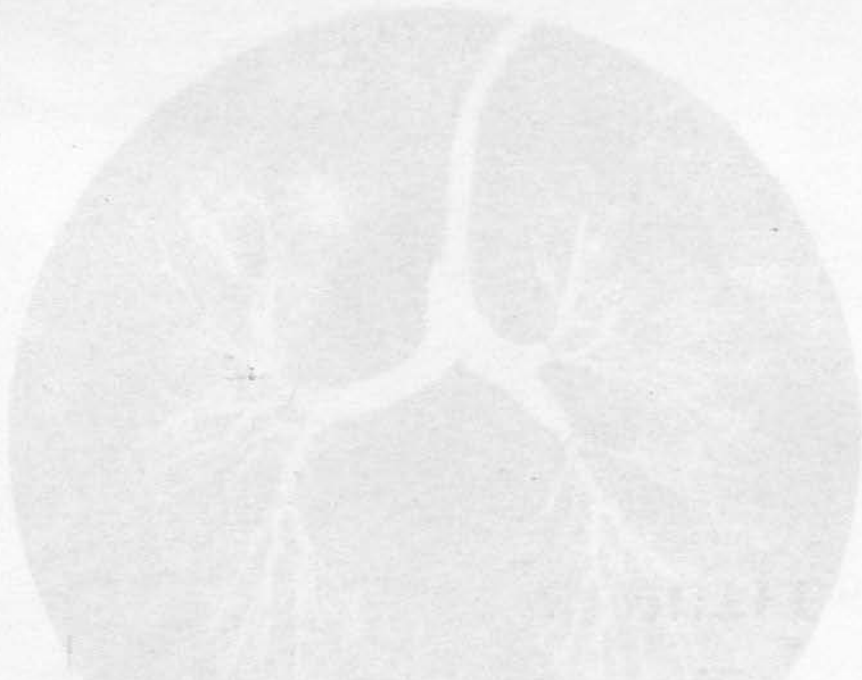
The page contains several faint, light-colored diagrams of the mediastinum. These diagrams illustrate the relationship between the bronchi and the aortic shadow. The diagrams are arranged in a vertical column, with one at the top and another at the bottom. They show the branching pattern of the bronchi and the position of the aortic shadow in the mediastinum. The diagrams are very light and difficult to see clearly.

Diagrams

The following four diagrams show the relationship between the bronchi and the aortic shadow in the mediastinum. They are tracings of films from lipiodol-injected bronchiectasis cases, reconstructing the bronchi and trachea as outlined by the streaks of lipiodol adhering to the walls.



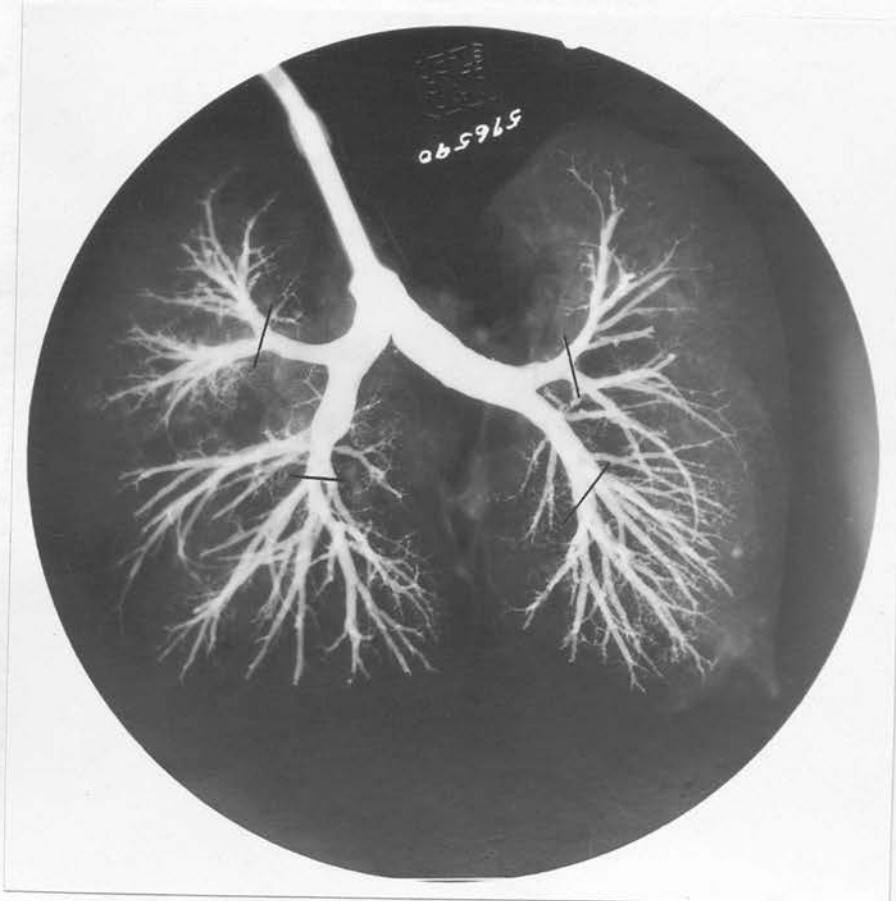
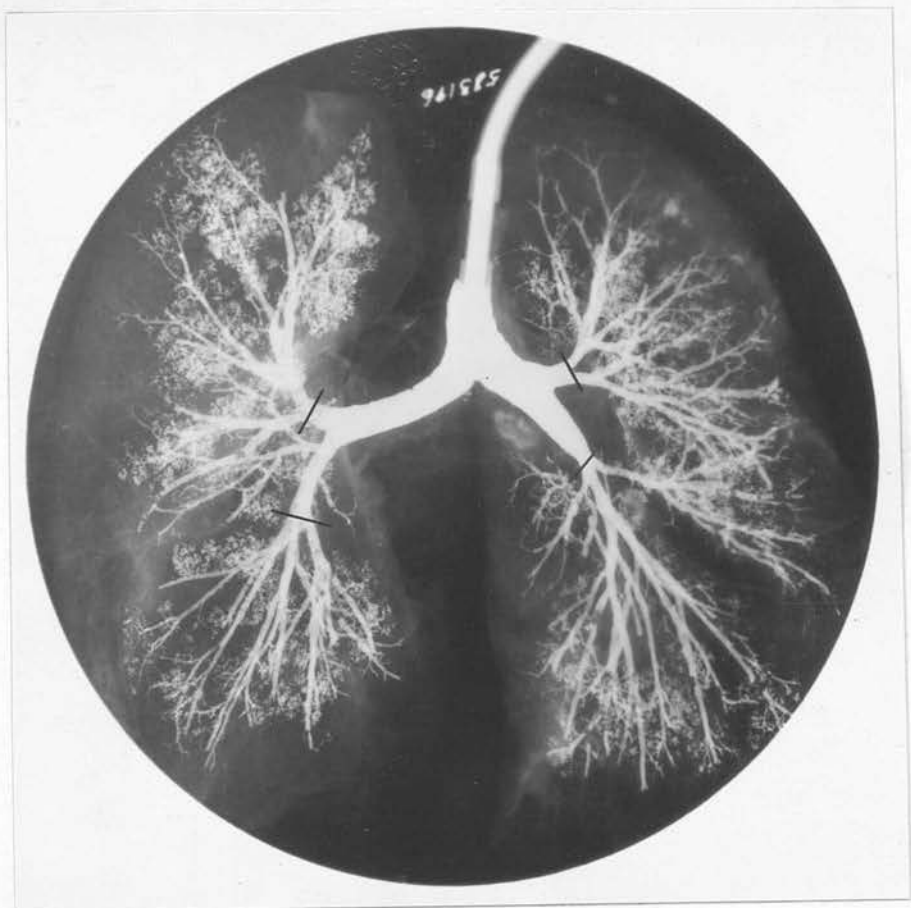


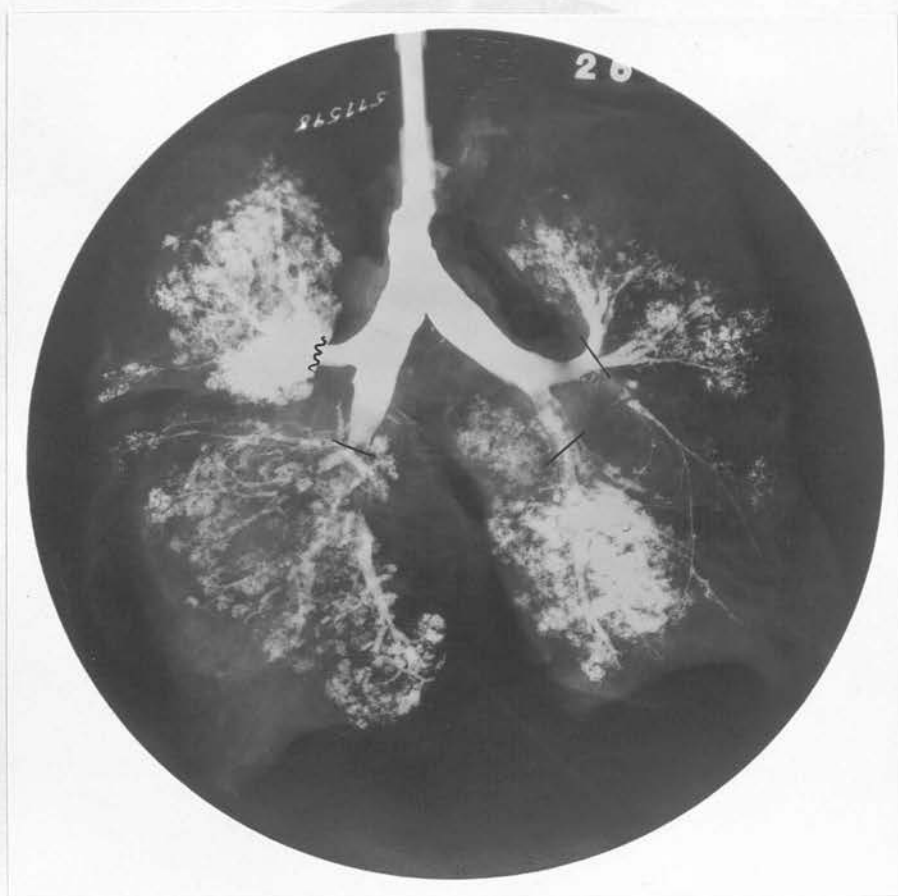
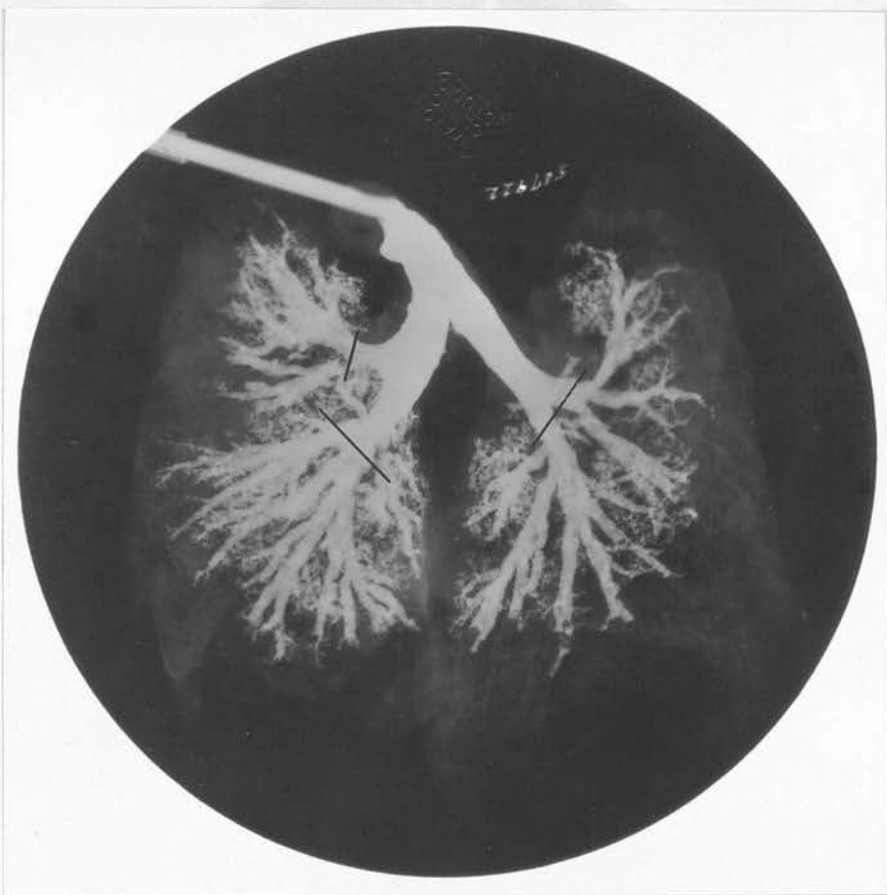


Illustration

The following prints show the variability in length of the bronchus before it breaks up into numerous branches. They are prints of x-ray films of barium-injected cadaveric lungs.









It will be seen that at times the bronchus breaks up very rapidly into numerous smaller components. Such a type will have little actual free bronchus within the clear spaces of the lung fields. Other types divide into two - or more rarely three - second degree but still quite large bronchi; this means that a reasonable sized bronchus lies quite a distance from the lateral edge of the "mediastinum" of the x-ray film.

Tracheal malignancy seems to be rare. All the carcinomas lie in this short length of bronchus. They may be anywhere in that length, but taking the bronchoscopic reports all-in-all the seat of election seems to be just about the region where the larger bronchi break up into numerous components - ? is the point of maximum irritation. As I have tried to show above, this point lies to a very variable distance into the x-ray lung "clear" space. At times the whole of an early growth will be intramediastinal and I think this explains the reason for an absence of hilar shadow in a percentage of cases. It is quoted that this condition represents a growth that has not yet erupted the wall of the bronchus. This may undoubtedly be the case with a really early lesion, but in the average case with normal length of history with symptomatology, I think the other is the real explanation.

The Characteristics of the Early Lesion: Taking the films of this group of cases altogether, can we get some sort of composite picture? I think so. The major characteristics are twofold:

I. A Hilar Density

II. An Atelectatic or Bronchiectatic Appearance

The Hilar Density is by far the more important. The literature perfectly realizes that a hilar density is the commonest lesion found but usually dismisses the subject somewhat as follows:

"Undistinguishable from any other hilar enlargement"; and therefore we presume "undiagnosable". While this is partly true, I feel that the question does not need to be so easily dismissed.

The X-ray Department of the Mayo Clinic has a principle which I have seen practiced nowhere else, that the radiologist best assists the clinician by making his ^{first} interpretation of the film without any history. In gastro-intestinal diagnosis Carman has reduced this diagnosis to such perfection that when the clinical history disagrees, the clinician, not the radiologist, has to think again! Ultimately with the progress of radiology the same perfection must be achieved for chest diagnosis.

I admit, however, that I have been disappointed in trying to establish an appearance that is peculiar to the hilar density of bronchial carcinoma, irrespective of the history. It can be simulated as I will show later, by other hilar enlargements but I think it has some particular characters and that no such particularized hilar lump should be dismissed as not malignant, except in the face of a clear history.

In my seven cases we have a hilar density in four, none in two and, if present, concealed by atelectasis in the seventh. Taking this as $4\frac{1}{2}$ in 7, we have an incidence of definite hilar density in 60 per cent of cases. Cases 4 and 6 lack it, and case 7 is neutral.

What are the particular characters of the malignant lump?

Hilar thickenings are very common. I investigated a very large number of films to pick out cases showing such thickening and the important distinguishing point is that 90-95 per cent of such densities are bilateral. These four films all show hilar densities on one side that are not present on the other. Other lesions with this unilaterality are not so common as to swamp the malignancies.

The density varies. Cases 2 and 5 are what I would like to consider as the typical picture. Case 3 is a softer lesion but none the less a definite unilateral lump. In shape the lesion is very roughly triangular, apex out. It has no clear-cut edge but throws out strand-like processes into the lung tissue, along the normal bronchial tree markings. Further it tends, while early, to have its point of central density just perceptibly demarcated off from the mediastinal margin. With growth, of course, it expands from the hilus, both into lung tissue and medially into the mediastinum obliterating this point of distinction. Even then, however, it remains centered at the hilus.

The site of the density is a fairly constant factor. It lies opposite the space between the 6th and 8th ribs with an average at the 7th rib posteriorly. In other words, it always occupies the hilus and the whole hilus; even a short distance off the hilus and you have a parenchymal lesion that may easily fail to give you the early symptoms and the bronchoscopic proof.

Atelectasis: This is the second characteristic but it is not so constant. It is, however, of great value for those intra-mediastinal lesions noted above. Two of these cases, cases 4 and 7, show clear forms of this. Case 4 shows a mid-lobe atelectasis, case 7 a total atelectasis. Both have the smooth homogeneous

density, anatomically limited, and carrying normal lung markings, that is typical of atelectasis. They are not diagnostic of malignancy but they are almost diagnostic of organic broncho-stenosis, for which a cause must be sought.

Apart from clean-out atelectasis such as these, we have two cases in which the probability is that the basal densities are partly atelectatic. These are cases 1 and 6. Of the cases definitely lacking atelectasis two are the denser hilar densities noted so that every one of the cases shows one or other of these two features.

The diaphragmatic and tracheal displacement factors of an atelectasis we have noted already. These are well brought out by case 7.

Bronchiectasis is the other feature. Three cases, 1, 6, and possibly 4 also, show the mottled fan-shaped density of the costo-phrenic angle typical of bronchiectasis. In case 6 the history showed this to be a real bronchiectasis. Moreover, this case has no hilar lump at all: It must diagnose as a "bronchiectasis" and if to be discovered will only be so by having to find a cause for that, in the absence of previous inflammatory disease.

The other two, with the absence of confirmatory history and leucocytosis, I believe to be a pseudo-bronchiectasis due, I think, to the collection of blood, by gravity and aspiration, below the lesion, giving a density of the blood-filled bronchial tree.

Hence an appearance of bronchiectasis, without history, is like atelectasis in being a suggestive picture.

If we really have an early lesion, there should be no other characters present. The unaffected lung must be perfectly clear; the upper mediastinum should not show thickening; we should never have an appearance as of metastasis distal to the lesion and rarely pleurisy. If we have appearances which might be taken as any of these, we must look for a larger primary lesion to keep the picture in proportion, or we must consider another lesion. For instance, a small unilateral hilar density with widened upper mediastinum should not be a malignancy with gland metastasis, but rather a Hodgkin's, or again a small hilar lump with peripheral metastasis will rather be entirely a metastatic business or we could expect a larger hilar primary.

Summarizing then, a unilateral hilar density, occupying the whole hilus, usually perceptibly separate from the mediastinum, and ramifying out into the parenchyma, especially if associated with apparent bronchiectasis or with lung atelectasis, must be checked against the clinical history before being dismissed as other than a malignant lesion. And secondly, though less easy of accomplishment, the appearance of atelectasis or bronchiectasis in an elderly person must have a cause found for it.

The "Probable" Group:

In presenting merely seven cases, even though of a lesion so rarely discovered early that seven early cases have never previously been collected, one realizes the possible falsity of the reasoning based on a small group of cases and I would, perhaps, have hesitated to present these were it not that I have also been able to collect other sixteen cases, probably bronchial; and I feel that this group almost completely bears out the findings of the other group in a convincing enough manner. All of these cases I have analyzed, for the sake of the symptomatology, in Table II. Of the sixteen I am presenting reprints of the x-ray in ten cases which I think are based on sufficiently sound evidence to be considered as good as proven. Of the ten I include four which illustrate, rather, the later stages.

On the average, as is to be expected, they are in a more advanced stage than the others if not acutally late. In none of them do we get the hilar density as an unaccompanied entity. It is present in four, absent in one only, and in the others may or may not be concealed in the atelectasis. This group, however, brings out much more markedly the incidence of atelectasis in this disease. Five cases show a pronounced type and two are suggestive. My pseudo-bronchiectasis is definitely shown in only one case in this series. This one gives a complete absence of any history suggesting a cause for a bronchiectasis, and shows no leucocytosis.

I think the most profitable way to use these cases is to take

them serially from the point of view of the x-ray diagnosis, but, as they are not proven, and can have no permanent value, give only the salient points of the clinical features; the summarized details of the histories can be seen by reference to the tables. While the prints are as good reproductions as are possible on paper, yet, as always with prints, they will sometimes fail to bring out the finer details as do the films; where this is so the reader will have to take my description of the films as accurate. Further, the fact that the originals were examined stereoscopically makes a very considerable difference.

The first three cases, cases 8, 9, and 10, I present first for their extreme similarity to three of the proven cases.

The first six cases show interesting variations in the atelactatic factor, case 8 of the lower lobe, case 9 of the mid lobe, cases 10 and 11 of the whole lung, and cases 12 and 13 of the upper lobe, this last a feature we did not pick up in the proven group.

Case No. 8

This man, aged 31, Clinic No. 573607, gave a history of four months of fatigability and weight loss, and some dysphagia, with, rather more recently, cough and blood-streaked phlegm but never real sputum. When he came to the Clinic he had some trouble in swallowing, a sense of pressure in the chest and painful swollen glands in the axilla and neck but no other localizing history. Physical examination showed limited expansion on the right; the white cell count was 8300; the thick barium x-ray of the esophagus was negative. He was bronchoscoped and a deformity of both bronchi with a bleeding obstructive lesion of the right bronchus was seen. The biopsy section showed only inflammatory tissue but may have been from the edge of the growth. One of the neck glands was excised and was definitely adenocarcinomatous.

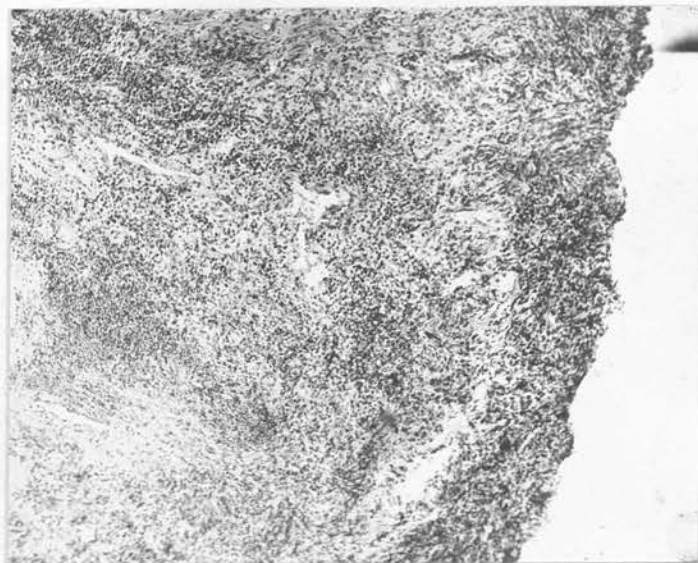
Examination of the sections (see photographic reproduction) shows in the bronchus fragment a cellular tissue which no one could safely say was not inflammatory, and which, therefore, cannot be reported malignant, yet which does show a little irregularity of cell arrangement and occasional suspicious looking cells. To match this the neck gland section, showing a vaguely adenomatous arrangement, is also of a very irregular type. In the absence of other demonstrable lesion, I think that the proof is good enough - especially as the patient died three months later.

The film I would contrast with proven case No. 1. It shows the same unilateral hilar shadow, continuous with an apparent basal bronchiectasis, for which there is no history and no leucocytosis. The other lung is absolutely clear and contrast of the two sides shows a certain amount of lack of aeration in the whole lower and mid lobes of the involved side.

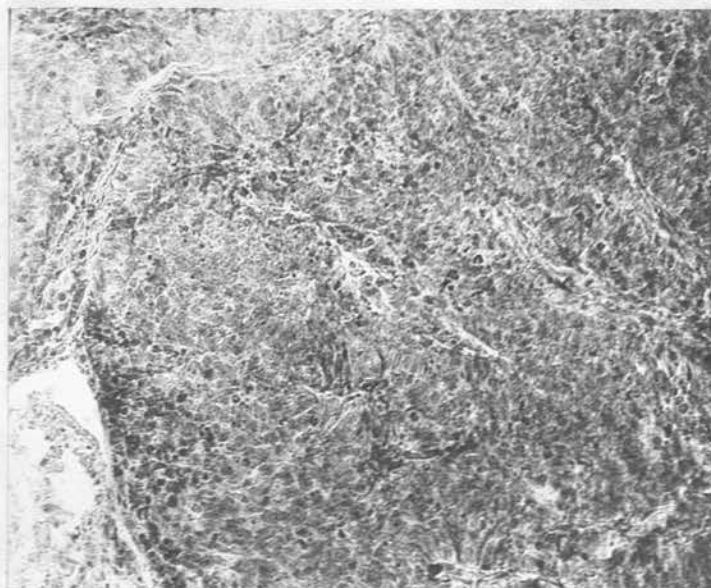
Case No. 8

Clinic No. 573607

Microphotographs from Biopsy Section and from Excised Neck Glands



- A. Bronchus Biopsy Section. Low Power: x 60. Note the extreme cellularity and the absence of normal structural arrangements, although there are no actual apparently malignant cell groups.



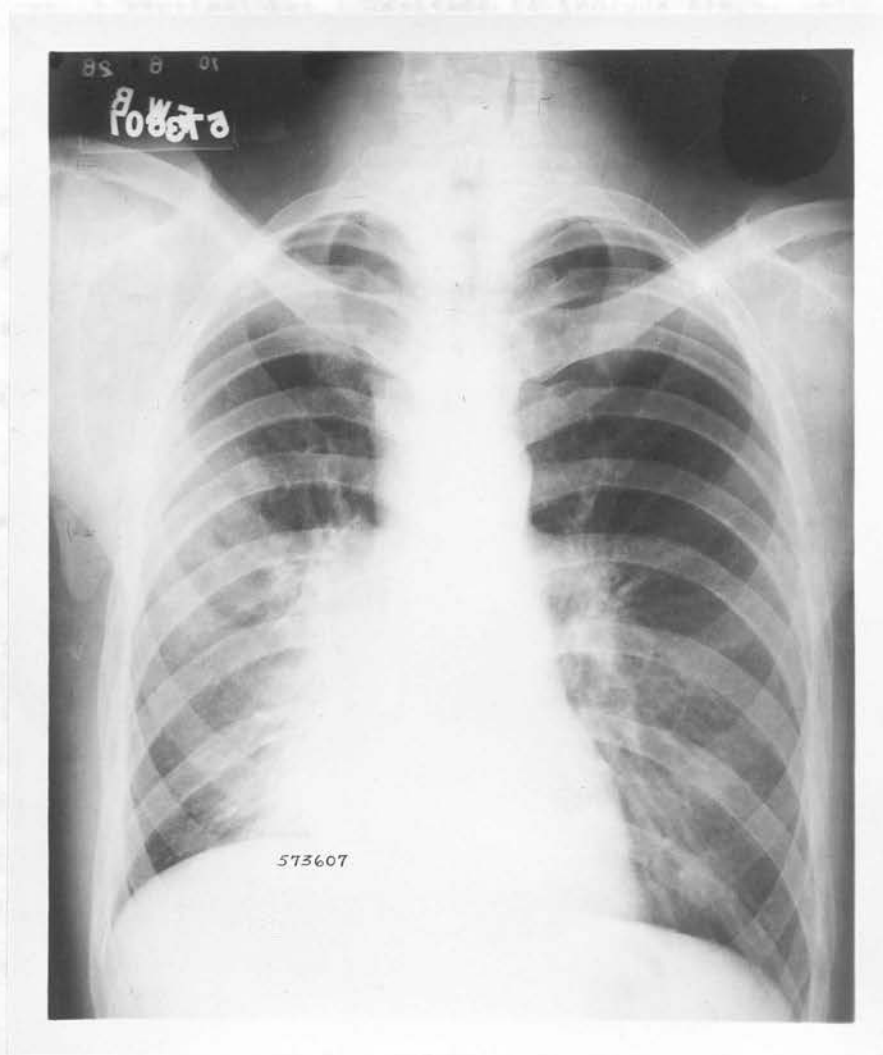
- B. Neck Gland. High Power: x 120. Shows clearly malignant tissue with a somewhat adenomatous arrangement. Extremely cellular with very little stroma.

Case No. 8

Clinic No. 573607

Reduced Print from X-Ray Film

Carcinoma Right Main Bronchus



Case No. 9

This man, aged 50, Clinic No. 467186, has a proven bronchoscopic biopsy section showing a grade III carcinoma (of which I was unable to get a repeat section) but I hesitate to include him as proven absolutely, because he had a large bladder tumor removed nine years before and a recurrence cauterized a year ago. The microscopic appearance of the two tumors was not the same and the clinical consensus of opinion was that this was an independent lesion but - there must always be the doubt.

He gave a history of one month of persistent hacking cough, commencing with a hemoptysis and always since producing blood. Apart from weight loss of ten pounds he had no other symptoms and the bladder was all right. The bronchoscope showed an ulcerated mass on the left wall of the right main bronchus at the junction of the mid-lobe bronchus. Five months later he wrote to say he was not much worse.

The film is about twin to that of case No. 4, and I take it to be nothing but a mid lobe atelectasis. The hilar lesion does not show but in this connection one notes the fact that the lesion was on the mesial wall and early. As in case 4, the diagnosis must be made by having to find an organic cause for the bronchial obstruction - and there is a perfectly crisp history.

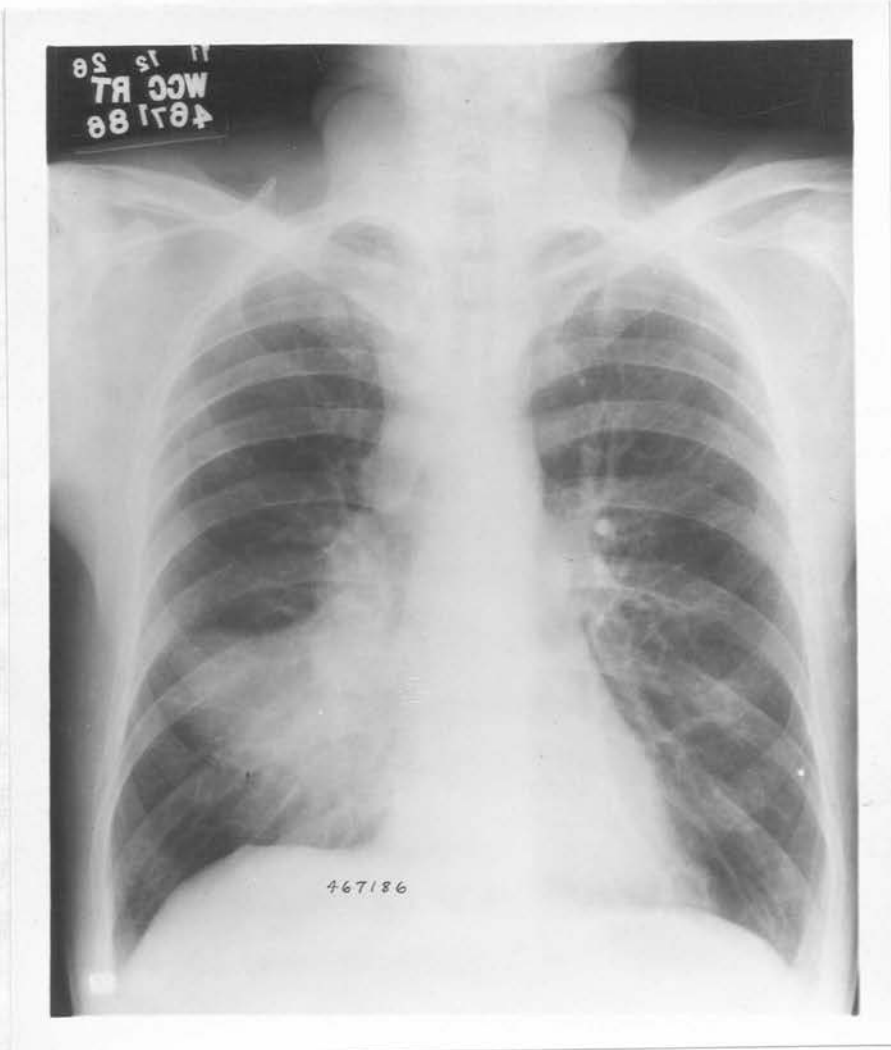
If it is a metastasis, it must have been right up against a bronchus and have involved it early.

Case No. 9

Clinic No. 467186

Reduced Print of X-Ray Film

Carcinoma Right Bronchus Obstructing
Middle Lobe.



This man, aged 57, Clinic No. 573670, came to the Clinic in October 1926, with complaint of two months persistent chronic cough, bringing up little sputum and, only within the preceding two weeks, blood. He had pain high up in the front of the chest, especially when lying down. Weight loss was slight and there was no fever or any other suggestive history. On physical examination the whole left chest was somewhat duller to percussion than the other, and the breath sounds were much weaker. On the x-ray diagnosis of lung tumor he was bronchoscoped and a lesion of the main left bronchus found. Although the biopsy showed only inflammatory tissue, Dr. Vinson, the bronchoscopist, states that the visible lesion was, in his opinion, absolutely typical and that he considered the case a "clear-cut" case. Three months later the patient wrote that he was in much the same condition.

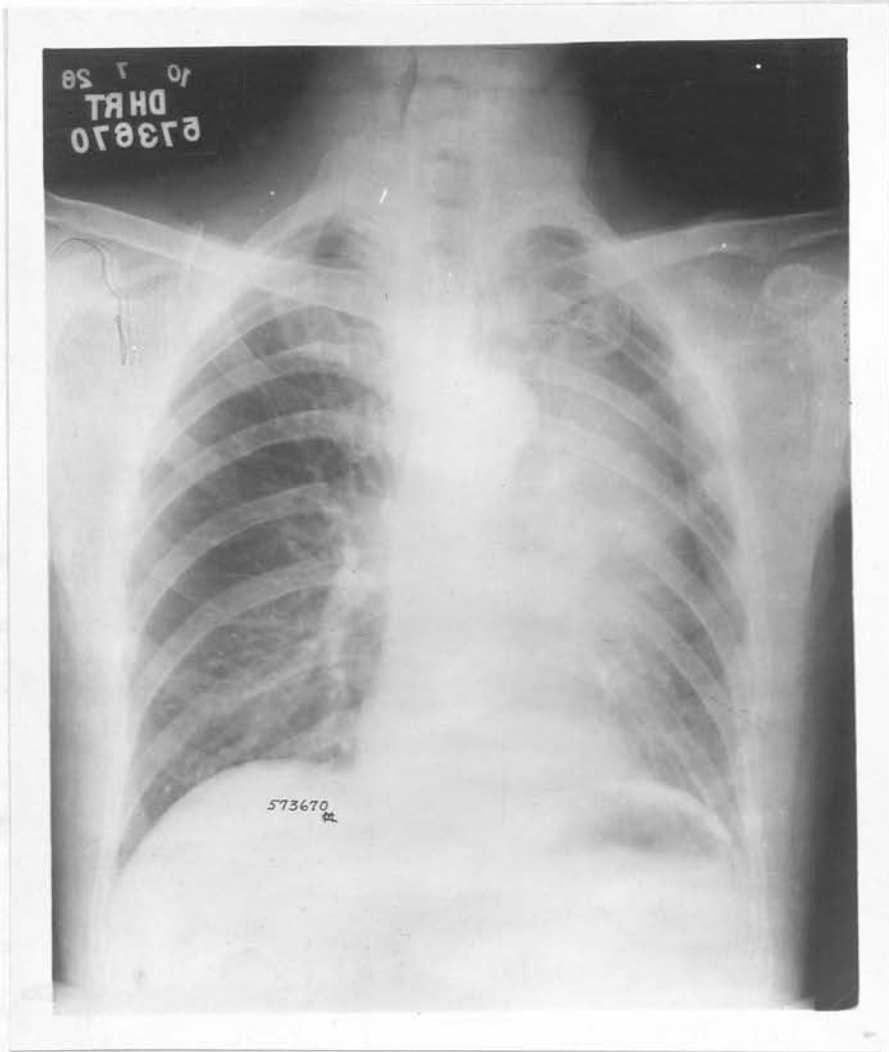
The film is like that of case No. 7 but at an earlier stage. I think the whole visible lesion is an atelectasis: The heart is over a little; the ribs are slightly depressed; the left diaphragm is up on a level with the right, and the texture of the "consolidation" is of that peculiar semi-translucent nature, which I believe represents a collapsing lung. It may, indeed, be all lesion, but the history is short and it lacks both differentiation from the lung texture and the irregularity of the typical infiltrative processes of carcinoma. We can correlate, too, with the fact that the lesion was of the main bronchus.

Case No. 10

Clinic No. 573670

Reduced Print from X-Ray Film

Atelectasis due to Epithelioma
Left Main Bronchus



This case, Clinic No. 103523, was an old woman of 67 who came to the Clinic complaining of a "severe cold" of five months duration. On questioning, this cold proved to be a non-productive, irritating cough, without any fever or weight loss. Two days before coming to the Clinic she had coughed up blood but that was the first occasion. On examination she was found to have a hypertension of over 200 systolic; the chest showed some dullness and impaired sounds on the left side and was interpreted as a stenosed bronchus. She said that two months before she had had a transient paralysis of left arm and leg for one and one-half hours, but there was no clinical evidence of this. The x-ray was as shown in the print and after correlation of the x-ray with clinical findings a diagnosis of malignancy (70% probability) was made. She was not bronchoscoped because of age. On following up this case she was found to have died three months later with cerebral symptoms - ? of brain metastasis.

This is not a proven case, but it is an orthodox history and the x-ray falls in with the group. Indeed it makes an excellent "later stage" of the previous case.

The x-ray, I think, shows both the hilar density and marked evidence of bronchostenosis. The heart is over, the thorax has fallen in a bit on that side, the diaphragm is well up and there is a lack of aeration. The hilar density just shows - using imag-

ination: - that cleft of separation from the mediastinum that I discussed. It certainly shows typical infiltrative processes.

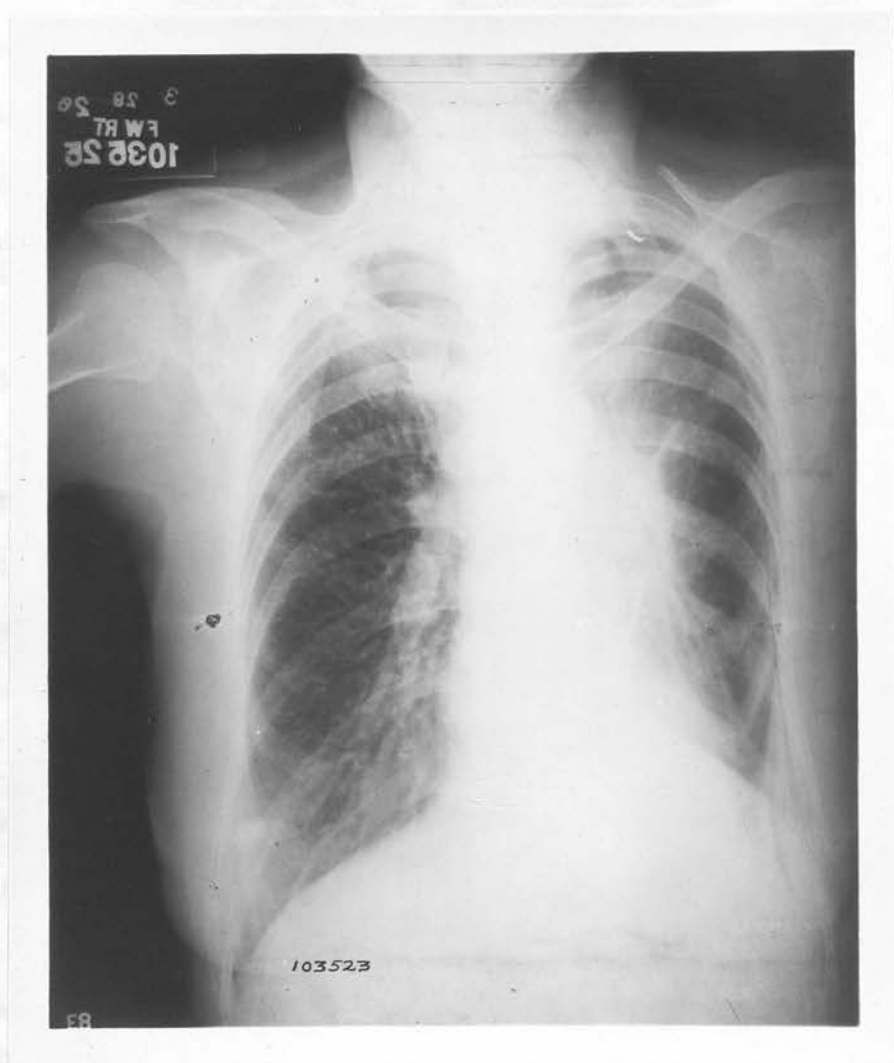


Case No. 11

Clinic No. 103523

Reduced Prints of X-Ray Film

Bronchial Carcinoma -
Site Unknown



This man, aged 56, Clinic No. 567074, came to the Clinic in August 1926, complaining of cough, loss of weight and of strength. He had suffered from an old dry winter cough for years, but in the previous January the cough had become much more definite, more constant and had begun to produce sputum, usually blood-stained. On physical examination he showed diminished sounds over the right upper chest. He had a mild leucocytosis and palpable adenomata of the thyroid but with no toxic signs associated. Otherwise he yielded no suggestive evidence. He was bronchoscoped. There was a soft ulcerating lesion of the right main bronchus, occluding the opening of the upper right branch. In spite of the fact that the biopsy showed only inflammatory tissue, Dr. Vinson felt quite certain that he had a typical epithelioma. He asked for a second bronchoscopy but the patient refused. The patient died the following November.

The x-ray is unusually interesting. The hilar density is present but is higher than in the others. The bronchoscopist found the lesion at the entrance to the upper bronchus. The "consolidation" above that is the query; on first glance it looks like an upper mediastinal mass with definite edge, ordinarily typical of one of the lymphoblastoma group. On examination, however, the area outside of this is hardly consistent with compressed lung and we should have the apex clear. Further, the mass just lacks the density and

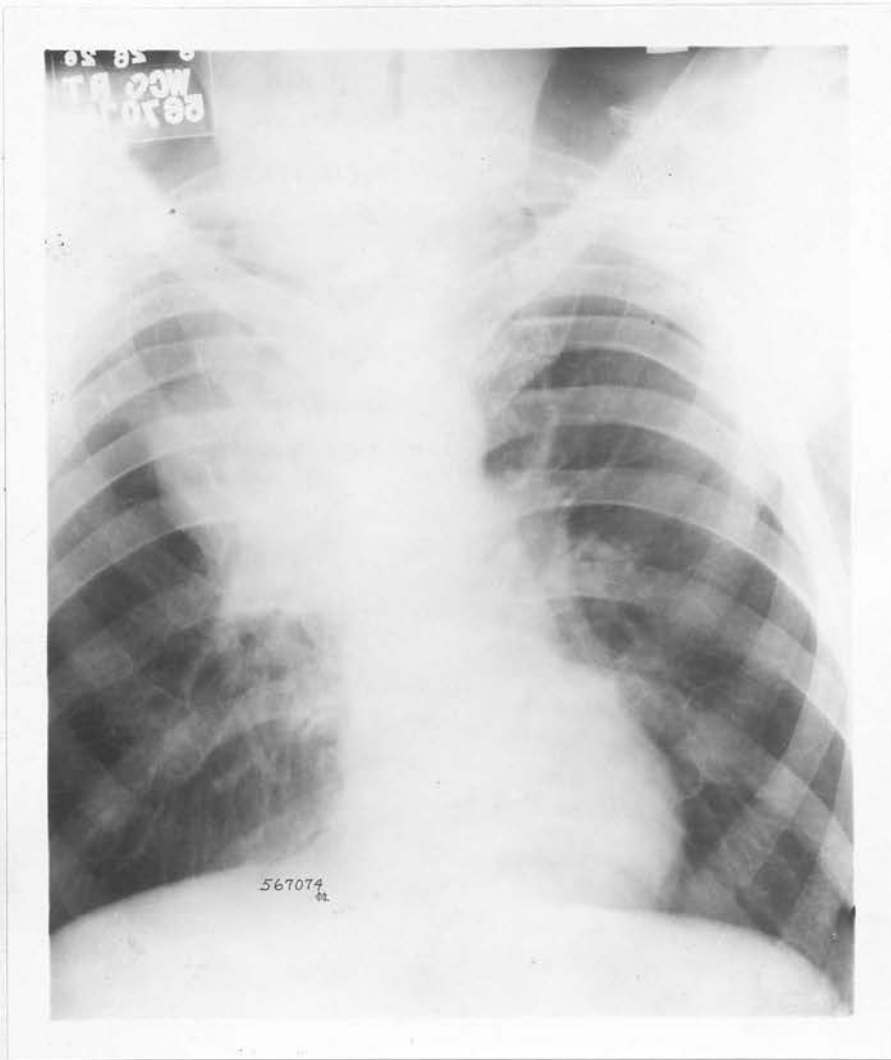
the roundness of edge of a lymphoblastoma or Hodgkin's, though it has its perfectly sharp edge. Taken with the bronchoscopic findings, I think there is little doubt that this is an atelectasis of part of the upper lobe with the lower and middle lobes ballooned out, emphysematously, upwards to compensate. The sharp lower edge lying obliquely is the normally horizontal lower border of the right upper lobe. Again, the diagnosis depends on the combination of a hilar density with atelectasis and a typical history.

Case No. 12

Clinic No. 567074

Reduced Print of X-Ray Film

Carcinoma Upper Right Bronchus



Case No. 13

This case, Mr. H. H. G., aged 56, Clinic No. 366319, gave a history of cough of the bronchitis type for the whole of his adult life. Four months before admission, however, the cough quite suddenly became much more severe and the patient developed constant vague pain in the chest and some dyspnoea. He had lost twenty-eight pounds in the four months. The cough was productive of some sputum but never was excessive, did not show tubercle bacilli, and was never blood-stained. For a short time prior to admission he had been suffering from laryngeal hoarseness. He had a leucocytosis on admission of 16,000. We were unfortunately unable to follow up this patient. He was not bronchoscoped but the x-ray report was definitely carcinoma of the lung and is so typical that I think it justifiably included.

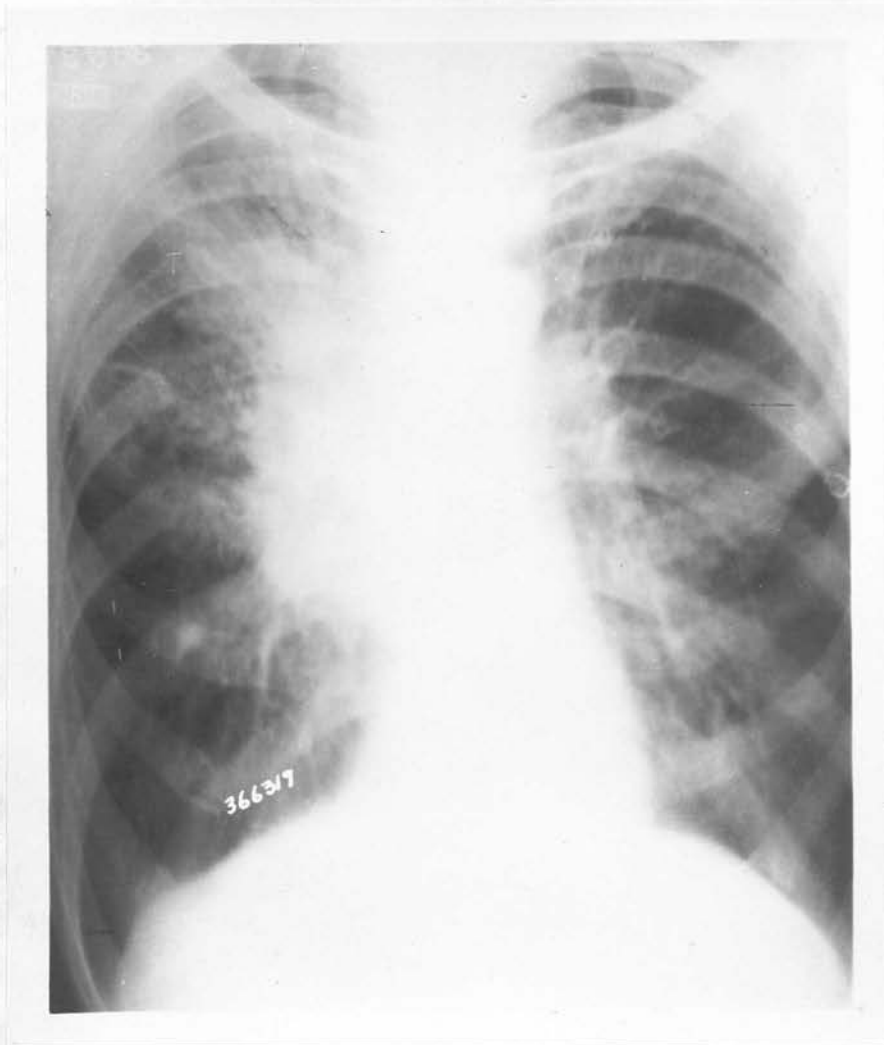
The film shows a definite irregular, infiltrating hilar mass, the infiltration tending to be towards the apex. The apex itself does not light up well and though the appearance may be all due to lesion, yet is most likely an atelectatic feature again.

Case No. 13

Clinic No. 366319

Reduced Print of X-Ray Film

Carcinoma of Bronchus



The End Result:

The next four cases, Cases 14, 15, 16 and 17, show a definitely later group of cases. After a certain stage the bronchial and the parenchymal carcinoma blend into a common picture. Case 17 is the ultimate result and as far as the x-ray goes may have a focus of origin anywhere. For this reason cases coming to the post-mortem table are of little value as an illustration of the early lesion. In the Post-Mortem Museum of the Mayo Clinic Pathological Laboratory there are a number of lung carcinoma cases. Of these, only one, Case No. 14, a very recent case, was illustrative of the bronchial carcinoma, and that only because the primary lesion had remained relatively small and had caused death by wide metastasis. In all the other cases the lungs were so widely infiltrated that it was impossible to say where the original growth began. A fatal result with a lesion showing no more radiologically than Case No. 14 would be unusual. More usually one would get a large growth such as seen in Case No. 15 with evidence of wide metastasis to the rest of the lung and the other lung, rarely advanced bronchiectasis, while, probably most often, the x-ray picture is merely that of a chest full of fluid, as in Case 17.

Case No. 14

This man, a miner aged 38, Clinic No. 585575, came to the Clinic in January 1927. On admission he was in extremely poor condition. Up till four months before he had been perfectly well. He then commenced to have a non-productive, irritating cough, constant since, and productive only just before admission. A fortnight before he began to have dyspnoea and on admission this was extreme. He had no fever but said he had lost fifty-seven pounds in four months. Physical examination of the chest was negative but there were large gland masses in right neck and axilla. An x-ray diagnosis of lymphoblastoma was made and he was sent to hospital for radiation therapy. He died suddenly of dyspnoea within a few days. An autopsy was granted.

The x-ray is of interest in that it is the only case where one could say that an early primary lesion came to autopsy. On the film a diagnosis of lymphoblastoma was made. We see the large mediastinal mass, both upper and lower, and that the density projecting down from the hilus has a smoother, non-infiltrative edge than the densities of a malignancy. There is an area of atelectasis in the base of the upper right lobe but with masses such as those present there is no need to presuppose an intrabronchial lesion. There are small metastatic areas in the right base. I do not think that on the film one can say more than that there is a mediastinal aden-

opathy present, and, because of the metastasis, that it is malignant. How does the film contrast with the autopsy findings?

I show a photo taken of the excised specimen. We see at once that the masses seen x-ray consist of numerous matted (to the feel densely hard) glands lying along the trachea and reaching out along the lower right bronchus but distinctly encapsulated from lung tissue. I could peel off the lung parenchyma quite freely. The primary focus is the superficial, papillary type of growth seen occupying the bifurcation and extending along the surface of both bronchi, especially the right, and partly filling up the lumen. Microscopic section shows a squamous epithelioma of the bronchus.

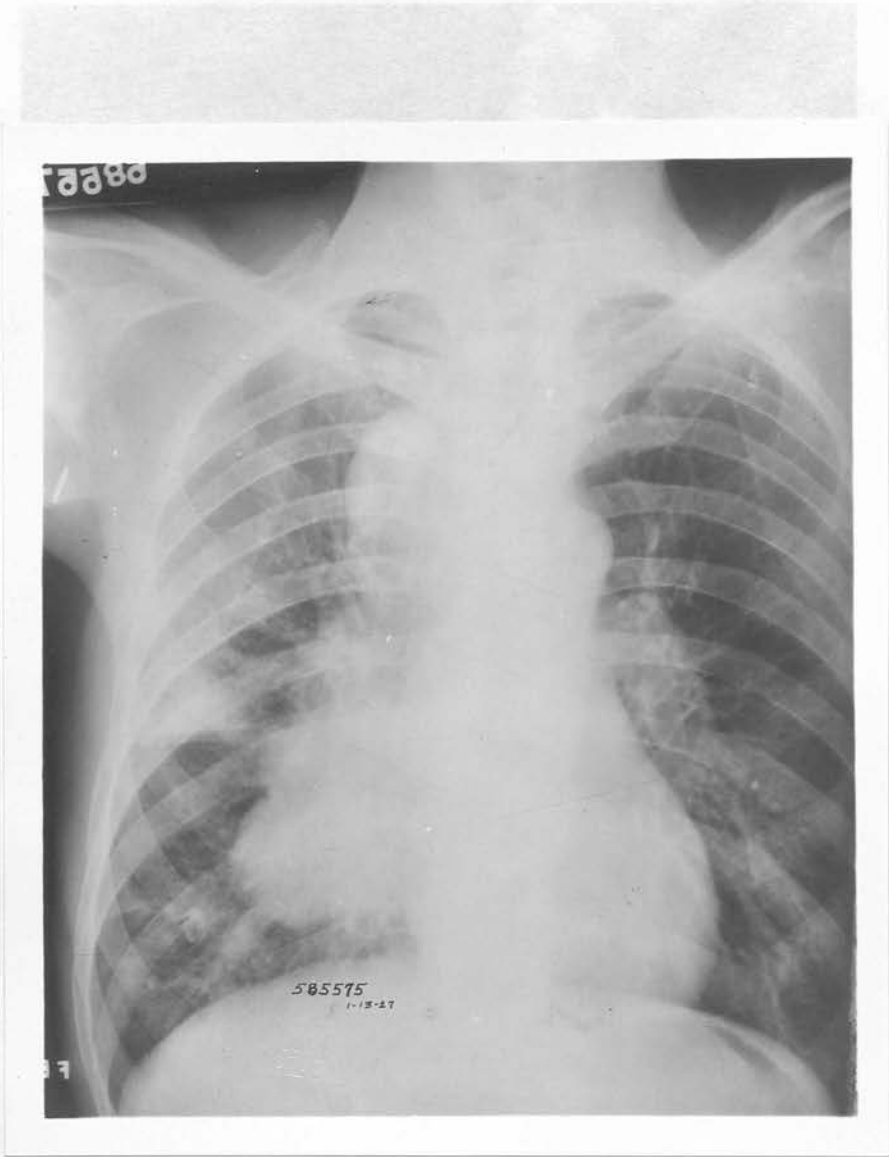
This explains the atypical picture seen in the x-ray. The dense masses interpreted as a lymphoblastoma were a multi-adenopathy, but happened to be due to a primary carcinoma bronchus, the radiological evidence of which was totally masked by its own gland metastasis.

Case No. 14

Clinic No. 585575

Reduced Print of X-Ray Film

Carcinoma Bronchus with Multiple
Mediastinal Gland Involvement



The large white masses are all dense. The width of mediastinal vessels to the left is the normal diameter. The papillary shadow of the bronchial growth is well shown.

Case No. 14

Clinic No. 585575

Photograph of Autopsy Specimen

Showing Central Mediastinum,
Bronchus and Right Lung



The large white masses are all glands. The strip of muscular tissue to the left is the opened esophagus. The papillary nature of the bronchial growth is well shown.

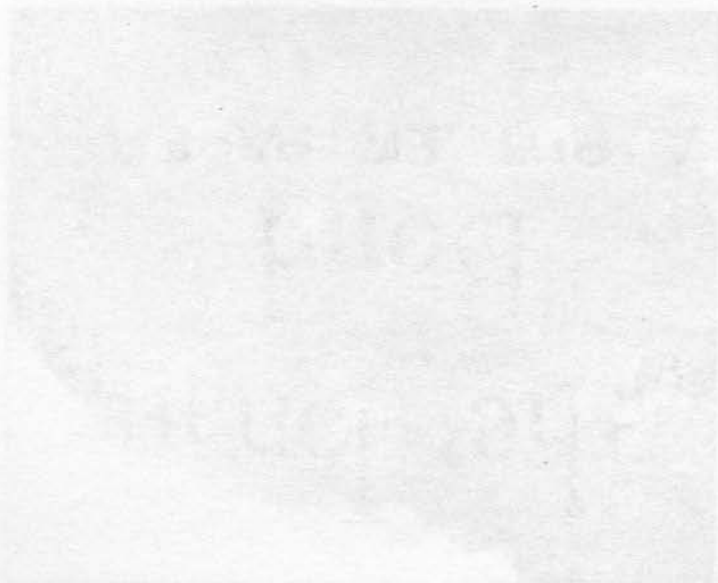
This man, Clinic No. 577866, aged 40, on admission gave a history of a "run down" feeling of one year's duration. Questioning brings out a vaguely gastric history running through this period. For five months previous he had suffered from severe cough with expectoration and dyspnoea. He never coughed blood. Twice he had had to have a pleurisy tapped. He had lost thirty-nine pounds in weight. Physical examination showed an absolutely dull left base. Gastric x-ray was negative. He was bronchoscoped and the right lower bronchus was found compressed and bleeding. A biopsy fragment taken then showed a Grade IV carcinoma.

This is almost certainly a primary bronchial case, which the films show to be a later case than the others. But both because of this and because of the vague gastric history preceding suggesting a possible metastasis, I include it here rather than with the other group.

The microphotograph from the biopsy section shows a tag of normal bronchus, with epithelium, muscle and glands, infiltrated with irregular clusters of malignant cells; in the actual section these cells had a squamous appearance.

The earlier film shows a density of the whole lower part of the lung, centered at the hilus; the free upper edge is infiltrative. The costophrenic angle shows a translucency without any lung texture in it. I think this is a large hilar mass with total lower lobe atelectasis. The diagnosis would have to be from an inflammatory lesion as it is very like pneumonic consolidation, but the clearer

periphery and lower angle negative free fluid present at examination and suggest a collapse factor. Close examination shows metastatic areas involving the other lung and these show more clearly in a film taken twenty days later. This then illustrates the generalizing metastasis type of later case.



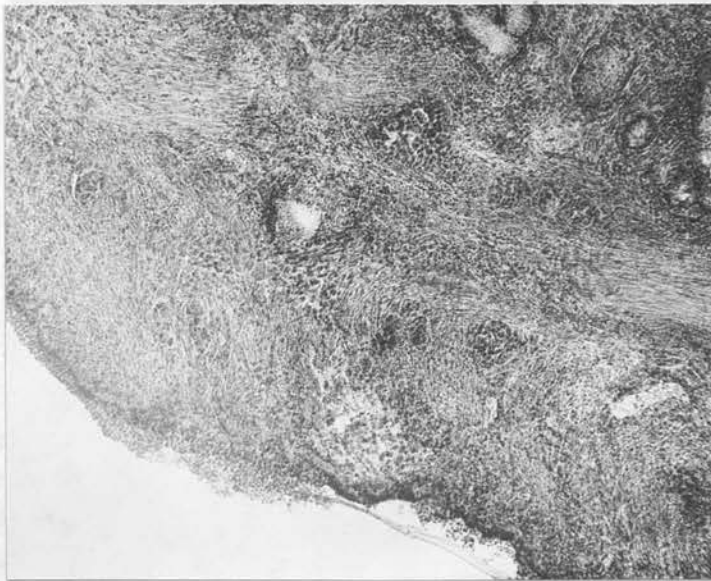
The lower part of the image shows several small, dark, irregular spots scattered across the field, which may represent metastatic lesions or artifacts from the scanning process.

Case No. 15

Clinic No. 577866

Microphotograph from Biopsy Section

Carcinoma Grade IV



Low Power: x 60. Shows normal bronchial tissue infiltrated with carcinoma cell clusters.

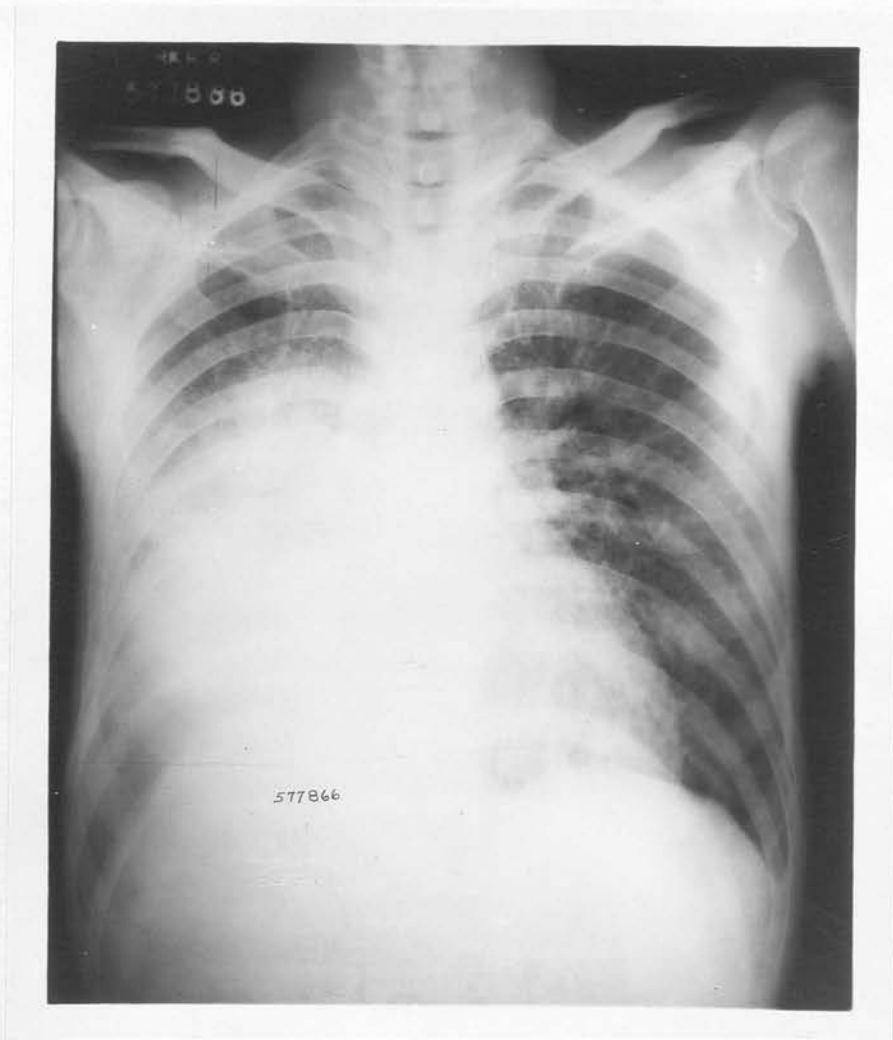
Case No. 15

Clinic No. 577866

Reduced Print of X-Ray Film

Carcinoma Right Lower Bronchus

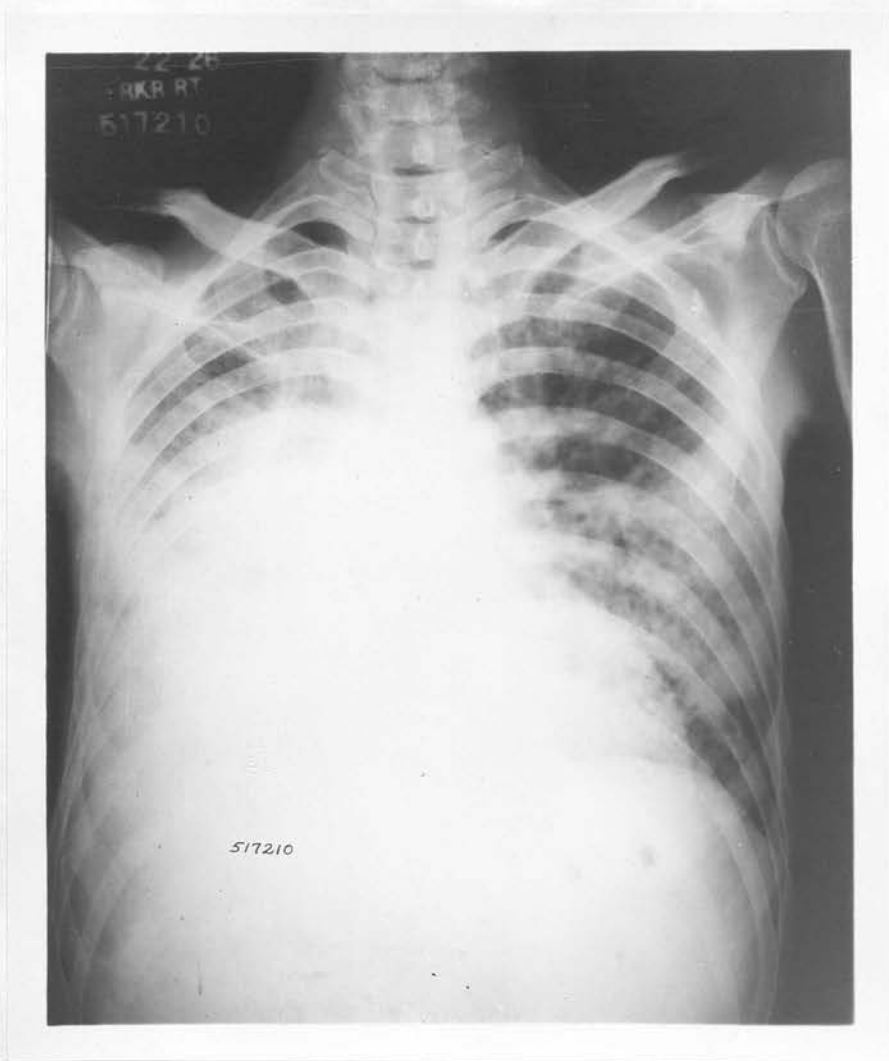
Film taken on admission.



Case No. 15

Clinic No. 557866

Film taken ten days later.



Case No. 15

This man, Clinic No. 577866, aged 40, on admission gave a history of a "run down" feeling of one year's duration. Questioning brings out a vaguely gastric history running through this period. For five months previous he had suffered from severe cough with expectoration and dyspnoea. He never coughed blood. Twice he had had to have a pleurisy tapped. He had lost thirty-nine pounds in weight. Physical examination showed an absolutely dull left base. Gastric x-ray was negative. He was bronchoscoped and the right lower bronchus was found compressed and bleeding. A biopsy fragment taken then showed a Grade IV carcinoma.

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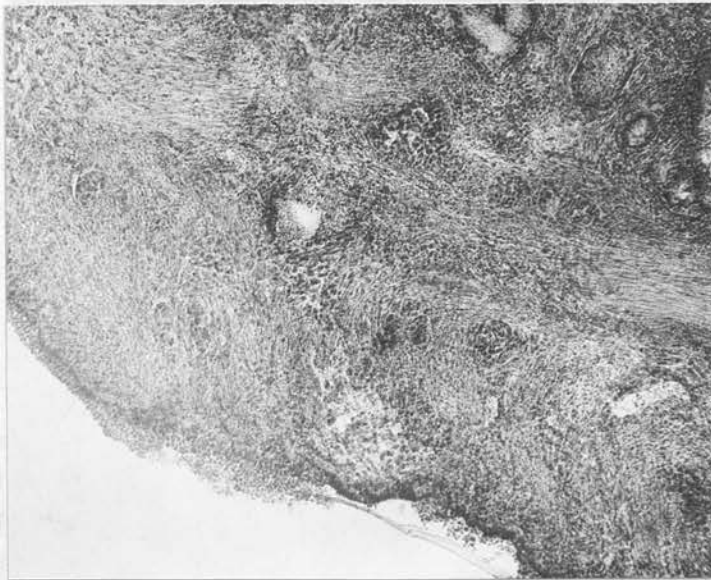
periphery and lower angle negative free fluid present at examination and suggest a collapse factor. Close examination shows metastatic areas involving the other lung and these show more clearly in a film taken twenty days later. This then illustrates the generalizing metastasis type of later case.

Case No. 15

Clinic No. 577866

Microphotograph from Biopsy Section

Carcinoma Grade IV



Low Power: x 60. Shows normal bronchial tissue infiltrated with carcinoma cell clusters.

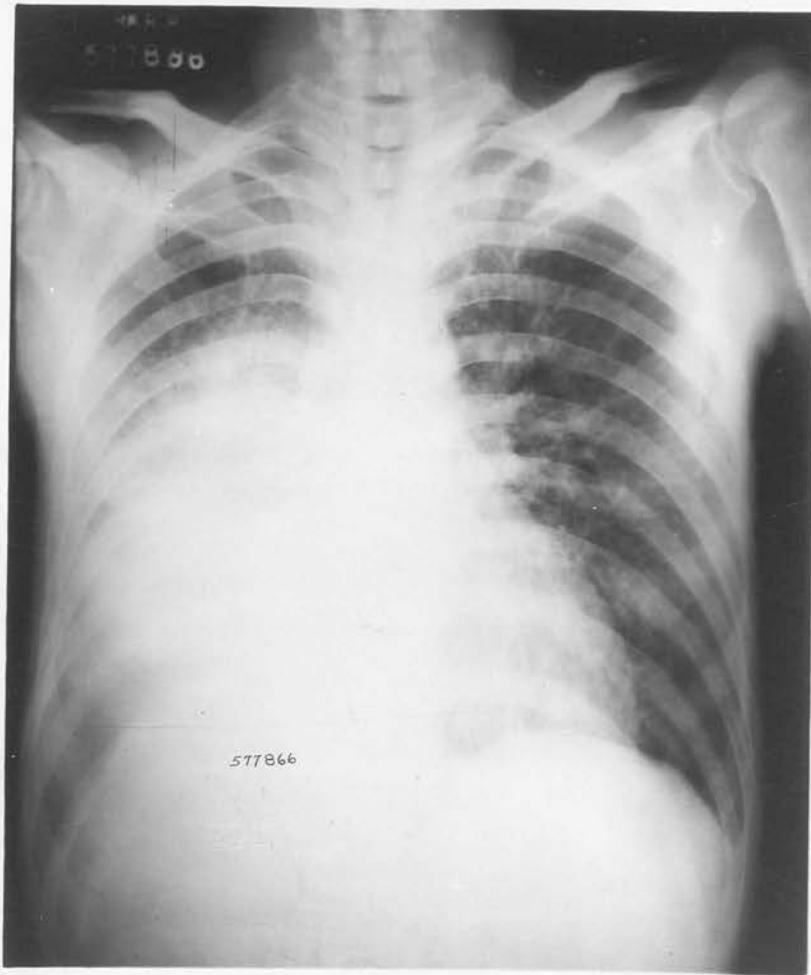
Case No. 15

Clinic No. 577866

Reduced Print of X-Ray Film

Carcinoma Right Lower Bronchus

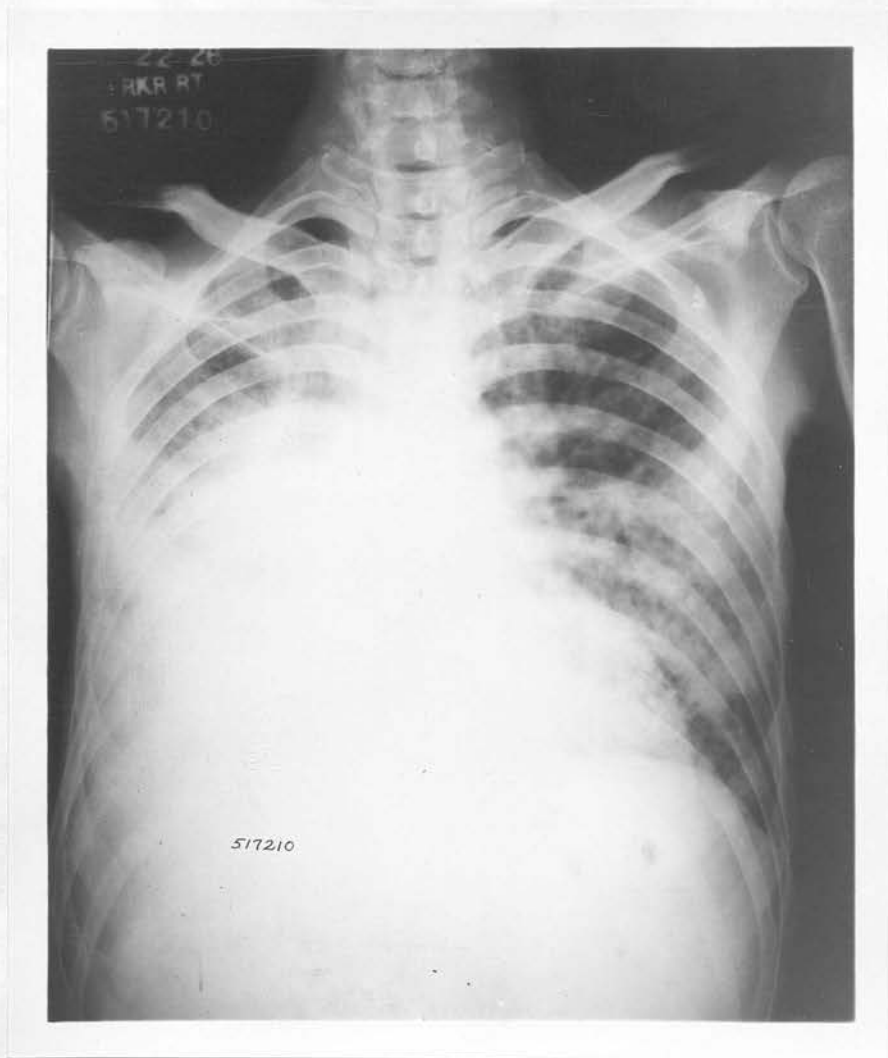
Film taken on admission.



Case No. 15

Clinic No. 557866

Film taken ten days later.



Case No. 16

This man, Clinic No. 406584, came to the Clinic complaining of four months of substernal pain, cough, and considerable sputum. Three months before he had been laid up for a few days with a feverish attack. Examination of the sputum showed it blood-streaked. Specimens sent for examination for "T. B." were thrice reported negative. He had a dullness of the left base, with rales above that. There were multiple enlarged glands in the neck and a biopsy taken from one of these showed a carcinoma. He died three weeks later.

We have seen a gland type of late case, and an atelectatic and metastatic late case; this case is, I think, a real bronchiec-tatic late case. The hilar density is there but there is no atel-ectasis. The whole base is occupied by an irregular infiltrative process radiating from the hilus; above this may be actual growth; below it is characteristic of bronchiectasis, and the history con-firms this.

Case No. 16

Clinic No. 406584

Reduced Print of X-Ray Film

Carcinoma Bronchus - Site Unknown



Case No. 17

This man, Clinic No. 504254, had a twenty-one months history of cough, with some but never abundant sputum, and always with blood. Recently he had considerable fever, night sweats, malaise, pain, and dyspnoea of insufficient exertion. He had a mild leucocytosis and an absolutely flat left lung. The sputum was negative for "T. B." He had lost twenty-five pounds. He died three months later.

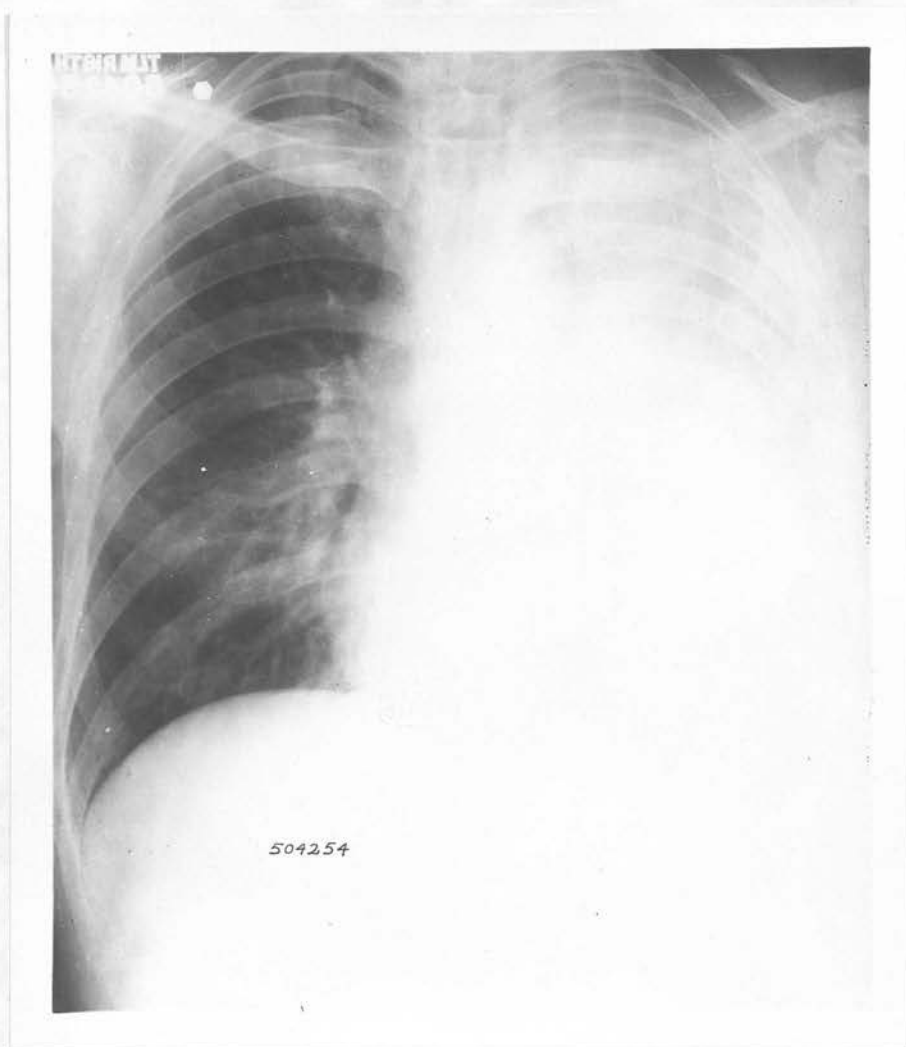
This film shows the most common end result - a massive pleurisy. From the film a diagnosis between bronchial and parenchymal cannot be made - it is the late stage of either; we have a pleura filled with fluid and a vaguely infiltrating density of the whole lower lobe, faintly seen through the fluid. The history indicates a bronchial origin.

Case No. 17

Clinic No. 504254

Reduced Print of X-Ray Film

Advanced Carcinoma Bronchus



Parenchymal Carcinoma

Detailed discussion of the x-ray picture of this group is outside the scope of this article. Table III was introduced to bring out the contrast between the symptomatology of the two groups. From this I am detailing six cases to show that there really is a radiological picture for the early parenchymal lesion totally different from that worked out for the bronchial lesion.

Four cases show the nodular type in different forms (the first three bearing some resemblance to hilar lesions); one shows a true early lobar type; and the last is a sarcoma of lung, which cannot be distinguished from a hilar lesion.

Apart from the fact that the lesion is seldom hilar in location, it is less dense but more circumscribed (though not so sharply defined as a nodular metastasis) and gives the appearance even when mesially placed of being totally within lung tissue.

As will be seen, the lesions usually are so different that the problem of differential diagnosis will not arise. Where it does so it is because, as in the last case, the bronchus has become secondarily involved.

Case No. 18

This woman, Clinic No. 494886, aged 54, came to the Clinic with a history of eight months of vaguely localized, dull, constant aching in the left scapular region. Three months later the pain was also present in the front and she commenced to have dyspnoea. She had a weight loss of twenty-five pounds. She reported no cough or other chest localizing signs. A careful examination revealed not the remotest suspicion of any other lesion. The x-ray showed a typical nodular lesion of the upper lobe diagnosed as malignant. The patient died three months after being at the Clinic. No neck glands were available but the early death I take as reasonably conclusive.

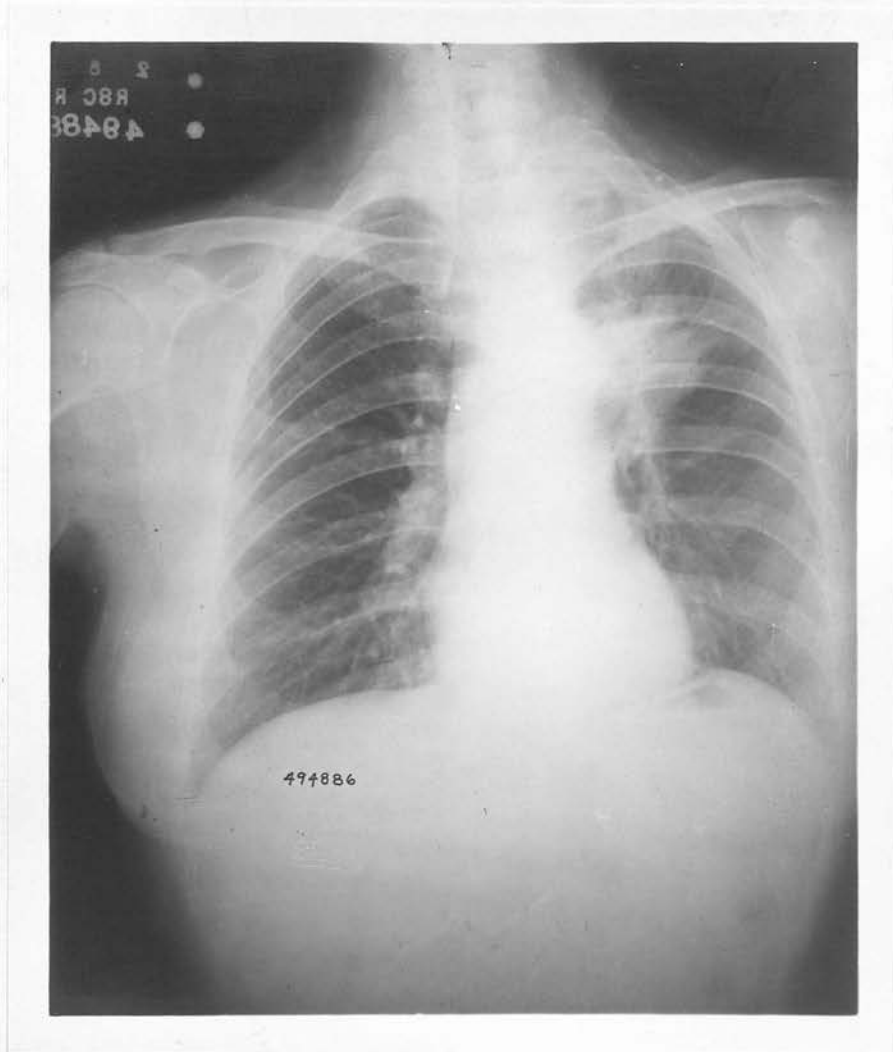
The film shows a roughly circular area of consolidation with an infiltrating edge, lying opposite the fourth and fifth interspaces posteriorly. The two differential diagnoses would be from abscess and metastasis. There was no leucocytosis and no suggestive history for the former and a first metastasis is rarely upper lobe and does not have this type of infiltrating edge.

Case No. 18

Clinic No. 494886

Reduced Print of X-Ray Film

Early Nodular Carcinoma of Lung



Case No. 19

This man, Clinic No. 516648, a fisherman, aged 50, gave a history of having smoked fifty cigarettes a day for years. He came to the Clinic in 1925 with a ten months history of constant pain in the left chest, and some dyspnoea on exertion. He had a mere trace of cough and on only one occasion brought up blood. He had a weight loss of twenty-seven pounds but, other than that shown in the x-ray film, not the least evidence of any lesion. He has since died but the date is uncertain.

The x-ray film shows the one lesion that Carman described as pathognomonic of lung malignancy - a single nodular lesion very like that of the previous case but with numerous satellite metastasis peripheral to it.

Case No. 19

Clinic No. 516648

Reduced Print of X-Ray Film

Early Nodular Carcinoma of Lung



Case No. 20

This case, Clinic No. 580151, a woman who came to the Clinic in December 1926, also gave a history of pain and weight loss - and nothing else. For six months she had had a pain in the right scapular area, constant but eased by heat. For two months this pain had been severe. She had lost eighteen pounds weight. There had never been cough or sputum. On physical examination nothing tangible was found in the chest; a bronchoscopic examination was negative. There were palpable adenomata in the thyroid and palpable neck glands. Biopsy section of one of the latter showed a highly malignant carcinoma. There was no other evidence of lesion and a gastric x-ray showed no gastric carcinoma. This patient was still alive two months later.

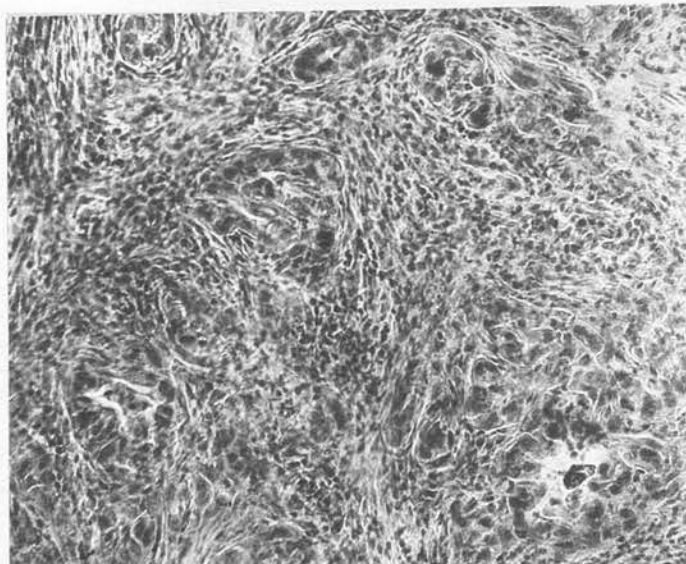
The biopsy section, from which a microphotograph is given, shows an adeno-carcinoma with considerable fibrous tissue: The malignant cells are in clusters, roughly acinous, with marked proliferation into the acini. The acini are smaller than normally found in breast cancer but are quite like that of stomach or prostate.

The film is of interest, as it shows about as early a visible lesion as is possible, and that it lies very near the hilus. But it is roughly circular, and does not occupy the whole hilus - indeed the hilus can be seen as separate structure. It is so early that an x-ray diagnosis would be almost impossible.

Case No. 20

Clinic No. 580151

Microphotograph of Section of Neck Gland Tissue Adeno-Carcinoma



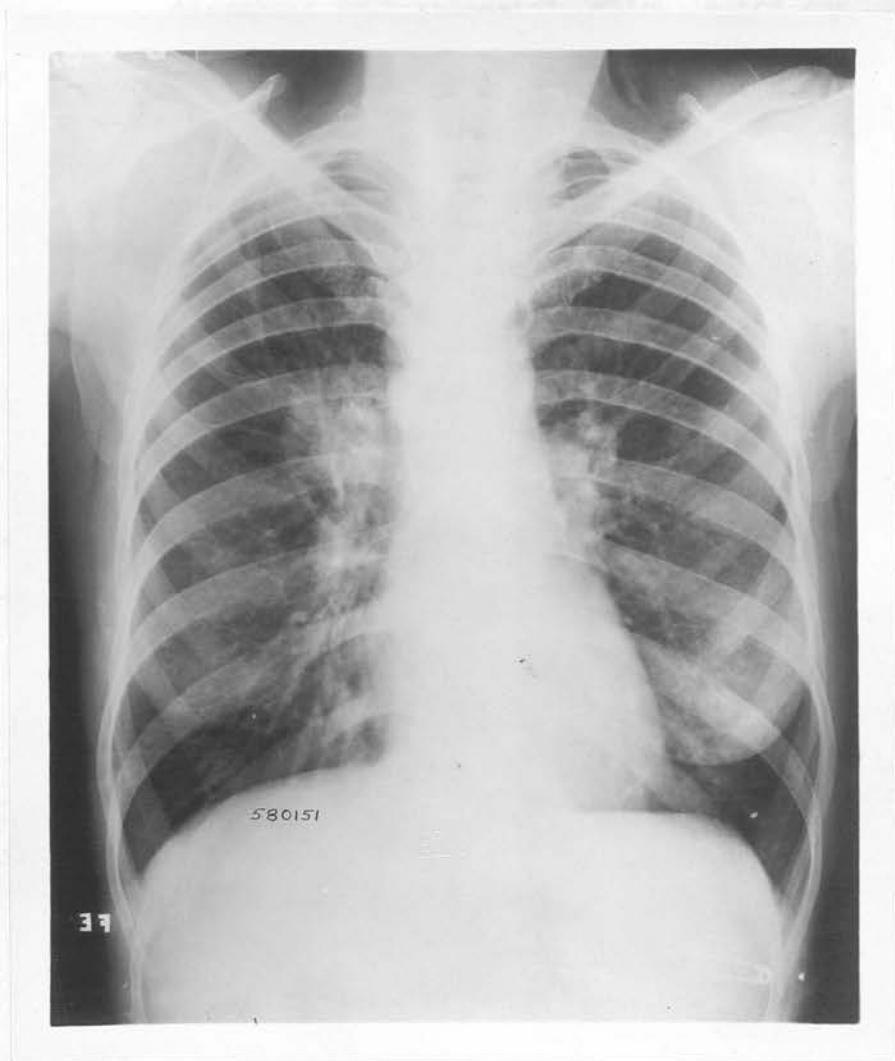
High Power: x 120. Shows the adenomatous arrangement and the marked interacinous proliferation of the cells.

Case No. 20

Clinic No. 580151

Reduced Print of X-Ray Film

Early Nodular Carcinoma of Lung



Case No. 21

This man, aged 57, Clinic No. 462306, came to the Clinic complaining of nine months of gradually increasing cough, in the mornings with spitting of blood. Five months ago he had a definite feverish illness diagnosed as "pneumonia", which lasted one month. After recovery from this he always had sputum with the cough and, at times, considerable blood. There was no evidence of any lesion other than the nodule seen in the x-ray of the chest and some neck glands, one of which was excised and showed adeno-carcinoma Grade IV. The patient died three months later.

The history is atypical in comparison with the film; but we have the lung lesion and the neck glands in the absence of any findings, symptoms or sign of other lesion, and conclude that this is a primary lung.

The x-ray shows an infiltrative nodule very like that of Case 18 but farther out. It demonstrates the obviously parenchymal early type.

Case No. 21

Clinic No. 462306

Reduced Print of X-Ray Film

Early Nodular Carcinoma of Lung



Case No. 22

This man, Clinic No. 503157, came to the Clinic with a clear-cut syndrome of brain tumor and absolutely no chest symptoms at all. He had neck glands and an excised section showed a Grade IV carcinoma. He died a month later. The film showed a basal density in the right lung, as representative of an inflammatory lesion as of a malignant. But there is no evidence whatever to bear out an inflammatory lesion. Either brain or lung must be primary but considering the frequency of brain metastasis from lung malignancy, and the presence of the cervical gland nodes, we may take the lung as a primary.

The microsection shows ordinary lymphoid gland tissue, impregnated with masses of squamous-looking cells, with very little real arrangement and with here and there areas of necrosis.

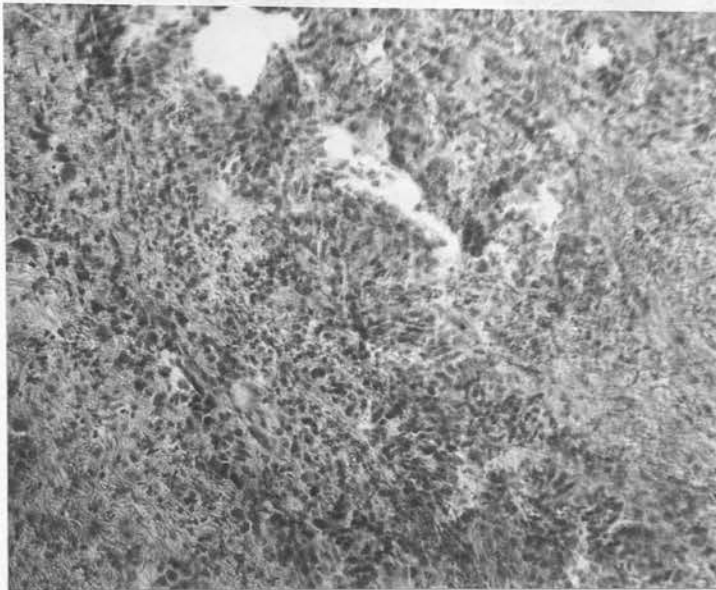
The film is the only early example I have found of a truly lobar type of malignancy. It shows a generalized consolidation of the base, less dense than an ordinary pneumonia, and with a different distribution from a bronchiectasis.

Case No. 22

Clinic No. 503157

Microphotograph of Section of Neck Gland Tissue

Epithelioma



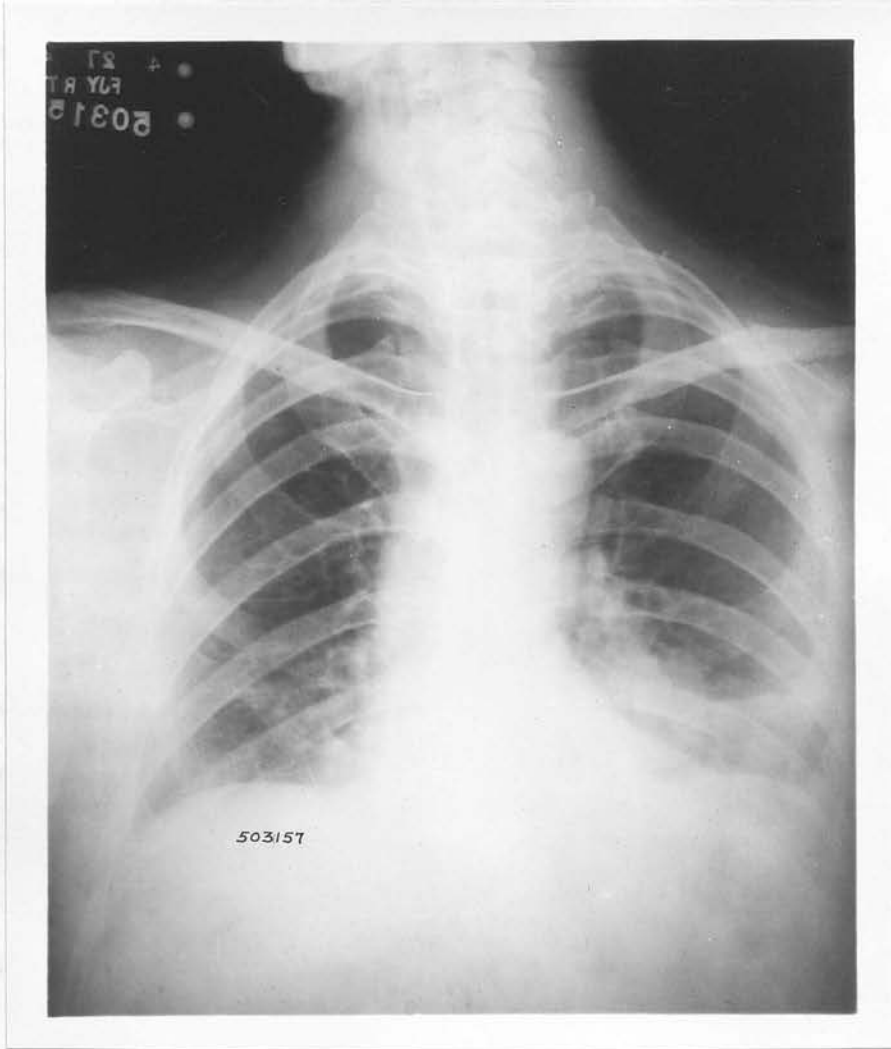
High Power: x 120. Shows lymphoid tissue impregnated throughout with irregular masses of squamous-type cells.

Case No. 22

Clinic No. 503157

Reduced Print of X-Ray Film

Early Lobar Carcinoma of Lung



This man, Clinic No. 571356, had been ill for between two and three months, the chief complaint being dyspnoea, but he had also cough in the mornings with mucoid sputum and traces of blood. He had lost twenty-five pounds. Physical examination was negative. He was bronchoscoped and a lesion of the lower right lobe bronchus was seen. Dr. Vinson considered this as probably carcinoma. The biopsy section, however, showed a lymphosarcoma. This diagnosis is consistent with the fact that he replied to his follow-up letter saying that he was very much improved after a course of deep x-ray therapy.

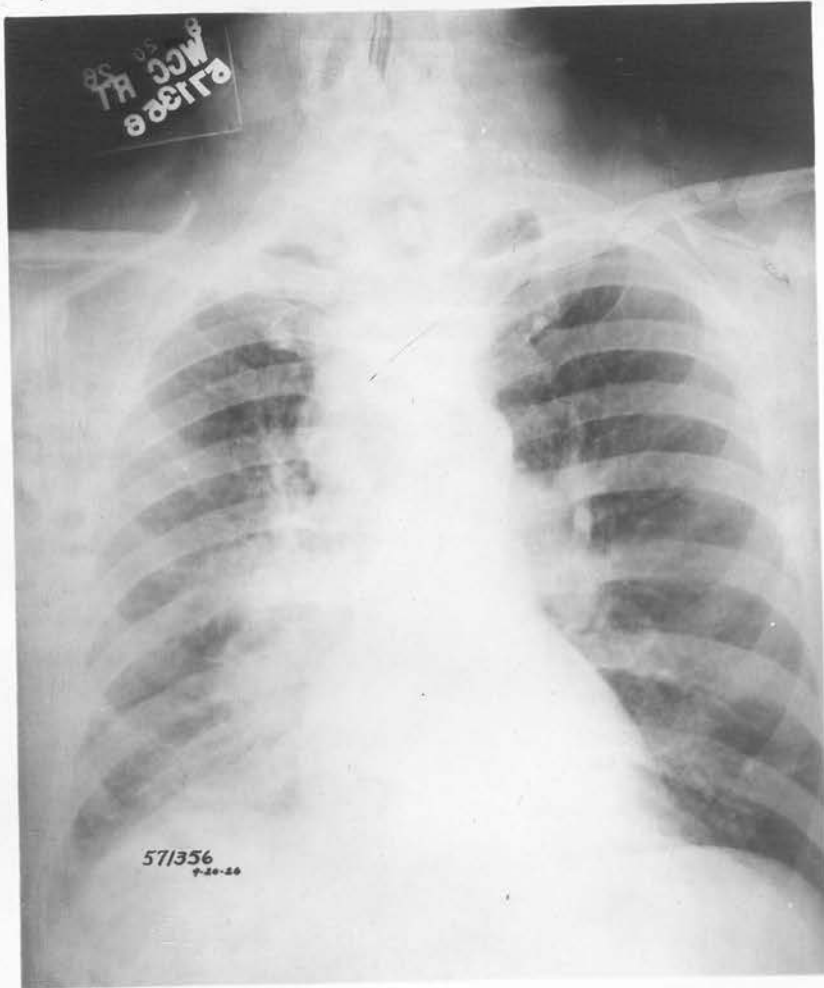
I include this case because it answers every one of my criteria of early bronchial malignancy - hilar infiltrating density, apparent bronchiectasis, and some atelectasis - except that it has also an enlarged upper mediastinum. As the bronchoscope showed, it is a primary sarcoma arising somewhere near the bronchus and ulcerating into it and hence giving all the appearance of a primary carcinoma. Its actual first source of origin must remain a moot point. Possibly it was primary in a hilar gland, infiltrating lungs and metastatic to mediastinum.

Case No. 23

Clinic No. 571356

Reduced Print of X-Ray Film

Sarcoma Possibly Primary Lung



Differential Diagnosis

The diagnosis cannot be made on the x-ray alone; the clinical history must complete the segregation of the cases; and even then non-malignant cases will go to the bronchoscopist, but it will have been justifiable to ^{have} sent them. I have, in searching for films illustrative of the differential diagnosis, been able to pick up films almost exactly duplicating the films of malignancies - but the history was seldom other than distinctive. These are seen in Figures 4, 7 and 11.

On the other hand, there are many lesions which give a similar kind of picture but one in which details differ, details that the radiologist must learn to pick up.

The three characteristics of early malignancies are hilar density, atelectasis and bronchiectasis. We must consider, then, the other things that will give these appearances.

First we consider the things giving hilar density, or an appearance of hilar density. In a very recent interesting paper Baum (24) discusses this problem and finds that the chief diseases giving increased density in the hilar shadow are carcinoma, tuberculosis, venous congestion and the Hodgkin's group, and few others.

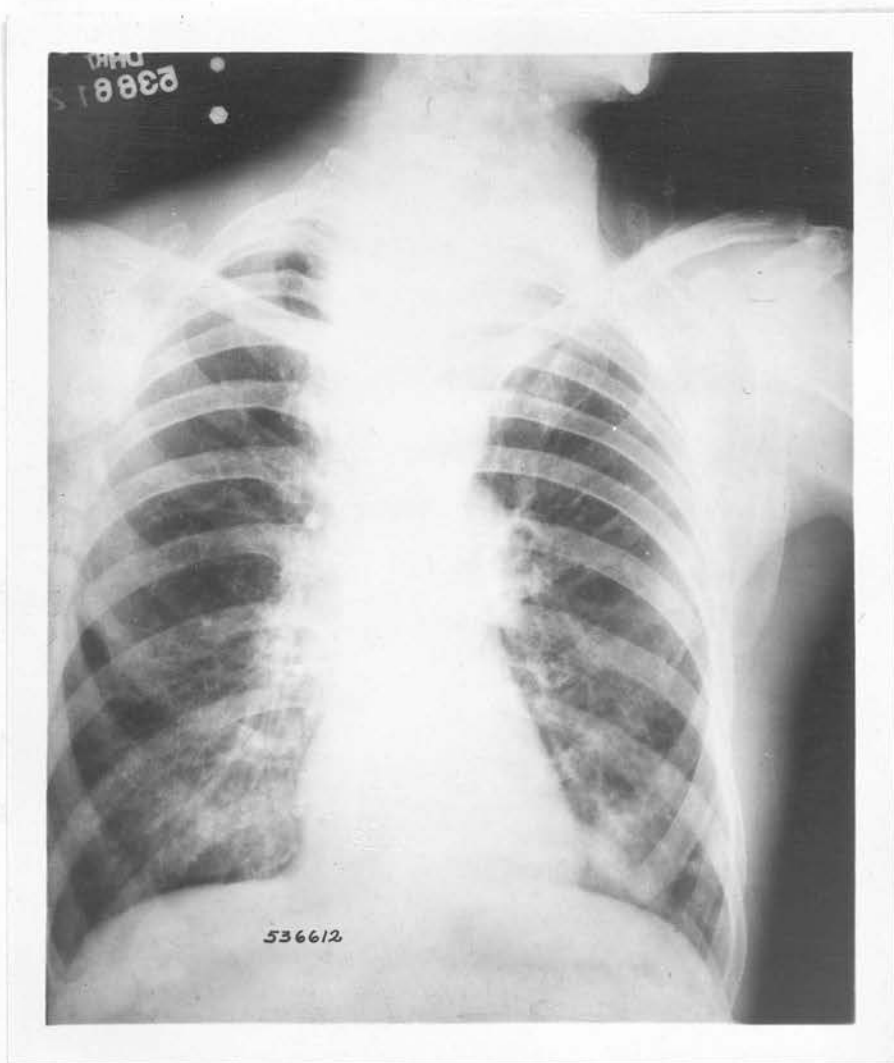
The hilus of the lung consists of bronchus, vascular trunks and glands. In the healthy hilus the first and the last cast no shadow. Pathology in any of these structures may then produce an appearance of hilar density. Chronic bronchitis or pneumoconiosis will give a generalized fibrosis, centered at the hilus - and there-

fore a "hilar density". Figure 1 shows a proven case of old bronchitis of twenty years standing; Figure 2 was the chest of a quartz miner. The vascular roots will show increased density in all congestive conditions. Figure 3 was from a case of definite cardiac insufficiency. The density in all such conditions will always be of a bilateral nature and the degree of apparent "infiltration" will be much greater than the malignancies produce.

The glandular conditions are a little more difficult as they do show unilaterality, though uncommonly. Any general adenopathy, such as leukaemia, lymphoblastoma, Hodgkin's, and the like, or any intra-abdominal lesion, infective or malignant, with gland spread up the lumbar and dorsal gland groups, may step over on to the root glands and give hilar shadows. Figure 4 shows a perfect unilateral hilar lump with no accompanying lesion. As an x-ray diagnosis it may be a malignancy. But the patient had obstructive jaundice, a palpable liver, an enormous palpable abdominal tumor and a hematoma. Thus a diagnosis of ascending glandular malignancy was fairly certain even before the clinching operative diagnosis of enormous left-sided retroperitoneal tumor (possible hypernephroma). Yet the x-ray film is not unlike that of Case 12. Figures 5 and 6 show the hilar densities of a lymphoblastoma and of a leukaemia. Even were they not to some extent visible on both sides, they have a rounded contour and a smoothness of edge that is not like a primary malignancy. Indeed, in general, this is characteristic of the glandular enlargements and we might compare Figure 6 with Case 14,

Figure 1

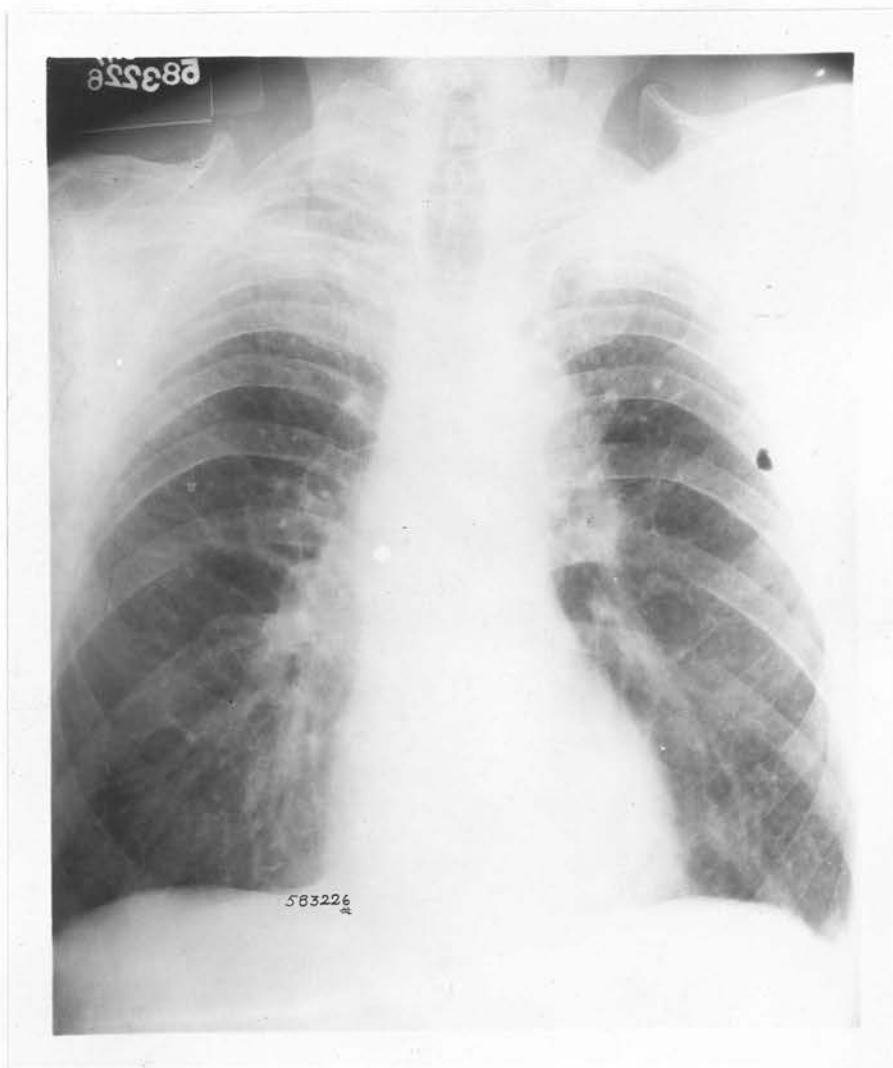
Clinic No. 536612



Film shows the generalized fibrosis of a chronic bronchitis of twenty years standing. The patient had a chronic cough, worst in winter, and physical examination gave signs of emphysema.

Figure 2

Clinic No. 583226

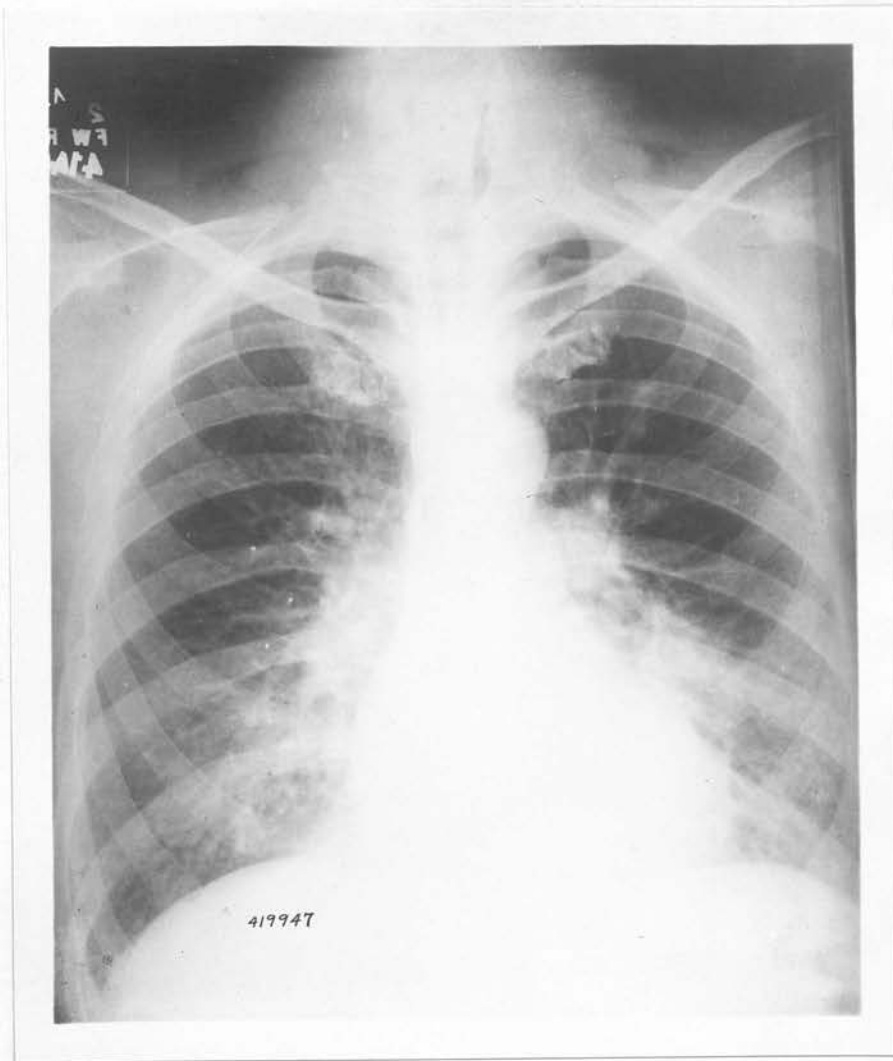


Case of pneumoconiosis. The patient was an old quartz miner.

[Faint, illegible text, likely bleed-through from the reverse side of the page.]

Figure 3

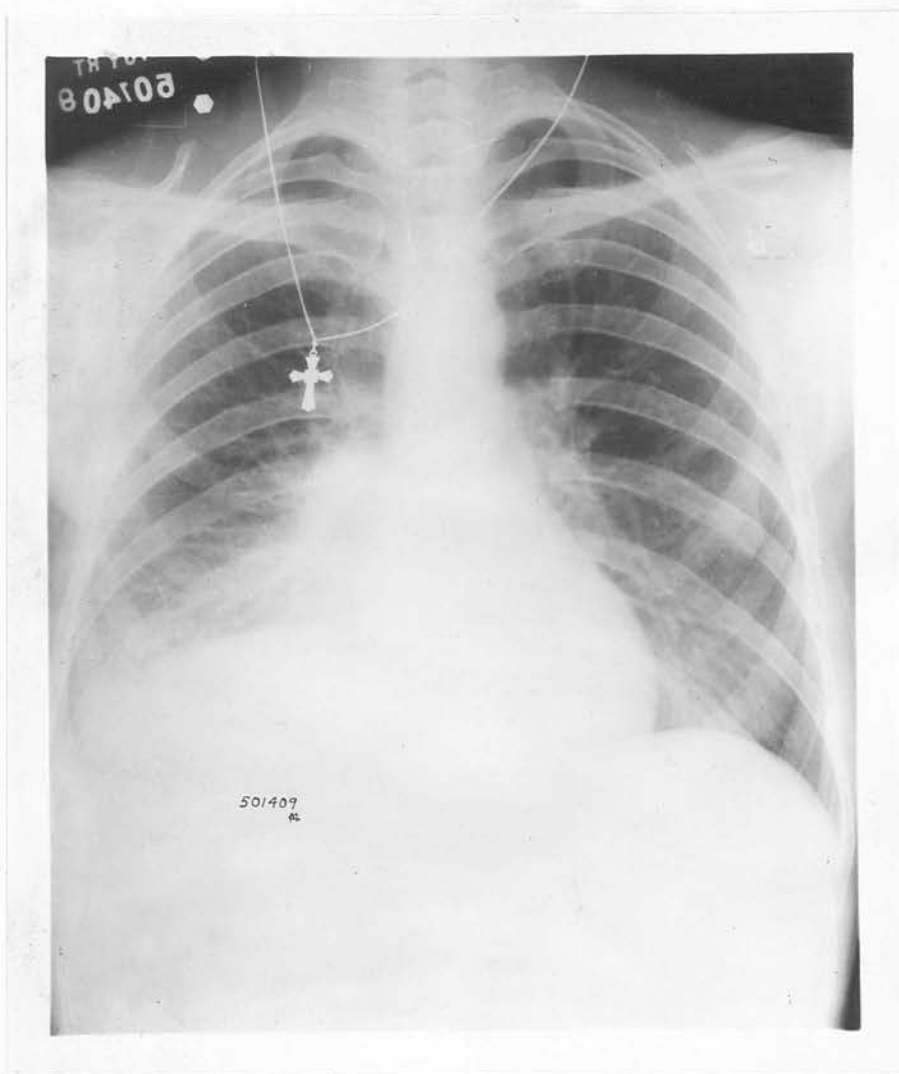
Clinic No. 414947



X-ray of chest showing chronic venous congestion due to heart insufficiency of one year's duration. Patient also had dyspnoea, oedema, palpable liver, fatigability, etc., and clinical evidence of a mitral lesion.

Figure 4

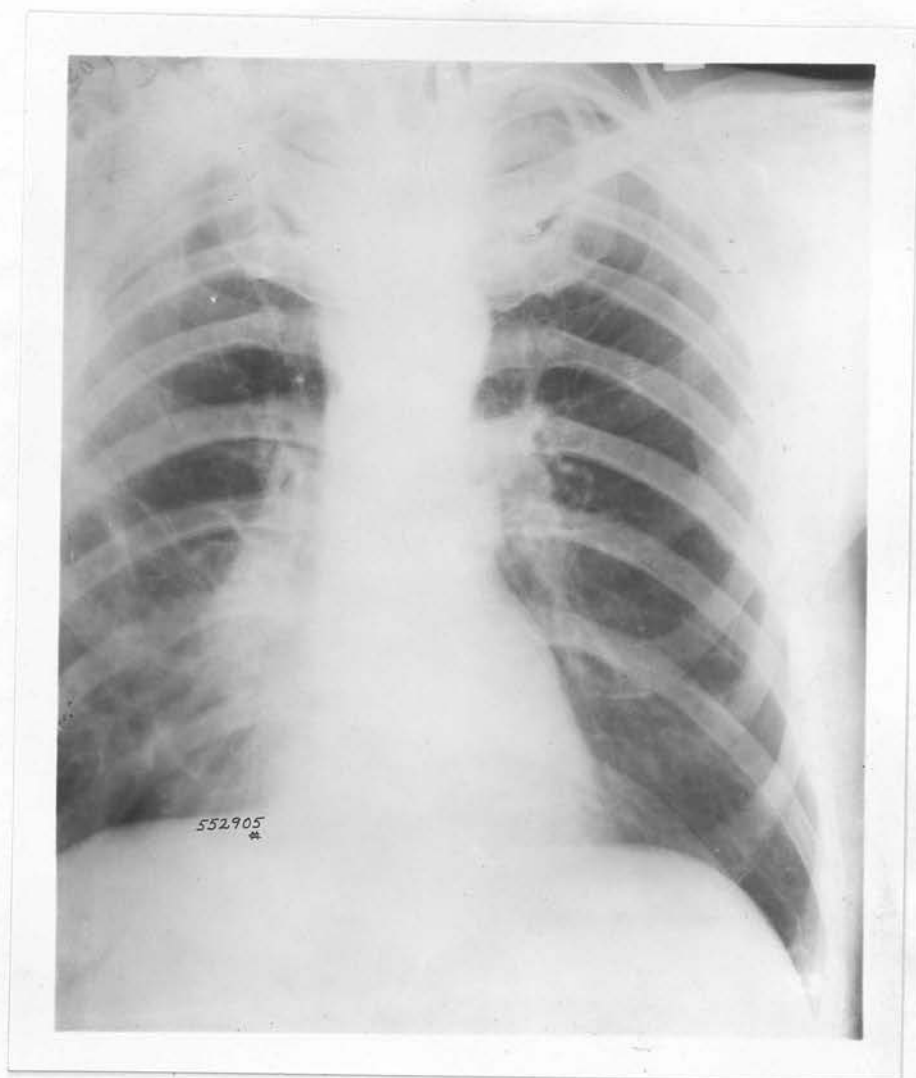
Clinic No. 501409



Film shows hilar gland metastatic malignancy from a huge retroperitoneal tumor, seen in the film pushing up the diaphragm.

Figure 5

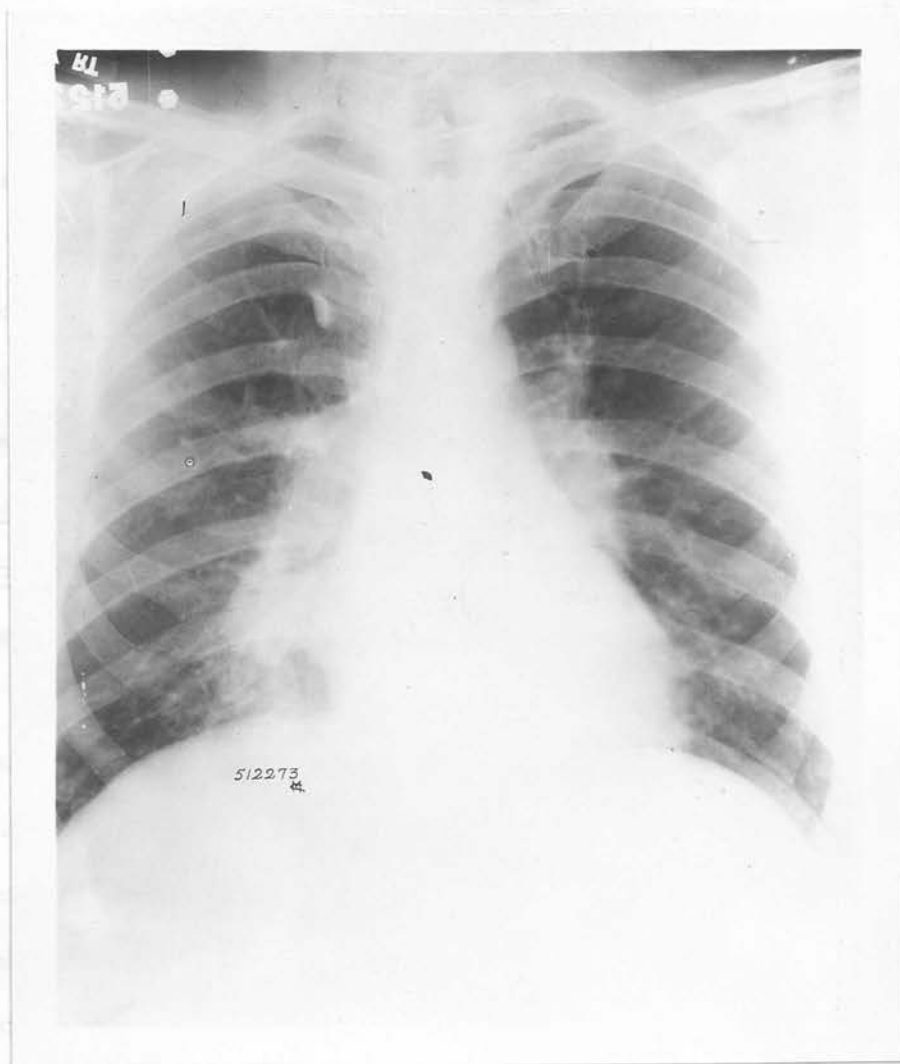
Clinic No. 552905



Mediastinal gland masses of a lymphosarcoma of six weeks duration, with palpable glands in neck, axillae and groins. Neck gland was excised and found lymphosarcomatous.

Figure 6

Clinic No. 512273



Mediastinal gland masses in a case of lymphatic leukaemia of two years duration. The patient had typical count and a general adenopathy.

as both show the same tongue-like process. We saw, however, that Case 14 was not a typical picture but rather a mediastinal multi-adenopathy that happened to be from a primary malignancy. There are cases, however, in which the lymphoblastomata take on an infiltrative character; usually the widening of the mediastinum will be the clue but where quite unilateral the differential diagnosis will be difficult.

The real hilar enlargements, not malignant, are then more or less simple to distinguish radiologically. A more difficult group on the film alone is that group of other mediastinal lesions, which give masses, apparently in the hilus. Such will include aneurism, carcinoma of esophagus, benign tumors, gumma of mediastinum, mediastinal abscess, and rarely such things as Pott's disease with abscess, and chondroma or sarcoma of the spine.

In their typical forms each of these has no great resemblance to bronchial malignancy, but if they take on a somewhat unusual form they may easily be mistaken in a chest film. The history or other form of examination, such as barium meal or spinal ray, should clear up the doubt. But at times it may be rather indefinite. In looking through films for examples of hilar densities I have picked out films of each of the above lesions. Usually the lesion should show a smoother and less infiltrating edge, but those reproductions will illustrate how easy it is to be deceived in a chest film alone. Figure 7 is the film from a case of esophageal carcinoma, proved by barium, esophagoscope and by death. Yet the film going through

Figure 7

Clinic No. 492582



X-ray film of chest in a case of carcinoma of esophagus (lower third) proved by barium mixture in esophagoscopy.

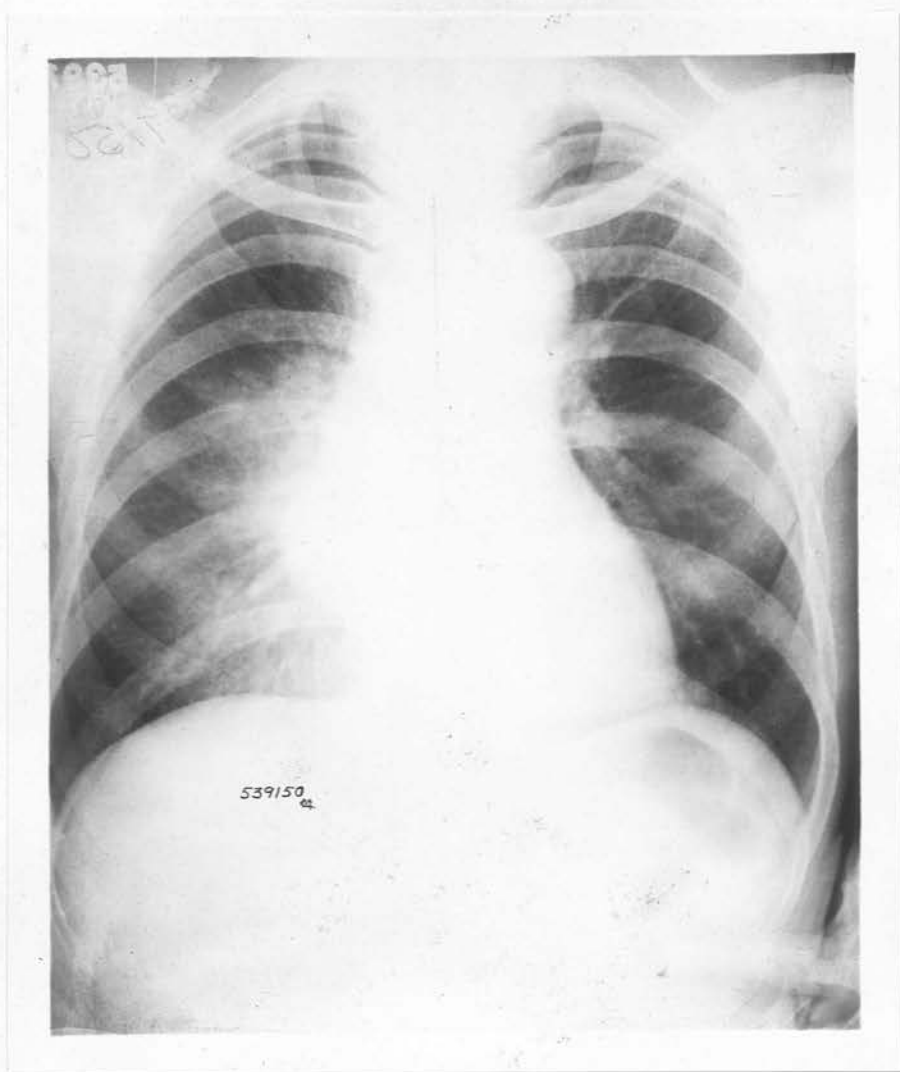
as a routine chest film is diagnosed as a lung malignancy -- and looks it. Figure 8 is even more interesting and merits description. The patient had a 4+ Wasserman and came to the Clinic with a history of two recent severe hemoptyses lasting only a matter of hours but with "blood welling up in his throat" and without any cough, fever, or, indeed, any ill health between. In spite of the fact that on the fluoroscope the tumor seemed to pulsate a little, he was considered as a possible malignancy and was put down for bronchoscopy. While in hospital, however, at eight weeks after the first hemoptysis, the aneurism ruptured properly into his bronchus and he died within a few minutes. I had several other films of aneurism but all show a clearer edge than this. The pseudo-infiltration here I take to be the effects of the first "seeping" blood losses. But the density has a smooth crescentic shape hardly like the irregular density of, say, Case No. 2.

Figure 9 was almost equally interesting and illustrates the possibilities of benign tumors. The density looks just like a hilar density a shade high. He had a history of, at first dry, cough and one slight hemoptysis. A leucocytosis of 23,000 and a biopsy of an "inflammatory" gland from the neck were against malignancy, but with an x-ray picture like that he would have had to be examined had he not made his own diagnosis of dermoid by bringing up numerous white hairs in the expectoration. He has continued to do so for three years now and the x-ray picture remains unchanged.

In discussing the non-malignant masses due to hilar glands I left out the question of tuberculosis as I think this the most

Figure 8

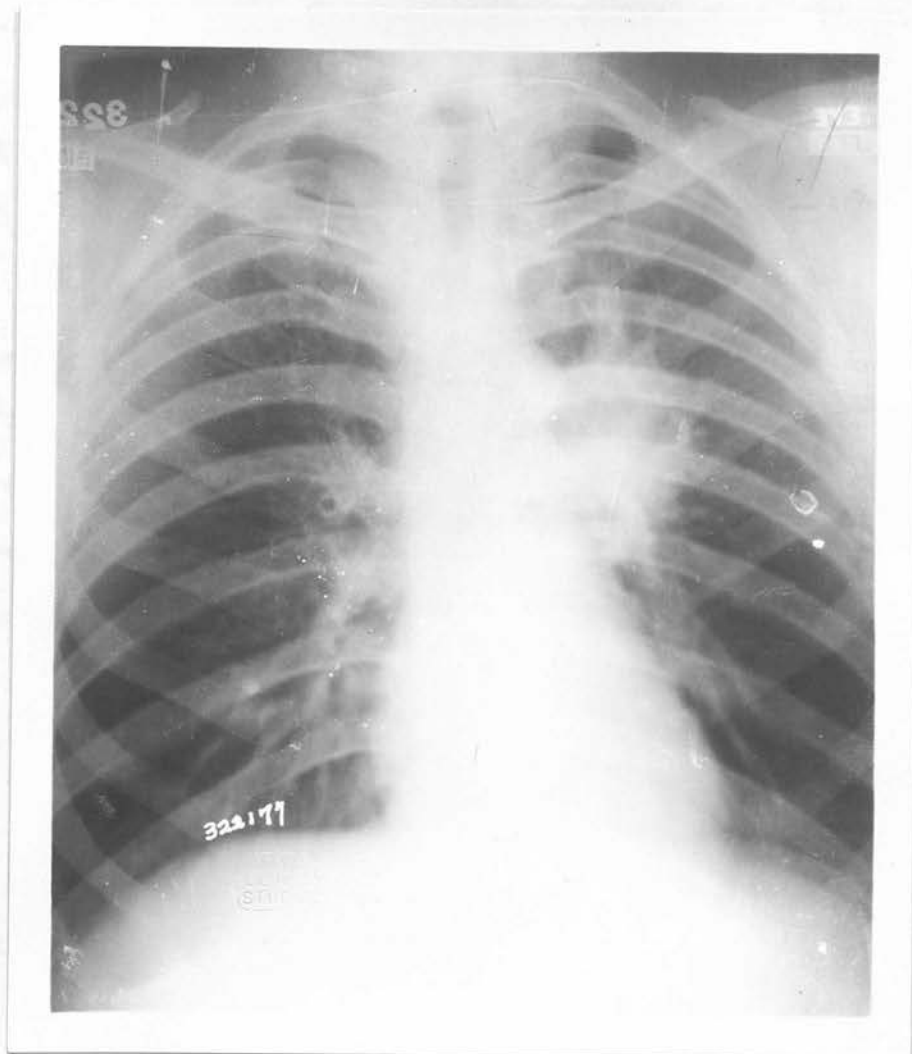
Clinic No. 539150



X-ray film of chest in a case of aneurysm shortly before its rupture into a bronchus.

Figure 9

Clinic No. 322177



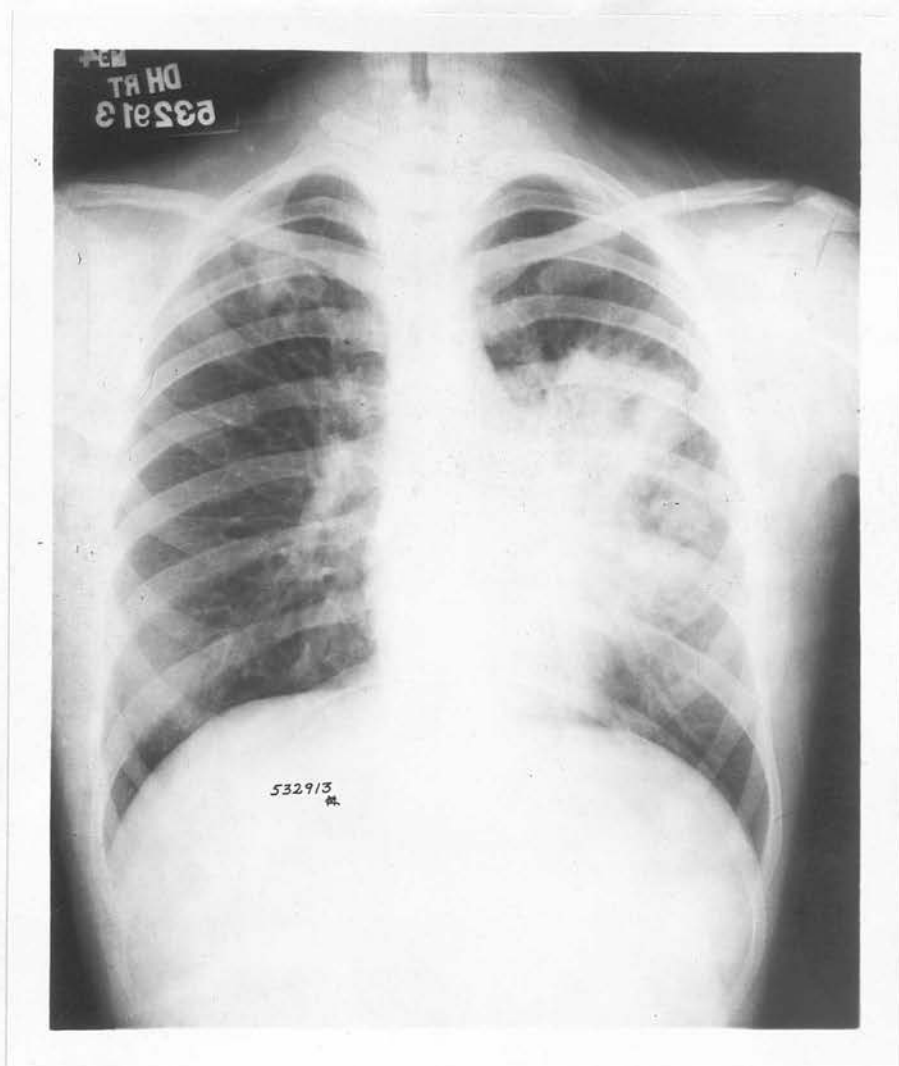
X-ray film of a hilar mass which turned out to be a dermoid of mediastinum and has remained unchanged for three years.

important of all the differential diagnoses. The history may often be of no help, as we get cough and hemoptysis - and weight loss too! There seems to be common agreement that true hilar tuberculosis after childhood is a rarity, so that age is a useful diagnostic point. With adult pulmonary tuberculosis the hilum quite often shows an associated affection, but the picture of patchy areas of consolidation in some part of the lung, with an apical tendency (malignancy tends to spare the apex) and with a tendency to cavitation is, usually distinctive. A case like Figure 10, where the left apex is spared and the hilum dense, suggests malignancy but lacks the appearance of centering to the hilus and shows a mottled patchy nature. The right apex is obviously tuberculous while the patient was only twenty-two and had a "T. B.+" sputum. But there will be the rare case where we have a true hilar disease, where there is a hilar mass of tubercular nature. Figure 11 is such a case, and was diagnosed as "possibly malignant". Only the ultimate follow-up investigation proved the real nature of the case. Bronchoscopy showed no lesion. The sputum was negative even to GP inoculation, but there was a history of cough, pain, and hectic fever and a neck gland biopsy showed typical tubercular tissue. After five months sanatorium treatment the patient returned clinically well and gave a normal chest x-ray. The film here is certainly twin to Case No. 1 and must diagnose as possibly malignant. However, it is rare to get a tuberculosis without some of the normal characteristics of that disease.

A glance down the column of routine x-ray diagnoses in Tables I

Figure 10

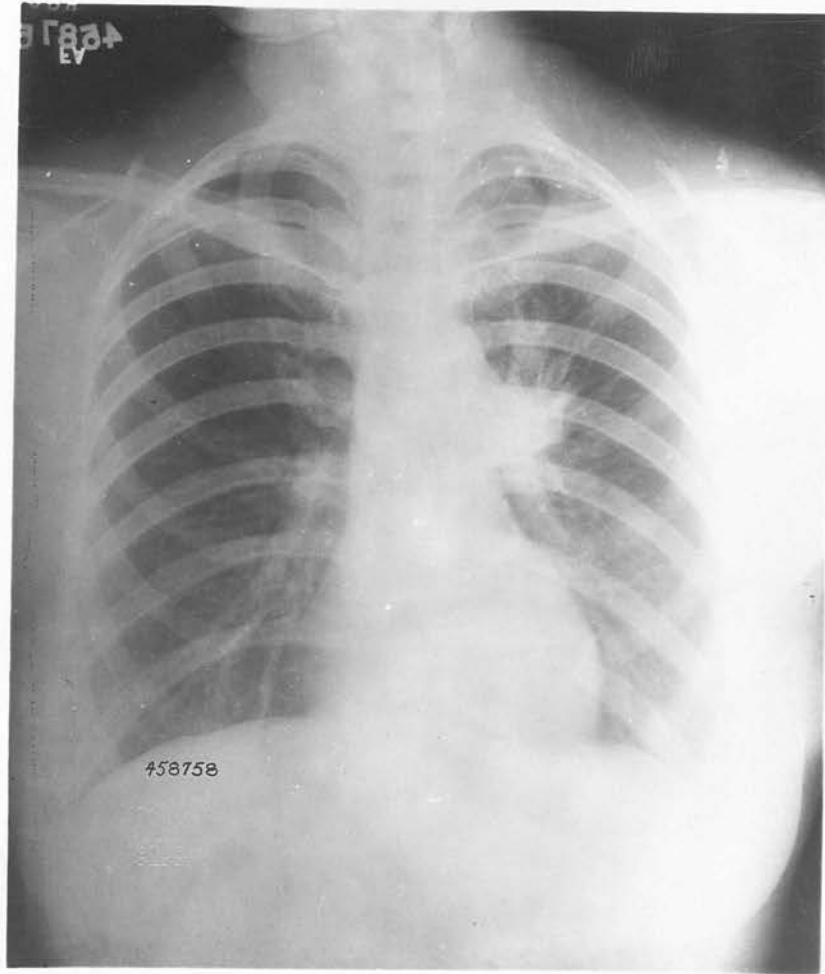
Clinic No. 532913



Case of tuberculosis in a girl of 22, with typical tuberculosis history and tubercle bacilli in the sputum.

Figure 11

Clinic No. 458758



X-ray of chest of a man of 28 with only three weeks history of illness ultimately diagnosed as tuberculosis from neck gland biopsy and the effect of sanitarium treatment.

and II impresses one with the frequency of inflammation as a tentative diagnosis. Abscess was diagnosed six times in the whole group while only eight were from the first diagnosed as malignant. It will thus be seen that the chief source of error is the inflammation group including various forms of pneumonitis, pneumonia, abscess and pleural affections - plaques or localized fluid collections. This occurs for two reasons:

(1) That the really early hilar density shows a separation from the mediastinum and is therefore apt to be confused with an interlobar empyema or a circumscribed parenchymal collection of pus;

(2) That the natural tendency is to consider the consolidation appearance produced by atelectasis as some form of pneumonic consolidation.

A true pus collection or a pneumonitis - omitting, of course, discussion of obvious abscesses with fluid levels - tends to be more circumscribed and less infiltrative than a malignancy, and further the lesion will very often present an appearance of multiplicity in some way, that no single cancer can present. Figure 12 shows the appearance in a case of resolving pneumonia: There is a hilar density and, while it is not divided off from the lung like the mediastinal masses, yet it has not the strand-like infiltration of a malignancy, and we have a couple of nodes farther out to suggest multiple foci.

An atelectasis consolidation, besides showing a peculiarity of texture, will also show at least one sharply defined edge without any increased density along that edge such as occurs with an abscess wall or cyst: It will always be continuous with the hilus.

Figure 12

Clinic No. 366380



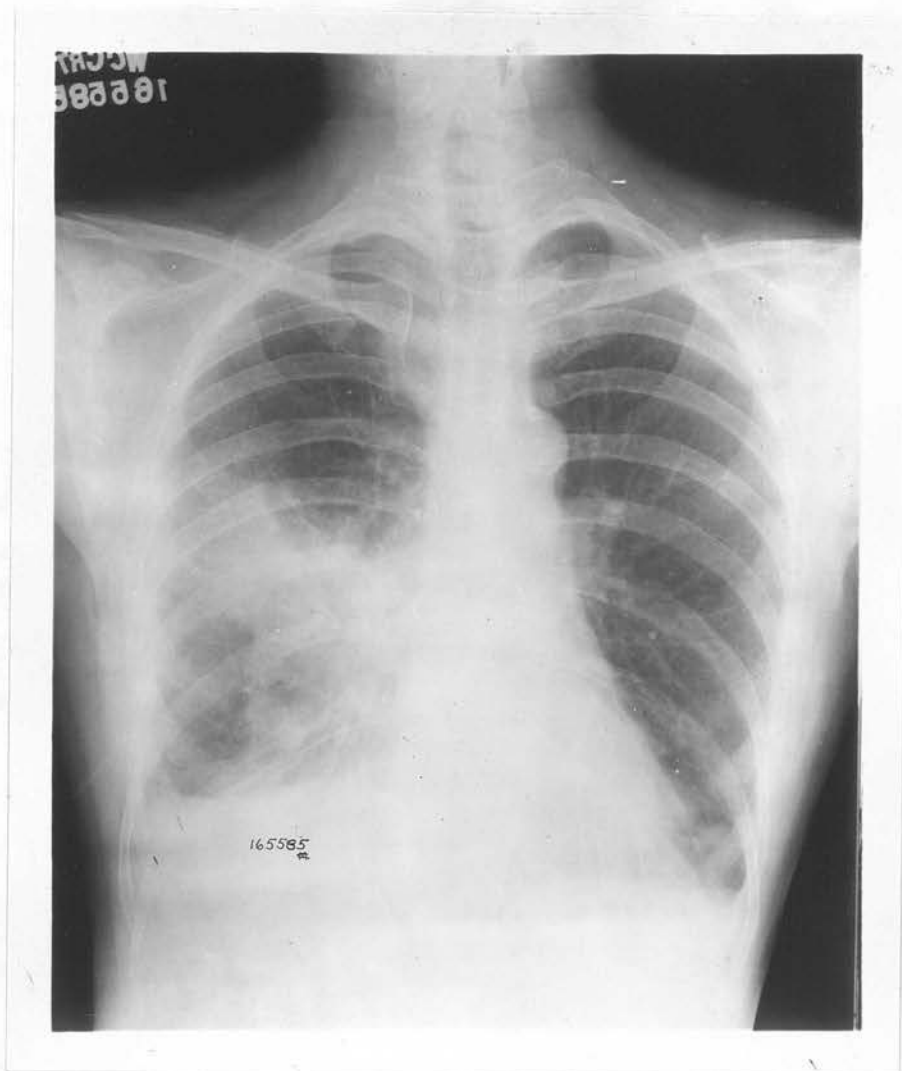
Film from x-ray of chest of a child of 12 who had had pneumonia some time before, yet was clinically well and showed no evidence of abscess. The film shows an unresolved pneumonia.

Figure 13 shows a hilar density, an apparent bronchiectasis and a shadow peripherally. Were this last atelectatic mid lobe it would have a sharp upper edge. It is not continuous with the hilus and the multiple lesions - there is also pleural fluid - suggest rather an inflammatory lesion. But the history was not too definite and a bronchoscopic examination safer. This was done and the patient given lipiodol that way. Figure 13A shows the bronchiectasis that was discovered and the area of true consolidation above it. Or, again, Figure 14, which is from a pneumonia and empyema, resembles atelectasis but has far too patchy an appearance for atelectasis, has no edge and is made definite by noting the pleural fluid and the mediastinal displacement away from the lesion. As the stereoscopic view shows, the density is probably thickened pleura. Figure 15 raises another problem. There is dense atelectasis and atelectatic displacement, there is a hilar lump, but the base is too dense for a pure pseudo-bronchiectasis and again we have that mottled patchy nature to the edge of the lesion indicative of an inflammatory lesion. The history was clear. It was an advanced foreign body bronchiectasis.

One would scarcely ever get so far advanced a bronchiectasis with a malignant obstruction - this case had several years history. But it should be emphasized again that a pure bronchiectasis even as typical as that shown in Figure 16 - a pure influenzal bronchiectasis - may, if no other cause be found for it, be due to a malignancy, though such a latent malignancy is rare.

Figure 13

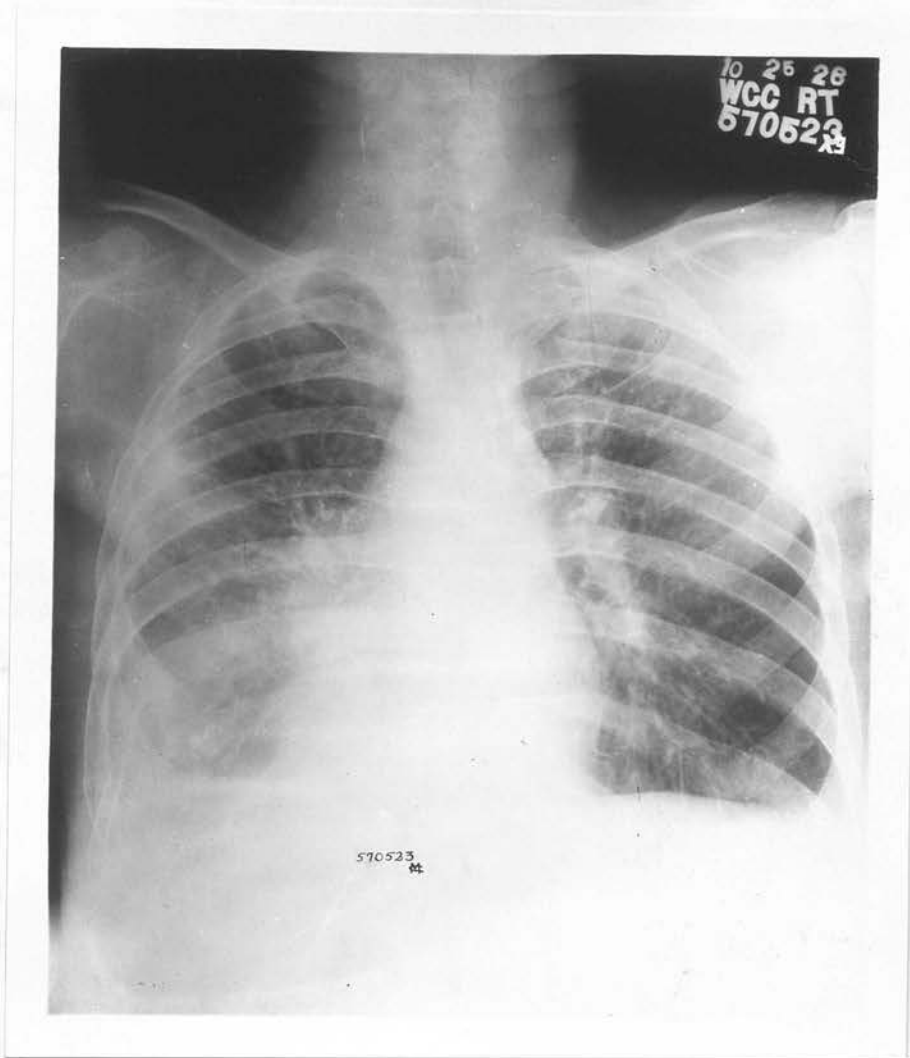
Clinic No. 165585



Case of a man with productive cough, blood-stained, and much fever of two years duration. Diagnosed by bronchoscopy as a typical bronchiectasis.

Figure No. 14

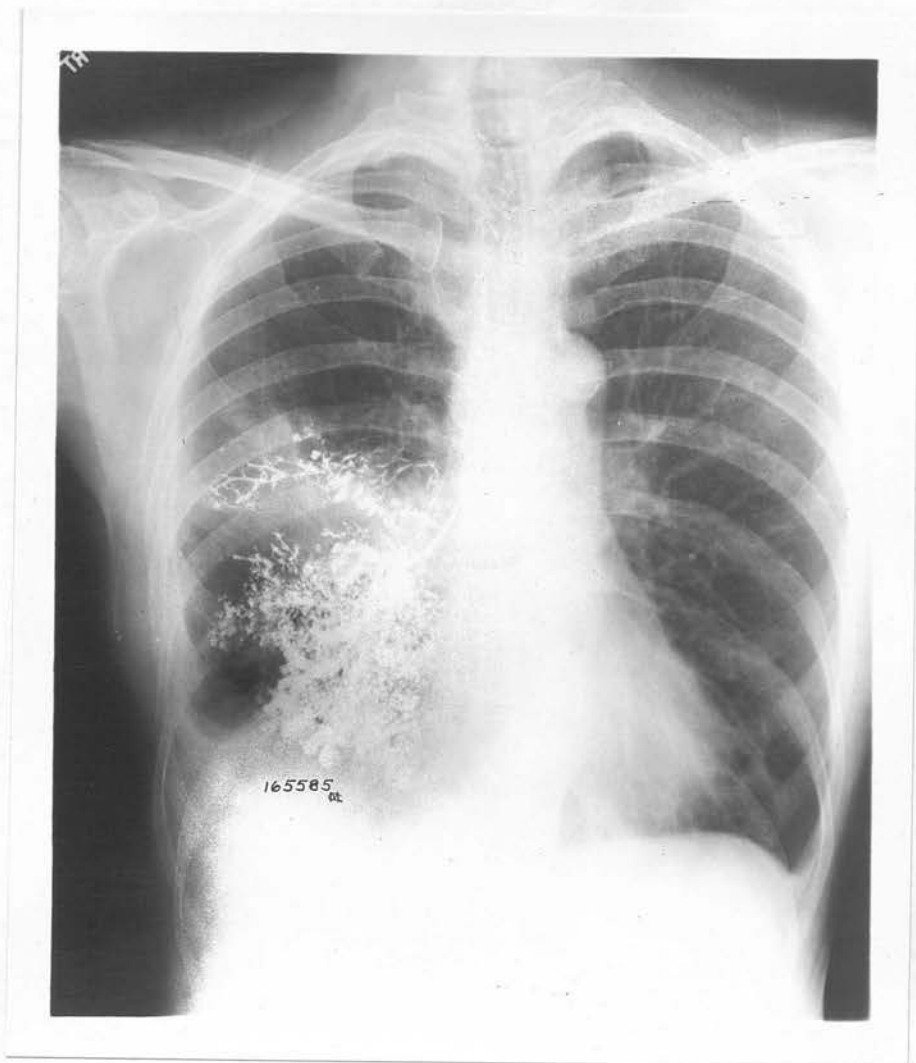
Clinic No. 570523



Case of thickened pleura resulting from drainage of an empyema.

Figure 13A

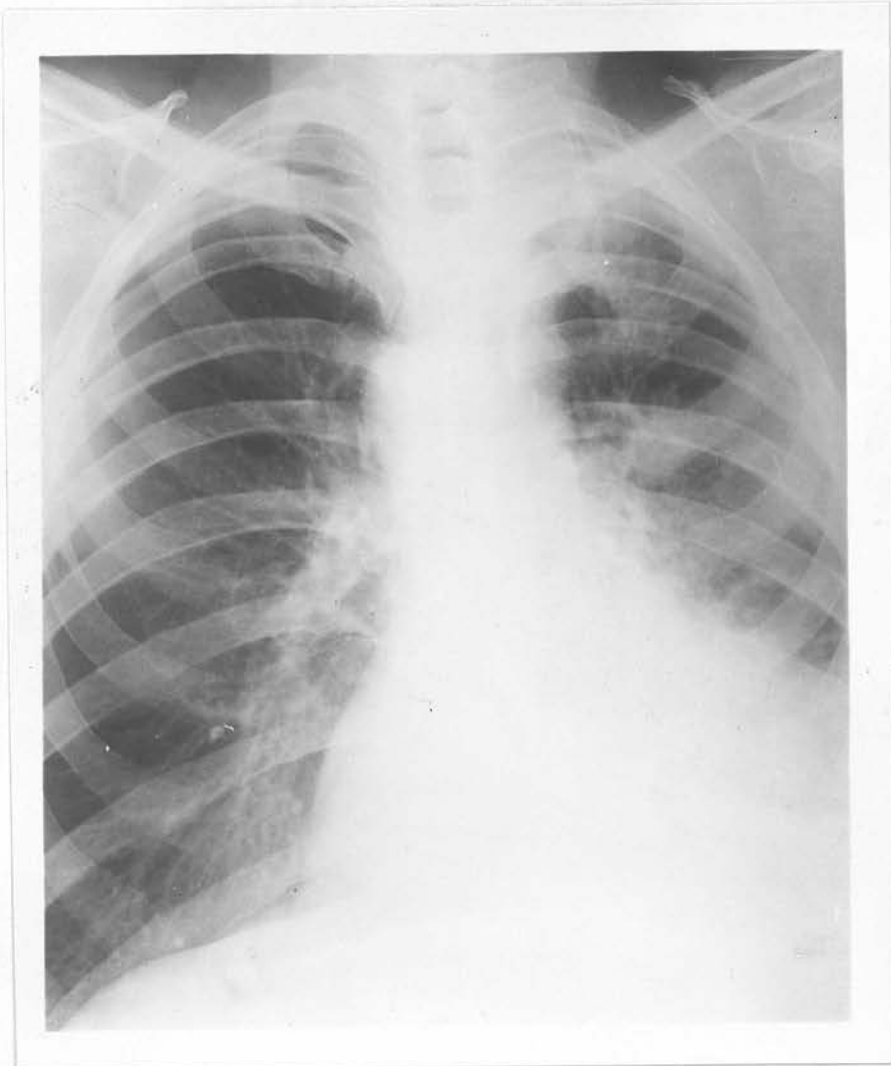
Clinic No. 165585



Same case as previous with lipiodol injection, showing the bronchiectasis.

Figure No. 15

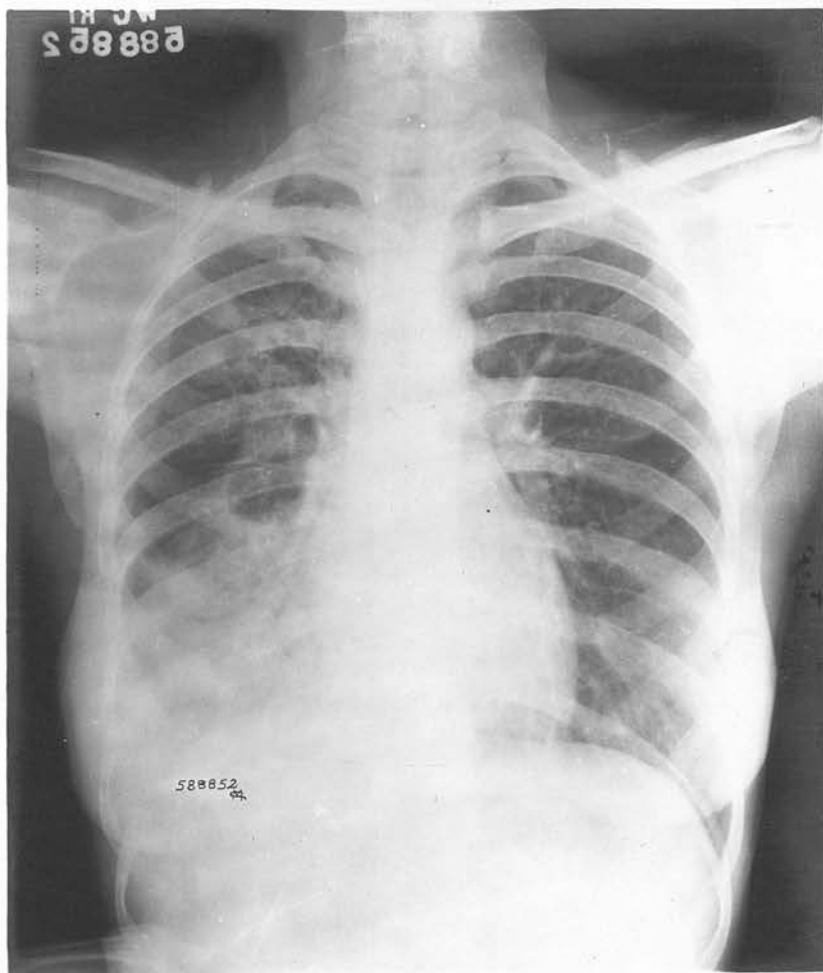
Clinic No. 503720



Case of advanced multiple bronchiectatic abscesses resulting from swallowing a toothpick which was in bronchus over a year before it was aspirated.

Figure 16

Clinic No. 588852



Typical x-ray picture of bronchiectasis. Note the correlation towards the hilus, where in the pseudo-bronchiectasis there would be the hilar density of the malignancy.

The inflammatory lesion, then, is the one that must be watched, and in the end, as in Case 13, where whatever the suspicion the appearance of malignancy cannot be excluded, the case must go to the bronchoscopist's court of appeal.

TREATMENT

Literature on the subject of lung malignancy is voluminous but it stops - at prognosis: Why is this? Probably chiefly because a diagnosis of carcinoma of lung is still considered an absolute death warrant, and in the early case, with evidence poor, the physician says, "Treat expectantly: If it is malignant we can do no good anyway." And so the surgeon gets only the later cases to tap pleural effusions or to do what Lilienthal (14) calls a thoracic decompression. Adler even sums up, "Optima hic est medica, medicam non facere."

And even to-day we can only ask, "What of the future?" The surgeon must get early cases and this can come only where the physician looks for this disease as at present he looks for phthisis. I believe that the x-ray will become more and more important in isolating early possible cases. Lilienthal in his well-balanced article stresses the need for, if necessary, an exploratory thoracotomy, just as to-day we do a laparotomy.

What can be done?

Complete unilateral pneumectomy has been done in dogs.

Lenhartz quoted by Playfair (12) operated on five cases by partial lobectomy: One case lived two and one-half years. This is probably the first authentic operation case.

The Sauerbrüch Clinic (16) reports fifteen cases (of which five were attempted radicals) with one five- and one three-year survival. They advise a wide rib resection and exposure and ligature

Moriston Davies (15) outlines another technique and quotes one survival case.

Just recently Brunn (19) reported two cases of which one recovered from operation and lived eight months.

Hence the operation is possible, and it is, unlike the now frequent enough lobectomy for suppurative conditions, a clean operation. "What man has done man can do," and ultimately, we would hope, with reasonable safety. A generation ago colectomy or total gastrectomy was an historic event.

But through all this runs the theme that this is only possible for a parenchymal tumor. The true bronchial is too near the mediastinum to be got at radically by that method.

What of radiation?

Here as yet we are only in the land of conjecture and yet by analogy there ought to be - and there will be - some success. Schnoeder (quoted by Lilienthal) gives an apparently cured x-ray case. Rolland (17) is reported in some of the papers as quoting a deep therapy cure, but reference to his article shows that the lesion was almost certainly sarcoma and, moreover, that the patient died:

I would have expected to have found reference in the literature to what seems to me to be the most hopeful method in bronchial cases - namely, radium needles or tubes placed in the tumor via the bronchoscope, but can find none.

We do have radium cures in cases of cervix, rarely in cancer of the oesophagus, and commonly in the skin. Why not here where

one can also get right onto the tumor? Some day it will be tried and with what results? On this note of conjecture I would end, and with the hope that before long the diagnostic radiologist and the clinician working together will be able to give the radium therapist and the bronchoscopist something early enough to offer possibilities, and yet in which surgery offers little.



Summary

1. Carcinoma of the bronchus - by which is meant a bronchus of dimensions visible to the bronchoscopist - has a distinct clinical entity of its own, distinct from true lung tumors, with which it has previously been grouped.
2. Lung and bronchial tumors are moderately rare but are becoming more frequently diagnosed, and may be much more common than at present realized, owing to the frequency with which they are treated as tuberculosis.
3. A male preponderance and a right-sided maximum incidence seem to indicate a relationship to chronic irritation as an etiological factor, but in the group of cases presented no marked relationship could be established to tuberculosis, influenza, occupational diseases or over-smoking.
4. The clinical syndrome of the primary bronchial tumor is an absolutely persistent cough with either hemoptysis or scant but blood-stained sputum and the lesion is visible on bronchoscopy. The syndrome of primary parenchymal tumor, a much more latent lesion, is severe, otherwise unexplained, weight loss, associated with vague but constant chest pain, or dyspnoea, or the cough-blood combination of the bronchial group.
5. The two groups do not separate pathologically in the same manner. The gross pathology of parenchymal includes nodular, lobar and infiltrative forms, while the bronchial are all infiltrative.

Microscopically we get all forms of adeno-carcinoma but also some squamous-celled carcinoma, and of the primary bronchial group reported six out of seven cases were of the latter type. This probably represents a metaplasia to an embryonic cell type latent in the development of the trachea and bronchi from the oesophageal bud. The growth tends to be of a highly malignant type.

6. The radiological literature describes a relatively late case. It groups the appearances as hilar or lobar of which the hilar is the more frequent, but at the stage at which the lesion has been previously recognized secondary effects, stenosis, infection, pleural effusion or metastasis, usually complicate the picture.
7. The early diagnostic picture must be recognized in the routine films of the chest, and therefore a special technique is not called for, although stereoscopic films are of great assistance.
8. There are three characteristic factors suggestive of bronchial malignancy:

 - (a) A hilar density, unilateral, occupying the whole hilus, usually just perceptibly separate from the mediastinum, ramifying out into the parenchyma in irregular strand-like processes and unassociated with any other mediastinal deformity, occurs in the majority of cases. This may be alone or be associated with one or other of the next two factors.
 - (b) Atelectasis of a whole or part of a lung without discoverable causal history, is very frequent.

(c) A pseudo-bronchiectasis , an appearance radiologically identical with true bronchiectasis but caused by blood-filled bronchi.

9. Contrasting with this the parenchymal tumor is less dense, either roughly circular or lobar in shape, rather less infiltrative, and is seldom even apparently hilar in location.

10. This radiological picture of the early bronchial carcinoma must be distinguished from the following groups of lesions:

(a) Other hilar densities such as bronchitis, pneumonia, venous engorgement, will give a more diffuse infiltration and will always be bilateral.

(b) Apparent hilar densities such as carcinoma of esophagus, aneurism, and such like, will show a certain definition of edge separating the lesion from the lung, even where there is apparent root infiltration.

(c) Tuberculosis will mostly give the features peculiar to that disease - an apical tendency, an irregular mottling rather than strand-like infiltration and an absence of hilar centering.

(d) Other gland lesions have a definite edge and a crescentic shape rather than the projecting shape of the malignancy, and even if unilateral tend to show a general widening of the mediastinum.

(e) Inflammatory lesions are the most difficult as they are so protean in form but they have a general mottled nature, a tendency to multiplicity, an absence of hilar centering and a

narrower limitation of the width of the infiltrating edge but never the smooth finished uninfiltrating edge of an atelectasis.

11. Although there are isolated reported cases of successful lobectomy for parenchymal carcinoma, nothing has yet been done for bronchial; but radium in the bronchus is suggested by the author.

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