

CARCINOMA OF THE LUNG

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by

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CARCINOMA OF THE lung has become a problem of some importance in this country in that its incidence has increased in frequency about six times since the first decade of this century, and is now more common than carcinoma of the stomach.

The disease is predominantly that of males, the ratio of males to females varying between 6-1 and 10-1 for different statistics ; personal statistics being 10-1.

Town dwellers are more frequently affected than country-folk.

The causation of the increased frequency is as yet unknown, but certain factors have been adduced to explain it ; the increased use of heavy hydrocarbons, both in internal combustion engines, especially in the confined atmosphere of large towns, and in the tar spraying of roads, and latterly the increase in cigarette smoking ; it is true in this connection to note that a large percentage of patients suffering from the disease are heavy cigarette smokers. It is interesting to note that our experience is almost exactly duplicated in the United States. Conversely, however, in Norway, no such increase in frequency has been noted and there is not the same disparity between town and country dwellers or the same sex disparity ; this seems to support the thesis that the increased use of heavy hydrocarbons may be an important factor. Norway has nothing like the same degree of mechanisation as occurs here, and tar spraying of roads is so little as to be negligible. Apparently in Yugoslavia, where local conditions are somewhat comparable with Norway, experience with this disease is similar.

Age Incidence.—The great majority of cases occur in the sixth and seventh decades, but cases have occurred in all decades from the second to the ninth.

Despite the marked frequency in the incidence of the disease, the percentage of cases in whom surgical intervention is not contra-indicated on clinical and radiological grounds is only 15-20 per cent., and of these, only about 60 per cent. eventually prove to be removable. This is a lamentable state of affairs, and it becomes more so when it is considered that the average length of time which elapses between the onset of symptoms and the patient's seeking his doctor's advice, is over three months, and added to which the time between the first consultation with his doctor and his arrival at hospital is over five months, and again a further month to six weeks may elapse before the patient's admission to a hospital

bed. The high percentage of cases which are inoperable when they arrive is easily understood when it is appreciated that the average expectation of life after the onset of symptoms is 12 months, and after diagnosis six months. Only recognition in the early phase of the disease can lead to an alteration in the state of affairs, and primarily this must rest on clinical grounds.

Pathologically, two types of tumour can be recognised, the main bronchus type and the circumscribed type of tumour.

(a) The main bronchus type occur as endobronchial tumours, arising in either the main, lobar, or segmental bronchus, in other words, a large majority of these tumours are within bronchoscopic telescopic vision, and of these, a fair percentage are amenable to biopsy.

These tumours, apart from haemoptysis, produce their symptoms by occluding the bronchus. Subsequent changes depend on the absence or presence of infection beyond the tumour. In the former case, a simple atelectasis occurs, but when infection is present, depending on its severity, and to a certain degree on the type of organism, all the phenomena of pulmonary infection may be manifest, bronchiectasis, suppurative pneumonia or lung abscess.

These tumours spread locally up and down the bronchus, or even submucosally, although this is a slow process, or there may be an extension through the bronchial wall into the surrounding lung substance, the latter being rarely of great extent.

(b) The circumscribed group arise from the smaller bronchi, occurring as tumours in the lung substance and having a remarkably clear cut circumscribed margin. These tumours are prone to undergo degeneration and to rupture into a bronchus of larger degree. When the latter only occurs, the tumour partially extrudes itself into the bronchus, like tooth-paste out of the tube, the extruded portion having no attachment to the mucosa of the bronchus into which it has been extruded—probably it is such a portion which is occasionally coughed up. When both degeneration and rupture have occurred, the degenerated portions are coughed up, leaving an air-filled cavity in the growth. These tumours grow concentrically, and because they originate in the smaller bronchi, in the majority of cases, the visceral pleura eventually becomes involved and subsequently surrounding structures, parietal pleura and eventually chest wall, mediastinum, pericardium or diaphragm.

Both types of tumour, as with all carcinomas, spread also by lymphatic and blood stream.

Personal experience suggests that the main bronchus type is more responsible for early metastasis to the parahilar and mediastinal glands than the circumscribed type, although there is far from unanimity on this point. It is, however, generally accepted that blood borne metastases occur earlier when the tumour is of the circumscribed variety, and this can be understood when it is considered that these tumours occur in

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the area of the main vascular bed ; not infrequently the tumour is found to be growing along the pulmonary veins.

The gland groups involved are the intra-pulmonary nodes, which occur at the site of the bronchial bifurcation, and these probably account for the later metastasis to the next group, the parahilar group. The other groups are the inferior tracheo bronchial and the lateral tracheal glands. The supraclavicular and axillary glands may also become involved, without radiological evidence of paratracheal or inferior tracheo bronchial involvement, and on two occasions, inguinal glands have been involved. Distant metastases occur in the liver, spleen, suprarenals, kidneys, brain or bones.

These tumours all arise from the basal layer of the bronchial epithelium as was pointed out by Barnard. These cells normally give rise to typical respiratory epithelium with its columnar ciliated and goblet cells, but it is also capable by metaplasia of producing stratified squamous epithelium. The cause of this metaplasia is not known ; it rarely occurs in the presence of gross infection ; although bronchial epithelium readily regenerates, in fact it is not uncommon to find ciliated epithelium lining either partially or nearly completely a lung abscess. This faculty of bronchial mucosa to change its character undoubtedly explains the pleomorphism of these tumours.

Histologically they present as squamous celled, oat celled or adeno-carcinomas.

(a) Squamous celled tumours form about 60 per cent. of the whole group, and are most commonly fairly well differentiated, but may show varying degrees of anaplasia.

(b) Oat celled tumours form about 20-25 per cent. of the total. They usually occur in younger age groups and are then rapidly growing and show markedly invasive properties, and generally the cases are inoperable by the time they are diagnosed. When this group occurs in the older age group, however, for some inexplicable reason, they often run a relatively benign course.

(c) Adeno-carcinomas are generally well differentiated tumours and in some cases exceedingly so, in the latter group sometimes producing large quantities of mucus, enough so to have been designated mucous celled carcinoma, an unnecessary elaboration. Some difficulty may arise in determining whether or not the lung tumour is primary or secondary to a carcinoma in the alimentary tract.

Symptomatically, the case presents in one of the following groups, although there is naturally a great deal of overlapping of groups in some cases.

I. Those presenting with symptoms referable to the respiratory tract.

(a) The symptoms may be of the chronic type.

These symptoms are, of course, common to any of the pathological conditions affecting the lungs, but certain points should be stressed as they appear to be indicative of carcinoma rather than the other lesions.

(1) *Cough* when it is non-productive and persistent, should promptly give rise to a suspicion of an endobronchial tumour. Such a cough is an index of bronchial irritation and without sputum connotes a lesion which needs investigation. Certainly the lesion may be a benign tumour, a fluid collection trying to rupture into a bronchus or rarely a foreign body ; it is nevertheless a symptom of serious significance.

(2) *Sputum*. This may be of any character, mucoid, purulent, foetid or non-foetid, and this, of course, depends on the degree and character of an associated infection.

(3) *Haemoptysis*. This is a valuable symptom when present early as it is liable to impress not only the patient but also his medical attendant. Only 60 per cent. however have haemoptysis, and if it be considered a cardinal symptom, then 40 per cent. of cases will be overlooked.

(4) *Pain*. This may be of two types, (a) *Pleural* in which the pain may be local over the site of the tumour or radiating in the usual manner of pleuritic pain. This is due to involvement of the parietal pleura either by the growth itself, or by an inflammation of the lung behind the growth. This type of pain when it occurs without any constitutional disturbance is often lightly diagnosed as fibrositis ; such a facile diagnosis for persistent chest pain cannot be too strongly deprecated, and its presence should promptly suggest an X-ray examination of the chest. (b) *Substernal*. This type of pain may be either a dull ache, or not infrequently, more sharp. In the former type, it is often dismissed as indigestion and not infrequently these cases are discovered when the chest is screened during a Barium meal examination. Screening of the chest at such an examination is, or should be, a routine procedure. The cases with the more acute type of pain are often mistaken for a small coronary thrombosis. These cases usually have a radiograph of the chest taken, but any suspected cases of coronary occlusion which is atypical should be so examined. The causation of this type of pain is not clearly understood, as it occurs when there is no involvement of either visceral or parietal pleura by either the tumour or an inflammatory process. One thing only is certain ; its complete relief after the lung and tumour have been excised ; to say it is visceral in origin merely begs the question.

(5) *Dyspnoea*. This is possibly the most constant symptom of the condition, though not the commonest presenting symptom, which is cough. The mechanism of its production cannot be satisfactorily explained in all cases, but in large numbers there is a fairly easily recognisable positive pressure emphysema which results from expiratory stenosis of the affected bronchus. During inspiration, the bronchus opens sufficiently to let air enter the bronchus beyond the block, but it closes before the air thus admitted can escape ; in this way, the air behind the block does not form part of the ordinary bronchial air stream and thus the blood circulating in this area is not fully oxygenated, hence there is a decrease in the oxygen tension in the arterial stream. It is possible too

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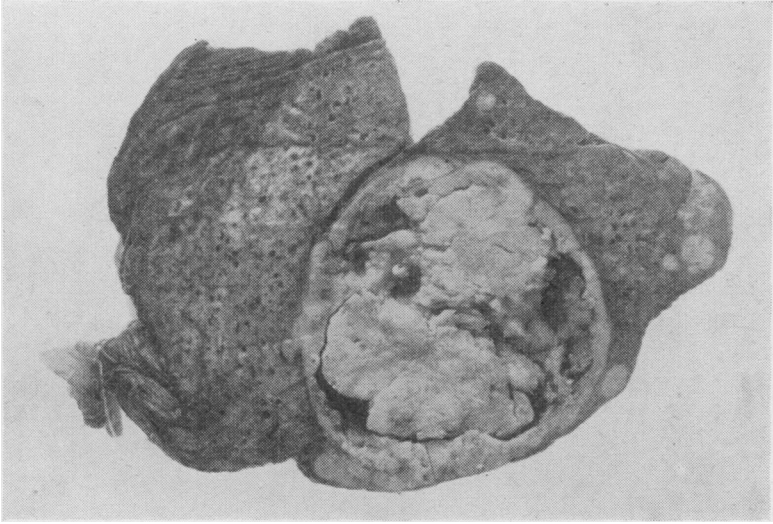


Fig. 1.

Circumscribed carcinoma involving visceral pleura and showing well marked degeneration. Histology : squamous celled.

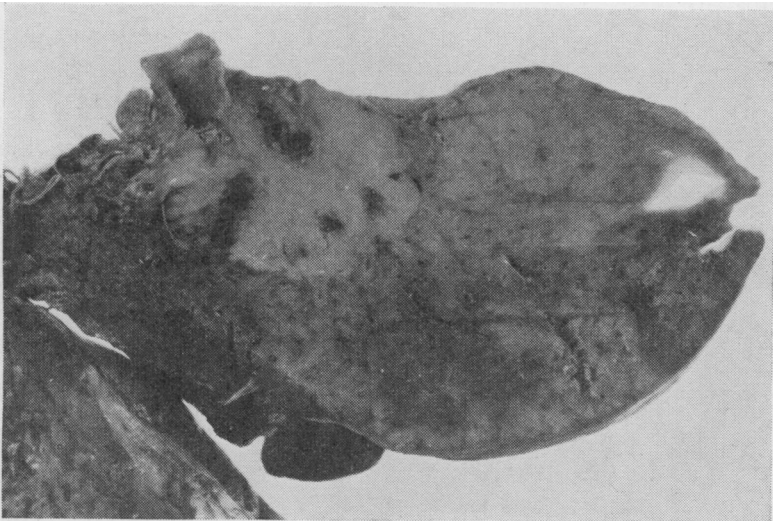


Fig. 2.

Main bronchus type of carcinoma showing extension outside bronchial wall and marked suppurative inflammation of the lung beyond site of tumour.

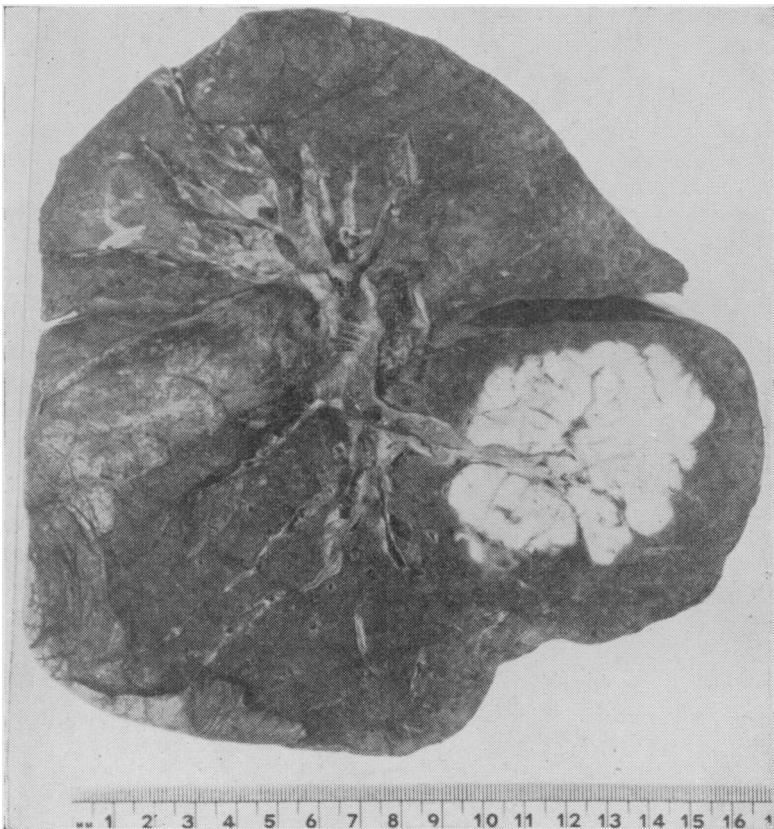


Fig. 3. Circumscribed carcinoma. Histology: squamous celled type showing a well marked circumscription of the tumour.

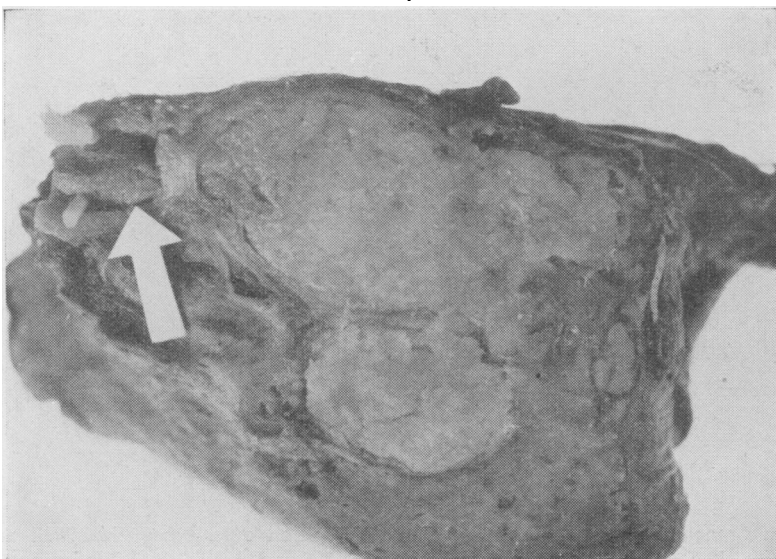


Fig. 4. Circumscribed carcinoma showing secondary rupture into main bronchus and extrusion of the tumour as shown at site of arrow.

that the tension built up inside this part of the lung contributes to the production of the dyspnoea.

Whatever be the cause, the relief of this symptom after resection is quite dramatic.

(b) Cases presenting with symptoms of acute respiratory disease are invariably diagnosed as pneumonia and usually rightly so, because the symptoms result from infection of the lung behind the tumour in the bronchus. It is a policy of the ideal that all cases of pneumonia should be radiographed and kept under radiographic control, but this is impracticable; however, should there be either a recurrence of the pneumonia in either weeks or months, or should the patient fail to react to chemotherapy, then recourse should be had to radiography. A persistent temperature and malaise does not necessarily indicate infection as it does accompany a non-infective degeneration of the tumour, where the pyrogenic factor obviously is absorption of the products of such degeneration.

II. The second main group are those patients which present without symptoms referable to the respiratory tract. They again can be subdivided into two headings.

(a) Patients who complain only of lack of energy, loss of weight and general malaise. A symptom complex which is not uncommon with other diseases, as for example, pernicious anaemia and carcinoma of the stomach. This group, though rare, is not as infrequent as would be expected and it is a case of forewarned is forearmed.

(b) The group whose symptoms can be classified loosely as those of rheumatism. These symptoms may be (a) chronic in which there is polyarthritis, with or without typical finger clubbing, and not infrequently they show radiologically new bone formation at the lower ends of radius and ulna and tibia and fibula, when the classical picture of hypertrophic pulmonary osteoarthropathy is present. Any of these manifestations may be present singly or in combination. The causation of this syndrome again is not understood; it can also occur with conditions other than carcinoma; it has been seen personally with mediastinal sarcomas, intrathoracic fibromas and chronic empyemas. The condition regresses dramatically after removal of the tumour or infection, and its similarity to chronic rheumatism suggests that the tumour acts as a trigger which releases a similar mechanism to that operating in the rheumatic diseases.

(c) In those cases with the more acute phenoma, the polyarthritis is the predominant feature. Its onset may be quite sudden, coming on in the course of a day, and it need not necessarily attack all the joints. It can be severe and widespread enough, however, to make the patient quite helpless, and the pain be so severe as to need morphia in order to carry out necessary nursing procedures. Again, the result of resection on the symptoms is very dramatic; pain disappears in the first 12 hours, and the joint effusions almost as quickly.

These latter cases are more common than was hitherto thought, and it is now in one centre a routine to X-ray the chests of all cases with chronic rheumatism ; in this way, many more cases are coming to light.

A full clinical examination should be carried out in every case, although there are no specific clinical signs of the disease other than the possible evidence of metastasis. Physical signs may be completely absent, or there may be any of the signs which are associated with pulmonary pathology. The supraclavicular and axillary fossa should be examined for enlarged glands, and the sites of distant metastasis kept in mind. Abdominal examination may show liver or splenic involvement, renal symptoms, or the presence of blood in the urine, either macro- or microscopically, should lead to a full renal investigation, as in this way an unsuspected renal tumour may come to light. Bone pain is an indication for radiography, although not infrequently a negative X-ray does not exclude a metastasis, as spontaneous fracture has occurred a day following an apparently normal radiograph. Hence a persistent localised pain in a bone is more safely considered as being due to a metastasis. Cerebral metastasis will be obvious when the motor areas are involved, but when the metastasis is in a silent area, diagnosis becomes more difficult ; often, however, a change of temperament may give an indication, a placid individual becoming irritable and argumentative, or the reverse should be considered as evidence of cerebral involvement.

Radiological investigation is essential. The type of radiological picture will vary, according to the type of tumour under investigation. In the main bronchus type, the picture is that of collapse or of consolidation, the size of the obstructed area of lung depending on the presence or absence of infection. The site of the radiological shadow will depend on the site of the occlusion, either in the main, lobar or segmental bronchus.

In the circumscribed type, the tumour presents as a circumscribed shadow, not infrequently quite clear cut. If the tumour has extruded into a larger bronchus, there may be an associated atelectasis resulting from the occlusion of the larger bronchus, and this may obscure the outline of the tumour. If degeneration and rupture into the bronchus has occurred, the shadow shows a central excavation, with or without a fluid level. This latter appearance sometimes mistakenly gives rise to a diagnosis of a lung abscess ; the well defined margin of the shadow and the thickness of the cavity wall should indicate the correct diagnosis, for an abscess with a thick cavity wall must be a chronic one, and under these circumstances, there will be such a surrounding pneumonitis or fibrosis that there will be no relatively sharp demarcation of the edge of the shadow, which will blend insensibly into the lung field.

Evidence of a pleural effusion will be obtained on the ordinary radiograph. Fluoroscopy will give evidence to paradoxical movements of the diaphragm when it is paralysed, the fact that the hemidiaphragm is high does not necessarily indicate a paralysis, as not infrequently it may be high when any atelectasis is present. Similarly a difference in the lighting up

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of the lung fields during inspiration can be assessed. A decrease in such lighting up is one of the earliest signs of commencing atelectasis, being a sign of deficient air entry. Conversely, an area which is more radio-translucent and which shows little change in the expiratory phase is an indication of a positive pressure emphysema, in this case due to the pressure of the tumour causing an expiratory stenosis.

In difficult cases, tomography may be of value, although its chief value will be in identifying enlargement of paratracheal and inferior tracheal bronchial glands which may not be assessable by ordinary methods, the latter by showing widening of the carinal angle.

Bronchography is of no particular value in this connection ; it merely demonstrates a bronchial occlusion which can be adduced from the atelectasis showing on the ordinary radiograph, but it gives no information as to the true nature of the occlusion.

Radiographs may also show involvement of the ribs due to direct extension of the growth.

Bronchoscopy should be undertaken in all cases ; in fact it is the usual practice to bronchoscope all patients who are submitted to thoractomy, and certainly in all cases in which there has been haemoptysis when there is no evidence of pulmonary tuberculosis, and even in those cases where radiographs fail to show any abnormality.

Bronchoscopy will give positive evidence of an endobronchial tumour in only about 60 per cent. of cases ; in the remainder the bronchial tree may appear to be normal or may show only features which by deduction lead to a diagnosis, such as distortion of a bronchus by an extra bronchial mass, widening of a secondary carina, or unnatural rigidity of the bronchus.

Often a specimen of the tumour may be removed for histologic examination.

Other information may also be obtained by bronchoscopy.

(a) *The site of the tumour.* Obviously resection should be carried out through healthy tissue, and if the trachea itself is involved, operation is impossible. It has been suggested that involvement of the orifice of the right upper lobe bronchus precludes operation ; this, however, is certainly not the case, provided that the resection is carried out on the lateral tracheal wall, and in fact in one patient in which the left main bronchus was involved to the level of the carina, the resection entailed removal of about the lower inch of half the lumen of the trachea with the carina and a portion of the inner wall of the right main bronchus. It was incidentally found to be possible to suture the bronchial wall to the margin of the trachea, the patient surviving to-day, 18 months after operation, without recurrence*

(b) Indication of glandular involvement of the paratracheal glands by localized deformity of the trachea or the inferior tracheo-bronchial glands

* This patient has now been admitted to hospital three years after the operation with recurrence at the site of the suture line.

by widening of the carina. The earliest indication of the latter is subcarinal widening, the crux of the recognition of this condition is that the inner wall of the main bronchus should project and then recede from view ; this has to be distinguished from recurving of the bronchus which nearly always occurs when the upper lobe is atelectatic and the main bronchus is pulled upwards ; under these circumstances, the inner wall of the bronchus remains in view even when the head is well rotated to the opposite side.

(c) Paralysis of the recurrent laryngeal nerve, usually the left. This is assessed before the bronchoscope is introduced. In cases of doubt, the suspected paralysis or paresis should be checked by laryngoscopy, because, sometimes the beak of the bronchoscope may be interfering with one of the aryepiglottidean folds and embarrassing the movement of the arytenoid cartilage on that side.

Examination of the sputum for malignant cells.—This examination may afford additional valuable evidence, but it is a prerequisite before accepting such evidence that the observer must be well skilled in the procedure ; there are many pitfalls and considerable experience is needed before a valuable opinion can be given. Dependence solely on this result of this investigation for establishing a diagnosis should not be resorted to, just as elsewhere all the evidence must be taken in conjunction. There is perhaps a tendency, however, to accept a positive finding of malignant cells in the sputum with the same confidence as a positive biopsy report, forgetting that the procedure used to obtain the latter entails visualisation of the lumen itself.

The treatment which offers the best prospect of cure and relief from symptoms at present is radical excision.

It has already been pointed out that only 15-20 per cent. of cases are suitable for exploration and only about 60 per cent. of these are suitable for removal.

The pre-operative contra-indications to operation are as follows :—

(a) *Age.*—This does not of itself contra-indicate except in extreme old age, the condition of the patient's cardio-respiratory reserve being of more importance. The youngest patient submitted to operation was 21 years old, and the oldest, 69 years.

(b) Serious general disease which contra-indicates operation of any kind.

(c) Involvement of superficial lymph glands, supra-clavicular, axillary, rarely inguinal, and radiological or bronchoscopic evidence of para-tracheal and inferior tracheo bronchial glands. These latter two groups may be found at the time of operation and be excisable, but the prognosis is then considerably worsened.

(d) *Involvement of the recurrent laryngeal nerve.*—Generally speaking, this forms a classical contra-indication, but in one such patient, when the vagus and recurrent had perforce to be excised, the patient has survived seven years.

(e) *Involvement of the phrenic nerve.*—This contra-indicates operation, with perhaps the exception of those cases in which the paralysis has occurred while the patient is under observation and in association with a pyrexial illness when it can be assumed that the inflammatory process has been responsible, and also in those cases where the growth lies over the pericardium, where possibly the pericardium with the area of involvement may be excised.

(f) *Pleural effusion.*—If the effusion is obviously malignant, that is either blood stained or contains malignant cells or both, operation is completely contra-indicated. In cases, however, where the effusion has occurred in association with an infection, and the fluid is clear or at most opalescent, possibly containing polymorphonuclear leucocytes, then operation may be justifiable, and has been carried out successfully under these conditions.

(g) *Radiological evidence of involvement of ribs.*—When this has happened, it is of little value to attempt radical removal.

(h) *Evidence of distant metastasis.*—Contra-indication to radical surgery at the time of operation. Generally speaking, this means extension of the disease beyond the scope of excision. Involvement of certain structures does not, however, rule out the radical procedure.

(1) *Involvement of the pericardium.*—Provided the growth has not ulcerated through the pericardium, the latter can be excised, and for that matter, a portion of the auricular wall can be taken as well, as has happened on five occasions. The defect left in the pericardium should not be closed by suturing the margins of the defect, for even when this is relatively small, the capacity of the pericardium is decreased, and in one patient, it was thought that such a constrictive effect was the cause of a fatality. If the area of pericardium removed is large, the gap should be closed by a graft of pleura ; failing this it is essential to nurse the patient lying on the sound side for the first 10 days, otherwise the heart will dislocate out of the pericardium with an ensuing ventricular fibrillation, as pointed out by Cameron Haight.

(2) *Involvement of the diaphragm.*—The diaphragm, at least a large segment of it, can easily be excised, and in two cases the capsule of the liver was also removed. The gap can usually be easily closed.

(3) *Involvement of the parietes.*—The parietal pleura can easily be removed with the tumour ; in fact it is advisable if the lung is adherent to strip the pleura from the chest wall in preference to trying to do it intrapleurally. If there is the slightest difficulty in stripping the parietal pleura, which should come away easily with the finger from the chest wall, then it is advisable to take away that portion of the chest wall. When the mediastinal pleura is involved, it is rarely possible to do a radical operation as by this time the tumour has usually invaded the mediastinum. Adherence to the vena cava, if not too extensive, lends itself to excision of a portion of the vessel wall with lateral suture.

Pneumonectomy is the ideal procedure in that a more complete removal of the lymphatic drainage area can be carried out. Some patients, however, with a poor respiratory removal will not tolerate this procedure, and again in certain cases with very small tumours (those picked up by mass radiography) it seems scarcely to be warranted, and consequently lobectomy is undertaken. Decision as to the latter course can only be taken at thoracotomy, and generally speaking the following criteria should be filled. Firstly, the tumour should be of the circumscribed type and sufficiently peripheral to allow of a lobectomy to be performed through healthy tissue. Secondly, there should be no evidence of gross lymphadenopathy in the paratracheal area as shown by inspection, or of the inferior tracheo bronchial region as demonstrated after the mediastinum has been explored, and this area duly exposed. It is true that any certitude as to the presence or absence of metastasis of any glands can only be gained by histological examination, as many enlarged glands are merely inflamed, yet the assumption that the pathology is that only of inflammation is a dangerous one and gross glandular enlargement should indicate pneumonectomy if at all possible.

Results of Cases Submitted to Resection

Total Number of Cases	214
Total Number of Deaths	134
Early Deaths	37
Late Deaths	97

Survival Rates of Late Deaths

Less than 1 year	55
Less than 2 years	22
Less than 3 years	13
Less than 4 years	3
Less than 5 years	2
Less than 6 years	2

Cases Surviving

Total Number of Cases	80
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Years of Survival Following Resection

Less than 1 year	19
More than 1 year	21
More than 2 years	8
More than 3 years	8
More than 4 years	4
More than 5 years	7
More than 6 years	2
More than 7 years	3
More than 8 years	4
More than 9 years	2
More than 10 years	2

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Results of Cases Operated on up to 30th June, 1947

Number of Cases resected	104
Total Deaths	82
Early Deaths	25
Late Deaths	57

Years of Survival of Those Dead

Less than 1 year	25
More than 1 year	16
More than 2 years	9
More than 3 years	3
More than 4 years	2
More than 5 years	2
<i>Total Number of Cases surviving more than 5 years following operation (21.15 per cent.)</i>	22
Total Number of Cases still surviving and followed up	20
Lost trace of after 1 year	2

Years of Survival of those Still Alive

Over 5 years	9
Over 6 years	1
Over 7 years	4
Over 8 years	1
Over 9 years	3
Over 10 years	2

The two untraced cases must be presumed to be dead, but no record of registration of their deaths can be traced at Somerset House.

The results of treatment when placed beside the number of people inflicted with this disease in the whole population are very discouraging, but of those cases which are submitted to resection, the results are certainly superior to those maintaining for carcinoma of the stomach and until we have a more certain and preferable way of treating cancer in general, it certainly offers for the individual the best hope of recovery.

MONTHLY DINNERS

The dinners will be at 7 p.m. on the following Wednesdays: November 12 and December 10, 1952. January 7, February 11, March 11, April 8, May 13, June 10, July 8, 1953.

The cost is £1 10s. 0d. which includes cocktails before dinner and wine at the table. Applications for tickets, accompanied by a cheque for the appropriate amount, must be sent to the Deputy Secretary at least a week before the date of the dinner. Cheques should be made payable to "Royal College of Surgeons of England." The dress is Lounge Suit.