

The pleura¹

With special reference to fibrothorax

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We have met to honour and to remember Arthur Tudor Edwards, who died after the Second World War and who devoted much of his professional life to the advancement of thoracic surgery.

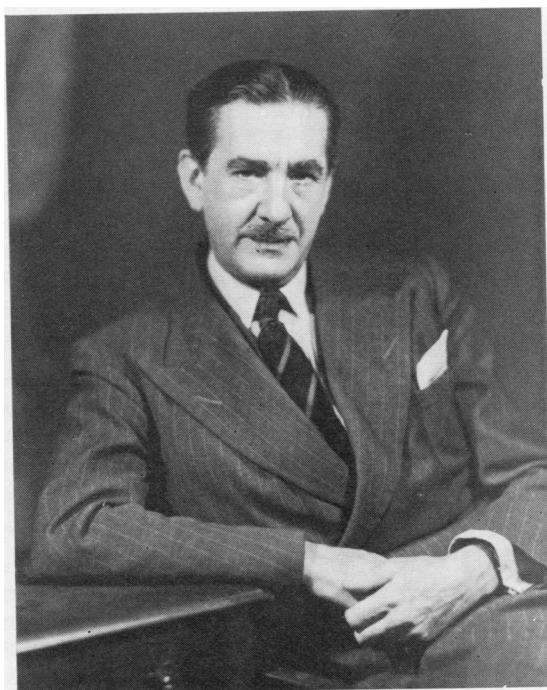
He lived and worked towards the end of an era when surgeons were 'prima donnas'. He was a man of handsome and commanding appearance: his convictions were strong and to his friends he was a staunch ally; the others he allowed to cultivate their own gardens.

He was a pioneer in his own field and became one of the first thoracic surgeons in the United Kingdom to achieve an international reputation. He deserved more recognition from his contemporaries in England than they gave him; indeed, his only honour was a medal from his colleagues in Norway. The reason was that thoracic surgery was not at first accepted as more than a foray into unlikely and hazardous territory.

Tudor Edwards was a surgeon to the Westminster, the London and the Brompton Hospitals and he combined these activities with those of a busy private practice. The latter brought him wealth and luxuries that he enjoyed and shared with friends; but this is not his memorial. It rests upon his contributions to thoracic surgery; these were not all new discoveries but steady improvements in therapy and technique that did a great deal to establish and to justify the new specialty. In particular, he made thoracotomy safe, and this enabled doctors for the first time to study the origins of thoracic diseases. Throughout his creative period he was helped by many people, but in particular by Sir Ivan Magill, who revolutionized the techniques of anaesthesia that led to controlled respiration, and by the late Mr. R. Schranz of the Genito-Urinary Company, who designed and made a number of appropriate and superb instruments. His surgical colleague was Sir Clement Price Thomas, who poured oil upon waters that were sometimes troubled and who was

always at his side; amongst the physicians, Sir Geoffrey Marshall helped him to found the Thoracic Society in 1945.

Looking back upon the 1920s one can see that the emblems were not favourable for thoracic surgeons. J. E. H. Roberts and Tudor Edwards had no beds of their own at the Brompton Hospital; they were at first at the beck and call of the physicians who decreed the operations they considered appropriate. The majority of these were for general surgical conditions; little could be done for chest diseases. But within a decade the picture had changed: the Brompton had become a Mecca for all who were interested in



[Rosalind Maingot, F.R.P.S.]

Arthur Tudor Edwards

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the new surgery. It was as exciting in those days to watch the chest being opened as it is to follow replacement surgery today. The hospital was full of visitors.

To justify and to establish any new therapy demands that sure principles be enunciated and proved. The fundamentals in those days seem obvious now; but they were new to surgeons. The lore and the practice of abdominal surgery, which had remained relatively unchanged for half a century, was inadequate for chest operations. It soon became obvious that the differences between respiration and efficient respiration were vital, and that to ignore this exposed patients to the risks of becoming respiratory cripples—or to death. The close association between the physical work and the physiological function of the heart and the lungs—combined as a unit—had to be accepted. To operate upon the one was to involve the other: both were concerned in health, in disease, in intervention and in convalescence. Surgeons for the first time became concerned with the heart as a pump, which needed priming with an adequate volume of liquid: they became aware of the mechanics of respiratory movements, and of the ways in which disease could cripple ventilation.

Nobody who experienced the excitements, the optimism and the enthusiasm of those of us who were associated, even in a humble way, with a pioneer will forget the early days of thoracic surgery at the Brompton Hospital.

You will remember that it was in the 1930s that the first serious attempts at pulmonary resection by dissection were made. Some will have read the dramatic account, by Evarts Graham, of the first resection of the lung for carcinoma. The patient was a friend and colleague and, as happens occasionally to those who are brave enough to be the first, he recovered and was cured. But during the operation the critical point came when the pulmonary artery was about to be tied: nobody knew what would happen. These are moments that everybody who was there remembers: but, in the day-to-day management of less taxing conditions there were many that were straightforward for the surgeons but painful and anxious for the patients; in these, new things were often discovered. Many questions involved the pleural cavity, and it is for this reason that I have chosen to talk about this aspect of the work. In so doing I begin by reminding you that every generation of doctors is ignorant of much that their fathers knew because the knowledge that was available seems no longer to be relevant to the work in hand: but one day, sometime in the future, the

wheel will return, and some of these things will be called back from oblivion and used again.

I had another reason for talking about the pleura. I have often been asked by surgeons, looking for a suitable subject for a thesis, to help them acquire some bright and expensive piece of laboratory equipment with which they might perchance reveal a tiny, and probably irrelevant, piece of the unknown. My advice has been to urge them to return to the difficult, but readily available, problems that beset clinical surgery. This does not imply collecting and reviewing a series of cases, but thinking about the gaps in our knowledge concerning almost every surgical condition. Significant advances can still be made by discussion and accurate clinical observation, and it is in this spirit of enquiry and ignorance that I shall talk to you about the structure of the pleura; and thence to the effects of fibrosis in the visceral and the parietal layers. I shall underline my suggestions by a brief comparison between fibrothorax and some pleural neoplasms.

In collecting my scattered thoughts I have had help and advice from my colleagues, Dr. K. F. W. Hinson of the Brompton Hospital and Professor Herbert Spencer of St. Thomas's.

'Few of us are big enough to stand alone.' (W. Mayo)

THE STRUCTURE OF THE PLEURA

After more than a century of debate the histological structure of the pleura is still discussed; thus it is necessary for me to make some observations upon this topic before embarking upon my journey of speculations.

The reasons that there are uncertainties are these. Parts of the pleura are so frail that it is difficult to make good histological preparations. Its thickness varies not only in different places in the same animal, but as between species. In man, for instance, the pleura is thin and closely applied to the superior vena cava and the pericardium whereas it can be peeled off the chest wall as a layer. Upon the lungs it is relatively thick in man but not only does it blend with the superficial stratum of these viscera but it sends prolongations that enter the substance of the lungs at right angles to the surface. These are the interlobular septa, and their presence makes it difficult to understand how the lung could be decorticated simply by stripping off the pleura. By comparison the parietal pleura has no such extensions: it is applied flatly to the endothoracic fascia upon which it rests, and it can be separated as a flap.

But this is not the whole story because the diaphragmatic pleura has no inward prolongations, and yet this cannot be separated from the underlying muscle. These points will be developed later on.

There are other controversial issues; what, for instance, is the boundary between the pleura and the structures upon which it rests?

Snow Miller, whose authoritative descriptions of the pleura are concerned chiefly with the visceral layer, defines it as 'a serous membrane covered with a layer of mesothelium which rests upon a subserous layer of connective tissue and a few elastic fibres. Within the subserous layer the blood vessels, nerves and lymphatics are found'.

The surface mesothelium, which is difficult to demonstrate as an intact membrane, is the same in all parts of the pleura. It is said to differ from epithelium because it derives from the mesoderm and because it has no basement membrane. These points are not of practical importance but it is relevant for surgeons to know how an area of chest wall or lung, denuded of pleura, heals. Ellis, working in the peritoneum, has shown that the raw surface is rapidly covered by cells indistinguishable from mesothelium which have grown from the granulations and not from the epithelium at the margins of the defect. This observation has been confirmed by Levene, who used synovial defects and who considered that the new mesothelium grew by metaplasia of fibroblasts. It becomes especially interesting when we come to question whether mesothelioma of the pleura could be connected with, or even derived from, pathological fibrosis in that membrane.

Another strange thing about the pleura is that foreign bodies, such as particles of carbon or fibrils of asbestos, can appear in the parietal layer even in the absence of adhesions or pleurodesis. Some have tried to explain this by postulating that there must be stomata in the mesothelium; or, alternatively, that the particles have been ferried across in macrophages. Neither of these ideas is acceptable. The fact, however, is important because cells can migrate from the lung to the parietes and some conditions, such as neoplasms, can spread across the open pleura.

Carbon particles are also normally found in the most superficial layer of the lung that contains the subpleural lymphatics. These fragments lie both inside and outside the lymph channels and, in pathological conditions, their presence has been used to indicate the original junction between the lung and the visceral pleura. Other pathologists

prefer to regard the boundary between the pleura and the lung as the deep elastic lamina.

Snow Miller tells us that the loose connective tissue beneath the mesothelium of the pleura contains many elastic fibres that are disposed in two ways. Superficially there are a number of isolated strands that intertwine loosely, and deep to these is a definite elastic membrane which is called the deep lamina. He regards the deep elastic lamina as part of the lung itself and not of the pleura. But if we examine the parietal pleura, of which he gives no separate description, we find that it, too, has a deep elastic lamina. This can have nothing to do with the lung. Thus it seems to me that we should regard this membrane as part of the pleura, and when we come to discuss whether a particular lesion has or has not originated in the pleura, and grown from thence into the lung, we should take the deep elastic lamina as the natural fence between the two.

As far as I am aware, nobody has made an anatomical and pathological study of the lymphatics in the visceral *and* the parietal pleura. I shall therefore refer only briefly to this subject although it must be relevant to the points I wish to discuss; relevant because the pleural and the subpleural lymphatics communicate and thus form a bridge between the pleura and the structure upon which it lies. The lymphatics in the visceral pleura certainly communicate with those of the lung, but the valves are so arranged that the lymph can flow only from the lung outwards. The reasons for this arrangement are not understood but it accounts for the frequent finding of metastatic malignant cells in the visceral pleura. How these cells get into pleural effusions and how they often reach the parietal layer of the pleura are points that need elucidation.

Some writers have stated that the lymph in the pleural vessels could lubricate the contiguous surfaces; but, in my opinion, this is more likely to be done by the mucus that electron microscopy reveals on these surfaces.

The intrapleural nerves are plentiful and of unknown function. The pain registered in the parietal pleura is probably transmitted by the intercostal nerves which are said not to communicate with those in the pleura itself. Thus the pain registered in pleurisy probably originates in the endothoracic fascia, upon which the pleura rests, and not in the membrane itself. This is borne out to some extent by the observation that a needle introduced towards the pleura from without hurts, whereas the parietal pleura can often be touched at thoracoscopy without sensation. The visceral

pleura does not register pain, and perhaps the nerves in it are more concerned with the stretch mechanism that controls respiration than with sensation.

The normal pleura adapts itself in area to the size of the surface it covers. The variations that occur in the volume of the lung and the chest wall might be expected to make the pleura taut at one moment and redundant at the next. But this is not so. It is also surprising that, with the chest open, the lung can be inflated and deflated without *greatly* altering the intra-bronchial pressure. These properties of stretch without great tension are in contrast to the limitations of lung movements imposed by a thin layer of fibrin deposited upon the surfaces of the pleura.

There is another point that should be understood and emphasized by any who wish to describe pathological conditions affecting the pleura. It is in the accurate use of words describing the thickness of the pleura. The pleura in all animals is, or appears to be, of different thicknesses for these reasons:

- (1) There are variations in the amount of supporting and elastic tissue that have the effect of making the normal pleura thicker in one place than another—for instance, upon the chest wall, as opposed to the covering of the superior vena cava.
- (2) The normal thickness varies from species to species.
- (3) The pleura may be thickened because it contains additional tissue or is infiltrated by cells from without.
- (4) It may appear to be thickened because some additional tissue has been laid upon its surface, such, for instance, as fibrin.
- (5) There may be a combination of 3 and 4.

NATURAL AND ARTIFICIAL PLEURODESIS

In man, and perhaps in all mammals, the pleural cavities have become anatomical luxuries and pathological hazards. We would be better off without them, but, be it plainly understood, only under certain conditions. The lungs in mammals cannot function unless they are outside the coelom; and, if the pleural cavities are to be disposed of, then they must be replaced by tissue that does not provide vascular or lymphatic connexions across the obliterated spaces. I shall dilate a little upon this point, because some of the conditions that I shall discuss involve pleurodesis.

Only one species of mammal—the proboscidea—has tried the experiment of doing without

pleural cavities and, in them, the issue has been forced, not by a desire to eliminate some unpleasant diseases, but by the evolution of a trunk. The early foetus of the elephant has pleural cavities but these disappear before birth and are replaced by elastic tissue. Zoologists believe that the development of a trunk has two relevant consequences; it increases the length of the narrow air passages, and it demands that the force of inspiration shall be greater than in other mammals. It is thought that if there were pleural cavities, and if the elephants used costal respiration, which they scarcely do, the superficial parts of the lung would probably be torn by the high negative pressure on the surfaces. In addition to a powerful diaphragm the elephant needs strong abdominal muscles to force respiration. When it drinks it sucks up to 2 gallons of water into the trunk, and this is blown into the oesophagus. Whatever be the cause of the experiment in pleural obliteration that elephants have made, experience shows that in them it works.

In man, obliteration of the pleura often occurs as a part of lung disease and, although it does not always embarrass the efficiency of respiratory movements, it can do so and it can result in the spread of disease from the lung to the chest wall or vice versa. In elephants, the pleural spaces are obliterated by relatively avascular elastic tissue that allows some movement between the ribs and the lung; and the vessels in that elastic tissue do not function as anastomoses between the parietal and the pulmonary circulations. By contrast, pleurodesis in man is a pathological process, and one that not only can cripple respiratory movements but may spread disease. This fact began to be appreciated a long time ago.

During the eighteenth century John Hunter made a number of preparations that demonstrated blood vessels in pleural adhesions. He understood that these were new developments and that they must connect the circulations in the lung and the chest wall.

The next advance came in 1853 when Virchow found that there was a connexion between pulmonary suppuration and cerebral abscess; but it was not until about 20 years ago that the explanation of these facts came to light.

The dangers of pathological pleurodesis—dangers that include not only limitation of chest wall movement but 'pleural shock', that is cerebral air embolism, metastatic brain abscess the result of pulmonary suppuration, and some cerebral metastases from carcinoma of the bronchus—are usually due to abnormal vascular connexions

between the lung and the chest wall. These pathological blood vessels that traverse the adhesions in the pleura can transmit organisms, air bubbles or cells from the lung directly into Batson's paravertebral plexus of veins and so into the cerebral venous sinuses.

FIBROTHORAX

This term defines the scar that can replace the pleura and obliterate the pleural cavity, completely or in part, as an end result of a variety of pathological conditions.

The clinical importance of fibrothorax is not as great today as it was when pulmonary tuberculosis was rampant and chronic empyema was the dreaded end-result of unchecked lung suppuration. It remains as an important problem in countries where medical practice is backward; and it persists in England as a final complication of some multiple injuries, where it has been difficult to treat all the defects from which the patient suffers simultaneously.

Fibrothorax is not only a severe deformity for any patient to endure, but the manner of its generation remains in many ways mysterious. Indeed, it would be true to say that the ubiquitous fibroblast is concerned with a wide range of conditions that are described in other parts of the body but are not understood. Consider, for instance, such variations upon a theme as Dupuytren's contracture, idiopathic mediastinal and retroperitoneal fibrosis, Reidel's disease, the healing of wounds, and fibrothorax. These are like the pieces of a jig-saw puzzle that seem to be of the same hue but do not fit: secure one, and you might elucidate the place of another.

As far as I am aware, nothing comparable to fibrothorax occurs in other parts of the body. Even in the peritoneum, from which the pleural cavities are diverticula, it is unknown. It is a variety of fibrosis that appears to be governed by its own conditions, and once initiated, it can be progressive, destructive and invasive.

Some think of fibrothorax solely as an end result of chronic empyema; but the significant fact is that it is not consequent upon, or due to, any single aetiological factor. It has many causes. It can arise as a result of pleural effusions of various types, chylothorax, empyema, haemothorax, and bacterial inflammations in the lungs. If the patient survives, the end result can be a fibrothorax.

In the beginnings of all these conditions, it is the cause that occupies the attention of the clinical

and time often elapses before it becomes evident that the patient is developing a fibrothorax. Empyema is a case in point. The word 'acute', when used in reference to empyema, should not refer to the time that the lesion has been present but to the fact that the pleural cavity contains an acute inflammatory exudate which, under correct treatment, will resolve, leaving no important residual abnormality. If, for any reason, resolution is delayed, the walls of the pus-containing sac are slowly converted to fibrous tissue that is permanent. There is no hard and fast boundary between an 'acute' and a 'chronic' empyema, and no certain clinical way of assessing the exact state of affairs within the cavity. The difference is in its pathology: it is between an inflammation that can resolve completely and one that cannot; it is the difference between granulation tissue and scar.

But, you will say, there is another obvious difference between a fibrothorax caused by a chronic empyema and one due to a haemothorax. The former is a septic cavity in the pleura lined by a pyogenic membrane, and the latter a sac lined by organized, sterile fibrin. This is true; *but the significant and important point is not the lining of the cavity, be it septic or sterile, but the events that are happening on the other, or deep, side of the lesion.* This side is sterile, whatever the cause, and it is the fibrous tissue here that can compress, invade, replace, or deform the chest. And, since the cause is not so significant as the result, I shall discuss the early development of fibrothorax, as it occurs in haemothorax, and the ultimate result in empyema.

HAEMOTHORAX

I have chosen haemothorax, as illustrative of the early changes, because many believe that they know what happens in this condition: and there is some truth in this because from the moment when surgeons began to decorticate the lung they had the chance to study events. But, in spite of world-wide experience, there is still no unanimity of opinion. Thus I feel justified in giving you mine.

Practically everybody will tell you that the management and the progress of a haemothorax depend upon whether the blood in the pleural cavity clots or not. And it is true that, in so far as the professed object of early treatment is to evacuate the blood and expand the lung, the clot can interfere.

But this emphasis on whether the blood in a haemothorax clots or not has led to two misconceptions—the first that clotting is the key to the future, and the second that clotting in a haemothorax is a bad thing. It is upon these issues that I want to speak.

Here is a quotation from a recent textbook of chest diseases. 'Intrapleural blood clots at once; but this clot is usually rapidly broken up and dispersed by the movements of the heart and lungs. The blood is thus defibrinated and the fibrin is either deposited on the pleura or sinks to the bottom of the pleural space.' It is statements such as this that Samson Wright must have had in mind when he wrote: 'The field of blood coagulation is one in which medical men and biological scientists have created such chaos that they do not understand what other workers in the field are talking about; far less the clinician or the medical student.' In practice, one finds that few experts will give a definite opinion about controversial points; everything needs qualification.

But to return to the quotation from the book. Experience in many hundreds of thoracotomies done to treat haemothoraces indicates that, unless there has been a lot of trauma to the chest wall, releasing much thromboplastin, all the blood in the pleural cavity does not clot immediately. Why should it? The pleura is a natural body cavity lined by a smooth mesothelium. This idea arose perhaps because blood, injected into the pleural cavity of dogs, clots; but this is due to the fact that the blood has been changed by aspiration and reinjection. The statement goes on to explain that, having clotted, the blood is then defibrinated by the movements of the heart and lungs. How can this be? Having clotted, the fibrin becomes part of the clot.

I suggest we look at this problem from two different standpoints. First, the blood in the pleura. This has come practically always from the parietes and not from the lung: it is oxygenated blood, and some of it clots. Pieces of fragile clot form and sink to the bottom of the pleural cavity or float in the bloody serum that separates from the contracting clots. But more important than this is the fact that, when the blood enters the pleura, it is partly defibrinated by the cardiopulmonary movements, and a proportion of the fibrin, *that would in other circumstances be available to take part in the clotting*, is removed and deposited as a membrane on the visceral and the parietal surfaces of the pleura. The idea that the recently spilt blood is defibrinated by the cardiopulmonary movements is itself open to question.

Even if it is true at the beginning of the formation of a haemothorax, it does not operate for more than a short time because the fibrinous sac that forms round the liquid blood holds the visceral walls of the sac almost immobile.

Thus within a few hours the haemothorax is converted into a blood cyst. Its contents are serum and clots which, being deprived of a full complement of fibrin, are soft, retract poorly, and are easily broken up. The future of this lesion depends upon what happens to the fibrin sac much more than upon its contents.

John Hunter was aware of the importance of fibrin deposited upon the surfaces of serous cavities. In his works (Vol. III, p. 349) he wrote: 'In all large cavities where we can make an observation with certainty . . . we find (in inflammation) diffused over the sides, or through the cavity a substance exactly similar to the coagulating lymph when separated from the serum and red blood after common bleeding. . . .'

If massive clotting occurs early, the majority of the fibrin must be in the clot and not on the surface of the pleura. Thus the pleura would be untrammelled by a heavy coat of fibrin, and it is probable that it would have no difficulty in absorbing the whole of the extravasated blood within a few days. In has been shown experimentally that a large dog, with a normal pleura, can reabsorb as much as 500 ml. of blood and clot within 24 hours. I have seen large clotted haemothoraces absorb quickly, spontaneously, and without aspiration, and others that have remained unabsorbed.

It has been stated repeatedly that a collection of blood in the pleural cavity acts as a foreign body and causes a secondary inflammatory exudate. It is also said that this late effusion accounts for late clotting in haemothoraces. But why should it? It is more likely that the fibrin, in this secondary effusion, will be deposited upon the existing walls of the cavity and thereby add to their thickness.

Thus I submit that it is more important to think of a haemothorax as a collection of partially defibrinated blood held in a sac, within walls of fibrin, than to bother about whether the contents are clotted, partially clotted, or liquid. It is the sac that determines the future.

The relevant properties of this sac are soon evident. It lies upon the surface of the intact pleura and can be peeled off without damaging the underlying lung or parietes. Thus it is wrong at this stage to say that the patient has a 'thickened pleura'. On the other hand, though at

first thin, the fibrin is so strong that it prevents respiratory movements in the underlying lung and if the contents of the haemothorax are merely aspirated the lung cannot always be immediately re-expanded. It is like a piece of cellophane, that is, strong, until it tears. It is because it is at first easily torn that surgeons do not advise decortication too early.

But, to return to the changes that occur in the sac of the untreated, or unabsorbed, fibrothorax, the sac itself gets thicker as more and more fibrin is laid down upon its surface. The additional fibrin cannot all be supplied from the original collection of blood, and much of it must come from the secondary exudate that the blood in the sac evokes. That this is so is suggested by daily red cell counts, upon the blood in the sac, and the finding that, although it may appear to be unchanged, it is being diluted all the time.

We have now reached another point that demands clarification. Surgeons who have done decortications upon haemothoraces that are several weeks old are agreed about the accuracy of the following statements. The fibrinous sac can at first be peeled off the lung, leaving a surface that looks normal and a lung that can be re-expanded immediately by increasing the intra-bronchial pressure. Sections of the peel so removed show that it contains no elastic tissue, and therefore that it has lain upon the surface of the pleura and not been incorporated in it. But these sections also show that *there are young fibroblasts in the fibrin*, and the question is how did these get into the fibrin, considering the fact that, up to this time at least, no granulation tissue has formed between the lung surface and the peel.

The explanation can only be that the young fibroblasts have migrated out of the pleura into the fibrin without granulation tissue forming at first. Fibrosis without granulation is recognized in other parts of the body. It occurs, for instance, in the conversion of oedema to scar, and is then called 'gefasslose' by German pathologists.

Some authorities have written that this is the beginning and the end of the story of haemothorax, namely that, even though the fibrin slowly converts to scar, it remains as a membrane laid upon the surface of the lung and that membrane can thereafter be peeled off the lung leaving a normal surface beneath it. I shall show you that this is untrue.

If a haemothorax remains sterile the pathological processes seldom advance beyond the point so far described. It seems that, as the supply of fibrin in the contents of the cavity ceases, there

is less and less to be deposited upon the wall of the sac and progressive fibrosis comes to an end. The importance of this lies in the clinical management of these cases. It has been my experience that, in the fullness of time, untreated (or partially treated) haemothoraces tend clinically to resolve spontaneously. That is, several years later, there may be some residual flattening with diminished movements on the affected side, but one rarely sees a respiratory cripple from this cause. If this is true it can only be due to something having halted the increasing fibrosis, and one must postulate that some of the existing scar must also disappear. My feeling is that an uncomplicated haemothorax should be given ample time to resolve before decortication is considered.

CHRONIC EMPYEMA

We have studied the development of fibrothorax as far as the formation of the sac, and said that at this point the process often resolves either as a result of treatment or, given time, spontaneously. But the outcome is less favourable if a chronic fibrothorax forms, and we can follow events by studying the changes in chronic empyema.

Although the early stages of haemothorax and chronic empyema are different, both reach a stage in which the histology of the greater part of the lesion is identical. It is only the superficial or cavity surface layers that are different. One is sterile, the other is infected. Below the surface layers, and where the scar of the sac impinges upon the deep structures, the histological appearances are identical whether the lesion be an acute inflammation or of other aetiology. The deep surface is a sterile advancing fibrosis, and it is this that deforms the patient.

A matter of practical relevance is that in tuberculous empyema the only place that giant-cell systems exist is in the sub-surface layer of the empyema sac.

A long time ago, surgeons wishing to excise lungs destroyed by suppuration found that whereas it was necessary to cut the lung away from the chest wall to which it was intimately fused, the dissection became less difficult as the mediastinum was reached until, at the hilum, a plane of cleavage could generally be found in which the great vessels could be accurately displayed and ligated.

Not only is the thickness of the empyema sac different macroscopically upon the visceral and parietal layers of the pleura, but there are histological differences as well. In considering these I ask you to distinguish in your minds between the

changes that occur in the pleura immediately overlying disease in the lung and those we are about to consider, in which the sac of a chronic empyema encases parts of the lung that are constricted by it but are otherwise not diseased. For the surgeon the interest lies in the feasibility of decortication; for the pathologist the nub is whether the sac remains as a foreign body planted upon the surface of the original pleura or whether it becomes incorporated in, and inseparable from, the lung and the chest wall.

In discussions that concern these late pathological changes of fibrothorax it is essential to have a way of recognizing the original limits of the pleura and the original surface of the lung, or of the endothoracic fascia upon which the parietal pleura rested. In this matter there are two points that might help. The first is the demonstration, amidst the pathological changes that may engulf it, of the original elastic lamina that formed the base of the normal pleura; the second is the finding of a line of microscopic carbon particles that lay originally on the surface of the lung itself between the alveoli and the elastic lamina.

In the past, emphasis has been placed upon the belief that in the circumstances we are considering the pleura itself remains intact and it is 'thickened' by tissue laid upon it. This is important to surgeons who believe that, as a general rule, in fibrothorax due to haemothorax or chronic empyema, the abnormal sac can be stripped off the lung leaving the original pleura intact. This belief needs adjustment if it is to be accurate.

If one looks at the cut surface of a chronic empyema, lying upon a lung that is not itself diseased, it appears that the lung and the sac of the empyema are separated from each other by a sharp and definite boundary zone; and in decortication it would be along this plane that cleavage might be possible. From these macroscopic appearances some have deduced that, even in a chronic empyema, the pleura is normal and that the fibrous, inflammatory sac is laid upon it. This is untrue. Histological sections taken through the *visceral wall* of a chronic empyema reveal the following strata. Upon the exposed surface there is a membrane of septic granulation tissue: beneath this are some chronic inflammatory cells that merge into a layer of dense, white, sterile and almost acellular collagen. Deep to the collagenous layer are some more small round cells mixed with a few polymorphs and the remnants of the deep elastic lamina. But the fibroblastic activity does not stop at this lamina, as one might expect; on the contrary, there is inflammatory involvement of

the surface of the lung itself, and this extends as far as the superficial alveoli. One may feel certain that the surface layer of the lung is involved because the inflammatory zone includes the carbon particles.

We should note that the changes described above apply only to those parts of the empyema sac that are in direct contact with normal lung: where the sac covers lung that is diseased it is fused by scar and cannot be decorticated.

Thus the sac of a chronic empyema includes not only the original pleura but the tissue that lay between the superficial alveoli and the deep elastic lamina. How then can decortication be possible? Surely only by taking away a tiny part of the surface of the lung; and experience shows that this does not matter.

I must now say a word about the changes that occur in the parietal, as opposed to the visceral pleura.

Even a cursory look at the chest wall shows that there is no line of demarcation between the scar of a fibrothorax and the underlying structures. It invades and destroys the intercostal structures. The fibrous tissue not only replaces the endothoracic fascia, causes thickening of the periosteum of the ribs (by a deposition of fat beneath the periosteum), and eventually an alteration in shape from flat to triangular; but it replaces the intercostal muscles and, by contracting, it approximates the ribs until they come into contact, fuse together, and form a carapace of bone. With the passage of time local or general calcification occurs in the collagen.

These important changes lead to serious clinical deformities. The chest wall is at first flattened upon the affected side, and respiratory movements are progressively limited. They can be abolished. The muscles of the shoulder girdle waste, movements become restricted and the patient develops a scoliosis. In long-standing cases compensatory curvatures appear above and below the chest.

For reasons that I cannot explain, the interaction between the sac of a chronic empyema and the diaphragm is different from that of the chest wall or the lung. At first sight the diaphragm resembles the chest wall: it is a muscle, covered above and below by mesothelium and liberally supplied with lymphatics that drain into the chest wall and the mediastinum. These lymph channels have ends that are closed and there is no good explanation of how a particle of India ink can travel so easily and quickly from the peritoneum to the mediastinum, nor, in view of this, is it easy to understand why patients who have peritonitis

do not develop mediastinal suppuration. Although infection from the sub-phrenic space can pass across the diaphragm into the pleura, the reverse does not occur; nor does the scar of a chronic empyema sac transgress the muscle. The factor that prevents this is not easy to determine.

Until we can find some convincing explanations for all these discrepancies we cannot begin to understand the intricacies of fibrosis.

MESOTHELIOMA

I wish briefly to compare the pathological effects of fibrothorax and mesothelioma of the pleura. The latter is now accepted as a primary tumour of the pleura that is frequently a sequel to the inhalation of asbestos fibrils. It is a pleomorphic tumour that contains epithelial and connective tissue elements, but pathologists accept that it derives from the mesothelium of the pleura. I shall not argue the possible connexions between the various types of fibrous proliferation that occur in the pleura and that can complicate pulmonary asbestosis, nor the reasons why the fibromata may, or may not, be the initiators of mesothelioma; but I would remind you that, in healing, the pleura derives from the metaplasia of fibroblasts. The latter can form mesothelium.

By the time a mesothelioma is first diagnosed it is usually far advanced and it may involve all parts of the pleura. The thick membrane of white malignant tissue, that encases the lung, looks like a chronic empyema. It does not at first invade the lung and, as in empyema, there is a line of demarcation between the malignant growth and the lung alveoli. In the chest wall the lesion is not so confined; it spreads out between the ribs and often comes eventually to the surface, presenting as hard masses of malignant tissue. In all these respects a mesothelioma seems to be partially confined by the same limiting factors that operate in fibrothorax. But it is when we examine the behaviour of mesothelioma in relation to the diaphragm that we see that this muscle is a law to itself. The malignant cells pass right through the diaphragm with equal ease in either direction. Thus it is necessary to explain the differences that exist between the visceral pleura on the one hand and the chest wall and the diaphragm on the other.

I have already said that, taken by itself, this is a problem that seems to be negligible in the wide sweep of medicine, but I believe that all correct information helps to lighten the darkness of ignorance and may have a wider application than is at first apparent.

CONCLUSION

I conclude with a suggestion. A reason why the lung seems to be able to resist invasion by fibrous tissue or mesothelioma could be that the sub-pleural layer is supplied with arterial blood from the bronchial arteries, whereas the alveoli beneath this receive venous blood from the pulmonary circulation. Thus there is a difference between the pleura and surface layer of the lung on the one hand and the alveolar tissue of the lung on the other. By contrast with this the conditions in the chest wall are propitious for the spread of fibrosis or neoplasia; the further the pathological process goes, the better the cells are supplied with arterial blood.

This slender guess may be appropriate to explain conditions in the visceral and parietal pleura but it does nothing to unravel the mysteries of the diaphragm. This extraordinary muscle, that surgeons have scarcely thought about in particular, is not only the prime mover of inspiration but it has functions in the containing of some spreading diseases.

In this address I have spoken in particular about things I have never understood, and I have done this to underline my belief that clinical surgery still has a great deal to interest a man who wishes to do some original work.

Some of the questions I have raised have been left over from the pioneer days of thoracic surgery and were discussed by Tudor Edwards himself. They have lain fallow ever since and, perhaps, they would lend themselves to rescruity using new information and modern tools. The time is ripe to think again about the pleura, for there is much in health and disease that needs better explanations than I have given.

During the course of this lecture lantern slides were shown to confirm the opinions expressed.

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