localization and there seemed to be something really typical in them, further experience showed that that was an error. *So these findings mean nothing in the definition and classification of disease entities.* Their fundamental value, rather, consists in showing something common to all these diseases, *etiologically and clinically so very different*; not anatomical forms of disease, but similar pathogenic complexes. . . . It can be seen how the most varied injuries, by a more or less long chain of causes, finally lead to the same pathophysiological process." (Italics mine.)

These are weighty words; they represent with exactness the conclusions I myself reached some time ago; though applied by Spielmeyer more especially to vascular disturbances, they stand for a principle capable of much wider application. What the neuropathologist sees is a tissue response, the expression of a pathophysiological process; one and the same process is capable of being called into being by etiological factors differing among themselves and causing clinical symptoms also differing in their type.

One or two other questions of pathological interpretation remain for brief allusion.

Such expressions as "acute haemorrhagic encephalitis," "acute disseminated encephalomyelitis," "acute parenchymatous degeneration," and other analogous terms, are merely descriptive names for pathological reactions; they correspond pathologically to such clinical expressions as "headache" or "paraplegia," and are devoid of meaning from a nosological or etiological standpoint. And it is of prime importance to note that *differing* reactions may and do sometimes occur in the *same* affection. For example, parenchymatous degeneration without obvious mesodermal hyperplasia characterizes some cases of epidemic encephalitis, as is now fully recognized; further, a number of disease conditions—for example, epidemic encephalitis, rabies, neurotubercle, neurosyphilis, and still others—may exhibit both types of reaction in one and the same case, in different parts of the neuraxis, and seemingly in complete independence of each other. Attention has lately been directed by Jakob,¹⁴ Spielmeyer,¹⁵ and other workers to the occurrence in the cortex of regions of general parenchymatous necrobiosis, pale or bleached in appearance, often without well-delimited margins, and visible only in Nissl preparations. They are best seen with a low power. Whether they are of vascular origin does not concern us for the moment; what is significant is their identical development in morbid conditions that differ fundamentally in etiology and in clinical character, and their coexistence with, but separation from, reactions of mesenchymal type. Clearly, the inference is again justified that some of the morbid states which we have thought constituted disease entities possess no specific pathological reaction on which to base that assumption; while, on the other hand, a seemingly definite pathological reaction is common to a number of diverse clinical states.

A final consideration bears on the question of modifications undergone by nerve cells during the normal activities of life and after dissolution has set in. Histological differences between resting and actively functioning cells are sufficiently well known; an extensive series of studies by Dolley¹⁶ has demonstrated the orderly sequence whereby changes in the quantity and distribution of chromidial substance and variation in the nucleus-plasma ratio are natural results of activity and depression. After activity, indeed, a cell may be practically dechromatinized and yet recover its full complement of chromatin during rest. The details of these changes need not delay us, but their import should not be overlooked. For in the examination of nervous tissues after death departures from the pattern of the resting cell do not all of necessity indicate the existence of pathological circumstances; on the contrary, they may equally well be physiological, and equally, therefore, indicative of health and not of disease.

Analogously, it becomes of cardinal importance to note that in toxic conditions, as well as in "natural" conditions, changes take place in nerve cells in accordance with the period after infection at which tissues are fixed and examined. This has recently been well demonstrated by Barros.¹⁷ He has injected tetanus toxin into guinea-pigs and shown by the microscope that if the tissues studied are fixed two hours after inoculation the ganglion cells of the spinal cord yield a normal Nissl picture; if

after six and a half hours, the cell exhibits early chromatinolysis; if after seventeen, it presents much more definite resemblance to the ordinary picture of a toxically degenerating cellular element. Evidently a toxin may be at work dynamically interfering with cell function before histological change can be detected.

The general bearing of these various observations, to which some discussion has been allotted, will not escape the inquiring mind. They indicate the desirability, nay, the necessity, of regarding "disease processes" as calling forth vital efforts to cope with noxae; many symptoms are proof of health, many "lesions" are evidence of attempts at repair. Along such lines of thought, I believe, we shall gain a truer insight into the activities of the nervous system.

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INFLAMMATION OF THE DIAPHRAGM.*

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(With Special Plate.)

INFLAMMATION in the neighbourhood of and implicating the diaphragm is fairly common, but the symptoms resulting vary enormously in their severity; they may be anything from a slight discomfort in the side to those suggestive of an acute abdominal condition. Some of the cases which I have chosen to call chronic may exist, I think, without any symptoms, while some of the misleading and urgent symptoms of acute pneumonia may be the result of implication of the diaphragmatic pleura in the inflammatory process. For descriptive purposes I propose to divide the subject into two parts: (1) Inflammation of the upper surface, or diaphragmatic pleurisy. (2) Inflammation of the under surface, or subdiaphragmatic abscess. It must, however, be remembered that inflammation of the upper surface may produce symptoms resembling an acute abdominal condition, and that inflammation of the under surface may, on account of the distribution of the phrenic nerve, produce pain about the shoulder in the supraclavicular region.

It would here be convenient to remind you of the innervation of the diaphragm. Excluding the sympathetic fibres, the diaphragm receives branches from (a) the phrenic nerves, (b) the lower six or seven intercostal nerves. The phrenic nerve arises from the third, fourth, and fifth cervical nerves, but mainly from the fourth. It arises from the same segment of the cord from which the supraclavicular region receives its cutaneous nerve supply, thus accounting for pain being referred to the supraclavicular region—the so-called shoulder-tip pain of diaphragmatic pleurisy. On reaching the diaphragm most of the phrenic nerve fibres pierce it and are distributed on its abdominal surface. The phrenic nerves contain afferent

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as well as efferent fibres, the former constituting about one-third. They are the sole motor supply of the diaphragm in man. Their sensory fibres are more limited, and are mainly distributed to the more central part, and particularly to the more central part of the abdominal surface; and the fact that the shoulder-tip pain previously referred to is the result of irritation of the branches of the phrenic is of interest, in that it indicates that the central part of the diaphragm is affected. Branches from the lower intercostal nerves can be traced into the diaphragm. It is doubtful if they contain any efferent fibres, but their afferent innervation is of interest. Their sensory field is the more peripheral part of the diaphragm. Irritation of this part of the diaphragm is therefore more likely to induce pain in the cutaneous distribution of the lower intercostal nerves, which embraces not only the lower costal region, but includes, of course, the anterior abdominal wall, and in that way may lead to difficulties in diagnosis.

DIAPHRAGMATIC PLEURISY.

In view of the wide variation of the symptoms of this condition I propose to subdivide it clinically into (a) acute, (b) subacute, and (c) chronic.

(a) Acute.

The onset is very abrupt. The patient is seized with severe pain and vomiting. The pain in a typical case is referred to the lower costal region, but it frequently extends to the upper abdomen and tends to radiate round the lower thorax, and, if the central part of the diaphragm be implicated, pain is also complained of in the supraclavicular region of the shoulder on the same side; it does not radiate to the shoulder, but is felt there in addition to being felt in the lower costal region; in this way it can be distinguished from the pain of acute cholecystitis, which seems to pass through the side as if a red-hot stiletto had been plunged through the liver to come out at the lower end of the scapula. Again, the pain in acute cholecystitis is, at its height, often referred to the epigastrium, whereas, when it has subsided a little, it tends to be located over the gall-bladder. It may happen, however, that the initial pain is referred almost entirely to the abdomen, the patient making little or no complaint of pain in the lower costal region. It is in these cases, particularly if vomiting is a conspicuous and urgent symptom, that great difficulty in diagnosis is apt to arise, and operations may be undertaken in the mistaken belief that the case is one of appendicitis, cholecystitis, or even perforative peritonitis or acute haemorrhagic pancreatitis, according to the situation of the pain, though usually in these conditions the degree of abdominal rigidity is greater than in diaphragmatic pleurisy. Of all the conditions the pain is perhaps most intense in acute haemorrhagic pancreatitis. There is usually moderate pyrexia, though this does not appear to be essential at the outset, as is instanced by the following case.

A woman, aged 41, complained of severe pain in the left lower costal and left upper abdominal regions, associated with urgent vomiting. The history was that four days previously, after a supper of veal and ham pie, she went to bed feeling in her usual health. In the middle of the night she woke with what she described as "terrible pain" in the left lower costal region and "could not get her breath." About 9 a.m. she began to vomit, and vomited so violently that she fainted. From this time onwards she had vomited everything she had taken. At first there was no pyrexia, and not until two days after the onset did the temperature rise to 99.6°. It then continued to rise gradually until, when I saw her on the fourth day, it was 102.8°; the pulse was 112 and respirations 20. Examination revealed marked hyperaesthesia over the left costal margin and left upper abdomen, but no striking rigidity. A diagnosis of diaphragmatic pleurisy was made, which apparently was correct, for the next day a friction rub made its appearance on the left side. Ultimately the patient made an uninterrupted recovery.

The pulse is rapid and small. The breathing is impeded, but not always appreciably accelerated, and is often entirely thoracic. The skin over the painful area is markedly hyperaesthetic, so that touch or light pressure causes intense pain, whereas firm pressure with the hand is infinitely less painful, and may even give relief. The absence of abdo-

minal rigidity is most striking, and this, combined with hyperaesthesia of the skin and the character of the breathing, is of the greatest service in differentiating from an acute abdominal condition. Later the diagnosis is often put beyond doubt by the detection of a friction rub at the base or by the supervention of unmistakable signs of pneumonia.

Treatment.

Once the diagnosis is established, it is advisable, if the pain is very acute, to give a dose of heroin or morphine hypodermically and to apply a fomentation locally.

(b) Subacute Diaphragmatic Pleurisy.

In these cases the pain is not so severe. It is located in the lower costal region, with or without referred pain in the supraclavicular region of the shoulder. As a fairly typical example I would quote the following case, which I saw on January 9th, 1925.

The patient was a schoolgirl, aged 15, with a history of having contracted a cold five days previously. Three days later she complained of severe pain in the left lower costal region, which, in the course of the day, was referred to the outer side of the left shoulder but did not affect the arm. The temperature was 99°. She had a slight, a very slight, cough, but no expectoration. The pain in the costal region was greatly intensified by breathing. When I saw her the temperature was normal; the respirations were short and rather rapid—namely, 26. The chest over the lower costal margin was tender, but there was no friction sound. The outer side of the left shoulder was also slightly tender, but there was no swelling, and the movements at the joint were good. There was no affection of any joints. The next day a friction sound was heard at the base of the left lung.

In some cases the pain over the shoulder is the first to make its appearance.

A patient, admitted to the Manchester Royal Infirmary on June 18th, 1927, for right-sided pleural effusion, gave a history that, four weeks previously, he was seized with sharp stabbing pains at the top of the right shoulder which lasted for two hours and recurred frequently until, a day or two later, pain began in the lower costal region.

(c) Chronic Diaphragmatic Pleurisy.

This group comprises those cases in which old adhesions exist between the visceral pleura and the diaphragm.

FIG. 2.

Many of these cases do not appear to give rise to any symptoms. In others the presence of certain symptoms may lead one to suspect the presence of adhesions, but the diagnosis can only be established when confirmed by x-ray examination. The patient may complain of a frequently recurring sharp pain in one or other lower costal region, with occasional pain in the supraclavicular region of the shoulder, which, if present, is a great help in diagnosis. Examination will reveal some impairment of movement with diminished air entry at the base of that lung. There are three main types of these adhesions as revealed radiologically.

Type 1.—Adhesions between the diaphragmatic surface of the pleura and the diaphragm. These adhesions may occur at any point, but not uncommonly may be seen (Fig. 1), in a radiogram taken laterally, as pointed out by Twining,¹ to extend from the diaphragmatic part of the fissure between the upper and lower lobes on the left side or between the middle and lower lobes on the right side, causing "tenting" of the diaphragm. The oblique fissures were shown by Kreuzfuchs and Schuhmaker² to extend to the diaphragmatic surface of the lung (Fig. 2).

Type 2.—Adhesions along the periphery of the diaphragm or at the costo-phrenic angle or mediastino-phrenic angle hooking up the diaphragm (Fig. 3). The following case is an example.

A foreman calico printer, aged 41, complained of tiredness, shortness of breath, pain in the left side on yawning or sneezing, and occasional sharp pain at the tip of the left shoulder. The history was that four months previously he had dry pleurisy at the base of the left lung, and that ever since he had run an intermittent temperature, rising in the evening to between 100° and 101°, with occasional night sweats and steady loss of weight. Cough had only been very slight and accompanied by very little expectoration, which had on three separate occasions been examined for tubercle bacilli with negative results. Examination revealed deficient movement, impaired resonance, and diminished breath sounds at the left base, but no adventitious sounds and no cardiac displacement. X-ray examination of the chest showed the left diaphragm to be fixed, and obliteration of the left costo-phrenic angle with some pleural thickening.

Type 3.—Adhesions arising from the mediastinal surface of the lung and connecting it with either the diaphragm or, as mentioned above, with the pericardium (Figs. 4 and 5).

The explanation of the formation of the adhesions arising from the interlobar fissures is interesting. In an antero-posterior view a pleural effusion is represented in a radiogram by a more or less uniform shadow, and if the effusion is insufficient to fill the chest the shadow is seen to have a convex upper margin rising to its maximum height in the axillary line. Fleischner,³ however, has shown that, in a lateral view, this shadow may be seen to dip into the interlobar fissures, the effusion having separated the lobes of the lung by invading these fissures (Fig. 6). In some cases this interlobar exudate disappears entirely by absorption, in others it becomes organized, and in this way is, I believe, responsible for the formation of adhesions arising from the fissures. Such adhesions, we have seen, may connect an interlobar fissure with the diaphragm or with the pericardium, and may, by their contraction, cause so-called "tenting," though actually this is very slight, for careful examination shows that the "tent" is composed almost entirely of adhesion.

SUBDIAPHRAGMATIC ABSCESS.

Any abscess in contact with the under surface of the diaphragm (except when in the liver or spleen) is spoken of as a subdiaphragmatic abscess. Such an abscess may be either right-sided or left-sided, and may, in addition to pus, contain gas (Fig. 7). These characteristics will, in great measure, be determined by the underlying cause of the abscess. The commonest cause of subdiaphragmatic abscess is perforation of a peptic ulcer, the resulting abscess being usually on the left side, and in view of the direct communication with a hollow viscus will contain gas in addition to pus.

The perforation may be subacute or acute, for the relief of which immediate operation may have been performed. Hurst and Stewart,⁴ in dealing with this subject, while admitting that immediate operation for gastro-duodenal perforation has enormously reduced the mortality of this complication, doubt if the frequency of subdiaphragmatic abscess has been appreciably affected, the process of loculation having begun before the patient is seen by the surgeon, or the peritoneal drainage provided being inadequate. Later in the same article, when discussing the symptoms, they state that "if the temperature remains raised, or if after an initial fall it rises, and symptoms of a general infection occur about the fifth day after an operation for a perforated ulcer, a localized abscess is probably forming. If abdominal and rectal examination show that there is no obvious local abscess in the abdomen or pelvis, a subdiaphragmatic abscess is probably present."

When the perforation in the original peptic ulcer is very small the resulting abscess may not contain gas.

Of the other causes of subdiaphragmatic abscess, perhaps one of the most frequent is the tracking up of an appendicular abscess. These abscesses are usually on the right side and are non-gas-containing, though it must be remembered that occasionally such an abscess may contain gas as the result of infection by putrefactive bacteria.

Symptoms and Signs.—The general symptoms of subdiaphragmatic abscess are those of a collection of pus anywhere in the body, and consist of languor, loss of appetite, emaciation, constipation, and dry furred tongue, with irregular pyrexia and rapid pulse, sweating, and occasional rigors. The onset and signs and symptoms, however, will vary with the cause and situation of the abscess. In cases following an appendicular abscess, or the operation for perforation of a peptic ulcer, the onset is usually insidious. If five or six days after the operation pyrexia persists without any local condition to account for it, and the patient complains of pain in the lower costal region, with impeded, though not necessarily accelerated, breathing, the formation of a subdiaphragmatic abscess should be suspected. The subsequent signs will depend upon whether the abscess is situated posteriorly, when the signs will be mainly thoracic, or anteriorly, when they will be mainly abdominal. With a posterior abscess an area of dullness appears at the base of the lung and gradually increases in size, but the upper border of the dullness, being limited by the diaphragm, retains the curve of the diaphragm but with an increased convexity, and does not rise towards the axilla as in the case of pleural effusion. Again, the apex beat is displaced upwards, and not laterally as in cases of pleural effusion. Not uncommonly, however, a subdiaphragmatic abscess is complicated by the pressure of pleural effusion, and when this occurs the convex upper border of the diaphragm cannot be defined by percussion, and the apex beat is displaced laterally as well as upwards. Over the area of dullness there is marked tenderness, which, as pointed out by Hale-White,⁵ is a very valuable sign. Owing to compression of the lung there may be bronchial breathing, and sometimes, as a result of concomitant pleurisy, a friction sound may be heard. If the abscess is on the right side the liver may be palpable; if on the left side, the usual resonance of the stomach and splenic flexure of the colon may be replaced by dullness. Exploration in the tenth intercostal space in the axillary line—the needle being pushed boldly on through the diaphragm—may reveal pus, though such a procedure is not without the risk of infecting the pleural cavity. When the abscess is situated anteriorly, a rounded tender swelling may be felt in the upper part of the abdomen and the thoracic signs may be insignificant. Such a swelling should not be punctured. Should the abscess contain air as well as pus, the signs of pyopneumothorax are present. X-ray examination will prove of the greatest value in the diagnosis of a gas-containing abscess, and reveals an air-containing space, separating the arched raised diaphragm above from the flat-topped shadow of pus below. In simple or non-gas-containing abscesses x-ray examination is not so helpful, for, as a rule, all that can be seen is that the diaphragm is elevated, fixed, and immobile, while any shadow below the diaphragm cannot be distinguished from the liver shadow.

Prognosis.—In all cases of subdiaphragmatic abscess the outlook is grave, but more so in those cases which contain gas as well as pus.

Treatment.—Surgical.

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ALBERT RABENBOTT: INFLAMMATION OF THE DIAPHRAGM.

FIG. 1.

FIG. 3.

FIG. 4.

FIG. 7.

D. R. E. ROBERTS: RENAL CYST
CONTAINING CALCULI.

FIG. 5.

FIG. 6.