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Thoracic lymphatics

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THE CONCEPT OF THE LYMPHATICS OF THE LUNGS, HEART, AND DIAPHRAGM WITH AN EVALUATION OF PRESENT KNOWLEDGE OF PLEURAL ABSORPTION

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CONTENTS

When knowledge of the lymphatics is compared to most other systems of the body, it us is usually found to be deficient. This is nowhere more true than in the thoracic cavity.

Although understanding of diseases of the thorax has sharply risen, the lymphatic system of this region has not kept pace. It is loosely used to explain a group of phenomena not well understood, with confusion or a false interpretation generally resulting. The evaluation of the present knowledge of thoracic lymphatics is thus indicated.

In this thesis, the literature on the structure and function of the lymphatics of the lungs, heart, and diaphragm will be reviewed and evaluated, as will that concerned with pleural absorption. On this basis, the concept of structure and function of these lymphatic channels will be presented.

In every section an attempt will be made to establish the developmental pattern. This will be followed by the microscopic and gross anatomy of the lymphatic vessels. Physiologic considerations will then be reviewed. The summary of conclusions in all of these sections will comprise the total concept. Since this subject in general is so unexplored, the final portion of each section will be devoted to the problems remaining in each field.

ABSORPTION FROM THE PLEURAL CAVITY

The absorption of colloidal material from the pleural cavity has been generally considered a function of the lymphatic system. Considering the clinical importance of this process, it is surprising that it remains such a vague entity today. This section will be devoted to a better understanding of this process.

It is rather surprising that it has not recieved more attention, and we are considerably handicapped by a lack of investigation into some phases of this problem.

THE ANATOMY OF THE PLEURAL LYMPHATICS

There is no literature recording the microscopic structure of the lymphatic channels of the costal pleura. We are no doubt correc in assuming that these are endothelial lined vessels lying beneath a layer of mesothelium, but the interposed tissue is not clearly defined. The gross appearance of these channels is discussed with the topic of the gross drainage of the pleural cavity.

The lymphatic vessels in relation to the mediastinal pleura, which will be shown very active in the process of pleural absorption, have not been described.

THE REACTION TO AND REMOVAL OF FOREIGN SUBSTANCES FROM THE PLEURAL CAVITY

Although studied to some extent for the past two hundred years, the removal of foreign particles from the pleural cavity still constitutes a problem as yet unsolved. This is true especially as concerns the mechanism of absorption and to lesser extent the pathways taken by the absorbed material. Likewise, the factors which influence the efficiency of this process remain in considerable doubt, both as to actual effect and the mechanism by which these factors may act. In this discussion, an attempt will be made to present the experimental basis for those facts which we may reasonably accept as being true, those which must be held in doubt, and those problems which confront us at the present time.

The earliest work on pleural absorption involved the investigation of the fate of crystalloid solutions and was carried out by Starling and Leathes (1895). These workers injected sodium chloride solutions of various concentrations, noting the speed of removal of this fluid and the concentration of the fluid remaining in the cavity. They found that hypertonic solutions were absorbed very slowly if at all, and in most cases found that more fluid was present than was origionally injected, this fluid being of less concentration than that origionally injected. Conversely, hypotonic solutions were absorbed with extreme rapidity and remaining fluid was of greater concentration than the injected solution. Normal saline was absorbed only very slowly with no change in concentration of the remaining fluid. From such observations, the authors concluded that the absorption of crystalloid solutions followed osmotic patterns alone and that there was no vital activity on the part of the cell in this process. The injection of a weak solution of sodium flouride (designed to kill the pleural mesothelial cells) with the sodium chloride solutions did not alter the fate of the injected solution. Some idea of the relative efficiency of this process was gained through the efforts of Corfer (1929), who found that the disappearance of sulphocyanate from the pleural cavity occured more slowly than from the parenchyma of the lung and more rapidly than from the peritoneal cavity. This was determined by the intratracheal injection of 2% sulphocyanate with subsequent determination of the blood level. Investigating the effect of pneumothorax, Maier (1939) duplicated almost exactly the picture produced by Starling and Leathes, and felt that they were correct in their conclusions. The work of these two groups seems amply to confirm this supposition. As a further index to the efficiency of the removal of crystalline solutions from the pleural cavity, the observations of Stevens, Taliaferro, and Haag (1941) serves to show that the pleural cavity is a relatively efficient absorber of crystalloid substances. They found that sulfathiazole absorption from the pleural cavity occurred more rapidly than from the intestinal tract and from the peritoneal cavity. This absorption was judged by blood levels of the drug at hourly intervals after injection. At one hour, the level in the intrapleurally injected animal was about 33% higher than the intraperitoneal, and for the next three hours remained about 25% higher. It then dropped to the blood level of the fluids introduced at other sites.

The other great class of material studied includes the various colloidal solutions adaptable for animal experimentation. In this sort of study there has been a general acceptance that lymphatics are largely, if not entirely, responsible for the removal of such substances from the pleural cavity. It must be borne in mind, however, that the majority of the studies made have not attempted to evaluate the role of the blood stream in this process.

The few articles which have concerned themselves with this question are in a state of disagreement. Katsura (1924) followed the absorption of aniline dyes in the normal peritoneal and pleural cavities of dogs and rabbits. He concluded that crystalloids (even in powder form) were rapidly absorbed by the blood stream, dependent upon the amount introduced. Colloidal dyes were found to be resorbed much more slowly through lymph channels. Brodsky (1928), on the other hand, believes that crystalloids must first pass through lymphatic channels before reaching the blood stream. He concludes this through studies on the lung, using potassium ferrocyanide as the substance traced. So it is very apparent that in the thorax, as in other places, the dispute as to the specificity of lymphatic and blood vascular endothelium rages.

There has been a wide variety of substances injected into the pleural cavity with only the observations recorded and very little suggestion as to the composite picture of pleural absorption. These studies have been very helpful, however, in establishing the functional capabilities of the cells of the pleural mesothelium. The earliest of these miscellaneous studies was undertaken by Cooper and Renoch (1921) who injected 7% gum acacia into the pleural cavities of rabbits, both normal and sensitized by injections of tubercle bacilli. The blood level of the acacia at various times after injection was taken as the index as to the efficiency of absorption. They found that the acacia soon appeared in the blood stream and that sensitization by the tubercle bacilli did not affect the rate or efficiency of absorption. No microscopic study was done. Binet and Verne (1924) found that ten days after the injection of rancid oil into the pleural cavities of dogs, pseudomembranes were found on the surface of the lung and pronounced proliferation of the connective tissue beneath the pleural mesothelium was present. The oil did not seem to be absorbed. Injection of oil which did not contain fatty acid was followed by absorption of the oil. The authors suggest that absorption probably occurs directly through the pleura and assume that the oil reappears in the lung and is there destroyed. Fat corpuscles were not found in the pleural mesothelial cells. Desbaillet (1927) studied the response of the pleural mesothelium of the guinea pig to tar and olive oil. The pleural mesothelium was seen to hypertrophy, acquire an apical brush, and foreign material was found within the cell. Tissue proliferation with verrucosities, villosities, or more often fungoid masses with a contorted surface was observed. After absorption, the pulmonary parenchyma showed simple hypertrophy of the alveolar epithelium and proliferation with an adenomatous aspect. The tar emulsion was split up by the pleura, the oil being absorbed and the tar caught up by tissue proliferation or devoured by large mononuclears. Merklen, Waitz, and Kabaker (1932) found that india ink and trypan blue injected intrapleurally could be found phagocytized by vacuolate and endothelial cells and by monocytes. Bradley and First (1938) studied the response of the pleural mesothelium to the implantation of various dusts. In a series of fifty rabbits, amouphous silica (10 animals) gave a proliferative response with fairly large confluent nodules scattered over the pleura and pericardium, with numerous small deposits scattered over the lung and mediastinal pleura. Numerous adhesions were observed. The diaphragmatic pleura showed far less reaction than did pleura in other sites. White rouge gave the same response with the same number of animals. Calcium carbonate (10 animals) showed complete absorption with no lasting changes, with the exception of a few hard deposits on parietal and visceral pleurae. There was no evidence of cellular proliferation. Magnetite (10 animals) showed an inart response. White rouge caused proliferation of what were apparently macrophages containing foreign material. Aggregations of giant cells were seen and fibroblasts were prominent. Magnetite seemed to be phagocytized by large cells just beneath the serous membrane. Haviland and McManus (1941) demonstrated that the concentration of antipneumococcal antibodies (horse and rabbit sera) in the pleural cavities equalled that of the blood stream. Singer (1942) injected thorotrast intrapleurally in an attempt to demonstrate the paths of drainage of the pleural cavity by roentgen examination. He found that on examination of the pleura grossly there were lines and patches of the thorotrast fixed on the pleura and microscopically some of this material was seen fixed in macrophages. He found the parenchyma of the lung to be void of the substance, but lymph nodes of the mediastinum contained thorotrast.

At an early date Marchand (1896) studied the effects of bacteria injected intrapleurally and found that these bacteria induced no reaction with the exception of a temporary local reaction on the surface of the pleura at the site of injection. If, however, there was a marked disturbance of the blood or lymph circulation, or if there is an initial injury to the pleural mesothelium, an empyema results. Grober (1901) confirmed Marchand's results on the intact pleura. He found that if a chemical irritant was first injected a purulent empyema resulted in a very short time. He concluded that the integrity of the pleura to bacterial invasion is dependent upon the integrity of the lymph vessels and their ability to remove bacteria to the main blood stream. Noetzel (1927) duplicated these results.

While these investigations give us valuable information, the most informative work has come from men who have used carbon particles in some form as their tracer material. Karsner ans Swanbeck (1920), in a careful study of the reaction of the pleura to india ink and carmine, found that the mesothelial cells of the pleura are definitely capable of phagocytizing ink particles in situ. Two percent lamp black solution was injected intrapleurally into cats. They found that pleural mesothelium over all surfaces, particularly over mediastinum and lung, contained carbon or carmine, depending upon which was injected. The ingestion was not of a diffuse nature but was round in small groups of cells. The mediastinum showed great numbers of large mononuclear cells loaded with particles in the lymphatics, and lymphatic endothelium also containing pigment. Occasionally a mesothelial cell could be seen dipping into the underlying tissue to pass into a lymphatic channel. The parietal pleura showed phagocytosis to much less extent than did other portions of the pleura, as was true of the diaphragm. Lymph nodes from the mediastinum all showed pigment in most cases. The authors believe that phagocytosis must precede removal of carbon particles from the pleural cavity. They also conclude that the mediastinal pleura shows the most activity, that of the lung next, with costal and diaphragmatic pleurae the least. Wadsworth (1922), in attempting to determine the relative role of phagocytosis and respiratory movements in the entry of foreign granular material into the lymphatics, injected india ink intrapleurally and found the parietal pleura to have a greater activity in removal of particles than the visceral pleura. Some phagocytosis was seen in the parietal pleura, with very little in the visceral pleura. Although he found that phagocytosis was a response of the pleural mesothelium to this granular material, his opinions on the role of this response in the total picture of absorption will be discussed later. Bettman (1925) confirmed the above findings.

By far the most exact and comprehensive study of the cytologic aspect of pleural absorption has been made by Lemon and Higgins (1930). They injected variable amounts of carbon suspensions into the pleural cavity of dogs and microscopically evaluated the response at various times. This work is finely done and in many respects embodies the conclusions of the problem to date, and for this reason considerable time will be spent in describing their results. After intrapleural injection of 15 cc of this preparation, from 50 to 75 cc of black, serous exudate may be recovered in the first hour. This exudate is rich in polymorphonuclear leukocytes (87%) with small and large lymphacytes constituting 10% to 12% of the total. Both neutrophiles and monocytes were seen to be phagocytic. In this same space of time, the entire mediastinum and pulmonary ligament were superficially blackened while the remainder of the pleural surfaces were relatively free of the pigment. Three hours after injection the exudate was essentially unchanged. In many places, especially over the anterior mediastinum, there were large masses of accumulated exudate hanging as black festoons while in most places the carbon was evenly distributed. Both lungs were free of graphite. Some polymorphs containing pigment were seen in the mediastinum at this stage. The festoons were seen to consist of polymorphs which were densely packed with carbon, few monocytes, some erythrocytes, all being held together by a matrix of fibrin. Six hours after injection only 35 cc of exudate could be recovered and cellular infiltration into the mediastinum and pulmonary ligament was far more marked. Costal and diaphragmatic pleurae showed no response. Eighteen hours after injection, however, edema and cellular infiltration of the costal pleura was very apparent. The subserous connective tissue was markedly edematous and contained numerous graphite laden polymorphs. The clasmatocyte was seen for the first time in this tissue and in the exudate. The mesothelial cells were enlarged to several times their normal size and to desquamate or to migrate to deeper tissues. Edema characterized all pleural membranes at this time with extensive hyperemia manifest. For the first time, granules of graphite were recognized in the reticulo-endothelial components of the spleen and bone marrow.

No free graphite remained in the exudate, 45 cc of which was recovered from the pleural cavity. Polymorphs comprised about 80% of the cells in the exudate. In subsequent experiments in which the time was increased, the percentage of all cells in the exudate except the lymphecyte changed. After 72 hours, 72% of all cells were clasmatocytes and 12% were neutrophiles. Sections of the pleura examined four, five, and seven days after injection showed many groups of mononuclear cells heavily packed with graphite, with some evidence to show that these cells were of mesothelial origin. Following the absorption of the graphite and the infiltration of the graphite-laden cells into the pleural membranes, cellular differentiation went on. Endothelial cells of vessels near the pleura were swollen and some were seen to contain graphite in their cytoplasm. Three types of cells abounded within the edematous mesenteries: Large mononuclear cells of mesothelial origin containing no or very little pigment and which showed signs of becoming fibroblasts; large and small lymphocytes which were slightly phagocytic; clasmatocytes containing large amounts of graphite. At five to seven days, organization of the festoons described above was in progress, with fibroblasts being prominent. The visceral pleura and pericardium did not take part in the removal at any time. Superficial collections of graphite over the diaphragmatic pleura could be easily brushed off and were the only signs of carbon on this division of the pleura.

Subsequent changes were only a continuation of the processes started during the first few days. The costal pleura, the mediastinum, the pulmonary ligament did not clear and contained no free graphite. In a period of months, these large clumps of cells on the surface of the mediastinum were organized and slowly removed in much the same manner as is a blood clot.

After reviewing the literature above, we are now in a position to evaluate and to form our conclusions on the cytologic aspect of plaural absorption.

From the investigations of the workers quoted, we must conclude that the absorption of crystalloids from the pleural cavity is dependent purely on the laws of osmotic pressure. The methods used by Starling and Leathes and by Maier are crystal clear and can leave little if any question. We are entitled to conclude that this is a relatively efficient process. It is probable that these crystalloids are absorbed directly into the blood stream, though the relative role of blood and lymph in this process is not clear.

We can well afford to be less dogmatic in our conclusions on the fate of colloidal material in the pleural cavity. The first line of reaction to such material is, of course, the pleural mesothelium. The mass of evidence presented permits us to accept these cells as being extremely active and of great functional capabilities in their response to foreign particles in the pleural cavity. We may also conclude that these cells possess phagocytic properties under the proper stimulus, that stimulus comprising the presence of foreign colloidal material in the pleural cavity. The chief response of these cells seems to be the production of many fixed and an unknown number of wandering macrophages.

The painstaking efforts of Lemon and Higgins and of Karsner and Swanbeck are adequate evidence that the pleural mesothelium differs in its response according to its location within the pleural cavity. We may accept the mediastinal pleura as most active in its response to granular material injected intrapleurally, followed by the costal pleura, with the lung as quite unresponsive and the diaphragmatic pleura as inert. We can come to absolutely no conclusion as to the reason why these cells of morphological identity and of identical embryologic origin should show these gradations in activity. It would seem almost impossible that these cells should be intrinsically different in different locations. One cannot avoid consideration of the analogous activity of the mediastinal pleura and of the greater omentum in their response to colloidal material.

The relative role of blood stream and lymphatics in the removal of foreign colloidal material from the pleural cavity is also undetermined. It is deserving of further investigation. We can conclude without question that colloidal material injected intrapleurally will be found in lymphatic channels which act as efferents from the pleural cavity, but must qualify this by stating that the amount carried by the blood stream is not known. The delayed appearance of foreign particles in the reticulo-endothelial cells of spleen and bone marrow suggests that the lymphatic system plays the predominant part.

That the blood stream plays a part in the response to foreign colloids is evidenced by the number of polymorphs in the exudate.

GROSS LYMPHATIC DRAINAGE OF THE PLEURAL CAVITY

As shown above, there can be no doubt that the lymphatic system plays a definite role in the removal of colloidal material foreign to the pleural cavity. Although the relative role of the lymphatic system in such a function cannot be accurately evaluated at present, it is definitely of value to understand the pathways of such drainage for reasons which become apparent when one considers disease processes within the pleural cavity. It is obvious that these are only a continuation of the local reaction to the noxious agent, whereby it is carried from the site of insult to open new locations of infection or neoplastic growth. Thus these pathways must be understood for the intelligent treatment of any disease process in the pleural cavity.

In presenting such a subject, we must realize that we can accomplish only the description of the afferent and efferent connections of the lymph channels and nodes and the gross appearance of the pleural cavity after injection of the tracer substance.

Once again we refer to Karsner and Swanbeck (1922) for a gross description of the pleural cavity a short time after the injection of india ink or carmine. Within two hours the mediastinum, especially the anterior, is very well demarcated from the remainder of the structures of the pleural cavity by the intense concentration of the dye on its pleural surfaces. It hangs as a curtain separating the two pleural cavities and is of the color of the material injected. Considerable pigmentation of the mediastinal nodes may be seen. Superficial accumulations of carbon are seen on other pleural surfaces, but may easily be brushed off. After 24 hours the picture is essentially the same with the exception that lymph nodes contain more pigment. This gross description is in full agreement with Lemon and Higgins (1930). Bettman (1925) adds to this description a picture of the marking of the intercostal lymphatic vessels (lying close to and parallel to the intercostal vessels and nerves) at a time four days after injection.

The brief and superficial summaries of the efferent lymphatics of the pleural cavity which are found in standard anatomy texts can hardly suffice for full understanding of this pathway. Their description, while agreeing with the findings described below, is not complete and is included in the substance of what follows. For this reason these descriptions will not be specifically considered in this paper. Unfortunately, these are almost all of the descriptions given.

Lemon and Higgins (1931) in a paper designed to show the gross features of pleural absorption in the dog, cover the pathways of absorption very carefully and adequately. A solution of graphite particles was injected intrapleurally into dogs and the delineation of lymphatic channels and nodes was allowed to proceed by purely natural processes. This method revealed the lymph nodes of the thorax to be naturally divided into parietal and visceral groups. The parietal group comprises the sternal, vertebral, and the diaphragmatic nodes; the visceral group including the mediastinal, pulmonary, tracheobronchial, tracheal, and bronchial nodes. The sternal nodes are quite constant and are seen to drain the peritoneum as well as portions of the costal pleura. Vertebral nodes are not constantly segmental on either right or left side, but are more constant on the right than on the left. Diaphragmatic nodes are very inconstant. The mediastinal nodes are also of the inconstant variety, comprising a group of three or four nodes lying between the vena cava and the trachea. Tracheal nodes, while always present, are very inconstant in number and size, lying along the trachea from the junction of the azygos vein and vena cava to the level of the first interspace. Tracheobronchial nodes lie in the bifurcation of the trachea and are constant in number and size.

The lymph drainage associated with these nodes may be grouped into six main routes, two of which conduct lymph caudad and four of which conduct lymph cephalad. The line of demarcation between these two directions of drainage lies at about the eighth or ninth interspace. Beneath this level, lymph vessels pass caudad and empty into a large node which lies dorsal to the anterior pole of the kidney. Efferent vessels from this node pass directly to the cysterna chyli. The cephalad drainage from this point of demarcation is less easily demonstrated and is imperfectly formed in the majority of cases. In general the intersegmental collecting vessels are more constant on the right than on the left and form a trunk which empties into the lower tracheal nodes on the right. On the left side, the collecting vessel, if present, empties into the anterior mediastinal nodes. This channel on the left usually reaches the level of the third rib, and eventually anastomoses with sternal nodes before entry into the thoracic duct. Ventrally, small lymphatic channels lie in and beneath the transversus thoracis muscles. A vessel was seen to lie on both the inferior and superior surface of each rib. These vessels unite to form a plexus which is independent of the lateral sternal channels from the diaphragm and lies lateral to it. These vessels pass into one of the sternal nodes at the level of the third interspace. Anterior to this, the channels emptied into the anterior of two sternal nodes lying opposite to or above the first rib.

Rouviere (1938) in his description of the lymphatics of the human pleural cavity divides it into definite regions of drainage. He agrees with Lemon and Higgins in the general features of anterior and posterior direction of drainage, but in addition adds regions of costal drainage. The first of these regions includes the parietal pleura covering the first costal arch, the first intercostal space (exclusive of its extremities), and the entire pleural dome. The efferent vessels from this region reach the superior aperture of the thorax and generally terminate either in a node of the transverse cervical chain or internal jugular chain, or in the mediastinal lymph nodes. The second lymphatic region extends from a point below the first rib to the fourth rib, inclusive. Its anterior and posterior boundaries almost merge with those of the medial wall of the axilla. In addition to the general principle of anterior and posterior drainage, some lymphatic trunks traverse the thoracic wall to end in the axillary nodes. The third region extends below the second region and terminates at the sixth rib. Some collecting vessels from this region drain into the axillary nodes.

After presentation of this literature and briefly reviewing the classical picture, two things become apparent. The pattern offered by our present anatomy texts has become generally accepted. It is at present impossible to determine the experimental basis for this summary. Secondly, experimental results on the dog confirm the findings presented in these texts. Our opinions on the efferent lymphatics of the pleural cavity have thus reached a static phase with the opinions well formed. There can be no real objection to accepting this pattern as described by Lemon and Higgins, with the reservation that the number and exact location of the lymph nodes may vary in the human.

Rouviere's areas of drainage are very pleasing to think about, but unfortunately we cannot evaluate his conclusions because we do not know the experimental method used in demonstrating these lymphatics.

PHYSIOLOGIC CONSIDERATIONS: FACTORS DETERMINING EFFICIENCY OF ABSORPTION AND THE RELATIVE ROLE OF DIFFERENT PROCESSES IN ABSORPTION FROM THE PLEURAL CAVITY

In consideration of a topic of this sort it is only fitting and proper that the effect of respiration on the absorption of foreign particles and solutions from the pleural cavity and its relative role in such a process should have been questioned. This was suggested very early and since has come to occupy one of the most controversial points in the entire problem. The constant changes in size of the thoracic organs and the constant changes in pressure relationships within the thoracic cavity have naturally caused no little speculation and various attempts have been made to explain phenomena of absorption by such processes. We will, therefore, review the theories which have been advaneed as to the mode of action of the respiratory process on the question at hand and the experimental basis for these theories.

Some years ago a controversy arose as to the manner in which foreign materials are removed from the pleural cavity, with the result that two schools of thought have arisen on this mechanism. In the last analysis, we probably are not dealing with two separately functioning entities, but rather with processes which act together to produce the final disappearance of the colloidal material. The first of these schools holds that mechanical change induced in tissues by virtue of the stresses of the respiratory movements are responsible and that the direct action of the cells on the foreign substance is not necessary for absorption. Dybkowsky (1866) was the first to suggest such a possibility and from him we quote directly.

> "With each inspiration the intercostal subpleural lymphatic network is opened out and filled with fluid from the pleural cavity, the forces affecting this being the elasticity of the lung on one side and the tightening of the intercostal fascia by the inspiratory movements on the other. With each inspiration the intercostal fascia is relaxed and bulges inward, the capacity of the subpleural lymphatic network is

> diminished and its contents are emptied into the efferent lymphatic vessels. The pumping action varies with the vigor of the inspiratory movements and the elastic force exerted by the lung."

By this explanation, Dybkowsky attempted to explain the disappearance of fluids and granular material from the pleural cavity. In this same year the first of the gravity experiments was done on the diaphragm by Ludwig and Schweigger-Seidel (1866). This procedure consists of placing the animal in such a position that the head of the animal lies below the level of the diaphragm. Following this, the granular or protein material is placed in the concavity of the diaphragm and filling of the diaphragmatic lymphatics of the dead animal is observed. Gravity is the only means of explanation for the filling of these lymphatics from the inferior surface of the diaphragm. The same may be done by intraperitoneal injection followed by artificial respiration. Results of this sort would tend to support a mechanical factor as being responsible. Other support for this mechanical factor will be found below, in addition to the following important reference. Wadsworth (1922) in attempting to evaluate the role of the respiratory movements in the removal of india ink from the pleural cavity of the rabbit. The animals were sacrificed and the trachea cannulated to a positive pressure respirator. Intrapleural injection was made and artificial respiration begun. After a period of about one hour of artificial respiration the animal was examined and the ink particles were seen to have progressed almost as far as in the living animal. Wadsworth naturally concluded that respiratory movements were the prime factor in the passage of carbon particles from the pleural cavity into the mediastinal nodes. Of recent years, Allen and Vogt (1939) have again considered the problem of the effect of changing volume on the removal of foreign material from the serous cavities. Although this investigation was primarily concerned with the diaphragm, their impression is believed to hold true for the costal pleura as well. These workers excised portions of the lining mesothelium and their subjacent tissue and placed a small amount of carbon suspension on the mesothelial surface. On alternate stretching and relaxation of the tissue, the suspension was seen to enter the lymphatics beneath the serous layer and to flow through the lymphatic channels. In such a supposition, they of necessity take the viewpoint that stomata in some form exist between the mesothelial cells, a view held in disfavor by the majority of anatomists today. In opposition to this point of view Karsner and Swanbeck (1922) found all carbon intracellularly and came to the conclusion that carbon particles must be phagocytized before entry into the lymphatic channels.

The role of respiration in the question of absorption from the pleural cavity has to date concerned itself chiefly with the effect of pneumothorax on the effieiency of pleural absorption. Detailed tissue work to corroborate the above theory of absorption has not been a part of the majority of this work. The common use of therapeutic pneumothorax today makes it obvious that we should attempt to understand fully the effects of this condition.

Bettman (1925) made a brief study of the effects of pneumothorax from the pleural cavity of the dog. He found that injection of india ink into the pleural cavity of normal dogs left only the markings of the intercostal lymphatics four days later. In animals in which an artificial pneumothorax was induced he found all pleural surfaces stained and the lymphatic channels less definitely defined after the same time interval. Cross section of the lungs showed them to contain no carbon, but a diffuse staining was otherwise present. In an attempt to determine the possible reason for such a change, Bettman induced a pneumothorax without carbon injection and could discern no change in the mesothelium. Thinking that perhaps separation of the pleurae might be the cause, he injected normal saline and found no change. He ventured no opinion. Corfer (1926) also investigated the effect of pneumothorax on the absorption of 2% sulphocyanate from the pleural cavity and by determining blood levels of this substance concluded that pneumothorax was without effect. Returning again to particulate matter, Noetzel (1927) injected twenty four hour bacterial boullion cultures into the pleural cavity of dogs. He found that in the normal animal this suspension caused no appreciable reaction except for a localized inflammatory process at the site of injection. If, however, an artificial pneumothorax was induced at the same time, the injected material not only remained in the pleural cavity but also produced an empyema. He concluded that the pneumothorax greatly interfered with the lymph and blood circulations. Just how he believed that this mechanism operated, he did not say. This work was followed in two years by Dolley and Weise (1929), who attempted their study on the living dog. After cannulating the junction of the confluence of lymphatics on the left side (exclusive of the thoracic duct), trypan blue was injected intrapleurally on the left. After a control period, a massive pneumothorax (250 cc of air) was induced on the left side. Every dog showed a substantial decrease in the amount of lymph taken over periods of one half to one and one half hours. In addition, the authors found that if pneumothorax was induced before injection that greater time was required before the stained lymph appeared in the cannula. Chyle from the thoracic duct was also decreased in amount for the first few minutes of the pneumothorax. Dolley and Weise also believed that in pulmonary edema, fluid entered the pleural cavity rather than remaining within the lung. This conclusion was confirmed by Brock and Blair (1931), who noted that the induction of pulmonary edema was rapidly followed by pleural effusion. Brock (1934) attempted an investigation of the fate of fluids in the pleural cavity of the rabbit under varying conditions. The efficiency of the absorption of these fluids was judged by the amount of fluid remaining in the pleural cavity and by the length of time required for the absorption of one minimum lethal dose of strychnine. He observed that with pneumothorax the efficiency of removal was increased by about 500% over normal. Deep and rapid respirations still had a marked effect and could increase the rate still further. The most accurate evaluation, as concerns quantities, was made by Maier (1939) in which he injected salt solutions of various concentrations into the pleural cavities of dogs and later noted the quantity of sodium chloride and the quantity of fluid remaining in the pleural cavity two hours after injection. He found that simple artificial pneumothorax decreased the absorption of sodium and chloride by 17% to 50%, with greatest average decrease seen with isotonic solution. He also found that deep respirations increased the rate of absorption, in some cases increasing the efficiency to above normal in the face of the pneumothorax. In conjunction with the above findings it would be wise to include the findings of Petersen and Drinker (1942) whose observations seem definitely to prove that movements of respiration do play a part in controlling the amount of lymph and the rate of lymph flowing in the thoracic cavity. They cannulated the trachea of dogs and a lymphatic channel in the superior mediastinum which was assumed to represent a cross section of the general lymphatic situation in the thoracic cavity. Cotton wool could be inserted into the trachea and by this means forced respiration was induced. Immediately pressures reached a maximum of -56 mm in inspiration and the flow of lymph through this cannulated channel immediately increased in volume with red blood cells appearing in the lymph. The composition and amount of lymph returned to normal as soon as the obstruction to respiration was removed. The authors concluded that movements of respiration definitely influenced the flow of lymph in the thoracic cavity, with increased respiratory excursion (and consequently altered pressures) causing the increased flow of lymph.

Other factors influencing the efficiency of pleural absorption have not been fully investigated, and, in fact, have suffered from neglect. Notkin (1925) concluded that the absorption of hemoglobin was delayed from an inflammed pleural surface and concluded that the lymphatic vessels play a part in the economy of the living animal because it is only through these channels that tissue fluids can be absorbed. Corfer (1926) was of the same opinion as a result of his investigations with sulphocyanate. On the other hand, Brock (1934), using turpentine inflammation and judging the efficiency of absorption as described before, concluded that the rate of absorption was markedly increased. Two days after the inflammation was induced, he found that the rate was three times normal and even after fifteen days the rate was twice normal. Deep breathing further ~~decreased~~ the survival time by 30% to 50%.

Volumetric examination of fluid remaining in the pleural cavity confirmed the above results almost exactly. Brock also found that the rate of absorption increased with increasing amounts injected until a total of 75 cc was injected.

In evaluating the literature above, it is seen that the relative roles of phagocytosis and movements of respiration in the removal of foreign colloidal material from the pleural cavity are certainly worthy of further investigation and that we cannot at present draw any definite conclusions. There is ample proof that either may be responsible and both are well documented. If one were forced to lean in either direction, he would have to conclude that possibly respiratory movements have been more consistently shown to be responsible here and in other sites (see diaphragm). We can only speculate on this problem, but it seems possible that the two may operate at different times and under different conditions in the pleural cavity.

In attempting to evaluate the effects of pneumothorax on the efficiency of absorption from the pleural cavity, we need not look far to note a discrepancy. The experimental study thus far has been based on similar methods, all of which seem to be quite accurate. The results of these studies must lead us to the conclusion that pneumothorax does impede absorption from the pleural cavity, this being true for both crystalloids and colloids. Brock stands as the exception, both as to method used and to results obtained. This one piece of work should not force us to reverse our opinion. While Brock's work is done with considerable care, we must remember that he used strychnine as the basis for his opinion of the rate of absorption. When we consider that this is not an inert substance in any sense of the word and that the susceptibility of a given series of animals will vary, we must reserve our opinion on the value of such a procedure. As in other phases of the absorptive process, the mechanism of pneumothorax is obscure. Decreased expansion of the thoracic acvity with its contained lung; disturbance of the capillary action between contacting pleural surfaces; gravitation of fluid to the inferior portions of the pleural cavity have been suggested as causes of the decreased absorption, but none has ever been proven.

Allied to the problem of pneumothorax, we have the question of the effects of hyperpnea. All who have investigated this phase are agreed that hyperpnea increases the rate of pleural absorption. The methods used have been much the same as for pneumothorax and are reliable. We may accept hyperpnea as increasing pleural absorption.

Conclusions as to the effect of other factors are not justified and cannot be based on adequate evidence. One very disturbing feature is that the effect of inflammation has not been evaluated. Again Brock's work is the most comprehensive to date, but must be held in reserve. It is surprising that this has not recieved more attention.

THE CONCEPT OF PLEURAL ABSORPTION

Pleural absorption has been a process quite unappreciated to this date, with the result that no clear concept of this process has been established. That this is the case is understandable and a tribute to the technical difficulties which are so obstinate in this region.

After reviewing the literature of the various phases of this problem, it is apparent that we can state the features of such a process only with the realization of the work which remains undone and the problems which yet face us. It is with the realization that the present evaluation of this process is attempted and only experimentally proven facts are used in the formation of this concept. To say that it is incomplete is an understatement, but with the solution of the remaining problems in the following section we should have a well defined and complete understanding of this process. We may accept pleural absorption as occuring after the following pattern.

When foreign substances in solution (such as colloidal dyes) are injected into the pleural cavity of mammals, that material is spread diffusely over all pleural surfaces. Within a short time two processes are operative in response to the presence of this material. Within one hour, an exudate is present within the pleural cavity. This exudate is composed of polymorphonuclear neutrophilic leukocytes which are phagocytic to the dye particles and of few large, phagocytic mononuclear cells of unknown origin. The second process operative at this time is the factor of respiratory movements which is also responsible to some degree for the disappearance of the particles of dye from the pleural cavity while causing the dye to bathe all surfaces. At this early stage the differential response of the pleura may be observed, with the mediastinum and pulmonary ligament infiltrated with dye and the remaining pleural surfaces free of dye.

As this process proceeds, we find several gradual changes which occur simultaneously. Over a period of days the number of neutrophiles in the exudate decrease in number with a commensurate increase in the number of macrophages, all of which are phagocytic. Masses of carbon in both types of cells are seen to be clumped together by fibrin and to be "pasted" to the mediastinal pleura by the same substance. This is first marked in the mediastinal pleura, later in the costal pleura. The pleural mesothelial cells become phagocytic in situ and produce some wandering macrophages. At this time a typical inflammatory response is seen in the subpleural tissues, with intense hyperemia. Mediastinal lymph nodes and sternal nodes are observed to contain pigment at this stage. Over long periods of time, dye particles are removed from the pleural surfaces by organization and removal of carbon.

An undetermined amount of the dye is removed via the efferent lymphatic vessels of the pleural cavity. Some enters these vessels in cells, other particles entering due to some change induced by movements of respiration. In this process, intercostal lymphatics carry the dye to sternal and mediastinal nodes chiefly.

The respiratory movements influence this process, with deep, rapid respirations increasing and pneumothorax decreasing the rate of absorption. Other than this, we do not possess adequate knowledge of other influencing factors.

PROBLEMS REMAINING IN PLEURAL ABSORPTION

The problems which remain unsolved are, unfortunately, the key to the concept of pleural absorption. A brief resume of these problems will be given.

The most annoying of these is our lack of knowledge of how the foreign particles enter the lymphatic channels. By this is meant that the activity of the lymphatic endothelium is not understood. This applies both to carbon within cells and free.

Although we are well aware that the lymphatic system plays a role in the removal of foreign particles from the pleural cavity, the relative role of the blood stream in this process is not known.

The differential response of the pleural mesothelium cannot be explained with the least degree of certainty.

The manner in which respiration influences the efficiency of absorption is not known. Another method of stating this problem is that we do not know just what changes in the lymphatic endothelium (if any) are induced by the changes of shape and volume secondary to the movements of respiration.

The influence of inflammation is not defined.

The nature of the processes in action in the mediastinum are completely obscure as are the pathways. The mediastinum has not been explored in relation to this problem and is the most important area.

The source of the macrophages in the pleural exudate is not known.

The investigation of the lymphatic channels of the costal and mediastinal pleurae should be done microscopically and with great care.

THE PULMONARY LYMPHATICS

A subject which we may well consider is the topic of the complete lymphatic picture of the lung. The importance of this system in relation to pulmonary disease is adequately emphasized, but the anatomy and physiology of this portion of the lymphatic system have not been entirely clarified.

It is interesting that there are two extremes of investigation of the various phases of this system. While the anatomic patterns have been studied since very early times, the physiologic considerations have only recently come into prominence and comprise virtually an unknown field.

DEVELOPMENT OF THE PULMONARY LYMPHATICS

Problems arising in the definition of adult anatomy and in problems arising therefrom can often be answered after a thorough study of the developmental processes and relationships of the given part. While the literature concerning the development of the lymphatic channels within the lung and the efferents of these channels is not voluminous, the work done is very careful and quite informative. This process of development will be reviewed, for in the case of the lung, its understanding clarifies the adult relationships to a considerable extent and forms the basis for some healthy doubts.

The exhaustive investigations of Flint (1906) into the development of the pig lung included the development of the lymphatics of that organ. He was considerably handicapped by lack of injection methods and serial sections, yet his contribution is not inconsiderable. Flint's study was the first to approach the understanding of the adult lymphatic system of the lungs through developmental observations. His work is confined to the intrapulmonary lymphatics. At a stage of 3 cm, he found that a few dilated lymphatic vessels are present at the root of the lung, but that they have not yet penetrated the parenchyma. These lymphatics are found to lie near the bronchi and blood vessels. At a stage of 5 cm, however, lymphatics extend for some distance into the developing lung, still being confined to the immediate vicinity of the major bronchi and cheir chief subdivisions. They are fragile structures with valves present in some cases. In more distal portions of the lung, plexuses of these lymphatics are seen to lie midway between the bronchi, having become as far separated from them as possible in the most distal portion of the bronchi. These plexuses reach the pleura at this stage and the lung is given a lobulated appearance, the lymphatics serving as interlobular markings. Valves are seen in the subpleural portions which, in general, point away from the pleura. At the 13 cm stage, obvious plexuses of lymphatic vessels are seen surrounding the bronchi and the large vessels entering the lung. This arrangement is constant as the structures pass into the lung, with interlobular lymphatics following the pulmonary vein as the periphery of the lung is approached. This forms a dense plexus, with occasional vessels seen entering the lobules of the lung. Until 23 cm is reached, there is no change in this pattern and at this time the first submucous plexuses are seen in the bronchi. These, in brief, are the findings of Flint and seem well borne out by later investigations.

Cunningham (1916) augmented this study with an extremely complete and painstaking observation of the lung lymphatics of the developing embryo pig. His report on this is very comprehensive and exact, but for the sake of brevity only the gross features of his results will be reviewed. In this he combined injection, serial section, and reconstruction in interpreting the developmental changes. Cunningham, who believes that lymphatics are derived from the endothelium of the venous system, states that the lung lymphatics are derived from three sources: The thoracic duct, the right lymphatic (thoracic duct) duct, and the retroperitoneal lymph sac. Arbitrarily, he divides principal developmental stages into the following:

Stage 1 The downgrowth of the right and left ducts from the jugular sacs, and the completion of the primary lymphatic system. This is complete at 2.3 to 3.5 cm.

Stage 2 Includes the migration of the heart; the coasescence of the cardiac and right lung drainage; the formation of the tracheal plexuses and the plexus on the arch of the aorta; the growth of the vessels in the lung from the earliest sprouts along the bronchi to the primitive pleural plexus and the early marking off of the connective tissue septa; the growth up from the retroperitoneal sac through the ligamentum latum and the anastomosis in the primitive septa into which the vessels grow. Complete at 3.5 to 4.5 cm.

Stage 3 The completion of the primary system of the lung; that is when the entire organ is supplied and the further development is an increasing complexity of the plexuses already present, incident to the increase in size of the organ and its assumption of mature activities. During this period the formation of the valves and nodes begins. This stage is complete at 4.5 to 7 cm.

Stage 4 The remainder of the development is considered a period as it is in reality an adaptation of the system already present to the increasing needs of the organ. This includes the differentiation of the drainage lines and the final development of the nodes.

Gunningham found that the thoracic duct was complete at 2.5 cm and at the point where it bends dorsally to pass the arch of the aorta, a bud is given off which passes toward the trachea. Vessels arise at a lower level from the thoracic duct, pass upward toward the trachea, and join the origional bud on the left side. Proliferation of this anastomotic loop (actually a plexus at the time of anastomosis) along the left margin of the trachea gives rise to the origional left tracheal plexus at 3 cm. From this plexus, vessels pass dorsally and ventrally over the surface of the trachea to unite with a plexus on the right side of the trachea (to be described below). This left tracheal plexus covers the greater portion of the ventral surface of the trachea, and in addition supplies a large portion of the lymphatics which come to cover the right bronchus. While these plexuses are still developing, vessels arise from the buds described above reach the lung at a stage of around 2.8 cm and lie irregularly grouped around the hilus. On the right side, the development is in general similar to that on the left. The right duct, however, passes caudad in very close relationship to the superior vena cava. At the point where this vessel arches ventrad to reach the heart, the duct splits and a definite branch is given off which passes to the heart. A larger continuation of the right duct passes along the right side of the trachea to reach the upper lobe of the right lung chiefly (after following the right primary bronchus), but is distributed to other portions of the lung as well. A few vessels arise from the cardiac branch and are distributed mainly to the upper lobe of the right lung. Between 3.3 and 4.5 cm the two tracheal plexuses anastomose freely, dorsally and ventrally and the left duct is clearly seen to give a great number of lymphatics to the inferior surface of the right primary bronchus. In the meantime, the heart is migrating caudally and at 4.5 cm has come to lie at the level of the hilus of the lung. The vessel which origionally branched off the right duct is no longer distinct and the lymphatics of the heart come to mingle with those of the tracheal plexus at the bifurcation of the trachea and the plexus of lymphatics at the hilus of the right lung.

At 3 cm there are two primary bronchi and two veins and two arteries to either side, one to each upper and lower lobe. From 3.5 cm these branch rapidly and bronchi especially come to occupy a great part of the developing lung. At this stage, the veins are located as far as possible from the distal bronchi while the arteries are very closely associated with these structures. This point becomes of special significance when one considers the position of the pulmonary vein and its associated lymphatics. In the essential points of intrapulmonary development, Cunningham agrees with Flint but he emphasizes several points which do have considerable significance. He emphasizes that lymphatics grow chiefly along the veins of the lung and with this the greater concentration of lymphatics in the perilobular location is explained. Branches growing along the bronchi were observed to grow more slowly than at any other site in the lung. He found that branches were given off to the periphery of the lobule where bronchi branch. In this way the plexuses of the lung are formed, and form in themselves a system of anastomosing lymph vessels. Connective tissue septa develop early.

At a stage of 3.4 cm, vessels were first seen passing from the retroperitoneal sac through the pulmonary ligament and into the lung. These vessels are distributed almost entirely to the inferior and lateral surfaces of the lower lobes. When these vessels reach the middle of the ligament, they divide into two fork-like plexuses which pass to the surfaces which they will invade. Upon reaching the surface of the lung, they pass into the lung at the interlobular septa and at 4 cm have completely anastomosed with vessels which are already present. It is impossible to differentiate these vessels from those already present at 4 cm. The lower half of the pleura and the lower lobe of the lung are said to be drained by these channels.

The relationships thus demonstrated in the mediastinum were confirmatory to Heuer (1909) and were again found true by Cash (1917).

In his study of the development of the valves of the human lung lymphatics, Kampmeier (1928) could find no valves before 3.5 months. The first valves present were near the hilus of the lung, especially on surfaces in contact with the pericardium. He found that all of these valves pointed toward the hilus of the lung. At a slightly later stage, valves could be found beneath the pleura which pointed outward at the pleura. The mode of valvulogenesis was not different than in other vascular channels with valves of this sort.

The latest observations on the development of the lung lymphatics are those of Harvey and Zimmerman (1935). They studied development in a series of human fetuses by means of serial sections and in general confirmed the observations of previous workers as regards the intrapulmonary lymphatics. At a C-H length of 75 mm, however, they found isolated spaces in the subpleural area while vessels were seen in the interlobular septa. These isolated spaces were seen frequently around blood vessels. At a stage of 112 mm these separate plexuses had united and a free connection existed between deep and superficial lymphatics. In addition, Harvey and Zimmerman found evidence of intralobular lymphatic channels at 188 mm. A few suggestive lymph spaces were found in the secondary lobule, but no actual invasion of the lobule was seen. At a C-H length of 248 mm the intralobular system was complete.

At present, the majority of anatomists are in agreement with Sabin (1901) that lymphatic endothelium is derived from venous endothelium by a process of budding and that further growth of lymphatic vessels is centrifugal from the origional points of budding. It is this pattern of development which is used by the first two authors, and to a large extent by the last.

A number of different methods have been used and used by men whose work is quite dependable. As shown, their findings are in general agreement and we may draw some definite conclusions.

From this evidence we must conclude that lymphatic channels enter the lung at the hilus after growth along the trachea and bronchi to that organ. Upon reaching the lung, they grow distally in that organ along the course of the blood vessels and bronchi. The chief concentration of these vessels is along the pulmonary vein, resulting in a profusity of interlobular lymphatic channels. That this peripheral growth is very rapid is evidenced by the fact that the pleural plexus forms while the plexus of the pulmonary vein is not yet complete. Although Harvey and Zimmerman imply an objection to this method of growth in the lobule, this cannot be accepted without qualification. They depended entirely upon serial section, using no injection, and may have failed to observe connection between perivenular and pleural lymphatic plexuses.

With the pattern of growth described, the lobule of the lung becomes outlined by lymphatic channels in a plexus in a plexus arrangement. Within the lobule, lymphatic plexuses grow in relation to the pulmonary artery and bronchi. These lymphatics are not as concentrated as those about the vein and communicate with the perilobular lymphatics, especially at points of bifurcation of the bronchi. Peripheral growth of the lymphatics along the bronchi occurs more slowly than that along blood vessels with the submucous bronchial lymphatic plexus appearing relatively late. Lymphatics in relation to the very distal parts of the bronchial tree have been seen only by Harvey and Zimmerman, who believe that they arise as isolated tissue spaces which are secondarily connected to the perilobular lymphatics.

There is adequate evidence in the pig, at least, that the chief lymphatic supply of the lungs is derived from the thoracic duct, with the right lymphatic duct contributing only to the upper and middle portion of the right lung. The question naturally arises as to just how fully this picture as seen in the pig conforms to that of the human. The pattern is probably nearly the same, for the relationships implied in other parts of the development are confirmed in the lung of adult mammals in general, human included.

The significance of the extrapulmonary lymphatic development will be discussed with the gross drainage features.

THE ANATOMY OF THE PULMONARY LYMPHATICS

It is agreed that the lungs present a profuse network of lymphatics which, as will be shown, is quite a paradoxical comdition. In this review only the pertinent papers will be reviewed since the general pattern of the lymphatics of the lung is well agreed upon.

According to Miller, Rudbeck (1653) first observed the lymphatic channels of the lung. These were observed in the dog and apparently only a few vessels at the hilus were seen. Miller also states that Thomas Willis (1675), by preventing the discharge of the contents of the thoracic duct into the subclavian vein in a dog that had eaten and drunk largely, caused the superficial lymphatics of the lung to fill and become very apparent.

Passing over an interval of 100 years, Cruikshank (1790) and Mascagni (1797) both described a superficial and a deep set of lymphatics in the lung, which sets communicated with each other. Both confined their description to the superficial set. This description corresponds to the present concept which has been mentioned.

Again another century passes before the investigation of Wywodzoff (1866). He demonstrated deep lymphatics as arising from fine lymph capillaries situated in the walls of the air spaces, thus introducing a very controversial point in the lymphatics of the lung. These lymph capillaries ran at an angle to the blood capillaries. Larger lymphatics were seen situated in and around the walls of the bronchi and blood vessels. These two sets of lymphatics communicated with each other. Superficial lymphatics were described as destitute of valves, the deep possesing valves. He believed that superficial and deep sets were connected by lymphatic channels which coursed along the pulmonary vein from the pleura to the interior of the lung.

In his first paper on the lymphatics of the lung, Sikorsky (1870) describes a system of fine capillaries and lacunae in the wall of the air spaces, similar to that of Wywodzoff.

He also describes a system of fine capillaries between the ciliated cells lining the bronchi. In a second paper (1872) he makes no reference to these findings and apparently abandoned them.

Sappey (1874) made quite a noteworthy contribution in his description of the markings of the secondary lobules by the pulmonary lymphatics as seen on the surface of the lung. He also described superficial and deep networks which communicated freely.

Klein (1875) described pleural, peribronchial, and perivascular lymphatics. He stated that the arrangement of the lymphatics around the arteries and veins was similar, but that smaller veins were surrounded by perivascular lymph spaces.

Councilman (1900) first observed the perilobular (interlobular) lymphatics, though his descriptions are quite vague.

Miller (1937) presents an excellent summary of our present opinions concerning the morphology of the lung lymphatics. An understanding of the development described leads to a full understanding of the arrangement of these vessels. Miller finds peribronchial, periarterial, perivenous, and interlobular lymphatic networks in addition to the pleural (superficial) lymphatics of the lung. Lymphatics of the bronchi consist of submucous plexuses which anastomose freely with plexuses found surrounding the cartilage of the larger bronchi. Smaller bronchi which have no cartilage in their walls possess but one plexus and this becomes finer until it is no longer visible at the distal end of the ductuli alveolares. Thus no lymphatic vessels would be found in the walls of the air spaces. The lyjphatics accompanying the pulmonary artery form a complex anastomosing plexus which seems at times to be common to the peribronchial plexus. These vessels also become finer as they pass distally in the lung and can no longer be seen beyond the ductuli alveolares. Smaller divisions of the artery are frequently accompanied by a single lymphatic vessel. The plexus accompanying the pulmonary veins is formed distally in the lung from three sources according to Miller. The distal end of the ductuli alveolares, the point at which bronchi divide, and the pleural network contribute to the formation of these perivenular lymphatics. As the veins increase in size, the complexity of the lymphatic network surrounding them does likewise. Those lymphatics of the interlobular septa form a lattice work between the pulmonary veins, and may actually be considered as a part of the perivenous lymphatics. The lymphatics of the pleura are arranged in irregular polyhedral rings, having four or more unequal sides. Miller states that there is only a single plexus of lymphatics in the pleura, though a pleural and subpleural plexus have been mentioned. The large lymphatics which take part in the formation of these rings mark out the secondary lobules of the lung. Within these, the markings of the primary lobule can be recognized. These lymphatics of the pleura form a dense plexus, the vessels being freely interconnected but not allowing flow of injected substances into the deep lymphatics due to the presence of numerous valves. These channels unite to form a variable number of trunks which drain into the lymph nodes at the hilum.

It is quite significant that the observations of the pulmonary lymphatics have been made on a number of different mammals and that the same general plan is observed in all. The arrangement of lymphatics of the adult lung correlates beautifully with the findings in the developmental stages and at once becomes apparent with an understanding of the latter.

The morphology of the lymphatics of the adult mammalian lung has been well established and there is no reason why they should be refuted. The pattern has been repeatedly confirmed and the embryologic and histologic bases are established. The conclusions will be given briefly.

The superficial lymphatic plexus and the deep lymphatics are functionally distinct by virtue of their valves which prevent deep flow from the superficial set. They cover the entire lung and terminate at the hilus of the lung by uniting with deeper lymphatics of the lung. Each lobule of the lung is outlined by a plexus of lymphatics which is seen to accompany the pulmonary veins. This perilobular plexus is carried to the pleura and by virtue of this arrangement the markings of the lobules may be seen on the pleural surface.

In addition, plexuses of lymphatic vessels accompanying the pulmonary artery and bronchi are present and communicate with the perilobular plexuses.

It is generally agreed that there are no lymphatic channels distal to the alveolar ducts.

The lymphatic channels described (peribronchial, periarterial, and perivenous) unite with the pleural lymphatics at the hilus and pass to the nodes to be described.

The lung is profusely supplied with lymphatic channels.

GROSS LYMPHATIC DRAINAGE OF THE LUNG

The gross lymphatic drainage of the lung is again a subject which has a tremendous importance to the clinician in his treatment of diseases of that organ. The features of this drainage are rather well agreed upon today, with certain notable exceptions which will be discussed below.

Before reviewing these opinions on the pattern of drainage of the lung lymph, it will be well to summarize briefly the developmental pattern described by Cunningham. In doing so, we must realize that his investigations were made on the embryo pig, while the present descriptions apply largely to the human lung. However, it is probable that the pattern of drainage would be essentially the same for mammals in general. If this assumption is correct, we should expect the adult drainage to follow the pathways as laid down in the developing organism. Cunningham found that the entire supply of lymphatics of the left lung was derived from the throacic duct as were the lymphatics of the inferior portion of the right lung. The cephalic connection of these channels was retained. The superior and middle portions of the right lung recieved the majority of their lymphatics from the right lymphatic duct. The lower portion of both lungs was supplied with lymphatics from the retroperitoneal sac. In our adult pattern, then, we should expect the entire left lung and the more inferior portions of the right lung to be drained through channels which pass along the left surface of the trachea and which empty into the thoracic duct or confluence of lymphatics at the junction of the subclavian and internal jugular veins on the left side. On the right, the superior and greater part of the middle portion of the lung will drain into channels which run along the right side of the trachea to empty into the right lymphatic duct or into the confluence of lymphatics at the junction of the right internal jugular and subclavian veins. Channels would be expected from each lung which drain to the upper abdomen.

The pattern which most anatomists accept today agrees essentially with that above. This is found in anatomy textbooks and in surgery texts in which the pattern of efferent lymphatics of the lung is described. Individual discussion of these references would contribute nothing to this paper and the reader is referred to the texts of Gray, Cunningham, Morris, or Piersol for further descriptions of this pattern.

Efferent lymphatics of the lung, in their course to the venous system, pass through numerous lymph nodes lying in close approximation to the trachea and bronchi. As they pass from the lung at the hilus, they are roughly grouped into peribronchial, perivenular, and periarterial plexuses. In effect, this is a single system due to the numerous anastomoses between the various plexuses of lymphatics. In their course along the bronchi, they pass through the nodes located at the periphery of these structures. Although not specifically stated, it is presumptive that lower lobe lymph passes chiefly to the interbronchial nodes. The channels then pass upward along the course of the trachea, being found on the lateral surface of that structure. In this course they pass into the laterotracheal nodes. These channels, efferents and afferents of the tracheobronchial nodes, collectively form the right and left bronchomediastinal trunks after joining the efferents of the internal mammary and anterior mediastinal lymph nodes. The right bronchomediastinal trunk then may join the right lymphatic duct, but more often opens independently of this duct into the junction of the right internal jugular and subclavian veins. On the left, this trunk may terminate in the thoracic duct, but more often empties independently into the junction of the left internal jugular and subclavian veins. In brief, then, the right lung drains to the right and the left lung to the left.

Drainage of the lung into the upper abdomen is not described. The common autopsy finding of carbon in the tracheobronchial nodes of city dwellers confirms the drainage into the tracheobronchial nodes.

A dissenter to this method of drainage is Rouviere (1938), who finds that the direction of lymph flow from the human lung is chiefly to the right. He states that the inferior half of the left lung and the entire right lung are drained through the right lymphatic duct or the bronchomediastinal trunk. In addition, he divides each lung into upper, middle, and lower portions with each having its own lymphatic drainage into a specific group of nodes. Thus the superior third of the right lung was said to drain into right laterotracheal nodes; the right middle third into the laterotracheal and interbronchial nodes on the right; the inferior area of both the right and left lungs into the interbronchial nodes; the left middle into the interbronchial and left anterior mediastinal nodes; the left superior third into the left laterotracheal, left anterior mediastinal, and nodes on the arch of the aorta. He believes that the interbronchial group drain to the right. Unfortunately, Rouviere does not describe his experimental method by which he concluded the above.

As a result of dissections and intrapleural injections, Petersen and Drinker (1942) speculated briefly that the right lymphatic duct may drain both lungs of the dog, with the exception of the upper segment of the left lung.

Drinker and Warren (1942) investigated this possibility further by intrabronchial injections of T-1824 into the specific bronchi. Careful precautions were taken that the dye should enter none but the bronchi injeted and all lobes of both lungs were injected. Right lymphatic and thoracic ducts were cannulated and collected lymph observed for the presence of the dye. After death of the animal, a thorough post mortem examination was done to determine further the fate of the dye. Invariably, they found dye first and in greater concentration in the right duct. Examination of the mesenteric lymphatics about one hour after injection showed them to be slightly stained. In only one case did the dye appear in the thoracic duct, and when seen it was two hours after injection and an hour and a quarter after its appearance in the right duct. Interbronchial nodes were always deeply stained. Drinker and Warren thus believe that the right lymphatic duct carries lymph from both right and left lungs in the dog.

In an examination of a series of 1298 cases of carcinoma of the lung, Oschner and DeBakey (1942) found the tracheobronchial nodes to be involved in 69.7% of cases, far more frequently than any other site. Abdominal nodes were involved in 20.7% of cases. In a series of 3047 other cases, regional lymph nodes were involved in 72.2% of cases.

As a result of this review, three schools of thought must be evaluated.

We must first examine the conventional picture of lymph drainage from the lung. This is the pattern as described for the human lung and it is unfortunate that we are unable to examine the experimental method and the opinions from which the opinion was formed. Be that as it may, this is the pattern which is accepted as correct and to disprove it experimental evidence must be offered. At present evidence cannot be offered that proves this to be false. This pattern must thus be accepted as true and comfort is gained by the fact that it corresponds most closely to that found in the development of the lung lymphatics of the embryo pig. An attempt to determine the origin of the lymphatics of the human lung is definitely indicated in the clarification of this concept.

We should next examine the observations of Drinker and Warren in their study of the lymphatic drainage of the lungs of the dog. There is no criticism of their experimental method, but it is impossible to state whether this pattern is true for the human. No further proof should be required to establish the drainage pattern of the adult dog. This observation does, however, create some doubt and the problem of the direction of drainage of the lung lymph should be re-opened.

The third feature is the opinion of Rouviere. His opinions as to areas of drainage are very attractive in that they would offer exact drainage areas and in addition offer lymphatic drainage to the right side in the human. There are, however, two aspects which cast considerable doubt on his ideas. In the first place, we have no idea as to the basis for his opinions and cannot evaluate them. Secondly, the indiscriminate manner in which he crosses the natural boundaries of the lung to create his drainage areas leaves one breathless. Although this is not impossible, it certainly cannot be accepted without a thorough examination of the observations upon which he bases his interpretation. His beliefs are quite a departure from our conventional pattern and it is unfortunate that we are unable to evaluate them.

REMOVAL OF FOREIGN SUBSTANCES BY THE PULMONARY LYMPHATICS

As in other phases of the behavior of lung lymphatics, we are deficient in our knowledge of the reaction of these vessels to foreign substances, specifically colloidal material. Certainly our ideas of the pathogenesis of pulmonary infections must be questioned without it. The rather limited literature on this subject will be considered in an attempt to clarify this somewhat.

That carbon particles injected into the substance of the lung will be found in lymphatics has been adequately proven. Hilton (1933) has found that after injection of a suspension of carbon particles into the lung, the material may be found in the lymphatics of the lung four months after injection. Earlier stages were not investigated since this work was done for another purpose and this was but a part of the picture obtained.

In more recent work, Drinker, Warren, and McLanahan (1937) injected horse serum, crystallized albumin and crystallized egg albumin into the lung of the dog and attempted to find the method of removal of these substances from the lung. Contrary to their expectations, these substances were removed via the blood stream and not the lymphatics. It is true that this is not acutally particulate matter, but each is composed of very large molecules supposed to be of such size that they must be taken up by lymphatics.

Technical difficulties in obtaining lung lymph have delayed the investigation greatly as concerns mammals, but Gillian and Conklin (1938) have succeded in obtaining lymph from the lung of the indigo snake. The considerable difference in the gross anatomy of this lung from that of the mammal made this possible. A lymphatic at the hilus was cannulated and various substances introduced through the bronchus. Lymph flowing from this cannula was examined after injection. Substances such as hemoglobin and Vital Red that form true solutions in water were readily removed from the lung by lymphatics, the maximum concentration being reached in 30 to 45 minutes after injection. Particulate matter (carmine, hydrokollag, calcite) with particles no greater than two microns in size was also removed from the lung by lymphatics. It was found issuing from the cannula on an average of 4.25 minutes after injection. They recognized that a small part of the foreign colloid was picked up by phagocytic cells, but due to the time element believed that it must play a very inconsiderable part. They found respiration to be an important factor in movingmatter through the lung of the snake in lymphatic channels. In almost every instance the concentration of the substance in the lymph and the speed of its appearance was in proportion to the rate and depth of respiration.

As a result of the findings of Gillian and Conklin and of Hilton, foreign material in the lung may be concluded to be removed from the lung by lymphatic channels. This is true whether introduced intratracheally or by direct injection into the parenchyma.

It is rather surprising at first glance that Drinker, Warren, and McLanahan would find molecules of such large size to be taken up by blood capillaries rather than by lymphatics. Actually, however, there is no given reason why such substances should enter lymphatic channels in preference to blood vascular channels.

Gillian and Conklin have accomplished a very carefully controlled piece of work and were fortunate in obtaining an animal on which technical difficulties were at a minimum. Their work is quite conclusive, but was carried out on the snake lung. The minor differences between this and the mammalian lung do not prohibit these findings from being accepted as true in the mammal. The conclusion that the absorption of colloidal material from the lung is very rapid is justified. The mode of entry here is not known, but does seem very rapid for phagocytosis to play the dominant part. The response to crystalloids is more puzzling. A plausible explanation for this may be the removal of the greater portion of the crystalloid by the blood stream with a lesser amount carried by lymphatics. Corresponding blood levels would have been very helpful in this case. Their observations on the role of the respiratory movements are well borne out by findings in the pleural cavity and may be accepted as true.

PHYSIOLOGIC CONSIDERATIONS: THE FORMATION AND FLOW OF LYMPH IN THE LUNG

Experimental investigation of the physiology of the lymphatic system of the lung has until recently been entirely neglected. This is due to the technical difficulties in the observation of this system in the living animal. It has not been until quite recently that lymph from the lung alone was obtained and until this date we could do no else than base opinions on general knowledge of lung and lymphatic system. Even so, this one experience has only proven that the composition and flow of lymph in the lung can be studied. In general, an entire new field has been opened for study. When one considers the application of such knowledge to a more thorough understanding of disease of the lungs, he is forced to feel that this problem should be attacked as soon as possible.

There are several great classes of problems in regard to the function and formation of lymph in the lungs. First and foremost, the source of lymph in the lungs must be determined. Secondly, the factors tending to influence the flow of lymph in the lung and the manner in which they act to produce change is as yet unsolved. Allied to this is the effect of pneumothorax. Thirdly, the response of the lymphatics of the lung (previously discussed) is not yet entirely clear. The genesis and resolution of pulmonary exudation is not understood.

The Formation of Lymph in the Lung

Before considering the literature, the special features of the circulation of the blood in the lung which make the formation of lymph here a physiological problem.

Since Starling (1895-1896) origionated the idea of the passage of water and crystalloids out of the capillaires as a result of the capillary blood pressure and passage into the capillaries as a result of the osmotic pressure of the blood protein, this theory has been generally accepted. Evidence to support him is far too extensive to cover in a paper of this sort, but suffice to say that he has been supported time and again. As applied to the systemic circulation, fluids, crystalloids, and some protein (a very small amount under normal circumstances) escape the vessel at the proximal end of the capillary loop. This results in a decrease in hydrostatic pressure, an increase in osmotic pressure with the increase in concentration of the contained protein, these changes continuing as the blood passes distally in the capillary. Eventually, the osmotic pressure of the contained protein becomes great enough that fluid and crystalloid are again drawn into the closed circulatory system. As a result of this process tissue fluid is maintained, with some of the capillary filtrate removed by the lymphatics. Drinker and others have shown on numerous occasions that the composition of this tissue fluid is identical to lymph and to plasma (with the exception of non-diffusible substances contained in the blood plasma) and it is by the above mechanism that most authorities hold that lymph is formed.

When the pulmonary circulation is considered, however, its differences from the systemic circulation become apparent at once. A large amount of blood is delivered to the pulmonary capillaries under a relatively low head of pressure and to a circulation which does not readily accomodate itself to changes in pressure. A low peripheral resistance is offered to this flow of blood under low pressure. These modifications are acrried to such an extent that the osmotic pressure of the blood in the pulmonary capillaries exceeds the hydrostatic pressure. Under such circumstances it becomes theoretically impossible that fluid should escape the pulmonary capillaries, with the result that lymph would not be expected to be formed from the pulmonary capillaries. This in spite of the fact that lymphatics are found in great numbers in the lung. The bronchial circulation, which follows the pattern of the systemic circulation, would be expected to form lymph but in rather small amounts.

Attempts by Drinker (1931) to obtain lymph from the lung failed and the above concept seemed to be supported. In this effort, he cannulated the right lymphatic duct of the dog (which should contain largely lung lymph if cannulated in the right place) and failed to obtain more than a very slight amount of lymph. Repeated attempts to cannulate lymphatics at the hilus of the lung failed due to technical difficulties until Drinker and Warren (1942) successfully cannulated lymphatic channels in the pulmonary ligament of the dog. It must be understood that this does not represent the total lymph flow from the lung and probably not even a major portion of it. The cannulation was done under conditions of pneumothorax by necessity, but positive pressure respiration was maintained and expansion of the lungs and respiratory rate were kept as near normal as possible. Drinker and Warren obtained what they considered a large amount of lymph from a channel of such size and with their considerable amount of work on these procedures there is little doubt that they considered correctly. In a series of 18 dogs, lymph flow was constant under these circumstances though the amount of lymph varied considerably in different animals. The average composition of the lymph collected averaged as follows: Protein 3.66 gm% (range of 2.81 to4.65 gm%); albumin-globulin ratio equal to that of blood and lymph from other regions; fibrinogen was present and lymph clotted; lymphocytes 22,206, somewhat higher than normal, but explained by the fact that lymph had passed through several nodes; red blood cells 9,553 per cmm, much higher than normal, but probably due to the faulty technique in the first operations, for the last ones showed no red blood cells.

It is seen that lymph is formed in the lung and probably in considerable amounts. These efforts by Drinker and Warren answer only that question. It is impossible to conclude definitely the source of this lymph, but in the amounts described it is probably formed in large part from a source other than the bronchial circulation. The only solution lies in further investigation.

Factors Controlling Pulmonary Lymph Flow

Here, as in the preceding section, we have but one piece of experimental evidence upon which to base any opinion. It is true that most workers have concluded that movements of respiration play an essential part in the movement of lymph through the lung, but actual experimental proof had never been given. The circumstantial evidence will be discussed in the following section.

Drinker and Warren (1942) attempted to determine the effect of some conditions on the lymph flow from the lung. They found the following:

Increased pulmonary ventilation (increase in oxygen supplied to the lung with respirations held constant) was found to decrease the flow of lymph from the lung. This cannot be construed as analogous to increased pulmonary ventilation in the intact animal, since the mechanism is entirely different in the latter.

Continuous intratracheal insufflation (with lungs held just beneath the position of full inspiration), in which the only massage could be caused by motion of the heart, caused an immediate and sharp drop in the flow of lymph, but did not stop the flow entirely.

Reduced oxygen (8.6% oxygen with 91.4% nitrogen for about one hour while respiratory movements were held constant) caused an immediate and sharp increase in the amount of lymph flowing from the lung. When the normal amount of oxygen was again made available, lymph flow returned immediately to normal. Though carbon dioxide content was markedly lowered during this phase, but it was later shown that oxygen lack alone was responsible.

Increased pulmonary blood pressure (induced by compression of the pulmonary vein) was followed immediately by a considerable increase in the flow of lymph. Definite oxygen lack was induced by this measure and the normal capillary pressure relationships of the pulmonary capillaries were certainly disturbed.

The main virtue of the findings presented here is in their value as a further stimulation to research on this problem. While incomplete they do serve as some indication of the processes which influence the lymph formation and lymph flow in the lung.

It may definitely be concluded that movements of respiration are vital to the flow of lymph in the lung. As is true of the thoracic cavity in general, increased respiratory movement increases the amount of lymph flowing from a cannula. The observation that lack of these movements decreases the flow of lymph adds to this conclusion. Anoxia of severe degrees may be concluded to increase the flow of lymph in the lungs just as it does in other parts of the body. The significance of the fact that increased pressure in the pulmonary artery increases the lymph flow in the lung is rather dubious. It does not offer any explanation as to whether lymph is normally formed from the pulmonary circulation, since the pressure relationships are badly upset by such an experiment. Although it is probably quite safe to say that the pulmonary circulation may form lymph when the hydrostatic pressure is increased, the behavior of the bronchial circulation under this circumstance is not known. As a consequence, the source of this increased lymph cannot be stated definitely.

The Effect of Pneumothorax on Lymph Flow in the Lung

There is adequate evidence that pneumothorax decreases the flow of lymph in the pleural cavity (and probably the thorax in general), but the specific study of the effect of this condition on the lymphatics of the lung has not been adequately evaluated. With the very frequent use of pneumothorax in the treatment of pulmonary disease, it would seem advisable that a review of our present knowledge should be undertaken. There is only the bare minimum of literature upon which to base any conclusion.

Shingo (1908) in working with rabbits and cats, induced the inhalation of soot and attempted to determine the effect of pneumothorax on the fate of this material. In animals with unilateral pneumothorax, the time required for removal of the foreign material was greatly prolonged. He attributed this to the immobilizing effect of the pneumothorax on the expansion of the lung. This, in his opinion, reduced the efficiency of lymph drainage from the lung.

Hilton (1933) attempted to determine the mechanism of pneumothorax, using rabbits as the experimental animal. Finely suspended carbon particles were injected into the trachea, followed immediately by collapse of one lung by artificial pneumothorax. At four months, controls showed the carbon largely removed, though phagocytes in the alveolar wall still contained some particles. With pneumothorax, much more of the material remained in the lung. It was grossly visible in this case. Lymphatic channels of the lung were seen to contain large amounts of carbon particles, especially toward the hilus and were grossly dilated on the side of pneumothorax. Some fibrosis around the lymphatic channels was observed. Hilton believed that lymphatic obstruction was the most logical explanation for the dilatation of the lymphatic channels.

From the evidence offered, it is fair to conclude that pneumothorax decreases the flow of lymph in the lung. That it enters the lymphatics is shown by Hilton, and the above conclusion is justified. Just what effect pneumothorax has on the entrance of these particles into the lymphatics is not known.

THE TOTAL CONCEPT OF PULMONARY LYMPHATICS

Our present concept of the morphology and function of the pulmonary lymphatics has been implied as nearly complete in some respects and almost totally incomplete in others. The previous review of the literature has shown the situation in the various phases. The concept will be summarized for the mammalian lung as it is formed on the basis of experimental investigation.

The lymphatic channels of the lung are derived from the right and left thoracic ducts of the embryo and grow to the lungs along the trachea and bronchi. Upon entering the lung at the hilus, they grow peripherally in relation to the pulmonary blood vessels and bronchi. The greatest amount of lymphatics develop along the pulmonary veins with the result that there is a profusity of lymphatics in the perilobular position. These channels reach the pleura and the pleural plexus is developed very early, with the result that the lobule is outlined very early. Growth of channels along the pulmonary artery and bronchi proceeds more slowly. Anastomoses are seen early between lymphatics at the periphery and core of the lobule. No lymphatics are seen distal to the alveolar ducts. In the pig, at least, the thoracic duct supplies lymphatics to the entire left lung and to the inferior portion of the right lung.

As a result of these developmental observations and of repeated examinations of the adult lung the knowledge of the morphology of the adult lymphatics is established. They are profuse in the mammalian lung and are found in four chief locations: Perilobularly (perivenous lymphatics); periarterial; peribronchial; and pleural. By this arrangement the lobule of the lung is surrounded by a profuse plexus of perivenous lymphatics and contains a core of lymphatic vessels in relationship to the pulmonary artery and bronchi. In addition, the lymphatics of the lung are divided into a superficial (pleural) and a deep set (parenchyma of the lung) by a large number of valves which prevent the flow of lymph from superficial to deep networks. Although these channels are described as located in four principal locations, they are united by numerous anastomotic vessels which in effect create a single system of anastomosing lymphatic vessels in the lung. There are no lymphatic vessels distal to the alveolar duct.

Superficial and deep lymphatics unite at the hilus of the lung. They are continued as peribronchial, periarterial, and perivenous lymphatics. There are numerous anastomoses between these networks. The efferent lymphatic vessels pass to the tracheobronchial lymph nodes which lie near the trachea and bronchi. With some reservation, the lymph from the right lung may be accepted as entering the venous system through the right lymphatic duct and that from the left through the thoracic duct.

Any opinion on the physiology of these pulmonary lymphatics is not on firm basis. One function of the lymphatics of the lung is the removal of colloidal particles foreign to the lung. The rate of removal of these substances is relatively rapid, this rate being dependent on the respiratory excursion of the lung. It is proportional to the rate of respiration and its depth. Crystalloids are also removed by lung lymphatics.

Lymph is formed in the lung, a statement shown to be significant. The flow of this lymph in the lung is dependent in large extent on the respiratory excursion of the lung. Anoxia increases the flow of lymph.

PROBLEMS REMAINING IN PULMONARY LYMPHATICS

Fortunately, problems remaining in pulmonary lymphatics are not so numerous as those in pleural absorption. They are centered chiefly around the physiology of these channels.

The source of the pulmonary lymphatics should be studied in the human, and the correlation of developmental pattern and adult drainage should be attempted in the same animal. In this way the adult drainage of the human lung may be better evaluated.

Although accepted that there are no lymphatic channels distal to the alveolar ducts, this portion of the pulmonary lymphatic system should be further investigated. This becomes apparent when it is shown that intratracheal colloidal dyes are seen in the pulmonary lymphatics. The pathway from alveolus to pulmonary lymphatics should be determined. In so doing, the problem of absorption from the lung will be clarified.

The source of the lymph of the lung is also deserving of further investigation. Although we now know that lymph is formed in the lung, it has not definitely been proved as origionating from the pulmonary circulation.

The factors which control the formation and flow of lymph in the lung require clarification.

The composition and flow of lymph from the lung areuin need of definition.

The transmission of bacteria within the lung lymphatics and the role of the lymphatics in pathogenesis of bacterial infections is a pathological study, but fits in well with investigation of the function of pulmonary lymphatics.

THE CARDIAC LYMPHATICS

The lymphatic system of the heart has been far overshadowed by almost all other phases of the anatomy and physiology of this organ.

That this is so is quite understandable. The lymphatic system here, as elsewhere, performs a function which is not understood and one which may not even be vital to the integrity of the organ. In the hope that a pattern for future reference may be established, the present knowledge of cardiac knowledge will be reviewed and evaluated in an attempt to establish better understanding of the lymphatic system of this organ.

DEVELOPMENT OF THE CARDIAC LYMPHATICS

Here, as in the lung, it seems advisable that developmental processes which lead to the adult form should be reviewed. In general, this topic has not recieved much emphasis. However, for a comprehensive picture of the cardiac lymphatics this should be understood.

To return momentarily to Cunningham's (1916) paper on the development of the lung lymphatics, his findings on the relationships of the right lymphatic duct will be considered. He states that the right lymphatic duct gives off a large branch to the heart, which branch passes along the vena cava to reach that organ. After reaching the base of the heart, this vessel passes around the bulbus to reach the anterior surface. Here it divides to form the primitive pericardial plexus. Cunningham makes no further remarks about this vessel, but states that other branches from the thoracic duct also pass to the heart. In view of the fact that the heart migrates caudad to such a point that its lymphatic channels are lost in the maze around the tracheal bifuraction and root of the right lung, it is impossible to make predictions as to the direction of drainage.

Because he felt that extensive lymphatic injections into the adult heart were impossible due to valves, Cash (1917) first approached the understanding of the lymphatic system of the heart from the developmental viewpoint. The injection method provided most of his preparations. Lymphatics of the heart (embryo pig) were fount to origionate from the right lymphatic duct and from the tracheal plexus, the greater number of channels arising from the right duct. The vessel from this duct was found to be joined by a smaller vessel from the tracheal plexus. These vessels pass together posteriorly under the pulmonary artery, lying between it and the left auricle to the auriculo-ventricular groove. Here, on the anterior surface of the heart, they form a plexus which gives rise to two main branches. These in turn divide to form the pericardial plexus, which covers the entire heart. After the pericardial plexus is formed, vessels invade the myocardium at a size of 150 mm. The myocardial plexus becomes less dense as deeper parts of the myocardium are reached. Cash finds no evidence of a sub-endocardial lymphatic plexus and believes that such has been mistaken for the injected bundle of His. The chief development of lymphatics occurs around the larger blood vessels.

In his general study of the development of the valves of the human lymphatic and blood vascular systems, Kampmeier (1928) did not find that the right lymphatic duct contributed to the developing lymphatics of the heart. He found the primary lymphatic vessel to the heart to origionate from the thoracic duct. This channel passes between the pulmonary artery and aorta, then ventral to the latter and along the coronary artery. The other vessel to the heart was found to be a derivative of the pretracheal lymphatic plexus. It was seen to pass behind and to the left of the pulmonary artery, then along the left coronary artery. Kampmeier believes that these channels are retained as the adult efferents. During the third month a net of growing vessels from these primary channels was seen to cover the entire heart. That over the auricles was seen to be less complete than over the ventricles. He agrees with Cash in the method of formation of the myocardial plexus, but makes no statement as to the subendocardial lymphatics.

Valves were first seen by Kampmeier at the end of the third month, being present in the primitive pericardial plexus. Most valves at this stage were seen along the larger cardiac vessels. Subsequently valves spring up in the myocardial plexus but in smaller numbers. In the fetus, more valves were found on the anterior than on the diaphragmatic surface. With few exceptions, valves occured only in the ventricular portion and none were seen deep in the myocardium.

In review of the above findings, it is seen that controversy exists concerning the right lymphatic duct as a source of cardiac lymphatics. Kampmeier does not agree that the right duct is a source, but states that the pretracheal plexus gives some lymphatics to the heart. This plexus, according to Cunningham, arises chiefly from the thoracic duct. There are two possible reasons for the source of controversy. First, different methods were used. Secondly, different animals were studied. As a result, it is not even known that the two are comparable and the findings of Kampmeier may be accepted as true for the human and those of Gash as true for the pig.

Cash and Kampmeier agree that the myocardial plexus is derived from the pericardial and that this plexus is complete before the myocardial is developed. This finding may be accepted as true. In addition, the conclusion that the ventricle is more profusely supplied is justified since it is well substantiated. The observation that no subendocardial lymphatics develop should be held in doubt, since adult studies show such a plexus to be present. Cash was unable to inject the cardiac lymphatics in embryos over 65 mm and it is possible that the subendocardial lymphatics may be a later development. Valves have been proven to develop quite early, those of the pericardial plexus appearing first.

THE ANATOMY OF THE CARDIAC LYMPHATICS

The first recorded observation of these lymphatics is that of Rudbeck (1653). He dissected a few subepicardial lymphatics of the dog and found that they terminated in some small mediastinal lymph nodes.

After the discovery by Fohmann (1833) that lymphatics could be injected by the indirect or puncture method, the investigation of the lymphatic channels was made much simpler and more accurate. A student of his, Lauth (1830), first used this method to investigate the structure and presence of the subendocardial lymphatics. He injected mercury indirectly into the lymphatics of the horse heart and found a superficial plexus of large anastomosing vessels in the epicardium. A deep plexus of smaller vessels closely applied to myocardium were also seen. He noted no communication between the plexuses. He asserted that the deep vessels lie parallel to the muscle fibers and were united by other vessels lying at right angles to the muscle fibers.

Gurlt (1844) reported the presence of large subepicardial lymphatics in the horse and Leyh (1859), who also studied the lymphatics of the horse, pointed out the presence of deep lymphatics in the myocardium. Teichmann (1861), using colored starch by indirect injection of lymphatic channels, noted only the presence of subepicardial lymphatics and did not describe them.

Two years later, His (1863) described subepicardial lymphatics lying directly on the myocardium and which were interconnected. He confirmed the lymphatics of the myocardium described by Leyh. Luschka (1863) also reported this deep plexus of the myocardium. He found that these vessels passed into subepicardial lymphatics which were located in the longitudinal sulci on the vortex of the heart. Eberth and Belajeff (1866), in a study of both human and other mammalian hearts, substantiated these findings in general but found a less dense plexus than that described by Luschka. Subendocardial lymphatic plexuses were claimed by these workers, who state that there is no noticeable difference between epicardial and endocardial lymphatics. Their subendocardial lymphatic plexuses were described as extending into the ventricular and semilunar valves. They injected blood vessels directly with colored solutions to differentiate them from lymphatics.

Quite a different school of thought on cardiac lymphatics was introduced by Henle (1868). He concluded that intermuscular fissures and spaces convey the cardiac lymph, on what basis cannot be determined at this time. However, Schweigger-Seidel (1871) also likened the heart muscle to a "lymph sponge". In the same year, Wedl (1871) confirmed the former findings of closed lymphatic channels on observations of the epicardium. Skvartzoff (1874), by indirect injection, found the myocardium to contain endothelial lined channels emptying into the subepicardial plexus. He was not successful in outlining subendocardial lymphatics. By the same method of study, Skowrzow (1874) described unlined lymph spaces which emptied directly into the subepicardial lymphatics and stated that subpicardial lymphatics were connected with the pericardial cavity by lymph spaces which pierce the epicardium. Bizzozero and Salvioli (1878) confirmed this. Salvioli alone (1878), using the indirect injection method was unable to inject lymph spaces and denied their existence.

Sappey (1885) again found and described an extensive subendocardial plexus which was united to the subepicardial lymphatics by vessels which passed between the muscle bundles of the myocardium. By direct mercury injection he found these vessels macroscopically visible in the heart of the horse and the calf and found them to cover completely the walls of the cavities. These vessels formed a loose meshed network. Bianchi (1886), returning to the indirect method, was unable to demonstrate lymphatic channels and returned to the idea of the lymph spønge.

The first physiological method used was that of Albrecht (1887), who injected colored substances into the myocardium of the living animal allowing the dye to be disseminated by the contractions of the heart alone. He reached the conclusion that a widespread endothelial lined lymph capillary system is present in the heart. Capillaries were seen which lay at right angles to the long axis of the muscle fibers and surrounded each individual fiber. Masini (1887) and Ranvier (1889), using methods not described, returned to the idea of the lymph sponge.

In an attempt to resolve the controversy between lymph channels and lymph spaces, Nystrom (1897) employed the indirect injection, modified Golgi impregnation, and uninjected microscopic sections. He reached the conclusion that both lined and unlined lymph spaces were present. He inferred, although he demonstrated none, that open communications existed between the two systems. He also briefly described subepicardial and subendocardial lymphatics and likened them to those described by Sappey.

Bock (1905), whose findings are generally accepted today, performed the most exhaustive study of the cardiac lymphatics to that date. He used indirect injection of lymphatics while perfusing the blood vessels with different colored solutions after blood was removed. Berlin blue was then injected under heavy pressure into the myocardium to inject lymphatics. The injected areas were then removed and sectioned. His description of lymphatics is, unfortunately, limited to the myocardium. Bock found a very profuse network of lymphatics lying adjacent to the blood vessels. Lymphatic vessels were seen to outnumber blood vessels and every muscle fiber had one or two lymphatic vessels following it. He found absolutely no connection between the two systems. In this way he met the criticism of confusion of blood and lymph channels on microscopic examination of the tissue.

Another differential examination was accomplished by Aagaard and Hall (1914), who directly injected the Purkinje system and attempted indirect injection of the subendocardial lymphatics. They stated that confusion between the Purkinje injections and the lymphatic injections does not exist, but that confusion between lymphatics and veins is possible. According to these authors, lymphatics of the endocardium lie superficial to the Purkinje fibers and, in part, parallel them. No communications between the two systems were found. In their injections of the Purkinje system with mercury, they claim to have duplicated the results of Sappey.

In addition to his study of the development of the cardiac lymphatics, Cash (1917) also attempted india ink injections into the myocardium of the live, anesthetized cat. He contended that the myocardial lymphatics formed a well woven plexus of vessels, the smallest of which were larger than blood capillaries. In accordance with his findings in the development of cardiac lymphatics, he found that vessels became fewer and smaller as the endocardium was approached. Cash was unable to inject any endocardial lymphatics and believes that all such claims are based on injections of the bundle of His.

Aagaard (1924) presented an extremely detailed investigation of cardiac lymphatics in man and some animals. His conclusions were based on the direct injection method. The myocardial plexus was said to consist of an interfascicular plexus of vessels of varying diameters. The smaller vessels paralleled, for the most part, the direction of the muscle fibers and were drained into the subepicardial lymphatics. His remarks on the subendocardial lymphatics were a repitition of his earlier findings with Hall.

Returning to the more physiological method of intracardiac injection into the living heart, Patek (1939) attempted to define the cardiac lymphatics of rabbits, cats, and dogs. Carbon suspensions were injected into the active heart and after sacrificing the animal, coronary blood vessels were injected directly with Ranvier's Prussian Blue solution in order to differentiate them. Gross and microscopic studies formed the basis for description. Patek found both lymph capillaries and collecting vessels in the epicardium, with collecting vessels following the course of the blood vessels. The myocardium is described as possessing a lymphatic capillary network uniform in density from subepicardium to subendocardium, with vessels lying in the interfascicular connective tissue and surrounding the muscle bundles. They accompany blood vessels and form an interconnecting plexus. The subendocardial lymphatic plexus was described as similar to the myocardial plexus, being formed entirely of capillaries. They lie in a single plane parallel to the surface of the endocardium and lie always superficial to the Purkinje system. The injected areas were in relationship to the longitudinal muscle columns of the ventricle. Lymphatic capillaries continuous with those of the papillary muscles were seen to accompany the chordae tendinae were seen to extend for a few millimeters. No lymphatics were found on the ventricular valves. In no instance were connections between the Purkinje system and the lymphatics observed. Kampmeier's findings on the valves of the lymphatics were substantiated.

In evaluating this literature, there is one obvious question which must first be answered. Are endothelial lined lymph vessels present in the heart? This question may definitely be answered in the affirmative, as there is abundant evidence for it in the literature reviewed. The question of unlined lymph spaces is more difficult to answer, for descriptions of the experimental method and results are lacking. It is to be noted, however, that the concept of the lymph space attracted no investigation after 1889 and this is apparently an idea entertained only by earlier investigators. Following only indirect injection into the non-functioning heart, it is quite easy to see how extravascular injected material could be construed as lying in unorganized lymph spaces and these spaces taken as the lymph pathways of the heart. Evidence to disprove the lymph space is scanty, but it is quite probable that the lymphatic system of the heart is composed solely of endothelial lined lymphatic vessels.

The presence of the subepicardial lymphatic plexus first described by Rudbeck has been well documented by every investigator who has sought to prove the presence of such a plexus. In this, as in other phases of cardiac lymphatics, the method most commonly used has been indirect injection of the lymphatic channels. If properly performed, there is no real objection to such a procedure, but a more satisfactory method is the injection of foreign material into the living heart under low pressure and allowing the filling of the lymphatics to proceed naturally. Direct injection of the blood vessels adds further accuracy. All of these methods have confirmed the presence of subepicardial lymphatics. This plexus is composed of collecting vessels and capillaries which communicate with the myocardial plexus. It is found in the connective tissue beneath the serous membrane surrounding the myocardium and the vessels lie very closely adjacent to muscle fibers in the deeper part of the plexus. Although these vessels communicate freely with the myocardial plexus, a large number of valves permit flow only into the superficial plexus. The fine channels of the subepicardial plexus unite to form the larger efferent lymphatics of the heart.

The myocardial plexus may also be described with some accuracy. Although earlier investigators were rather unspecific and expressed some doubt as to the profusity of such a plexus, later observers have established this as a rich plexus which surrounds the muscle bundles and fibers completely. The myocardial plexus may be accepted as formed of capillaries closely applied to muscle fibers and adjacent to blood vessels. They are located in the ventricles with few if any present in the auricles. These capillaries may be accepted as being in very free communication with the subepicardial and subendocardial lymphatic plexuses.

The bulk of evidence presented by those who have expressed opinion favors the presence of a subendocardial lymphatic plexus. Cash is the only one who has recorded his failure to observe such a plexus when it was sought. Patek and others, using methods identical to Cash's, have reported the presence of such a plexus and it would seem that the work of Cash could be re-checked for a better evaluation. His contention that the bundle of His has been confused with the subendocardial plexus is disproved by Aagaard and Hall and by Patek, who give descriptions of both. The subendocardial lymphatic plexus may be accepted as lying superficial to the Purkinje fibers and in part parallel to them, with no communication between them. The subendocardial plexus covers the entire interior of the heart and is composed of capillaries just beneath the endocardium. This system does not continue into the ventricular valves, but may be seen over the papillary muscle and proximal portion of the chordae tendinae.

GROSS LYMPHATIC DRAINAGE OF THE HEART

In contrast to the investigation of the lymphatic networks of the heart proper, the study of the efferent lymphatics of that organ and their nodes of termination has not recieved a great deal of attention. With one exception, all accounts are in the nature of a summary and the experimental method is not defined.

It is agreed that the heart proper is divided into areas which drain the right and left ventricles. Two main drainage trunks are described, named right and left by most authors according to the area drained.

Concerning the relationships of the right duct there has been some disagreement. Poirer, Cuneo, and Delamere (1903), after describing the origin of the right trunk in the right portion of the auriculo-ventricular groove, state that it lies on the anterior surface of the heart and ascends between the pulmonary artery and aorta. Bartels (1909) implies an anterior direction of flow as he finds that the right stem accompanies the right coronary artery to its origin and passes over the arch of the aorta. Of the standard anatomy texts, Morris agrees with this statement entirely. Gray, however, differs in that he describes the right lymphatic trunk as ascending in the posterior longitudinal sulcus, then running forward in the coronary sulcus and passing up behind the pulmonary artery. Piersol fails to distinguish between right and left lymphatic drainage trunks. He notes the formation of a large vessel in the anterior interventricular groove. On reaching the auriculo-ventricular groove, a vessel is described as bending to the left after its formation on the inferior surface of the heart. These two vessels then unite and the conjoined trunk passes upward along the posterior surface of the pulmonary artery, perforating the parietal pericardium in its passage. A similar independent trunk is described as arising on the right side of the right ventricle, passing parallel to the above trunk. Shore (1928), using indirect injection into fresh human hearts, substitutes the term "anterior" for right and states that this trunk lies on the anterior surface of the aorta. Patek (1939), in investigating the dog heart, concludes that vessels of several orders unite to form one large drainage channel which passes upward on the anterior surface of the pulmonary artery.

There exists similar confusion on the relationships of the left lymphatic efferent. Poirer, Cuneo, and Delamere (1903) and Gray are in agreement as to the relationships of this trunk, stating that the vessel ascends between the pulmonary artery and the left atrium. A posterior relationship to the pulmonary artery is thus suggested. Bartels (1909) modifies this description somewhat by finding that the left trunk proceeds backwards and outward below the pulmonary artery. It then passes under the aortic arch to an anterior position in the mediastinum. Morris merely states that the vessel passes behind the arch of the aorta to a destination which is presumed to be anterior. Shore (1928) finds that the efferent of the left ventricle takes a posterior course, passing behind the pulmonary artery.

The lymph nodes in which these cardiac efferent lymphatics terminate are located in the anterior mediastinal and (or) tracheobronchial group. Morris and Bartels (1909) find that the anterior mediastinal nodes are the point of termination of the cardiac lymphatics. Shore (1928) believes that only the anterior (right) lymph trunk terminates in this group of nodes. Poirer, Cuneo, and Delamere (1903), as well as Piersol, state that the lymphatic drainage of the heart is to the interbronchial nodes, with which Shore disagrees. Gray states nonspecifically that drainage is to the tracheobronchial nodes. Shore (1928) believes that the drainage of the left ventricle (posterior trunk) is directed into an extrapericardial node which is a member of the right superior tracheobronchial broup.

The situation here is quite analogous to that which was seen in the lung. In this case, however, the descriptions given are less specific. In addition, as a basis for subscribing to such beliefs, one can only site the fact that they are generally accepted and can be found in a textbook of anatomy, a weak basis at best.

Shore's investigation has been rather carefully done and is deserving of some attention. For such gross observation, there is no objection to very forceful injections into the myocardium. In addition, Shore used fresh human hearts in which no pathology was present. His conclusions may be accepted as the lymphatic drainage of the human heart. They are quoted directly:

> "The lymph drainage of the right ventricle is directed by an anterior lymph trunk to an extrapericardial group of lymph flands that lie in the superior mediastinum in relation to the left innominate vein. The lymph drainage of the left ventricle is directed by a posterior trunk to an extrapericardial gland which is a member of the right superior tracheobronchial group and lies in close relation to the superior vena cava, the aorta, and the right pulmonary artery."

REMOVAL OF FOREIGN SUBSTANCES BY CARDIAC LYMPHATICS

This phase, as such, has recieved no particular attention as concerns cardiac lymphatics. The mechanism of entry of the foreing particles (india ink, etc.) has not as yet been studied. It would seem, however, that the very rapid disappearance of carbon from the actively contracting heart would indicate that phagocytosis does not play an important part. It is only a matter of seconds until carbon first is seen in lymphatics after injection.

This section is hardly deserving of comment, but in passing it may be said that the problems of entry of foreign particles into the lymphatic system here are probably no different than in other regions. This is not a particularly vital phase of the cardiac lymphatic picture and the findings of such a study in the heart would probably indicate no different mechanism than in the diaphragm, for example, which is a much more convenient organ for study.

PHYSIOLOGIC CONSIDERATIONS OF CARDIAC LYMPHATICS

The physiology of the cardiac lymphatics has not been adequately determined. It would seem that the heart should be almost ideal for the study of lymph flow and the conditions affecting it, but it has apparently not been used as such.

The first recorded statements on the physiology of the cardiac lymphatics are those of Kampmeier (1928). After studying the valves of the lymphatics of the heart, he believes that the flow of lymph in the heart is from the depth of the heart to the exterior, thence to and through channels located in the furrows and into the efferent lymphatics of the heart. After filtering through one or more nodes, it then enters the blood stream. He postulates that during systole the muscular contraction forces lymph from the myocardial into the subepicardial plexus. This would be facilitated by the relaxation of the pericardium and the consequent augmentation of its lymph channels occuring when the ventricular diameter diminishes during the beat. He finds it evident that the extensiveness of the subepicardial lymphatic plexus is not the expression of any vigorous metabolism within the epicardium, but is of service as a lymph resorvior in close periodic sequence. Kampmeier also believes that the flow of lymph from the heart is relatively constant for both systole and diastole would tend to sustain it: Systole because of the shortening of the heart from apex to base; diastole because of the stretching of the pericardium during the filling of the heart. The factors tending to induce backward flow of lymph during the cardiac cycle include the sucking action of the lax myocardium. Kampmeier believes that the cardiac lymphatics function simply as a drainage system for products of cellular metabolism which are not taken up by blood vessels.

Patek (1939) feels that the physiology of the cardiac lymphatics has been well explained by Kampmeier. He feels that the very frequently seen lakes of dye seen in the subepicardial plexus indicate that these vessels do serve as a resorvoir. He adds that the venous pressure during diastole may force lymph through myocardial lymphatics by virtue of increased formation of lymph.

Drinker and Yoffey (1941), after cannulating efferent lymphatics of the heart, came to the conclusion that the flow of lymph from the heart was increased with increased activity.

Kampmeier's suggestions concerning the manner in which lymph is propelled in the heart, while quite feasable in most respects, are entirely lacking in experimental proof. His general opinion is quite shrewd.

There can be no doubt that lymph flow is directed from the myocardial and subendocardial plexuses into the subepicardial plexus. Patek and others have often observed lakes of injected material in the subepicardial plexus. In addition this plexus is far to large for the requirements of the connective tissue in which it lies. In addition, the only large lymphatic collecting vessels are seen on the external surface of the heart and these vessels have been shown to terminate in nodes.

It is logical to believe that systole should empty the cardiac lymphatics into the subepicardial plexus in the same way that blood is forced from the blood vessels of the myocardium. Arguments pro and con may be expressed on the effect of diastole on the volume of the subepicardial lymphatics and consequently on the fate of lymph in these vessels during that phase. A valuable conclusion cannot be reached at present.

That more lymph should be produced during increased functional activity is in full accord with present concepts of lymph formation.

THE TOTAL CONCEPT OF CARDIAC LYMPHATICS

Cardiac lymphatic channels are derived from the mediastinal lymphatic channels, notably the thoracic duct of the human embryo. These channels provide lymphatics also to the lungs, with the result that the lymphatic drainage of these organs is confluent. From these channels, vessels grow onto the surface of the heart and cover it in the form of a pericardial plexus. From this superficial plexus, lymphatics grow into the myocardium with the ventricles recieving the preponderance of vessels. Valves appear early which functionally separate myocardial and pericardial plexuses.

Endothelial lined lymphatic vessels are present in the mammalian heart. These vessels are found in plexiform arrangement in three principal locations: Subepicardial; myocardial; and subendocardial. The subepicardial plexus is a very rich network of vessels composed of capillaries and colecting vessels which covers the heart. This plexus is anatomically continuous with, but functionally separate from the myocardial plexus by virtue of a set of valves which permits flow only superficially into the subepicardial from the myocardial plexus. Vessels of the subepicardial plexus unite to form the large efferent lymphatic channels of the heart. The myocardial lymphatics are very profuse and are found in plexiform arrangement around muscle fibers and in association with the finer myocardial blood vessels. They are closely applied to each individual muscle fiber. On their deeper margin, the myocardial lymphatics communicate with the subendocardial lymphatics. The subendocardial plexus is found just beneath the endothelium lining the cavity of the heart. It lies chiefly in one plane and is composed of capillaries only. They lie superficial to the Purkinje system and are continuous with the myocardial plexus. Subendocardial lymphatic vessels are not found on the ventricular valves, but extend for short distances on the proximal portion of the chordae tendinae.

Grossly, the heart is divided into two drainage areas, right and left. For each of these areas, there is a rather large efferent lymphatic. The lymphatic efferent which drains the right ventricle passes cephalad, lying on the anterior surface of the aorta to terminate in nodes of the anterior mediastinum which are close to the left innominate vein. The efferent vessel of the left ventricle lies on the posterior surface of the pulmonary artery in its passage to nodes of the right tracheobronchial group in close relation to the superior vena cava.

Knowledge of the activity of these vessels is very deficient. Colloidal solutions, when injected into the living myocardium, are found in cardiac lymphatics within a matter of seconds. This is the only statement which can be made on this phase.

It is most probable that the direction of flow of lymph is into the subepicardial plexus from the deeper lymphatics of the myocardium. Systole may be accepted as emptying the myocardial lymphatics. The flow of lymph from the heart is increased with increased functional activity.

PROBLEMS REMAINING IN CARDIAC LYMPHATICS

Of the problems reamining in the field of cardiac lymphatics, the following are most important.

The developmental pattern of the cardiac lymphatics requires further study. The relative role of the right and left lymphatic ducts should be determined and and a study conducted on the same lines as suggested in the lung.

The response to foreign colloidal material injected into the myocardium should be given more careful study. The method of entry into the lymphatics here is not known, but is probably no different here than in other sites.

The fate of intrapericardially injected colloids has not been determined. This is a compound problem of the response of the pericardial mesothelium and absorption from the pericardial cavity.

The function and flow of lymph in the heart is deserving of investigation.

THE DIAPHRAGMATIC LYMPHATICS

Investigations of the absorption of particulate matter from the peritoneal cavity have focused attention on the importance of the diaphragmatic lymphatics. In addition, the frequency of abdominal disease complicating diseasees of the lungs has caused much speculation as to the circulation of lymph in this muscular organ. In attempting the definition of the structure and function of these lymphatics, peritoneal absorption will be discussed only as it applies to the demonstration of diaphragmatic lymphatics.

DEVELOPMENT OF THE DIAPHRAGMATIC LYMPHATICS

There is no complete report in the literature on the development of these lymphatic channels.

McCallum (1903), in his report on the absorption of granular material from the peritoneal cavity of dogs, stresses the desirability of an understanding of this phase of the diaphragmatic lymphatics. He states that it was found impossible to inject the lymphatics of the diaphragm through the thoracic duct of the embryo pig. McCallum feels that the apparent reason for this was the presence of intervening lymph nodes. The earliest stage at which an injection could be obtained by direct puncture was at a length of 40 mm. By staining the diaphragm in toto with silver nitrate, he found it possible to demonstrate endothelial lined lymphatics in the pig of 35 mm. Before this stage, the peritoneal cavity is fully formed and separated from the thoracic cavity by the diaphragm and McCallum proposes that lymphatics may grow into the diaphragm from its margins and that the intimate relationship to the peritoneal cavity be secondarily established.

THE ANATOMY OF THE DIAPHRAGMATIC LYMPHATICS

Diaphragmatic lymphatic vessels were probably first observed by Rudbeck (1653). Other early investigators, including Mascagni (1787) and Nuck (1692), also saw these vessels but their descriptions are not available.

McCallum (1903) found that the diaphragm was very active in the removal of granular material from the peritoneum. This led him to the examination of the lymphatic vessels in the course of tracing this material. Subpleural and subperitoneal plexuses were seen to be connected by a rather dense network of intermuscular lymphatic capillaries. He noticed a difference, however, between the surface lymphatics of the pleural and peritoneal surfaces. On the peritoneal surface, vessels were observed running parallel to muscle fibers and were placed more superficially (in some cases projecting beyond muscle fibers) than those on the pleural surface. These vessels were connected by capillaries which were superficial and transverse to muscle fibers. The superficial vessels (named lacunae by McCallum) were separated from the peritoneum only by isolated strands of reticular tissue, making the closest possible communication between peritoneum and lymphatic endothelium on the abdominal surface of the diaphragm. Lymphatics on the pleural surface were not so intimately related to the diaphragmatic pleura. Larger channels were seen to lie in a semicircular manner around the tendinomuscular junction and from these, channels were seen to pass anteriorly and posteriorly to the esophageal hiatus.

The picture of subpleural and subperitoneal plexuses united by intermuscular capillaries has been generally accepted by the anatomy texts and is so described there in rather brief form. Rouviere (1938) believes that larger collecting vessels are formed in the center of the diaphragm from the plexuses on the pleural and peritoneal surfaces. Other than the above, there are no descriptions available on the diaphragmatic lymphatics.

It is quite discouraging to attempt the review of the anatomy of the diaphragmatic lymphatics. With the exception of McCallum, there are no adequate descriptions. It is true that present descriptions are probably correct, but they are incomplete. This becomes especially true when the different response of the pleural and peritoneal surfaces is considered. It is possible that the activity of the peritoneal surface is due to the anatomical arrangement alone.

McCallum's observations are the kind which are now needed. His definition is very fine and exact, so much so that a single study of this type should be repeated before drawing any final conclusions. On his explanation, if true, the great activity of the peritoneum and the inertness of the pleura may be partially explained.

The formation of the larger collecting trunks is not entirely clear, but would not be expected to influence the relative efficiency of the two surfaces.

GROSS LYMPHATIC DRAINAGE OF THE DIAPHRAGM

As has been suggested, a knowledge of the lymphatic drainage of the diaphragm becomes essential to the understanding of the lymphatic drainage of the peritoneal cavity. The topic will be considered here, however, because the full examination of its functional relationship to the pleural cavity and thorax is not complete.

The present gross anatomy texts give a somewhat inadequate account of this pattern. Gray is representative and cites the following arrangement: The anterior set of diaphragmatic nodes are situated just behind the xiphoid process of the sternum and recieve efferent channels which pass through the diaphragm from the convex surface of the liver. Other anterior nodes are located at the junction of the seventh rib with its costal cartilage and drain the anterior portions of the diaphragm. The middle set of nodes are said to be situated close to the point where the phrenic nerve enters the diaphragm on either side. The afferent channels of these nodes drain the middle portion of the diaphragm and possess efferent channels which pass to the posterior mediastinal nodes. The posterior set of nodes consists of a few nodes situated on the back of the crura of the diaphragm and are connected on the one hand with the lumbar nodes and the other with the posterior mediastinal nodes.

Higgins and Graham (1929), following the intraperitoneal injection of hydrokollag into living normal dogs, established the most complete description of the efferent lymphatics of the diaphragm yet given. These channels are as follows:
The sternal route is by far the most important, carrying about 80% of the ink injected intraperitoneally. By this route, material passes through the diaphragm into the lymphatic plexus of vessels which lies posterior to the sternum. The further course of this route consists of passage into retrosternal channels which run parallel to the internal mammary vessels.
A pulmonary route was described as comprised by a group of vessels, generally more conspicuous on the left than on the right, which, after leaving the diaphragm, course forward along the pericardium parallel to the esophagus and the vagus nerves to terminate in the bronchial lymph nodes lying dorsal to the base of the lung. A lymph vessel also courses forward over the diaphragm and then runs parallel to the phrenic nerve.
It empties directly into the paratracheal nodes. Lymph from the main channel described above passes also to the paratracheal nodes and thence to the venous system, either by way of

vessels entering the right lymphatic duct or the thoracic duct just before it empties into the venous confluence. A third route consisted of channels which pass over the vault of the diaphragm and then cephalad on the posterior wall of the thorax to unite with the thoracic duct. The two posterior routes, the fourth and fifth routes described, lead from the peritoneum upward through the diaphragm and then backward and downward again through the diaphragm into the peritoneal cavity or into the retroperitoneal spaces dorsal to the two diaphragmatic crura. Of the two, the latter course is the more constant. The lymphatic channels in the lower right and lower left margins of the diaphragm carry the lymph backward, dorsal to the peritoneum, to a large lymph node which lies in the retroperitoneal space just above the kidney. From this node, channels pass into the cysterna chyli. The fifth group of channels courses over the dorsal half of the diaphragm and converges near the ventral margin of the aorta. These channels then go directly through the diaphragm, enter the peritoneal cavity and may be traced directly to a lymph node in the mesentery of the spleen. This node also is connected by small vessels to the cysterna chyli.

Lemon and Higgins (1929) confirmed these routes exactly, again using dogs as the animal upon which the description was based. Their experimental method was the same.

Higgins and Mills (1929), in attempting to find pathways from the lung into the abdominal cavity, failed to find any such functional pathway. Using dogs, they did, however, find the same abdominal routes as Higgins and Graham. They state that the vessels passing to the node in the mesentery of the spleen pass along the ventral surface of the stomach to reach this node. Lateral and posterior aspects of the diaphragm were found to drain into the retroperitoneal nodes.

Rouviere (1938) divides the collecting vessels of the diaphragm into subperitoneal, perforating, and subpleural collecting trunks. He is of the opinion that subperitoneal vessels may either remain below the diaphragm and terminate in abdominal nodes or pass through the diaphragm and terminate in supradiaphragmatic nodes. Subpleural vessels accompany the inferior phrenic blood vessels and terminate in pre-esophageal and juxta-aortic nodes. Perforating vessels are very numerous andmost enter a principal collecting trunk. Others terminate in nodes which lie near the inferior vena cava and the phrenic nerve. Rouviere also states that anterior portions of the diaphragm drain into sternal nodes, while posterior regions drain into intra-abdominal nodes.

The experimental results cited do not contradict the conventional picture, but rather add to it. The observations of Higgins and Graham are well founded and repeated identical patterns were used as the basis of conclusion. The fact that they are supported in their entirety by Lemon and Higgins and the abdominal routes by Higgins and Mills lends considerable credence. Whether this is the pattern of the human diaphragm is quite another question. The fact that it agrees in principle with the human pattern is quite suggestive, and these routes may be accepted with reservation as being present in the human. Rouviere's pattern supports the above.

PHYSIOLOGIC CONSIDERATIONS OF THE DIAPHRAGMATIC LYMPHATICS

The physiology of the diaphragmatic lymphatics is not at all defined. As in other phases of diaphragmatic lymphatics, present knowledge has followed intraperitoneal injection largely.

McCallum (1903) was immediately struck by the rapid appearance of carbon particles in the "phagocytic leukocytes" which abounded in the peritoneal exudate. He observed these cells to pass through the walls of the lacunae which he describes. He also found that the peritoneal mesothelium over the lacunae could become phagocytic and act in the same capacity as the leukocytes. The author felt that this process played some part in the removal of peritoneal exudates. He also found that dead animals under artifical respiration were capable of showing filled diaphragmatic lymphatics after intraperitoneal injection of india ink. Covering the diaphragmatic peritoneum with 10% formalin and other chemicals designed to kill the mesothelial cells did not appreciably alter the rate of absorption, McCallum reports that he found either phagocytosis or no phagocytosis, but never the two in the same specimen. He was of the opinion that the foreign particles passed into his lacunae through the intercellular substance of the peritoneum and lymphatic endothelium, but did not believe that stomata were present. Alternating size and shape of the lacunae were held responsible for the entry of carbon into the lymphatics.

Florey (1927) came to the conclusion that pressure alone was responsible for the filling of the diaphragmatic lymphatics from the peritoneal surface. Intraperitoneal carbon injections were used, followed by removal of the thorax. He could then observe the filling of the lymphatics of the rat, rabbit and guinea pig. Florey found that these vessels were very readily observed and that they pulsated independently at a rate of 15 pulsations per minute. The peritoneal mesothelial cells were outlined by dye particles and he quotes Kolosow (1893) as stating that the endothelium of the lymph capillaries of the diaphragm is similarly outlined. Phagocytosis was noted to occur long after peritoneal injection. A very interesting finding by Florey is that colloids escape from the diaphragmatic lymphatics at a pressure of 2.5 cm of water, and that these colloids are seen only to ooze from the peritoneal (not the pleural) surface of the diaphragm.

Lemon and Higgins (1929) also examined the part of the diaphragmatic lymphatics in the transport of intraperitoneally injected colloidal material. They noted that carbon appeared in the thoracic lymphatics of normal dogs in 3 to 5 minutes after injection and that channels on the right side of the diaphragm filled more efficiently than on the left. After unilateral section of the phrenic nerve, absorption occurred at a slower rate, but definitely did occur. Carbon was found in thoracic lymphatics 10 to 15 minutes after injection. Lemon and Higgins also believed that flow of lymph in the diaphragm was toward the pleural cavity and that passage of particles from pleural to peritoneal cavity does not occur.

Higgins and Graham confirmed this opinion. Their intrapleural injections failed to reveal the diaphragmatic pleura as an absorbing surface. This is confirmatory to observations on pleural absorption.

Allen and Vogt (1939) rather dogmatically state that the entire process of entry into diaphragmatic lymphatics is dependent upon changes in size and shape of the diaphragmatic lymphatics. They found that the time of appearance of carbon in intrathoracic lymphatics was closely correlated with respiratory rate, appearing sooner with rapid respirations. If carbon suspensions were placed on pieces of excised diaphragm and these pieces alternately stretched and relaxed, carbon entered lymphatics and flowed through the channels. They believe that entry is the result of dilatation of the channels and movement the result of compression during contraction of the diaphragm.

There are several phases of the activity of the diaphragmatic lymphatics which must now be evaluated. Although not discussed in order above, they will here be separated for the sake of clarity.

The manner of entrance of foreign particles into the diaphragmatic lymphatics presents much the same problem which was faced in the pleural cavity. In the diaphragm, the greater amount of evidence supports the view that mechanical factors alone are responsible for the entry of colloidal particles into the lymphatics. McCallum's observation that killing of the peritoneal mesothelial cells does not alter the absorption is certainly significant on this score. He believed that mechanical factors alone could be responsible, as did Florey. Allen and Vogt seem to have shown definitely that mechanical factors alone may be responsible. On the other hand, McCallum and others have shown that phagocytosis does occur and that dye laden cells are found in lymphatics. The relative role is not clear, but mechanical factors have the greater support.

Florey and McCallum each have seen that peritoneal mesothelial cells are outlined by carbon particles after intraperitoneal injection, which suggests that the site of entry is intercellular. This is not a fact generally accepted and it must be substantiated more before accepting this site of entry.

With mechanical factors held to be responsible for the entry of carbon particles into the lymphatics, variation in activity of the diaphragm should produce difference in efficiency of absorption. This has been proven true by Lemon and Higgins and by Allen and Vogt. It seems that the factor controlling the efficiency of the diaphragm in absorption and movement of lymph through its channels is the activity of that structure.

Perhaps the most intriguing feature of the activity of the diaphragmatic lymphatics is the difference in the response of the mesothelium of the thoracic and abdominal surfaces. On the other hand, there is the very active peritoneum and on the other the inert pleura. Both are of the same origin and form, yet there exists this definite difference. It cannot be explained at present.

Florey's observation that lymph flows from the peritoneal and not the pleural surface when injections into the diaphragm are made is allied to this problem. A thorough anatomical study is indicated, for no conclusion can be reached.

It has been established that lymph flow in the diaphragm is directed toward the thorax and not in the opposite direction. No conclusion can be reached as to why this should be so. It may be that lymph from the superficial plexuses passes into collecting vessels in the center of the diaphragm and that these vessels pass only toward the confluence of lymphatics. In all probability the answer lies deeper than this and a good definition of the anatomy of these vessels may give the answer which is sought.

THE TOTAL CONCEPT OF DIAPHRAGMATIC LYMPHATICS

The concept of the diaphragmatic lymphatics which may be formed leaves much to be desired. It is terribly incomplete. In some phases the technical difficulties attending such studies are responsible, while in others the only requirement is a more exhaustive investigation.

The development of the lymphatics of the diaphragm has not recieved adequate attention. No conclusions can be drawn.

The description of the lymphatic vessels of the diaphragm must consist only of the brief statement that this network is composed of plexuses of lymphatic capillaries which underlie the serous membranes on the pleural and peritoneal surfaces and which are connected by intermuscular lymphatics. The formation of the efferent channels is not clear. It is probable that there is some fine difference in the anatomical arrangement and relationships of the lymphatic vessels on the two surfaces.

The gross pattern of lymphatic drainage of the diaphragm is formed of channels which carry lymph into the abdomen and of others which carry lymph into the thorax. Of the cephalic routes, the sternal consists of channels which pass from the anterior portion of the diaphragm into vessels which lie posterior to the sternum. These vessels terminate in the sternal nodes. A second route in this direction consists of channels which course forward along the esophagus and vagus nerves to terminate in the bronchial nodes lying dorsal to the base of the lung. The third route is made up of vessels which arch over the diaphragm and run forward on the dorsal wall of the thorax to unite with the thoracic duct. The abdominal routes consist first of channels which pass through the diaphragm and arch over its vault to pass again into the abdominal cavity. By these channels lymph is carried into the nodes in the peritoneal cavity or into retroperitoneal lymph spaces dorsal to the two diaphragmatic crura. One of these channels terminates in a node which lies in the retroperitoneal space just above the kidney, while the other ends in a lymph node in the mesentery of the spleen. Both of these nodes of termination are connected with the cysterna chyli by efferent vessels.

Studies on the flow of lymph in the diaphragm, as based on the activity of the lymphatics of this organ in absorbing colloidal dyes, indicate the following facts. Lymph flow in the diaphragm is only toward the pleural surface, with the result that foreign particles pass from abdominal to thoracic cavity and not in the reverse direction. There is a marked difference in the absorptive capacity of the pleural and peritoneal surfaces, the former inert and the latter very active. Mechanical factors alone may be responsible for the entry of colloidal material into these lymphatics, though phagocytosis by peritoneal mesothelial cells can and does occur, with dye laden macrophages observed to pass into lymphatic channels. The activity of the diaphragm influences the efficiency of this absorptive process through the peritoneal surface, the paralyzed diaphragm absorbing more slowly than the actively functioning organ.

PROBLEMS REMAINING IN DIAPHRAGMATIC LYMPHATICS

The situation here closely resembles that encountered in pleural absorption. Although a limited concept has been formed, the most important problems remain unanswered. These will be discussed briefly.

The development of the diaphragmatic lymphatics should be investigated. The value of an understanding of this phase becomes very apparent when the present status of the anatomy of these vessels is considered.

The adult anatomy of the diaphragmatic is very deficiently understood. An exact knowledge of the relations of these vessels to surrounding tissues is required, for reasons discussed above.

Although a very good description of the gross picture of diaphragmatic lymphatic efferents has been presented, the clarification of the abdominal routes as they exist in man is desirable.

Closely associated with the problems above is the direction of lymph flow in the diaphragm. This cannot be explained at present and is of considerable significance. It is probable that this will be found on an anatomical basis.

The difference in the absorptive capacity of the two mesothelial layers covering the surface of the diaphragm is also closely associated with the problems above. This is quite a fundamental problem and may possibly be explained on an anatomic basis, but the probability is that it is much deeper.

Although two possible methods of entry of colloidal particles into the diaphragmatic lymphatics are known, the relative role and significance is not clear. In addition, the site of entry into lymphatics and through peritoneum is in need of clarification.

SUMMARY AND CONCLUSIONS

The conclusions presented are merely brief summaries of more complete descriptions which may be found in the text under appropriate title.

ABSORPTION FROM THE PLEURAL CAVITY

The development of lymphatic channels intimately associated with pleural absorption has not been adequately studied, nor have the microscopic lymphatics associated with the pleural cavity of the adult.

In its reaction to and removal of foreign substances from the thoracic cavity, the pleural mesothelium is very active. Crystalloids follow osmotic patterns in their absorption. Pleural mesothelium is of great functional capabilities in its response to colloidal material, such as carbon particles. These cells possess phagocytic properties in situ and produce an unknown number of wandering macrophages. Mediastinal pleura is most active in its response to dye particles, followed by costal pleura, with the visceral and diaphragmatic pleura inert. The relative role of blood stream and lymphatics in the removal of dye particles has not been determined.

Lymphatic efferents of the pleural cavity consist of intercostal lymphatic vessels. Those on the posterior wall drain to the vertebral nodes and those on the anterior wall to the sternal nodes. Channels draining into the upper abdomen are present in dogs, but have not been well substantiated in man.

The relative roles of respiratory movement and phagocytosis in filling of the lymphatics associated with the pleural cavity have not been defined. Both have been shown to be responsible. Pneumothorax decreases the efficiency of pleural absorption, with hyperpnea increasing efficiency. Other factors have not been adequately studied.

The concept of pleural absorption may be briefly stated as follows: Foreign colloidal material injected intrapleurally is spread diffusely over all pleural surfaces and enters lymphatics by mechanical or phagocytic processes. Exudation is pronounced very early, with polymorphonuclear neutrophilic leukocytes predominating which are phagocytic. In a matter of hours, phagocytic mononuclear cells predominate in the exudate. At a very early stage, the differential response of the pleural mesothelium may be observed. Phagocytosis in situ by these cells is observed as is the production of wandering macrophages. Large accumulations of carbon are seen on the mediastinal pleura. Mesothelial surfaces remain stained for long periods, with gradual removal of the dye containing cells.

Problems remaining in pleural absorption include the following: The method of entry of particles into lymphatics; the relative role of the blood stream and lymphatic system; the differential response of the pleural mesothelium; the manner in which respiration affects absorption; the influence of inflammation; the pathways of the mediastinum; the fine details of the structure of the lymphatics of mediastinal and costal pleurae.

THE PULMONARY LYMPHATICS

The lymphatic channels of the lung are derived from the primitive right and left thoracic ducts of the embryo. They pass to the lung along the trachea and bronchi. Upon entering the lung, they grow peripherally along blood vessels and bronchi, with greatest numbers found in association with the pulmonary vein. Pleural plexuses develop early from the perivenous channels. This results in the outlining of the lobule of the lung, with periarterial and peribronchial lymphatics lying in the core of the lobule.

Lymphatic channels in the adult lung are found in four principal locations: Pleural, perilobular (perivenous), periarterial, and peribronchial. Greatest numbers are found in the perilobular location. Anastomoses occur between these sets of lymphatics. Superficial (pleural) and deep lymphatics are functionally separated by valves which allow flow only into the superficial plexus. No lymphatics are found distal to the alveolar ducts.

Superficial and deep lymphatics unite at the hilus to form the efferent lymphatics of the lung. They pass to the tracheobronchial nodes. Efferents from these nodes carry lung lymph to the blood stream. The right lung lymph enters into the venous confluence on the right, while left lung lymph enters on the left.

The physiology of the pulmonary lymphatics is only incompletely understood. Lymph is formed in the lung. One function is the removal of foreign colloidal material. The flow of lymph in the lung is dependent on respiratory excursion to large extent. Anoxia increases the flow.

The concept of pulmonary lymphatics is formed from the above conclusions.

Problems remaining in pulmonary lymphatics include the following: The source of lung lymph; the pathway of dye particles in the distal portions of the respiratory tree; the factors which control formation and flow of lung lymph; the amount and composition of lymph formed in the lung.

THE CARDIAC LYMPHATICS

Cardiac lymphatics are derived from mediastinal lymphatic vessels of the embryo. Exact sources are in doubt. After covering the heart with a profuse pericardial plexus, these vessels grow into the myocardium to establish the myocardial plexus. Valves appear early which functionally separate these plexuses, flow being allowed only superficially.

Endothelial lined lymphatic vessels are found in the heart in three principal networks: Subepicardial, myocardial, and subendocardial. The subepicardial plexus is formed of capillaries and collecting vessels which unite to form the lymphatic efferents of the heart. The myocardial plexus is formed only of capillaries which are closely applied to muscle fibers. Subendocardial lymphatics lie superficial to the Purkinje fibers and are in communication with the myocardial lymphatics. They are not found on the ventricular valves, but extend for short distances on the proximal portion of the chordae tendinae. Auricles are poorly supplied in contrast to ventricles.

Grossly, the heart is divided into right and left drainage areas. The efferent draining the right ventricle passes cephalad on the anterior surfact of the aorta to terminate in anterior mediastinal nodes. The efferent of the left ventricle lies on the posterior surface of the pulmonary artery in its passage to nodes of the right tracheobronchial group.

Colloidal dyes injected into the myocardium are found in lymphatics in a very short time. The direction of flow of lymph in the heart is toward and into the subepicardial plexus. Systole empties the myocardial lymphatics. The flow of lymph is increased with increased functional activity.

The concept of cardiac lymphatics is formed from these conclusions.

Problems remaining in cardiac lymphatics include the following: The developmental pattern, that is the source of the cardiac lymphatics; the fate of intrapericardially injected colloidal dyes; the function and flow of lymph in the heart.

THE DIAPHRAGMATIC LYMPHATICS

The development of the lymphatics of the diaphragm has not been adequately studied.

The lymphatics of this organ consist of subpleural, subperitoneal, and collecting vessels.

Gross lymphatic efferents of the diaphragm pass into the thorax and abdomen. Routes carrying lymph cephalad include: The sternal route; a pulmonary route which carries lymph to bronchial nodes after passing along the esophagus; a route which passes to the thoracic duct after passage along the posterior wall of the thorax. Abdominal routes include: Channels which arch over the diaphragm to pass to a node at the upper pole of the kidney and to a node in the mesentery of the spleen.

Dye particles may enter the diaphragmatic by mechanical means or in phagocytic cells. Lymph flow in this organ is only toward the thorax, and particles do not pass from thoracic into abdominal cavity. The diaphragmatic pleura is inert in its response to colloidal dye particles, while they are rapidly absorbed through the peritoneal surface. The efficiency of the absorptive process on the peritoneal surface is dependent upon the activity of the diaphragm. Absorption occurs more slowly through the paralyzed diaphragm.

The concept of the diaphragmatic lymphatics is formed from the above conclusions.

Problems remaining in diaphragmatic lymphatics include the following: The development of these lymphatics; the finer adult anatomy of the diaphragmatic lymphatics; the direction of lymph flow and reasons thereof; the difference of absorptive capacity between pleural and peritoneal surfaces; the relative role of phagocytosis and mechanical factors in absorption via the diaphragm.

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