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RESEARCH ON LYMPH CIRCULATION IN HUNGARY

A Magyar Tudomány Tíz Éve
1945-1955 /Ten Years of
Science in Hungary 1945-1955,
1955, Budapest, Pages 213-222

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One of the most valuable chapters of lymph research is now being written in Hungary, following the line developed by Sandor Koranyi. By way of contrast, a negligible number of research projects were concerned with the physiology and pathology of the lymphatic system prior to Liberation. The earlier Hungarian technical literature in this field records smaller research projects by Buday, Genersich and Regeczy related to problems concerning the lymphatic system. In addition to these three researchers Koranyi and his pupil Roth postulated a brilliant theory of lymph circulation which still holds promise. However, these constitute the total of significant preliberation Hungarian literature in the field of lymph circulation.

The fact practically no Hungarian and very few foreign researchers were active in the field of the physiology and pathology of lymph circulation after the turn of the century is due in large part to the world-wide interpretation of the classical studies of Starling as implying that edema and fluid absorption could be satisfactorily explained without attributing a role to the lymphatic system in the pathological process.

As early as the 1930's the present author emphasized the fact that the solution of the many unsolved problems connected with edema is possible only through investigation of the lymphatic system. The studies conducted by the author and his associates, Doctors Mihaly Foldi and Gyorgy Szabo, have encompassed many years. This study, which originally was aimed at discovering the origin of edema, branched out to include investigation of lymph circulation and the importance of the latter not only in the origin of edema, but in the entire fluid balance of the body and in the functioning of the internal organs.

The sum total of the present conception of the conditions under which edema arises is derived from Starling. He was the first to point out the fact that two forces are opposed in the blood capillaries: one is the force which tends to force fluid from the capillary, which is due to blood pressure, and the other tends to reabsorb fluid which is in the tissue spaces, which is the reabsorbing power of proteins, or colloidal osmotic pressure. The establishment of this fact led to an attempt to explain the formation of an edema in the light of these forces. Krogh and his associates continued investigations along this line after Starling, and the present author also participated in this research 20 years ago. On this basis an edema results when the forces tending to express fluid from the capillaries are greater than those tending toward their reabsorption. This is the classical teaching of Starling and in its essence is still a generally accepted viewpoint. Upon careful reconsideration, however, it was realized that this explanation alone does not satisfactorily explain all types of edema. It is known, for example, that following the radical removal of the axillary lymphatic nodes in the course of surgical excision of mammary cancer an extreme edema may appear in the arm after a certain time, often without disturbance of blood circulation. Such cases cannot be explained on the basis of the above theory alone, because there has been no increase in capillary pressure, and no quantitative or qualitative change in the composition of protein composition. Thus it appears



that an edema may arise even without any pathological change in the factors taken into account in the Starling-type explanation, but when there is some sort of disruption of the lymph circulation. Another case in point is presented by edema accompanying heart disease. According to the old theory edema in decompensated heart disease patients was explained by an increase in filtration pressure and the fluid oozes into the interstitial spaces of connecting tissue. However, if the lymphatic system is unimpaired, it is not understood why the oozing fluid is not carried away by the lymph circulation. Thus at least 2 types of edema are not explained by the classical theory alone. Also, it is not understood why the fluid is not absorbed in inflammatory edema, where protein-containing fluid leaks from the blood vessels into the tissue as a result of an increase in capillary permeability, and why this fluid is not carried away by the lymph circulatory system.

The first problem investigated by the above research group was why edema occurs in thrombophlebitis (infection of the veins). This type of edema is in the class of common pathographies. According to the Starling theory, closure of an artery results in increased blood pressure in the capillaries, which in turn results in an increase in the escape of fluid. Here the question also arises, why the escaping fluid is not carried away by the lymphatic circulation. The matter is further complicated by the fact that it has been observed that tying off of the main vein, the vena cava inferior, does not always result in edema. This operation recently has been used as a therapeutic measure in edemic heart patients, and experience has shown that following this operation edema of the lower extremities not only does not increase, but often disappears. The French clinical specialist was the first to demonstrate that edema can be terminated in thrombophlebitic patients through the novocain narcotization of certain nerve trunks. At the request of the author, Imre Littmann and Pal Rubanyi studied this method and have obtained very good results.

The effect of novocaine, or sympathectomy (obliteration of certain nerves), cannot be explained by the Starling theory. The injection of novocaine has no effect on the conditions produced by closure of arteries. This is the reason why the research group thought the disruption must be due to the lymphatic ducts. Therefore, it was investigated whether spasms of the lymph ducts could take place, similar to arterial spasms. It must be noted that lymph ducts have their own innervation, and smooth muscle elements may be found in their walls upon histological examination.

In these investigations it was found that electrical stimulation of the same nerves which were narcotized with novocaine with a resultant therapeutic effect in thrombophlebitic edema, actually resulted in spasms of the lymph duct, or lymphangiospasmus.

On the basis of these investigations it was concluded that a contributing factor of thrombophlebitic edema is a reflex which causes spasmodic contraction of the lymph duct, preventing fluid from leaving the intersitium via the lymph duct.

Study of the phenomenon of lymphangiospasmus led to further investigation of the connection between the lymphatic system and the nervous system. It was found in the course of experiments that not all the fluid injected into a peripheral lymph duct reaches the main lymph duct, the ductus thoracicus, and thence into the blood system. It was found that part of the injected fluid enters the blood system by first passing through the walls of the lymph ducts, and part is absorbed into the blood system through the lymph nodes. Part of the fluid remains for a time in



the lymph ducts and in the lymph nodes. It was found that this phenomenon could be effected by Dibenamin, a drug which effects the nervous system. Experiments along this line led to the conclusion that contrary to the earlier theory, lymphatic circulation is not passive, but is regulated by the nervous system, similarly to the active nervous regulation of the blood circulation.

The edema of heart patients also was studied from the point of view of lymph circulation. In the latter 1880's Cohnheim expressed the opinion that edemic stasis is caused only by failure of the lymphatic system to carry away the increased amount of fluid in the interstitium. Volhard and Rouviere also have taken up this position in recent literature.

Because of the importance of this problem, and because of the contradictions appearing in the literature it appears necessary that an attempt be made here to clarify this problem in the light of several experiments.

Because the main lymph ducts empty into the venous system at the angulus venosus, it is possible that in decompensated heart patients the increased arterial pressure hinders the emptying of lymphatic ducts, and the stasis is transferred to the lymph ducts, also. It was demonstrated experimentally that if the pressure is increased in the large arteries, this pressure backs up to the ductus thoracicus. On the basis of these experiments it may be considered proved that an increase in arterial pressure causes edema only if the lymphatic circulation also is obstructed and that this is the reason for the difference detected between the requisites for a local increase in venous pressure and a general increase in pressure of cardiac origin.

The edema of kidney patients is equally important as the edema of cardiac patients. This problem also was investigated by the research group in the course of their research. It was found that the large efferent lymph ducts are greatly enlarged in animals made edemic by plasmapheresis, and cannulation of the ductus thoracicus showed the amount of lymph collected much greater than normal. Because the capacity of the lymph ducts is finite, if the amount of interstitial fluid exceeds this capacity the lymph ducts cannot carry away all the fluid and the fluid remaining in the tissue interstitial spaces forms an edema.

By way of a brief summary of the investigation of the research group in the field of the origin of edema it may be stated that the formation of an edema is impossible as long as the lymph ducts are capable of performing their function of conveying fluid. Edema results only when lymphatic circulation is deficient. Deficient lymphatic circulation may be caused by mechanical obstruction, anatomical irregularity, spasm of the lymph ducts, or increased venal pressure which hinders lymph removal. A dynamic deficiency also may occur if the peripheral production of fluid is so great that the lymphatic system cannot carry away all of the fluid. Although it still has not been verified, the possibility of peripheral absorption becoming deficient for some reason or other also must be allowed.

Following investigation of the role of lymphatic circulation in various types of edema the research group undertook investigation of the local influence of lymph circulation in the function of individual organs.



1. Kidneys

It is a generally known urological fact that closure, or experimental blocking of the ureter, the efferent urinary duct, causes no significant change in the kidney for a period of several weeks. According to the data of Babics and Renyi-Vamos the injection of various substances into the blood stream, such as inulin or indigocarmine, following tying off of the ureter resulted in the appearance of these substances in the tied-off renal cavity. Under similar conditions Jancso was able to demonstrate the presence of inulin in the cells of the uriniferous tubules by histochemical methods. According to Babics and Renyi-Vamos the continued functioning of the tied-off kidney is explained by the movement of the urine from the renal cavity into the renal tissue, from where it is gradually absorbed into the lymph ducts. In the light of this explanation there is no urinary stasis when the ureter is closed off. The flow of urine continues, with the lymph ducts carrying off the urine instead of its being passed through the ureter. This is the explanation for the fact that deterioration of a blocked kidney begins only after the lapse of a period of several weeks, and experience has shown that kidney blocking does not result in death, but in slow consumption.

If the lymphatic system has such an important role in the pathological conditions following ureteral closure the question arose as to what would happen if both the ureter and the efferent lymph ducts of the kidney were tied off.

It was established experimentally that tying off of both the ureter and the kidney's efferent lymph ducts was followed within 2 or 3 days by the most severe change, the death of the kidney.

The conclusions of Babics are important in this respect: if a condition of renal block by a kidney stone in a human is accompanied by inflammation of the renal peduncle, or pedunculitis, in which condition the lymph ducts passing through the renal peduncle are closed off, no attempt should be made at conservative treatment through removal of the kidney stone, but the entire kidney should be removed because according to his experience the kidney always is lost in such cases.

2. Liver

The investigation in connection with the liver was done with the cooperation of Babics and Renyi-Vamos at the Budapest Urological Clinic and Romhanti at the Pecs Institute of Pathological Anatomy.

The problem of the so-called Disse spaces has long been important from the point of view of clinical, as well as anatomical and histological studies. Although numerous publications have appeared on this problem, it still remains unsolved. The problem is whether in the normal state there are fluid-containing interstitial spaces between liver cell strands, or whether these spaces are an artifact.

The difficulty consists in the fact that the methods used were not adequate for solution of the problem. The method used by most researchers was the injection of various substances under high pressure into liver tissue, and histological examination of the distribution of these substances, later. Therefore, it is questioned whether the facts observed by this method are purely artificial or not.

The above research group proceeded on the theory that if the Disse space existed and was part of the liver interstitium, then blocking of

the efferent lymph ducts must result in expansion of the Disse space, because the protein-containing fluid could be led off from the interstitium on through the lymphatic system.

In liver research, lymph stasis was successfully produced in the liver by tying off of the lymph nodes of the liver. Histological examination revealed that under such conditions the Disse spaces were exactly as in liver inflammation caused by infection. On the basis of the experiments of this group it was established that the Disse space is not an artifact but is present in normal liver and is an integral part of the liver interstitium.

Further experiments, similar to the above experiments on the liver, were aimed at discovering the effect of tying off the efferent lymph ducts of the liver on the results produced by tying off the ductus choledochus, the common bile duct. These experiments showed that the tying off of both ducts led to far more serious consequences than tying off only the ductus choledochus.

3. The Heart

These investigations were performed with the participation of Ferenc Solti, Gyorgy Romhanyi of the Pecs Institute of Pathological Anatomy, and Antal Temesvari of the Budapest Clinic of Advanced Surgical Training. The experiments showed that blocking the lymphatic circulation of the heart leads to severe histological changes: the heart muscle becomes edemic, and in some cases small, scattered areas of dead tissue are formed. The most important observations were that cardiac lymph stasis has serious electrocardiographic results.

Although the above observations have no precedent in literature, several researchers already have described venous circulatory disturbances of the heart and their electrocardiographic consequences. Among the latter researchers are the Hungarians Temesvari and Kunos of the Budapest Clinic of Advanced Surgical Training. The essence of their results is that tying off of the principal venous cavity of the heart, the sinus coronarius, never leads to death of the heart muscle. At most, this leads, after a certain period, to a mild increase in connective tissue (fibrosis), and to a temporary depression in oscillations, or low voltage (Unghvary). There are no serious electrocardiographic consequences.

In light of the above, the question arose as to what would happen if the cardiac lymph ducts became obstructed when a condition of venous stasis prevails, and there is increased need for the efferent lymphatic circulation to maintain the lymphatic circulation of the heart muscle. Therefore the results of simultaneous venous and lymphatic stasis were investigated.

These experiments established that although tying off of either the sinus coronarius or the cardiac lymph ducts alone did not endanger the survival of the animal, the tying off of both ducts at the same time usually led to the rapid death of the animal. Post mortem dissection revealed the cause of death to be extensive hemorrhagic death of the heart muscle. The electrocardiographic results were similar to those obtained in human pathology in cases of blocking of the coronary arteries.

The research group drew several significant conclusions from these observations. Firstly, from a general standpoint these facts give a strong indication of the crucial role of lymph circulation in the life of the heart muscle. Secondly, these observations are important because of their implication in the cases in human pathology in which the death of



some patients is accompanied by all the symptoms of coronary occlusion, but autopsy reveals no pathological changes in the coronary arteries. From the investigations of this research group it may be concluded that closure of the cardiac arteries is fatal only if accompanied by closure of both the venous and lymphatic ducts. In connection with spasm of the lymph ducts mentioned above, or lymphangiospasmus, this group proposes that venous occlusion may lead to a lymphangiospasmus in the form of a reflex action. This area of research has such great theoretical and practical significance that further research on clinical patient material is absolutely necessary.

These investigations also have very important implications for the pathological course of certain human cardiac diseases, including cardiac decompensation. In cases in which exhaustion of the left side of the heart is followed by secondary decompensation of the right side of the heart, the systemic and the cardiac arterial pressure rises. Also, as was mentioned above, an increase in arterial pressure hinders the emptying of lymph from the lymphatic ducts into the large arteries. This causes a sudden deterioration of cardiac venous circulation which, as was seen above, has fatal effects on the heart muscle.

4. Lungs

It has long been known that the lung has an extensive lymph duct system. The clinical picture of pulmonary edema also has been known for a long time. Despite these facts, all the details of the origin of pulmonary edema still are not sufficiently well known, especially concerning the role of pulmonary lymph circulation in the fluid circulation of the lung under normal and pathological conditions. The theory generally held, which was first proposed by Welch, is that pulmonary edema rises when the left side of the heart becomes deficient and the right side of the heart continues normal. In this situation the blood pressure in the capillaries in the lung region of the inferior circulatory system greatly exceeds the pressure tending to keep the blood fluids within the blood vessels, and pulmonary edema results, with fluid filling the pulmonary vesicles. This hinders the exchange of gases, and if this condition extends to a large part of the lung the patient suffocates. In this instance, as in many other cases, the extensive lymph circulation of the lungs has been overlooked.

In experiments conducted by Janos Kepes, an associate of the National Scientific Research Institute of Nerve Surgery, Ferenc Robicsek, an associate professor of the Budapest Clinic for Advanced Surgical Training, and Miklos Papp, who is a degree aspirant under the sponsorship of the present author, it was established that pulmonary edema could be produced by tying off the efferent pulmonary lymph ducts. Although the edema produced in this way could be definitely identified, it did not extend to a majority of the pulmonary vesicles. When the heart valves of a dog were first damaged, however, tying off of the lymph ducts led to diffuse, extensive and serious pulmonary edema.

On the basis of these investigations this research group drew up a new definition of the origin of pulmonary edema: pulmonary edema results in all cases in which there is a discrepancy between the production of pulmonary capillary filtrate and removal of the latter, or in all cases in which the pulmonary lymph duct system is deficient and incapable of keeping the lung "dry." The occurrence of pulmonary edema, whether due to an increase in pulmonary capillary blood pressure, to a decrease in colloidal osmotic pressure (drop in the affinity of proteins for water), to an increase in the permeability of capillaries of the inferior circulatory system, or to the presence of water in the air passages, in the



final analysis the edema is always the result of some type of deficiency in the lymphatic circulation of the lungs.

One of the most important preparations of the field of physiology, pathology, and pharmacy is the so-called Starling heart-lung preparation. Study of his preparation led to discovery of most of the known laws governing the functioning of the heart. A very annoying circumstance is that the use of the Starling heart-lung preparation always leads to the spontaneous development of pulmonary edema after a certain period of time. Starling himself observed and recorded this fact, but its causes still have not been explained. Most authors attempt to explain this phenomenon by the liberation of toxic substances from the dog blood which is artificially pumped through the heart and lungs, and which have a damaging effect on the walls of the arteries. On the basis of its own experiments the above research group is able to contribute a very important fact to knowledge of this problem. The Starling heart-lung preparation requires the preliminary tying-off of the large veins leading to the heart. This hinders the emptying of lymph from the large lymph ducts into the large veins. This, however, does not preclude the possible toxic effect of the blood used for perfusion.

5. Thyroid Gland

These investigations were performed in conjunction with Harry Jellinek, an associate professor of the Budapest Institute of Pathological Anatomy No II. It is a long-disputed question, whether the metabolism-regulating hormone produced by the thyroid, the so-called acinus secretions, leave the thyroid gland via the blood stream or via the lymphatic ducts.

In the first group of experiments the lymph ducts of the thyroid gland were made visible by tying off the two principal efferent lymph ducts in the neck of a dog. This rendered visible the thyroid lymph ducts which otherwise are collapsed and cannot be observed even in histological examinations, and the course, location, and relation of these lymph ducts to blood vessels and to the acinus secretions could be studied in detail. The incisions were stained with extremely varied types of dyes and it was found that in every case the gland secretion in the acini and the lymph in the distended lymph ducts of the thyroid gland showed the identical staining results. At the same time, the lymph in the ductus thoracicus exhibited different staining characteristics. From these investigations it may be concluded that the content of the acini and of the thyroidal lymph ducts is identical, and that the lymphatic system of the thyroid has an active part in carrying off the hormone produced by the thyroid gland. Nevertheless, further investigations will be necessary to prove this hypothesis.

In the second group of experiments large numbers of human thyroid glands were examined. It was established that pathological changes may be found in the lymph duct system in cases of colloidal goiter, which most probably have an important role in the development of transformations, scarring and death of thyroid connecting tissue.

An extensive series of experiments was undertaken to determine the mechanism by which various substances present in the interstitium, such as fluid, protein, bacteria, etc, get into the lymph capillaries, which begin as a closed system, shaped like a glove. (It must be noted here that no one has had as much success as academician Miklos Jancso in his recent classical photographs which demonstrate that lymph capillaries originate in this manner.)



From these investigations it was concluded that the function of the endothelial cells which compose the walls of the lymph capillaries is the regulation, or active limitation in the living organism of absorption into the capillaries. It must be noted that this phenomenon is not unique in the life of the organism, and the same thing happens in both the stomach and the renal cortex.

The Urological Clinic, headed by academican Babics, plays an important role in Hungarian lymph research. The principal research results of Babics and Renyi-Vamos are described below.

Through electrophoretic experiments Babics and Renyi-Vamos have demonstrated that lymph taken from extremely diverse parts of the body (intestine, testicles, liver, kidney, appendages, ductus thoracicus) contains the same proteins which are found in blood. However, there is a definite, demonstrable difference between the composition of lymph and blood protein.

This research group demonstrated that in the hydronephrosis resulting from tying off of the ureter the lymph capillaries distend and they may be counted and their location may be studied. They showed that the liver contains many lymph capillaries, but contrary to earlier data there is no system of lymph ducts. The investigations of Babics and Renyi-Vamos along this line contributed greatly to the knowledge of the kidney lymphatic duct system.

In further experiments it was established that contrary to previous opinion, that in both humans and in experimental animals inflammatory processes of the renal nervous system do not invade the kidney substance via the lymph ducts, but through the fatty and connective tissue, with the exclusion of the lymph ducts.

The investigations of the Budapest Urological Clinic in the field of the pathology of pyelonephritis have great practical significance. In these investigations it was shown that the stasis and inflammation of protein in the kidney tissue and in the renal tunic causes the formation of scar tissue in the tunic, peduncle and in the fatty tissue surrounding the renal cavity, which compresses the efferent lymph ducts. These processes explain the phenomenon of the shrinkage of the kidney in pyelonephritis. On the basis of these observations a therapeutic standard was developed for the treatment of chronic pyelonephritis according to which surgical removal of the stone is insufficient, and if the kidney is worth retaining, the scar tissue must be removed as well. With such treatment the functioning of the kidney improves, and the pathological configuration of the renal cavity system also reverts to normal.

Renyi-Vamos and Gyorgy Rona, lecturer of the Institute of Pathological Anatomy No 1, investigated the problem of why the renal lymph capillaries do not distend in acute and subacute glomerulonephritis, despite the existing edema. In the opinion of these researchers deficient lymphatic circulation is one of the causes of the development of shrunken kidney, which is the fatal result of chronic renal infection.

Renyi-Vamos and Gyula Szalay, lecturer of the Budapest Institute of Pathological Anatomy, investigated the anatomy of the lymphatic system of the stomach, and the role of the gastric lymphatic system in the pathology of gastric ulcer.

Renyi-Vamos made some important new observations in the investigations concerning the testicle. On the basis of his observations he drew the conclusion that whereas, contrary to the general opinion there are no



lymph capillaries in the ducts between the testicle and the epididymis, such lymph capillaries can have no role in furthering the development of tuberculosis. Tuberculosis of the testicle, therefore, is not lymphogenous as was previously thought, but is transmitted directly to the testicle tissue.

Whereas there are no lymph capillaries between the testicular ducts, the removal of fluids accumulated due to edema of the testicular tissue during an illness or the increase of such fluid following hemorrhage caused by injury is very slow. This is thought to be the cause of the clinical observation of the rapid death of the testicle in testicular conditions accompanied by extreme edema. In less severe cases the result is not the death of the organ, but the formation of scar tissue. Based on the above, Babics developed the therapeutic conclusion that in cases of injury to the testicular integument the extruding testicular tissue should not be replaced, as is the present practice, but should be excised. It has long been known in clinical practice that novocaine treatment in cases of inflammation of the testicle and epididymis has a beneficial effect. Babics and Renyi-Vamos, then, are justified in thinking that in such cases elimination of the lymph duct spasms has some effect in the therapeutic treatment.

Finally, it may be mentioned that Babics and Renyi-Vamos have stated that if the Funiculus spermaticus (the fascicle containing the efferent duct of the testicle, the testicular arteries, lymph ducts and nerves) is thick, turgid, very sensitive, and the condition persists for 6 to 8 days, it is certain that the condition has spread to the testicle and the testicle no longer can be saved. In such a condition the efferent lymph ducts located in the funiculus have been blocked off, and the testicle must perish.

In conclusion, the research of Istvan Kubik, lecturer of the Budapest Institute of Anatomy, in the field of lymph circulation may be mentioned. Kubik was especially concerned with investigation of the factors which play a role in the maintenance of lymphatic flow. In another research project Kubik investigated the lymphatic system of the uterus and contributed to the clarification of the anatomy of the lymphatic plexus of the uterine mucous membrane. He established that this plexus has a definite embryonic character, because due to the rapid succession of sloughing off of the mucous membrane in menstruation the lymphatic plexus has no opportunity for differentiation. Another interesting observation of this research is that the lymph ducts originating in the outermost regions of the genital system pass through more lymph nodes than the ducts leading from the inner regions. Thus the regions which are exposed to greater possibility of infection are protected by greater filtration of the lymph.

In his book entitled A tudo segmentumok localisatioja a tajeki nyirokcsomokban /Localization of Lung Segments in the Regional Lymph Nodes/, Kubik discusses the possibility of localization of the smaller units of each lung lobe, the lung segments, within the lymph nodes of the hilus. On the basis of his experiments he was able to localize the lymph nodes of the individual lung segments, and he even succeeded in isolating the distribution of appropriate segments within individual lymph nodes. On the basis of this study the primary units which compose a lymph node may be defined. As a result of these investigations it may be demonstrated that from the point of view of lymphatic circulation the segmentum is an independent unit. The study of this problem is of importance to pulmonary surgery, also.



Kubik also investigated the problem of the innervation of lymph ducts, and after Zhdanov, he was the first to study this problem through utilization of silver-impregnation photographs. Kubik succeeded in demonstrating the so-called basic plexus of the intestinal folds, including the small secondary branches, the innervation of which never before had been demonstrated. He discovered a peculiar, network-like nervous plexus on the larger lymph ducts which, according to denervation experiments, apparently constitute a receptor grid. This problem is especially important in view of the fact that according to Soviet data various blood circulatory reflexes are governed by the lymphatic circulation. From Soviet literature it is known that experimental increase of the pressure in the ductus thoracicus results in an increase in blood pressure, and Kubik demonstrated that the same phenomenon may be observed in experiments with the abdominal and neck lymphatic vessels, also.

In the above the author has attempted to give a brief review of the work which has been done in Hungary since the liberation in the field of the physiology and pathology of the lymphatic system. This work already has had many new and interesting results and extends the hope that in the future it will further enrich medical science with knowledge of both theoretical and practical importance.

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