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Physiopathologie des chylifères chez le chien et chez l'homme. Intérêt dans les transplantations de l'intestin grêle.

Physiopathology of chyliferous vessels in dogs and humans. Relevance to small intestine transplants.

Marceau SERVEILLE

En janvier 1951, utilisant le rein d’un condamné à mort, nous avons réalisé la première transplantation rénale (1) avec une survie de 39 jours. Aussi, avons-nous suivi avec intérêt les autres transplantations d’organes (cœur, poumon et organes intraabdominaux).


PHYSIOLOGIE DES CHYLIFÈRES. GÉNÉRALITÉS.

Il y a 15 ans, au cours d’un voyage à Houston, nous découvrons un livre intitulé "GASTROINTESTINAL PHYSIOLOGY " par SERNKA et JACOBSON (1979) (3). Surpris de ne trouver aucun chapitre consacré à l’absorption par les lymphatiques de l’intestin grêle, nous avons cherché dans l’index pour trouver une seule référence sur ce sujet.

Par contre, Mark RAVITCH, en 1966, rassemblant en 2 gros volumes, les 269 publications réalisées par Alfred BLALOCK au cours de sa carrière universitaire : "THE PAPERS OF ALFRED BLALOCK." (4). Nous trouvons dans le tome 1,

**Key words** : Chyliferous vessels, chyle, animal, human, transplants, surgery.

Reprints requested to :
Marceau SERVEILLE
Chirurgien cardiovasculaire
16, rue Spontainie
F - 75116 Paris.

In January 1951, we performed the first kidney transplant (1), using the kidney from a condemned person, following which the patient survived for 19 days. We therefore followed other organ transplants with interest (heart, lung and intra-abdominal organs).

After an initial attempt at a liver transplant in 1963, Thomas E. STARZL, from Pittsburgh successfully carried out a human liver transplant in 1967. In his remarkable book, published in 1962, "THE PUZZLE PEOPLE: MEMOIRS OF A TRANSPLANT SURGEON. (2)] he summarises his significant clinical and experimental research, firstly into kidney transplants since 1965 and then into liver transplants and, in particular, perfection of the anti-rejection treatment. He then links small intestine transplants to these liver transplants. The present paper will deal specifically with the latter transplants.

PHYSIOLOGY OF CHYLIFEROUS VESSELS.

Fifteen years ago, during a trip to Houston, we came across a book entitled "GASTROINTESTINAL PHYSIOLOGY " by SERNKA and JACOBSON (1979) (3). We were surprised not to find a chapter devoted to absorption by the lymph vessels of the small intestine, we looked in the index to find only one reference on this subject.

On the other hand, in 1966, Mark RAVITCH compiled into 2 large volumes the 269 papers published by Alfred BLALOCK during his university career, "THE PAPERS OF ALFRED BLALOCK." (4). In volume 1, page 116, we find a publication entitled "CHYLOTHORAX AND CHYLOPERITONEUM " A 17-year-old woman presents a double effusion of chyle in the pleura and the peritoneum. Over a period of 19 months 550 litres of chyle are withdrawn by pleural and peritoneal punctures and 11 litres reinfected into the patient intravenously. The same article refers to another publication by BLALOCK, CUNNINGHAM and ROBINSON (Annals of Surgery, 1956) : these authors made a ligature of the superior vena cava of several dogs. Hall of the dogs present a chylotorax with a fall in blood proteins.

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PHYSIOLOGIE DE L’ABSORPTION INTESTINALE

LIGATURES DES CHYLIFIERES

Nous avons également étudié avec notre test d’hyperlipidémie provoquée l’effet des ligatures des chylifères chez le chien et chez l’homme ainsi que la physiologie de l’absorption par l’intestin grêle. Pour ce test d’hyperlipidémie, nous effectuons une prise de sang à jeun puis le malade ou le chien absorbe 50 grammes de beurre pendant 3 heures. Des prises de sang sont réalisées toutes les heures pendant 5 heures pour dosages des lipides totaux et des triglycérides ainsi que la densité optique. Sur la courbe normale, nous avons montré que les heures et en ordonnée les lipides totaux ou la densité optique. Chez le sujet normal, ce test montre que les lipides totaux sont à 6 grammes à jeun ; ils montent à 6,4 grammes à la première heure, à 7 grammes à la 2ème heure et atteignent leur sommet à 7,3 grammes à la 3ème heure, puis redescendent à 6,5 gr à la 4ème heure et se terminent à 5,5 gr à la 5ème heure. Ce test d’hyperlipidémie provoquée a été réalisé chez 500 antécédents anévrismatiques et chez 300 malformations des chylifères. Au-dessous de la courbe normale, on s’inscrit les courbes des lipides totaux des antécédents, des coronariens, des anévrysmes artériels et des cellules des fibres prênant la pilule. Au-dessus de la courbe normale, s’inscrivent les courbes des malformations congénitales des chylifères dont les manifestations cliniques sont variées et souvent graves. La courbe de densité optique a le même profil que la courbe d’hyperlipidémie provoquée, mais, à la 5ème heure, nous avons une densité optique à 10 fois qu’au temps 0 elle est à 5.

Toutes nos études des courbes d’hyperlipidémie provoquée après absorption de 50 grammes de beurre sont en totale contradiction avec ce qu’écrivait DAVENPORT dans son livre cité plus haut : "les graisses absorbées apparaissent dans la lymphe 13 heures après le repas gras."


CONCLUSION

All our clinical and lymphographic observations are of only theoricat value. We think that when the small intestine is taken from a donor for transplant, methyl butter in warm milk should be injected by gastrodenodal probe 3 hours beforehand to make it easier to find the intestinal lymphatic trunk which is to be severed, with covered thread to mark the section to be severed.
Apparition et croissance embryonnaire des lymphatiques du poumon et du cœur chez l’homme.

Origin and embryonic growth of lymphatics of heart and lungs in human.

RIQUET M. * **, LE PIMPEC-BARTHES F. *, DUPONT P. * **, HIDDEN G. **

* Service de Chirurgie Thoracique (Pr Debrosses) - Hôpital Laennec, Paris.
** Laboratoire d’Anatomie (Pr Lantuejoul) - Biomédicale des Saints-Pères, Paris.

RÉSUMÉ

Selon LINBORGH, des plexus lymphatiques parastrachéaux apparaissent chez l’embryon de 13 mm et un primordium unique sous la bifurcation trachéale à 22 mm.

De façon à étudier plus avant le développement des lymphatiques du poumon et du cœur, les coupes histologiques de 71 embryons et fœtus humains de la collection du Laboratoire d’Anatomie de l’I.E.R Biomédicale des Saints-Pères ont été revues. Leur taille calculée du vertex au sacrum allant de 16 à 92 mm : 49 étaient couplés en série transversalement, 15 sagittalement, 7 frontalement. Nous avons observé des vaisseaux lymphatiques dès 21 mm du tissu lymphoïde entre 33 et 42 mm et des lymphonœuds dès 69 mm. Ces éléments apparaissaient à la même période que soit la région anatomique observée : inter-trachéo-bronchique, sous-bronchique gauche, pré-trachéale droite et ligaments triangulaires. Les vaisseaux lymphatiques établissaient des connexions avec les veines de la face du cou et le canal thoracique dans le médiastin pratiquement en même temps qu’apparaissaient les premiers éléments lymphoïdes.

Les lymphatiques du poumon et du cœur sont donc construits et à leur place définitive avant la fin de la période de la croissance embryonnaire telle qu’elle est définie par PINEAU.

Key words : Lymphatics - heart - lungs - embryology - lymphangioma.

ABSTRACT

According to LINBORGH, paratracheal lymph plexuses appear in the embryo at 13 mm and a single primordium appears inferior to the tracheal bifurcation at 22 mm. In order to study the development of the lymphatics of the lungs, we have reviewed serial sections of 71 human embryos and fetuses from the Laboratoire d’anatomie de l’I.E.R Biomédicale des Saints-Pères. Their crown-rump lengths ranged from 16 to 92 mm : 49 were sectionned transversally, 15 sagittally and 7 frontally. We observed lymphatic vessels as early as 21 mm, lymphoid tissue between 33 and 42 mm and lymph nodes at 69 mm. These structures appeared at the same time whatever the anatomical site studied: tracheal bifurcation, left superior bronchus, right aspect of the trachea and pulmonary ligaments. The lymph vessels were connected with the cervical veins and the thoracic duct in the mediastinum as soon as the first lymph gland structures appeared. The lymphatics of the heart and lungs are formed and at the right place before the end of the embryonic growth period as defined by PINEAU.

— I —

INTRODUCTION

Studies about lymphatic drainage of intrathoracic organs are rare in embryos. About the heart, we must quote works of KAMPMEIER (7) and about the lungs, works of VAN DER PUTTE and of VAN LINBORGH (9, 13). The purpose of this study is to better assess the anatomy of this lymphatic system as early as in its embryonic origin.

La nature des structures observées a été considérée comme lymphatique et lymphoïde par leur aspect évolutif et sur le fait qu'elles ont été constatées au niveau des sites anatómiques ne contenant que ce type de structures chez l'adulte. De plus, les photographies reproduites par VAN DER PUTTE (13) au niveau du poumon et par KAMPMEIER (7) au niveau du cœur montraient les mêmes structures lymphatiques vasculaires que celles que nous présentions. Le tissu lymphoïde et les lymphocytes ont le même aspect que celui photographié par HAMILTON à 50 mm (6) et par BLECHSCHMIDT pour des tailles de fœtus plus grandes (4). Les amas lymphoïdes nous semblaient apparaître avant 60 mm, ce qui est en accord avec les observations faites par BAILEY (2). La réalité des lymphatiques observées ne semble donc faire aucun doute : la cœruleaïde pourrait être obtenue sur du matériel frais en utilisant des immuno-marqueurs mais ce matériel est difficile à se procurer actuellement.

Deux points embryologiques sont à souligner. Tout d'abord, le fait que les vaisseaux lymphatiques apparaissent tous au même moment dans les différents sites anatomiques et évoluent parallèlement va en faveur de l'origine centripète dans la lymphangénèse, théorie défendue notamment par KAMPMEIER (8) et à l'encontre de la théorie centrifuge (faisant dériver ces vaisseaux de structures veineuses) développée dès le début du siècle par SABIN notamment (17). Deuxièmement, l'existence de connexions avec les confluentes veineux mais aussi avec le canal thoracique est anatomiquement identique à celle que nous avons observée chez l'adulte (14) : ces connexions sont le siège des lymphangiomes cervico-médiasinaux du nouveau-né, considérés habituellement comme congénitaux et celui des lymphangiomes médiasinaux de l'adulte développés de façon probablement acquise au niveau de ces chaînes nodales.

Sur le plan de l'organo génèse, les lymphatiques apparaissent donc présents au niveau du cœur au stade embyryonnaire et dès la fin de la cardiogénèse telle qu'elle a été décrite par O'RAIHLLY (10) : ils sont également présents au poumon au stade embryonnaire (1), apparaissant dès la fin de l'organo génèse (1, 12) : leur mise en place définitive est complétée durant la première moitié du stade pseudoglandulaire (de la 2ème à la 17ème semaine) (5) qui prend place au début de la vie fœtale proprement dite des auteurs classiques. Cette période est celle définie par PINEAU (12) comme étant la phase de croissance embryonnaire : cet auteur ne fait en effet commencer la vie fœtale qu'à la fin de la 14ème semaine, la taille étant alors de 98 mm en moyenne.

**DISCUSSION**

We have considered that the structures we have seen were of lymphatic and lymphoid nature because they were observed at the anatomical sites where only this kind of structures exists by adults. Moreover, the photographies produced by VAN DER PUTTE (13) at the larv level and by KAMPMEIER (7) at the heart level show the same lymphatic vessels as those we have observed. The lymphoid tissue and the lymphoïdes compared with those photographed by HAMILTON at 50 mm CL (6) and by BLECHSCHMIDT for bigger fetal specimens (4). The lymphoid tissue appears at about 42 mm which is what was also observed lymphatique makes no doubt : certain would be afforded by immunohistology on fresh embryos but such a material is difficult to obtain at the moment.

Two embryologic points must be stressed (5). First the fact that all lymphatic vessels appear at the same time in different anatomical sites and then keep growing together favours the hypothesis of the centripetal origin of lymphangiogenesis as it was advocated by KAMPMEIER (8) and does not agree with the centrifugal theory which states that lymph vessels originate from the veins as it was advocated by SABIN (17). Second, connections of the lymph vessels with the cervical veins and with the thoracic duct in the mediastinum is exactly what we have already observed by adults (14). These connections are the sites of the cervico-mediastinal lymphangiomas observed by newborns which are considered as congenital and the site of the mediastinal lymphangiomas observed by adults which probably develop at the level of those nodal chains.

As far as organogenesis is concerned, lymphatic vessels are present in the heart by embryos as soon as cardiac tubes as describby by O'RAIHLLY (10) are formed ; they are present too in the lungs and mediastinum by the enteryo (1) and do appear at the end of organogenesis (1, 12) : they are definitely in place during the first half of the pseudo glandular stage (between 7 and 17 weeks of in utero life which begins with the fetal life as defined by embryologists. This period is the one PINEAU (12) named the embryonic growing period : this author thinks, that the fetal life begins at the end of the 14th week, the CR length being then of 98 mm.

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TABLE I

<table>
<thead>
<tr>
<th>Taille on tmm</th>
<th>Age moyen</th>
<th>Horizon streeter</th>
<th>Numéro</th>
<th>Poids (grammes)</th>
<th>Année</th>
<th>Origine</th>
<th>Fixateur</th>
<th>Collération</th>
<th>Coupe (micron)</th>
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<td>−</td>
<td>P 1087T 46</td>
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### TABLE III

Embryos sectionnés frontalement. — Embryons coupés frontalement.

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<th>Année</th>
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<td>P 5 CK</td>
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<td>33</td>
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<tr>
<td>34</td>
<td>59</td>
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<td>P 9 OC-DO</td>
<td></td>
<td>1930</td>
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<tr>
<td>50</td>
<td>69</td>
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<td></td>
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<td>55</td>
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<td>68</td>
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<td>91</td>
<td>90</td>
<td></td>
<td>P 9 AP</td>
<td></td>
<td>1929</td>
<td>Rouvière</td>
<td>F 10 %</td>
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### TABLE IV

Embryos sectionnés sagitalement. — Embryons coupés sagitalement.

<table>
<thead>
<tr>
<th>Taille en mm</th>
<th>Age moyen</th>
<th>Horizon stérilet</th>
<th>Numéro</th>
<th>Poids (grammes)</th>
<th>Année</th>
<th>Origine</th>
<th>Fixateur</th>
<th>Coloration</th>
<th>Coupe (mm)</th>
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<tbody>
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<td>46</td>
<td>XVIII</td>
<td>U-V</td>
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<td>21 mm</td>
<td>50</td>
<td>XIX</td>
<td>CL</td>
<td></td>
<td>1924</td>
<td>Nicols</td>
<td></td>
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<td>24 mm</td>
<td>52</td>
<td>XXI</td>
<td>EB</td>
<td></td>
<td>1939</td>
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<td>F 10 %</td>
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<td></td>
</tr>
<tr>
<td>24 mm</td>
<td>52</td>
<td></td>
<td>P 10 HT 15</td>
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<td>57</td>
<td>XXII</td>
<td>P 9 AV</td>
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<td></td>
<td>P 9 EN-EO</td>
<td></td>
<td>1935</td>
<td></td>
<td></td>
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</table>
FIGURE 3
Embryon de 44 mm (coupe frontale).
B = bronches ; amas lymphoides (latéro-ventral)
gross. X 10 ; col. Masson.
Embryo 44 mm (frontal slide).
B = bronchus ; lymphoid cells (anterior).
Magnification X 10 ; col. Masson.

FIGURE 4
Fetus de 70,5 mm (coupe transversale).
B = bronche ; lymphonœuds au sein de vaisseaux lymphatiques
Fetus 70.5 mm (transversal slide).
B = bronchus ; lymph nodes inside lymph vessels (arrows).
Magnification X 10 ; col. Morel and Basaul.
FIGURE 7

Embryon de 38 mm (coupe transversale).
Conversation médiane de l'ITB avec le canal thoracique (CT) (gross. X 10; col Trikrom).

Par 1 vaisseau lymphatique antéro-postérieur (flèche).

Corps vertébral = V; Aorza = A; Ésophage = E.

Embryo 38 mm (transverse slice).
Anterior-posterior lymph vessel (arrow).

Conveying the nodes of the thoracic bifurcation (ITB) with the thoracic duct in the mediastinum (CT).

V = vertebra; A = aorta; E = esophagus.

Magnification X 10; Col. Trikrom.
Ultrastructural study on the pleural stomata in human.

Etude ultrastructurale des stomates de la plèvre humaine.

JICHENG LI
Department of Histology and Embryology,
Zhejiang Medical University,
Hangzhou 310006 China

RéSUMÉ
Nous avons étudié l’ultrastructure des plèves diaphragmatiques et viscérales humaines en microscopie électronique à balayage et par transmission. Des stomates pleuraux, habituellement arrondis ou ovaux, d’environ 6,2 µm de diamètre ont été mis en évidence au niveau de la plèvre diaphragmatique. Nous n’en avons observé aucun sur la plèvre viscérale. La majorité de ces stomates pleuraux humains étaient profonds, constituant de véri-
tables canaux paraissant faire communiquer la cavité pleurale
avec les lucanes lymphatiques sous-jaunentes. D’autres ressem-
blaient à des pits peu profonds ouverts sur le tissu conjonctif
sous-jaunent.

Dans certaines régions de la plèvre diaphragmatique, les stoma-
tes pleuraux étaient bordés par de nombreuses expansions vil-
neuses des cellules mésothéliales qui en entouraient l’entrée. Ces
microvillosités étaient toujours plus longues et armées d’un
réseau plus dense de filaments que les autres expansions présen-
tes en général à la surface des cellules mésothéliales. Ainsi, les
cellules mésothéliales, par ces prolongements cytoplasmiques,
réalisaient à l’intérieur des stomates un dispositif valvulaire qui
autorisait en permanence l’épuration rapide de liquides de par-
ticules étrangères ou de cellules vers les lymphatiques dia-
aphragmatiques à partir de la cavité pleurale.

Key words : pleural stomata - pleural lymphatics - electron microscope - human.

Reprints request to :
JICHENG LI
Department of Histology and Embryology
Zhejiang Medical University
Hangzhou 310006
China

ABSTRACT
The ultrastructure of human diaphragmatic and visceral pleura
was studied by scanning and transmission electron microscope.
Human pleural stomata, which are usually round or oval in shape
with about 6.2 µm in diameter, were present on the diaphragma-
tic pleura. There were never found on the visceral ones. Majority
of human pleural stomata were quite deep, forming channels
which seem to connect pleural cavity with underlying lymphatic
lucane. Some of them occurred as shallow pits exposing compo-
nents of the underlying connective tissue. In some areas of the
diaphragmatic pleura the pleural stomata were furnished with
great number of microvilli of mesothelial cells surrounding their
openings. These microvilli were always longer and had denser
network of filaments in comparison with other on the surface of
mesothelial cells. In this way, the mesothelial cells formed valve-
like cytoplasmic processes into the pleural stomata, as a per-
manent structure, provided a rapid removal of fluid-particles and
cells from the pleural cavity into the diaphragmatic lymphatics.

INTRODUCTION
The peritoneal stomata were small openings of lymphatics which
open into the diaphragmatic peritoneum and connect peritoneal
cavity with lumen of lymphatics. The function of these stomata
has been to remove fluid, particles and cells from the peritoneal
cavity into the lymphatics. The peritoneal stomata were very
important for absorption when ascites developed, tumor cells and
bacteria were escaped from the peritoneal cavity (18, 7), haemolytic
disease of fetuses was treated by intrauterine transfu-
sion (8, 12) and ultrafiltration and solution clearance were
increased in long-acting peritoneal dialysis (10, 14).
A number of investigators (7, 17, 16, 19, 20, 13, 6) have studied
the ultrastructure and the function of the peritoneal stomata
in human and different animals.
Microlymphatic and thromboembolic disease in acute spinal cord injury.  
A morphological study on skin biopsies.

R. SCELSI, S. LOTTA *, Paolo POGGI **, R. BOCCHI * and Laura SCELSI

From the Department of Human Pathology, University of Pavia.  
* Rehabilitation Center " G. Verdi ", USL 3, Villanova d'Arda (Pez)  
** Institute of Normal Anatomy, University of Pavia.

SUMMARY

The thromboembolic disease (TED) of deep veins of legs is an important cause of morbidity and mortality in the first few months following traumatic spinal cord lesions in over 30 % paraplegic patients, in absence of chemical prophylaxis. In paraplegia, the main causes of the disease are the venous stasis following paralysis and immobilisation in the present condition, numerous paraplegic patients with documented ilio-femoral venous thrombosis developed the so called phlegmasia alba dolens with edema and stasis dermatitis of the lower extremities suggesting changes in the cutaneous lymphatic microcirculation.

Skin biopsies from 4 paraplegic patients with ilio-femoral TED were obtained from the lower lateral region of the involved leg and were studied with light and electron microscopy. Biopsies from 2 healthy subjects served as control. In all specimens, numerous lymphatics with dilated lumen and distended wall were present. The endothelial cells were attenuated and numerous open junctions and channels between contiguous endothelial cells were present. Perivascular collagen and elastic fibres were dissociated by presence of granula material.

These morphological alterations demonstrated a lymphatic microangiopathy in paraplegic patients with TED, with endoluminal lymph stasis and an increased transcapillary diffusion of the lymph material into interstitial dermit tissues, clinically resulting in edema with reduced removal of issue catabolites.

Key words : lymphatic vessels ; human skin ; paraplegia ; thromboembolic disease ; ultrastructure.

RéSUMÉ

La maladie thromboembolique (TED) des veines profondes des jambes est une cause importante de morbidité dans 30 % des sujets paraplégiques après lésions traumatiques de la moelle épinière.

De nombreux patients avec paraplégie et avec thrombose des veines ilio-fémorales montrent œdème et altérations cutanées au niveau des jambes (phlegmasia alba dolens).

Cealtérations suggèrent que la microcirculation lymphatique cutanée est impliquée.

Nous avons étudié les modifications morphologiques et ultrastructurelles des vaisseaux lymphatiques dans des biopsies cuta
nées des jambes chez 4 sujets paraplégiques avec TED.

Les principales modifications ont été : dilatation des vaisseaux lymphatiques, présence de nombreuses jonctions ouvertes et de canaux permi les cellules endothéliales, le tissu conjonctif en
toure les vaisseaux lymphatiques apparaissait désorganisé par la présence de granulations libres et de vésicules remplies de granulations fines.

Les résultats suggèrent que la microcirculation lymphatique cuta
nées des jambes des sujets paraplégiques avec TED est impliquée dans une pathologie produisant une stase lymphatique avec œdème et avec accumulation des catabolites dans le tissu conjonctif.

Reprints request to :  
Prof. Roberto SCELSI  
Department of Human Pathology  
Via Forlanini 14  
27100 Pavia (Italy)

A lymphatic vessel from the skin of a normal healthy subject is characterized by a thin endothelial wall, by open junctions and by perivascular connective tissue arranged in packed groups of elastic and collagen fibres (X 4,000).

Un vaisseau lymphatique cutané d'un sujet sain est caractérisé par une paroi mince, par des junctions ouvertes et par un tissu conjonctif avec nombreuses fibres collagène et élastique (X 4,000).

A lymphatic vessel from a paraplegic patient with TED showing a very dilated lumen filled by coagulated lymph. The perivascular connective tissue is disorganized by oedema (X 4,000).

Un vaisseau lymphatique de la peau d'un sujet paraplégique avec TED, caractérisé par une paroi élargie et disséminée. Le tissu conjonctif parait désorganisé par l'œdème (X 4,000).
FIGURE 5
An open junction between contiguous endothelial cells is present in the lymphatic wall. The perivascular connective tissue shows vacuolation and presence of free granular material between disorganized elastic and collagen fibres (X 10,000).

La paroi du vaisseau lymphatique montre une jonction ouverte entre deux cellules endotéliales. Le tissu conjonctif montre de nombreux vacuoles et des fibres collagènes et élastiques désorganisées (X 10,000).

REFERENCES
No free flow of oedema fluid along the tissue spaces after MLD

EDITOR.


They have achieved a "significant volume reduction in cases of post mastectomy lymphoedema treated with MLD and compression bandage" and question therefore our finding that there was no free flow of oedema fluid along the tissue spaces in patients presenting with chronic lymphoedema and treated by MLD.

We would like to point out that the explicitly declared aim of our study was not the assessment of the positive therapeutic results reported by the patients treated by MLD but the mechanism how these results were achieved.

For this reason, we decided to study the effect of just one session of lymph drainage of 30 min. duration. We focused on two variables.

Firstly on the haemodynamic changes of the macro circulation by monitoring the venous flow with a colour coded duplex scanner.

Secondly by getting deeper inside into the micro circulation by measuring interstitial tissue pressure. The results showing the correlation between these two variables were presented on the 14th International Congress of Lymphology in Washington in 1993 (MLD - Mode of action).

In all our studies, we have never questioned the possibility of decongestion after several sessions of MLD immediately followed by application of compressing dressing.

Our measurements simply demonstrated that the decongestion reported by HUTSCHEMREUTER and HERPERTZ was not effected by a mass (and therefore measurable) transfer of interstitial oedema fluid.

The haemodynamic changes, consistently recorded in the macro circulation and the indirect evidence from the micro circulation, suggest that oedema mobilized by MLD is transferred during each circulation cycle, step by step, i.e. in minute non measurable quantities from the interstitial into the vascular compartment.

DEREYEN - ASLAM - PFLUG
Swollen Limb Clinic
Hamnersmith Hospital
Ducane Road London W12

(1) HUTSCHEMREUTER P. and HERPERTZ U.

A propos de :

Pas de transfert libre du liquide lymphatique dans les espaces tissulaires après DLM

EDITOR.


Ils ont trouvé une réduction significative dans des cas de lymphoédème après mastectomie, traité par le DLM, suivis de bandages compressifs. Suite à cela, ils mettent en question notre constatation qu'il n'y avait pas de transfert libre du liquide lymphatique dans les espaces tissulaires chez les patients souffrant de lymphoédème chronique, traité par DLM.

Nous ambitionnons que le but de notre étude ne fut pas d'évaluer les résultats thérapeutiques positifs, rapportés par les patients traités par DLM, mais de retrouver le mécanisme par lequel ces résultats sont obtenus.

Pour cette raison, nous avons décidé d'étudier l'effet d'une session de DLM de 30 minutes. Nous avons exploré deux domaines.

Premièrement, les changements hémodynamiques de la macrocirculation sur le retour veineux à l'aide du scanner duplex coloré. Ensuite en approfondissant l'examen sur la microcirculation ; nous avons mesuré la pression interstitielle dans les tissus.


Dans toutes nos études, nous n'avons jamais mis en question la possibilité de décongestion après plusieurs sessions de DLM, suite immédiatement par l'application d'un bandage compressif.

Nos mesures démontrent simplement que la décongestion, rapportée par HUTSCHEMREUTER et HERPERTZ, ne fut pas effectuée par le transfert de la masse (et pour cela mesurable) du liquide interstitiel.

Les changements hémodynamiques, rapportés dans la macrocirculation et par la suite, indirectement dans la microcirculation, suggèrent que l'exemple, mobilisé par le DLM, est transféré pendant chaque cycle, pas à pas, c'est-à-dire par infime et non mesurable quantité des compartiments interstitiels vers le compartiment vasculaire.

DEREYEN - ASLAM - PFLUG
Swollen Limb Clinic
Hamnersmith Hospital
Ducane Road London W12

(1) HUTSCHEMREUTER P. and HERPERTZ U.
The interpretation of lymphoscintigraphy rate constants

THE EDITOR

Dear Sir,

Isotopic lymphoscintigraphy is now the preferred method of investigation in lymphedema because 1) it is less invasive than lymphography and 2) it provides functional information about the rate of removal of material by the lymphatic system. The term "quantitative lymphoscintigraphy" has become accepted in the literature to mean the ability to measure abnormalities of lymph drainage as determined from either colloid removal from the injection site or uptake of colloid in the regionally draining lymph nodes. We are concerned here with the former - colloid removal from the injection site.

While many users of lymphoscintigraphy are careful to point out that the removal rate constant does not measure lymph flow per se, it is often tempting to interpret the data as a measure of lymph flow. We felt it would be useful, therefore, to undertake a simple analysis of the rate constant, to see what it really measures. In doing this we employed Occam's razor, i.e. we made the simplest possible assumption, namely that the radioactive colloid is removed from the depot entirely by bulk flow (F) which, at least in normal subjects, is flow into the lymphatic system. More complex situations can, of course, be envisaged; we aim here merely to identify the most fundamental determinants of the measured removal rate constant.

Let mass \( m \) be injected at time \( t = 0 \). After time \( t \) there will be a smaller mass \( m \), remaining of mean concentration \( C \). If the volume of distribution of mass \( m \) is \( V_D \), then from the definition of mean concentration, \( C = m / V_D \). If the removal of colloid material is entirely by convection (our simplest assumption, for which there is much experimental support), and if colloid transport is not complicated by interaction such as partial molecular reflection then removal rate -dm/dt is:

\[
-\frac{dm}{dt} = C \cdot F = \frac{m \cdot F}{V_D} \tag{1}
\]

In order for equation (1) to give rise to a monoeponential curve, as usually observed, it is necessary to assume that the curve \( F \cdot V_D \) does not change significantly with time, i.e. \( F \cdot V_D \) is constant. If this is so, integration of (1) gives:

\[
\ln m = -\frac{F \cdot t + \ln m_0}{V_D} \tag{2}
\]

or

\[
m = m_0 \cdot e^{-F \cdot V_D \cdot t} = \frac{m_0}{V_D} \tag{3}
\]

Thus the simplest possible analysis of the lymphoscintigraphy rate constant \( k \) (units of min\(^{-1}\)) shows that it depends on the ratio of Flow to volume of distribution, \( F \cdot V_D \). The reciprocal of \( k \) is called the time constant \( \tau \) (units of minutes) and this is the ratio of volume of distribution to flow. Half-life, \( \tau_{1/2} \) is \(-0.693 \cdot V_D / F\).

The removal process can equally well be expressed in terms of "clearance". Clearance, \( C_l \), is by definition the virtual volume of a solution that is cleared of a solute per unit time. Thus \( C_l \) is \( (dm/dt)/C \) and has units of volume/time : the renal clearance of creatinine from plasma, for example, is 120 ml/min. For the lymphoscintigraphy colloid,

\[ C_l = k \cdot V_D \] (4)

If the clearance of the lymphoscintigraphy colloid is entirely by unimpeded convective transport into lymphatic vessels then \( C_l = F \), i.e. clearance rate equals lymph flow from the labelled region.

In comparing the removal rate constant in a normal and oedematous limb, one must therefore bear in mind the potential influence of volume of distribution of the injected colloid. If, in an oedematous limb, the tracer half-life is longer than in the control limb, one can state that the lymph flow per unit volume of distribution of tracer is reduced in the oedematous limb ; but the investigator may wish to ask whether this is solely due to reduced lymph flow or whether an increased volume of distribution of the injectate might play a part too.

In making the above simple analysis, we are struck by the necessity of assuming time-independence of \( F \cdot V_D \) in order to get a monoeponential removal process. One might expect, a priori, that even if \( F \) were relatively constant (the volume of injectate being small, around 0.2 ml), \( V_D \) would increase with time by diffusion. A truly monoeponential curve would seem to be telling us, therefore, that lymph flow per unit volume is uniform in the neighbourhood of the injection site. In conclusion, we suggest that measurement of \( V_D \) as well as \( k \) (or \( C_l \) or \( \tau_{1/2} \)) could usefully be made by imaging during lymphoscintigraphy, in order to clarify our understanding of the method and give us a clearer basis for interpreting differences in rate constants between limbs.

Yours sincerely,

Dr J R LEVICK (Dept Physiology)
Dr P S MORTIMER (Dept Physiological Medicine)
St George's Hospital Medical School,
Cranmer Terrace, London SW17 ORE

REVIEW
of the Prague symposium on lymphology
"LYMPHO 94"

In the second week of September 1994, Prague hosted an international symposium devoted to lymphology: "LYMPHO 94". Its organizer was the Czech Lymphology Society, in cooperation with the Groupement Européen de Lymphologie (GEL). The Czech Lymphologic Society is young, having been founded two years ago on the initiative of Czech lymphologists desiring to associate and to offer a strong organizational platform to the physicians and health care providers in this field that has become a modern interdisciplinary medical branch.

The topics of the "LYMPHO 94" symposium attracted well over one hundred of attendants, of that 17 from abroad. There were specialists in internal diseases among them, oncologists, surgeons, angiologists, dermatologists, pediatricians, radiologists, specialists in diagnostics, pathologists, anatomists, as well as theoreticians and experimental scientists. The comprehensive scientific agenda was divided into eight separate topical sessions in which 52 communications were presented.

Within the framework of the festive opening of the symposium, the first honorary members of the Czech Lymphologic Society were appointed: Prof. BARTOS, Prof. BELAN and Prof. BARINKA. They presented their communications that had been asked for, reflecting the contributions of the Czech specialists for the benefit of national and international development of lymphology. The following introductory session of the scientific programme comprised the papers of invited lecturers covering the essential groups of issues discussed at the symposium. The scientific agenda of the second day focussed upon problems of anatomy, physiology and pathophysiology of the lymphatic system. It brought many interesting communications, of which well deserved attention was invited in particular by the corner-stone papers of the German lymphologists, Prof. KASTENHOLZ and Prof. HUTZCHENREUTER, being of extraordinary practical importance for the clinical work.

A separate session was devoted to methods applied in the diagnosis of pathological conditions of the lymphatic system. This session centred around imaging methods the overview of which, including the contribution of the imaging the lymphatic structures by magnetic resonance (MRI), was the subject of the introductory paper. The proceedings of the symposium stressed the necessity of diagnostic orientation upon non-invasive modalities of examination, allowing timely detection of functional and morphologic changes accompanying the affections of the lymphatic systems. The clinical problems were dealt with in the sessions focussing upon lymphostatic diseases, lymphedemas, and on systemic diseases, lymphomas. Rational treatment of lymphedema including its methodology and the achieved results were presented and discussed. Much stress was laid on the comprehensiveness of lymphedema therapy that should be consistent and long lasting (practically life-long). It should be based, primarily, on full-scale physical therapy encompassing skin care, manual lymphatic drainage, special exercises and compression treatment.