

## The pioneers of modern lymphology in the early 20<sup>th</sup> century

Alberto Macciò

President of LymphoLab, Genova, Italy

### Abstract

We can state that modern lymphology was born from the pioneering work of the physicians of the first quarter of the 20<sup>th</sup> century. The turning point was definitely linked to the huge and precise work of the anatomists of the previous centuries and above all to the fine anatomical studies that resulted from the works of the second half of the 19<sup>th</sup> century. In the following decades, the possibility of specifically highlighting and studying lymphatic vessels and their physiology allowed the foundational step towards their clinical application and therefore the real understanding of pathologies and the first rudimentary therapeutic approaches. After the work of Von Recklinghausen (1863) and Sappey (1876), after the technical completion of the then modern Gerota staining (1896) and the postulates on the physiology of the microcirculation put forward by Starling (1894), three centuries after the intuitions of Aselli (1626), we saw the definitive emancipation of Lymphology as an independent medical subject.

### The pioneers of modern lymphology in the early 20<sup>th</sup> century

In order to understand the true pioneering role of those who ventured into the study of lymphatic circulation and the treatment of related diseases, it is necessary to focus on the state of the art in the early 20<sup>th</sup> century.

Edgar V. Allen from the Mayo Clinic in 1934 in the incipit of his article on *Lymphedema of the extremities* wrote *General information about lymphedema tends to be somewhat confused and vague, in spite of a considerable number of excellent reports that may be found in medical literature...*<sup>1</sup> (Figure 1).

One would not be hard pressed to believe that one could find a similar beginning in much more recent articles as well.

This is because the difficulty in studying and understanding diseases of the lymphatic circulation system still lies in its

complex physiology and in its peculiar anatomy, often very different from one subject to another and as a result of different morbid states.

As a matter of fact, the first years of the last century can be considered a real turning point - we owe the above all to the splendid work carried out by the anatomists of the 18<sup>th</sup> and 19<sup>th</sup> centuries, who contributed greatly to fill this initial gap and to create the conditions for the progress that followed.

If Gaspare Aselli (Figure 2) in the 17<sup>th</sup> century, in imagining an independent role for the chyliiferous vessels (*Quarta Vasorum Mesaraicorum genere - Novo Invento - 1627*)<sup>2</sup> (Figure 3).

laid the foundations for modern lymphology, it was the following centuries that defined the knowledge necessary to deepen the anatomo-pathological models to recognize their physio-pathological importance.

At the end of the 18<sup>th</sup> century, Mascagni (1787)<sup>3</sup> was the first to provide a systematic and complete description of the human lymphatic apparatus; after him, among many others, we can mention Von Recklinghausen (1863),<sup>4</sup> who studied the communication between blood and lymphatic circulation, and Sappey (1876),<sup>5</sup> who deepened the structure and importance of lymph nodes as active elements within the lymphatic apparatus.

Last but not least, in those years and specifically in 1894, Starling enunciated his theory of capillary *filtration and reabsorption*.<sup>6</sup>

It was in this context and with these solid foundations that the pioneers of the 20<sup>th</sup> century faced the challenges of diagnostics, clinical medicine and surgery of lymphatic diseases.

It is on these three strands of development that I intend to focus the subject of this editorial, although anatomists did not stop their work of consolidation of nineteenth-century knowledge.

In particular, Gerota (1896),<sup>7</sup> by describing an innovative technique of staining the lymphatic *capillary* networks (injection of Prussian Blue in turpentine oil and diaphanization of dissections), allowed a more accurate morphological study of the capillary networks of all organs and favored the subsequent work of Cuneò (1900),<sup>8</sup> Poirier (1909),<sup>9</sup> Bartels (1909),<sup>10</sup> Idanov (1930),<sup>11</sup> all of whom devoted a part of their writings to the detailed description of the lymphatic system of the thoracic-splanchnic and muscular-peripheral districts.

In 1932, after thirty years of studies, Rouvière<sup>12</sup> published what is still considered one of the most classic treatises on the anatomy of the lymphatic system.

Correspondence: Alberto Macciò, LymphoLab Onlus, via Marcello Staglieno 10/15, 16129 Genova, Italy.  
E-mail: segreteria@linfologia.it

Key words: Modern lymphology; 20<sup>th</sup> century.

Received for publication: 21 January 2021.

Accepted for publication: 21 January 2021.

This work is licensed under a Creative Commons Attribution 4.0 License (by-nc 4.0).

©Copyright: the Author(s), 2021

Licensee PAGEPress, Italy

*Veins and Lymphatics* 2021; 10:9631

doi:10.4081/vl.2021.9631

Going back to the times that revolutionized lymphology in the 1900's, we must remember who was primarily responsible for diagnostics.

Visualizing the circulatory system *in vivo* is, as in other medical realities, a starting point for the understanding of the pathology in progress and therefore for the setting of a suitable therapy.

The first years of 1900 were very laborious in this field, and it was thanks to the experiments that followed that Defrise (1929),<sup>13</sup> Ottaviani (1930),<sup>14</sup> followed by Funaoka (1930 - on live animals)<sup>15</sup> and Carvalho (1931 - on humans via translymph node)<sup>16</sup> laid the foundations of lymphography.

However, many years of work were still needed to find the best contrast medium and the best inoculation route, until the breakthrough of the intra-collector technique by Kinmonth and Taylor (1957).<sup>17,18</sup>

As said, with the solid basis of anatomy and physiology and with the help of a growing diagnostics, we could eventually start to understand the real lymphatic pathology that, as we all know now, is divided into primary (heredo-familial) and secondary acquired (more often post-surgical) pathology.

The pioneer of the early '900 I want to refer to for the study of primary lymphatic diseases is W.F. Milroy, who in 1928 published in JAMA an article that we can consider one of the cornerstones of modern lymphology. In the article entitled '*Chronic hereditary edema: Milroy's disease*' he gave a precise account of twenty-two cases of lymphedema in six generations of a family consisting of ninety-seven persons.<sup>19</sup>

Before him Sir William Osler<sup>20</sup> in the textbook '*The Principles and Practice of Medicine*' (1892) examined the disease but was in the article '*An Undescribed Variety of Hereditary Oedema*'<sup>21</sup> that Milroy

assumed the hereditary aspect of some types of edema of the lower limbs, as well as Henry Meige who in 1898<sup>22</sup> took the same conclusions. The work of Milroy was much more specific and detailed, putting, as mentioned, a further solid basis for a more methodical study of all primary forms of diseases of lymphatic circulation.

To end this overview on the assumptions that contributed to the history of lymphology and on the researchers who were its protagonists, one cannot overlook the fact that the first rudimentary surgical approaches for the treatment of lymphatic edemas of the limbs date back to the beginning of the 20<sup>th</sup> century.

However, these rudimentary surgeries, far from the more modern microsurgery,<sup>23,24</sup> are to be considered useful even for today's clinical lymphology and not completely abandoned.

The first interventions were based on two distinct assumptions: the more simply resective one, and the one based on the insertion of foreign bodies for drainage purposes.

With reference to the latter approach, we remember Handley who in 1910 proposed - not without complications - the insertion of silk threads from the ankle to the abdominal wall with the intention of increasing capillary drainage of the lymphedematous limb.<sup>25</sup>

We should also remember that W.S. Handley, besides being vice-president of the Royal College of Surgeons, proposed the *theory of centrifugal lymphatic permeation* as the main mechanism for the spread of cancer and for which Halsted (1921)<sup>26</sup> in turn proposed his radical mastectomy as the gold standard for the treatment of breast cancer.<sup>27</sup>

On the other hand, as far as more traditional surgical approaches are concerned, after the disappointing scarification proposed by Lisfranc<sup>28</sup> in the 19<sup>th</sup> century, in the first years of the 20<sup>th</sup> century many dabbled in the search for the best intervention for limb lymphedema.

Lanz in 1911<sup>29</sup> proposed excision of fascia flaps associated with bone drilling, Oppel (1911)<sup>30</sup> and Rosanow (1912)<sup>31</sup> also tried to connect the superficial and deep circulation systems with wide resections of fascia, Kondoleon (1912)<sup>32</sup> proposed the removal of part of the edematous connective tissue beyond the fascia, while Charles, who may be considered the most important representative of this school of thought, described in 1912 a surgery called *total superficial lymphangiectomy*<sup>33</sup> consisting in the complete removal of all connective tissue and fascia with direct suturing of the dermo-epidermal flap to the muscle masses

Classification of 300 Cases of Lymphedema

A. Noninflammatory	Cases
I. Primary	
Præcox .....	90
Congenital	
1. Simple .....	12
2. Familial (Milroy's disease).....	0
II. Secondary	
Malignant occlusion .....	32
Surgical removal of lymph nodes.....	61
Pressure .....	1
Roentgen and radium therapy.....	3
B. Inflammatory	
I. Primary (single or recurrent acute and chronic).....	41
II. Secondary (single or recurrent acute and chronic)	
Venous stasis .....	13
Triehophytosis .....	5
Systemic diseases .....	5
Local tissue injury or inflammation.....	34

Figure 1. Classification of 300 cases of lymphedema - Allen E, 1934.



Figure 2. Gaspare Aselli.



Figure 3. Quarta Vasorum Mesaraicarum genere - Novo Invento - 1627.

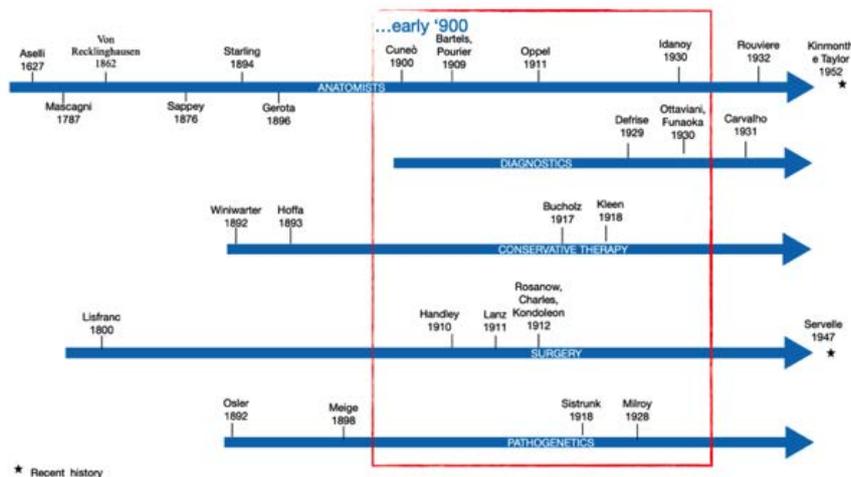


Figure 4. The pioneers of modern lymphology in the early 20<sup>th</sup> century.

(later further optimized by Servelle in 1947).<sup>34</sup>

Sistrunk (1918),<sup>35</sup> like Milroy from the Mayo Clinic in Rochester, was among the first to compare the various results obtained with the different techniques.

Last but not least and to complete this historical overview, I believe it is also important to remember the contribution of Alexander von Winiwarter. This Austrian physician, a former student of Theodor Billroth in Vienna, later moved to the University of Liège in Belgium - He is considered the true father of the conservative therapeutic approach to lymphoedema, for which he described special massages and compression approaches (1892).<sup>36</sup>

Although he worked at the end of the 19<sup>th</sup> century, it was the posthumous revisions based on his insights (A. Hoffa - 1893, C. H. Bucholz - 1917, E. A. G. Kleen - 1918)<sup>37-39</sup> that led the Danish biologist E. Vodder to optimise what came to be known as 'Manual Lymphatic Drainage', which he presented at the 'Santé et Beauté' Congress in Paris in 1936<sup>40</sup> (Figure 4).

I would like to conclude with this brief reflection: today as a hundred years ago, given the recent new discoveries, can we think that it will still be from the deeper understanding of the anatomy and physiology of the lymphatic circulation that the most interesting ideas for the development of Lymphology in the 21<sup>st</sup> century will come?

What is the importance of cerebral lymphatic vessels or thoracic-abdominal circulation in chronic inflammatory processes and infections?

Great progress is expected but knowing the past experiences will allow us to focus on the most promising goals.

## References

- Allen E. Lymphedema of the extremities. Classification, etiology and differential diagnosis: a study of three hundred cases. *Arch Intern Med* 1934;606-24.
- Aselli G. De Lactibus sive Lacteis Venis Quarto Vasorum Mesaraicorum genere Novo Inven-to Gasparis Asellii Cremonensis Anatomici Ticinensis Dissertatio. Milano; 1627.
- Mascagni P. Vasorum lymphaticorum corporis humani. Historia et ichonographia. Tip. Pazzi-ni Carli, Senis; 1787.
- Von Recklinghausen FD. Die Lymphgefäße und ihre Beziehung zum Bindegewebe The lymph vessels and their significance in connective tissue. Berlin: A. Hirschwald; 1862.
- Sappey Ph. C. Des vaisseaux lymphatiques. *Traité d' Anatomie descriptive*. Paris: A. De-lahaye & C.; 1876.
- Starling EH. The influence of mechanical factors of lymph production. *J Physiol* 1894;16:224.
- Gerota D. Zur Technik der lymphgefässinjektion. Eine neue Injektionsmasse der lymph-gefäße. *Polychrome Injektion. Anat Anz* 1896;12:216.
- Cuneò D, Delamare G. Anatomie et histologie des lymphatiques de l'estomac. *J Anat Physiol* 1900.
- Poierier V, Charpy A. *Traité d'Anatomie Humaine*, 2, f. 4, 1115, Paris, 1900.
- Bartels P. Das Lymphgefässsystem in Bardeleben's Handbuch der Anatomie des Menschen. Ed. Fisher, Jena, 1909.
- Idanov D.A. Die Lymphgefäße der Muskeln der oberen Extremität des Menschen. *Proc IV Congr. Zool. Anat Histol U.S.S.R., Kiev*, 1930.
- Rouviere H. *Anatomie des lymphatiques de l'homme*. Paris: Masson; 1932.
- Defrise A. Primo saggio di ricerca radiografica del Sistema Linfatico. *Atti Soc Ital Ant I Congr Monit Zool Ital* 1929;44:568.
- Ottaviani G. Indagini radiologiche sul sistema linfatico. *Arch Ital Anal Embr* 1930;28-38.
- Funaoka S. Der Mechanismus der lymphbewegung. Untersuchung über die physiologie der lymphbewegung. *Arb Anat Inst Kaiserl Univ Kyoto* 1930;1:1.
- Carvalho R, Rodriguez A, De Sousa-Pereira S. Sour la methode radiographique de mise en evidence des lymphatiques chez le vivant. *J Rad Électrol* 1934;18:180.
- Kynmonth JB. Lymphangiography in man. *Clin Sci* 1952;11:13.
- Taylor GV, Kinmonth JB. Lymphatic circulation studies with radioactive plasma protein. *Brit Med J* 1957;1:133.
- Milroy WF. Chronic hereditary edema: Milroy's disease. *JAMA* 1928;Oct 20.
- Osler W. *The Principles and Practice of Medicine: Medical Textbook designed for the Use of Practitioners and Students of Medicine*; 1892.
- Milroy WF. An undescribed variety of edema. *New York Med J* 1892;56:505.
- Meige H. Dystrophie oedémateuse héréditaire. *Presse Méd* 1898;6.11:341-3.
- Nielubovitz Olszewski W. Experimental lymphovenous anastomosis. *Br J Surg* 1968;55:449-51.
- Degni M. New technique of lymphatic-venous anastomosis (buried type) for the treatment of lymphedema. *VASA* 1974;3:479-83.
- Handley WS. Hunterian lectures on the surgery of the lymphatic system. *Br Med J* 1910;1:853-64.
- Halsted WS. The swelling of the arm after operations for cancer of the breast: elephantiasis chirurgica, cause and treatment. *Bull Johns Hopkins Hosp* 1921;32:309.
- Handley WS. Lymphangioplasty. *Lancet* 1908;1:783.
- Lisfranc J. *Clinique chirurgicale de l'Hôpital de la pitié*. Paris: Béchet Jeune et Labé; 1841.
- Lanz J. Er Öffnung neuer Abfuhrwege bei staung in Bauch und unteren extremitäten. *Zbl. Chir.* 1911;38:3.
- Samokhvalov IM, Tyniankin NA, Reva VA, et al. Oppel V., The military surgical legacy of Vladimir Oppel (1872-1932). *J Trauma Acute Care Surg* 2013;74:1178-81.
- Rosanow WN. Lymphangioplastik bei Elephantiasis. *Langenbecks. Arch klin Chir* 1912;99:645.
- Kondoleon E. Die lymphableitung, alshelmmittel bei chronischen oedemas nach Quetschung. *München Med. Woch* 1912;59:525.
- Charles H. A system of treatment. London: J.A. Churchill; 1912.
- Servelle M. La lymphangiectomie superficielle totale. *Rev Chir* 1947;85:294.
- Sistrunk WE. Further experiences with the Kondoleon operation for elephantiasis. *JAMA* 1918;71:800-6.
- Von Winiwarter A. Die chirurgischen Krankheiten der Haut und des Zellgewebes. Stuttgart: Ferdinand Enke; 1892.
- Hoffa A. *Technik der Massage*. Stuttgart: Ferdinand Enke; 1893.
- Herman Bucholz C. A manual of therapeutic exercise and massage, designed for the use of physicians, students and masseurs. Philadelphia and New York: Lea & Febiger; 1917.
- Kleen E. *Massage and Medical Gymnastics*. Churchill; 1918.
- Vodder E. *Manual de Lymphodreinae*. Congresso di Estetica di "Santé e Beauté", Paris, 1936.