

**Keynote Lecture**  
**Walchseer Lymphological Winter Conference**  
11th - 12th January 2019

**Lymphological expertise**  
**from Macro - to Microcosm**



Pic source: Cameron Gray in  
*FritjofCapra* December , 2015.

# Keynote Lecture Walchseer Lymphological Winter Conference Structure

I

- my personal and Life principles

## Lymphological Macro Cosmos

- Scientific star-hours "lymphological knowledge" from antiquity to the present in the fields of Anatomy-Pathology-Pathophysiology-Diagnostics-Conservative Therapy Methods.

- Prof.P. Hutzschenreuter : „ MLD (KPE) und Science“ - Literature -

## Lymphological Macro Cosmos

Bridges for research into the lymphological microcosm.

**"It must be assumed that the majority of our diseases are caused by micro-edema in the connective tissue."**

*Quote: Prof. H.Weissleder nach Prof.H.Wittlinger in „Eine kleine Geschichte der Lymphologie“*

**The Endothelium : the Chief Conductor in the human organism is a "systemic effective organ".**

**Keynote Lecture**  
**Walchseer Lymphological Winter Conference**  
**Structure**  
**II**

**Microcirculation**

**The phenomenon of chron. Inflammation in the vascular lymph system**  
relevant publications on the topic

**The Science of Microparticles - Sophisticated Vesicles !**

**The World of Microcirculation Research and its Importance for MLD**

**PMFT (pulsed magnetic field therapy) – complementary helpful for KPE :  
results of the pilot study 2015**

**Lymphological macro-micro-cosmos and beyond....**  
**The soul-body axis**

# Good quality of life thanks to information therapy



Rheumatism Clinic Bad Kreuznach  
Surgery Garmisch-Partenkirchen  
Dermatology Uni-Munich  
Internal Medicine Uni-Munich



Indian Medicine Andes/Peru  
Specialist practice Bad Feilbach - Chiemgau  
Head of German Acupuncture Centre  
Oncology Bad Aibling  
Medical Park Clinic Bad Wiessee  
Lymph Clinic Wittlinger Walchsee



Specialist in Internal Medicine ,  
Rheumatology-  
Cardiology - Lymphology  
Naturopathy , sports medicine  
Endothelial sciences

heart attack prevention  
endothelial diagnostics  
endothelial therapy  
endothelial research

Biophysical influences on the Endothelium  
Endothelial Acupuncture - Endothelial and Environmental Protection  
Endothelium and water quality  
Physical vascular therapy (information therapy)



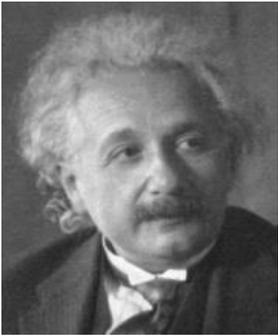
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## Maxime of my Life :



Fantasy is more important than knowledge, because knowledge is limited.  
But fantasy embraces the whole world.



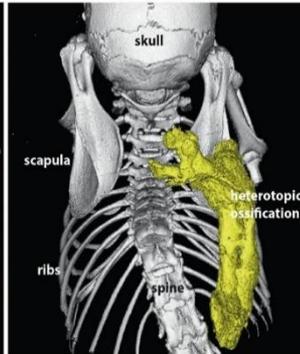
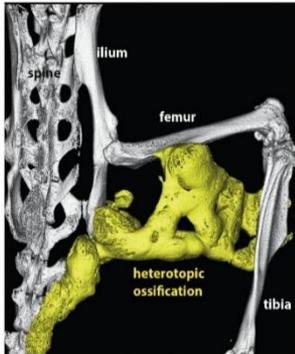
Academic freedom is the freedom to learn as much as you want.  
Two things tend to slow down the progress of medicine:  
authorities and systems.



"Any material structure, including the human body, can be understood as complex vibration system which is caused by interference with the innumerable individual frequencies of atoms and molecules and is absolutely specific to the type and composition of the respective structure and reacts individually to biophysical signals " !

**Don't ever forget to laugh...!**

## How it all started... In the Rheumaklinik Bad Kreuznach 1979 - Prof.Schilling



### 25-year-old female patient with the diagnosis :

Generalized soft-tissue Spine and joint ossifications ,  
(L'Homme du Bois) of both shoulder, hip, knee and ankle joints ,  
and predominantly polyarticular of the finger and toe joints,  
progressive since 15 years of age despite supportive therapy (cortisone/NSAR),  
**Significant improvement (!)** after six-monthly  
psycho-neuro-immunological therapy (mental behaviour training) .

### What happened here?

[Cell Tissue Res.](#) 2012 Jan; 347(1): 177–186.

Regulation of endothelial cell plasticity by TGF- $\beta$

[Laurens A. van Meeteren](#)

[Best Pract Res Clin Rheumatol.](#)

Published in final edited form as:

[Best Pract Res Clin Rheumatol.](#) 2008 Mar; 22(1): 191–205.

**Fibrodysplasia ossificans progressiva**

[J Bone Miner Metab.](#) 2008; 26(6): 521–530.

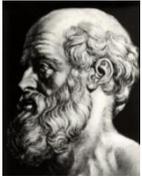
Published online 2008 Nov 1. doi: [10.1007/s00774-008-0879-8](#)

**Skeletal metamorphosis in fibrodysplasia ossificans progressiva**

**(FOP)** [Frederick S. Kaplan et al.](#),

# Lymphological Macro Cosmos I

History of Lymphology and Manual Lymph Drainage



## The white vessels

The ancient Greeks knew about the lymphatic vessels and spoke of the "white" vessels in contradiction to the "red" and "blue" vessels of the bloodstream. **Hippocrates (460-377 B.C.)** already spoke of the lymphatic system as "vessels that carry white blood".

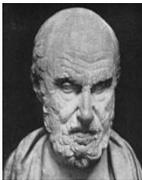


## Aristoteles (384-322 v. Chr.)

describes vessels that carry "white blood" in humans and animals as "ductus lactei"

In biology, Aristotelian views could persist until the 18th century.

Thus William Harvey, 1578 - 1657, assumed with the discovery of the blood circulation from Aristotle's principle that nature produces nothing unnecessary, and used it to determine the nature of the blood vessels and ventricles.



**Erasistratos** (\* around 305 v. Chr. in Julis, auf Keos; † around 250 v. Chr.) was a Greek doctor and naturalist, anatomist, surgeon and physiologist. As co-founder of the **Alexandrian medical school**, he describes "Milk vessels" in the "lamb".

**Abū Alī al-Husain ibn Abd Allāh ibn Sīnā** \* around 980 † Juni 1037 – short Ibn Sina and Latinized **Avicenna** - was a Persian doctor.

He is one of the most famous personalities of his time and has shaped the history and development of medicine in particular.



## Bartolomeo Eustachi,

(\* between 1500 and 1520 † 27. August 1574)

was an Italian doctor and anatomist. In 1552 he wrote a textbook of anatomy, the **tabulae anatomicae**, in which "lymphatic vessels" are described: "**Vena alba thoracis**" in the horse. The book, which was not published until 1714, contained a remarkable collection of anatomical drawings.

Pics source: Wikipedia

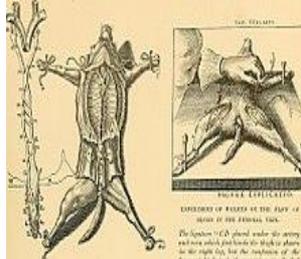
Text-source: Eine kleine Geschichte der Lymphologie :Ch. Schuchhardt und H.Wittlinger,H.Rabe: Viavital Verlag ,Köln 2003  
Scholars and scientists in the history of the lymphaticsystem. Journal of Anatomy. DOI: 10.1111/joa.12644



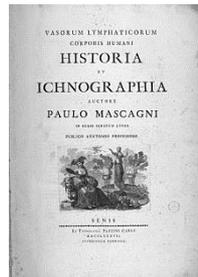
# Lymphological Macro Cosmos I

The 17th century was the golden age for the study of the lymphatic system with several discoveries:

**Caspar Asellius** (1581-1672) is considered the actual discoverer of the lymphatic system. In 1622 he discovered lymphatic vessels in dogs. He assumed that the newly discovered vessels were used to transport the resorbed food from the intestine to the liver.



**Jean Pecquet** (1622-1674) : succeeded in proving that the vessels discovered by Aselli did not flow into the liver but into a bag-shaped extension in front of the lumbar spine, called Cisterna Chyli. (In French this Cisterna is called "Cisterna Pecquet"). Pecquet also described the further path of the lymph through the large thoracic duct with its opening into the left angle of the vein. Pecquet was the first to prove the connection of the lymphatic vascular system with the blood circulation.



**Paolo Mascagni** (1752-1815) published his book **Vasorum lymphaticorum corporis humani historia et iconographia** in Siena in 1787, which identified him as a specialist in the human lymphatic system and established his reputation in Europe. His drawings of these fine ramifications are still valid today. He also described quite precisely the possible causes of lymphedema.

Pics source: Wikipedia

Text-sources: Scholars and scientists in the history of the lymphatic system. Journal of Anatomy. DOI: 10.1111/joa.12644.

The Discovery of the Lymphatic Circulation. Acta Physiologica Scandinavica. Supplementum, 463: p. 9-10.

# Lymphological Macro Cosmos III

## from Anatomy to Physiology

In 1650, the Swedish physician **Olof Rudbeck** intensively studied the lymph vessel system and recognized its importance. 1652 he discovered the lymph vessels of the intestine, the spleen and the liver. He was the first to discover that lymph flowing from the tissue via the lymph vessels to the body circulatory system.

**William Hunter** (\* [1718](#) † [1783](#) ) describes the entire lymphatic system of the body - this not only affects the belly area, but the whole body in the sense of a "large and general system".

**William Hewson** (1739-1774) knowing about the work of William Hunter he worked on physiological problems of "lymph formation"

**Carl Ludwig** (\* [1816](#) † [1895](#) ) : succeeded in the first cannulation of the lymph vessels - Berliner Blau for the depiction of lymphatic vessel. Increase in blood capillary pressure leads to increased fluid filtration and evacuation via the lymph vessel system.

**Cecil Kent Drinker** (1887-1956) :

He was the first to prove that blood proteins are able to leave the bloodstream and that these plasma components are only reabsorbed by the lymphatic vessels.

Text-sources:

Peter Zupan: *Der Physiologe Carl Ludwig in Zürich 1849–1895* (Zürcher medizinisch-geschichtliche Abhandlungen Nr. 188), Zürich 1987.

Heinz Schrör: *Carl Ludwig. Begründer der messenden Experimentalphysiologie 1816–1895* (Große Naturforscher 33), Stuttgart 1967

Lymphatics, lymph, and lymphoid tissue; their physiological and clinical significance, Cambridge, Mass., Harvard University Press, 1941.

Wikipedia

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# Lymphological Macro Cosmos IV

## The 20th century

### Therapeutic methods and instrumental diagnostics

Due to improving technical possibilities offered through imaging, it was possible to improve diagnostics and as a result to improve therapy methods.

**Alexander von Winiwarter** reports in 1892 about the treatment possibilities of Lymphedema with massages, bandages and mobility exercises.

**Estrid & Dr. phil. Emil Vodder** in Paris at the Beauty and Health Exhibition in 1936, manual lymph drainage was introduced as a universal therapy.

**In the 1930s**, Emil Vodder described a gentle, effective treatment of edema that stimulates lymph transport by increasing lymph vessel activity. In 1985 he was awarded the Rohrbach Medal by the Physical Therapy Association in recognition of his life's work. This award was also associated with the confirmation of a professional association that Emil Vodder is the creator and eponym of his method: **Manual lymphatic drainage according to Dr. Vodder**.

**Der Arzt J.Asdonk** got to know the "manual lymphatic drainage" according to Emil Vodder in 1963.

He introduced the subsequent compression bandage into the treatment scheme in order to maintain the volume reduction achieved by manual lymph drainage. In the meantime, this so-called complex physical decongestion therapy (KPE) has established itself worldwide as the most effective treatment for lymphedema. In 1967, the "Gesellschaft für manuelle Lymphdrainage nach Dr. Vodder" was founded in Essen. From this society the **German Society for Lymphology** was founded in 1976 with the participation of Eberhard Kuhnke, Gregl, Földi and Hohlbaum. Especially the cooperation with E. Kuhnke and Földi brought a lot of dynamism to the still young lymphology at that time, because they developed the theoretical basics of this therapy.

**Prof. Hildegard Wittlinger - The spirit of the house "Wittlinger"**

Massage therapist Specialist teacher for manual lymphatic drainage according to Dr. Vodder/KPE  
Co-founder of the "Gesellschaft für Manuelle Lymphdrainage according to Dr. Vodder", book author  
"Manuelle Lymphdrainage nach Dr. Vodder"

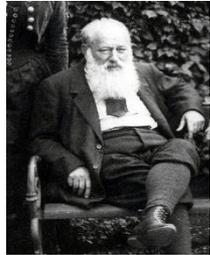
**Frau Prof.Wittlinger** travels to lectures and courses in many European countries and also overseas, mainly to the USA and Canada, where she introduced the Vodder Method in Manual Lymph Drainage to interested therapists. Due to its intensive teaching, the Dr.Vodder School Austria has gained a worldwide reputation.

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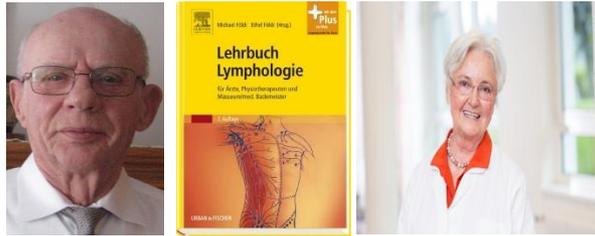
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# Lymphological Macro Cosmos V

## The scientific "lighthouses" in the field of lymphology



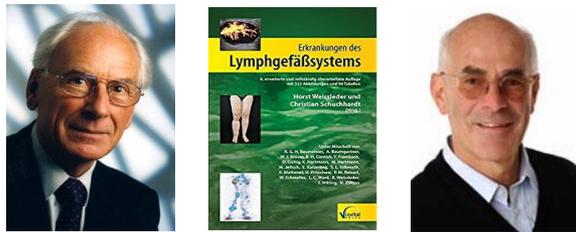
### Lymphology as a life mission :

**Prof. Prof. h.c. Dr. med. Michael Földi** with his wife **Dr. med. E. Földi**, as an internist, lymphologist and international capacity, has had a significant influence on lymphology in Germany and worldwide.

**Prof. H. Weissleder** : Former President of the German Society of Lymphology.

Expert in lymphological imaging: Example:

Diagnostics of the lymphatic system over time : direct lymphography, fluorescence micro-lymphography, capillary scintigraphy, sonography, computer tomography, Magnetic resonance tomography and MRI lymphography - Possibilities and limitations of the individual examination procedures - LymphForsch 16 (2) 2011



**Dr. med. Ch. Schuchardt** Internist, haematologist and internal oncologist - medical director of several schools for manual lymphatic drainage in Asdonk/Földi (Switzerland, Germany, Canada). Regular lectures at home and abroad. Former President of the German Society of Lymphology.



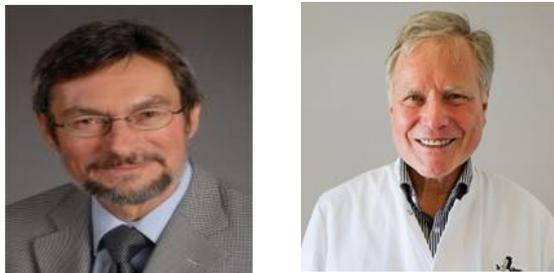
**Ao. Univ. Prof. Dr. E. Brenner**

Clinical-functional anatomy University of Innsbruck

**Prof. Dr. Dr. med. habil. R. Baumeister**

Consultant for Lymphology and Reconstructive Microsurgery

Specialist for: Surgery , Vascular surgery , Trauma surgery , Plastic surgery.



**Dr. med. W.J. Brauer** - Radiology : currently:

Possibilities and limits of sonographic lymph node diagnostics : how to do it, LymphForsch 22(2)2018

**Dr. F.J. Schingale**

Medical director of the Lympho-Opt-Klinik

Specialist in liposuction.



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# Prof.P. Hutzschenreuter : „MLD (KPE) and Science“ - literature-extract -

## Lymph formation and lymph transport in experimental lymphedema.

Hutzschenreuter P., Brümmer H.  
Aktuelle Beiträge zur Manuelle Lymphdrainage. 1992; 3: 8-11

## Spontaneous anastomosis of lymph collectors after lymphadenectomy - an experimental study.

Hutzschenreuter P., Brümmer H.  
Aktuelle Beiträge zur Manuellen Lymphdrainage: 1992, 3: 24-33

## Scar and lymphatic drainage.

Hutzschenreuter P., Brümmer H.  
Aktuelle Beiträge zur Manuellen Lymphdrainage: 1992, 3: 88/89

## The vegetative nervous system in patients and practitioners treated with manual lymph drainage according to Dr. Vodder.

Hutzschenreuter P., Wittlinger H., Hermann H., Silberschneider K., Kitzbichler M.  
Aktuelle Beiträge zur Manuellen Lymphdrainage. 2000; 7: 109

## The effect of manual lymphatic drainage on arterial occlusive diseases in the pAVK IIa stage.

Hutzschenreuter P., Ehlers R.  
Aktuelle Beiträge zur Manuellen Lymphdrainage. 1992; 3: 85-87

## Change of the microcirculation during the manual lymph drainage technique according to Dr. Vodder.

Hutzschenreuter P., Brümmer H., Kurz I., Wittlinger D.  
Aktuelle Beiträge zur Manuellen Lymphdrainage. 1992; 3: 44-52

## Manual lymphatic drainage and smooth musculature.

Hutzschenreuter P.  
Aktuelle Beiträge zur Manuellen Lymphdrainage. 1994; 4: 32-34

## Microcirculation in AVK and diabetes mellitus.

Hutzschenreuter P.  
Aktuelle Beiträge zur Manuellen Lymphdrainage. Band 6, Heidelberg:  
Karl F. Haug Verlag, 1998

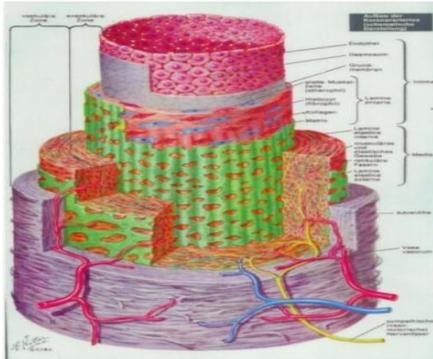
## The effect of lymph drainage on vasomotion.

Hutzschenreuter P., Brümmer H.  
Aktuelle Beiträge zur Manuelle Lymphdrainage. 1992; 3: 19-20

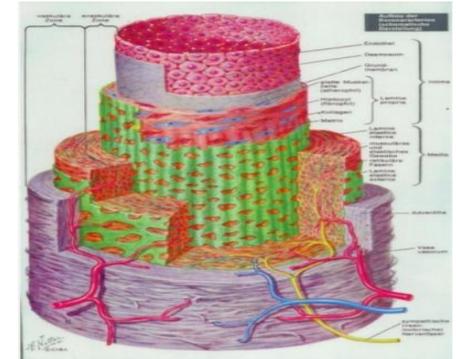
# Lymphological Micro Cosmos

## The Endothelium

# What is the Endothelium?



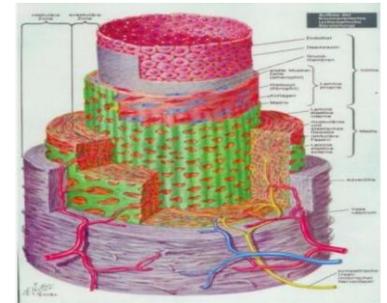
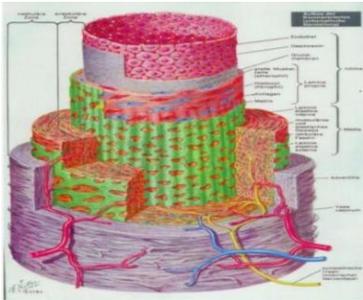
**pawelke**  
**prevent**  
Dr. Rainer Pawelke



# Definition : Endothelium

Single-layer cell structure which covers the inner vessel wall  
of arteries, capillaries, lymph vessels and veins.

The endothelium operates as a biological network system  
(biological sensor and signal generator) in response to all internal  
and external influences. and is responsible for the energy supply  
to approx. 80 trillion cells!



# Lymphological Micro Cosmos

## The Endothelium

The Endothelium - the "chief conductor" - is a systemic organ !

## THE ENDOTHELIUM

Covering an area of 6-8000 square meters  
Weight : 1,5 Kg.

**Biological Sensor :**

**Expression of endothelial receptors :**

Growth-factors : IGF, FGF, VEGF, ICAM, VCAM, P-Selektin, Cytokine, bakterielle Toxine, Neuropeptide, CRH

**Biological signal transmitter :**

Production of vasoactive peptides and hormones

**Vasodilators :** NO, Prostacyclin, EDHF, Bradykinin, Adrenomedullin, C natriuret. Peptid, ADP...

**Vasoconstrictors :** Endothelin-1, Angiotensin II, Thromboxan A2, Prostaglandine, Hydrogen peroxide, Freie Radikale.....

**Major Tasks of the Endothelium :**

**Regulation of homeostasis and haemostasis / thrombosis , immunomodulation  
vasorelaxation and constriction**

**vascular growth - vascular tightness - remodeling - apoptosis ...!**

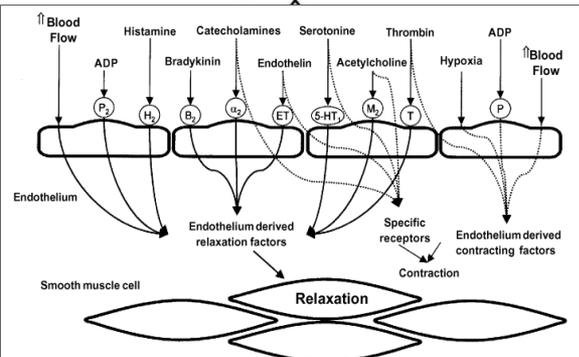
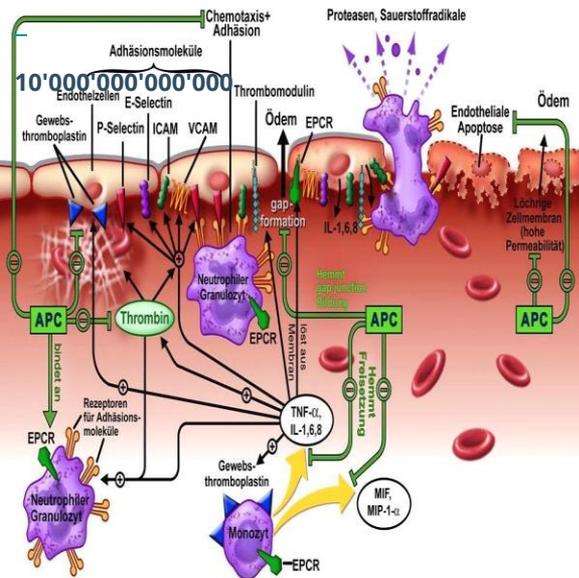


Fig. 1 - Diagram describing the action of various effectors on functionally intact endothelium. Receptor stimulation or direct action of these agents led to the liberation of endothelium-derived relaxation factors (nitric oxide, prostacyclin) that cause vascular smooth muscle cells to dilate. In contrast, serotonin, catecholamines, endothelin, acetylcholine, thrombin, hypoxia, and the stress of shearing (blood flow) may cause contraction of vascular smooth muscle cells. In functionally intact endothelium, vasodilatation predominates (1-12). Histamine receptor, a2-a-adrenergic receptor, 5-HT -serotonergic receptor, B-bradykinin receptor, M-muscarinic receptor, P-purinergic receptor, ET-endothelin receptor, T-thrombin receptor.



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# The Endothelium - the "Chief Conductor" - is a systemic organ !



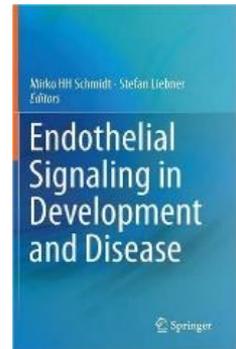
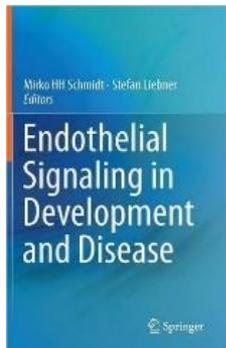
From conception to death, the Endothelium is **THE** coordination center of all "Life-creating, sustaining, and terminating mechanisms."

It is a **key factor for development and differentiation** of the entire **vascular and lymphatic system** :

VEGF and Notch Signaling in Angiogenesis :

Pericytes in Vascular Development and Function :

Development and Differentiation of the Lymphatic Vascular System



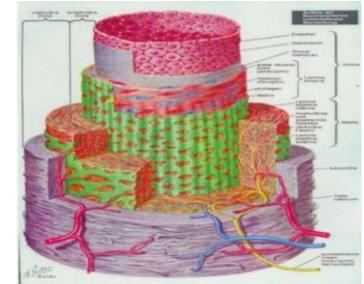
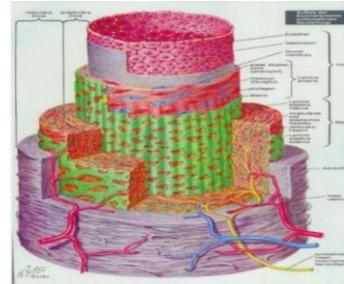
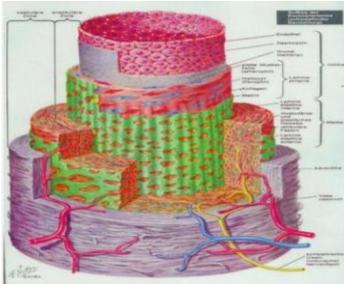
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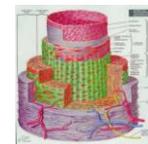
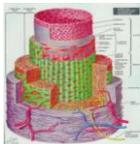
# What is the importance of keeping my Endothelium in good health?



A " well-kept "  
Endothelium gives  
statistically 14.2 years of  
life !

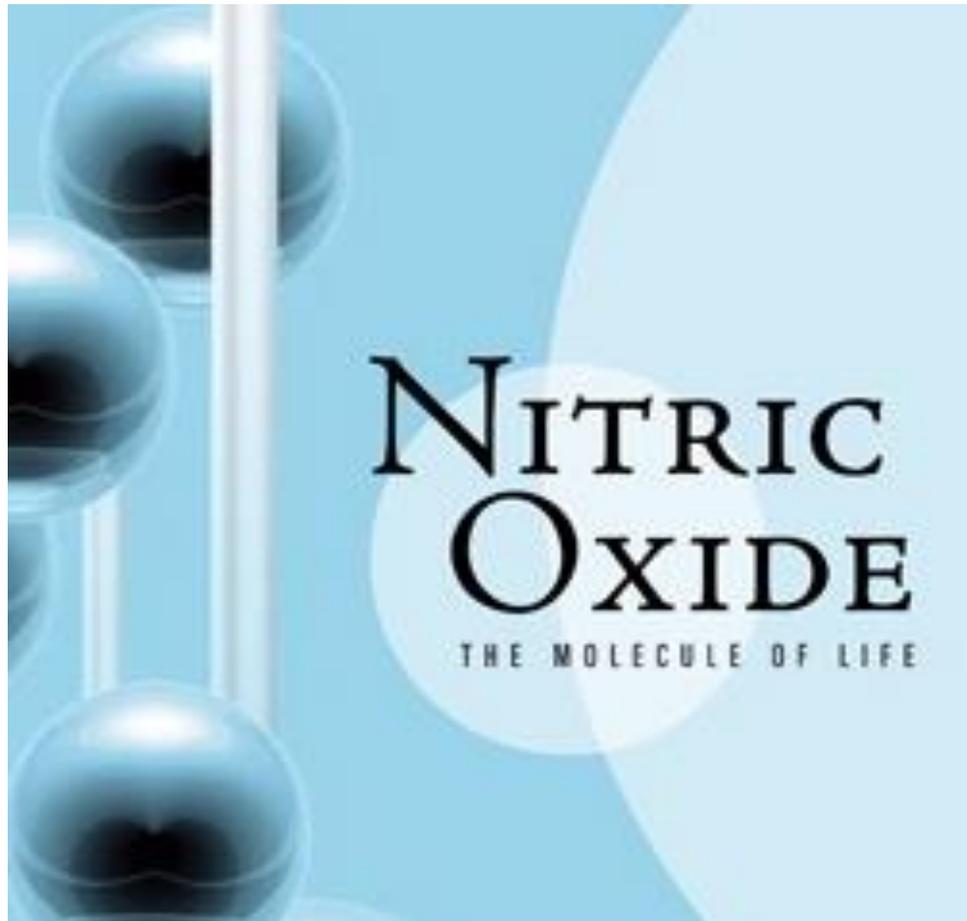
**NEJM 2012;366:321 : Cardiovascular Lifetime Risk Pooling Project**

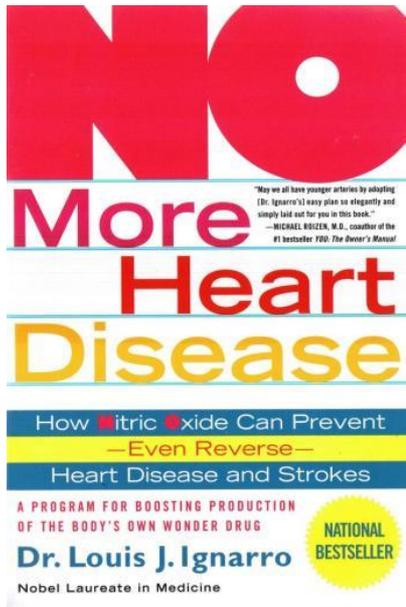
# Molecular reaction fields of the Endothelium



Group	Function	Receptor/Cytokine/ Protein
Receptors of the immune system	Cell adhesion and cell migration	<p>ICAM -1 = Intercellular Adhesion molecule -1 (CD54)                      ICAM - 2 = Intercellular Adhesion molecule -2 (CD102)                      VCAM-1 = Vascular Cell Adhesion Molecule-1 (CD 106)                      E-Selectin = Endothelial Selectin (ELAM-1) (CD 62E)                      P-Selectin = Platelet Selectin(CD 62P)                      PECAM-1 = PlateletEndothelial Cell Adhesion Molecule-1 (CD31) VAP-1 = Vascular Adhesion Molecule -1 <b>VEGF=VascularEndothelial Growth Factor</b>                      LFA-3 = Lymphocyte Function Antigen -3 (CD 58)                      Endoglin = TGF-β binding protein = Transforming Growth Factor β</p>
	Antigen-presentation	<p>MHC – 1 = Major Histocompatibility Complex Class I                      MHC – 2 = Major Histocompatibility Complex Class II</p>
Coagulation-active substances	Pro-coagulation	Tissue Factor (Thromboplastin) v.Willebrand Factor
	Anti-coagulation	PAF = Platelet Activating Factor (CDw 109) Kininogen
	Fibrinolysis	<p>TFPI = Tissue Factor Pathway Inhibitor (Fxa-Inhibition)                      PSBP= Endothelial Cell Derived Protein S Binding</p>
vasoactive substances	Dilatation	<p>tPA = Tissue Plasminogen Activator                      PAI-1= Plasminogen Activator Inhibitor                      HS = Heparansulfat (AT III binding)                      PG I-2 = Prostaglandin I-2 Inhibitor</p> <p><b>NO = Nitric Oxide</b></p>
	Constriction	<p>Endothelin -1                      ACE= Angiotensin Converting Enzym</p>
Cytokine / chemokine/ Receptors	TNF -alpha	<p>IL-1, IL-6, IL-8, MCP 1u3, G-CSF,GM-CSF, TGFβ,                      TNF-R-I (p55),TNF-R-II (p75),IL-1R, IL-3R,IL-6R                      PG=proteoglycan,Fibronectin,Elastase, Collagenase  <b>PIEZO 1</b></p>

# What is „NO“ ? !

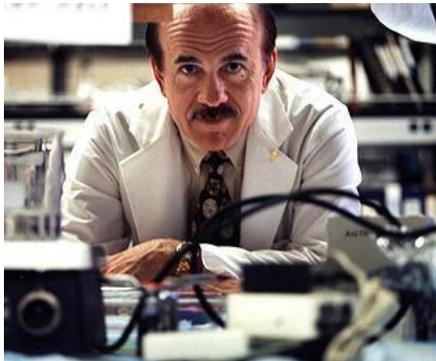




= NITRIC OXID

is the most important protector  
of the ENDOTHELIUM towards  
the vascular inflammatory process!

**EVERYWHERE !!**



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# NO is a gas.....

...which exists in the vessels and in the vascular bed in the form of a NO vapour and provides the adequate energy supply for the cells .... !

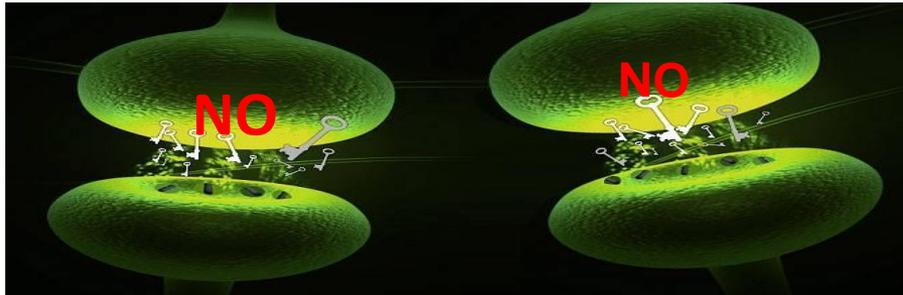


**NO regulates : the blood pressure !**

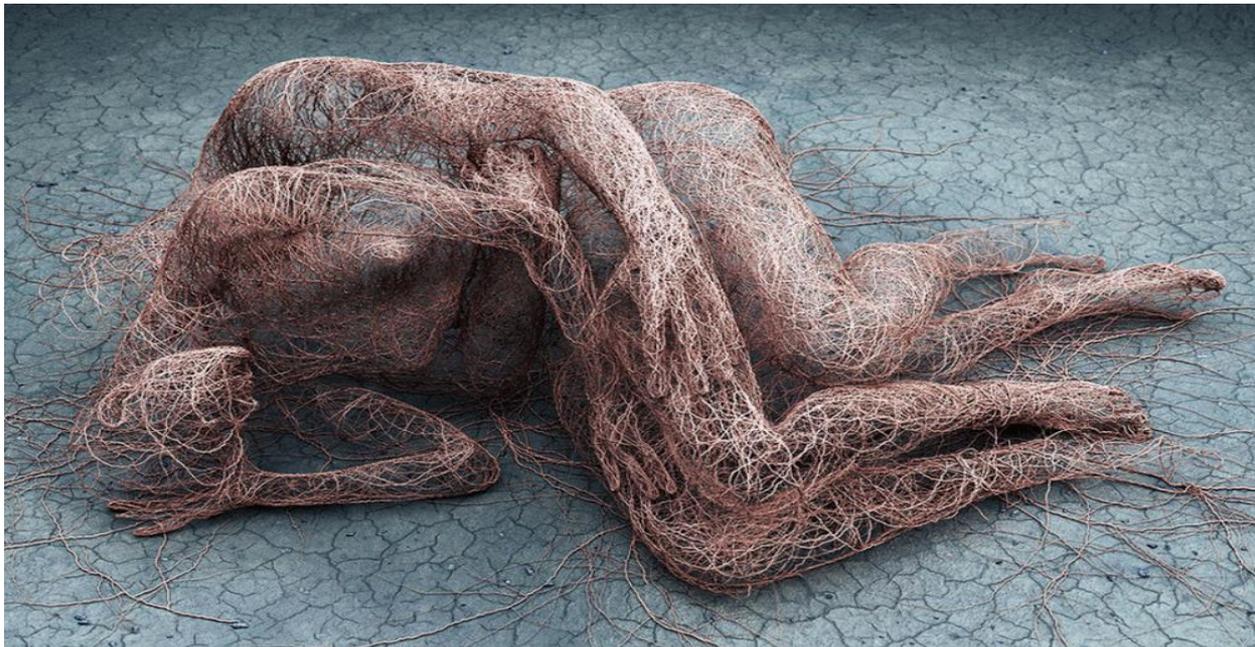


# NO regulates .....

the nerve signal transmission.  
the learning process! ...  
the memory !



**NO** regulates.... ..... the cell supply via the  
blood distribution adjusted to the need  
in the field of microcirculation !





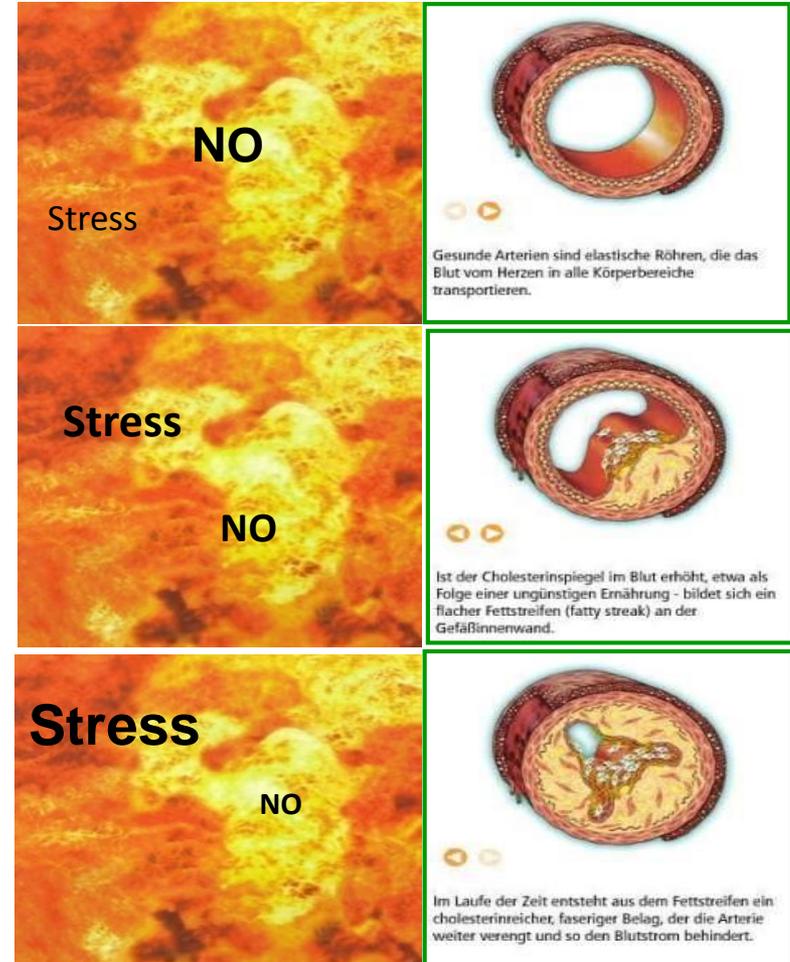
# NO-deficiency - Endothelial dysfunction - aging process

## NO-deficiency :

The reduced bioavailability of **NO** - the body's own "anti-rust agent" - plays a significant role in atherogenesis and in the dynamics of ageing processes.

The protection of **NO** is synonymous with arteriosclerosis prophylaxis.

Lüscher et al. / Zürich  
Ignarro et .al  
Drexler H.



# Endothelial medicine : Why does the endothelium get sick?

## Imbalance between aggressive factors (inflammatory stress) and the endothelial protection factor NO.

nicotine consumption , reactive oxygen species (ROS)

Physical / Chemical stress/ Water quality!

Environmental stress / pesticides / nutritional stress

Lifestyle / Family Amnesty

Sports inactivity / osteoporosis body weight

Chronic inflammation !!!! / Rheumatism

Elevated blood pressure

Fat metabolism disturbance/food additives !!

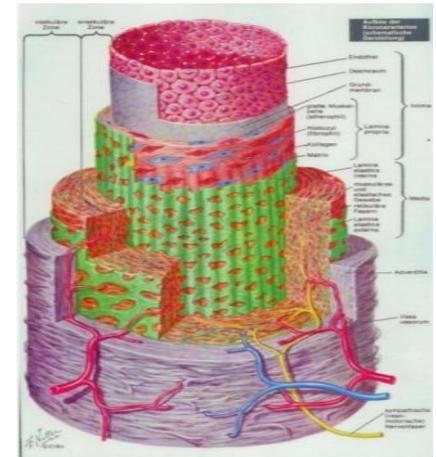
Diabetes mellitus

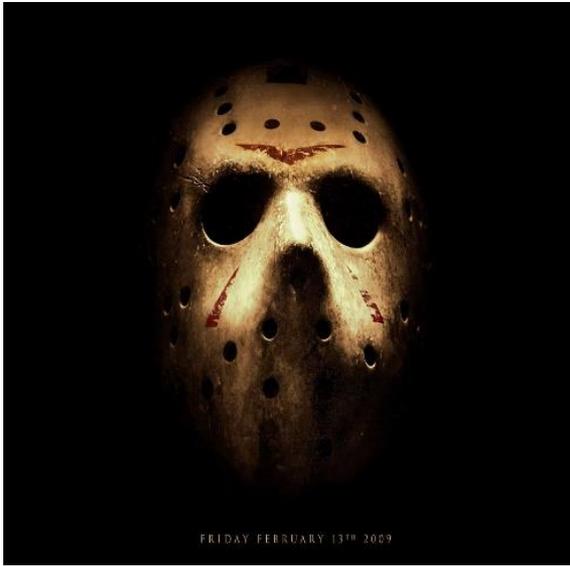
emotional and mental stress, noise pollution!!!

Depression, anxiety, panic Depressive episodes or chronic

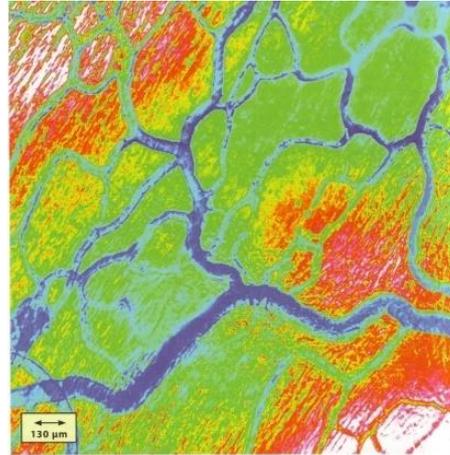
Depression are precursors of disease on the the way to coronary heart disease

**NO** ↓





**Stress !!**

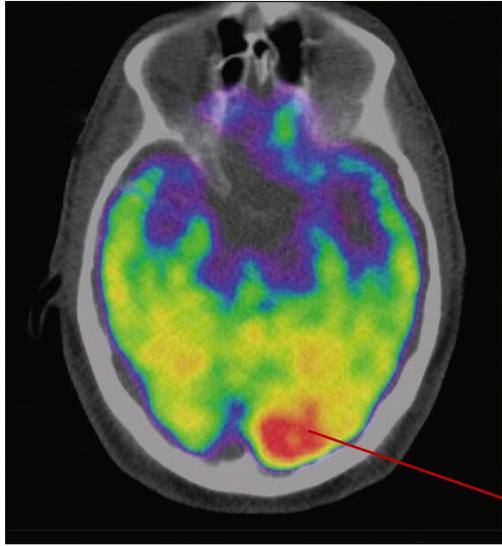


**Stress !!**



## Stress leads to inflammations in the body, without any germs.

The Lancet 2017, online .11.01.2017 Dr.Ahmed Tawakol Harvard, Boston

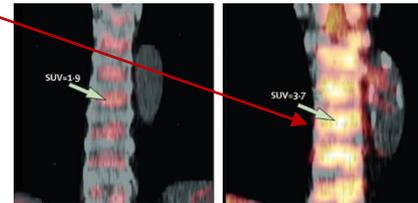
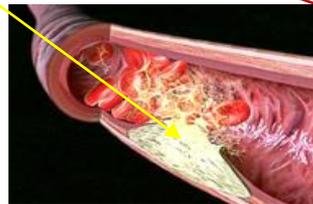


In this study, 293 patients received a combined PET / CT scan to document the activity and inflammation of their arteries in the brain, bone marrow and spleen.

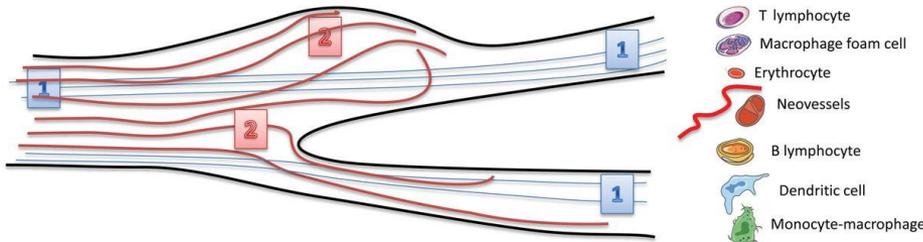
High activity of their amygdalae resulted in a 60% higher risk. (P <0.0001) for myocardial infarction, angina, heart failure, stroke and peripheral arterial disease.

During stress, signals are apparently sent from here to the bone marrow and other body regions to increase the production of white blood cells and other inflammatory substances.

Brain scans of volunteers showed in of the study increased activity of the amygdala.  
(Photo: REUTERS)



# Endothelfunction and Shear/Stress !



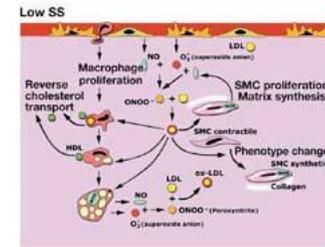
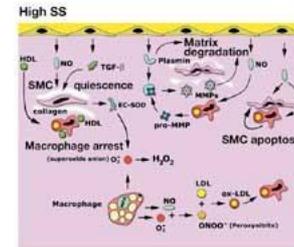
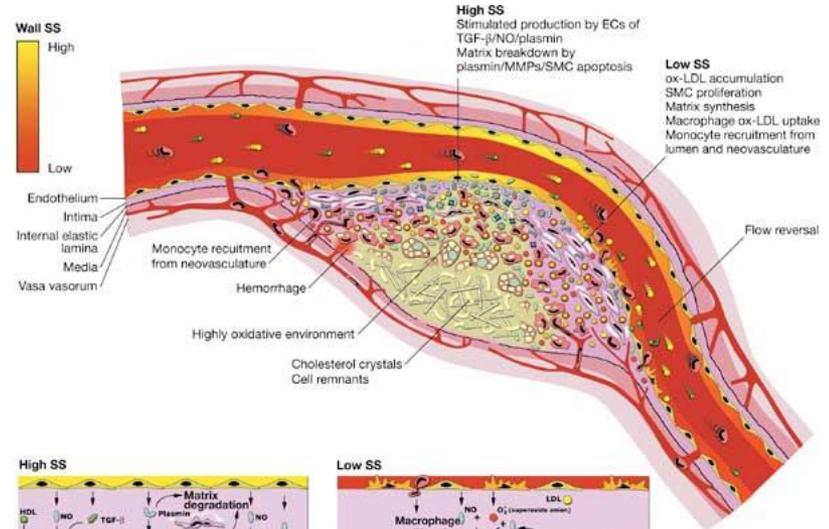
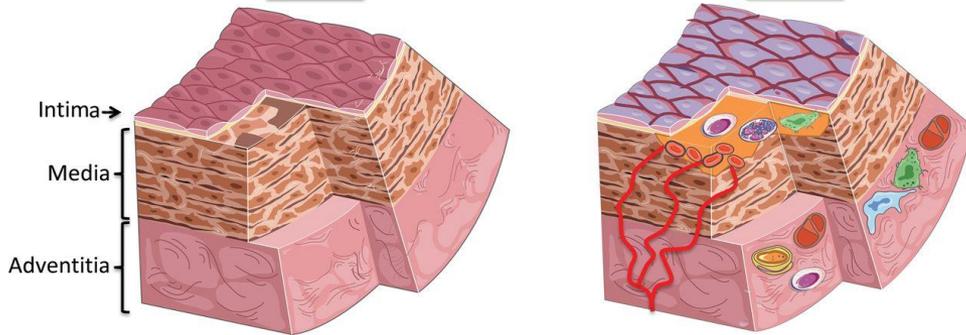
- T lymphocyte
- Macrophage foam cell
- Erythrocyte
- Neovessels
- B lymphocyte
- Dendritic cell
- Monocyte-macrophage

**1**  
 ↑ Shear  
 ↓ Strain

Functional endothelial barrier  
 Cell survival and low turn over  
 Anti-inflammatory, anti-coagulant  
 Low oxidative stress

**2**  
 ↓ Shear  
 ↑ Strain

Loosened endothelial barrier  
 Cell death and high turn over  
 Epigenetic modifications  
 High oxidative stress and inflammation  
 Neo-angiogenesis, haemorrhage, leucocyte extravasation

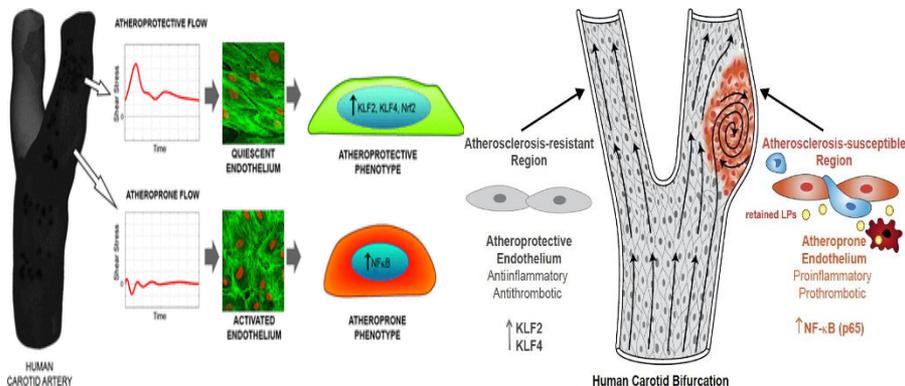


- EC—endothelial cell
- EC—apoptotic
- SMC—synthetic
- SMC—contractile
- SMC—apoptotic
- Monocyte
- Macrophage
- LDL
- ox-LDL
- HDL
- EC-SOD
- Plasmin
- pro-MMP
- MMP
- TGF-β
- NO
- O<sub>2</sub>
- ONOO<sup>-</sup>
- Collagen
- Cholesterol crystal
- Cell remnants

# Shear stress dependent **vascular inflammatory activity** at nuclear level Endothelial dysfunction

Endothelial cells exposed to **low oscillating shear stress (OSS)** show **proinflammatory response** due to the increased expression of **proinflammatory genes (VCAM-1, BMP4, MMPs) !**

Endothelial cells exposed to fast harmonic flow, high shear stress (HSS), react anti-inflammatory due to the expression/production of anti-inflammatory genes = atheroprotective genes (Klf2, Klf4, eNOS).



**Conclusion:**

**"Reduced vascular inflammation"** through sporting + mental activity / good water quality / trained stress management ...positive lifestyle (!) ..... (Avoid niggers and "know-it-all"!)  
....

Stress influences the quality of endothelial flow profiles and deteriorates thus pre-existing endothelial dysfunction disorders !

**Endothelial diseases are "curable"!**

## RESEARCH ARTICLE

**Shear-sensitive microRNA-34a modulates flow-dependent regulation of endothelial inflammation (Huvec)**

Wendong Fan, Rong Fang, Xiaoyuan Wu, Jia Liu, Mingzhe Feng, Gang Dai, Guojun Chen, Guifu Wu  
J Cell Sci 2015 128: 70-80

**"In the present study, we report that mechanosensitive miR-34a modulates the flow-dependent regulation of endothelial inflammation, partially through sirtuin 1 (SIRT1) and its downstream nuclear factor  $\kappa$ B (NF- $\kappa$ B) signaling pathway".**

# Diagnostik der Endotheldysfunktion:

Inflammatorischer Stress gilt heute als Hauptvermittler beschleunigter Alterungsprozesse.

## Risikomarker:

ox.LDL / LOX-1 , Pb,Hg,Fe,Cu

PAI-1, Vitaminmangel, spez. B-Gruppe , Selen, Homocystein...

IL-1,NT-proBNP,

Prostaglandin E2

VCAM-1 / sP-Selektin / ICAM-1

NFkB / IL-6 / TNF $\alpha$

Leucotrien B4

MCP-1, ADMA

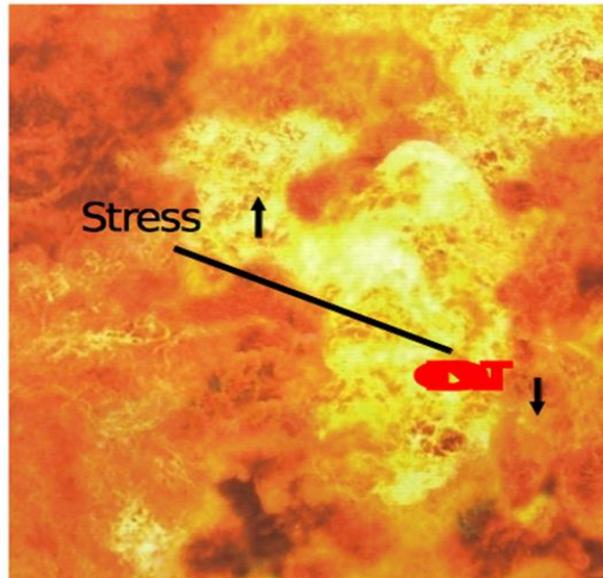
Myeloperoxidase

CRP, CD-40-Ligand

Platelete aggregation

Lipoprotein a ,EBV,CMV,

Herpes -Virus



Quellen:

NEJM: Vol. 349: 1595-1604, Nr. 17, Oktober 23, 2003

Cardiovasc Res. 2003 Jan; 57(1): 238-43

Biochem. Biophys Res Commun. 2001 Dec 14; 289(4):857-61

Eur J Clin Invest. 2005 Jan; 35(1):47-51

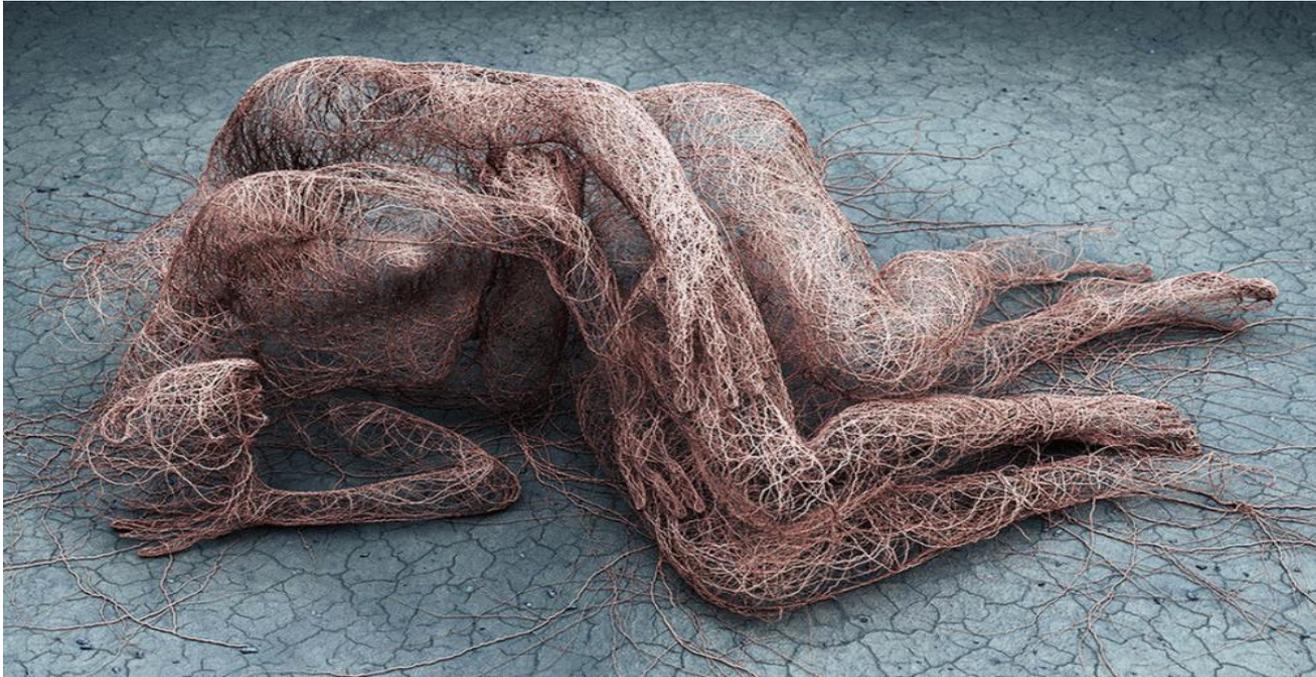
Clin Exp Pharmacol Physiol. 2004 Jul; 31(7):407-13

Atherosclerosis. 2002 May;162(1):179-85

Murad Atmaca et al. :Serum folate and homocysteine levels in patients with obsessive-compulsive disorder; Psychiatry Neurosciences 59 (5), 616-620; Firat University, School of Medicine, Elazig, Turkey:

Circulation:Vol.117, 2008:Extreme Lipoprotein a Levels and Risk of Myocardial Infarction..."The Copenhagen City Heart Study

# The Mikrocirculation !



[Circ Res.](#) 2016 Jan 8;118(1):157-72.

**The Human Microcirculation: Regulation of Flow and Beyond.**

[Gutterman DD](#)<sup>et al.</sup>

[J Am Heart Assoc.](#) 2016 Nov 4;

**"Small Blood Vessels: Big Health Problems?,"**

**Scientific Recommendations of the National Institutes of Health Workshop.**

# Microcirculation

the functionally most important part of human blood circulation.

Microcirculation includes:

The blood and its components, blood vessels with diameter( $d$ )  $< 100 - 200\mu\text{m}$  (arterioles, capillaries, venules),

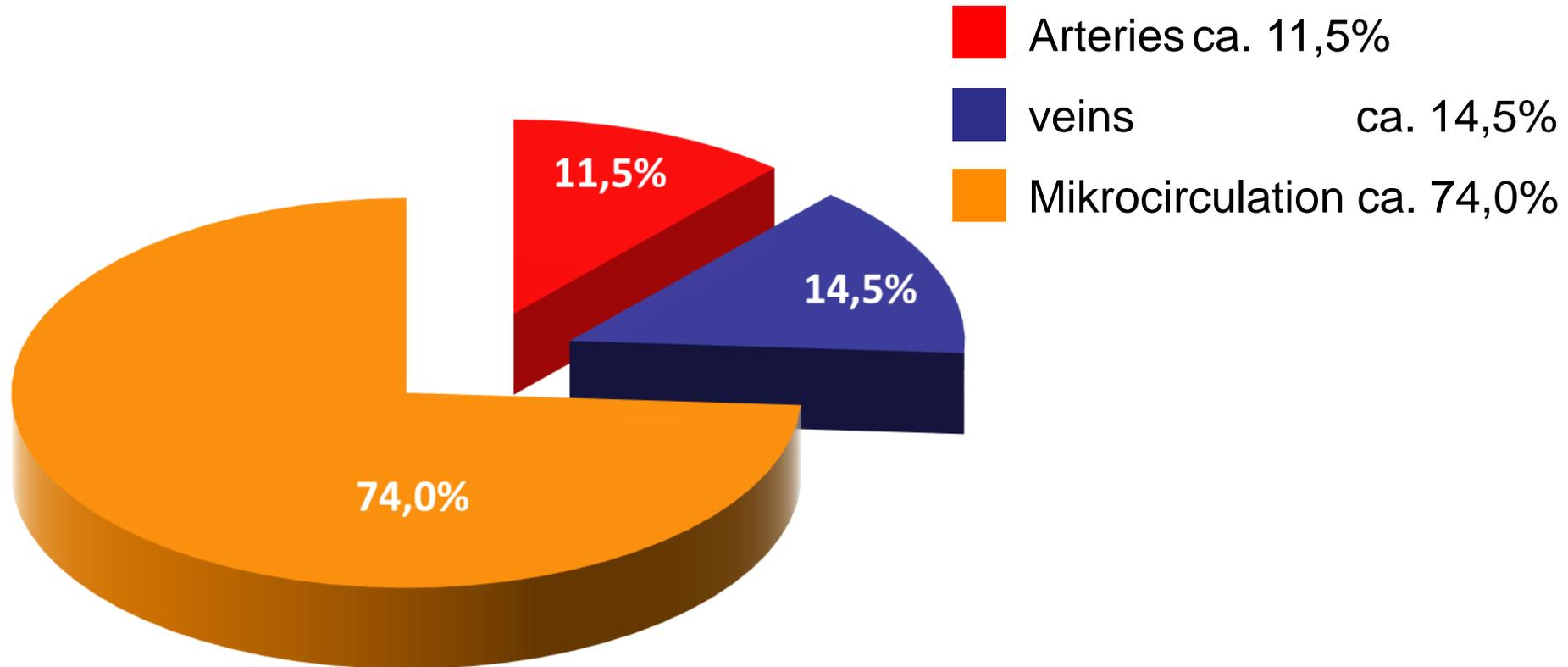
Initial lymphatic vessels/pre-collectors

Interstitial space  
(area between cells and vessels)

# The world of microcirculation research and its significance for MLD

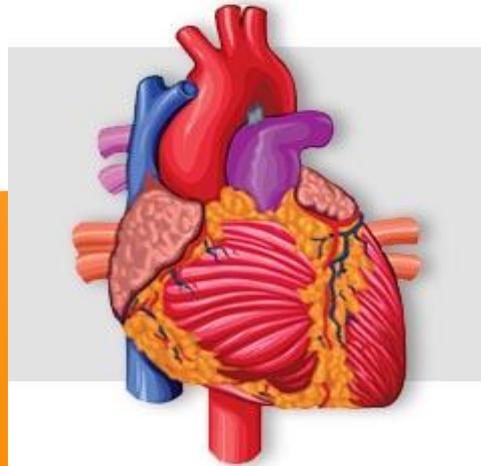
## Blood Vessels.

### Distribution of blood vessels in the body



# The world of microcirculation research and its significance for MLD

## Microcirculation : area and expansion



**Mikrocirculation**



**Area ca. 7.000 qm**  
**Expansion: 100.000 km**

# The world of microcirculation research and its significance for MLD

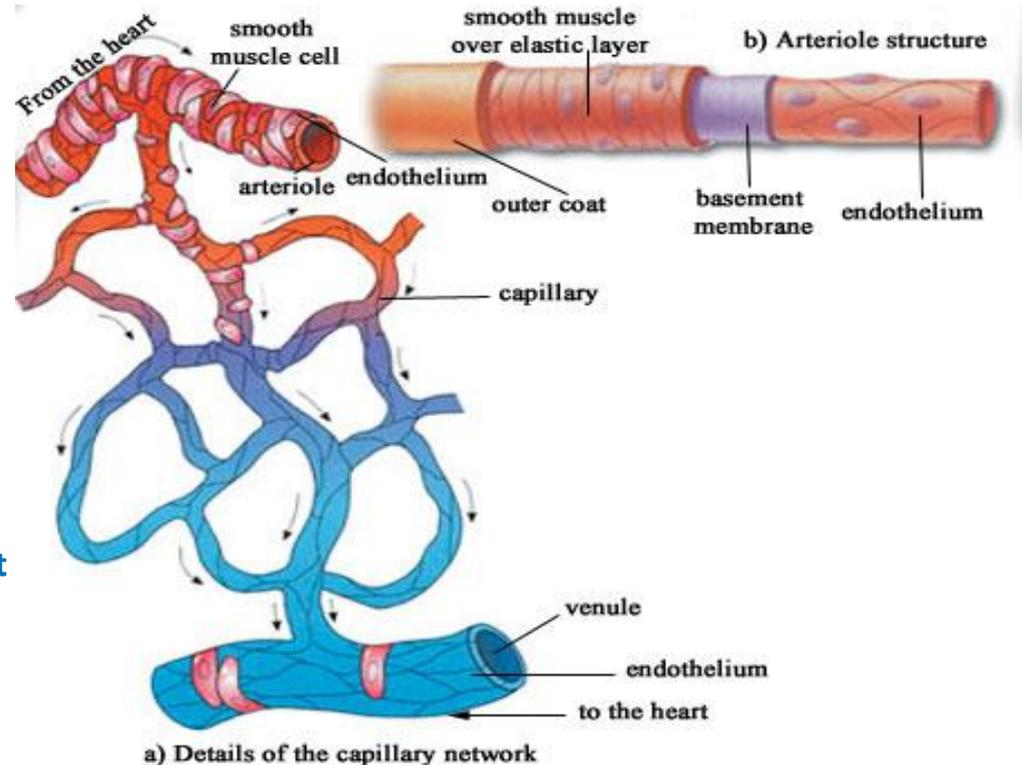
Zur Mikrozirkulation gehören:

Das Blut und seine Bestandteile, Blutgefäße mit Durchmesser (d) < 100 - 200µm (Arteriolen, Kapillaren, Venolen), das Endothel !

Initiale Lymphgefäße, LEC.

Interstitieller Raum

(Bereich zwischen Zellen und Gefäßen)



**Microcirculation the functionally most important Blood circulation.**

**What is the problem ??**

# Vasomotion

Rhythmic vascular diameter changes due to local tonus changes of the smooth musculature **independent** of heart rhythm, neuronal or humoral regulation in the microvascular regions.

Informational dynamics of vasomotion in microvascular networks: a review  
R. K. Pradhan<sup>1</sup>, V. S. Chakravarthy<sup>2</sup>  
Acta Physiologica Volume 201, Issue 2, pages 193–218, February 2011

„The“ triggers improvements in microcirculation

## Conditions Linked to Microvascular Dysfunction :

### Ischemic Cardiomyopathy :

Am Heart J. 2003 Sep; 146(3):549-54.

### Diabetes Mellitus : [Circulation](#). 2016 Nov 1;134(18):1339-1352.

**Prediabetes and Type 2 Diabetes Are Associated With Generalized Microvascular Dysfunction: The Maastricht Study.**

### Obstructive Sleep Apnea:

Am J Respir Crit Care Med. 2010 Dec 15; 182(12):1540-5.

### Aging : J Physiol. 2008;586:3301.

### Schizophrenia : Transl Psychiatry. 2015;5:e616.

### Dementia: [Cell Mol Neurobiol](#). 2016 Mar;36(2):241-58.

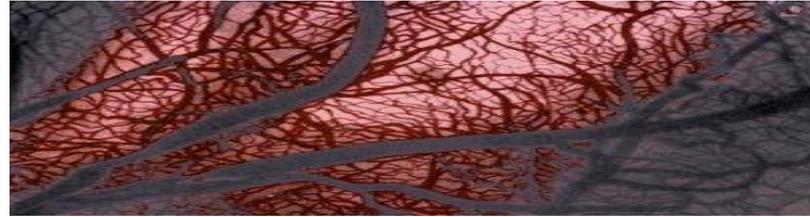
Epub 2016 Mar 17.

### Peripheral Neuropathy:

Curr.Diab Rep.2002 Dec;3(6):446-51

### Chagas Disease

### Amyloidosis :Int J Cardiol. 2010 Nov 5; 145(1):67-8.



### Lymphedema: [Int J Mol Sci](#). 2017 Jan; 18(1): 171.

Inflammatory Manifestations of Lymphedema

### Stress Related Cardiomyopathy: Annals of medicine. 2009;41:462–470.

### Systemic Lupus Erythematosus : ArteriosclerThrombVascBiol. 2006;26:2281–2287.

### Cerebral Vasospasm : Biomed Res Int. 2014; 2014():253746.

### Inflammatory Bowel Disease : Am J Pathol. 2008 Jun; 172(6):1457-66.

### Tobacco Abuse : AmJPhysiol Heart CircPhysiol. 2011;300:H109–H117.

### Hypertrophic Obstructive Cardiomyopathy: Coronary microvascular dysfunction and prognosis in hypertrophic cardiomyopathy. NEnglJMed. 2003;349:1027–1035.

### Obesity : The microcirculation in adipose tissue inflammation--Reviews in endocrine & metabolic disorders. 2013;14:69–76.

### Systemic Sclerosis

### Hypertension: Aging Cell, 2017 Mar 14

### Idiopathic Cardiomyopathy : Cardiology. 2011;119:191–196.

# Lymphedema: a systemic inflammatory process !

Lymphedema is a progressive disease caused by congenital anomalies, obstructions, injuries, or infections of the lymphatic system, usually due to lymph vessel injury damage during cancer treatment with risk factors such as extensive lymph node dissection and adjuvant chemo/radiotherapy.(1)

**If a lymphatic injury is present, the fluid flow is interrupted, leading to fluid accumulation, increased lymph flow, vasodilatation, valvular dysfunction and reflux. Changes in normal tissue function due to inflammation, tissue remodeling, lymphatic hyperplasia and adipocyte deposition subsequently occur and lead to lymphoedema phenotype.**

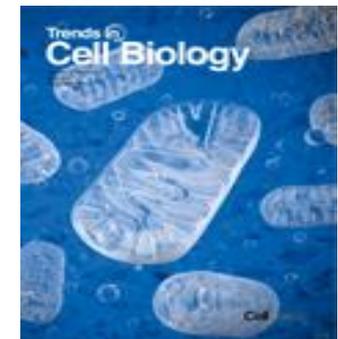
**"A histological feature of lymphedema is the infiltration of inflammatory cells and recent studies with animal models and clinical biopsy specimens have shown that this response plays a key role in the pathology of lymphedema.(2)**

**An increased liquid flow itself can serve as an early signal for inflammation. The TGF- $\beta$ 1 is an autocrine upregulation of the transforming growth factor  $\beta$ 1 - (TGF- $\beta$ 1) with differentiation into myofibroblasts and increased collagen production when lateral lymph vessels are not able, to compensate for the initial lymphatic damage, the resulting persistence of fluid accumulation in the interstitial space contributes to a sustained positive feedback loop of inflammation that ultimately leads to pathological changes in lymphedema.(3)**

1) Dtsch Arztebl 2017; 114(5): [14]; **Das Lmphödem**

2) Int J Mol Sci. 2017 Jan; 18(1): 171.  
**Inflammatory Manifestations of Lymphedema**

3) **A driving force for change: Interstitial flow as a morphoregulator.**  
Trends Cell Biol. 2007;17:44–50.



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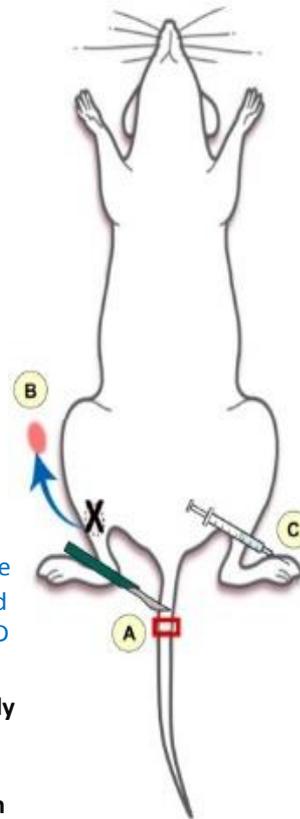


# Inflammatory manifestations of lymphedema

[Int J Mol Sci. 2017 Jan; 18\(1\): 171.](#)

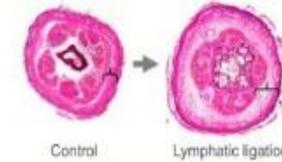
## Inflammatory Manifestations of Lymphedema

Both experimental and clinical studies over several decades have identified inflammation as a critical component in the pathophysiology of lymphedema. A histological feature of lymphedema is **the infiltration of inflammatory cells** and recent studies with animal models and clinical biopsy samples have shown that this response plays a **key role in the pathology of the disease**.



### A. Tail surgery

FibroadiPOSE deposition

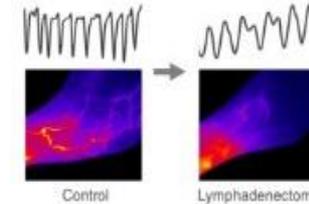


Inflammation

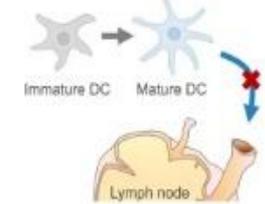


### B. PLND

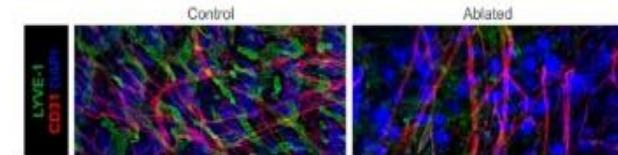
Decreased collecting vessel pumping  
Decreased collateral vessel formation



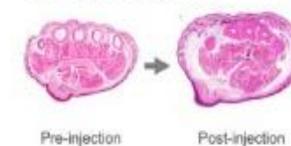
Decreased DC trafficking



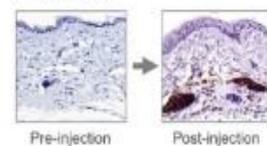
### C. Lymphatic ablation



End-stage swelling  
FibroadiPOSE deposition



Inflammation



# Lymphological Micro - Cosmos

The lymph-peri lymph system is a "systemically active organ." Lymphangiogenesis is a recognized hallmark of inflammatory processes in tissues and organs  
No region of the body is impenetrable to the flames of inflammation.

**Inflammation-associated lymphangiogenesis (IAL):** the basic drainage task of lymphatic vessels is a complex balance of locally processed and transported antigens as well as interstitial cytokine and immune cell signaling. "Inflammatory progression (IAL) is present in acute and chronic tissue pathologies throughout the body. Lymphatic vessels play physiological roles relevant to all medical fields as important regulators of fluid balance, immune cell trafficking, and immune identity. (1)

Importance of IAL in tissue inflammation pathologies: Examples:

Dermal inflammation and lymphangiogenesis

Lymphangiogenesis in intestinal inflammation

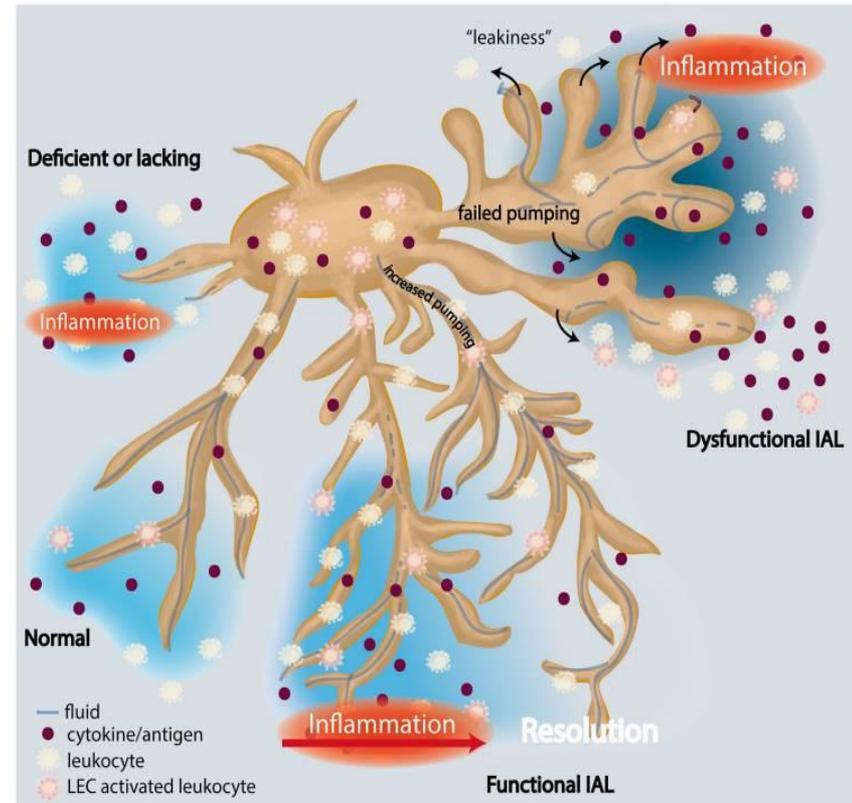
Adipose tissue, the metabolic syndrome, and lymphatic function (3)

Recently, more active roles for LECs in immune regulation have been receiving more attention.

LECs have the ability to - themselves take up and process antigens,  
- alter immune cell phenotype and function  
- serve as a site of immune cell interaction  
- secrete cytokines that propagate immune responses both locally and in the downstream node. (2)



- 1) **Lymphangiogenesis: fuel, smoke, or extinguisher of inflammation's fire**  
*Exp Biol Med (Maywood)*. 2017 Apr; 242(8): 884–895.
- 2) **Emerging roles of lymphatic endothelium in regulating adaptive immunity.**  
*J Clin Invest* 2014; 124: 943–52.
- 3) **Mechanisms of obesity and related pathologies: the macro- and microcirculation of adipose tissue.**  
*FEBS J* 2009; 276: 5738–46.



Picture from 1)

# Lymphedema: a systemic inflammatory process !

## III

In a study of affected patients undergoing CDT, for example, Foldi et al. noted that the expression of pro-inflammatory genes such as that for CD14, interferon-gamma (IFN- $\gamma$ ) receptor, tumor necrosis factor-alpha (TNF- $\alpha$ ), integrin alpha 4 beta 1 ( $\alpha 4\beta 1$ ; also known as Very Late Antigen-4 or VLA-4), tumor necrosis factor receptor p55 (TNFR1), and CD44 were increased prior to and significantly decreased after the first phase of treatment.

[Lymphology](#). 2000 Mar;33(1):19-23.

**Effect of complex decongestive physiotherapy on gene expression for the inflammatory response in peripheral lymphedema.**

[Földi E<sup>1</sup>](#), [Sauerwald A](#), [Hennig B](#)

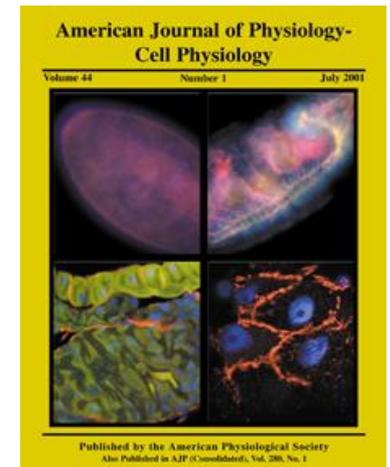
[Am J Physiol Heart Circ Physiol](#). 2014 May 15; 306(10): H1426–H1434.

**IL-6 regulates adipose deposition and homeostasis in lymphedema**

Current evidence suggests that a **variety of key players, including T helper cells, Tregs, macrophages, and dendritic cells**, play complex roles in the pathology of the disease by **elaborating inflammatory cytokines** and regulating the development of collateral lymphatic vessels.

[Int J Mol Sci](#). 2017 Jan; 18(1): 171.

**Inflammatory Manifestations of Lymphedema**



# Lymphedema: a systemic inflammatory process !

## II

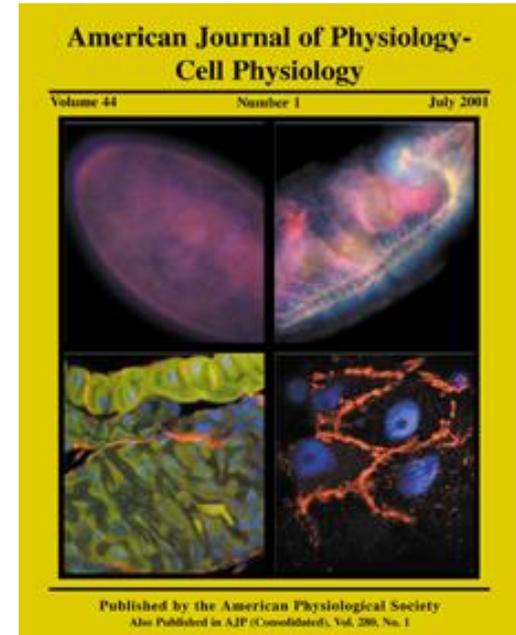
### Toll-like receptor deficiency worsens inflammation and lymphedema after lymphatic injury

Am J Physiol Cell Physiol. 2012 Feb 15; 302(4): C709–C719

“In conclusion, we have shown that TLR function plays an important role in homeostatic responses to lymphatic fluid stasis.

These molecules (**endogenous danger signals: extracellular matrix breakdown products (hyaluronan fragments), heat shock proteins (HSPs), members of the S100 family of proteins, and nuclear proteins, such as high-mobility group box-1 (HMGB1).....**

regulate a variety of effects like lymphangiogenesis, fat deposition, inflammation, and tissue fibrosis. These molecules are known to activate TLR 2, 4, and 9, suggesting that these **pathways play important roles in the regulation of tissue responses to lymphatic fluid stasis and inflammation processes.**”



# Lymphedema: a systemic inflammatory process!

## IV

### Summary of selected cytokines and growth factors involved in lymphedema

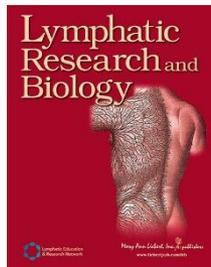
Cytokine	Function
IFN- $\gamma$	Impairs lymphangiogenesis Activates macrophages
IL-1	Induces DC migration
IL-13	Impairs lymphangiogenesis Promotes M2 macrophage activation
IL-4	Impairs lymphangiogenesis Promotes M2 macrophage activation
IL-6	Regulates chronic inflammation Decreases adipose deposition
TGF- $\beta$ 1	Mediates soft-tissue fibrosis Negatively regulates lymphatic vessel regeneration
VEGF-C	Promotes lymphangiogenesis

# Lymphological Micro - Cosmos

## The phenomenon of chron. Inflammation in the vascular lymph system Relevant publications on the topic (selection)



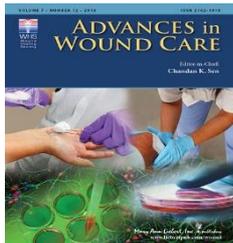
[Aging \(Albany NY\)](#). 2016 Nov; 8(11): 3065–3090.  
**Mast cells and histamine are triggering the NF- $\kappa$ B-mediated reactions of adult and aged perilymphatic mesenteric tissues to acute inflammation.**



[Lymphat Res Biol](#). 2008;6(3-4):123-37.  
**Lymphatic endothelial cells, lymphedematous lymphangiogenesis, and molecular control of edema formation.**



[Int J Mol Sci](#). 2017 Jan; 18(1): 171.  
**Inflammatory Manifestations of Lymphedema**



[Adv Wound Care \(New Rochelle\)](#). 2018 Jul 1; 7(7): 189–208.  
**Physiological Perspective on Therapies of Lymphatic Vessels**



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# Lymphological Micro - Cosmos

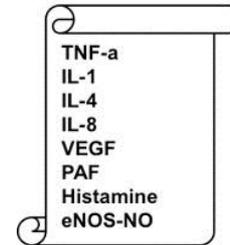
The phenomenon of chron. Inflammation in the vascular lymph system

Relevant publications on the topic (selection)

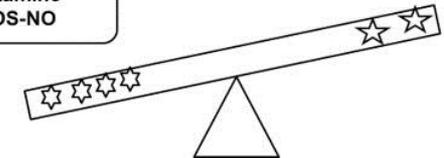


[Circ Res. 2016 Jul 8; 119\(2\): 178–180.](#)  
New member of endothelial arsenal  
against inflammation

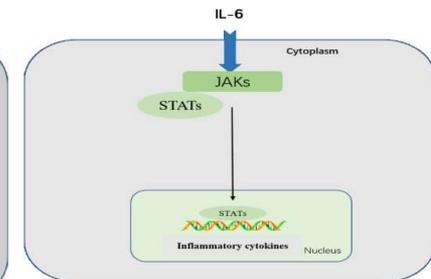
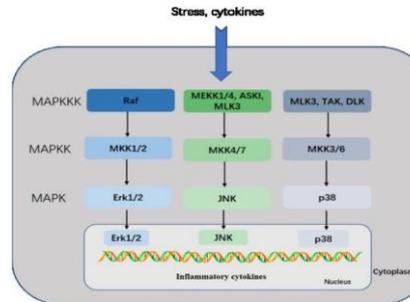
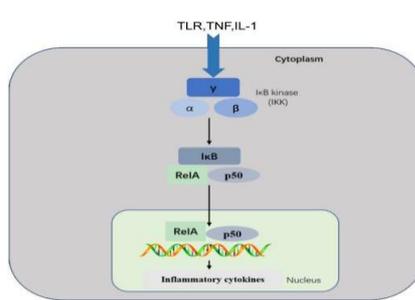
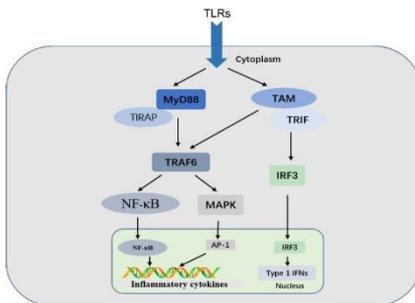
Cell- and Plasma-derived  
PRO-INFLAMMATORY  
Mediators



Endothelial and Vascular Cells derived  
ANTI-INFLAMMATORY Mediators



[Oncotarget. 2017 Dec 14;9\(6\):7204-7218.](#)  
Inflammatory responses and inflammation-associated  
diseases in organs.



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[Mei R. Fu](#) et al. :

**PRECISION ASSESSMENT OF HETEROGENEITY OF LYMPHEDEMA PHENOTYPE, GENOTYPES AND RISK PREDICTION**

Published online 2016 Jul 22. doi: [10.1016/j.breast.2016.06.023](https://doi.org/10.1016/j.breast.2016.06.023)

Fu et al. found that **inflammatory genes** were associated with a greater number of symptoms due to Lymphedema :

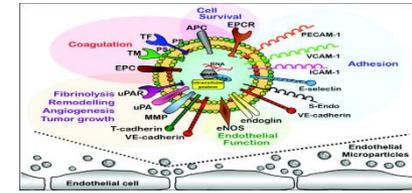
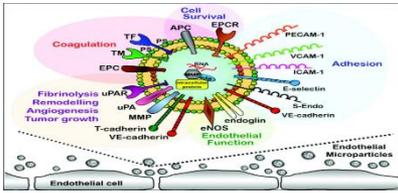
**IL-4 rs2070874** was significantly associated with phenotype of impaired limb mobility and fluid accumulation.

Phenotype of fluid accumulation was significantly associated with **IL6 rs1 800795, IL4 rs2243250 and IL4 rs2070874.**

Phenotype of discomfort was significantly associated with **VEGF-C rs3775203 and IL13 rs1800925.**



# Science of „Microparticles“ – Sophisticated Vesicles !



**Microparticles** are small (0.1-1 µm) large lipid-rich vesicles that are caused by various mechanisms such as mechanical stress (Diehl, Nagy et al. 2008), apoptosis (Barry, Pratico et al. 1997), (Mallat, Hugel et al. 1999) and cell activation (Beaudoin and Grondin 1991) of plasma membranes of multiple cells. They probably have many (patho)-physiological functions e.g. in the area of haemostasis and in the development and progression of diseases such as atherosclerosis and malignancies (Barry and FitzGerald 1999), (Diamant, Tushuizen et al. **A subgroup of microparticles** are **endothelial microparticles** (EMP) that originate from activated, destroyed and/or apoptotic endothelial cells and thus represent a marker for vascular damage".

Excerpt from : Cellular Internalization of Microparticles Dissertation On the acquisition of the Doctorate of Medicine at the Medical Faculty of the Ludwig-Maximilians-Universität Zu München Submitted by Géraldine Müller-Stoy from Munich 2013  
 Extract from: Inaugural dissertation for the award of a doctorate in medicine from the High Medical Faculty of the Ruhr University Bochum presented by Lisa Marie Niedballa from Seeheim-Jugenheim

## RESEARCH ARTICLE

### Shear-sensitive microRNA-34a modulates flow-dependent regulation of endothelial inflammation

J Cell Sci 2015 128: 70-80

### Role of flow-sensitive microRNAs in endothelial dysfunction and atherosclerosis – “Mechanosensitive Athero-miRs”

Arterioscler Thromb Vasc Biol. 2014 Oct;34(10):2206-16.

**“Emerging evidence indicates that alteration of flow conditions regulate expression of miRNAs in endothelial cells both *in vitro* and *in vivo*”.**

The key signaling pathways that are targeted by **these mechano-miRs** include the endothelial cell cycle, inflammation, apoptosis, and nitric oxide signaling.



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# Science of „Microparticles“ – Sophisticated Vesicles !

The majority of the microparticles present in healthy blood originate from thrombocytes.

Other cells of the entire vascular system, **such as erythrocytes, granulocytes, monocytes, lymphocytes and endothelial cells are capable of forming microparticles.** (Van Wijk, VanBavel et al. 2003) ,(Morel, Hugel et al. 2004). The fragments of the membrane with intracytoplasmic material are released into the extracellular space.

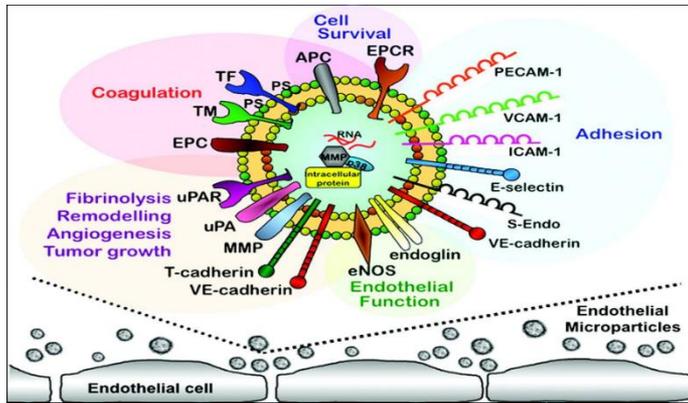
Recent reports identified particles containing micro RNAs that exert protective effects on downstream targets.

**“Microvesicles appear to be more than just biomarkers of vascular injury. They serve as important para/endocrine mediators in cell-to-cell communication “.** “Given its large volume, the microcirculation probably serves as the major source of endothelial microvesicles in the circulation”.

**Circulating microvesicles from patients with cardiovascular disease impair endothelial function in vessels from healthy animals !!** *Circulation.* 2001 Nov 27; 104(22):2649-52.

**The mechano-miRs** that are implicated in atherosclerosis are termed as **“mechanosensitive athero-miRs”** and are potential therapeutic targets to prevent or treat atherosclerosis. [Arterioscler Thromb Vasc Biol. 2014 Oct; 34\(10\): 2206–2216.](#)

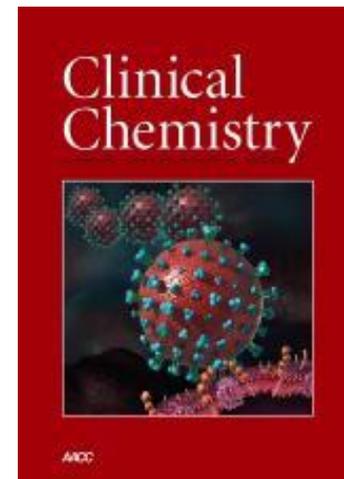
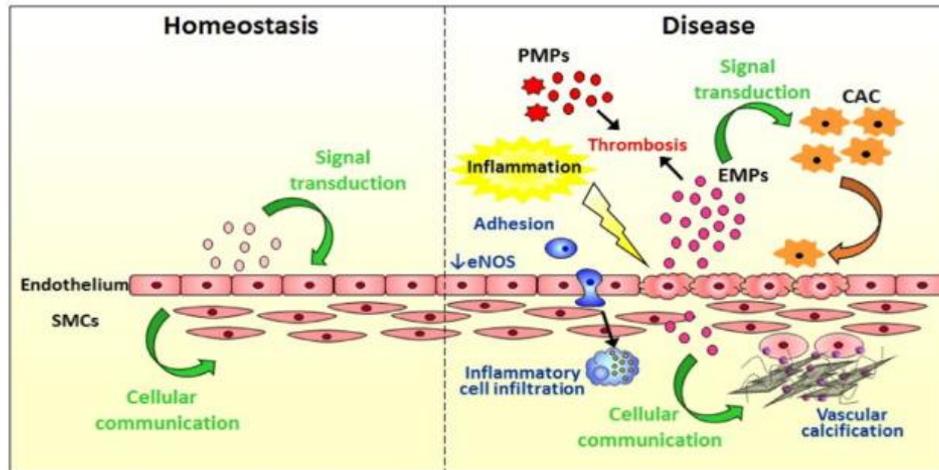
# Endothelial microparticles are jointly responsible for the Development of "endothelial dysfunction" and determinable as diagnostic marker.



Clin Chem. 2013 Aug;59(8):1166-74..  
**Evolving role of microparticles in the pathophysiology of endothelial dysfunction.**

Microparticles include membrane and cytoplasmic Cell parts: RNA, microRNA, lipids, but also "functional Endothelial NO-Synthase" !!  
 MP's are biomarkers for vascular damage and inflammation !

Size : 100 nm-1µm



# Cellular "Cross-Talk" in microcirculation!

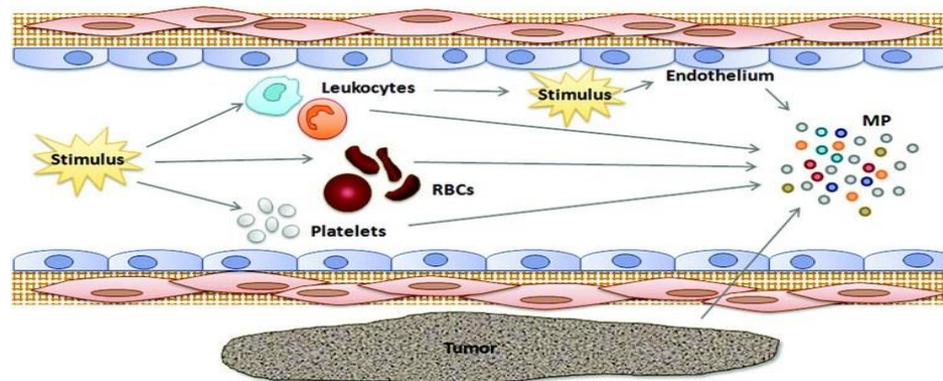
Role of flow-sensitive microRNAs in endothelial dysfunction and atherosclerosis –

"Mechanosensitive Athero-miRs" Sandeep Kumar,<sup>1,\*</sup> Chan Woo Kim,<sup>1,\*</sup> Rachel D. Simmons,<sup>1</sup> and Hanjoong Jo<sup>1,2</sup>

*Arterioscler Thromb Vasc Biol.* 2014 October

Recent publications have identified particles containing micro-RNAs that have protective effects on downstream targets. Microvesicles serve as important endocrine mediators in cell-to-cell communication. In view of its large volume, microvesicles probably serve as the main source of endothelial microvesicles in the circulatory system.

Circulating microvesicles of patients with cardiovascular disease interfere the healthy endothelial function in vessels of animals! *Circulation* 2001, Nov 27



# The world of microcirculation research and its significance for MLD

The lymph flow can be influenced by internal and external stimuli.

Sympaticolysis during MLD increases vasomotion and lymphatic volume

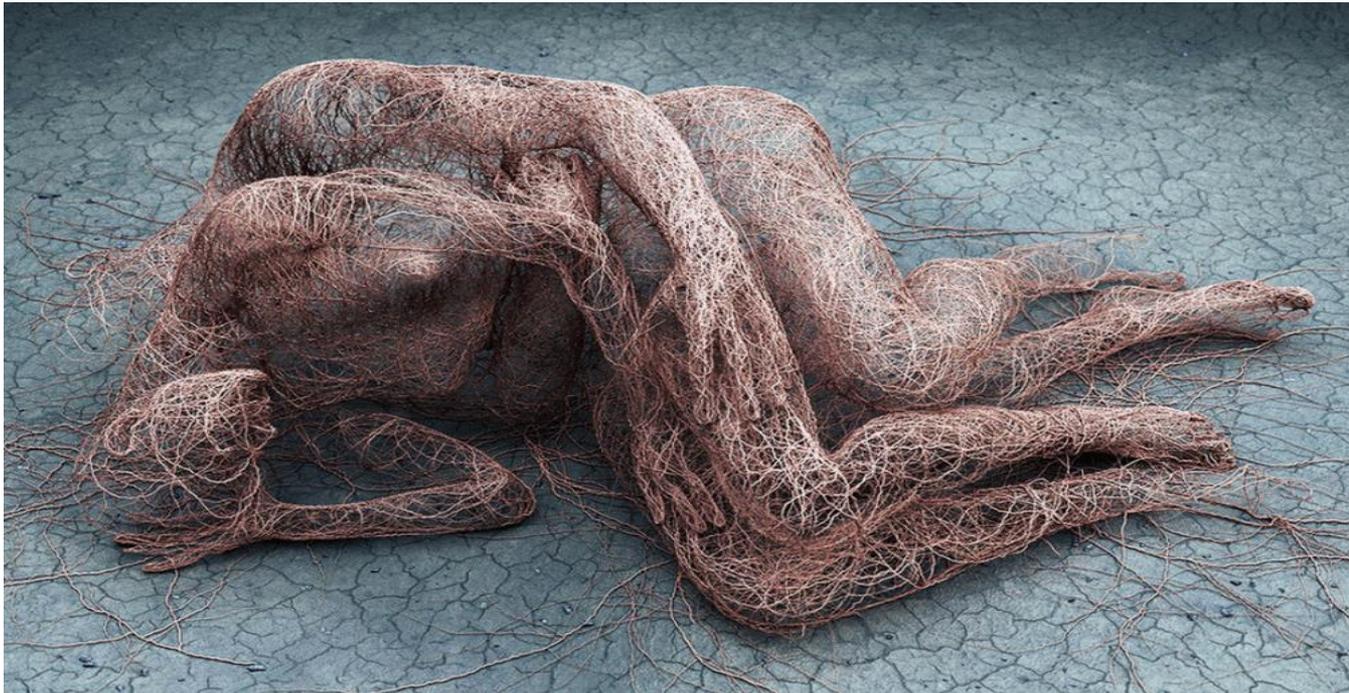
**Improved Vasomotion = Altered Shear Stress = Reduced Inflammation**

Professional MLD/KPE is the "**Manual Therapeutic Agent**" in the field of

**Microcirculation improvement !**

Physical improvements achieved through this usually result in the additional optimization of "emotional factors" (trust, hope, joy, self-acceptance) an improvement of the systemic inflammation process and immune strengthening !

# Microcirculation optimization through "Pulsed electromagnetic field therapy (PEMFT)"

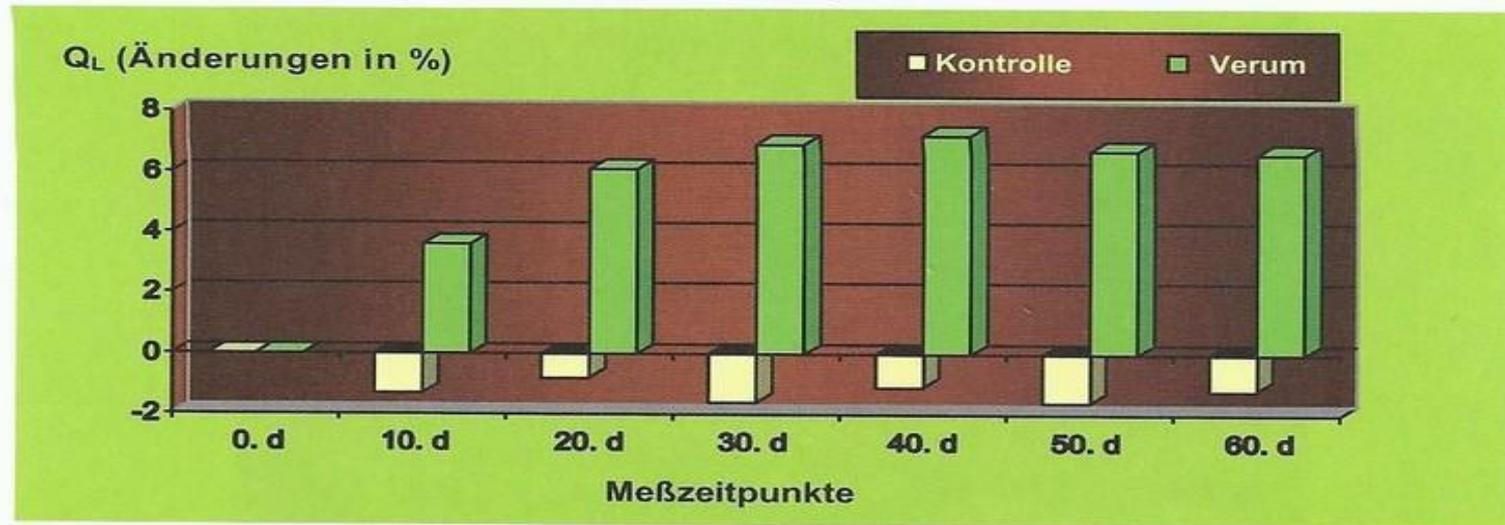


# Improvement of microcirculation in the lymphatic area through PMFT : Microcirculation in the focus of research

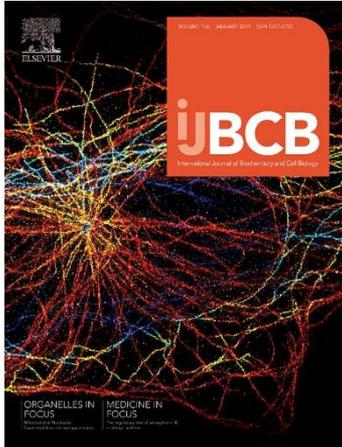
**Abbildung 341**

Meßdaten zum Merkmal „Strömungsfluß der initialen Lymphe  $Q_L$ “ (Mittelwerte) im subkutanen Targetgewebe in einem 60-tägigen Behandlungszeitraum bei einer Stichprobe aus geriatrischen Diabetikern mit Polyangioneuropathie, die zusätzlich zur kliniküblichen Therapie komplementär mit einem bestimmten elektromagnetischen Wechselfeld mit Vasomotionsstimulation behandelt wurde (Verum), im Vergleich mit einer Stichprobe, bei der keine komplementäre Behandlung stattfand (Kontrolle).

Signifikante Merkmalunterschiede zwischen den Meßdaten der Kontroll-Gruppe und den Meßdaten der zusätzlich mit einem bestimmten elektromagnetischen Wechselfeld behandelten Verum-Gruppe traten ab dem 10. Meßtag auf.



Klopp et.al. : „Mikrozirkulation im Fokus der Forschung“  
Mediquant Verlag 2008



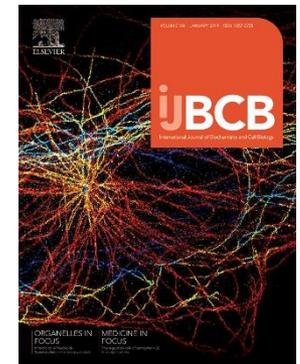
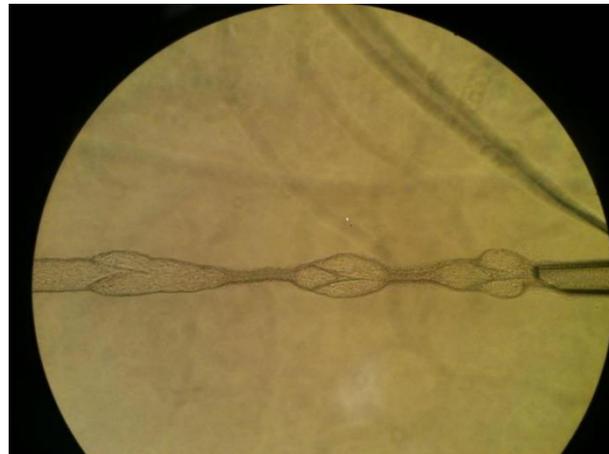
## Lymphatic smooth muscle: the motor unit of lymph drainage

[Pierre-Yves von der Weid](#),  
[David C. Zawieja](#)

Embedded into the wall of collecting lymphatic vessels and trunks, the **lymphatic smooth muscles** are cardinal to the functions of the lymphatic system. Their **intrinsic contractile property** — **the intrinsic lymph pump** — is **sensitive towards physical signaling ....!**

.... rhythmical and phasic contractions of the vessels, represent the principal mechanism by which lymph flow is generated.

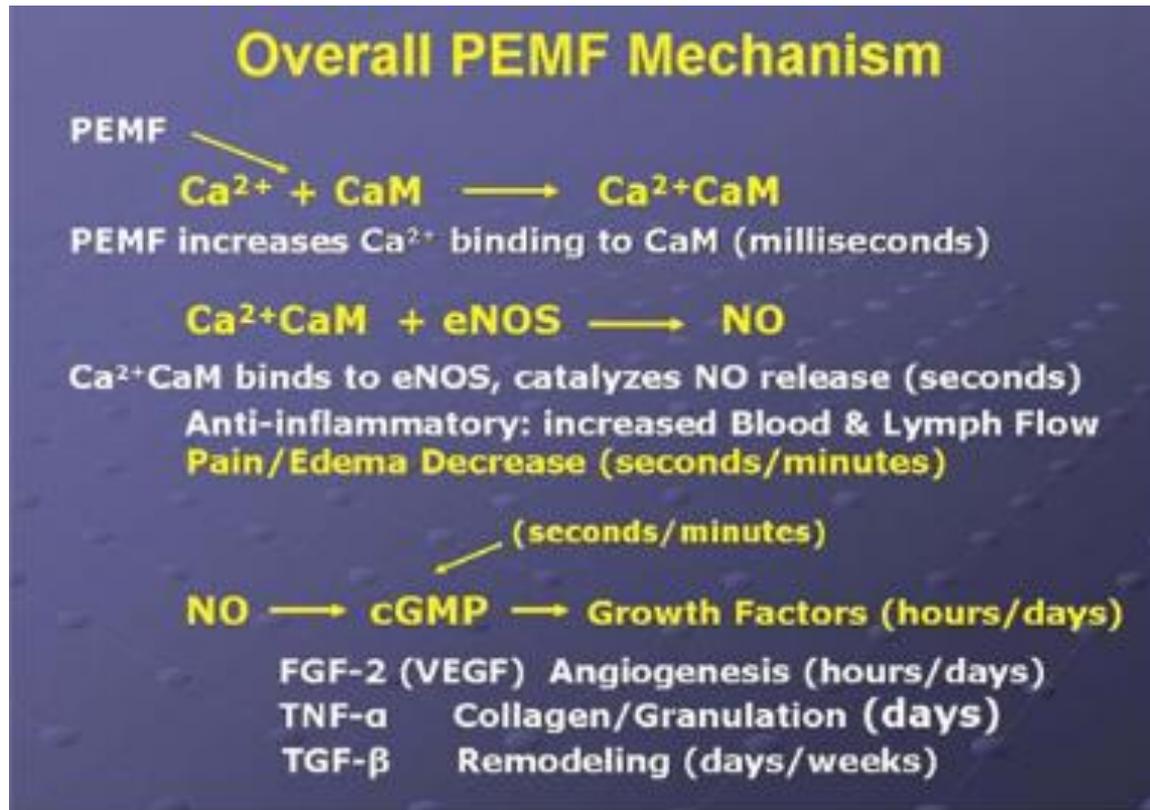
[The International Journal of Biochemistry & Cell Biology Volume 36, Issue 7, July 2004, Pages 1147–1153](#)



# Evidence-Based Use of Pulsed Electromagnetic Field Therapy in Clinical Plastic Surgery

Berish Strauch, MD, Charles Herman, MD, Richard Dabb, MD, Louis J. Ignarro, PhD, Arthur A. Pilla, PhD

Aesthet Surg J (2009) 29 (2): 135-143.



# Microcirculation improvement in the vascular/lymphatic system through PEMF therapy :

[Diabet Foot Ankle. 2013; 4: 10.3402/dfa.v4i0.22081.](#)

[Gaurav Thakral, MD, et al.: Electrical stimulation to accelerate wound healing](#)

[Am J Transl Res. 2018 May 15;10\(5\):1260-1272. eCollection 2018.](#)

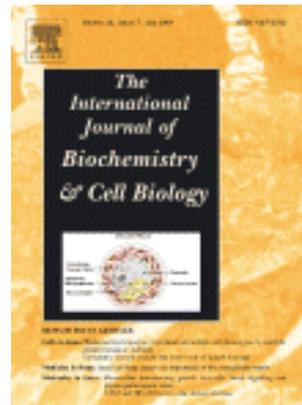
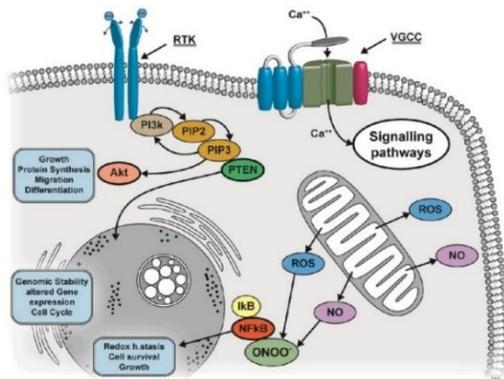
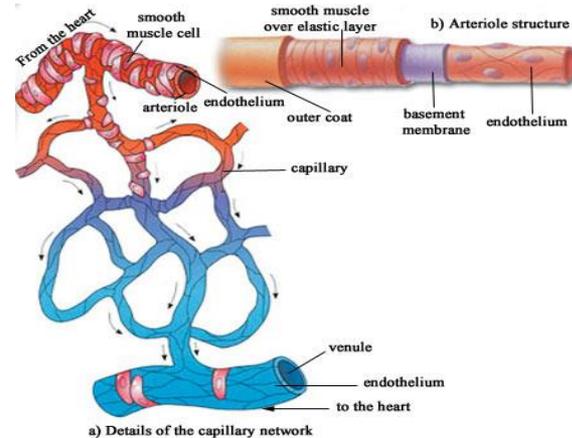
[Coupling of pulsed electromagnetic fields \(PEMF\) therapy to molecular grounds of the cell.](#)

[Funk RH<sup>1</sup>.](#)

[Br J Pharmacol. 2005 Mar;144\(5\):605-16.](#)

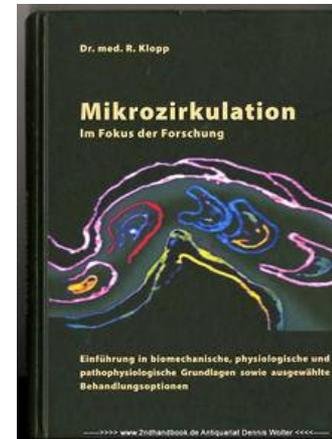
[Vasomotion: cellular background for the oscillator and for the synchronization of smooth muscle cells.](#)

[Aalkjaer C<sup>1</sup>, Nilsson H](#)



**Microcirculation: the focus of research ;  
Introduction to biomechanical, physiological and  
pathophysiological basics  
and selected treatment options**

**Lymphatic smooth muscle: the motor unit of lymph drainage**  
[Pierre-Yves von der Weid<sup>1</sup>, David C. Zawieja<sup>2</sup>](#)  
[The International Journal of Biochemistry  
& Cell Biology Volume 36, Issue 7,](#)  
[July 2004, Pages 1147–1153](#)



Different ways of PEMF-coupling to molecular biology of the cell:



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## Pilotstudy 2015 : Pawelke - Wittlinger – PMFT



Is there a specific effect of a specific PMFT signal in regard to oedema reduction and inflammatory parameters in addition to the established KPE therapy as part of a 3-week intensive therapy ?

**YES , clearly with all examined parameters !**

R.Pawelke : unpublished data 2015



## Clinical follow-up study - Pawelke/Wittlinger 2015

outcomes

In 10 consecutively admitted patients with prim./sek. Leg lymphedema the signal configuration BEMER (P3) was additionally tested twice a day for 20 minutes in addition to the standardized therapy program.

**All patients showed a significant reduction of oedema !**

without PEMF signal (previous stay !) : edema reduction between 3.09 % - 9.07 % on average of **6.68 %**.  
with PEMF signal : oedema reduction between 5.73 % - 12.41 % on average **of 8.96 %**

A comparison of the two groups showed an increase in oedema improvement with an additional Use of the PEMF signal configuration on an average of **37.23 %!**

Summed edema improvement of both comparison groups:

**WITHOUT PEMF therapy (previous stay) : 4,070 ml, average 678 ml.**

**WITH PEMF therapy : 5.332 ml ,average 892 ml.**

The collected laboratory data showed relevant changes in "inflammatory parameters".  
tendency proinflammat.parameter(TNF-alpha ,CRP increased ,) -and tendency anti-inflammatory  
(FGF reduced, VEGF,PDGFbb increased , MCP-1 reduced IL-6, IL-8 reduced) !

The score "general condition" - subjective patient information (0-10) showed improvements in the course of the study  
from scale value + 1 (7 to 8) to scale value +7 (2 to 9) -- on average improvement by 4.8 scale values



## Lymphological macro-micro-cosmos and beyond.... The soul-body axis !



**In view of the scientific data in the field of "Shear Stress" and "Microparticle Research", the fantastic seeming solution and dissolution of the "soul-body dualism to be realized by the communication network of "microparticles" !  
As a bridge between the individual spiritual world and the Human morphology down to the cellular and subcellular level.**

**Wouldn't it be wonderful, in the microcosm to get closer to the mystery of life ?  
The many still open questions of the micro-cosmos, the instant cell-cell communication between approx. 80 trillion cells, in reaction and in cooperation with the "Emotional feeling and processing" and the "Emotional being and consciousness" are in the future Call and order in the sense of sustainable prevention and therapy !**

**What protects and affects the endothelium, the blood/lymph flow conditions, the immune system, the world of microparticles ?**

**Loving...**



**Laughing....**



**Dancing...**



**Joy, friends and good atmosphere...!**

# Lymphological macro-micro-cosmos and beyond.... The soul-body axis !

This field of research, especially the knowledge of the mode of action of the "lymphological endothelial microcosm" gives it the significance of a "Systemic Organ" and "Lymphology" a more important medical interdisciplinary in the future, even a Pacemaker function in successful treatment systemically effective endothelial diseases.

In this sense....

... on to scientifically fruitful new shores ..... Thank you for your time !

