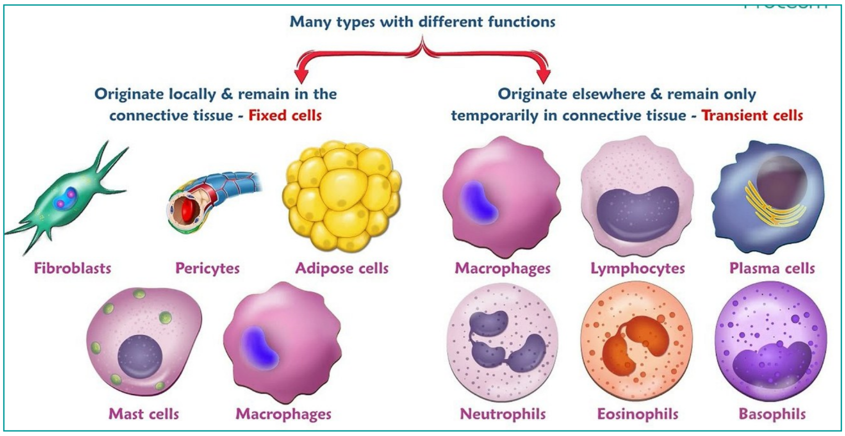
24.5. COMPONENTS OF THE BBRS

The different components of the Basic -Bio-Regulation-System are (summarized) the following:



24.5.1. Loose connective tissue

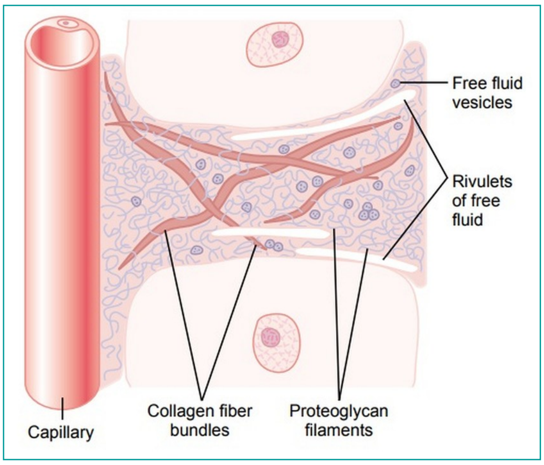
As already described in chapter 25.4. Connective tissue, the loose connective tissue consists of cells, tissue fluid, ground substance and fibers.

a. Cells

As discussed, these are the undifferentiated mesenchymal cells and their differentiation forms such as Fibroblasts, Macrophages, Mastocytes, Lymphocytes, Lipocytes and Plasmocytes. Their function is both specific and non-specific. The former mainly in terms of soil regulation and general defences, the latter in immune-biological terms.

b. Tissue fluid

It is known that morphology and theoretical physiology treat the extracellular fluid only indirectly. Clinical physiology, on the other hand, deals extensively with her. Schade in particular has paid attention to this, with his research on colloid and physico-chemistry, including the relationship between this fluid and capillary permeability.



Following in his footsteps is Eppinger, who was particularly interested in the so-called interstitium: a classic example of the loose-meshed connective tissue, albeit with a relatively high fibre content.

In contrast to morphology, he does not so much deal with the individual form elements, as with 'the all-important pore and fissure system' that 'is difficult to recognize under normal circumstances, especially within the large parenchymal organs'. Only with a pathological accumulation of fluid does it emerge.

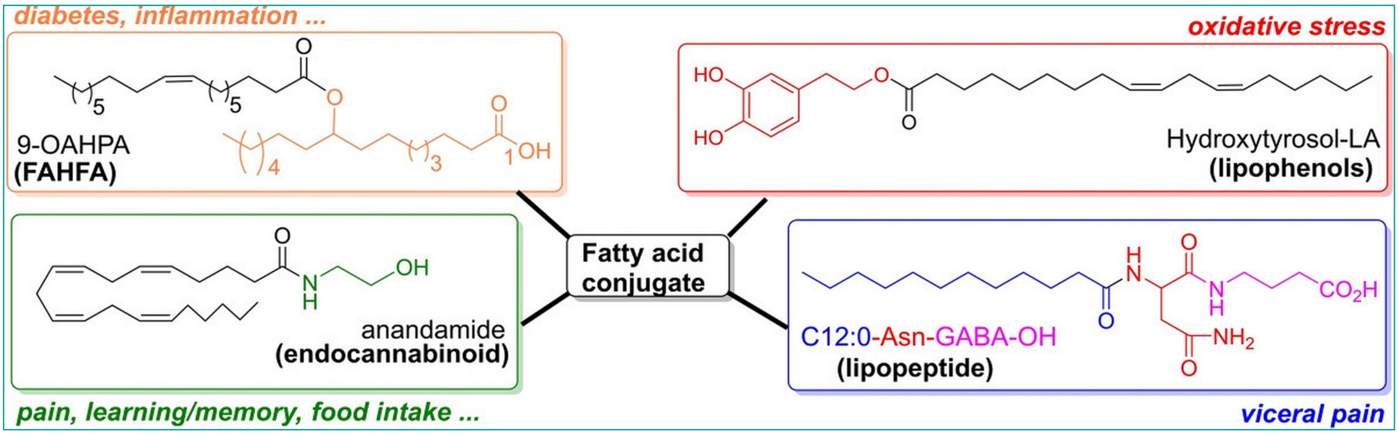
The interstitium is the seat of the so-called extracellular fluid. The composition is almost identical to that of blood plasma in terms of ions and solubles.

The tissue fluid is colloidally bonded to the matrix of the connective tissue (Glycosaminoglycans and Glycoproteins).

Eppinger was the first to point out that there are humoral substances in the serum and in the extracellular fluid, which have an important regulatory effect. He saw a relationship between these substances and the functions of the vegetative nervous system.

Pischinger discovered that these substances arose from the Leukocytes and also from the Fibroblasts. He called the active factor 'the factor M': active conjugated unsaturated fatty acids.

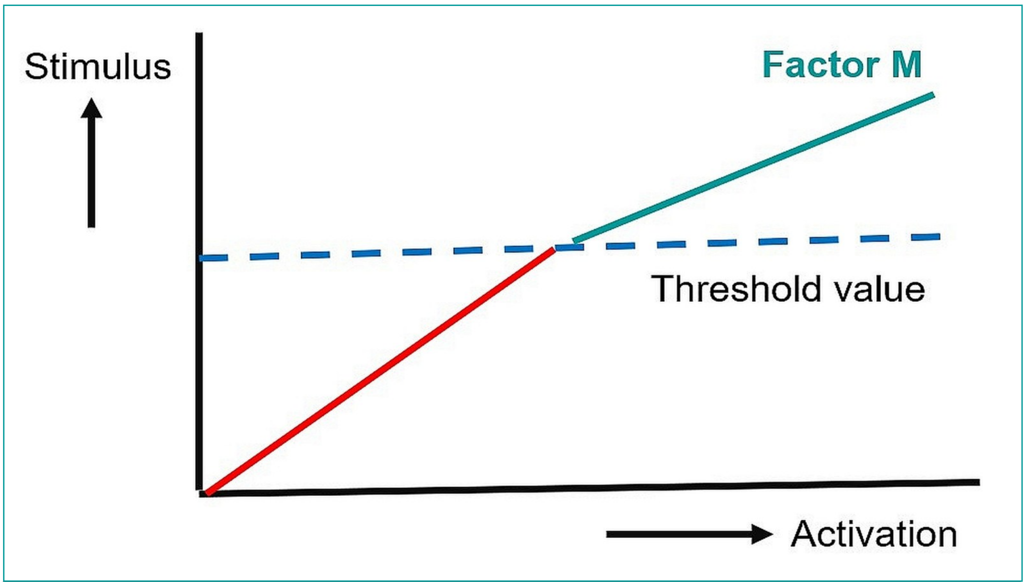
Sources:
- Eppinger, H., Die Permeabilitätspathologie, als die Lehre von Krankheitsbegin, Springer- Verlag, Wien, 1949.
- Pischinger, A. Prof., Dr., Med, Das svstem der grundregulation, Haug Verlag, Heidelberg. 1975



Subcutaneous injection with the factor M gave a significant increase in the Monocytes in the blood and at the same time an increase in the lysis (disintegration) of the Lymphocytes.

In 1961, Pischinger published his studies on this 'needle-prick-phenomenon'. He showed that at the slightest local irritation of the BBRS (in any place) the total regulation system in the body participated. After subcutaneous injection with the factor M, the following changes have been determined on the basis of various parameters:

1. the differential blood count (Monocytes rise).
2. the leukocyte count increases (leucolysis decreases).
3. change in iodine-fixation-value.
4. the polarization electrical properties.
5. the oxygen utilization measured in the periphery.



Stimulus —> non-specific immune response —> Factor M —> activation

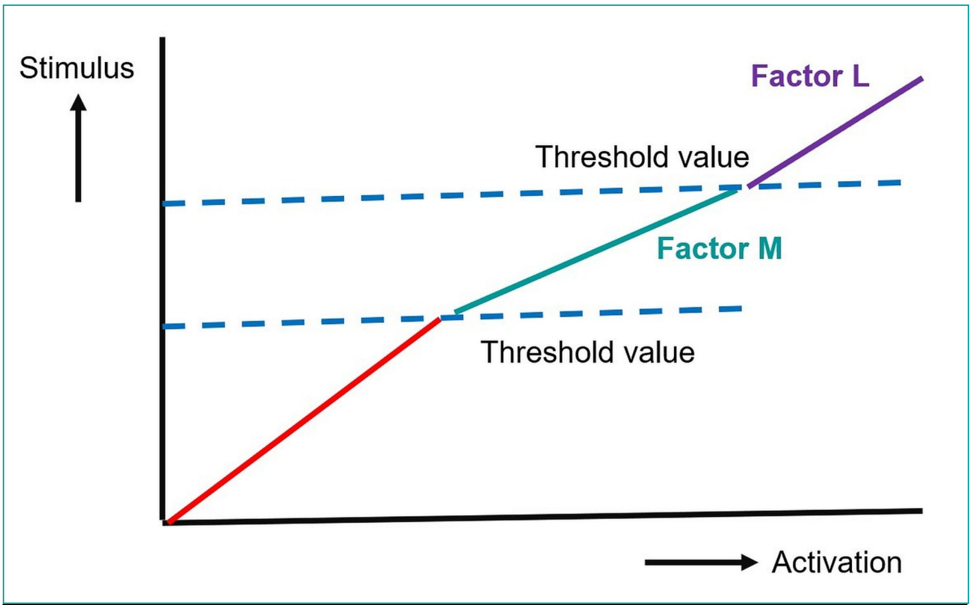
The triple-conjugated unsaturated fatty acids (factor M) activate the non-specific immune response. According to Perger, these substances can be referred to as the body's own humoral anti -shock substance. They take care of the polarity reversal within the non-specific immune-response from the shock-phase to the countershock-phase.

Pischinger also discovered a factor L that is produced by the Fibroblasts. This factor initiates the Lymphocytes to infiltrate a damaged area.

These investigations therefore show without further ado, that the totality function of the body is based on its own system: the BBRS. That system is present everywhere and always reacts as a unity (metaphysical and metapsychic).

This also brings us to a causal treatment of vegetative interferences (accompanied by medically untreatable pain). It is this (non-specific) therapy that affects the BBRS.

It is also clear by now that most naturopathic methods develop their effect through the Basic-Bio -Regulation-System.



Factor M sufficient high —> factor L —> specific immune response

The extra-cellular fluid (15-18 liters) was called 'the inner circulation system' by Eppinger. The term circulation is misleading in this case, but there is an uninterrupted exchange (Panta Rhei: everything that lives is always in motion). Due to its bio-electrical properties, the extracellular fluid interacts with the cells of the interstitium, but also with the parenchyma cells. As a transport -medium for the inner circulation, the connective tissue is the bedding for the humoral functions in terms of shape and physiology.

The effects of the exchange between the BBRS and the blood can be controlled by the arterio-venous anastomoses.

The highly unsaturated fatty acids in the extracellular fluid are highly sensitive to the Redox-potential. Together with the Glycosaminoglycans, they are responsible for the permeability of membranes and vascular walls.

The moisture composition of the tissue water is analogous to the seawater, only the calcium component is different. The amount of Calcium is controlled outside the soil regulation, by the parathyroid glands.

Calcium has many different functions in the body, both intra- and extracellular.

Sources:

- Eppinger, H., Die Permeabilitätspathologie, als die Lehre von Krankheitsbegin, Springer- Verlag, Wien, 1949.
- Pischinger, A. Prof., Dr., Med, Das svstem der grundregulation, Haug Verlag, Heidelberg. 1975
- Perger, F., Das Grundsvsteem nach Pischinger, Phys.Med.und Reh. 20e Jahrgang #6, 1979.
- Drews, U. (1993), Taschenatlas der Embrologie, Georg Thieme verlag, Stutgart / New York, 1993.
- Lamers, H., (1988), Neuraaltherapie en het Basis Bio Regulatie Systeem, Ankh-Hermes. Deventer, 1988.
- Alberts, B.; Bray, D.; Lewis, J.; Raff, M.; Roberts, K en Watson, JD. Moleculair Biology of the cell, Garland Publishing, Ine. New York & London, 1989.

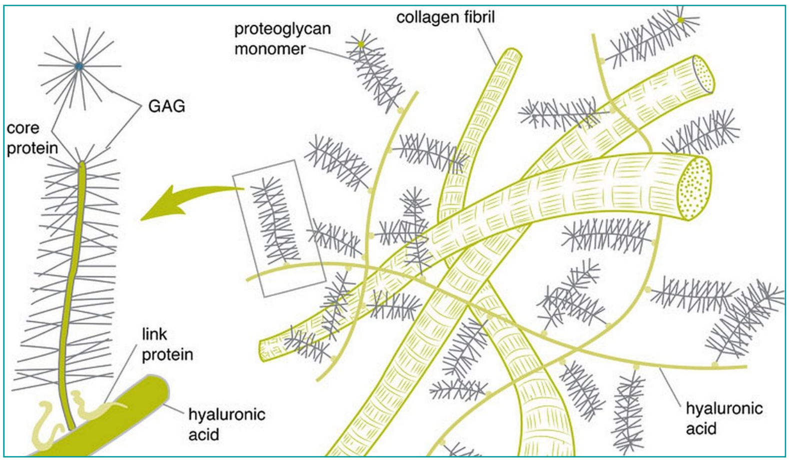
With regard to the Basic-Bio-Regulation-System, the most striking function is that Calcium is needed for the conversion from SOL state (soluble) to GEL state (jelly) in the connective tissue.

Calcium is only found phylogenetically in vertebrates and is necessary for the construction of the skeletal system (supply) and the function of the muscles. In vertebrates, we see the lymphatic system developing, which houses the specific defense. The Basic-Bio-Regulation-System is therefore actually the oldest communication system between the cells, with its own immune system.

The extracellular fluid is a very old system that already has its own specific function. Water can arrange itself (bio-electrically) and this appears to be important for the reporting in the BBRS, which goes outside the nervous system. The information is passed on via the Proteoglycans, the factor M and electrolytes.

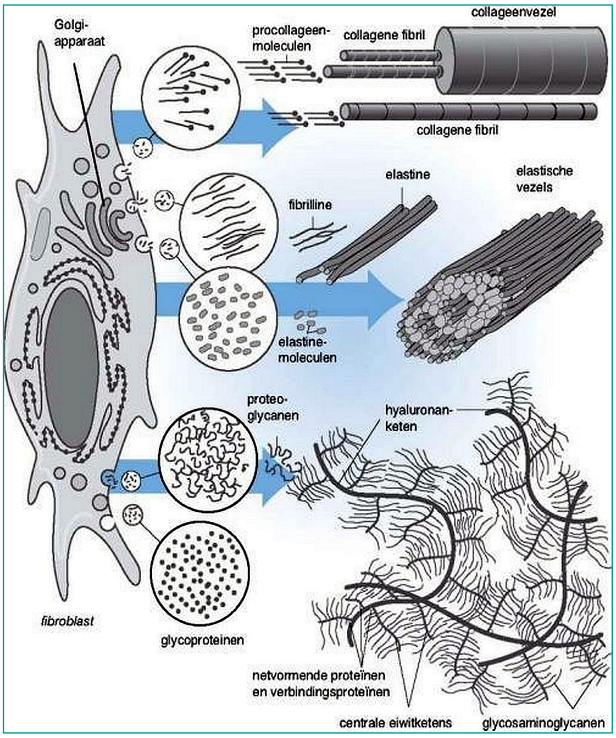
c. Ground-substance

The composition of the ground-substance of Glycosaminoglycans and Glyco-proteins has already been discussed. The importance of the negative charge group of the GAGs are mentioned before. The Proteoglycans are composed of Glycosaminoglycans attached to a protein-chain. Water-molecules arrange themselves as a water-mantle around the GAGs.



Proteoglycans have the potential for an almost limitless heterogeneity. They can vary in protein-component, molecule size and the number and types of Glycosaminoglycans per molecule.

Given this heterogeneity, it is illogical to assume that their function is limited to forming a hydrated space around and between cells. Proteoglycans form gels of different pore sizes and therefore function as molecular sieves for transport in connective tissue.



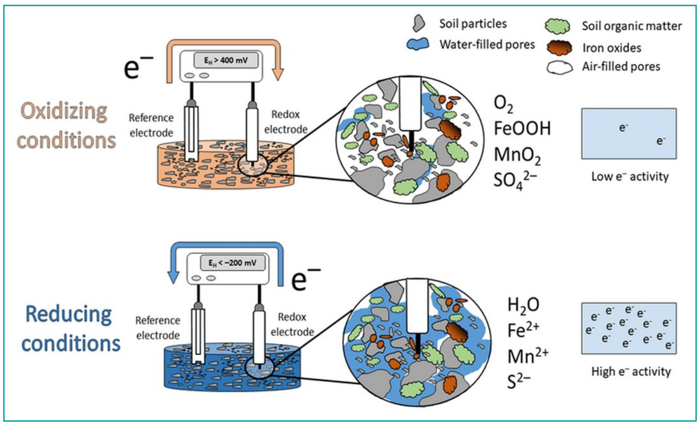
Some polysaccharides (the GAGs from the Proteoglycans) are known to organize into helix-like or ribbon-like structures. Two different polysaccharides can form a junction and change the matrix into a gel-form, when the compound detaches the matrix changes into a sol-form.

Prof. Heine (1985) has seen changes in the pattern of the Proteoglycans in all chronic diseases and also in all tumors. These changes usually run parallel to altered and uncontrollable redox potentials.

Proteoglycans appear throughout the Basic-Bio-Regulation-System as a continuous network, between which the water molecules attach.

Prof. Heine states that these biopolymers of water-sugar-protein complexes are the oldest information systems of the oxygen-breathing single- and multicellular organisms. Iso-iony, iso-osmia and iso-tony of the BBBRS are determined in this way by this composition of the biopolymers.

This guarantees and builds up a bio-potential for life, which can be measured as Redox-potential. This redox-system is excellently able, through the release and absorption of electrons, to store, further guide and process every information that reaches the Basic-Bio-Regulation-System. Moreover, this system is energetically open and in a healthy state it is able to neutralize burdensome energies, including reactions of free radicals.



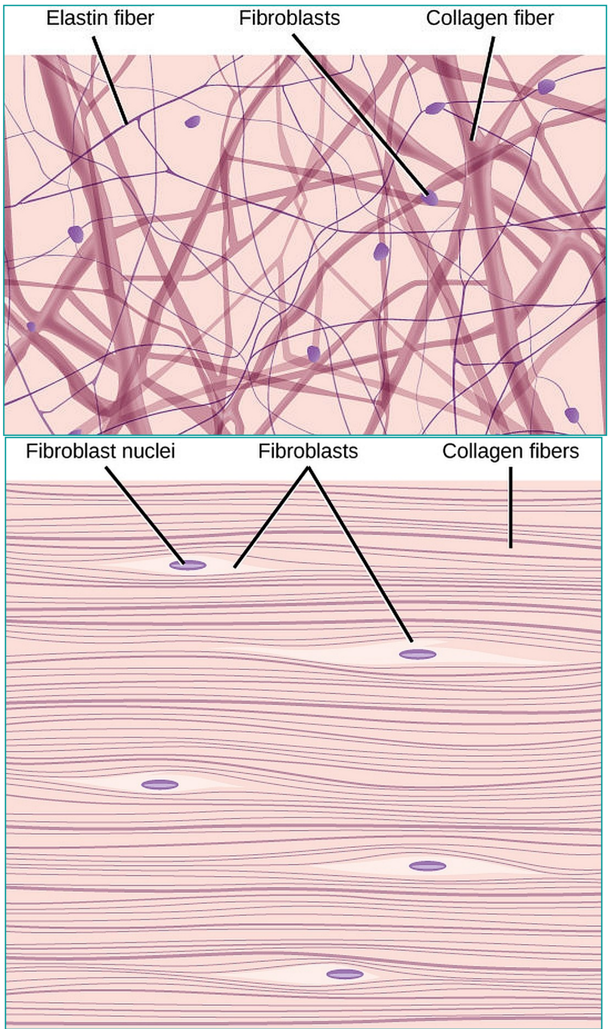
d. Fibers

The fibers in the BBRS (Collagen and Elastin) have already been discussed in terms of composition and subdivision. It is important to note that the production of collagen fibres takes place in the granular endoplasmic reticulum of the Fibroblast, which, given its pluripotent capacity, can synthesize different types of collagen fibres.

The stability and mechanical properties of collagen are determined by the nature and sequence of the amino-acids in the chains. There are regions in the chains, in which the amino acids with uncharged short side chains predominate. In other areas, amino-acids with a polar long side chain predominate (Glutamine, Lysine, Aspartic-acid). The alternation of neutral and polar regions in the procollagen is also important for the characteristic aggregation of the molecules into long collagen fibrils outside the Fibroblast.

The polarity of collagen (+charge) and the ionized NH^+ form of the (water-dissolved) amino group allow the electrovalent binding to the negatively charged Proteoglycans.

The Proteoglycans and Glycoproteins in the matrix form an extensive waterbound network and also determine the location of the fibers located in the matrix. The ratio of Proteoglycans in the matrix determines the rate at which forming collagen condenses and the thickness of the fibers. When loaded, the negatively charged Proteoglycan complexes ensure that the fibers shift according to relatively fixed routes and are guided in the right direction in a way that restores shape after defecation. The cells are anchored in this fiber network by means of Glycoproteins, such as Fibronectin .



Loose connective tissue, with loose woven Collagen and Elastine.

Fibrous connective tissue of a tendon has Collagen-strings ordered parallel.

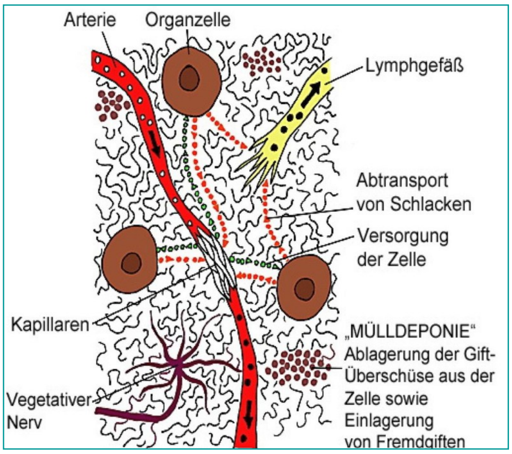
Sources:

- Alberts, B.; Bray, D.; Lewis, J.; Raff, M.; Roberts, K en Watson, JD. Moleculair Biology of the cell, Garland Publishing, Ine. New York & London, 1989.
- Lamers, H., (1988), Neuraaltherapie en het Basis Bio Regulatie Systeem, Ankh-Hermes. Deventer, 1988.
- Morree, drs.J.J. de, Dynamiek van het menseliik bindweefsel, Bohn Stafleu Lochem, Houten/Zaventem. 1993.

24.5.2. Capillaries and lymphatic pathways

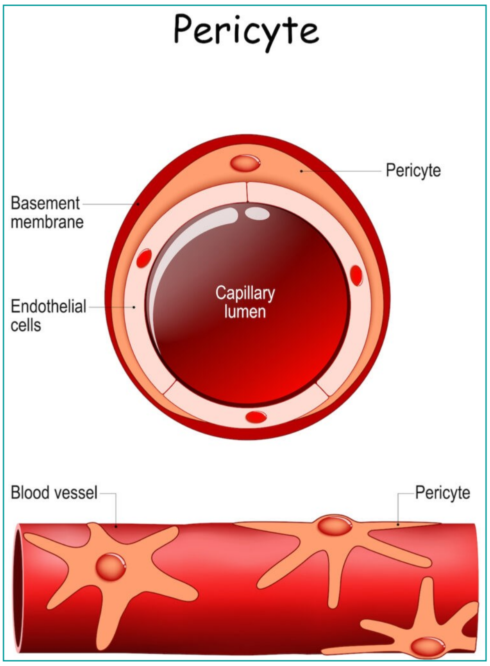
The capillaries do not have direct contact with the parenchymal cells. All substances leave an end-capillary are the first to enter the extracellular fluid. Subsequently, these substances react with the connective tissue-cells and only then does the influence of those certain substances on the specific parenchyma cells follow. In other words, the arterial nutrition of the parenchyma cells takes place from the connective tissue, while the drainage of the venous blood flows back analogously back into the veins, located in the connective tissue.

Disruption of the connective tissue causes disruption of the nutritional and oxygenation of the parenchyma cell and disruption of the disposal of waste products and carbon-dioxide



a. Capillaries

Capillaries are cylindrical tubes, which are bounded by a single layer of endothelial cells. At transverse cross-section, the wall consists of one or two, sometimes three endothelial cells. The endothelium is usually surrounded by a lamina basalis that can be surrounded by a thin fiber layer of type-III collagen, so that a basal membrane is formed. This fiber layer has connections with the connective tissue of the environment and as such fulfills an adventia function .



In many places there are branched cells against the wall of the capillaries that are connected to the capillary wall. These Pericytes are of mesodermal origin and are surrounded by a glycocalix that fuses with the lamina basalis of the endothelium.

Pericytes contain actin fibrils and have the ability to contract. In addition, they play a role in the growth of a new vascular bed. This process is similar to embryonic vessel formation.
The Pericytes affect the permeability of the capillary wall .

Where necessary, new capillaries are formed. The process of angiogenesis occurs by sprouting and duplication of endothelial cells. The signal for angiogenesis is given by the surrounding tissue, in relation to oxygen deficiency or inflammation, tissue repair and growth.

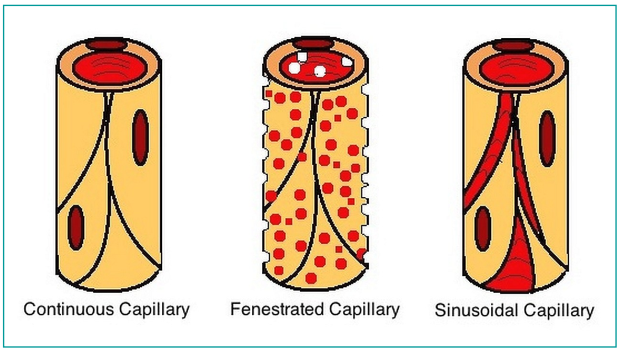
Two well-known factors are the 'acidic Fibroblast Growth Factor (acid-FGF) and the basic Fibroblast Growth Factor (basic-FGF)'. It is also known that Macrophages, Mastocytes and Lipocytes release factors for angiogenesis.

Sources:

- Lamers, H., (1988), Neuraaltherapie en het Basis Bio Regulatie Systeem, Ankh-Hermes. Deventer, 1988.
- Vander, A.J, MD.; Sherman, JH., PhD. en Luciano, D.S.,PhD. (1990). Human Phvsiologv, the mechanisms of bodv function,McGraw-Hill Publishing Company, New York. ISBN 978-0077350017, 2010.
- Morree, drs.J.J. de, Dynamiek van het menseliik bindweefsel, Bohn Stafleu Lochem, Houten/Zaventem. ISBN 9789031351978, 1993.
- Junqueira, L.C.; Cameiro, J en Kelley, R.O. Functionele histologie, Bunge, Utrecht, 1993.

On account of different construction of the endothelial wall, capillaries are classified into 3 types:

1. *Continuous capillary (type-I)* is the most common type. It has no openings and has a continuous lamina basalis surrounded by a layer of thin collagen fibers (muscle and nerve tissue).
2. *Fenestrated capillaries (type-II)* are characterized by fenestrations. These windows are closed by a membrane-shaped diaphragm (endocrine glands and intestinal tract).
3. *Sinusoidal capillaries (type-III)* have a wider lumen due to ingrowth of parenchymal cells in the thin-walled embryonic vessels (liver, bone marrow and adrenal medulla)



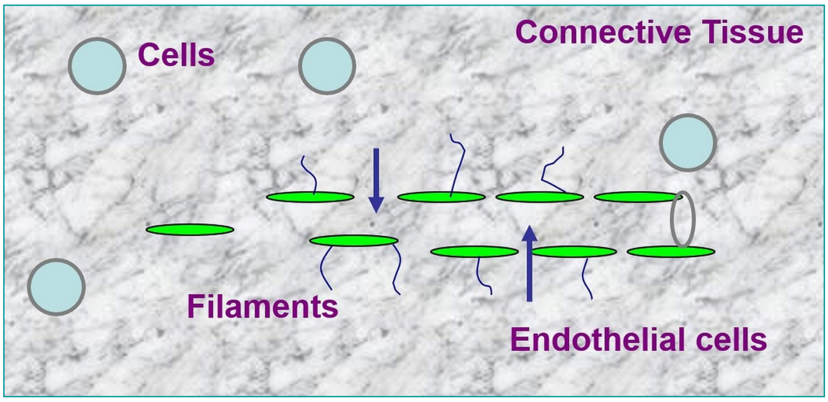
The exchange between capillaries and the surrounding tissue takes place through:

- the intercellular gaps between the tight junctions,
- exocytosis and endocytosis,
- diffusion, osmosis, carrier transport, filtration, etc.

The exchange is regulated by several factors:

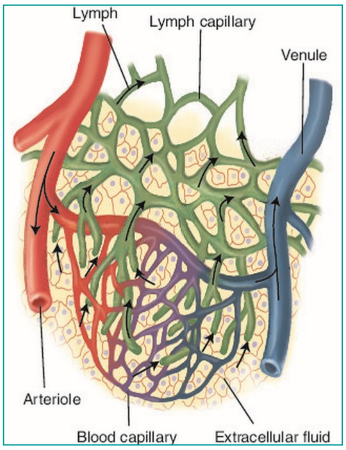
- endothelial signals, such as prostaglandin E_2 and E_3, Adenosine, Endothelium Dependent Relaxation Factor (EDRF), Endothelin, Addresin, etc.
- vasoactive substances, such as Bradykinin, Histamine,
- vasoconstrictors, such as Thromboxane A2,
- different neurotransmitters.

b. Lymphatic Pathways



Not all proteinaceous fluid that flows from the capillaries to the interstitium on the arterial side is reabsorbed on the venous side; a certain amount remains in the connective tissue, which is drained by the system of lymphatic vessels.

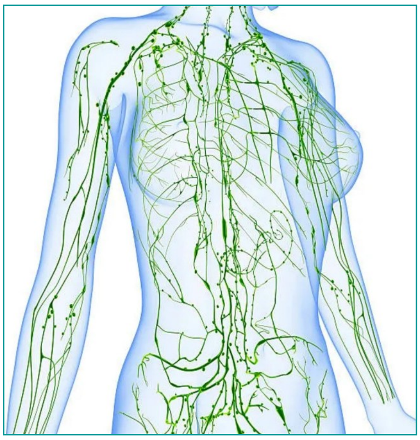
The lymphatic vessels have a blind origin at the level of the interstitium and are formed by a thin layer of endothelial cells separated from each other.



The endothelial cells are connected to each other by Glycosaminoglycans and linked to the matrix of the connective tissue by means of extracellular microfilaments. Lymphatic vessels are missing in some places, such as in the bone marrow and in bone tissue.

The endothelial cells of the lymphatic vessels do not connect exactly, so that a drainage system of lymphatic capillaries is created. There is no lamina basalis around the endothelium and no continuous basal membrane.

Fibers from the connective tissue attach to the endothelial cells as anchor fibers (extracellular microfilaments), which play a role in the permeability of the pores in the endothelial wall.



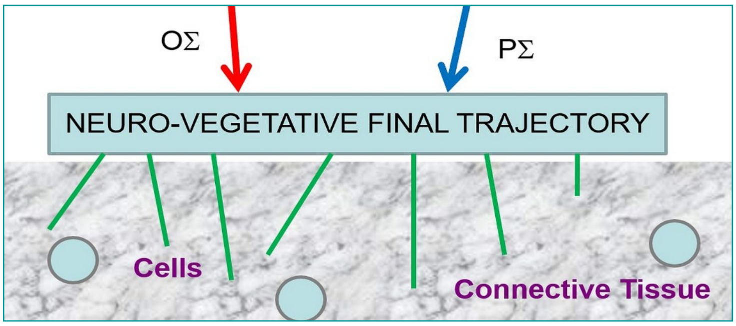
Originally, the lymphatic fluid is extracellular fluid. In the lymph ganglia, the composition of the lymph changes, partly due to the addition of large amounts of Lymphocytes. An immune response also takes place in the lymph nodes if necessary. In this way, both proteins and Lymphocytes are added to the bloodstream.

The parenchyma cell is therefore dependent on the loose connective tissue (BBRS) in terms of nutrition and drainage. The BBRS plays a role in the exchange through:

- the transmitter function.
- metabolic function.
- the hoarding function.
- the concentration regulation.

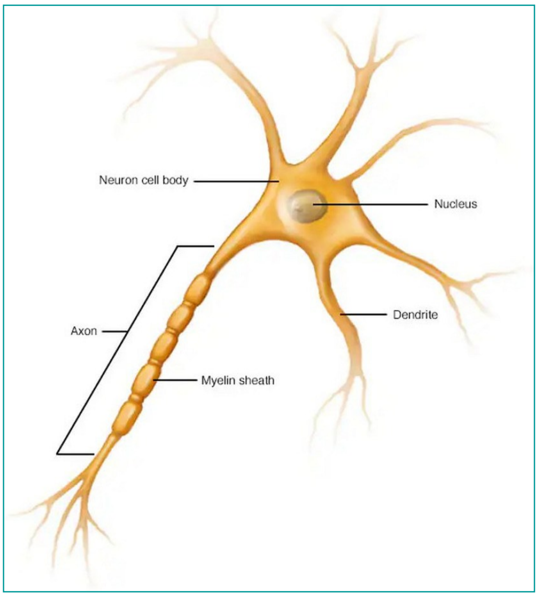
24.5.3. Neuro-Vegetative Final Trajectory

The nerve plexus at the end of the vegetative nervous system forms the so-called vegetative nervous periphery. This is a wide-meshed, spatial network of unmyelinated fibers. Distinguishing between ortho- and parasympathetic nerve fibers is impossible in this end-network. Classic direct synapses, as everywhere else between the nerve cells, are absent here. All the small nerve endings end freely in the extracellular fluid.



Birkmayer has also found that an axon approaches a muscle cell and a blood vessel, but remains at a certain distance from the target cells. The naked axons lie in the direction of the target cells in the extracellular fluid. He also found situations in which axons were located in loose connective tissue, close to mesenchymal cells and invaded Leukocytes.

The fibers in the syncitium consist of unmyelinated axons, embedded in the Schwan basal plasmodium, which consists of merless glial-cells. Pischinger has been able to determine on the basis of material from the dental pulp and the pulmonary valve, that the axons with their decreasing thickness of the fibers have no perineurium in this area, and become more superficial until the axons with increasingly wide surfaces come into contact with the surrounding environment (extracellular fluid).



The innervation in the ground-plexus appears to be focused on physiological activities. The activity of the final formation takes place by the release of transmitter substances, which causes chemical changes in the tissue fluid.

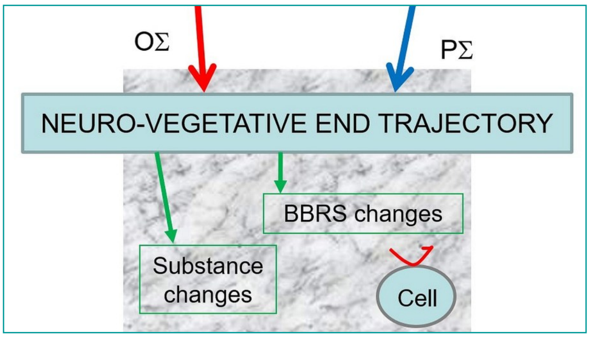
A physicochemical system is formed, with sympathetic secretion of Adrenaline and parasympathetic secretion of Acetylcholine, in addition to which there are paracrine secretions of various other neurotransmitter substances.

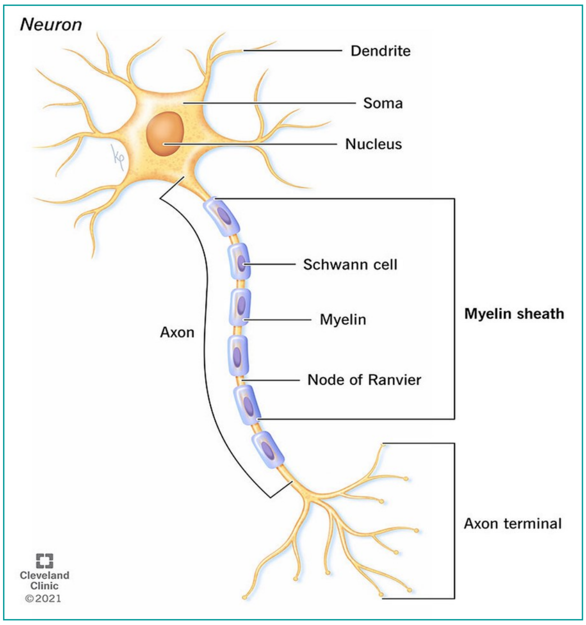
Sources:

- Birkmayer, W & Pilleri, G., Die reticuläre Formation des Hirnstammes und ihre Bedeutung für das vegetativ- affectiv Verhalten, Hoffman / La Roche, Basel, 1965.
- Pischinger, A. Prof., Dr., Med, Das svstem der grundregulation, Haug Verlag, Heidelberg. 1975

However, the secretion of these substances, or at least their action on the receptor cells, depends to a large extent on the state of the connective tissue (BBRS).

In other words, the neurovegetative final trajectory has no direct contact with the parenchyma cells and there is no synaptic stimulus transmission here. The neurotransmitter substances are released into the extracellular fluid and can therefore also modify the composition of this fluid.





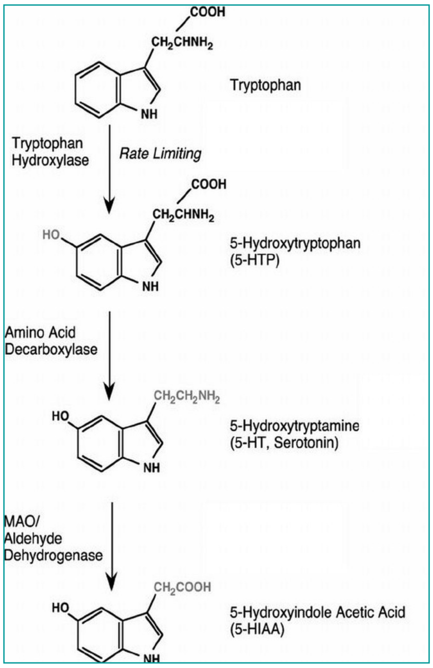
Where and how does the further conduction of the nerve impulse to the parenchyma cells take place? The conduction takes place via the neurotransmitter substances through the extracellular fluid and is then captured by receptors on the cell membrane of the parenchyma cell.

The principle of signal transduction also applies to neurotransmitters, especially the ion-channels and the receptors linked to G-protein.

We have already seen that the transfer systems are not limited to ortho- and parasympathetic impulses and transmitter-substances.

The total of neurocrine, endocrine, paracrine and autocrine systems can be considered to be part of the neurovegetative final tract of the Basic-Bio-Regulation-System, since the capillaries and the vegetative end-trajectory belong to the BBRS.

Physiological experiments have shown that the influence of the transmitter-substance cannot always be the same. This is reflected, for example, in the intestinal musculature, where the influence is mainly focused on the tunica muscularis. In the tissue and in the receptor cells there are modifying factors, for example Catechinonydases or Phenoloxydases. These substances convert Adrenaline into the inactive Adrenosine, they can also neutralize hormones, such as in the Uterus.



In the case of nervous transfer, one must take into account:

- the nervous pole (the final formation).
- the effective pole (the receptor).
- the transmitter substance.
- the local and general factors that modify the effect and adreoxinogenic factors, hormones and ferments.

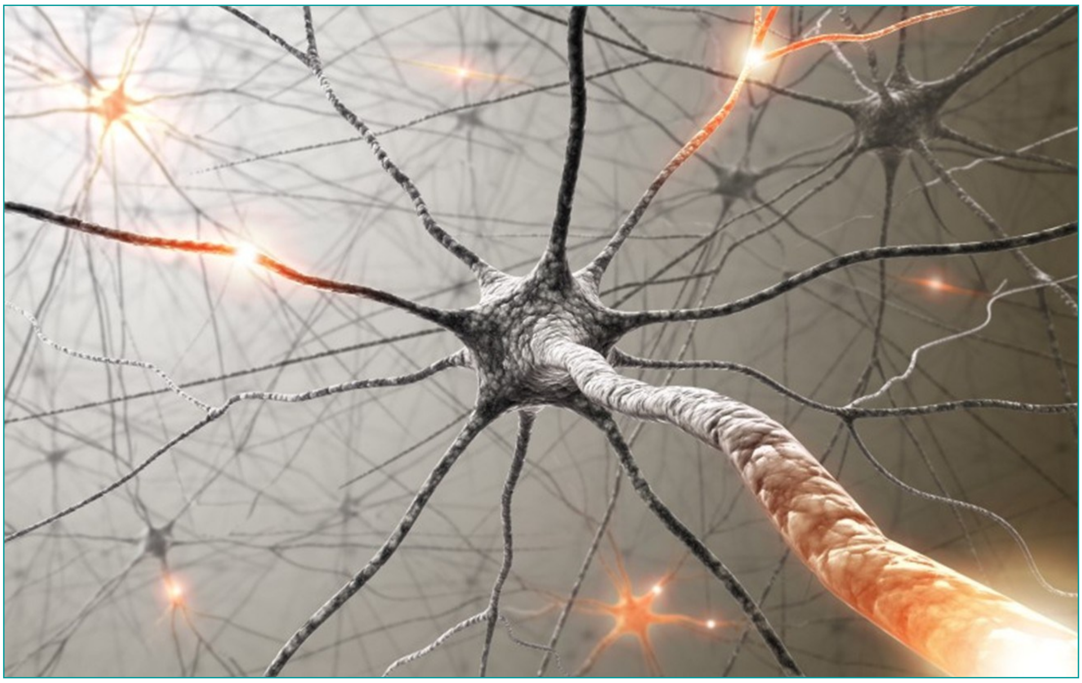
In the last point, of the general factors, the function of the capillaries is particularly important. In the case of local factors, it is specifically the tissue cells that exert their influence, such as the ferments contained in them (Phenol oxidases, 5-Hydroxytryptamine, MAO).

Sources:

- Kandel, E.R.; Scwartz, JH.; Jesse!, TM., Principles of neural science, Appleton & Lange, Connecticut, 1991.
- Zagon, S. & McLaughlin, P.J (1993), Receptors in the developing nervous svstems. Vol 1: growth factors and hormones. Vol 2: neurotransmitters, Chapman & Hall, London/New York, 1993.

This concept, that different types of neurotransmitters can be associated with characteristics of granulae, has received more attention in recent years. This concept, with the modification of the transmitter-substances in the Basic-Bio-Regulation-System, makes it possible to explain why so many functions of the autonomic nerves cannot be blocked by both the classical adrenergic and cholenergic inhibitors.

In terms of development, the neurovegetative final trajectory belongs to the archi level and is controlled in the periphery by molecules of the extracellular matrix. The information from the nervous part of the Basic-Bio-Regulation-System is passed on to the higher systems and inhibited if necessary. A continuous stimulus from the Basic-Bio-Regulation-System can exert a continuous influence on the higher levels of the nervous system.



24.5.4. The trias in the BBRS

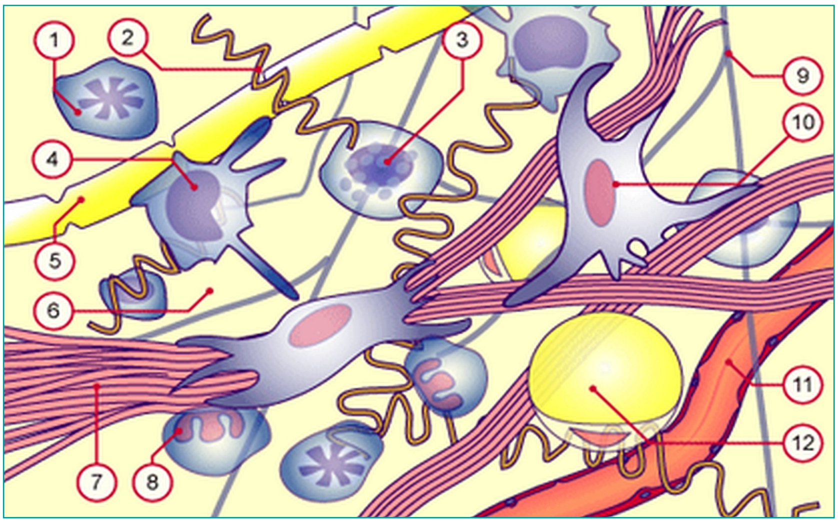
In summary, the Basic-Bio-Regulation-System includes:

1. Connective tissue cells,
2. Extracellular matrix and liquid,
3. Capillaries and lymphatic pathways,
4. Vegetative nervous periphery.

The nerves and capillaries therefore have no direct contact with the parenchyma-cells, and therefore the Basic-Bio-Regulation-System (BBRS) cannot only be seen as connective tissue.

The BBRS has its own producing secretion to the parenchyma-cells and its main function is to control the ground functions; the phylogenetically oldest homeostatic functions.

The Basic-Bio-Regulation-System is the carrier of the primary control and provides the conditions for the correct functioning of the specific parenchyma cells. The BBRS is present everywhere and continuously in the organism.



Basal structure of the Basic-Bio-Regulation-System:
1. Plasma cell.
2. Elastine.
3. Mastocyte.
4. Macrophage.
5. Neve-fiber.
6. Basis substance.
7. Collagen.
8. Neutrophile Granulocyte.
9. Reticuline fiber.
10. Fibroblast.
11. Capillary with endothelia cells.
12. Fat cell.

Topographical main locations of the Basic-Bio-Regulation-System are:

* tunica piallaris of the skin,
* Arachnoid and Pia mater,
* adventiva, perivascular and interstitial,
* tunica mucosa Tractus Gastro-Intestinalis (TGI),
* tunica mucosa Tractus Uro-Genitalis (TUG),
* content of the Haversian canals in the bone tissue,
* capsula synovialis,
* alveolar tissue of the lungs (TR),
* tunica mucosa of the Trachea,
* plexus Choroideus,
* Endocardium, heart valves and endothelium capillary (TC),
* Peritoneum and Mesenterium,
* interstitium of all organs.

All types of the Basic-Bio-Regulation-System are connected throughout the organism through the vascular and neural components.

The cells of the BBRS have specific functions, such as the biosynthesis and regulatory metabolism of Proteoglycans, proteins and lipoids. These cells regulate the basic principles of homeostasis and influence all its parameters, such as electrolytes, Redox-potential, acidity, temperature and basal metabolism.