I. THE ENVIRONMENTAL COMPLEX OF THE CELL

1. THE CELL

The basic regulating system serves the organism in its nonspecific defense performance.

The histological basis of this system has been called the cell environment complex by Pischinger, consisting first of all of cells of the soft, nondifferentiated connective tissue whose ancestral cell is the fibroblast, a cell which still exists in the adult organism as a totipotent cell.

All different forms of connective tissue cells, such as small and large round cells, histiocytes, resting migrating cells, lymph cells, plasma cells, granulocytes and mastocytes developed from the original ancestral cell. The cells of the so-called reticulo-histiocytoid systems, which serve in the general defense of the organism are, after all, specifications of the original ancestral cell of the mesenchymal connective tissue. The various cell differentiations from the mesenchymal ancestral cell can be seen in special cell cultures.

For instance, this is how under special burdens from fibroblasts monocytic, respectively histiocytic cells, are produced; vice versa we are able to realize from blood monocytes and other monocariocytes again fibroblasts. It was also possible in special culture media to change blood lymphocytes into reticulum cells,

this was largely accomplished via an intermediate stage of large round cells which are commonly called lympho- or germinoblasts. These experiences lead us to the conclusion that there are genetic connections between the various cell types of the stroma. Therefore, we can also infer that the cell stock is subject to strong changes due to functional conditions, even without a new cell supply received from the blood, respectively the capillaries.

As further discovered by PISCHINGER and his colleagues who worked on cell cultures, fibroblasts function not only through appropriate differentiation in special cell forms and environments, but also influence directly their surrounding environment. If the environment is subjected to stress such as, for instance, the elimination of organic nutrients in culture media, the cells will secrete zytoplasm droplets, possibly due to changed border area conditions. These sequestered droplets bring substances from the living cells into the environment and modify it to such an extent that the cells are able to stay alive. We can see, therefore, that there is an intimate functional connection between the cell and the environment which is apparent in the sense of life maintenance and defense against harmful irritations. All these experiments and observations show similar results, i.e. cells exist with their environment in a changeable regular connectivity. We are dealing here with biological ground functions which concern the primary regulating system of the one-cell life as well as the higher organisms.

In conclusion, deviations from the normal condition in the environment, whether in the chemical sense (acid-base economy), in the electro-chemical tension field (disturbance of ion guidance), in the oxyreductive potential (acute O_2 deficiency) or due to the effect of a toxic irritation to a cell, namely the dispensing of metabolic products which can normalize the troubled environmental system.

2. THE INTERSTITIAL ENVIRONMENT

The regulating principle in the cell's environmental system shows the effort to construct harmonic connections between cell and extracellular liquid. Seen from a biological viewpoint, one cannot look at the notion of a cell without its life environment in an isolated context. This life environment of the cell represents <u>in vivo</u> the extracellular liquid which surrounds the cell elements, most generous in the soft, respectively in the cell-rich stroma. This cell environment system occurs in its purest form in the early embryonal mesenchyme. The various vibrils occur later, but they do not play a role in the ground regulatory system; however, more attention must be given over to the extracellular liquid because no cell can fulfil its function without it.

The extracellular liquid, also called the interstitium, is filled with the so-called ground substance, according to H. Gibian. Chemically unstructured, this ground substance contains

several, perhaps many elements and groups of substances. The accumulated fibers or cells are functionally cemented by this fluid and this fluid is therefore responsible for the permeability of membranes and vaascular walls, storing the major portion of the extracellular and extravascular body liquids. The metabolic products are transported to and fro between the vessels and cells in this fluid, enabled by the chemical-physical properties of this ground substance. A diversity of fermentative and hormonal mechanisms appear to play a role in its steering. The interstitial ground substance contains proteins of unknown composition as well as lipids and many carbohydrates. A special role are played by the mucopolysaccharides since these substances permit diffusion regulations. The biosynthesis of the mucopolysaccharides occurs in the preliminary phases, probably in the fibroblasts.

3. THE CAPILLARIES

As the next item we will look at the position of the capillaries as they relate to the connective tissue. For this we must take a side trip into ontogenesis. Capillaries occur, like all vessels, as nodular cell accumulations in the mesenchyme -- the so-called blood islets -- which then spread and connect into nets. The outer cells turn into endothelial tubes while the inner cells lose their reciprocal cyoplasma contacts, grow into spherical form and finally into primary blood cells. The extracellular liquid increases and turns into primary blood plasma. This

developmental stage shows that the capillaries, like all vessels, are products of the embryonal mesenchymes. Besides, this is also shown in the regeneration of capillaries. Blood cells, respectively blood corpuscles belong to the group of connective tissue cells, although with a differentiation. The blood plasma is logically an analogue to the extracellular liquid. Just like in the case of the former embryo, there remains in the fully-grown organism the immediate sphere of action of the capillaries the soft basic tissue, which is the cell environmental system.

The substances passing in the endothelial arrive in the extracellular fluid, with which the connective tissue cell reacts. An influence on specific organ cells can only occur indirectly. Nowhere in the organism is there a direct contact between capillaries and parenchymal cell, connective tissue is interspersed everywhere. Because of this special quality, the interstitial space is also identified by the term of Transittract. (The only area where this basic building plan is modified is found in the central nervous system, where around the capillaries no extracellular region could be found which permits the free diffusion of substances trespassing from the bloodstream. The functions of transportation are being performed here immediately by the cell membrane, where intracellular transport and distribution mechanisms are reversed). We see therefore the central and exclusive mediator role of the extracellular spaces, which accept the supply coming from the capillary circulatory system, before the cellular metabolic events can begin.

capillaries and also in the tissues fluorescent substances which were ultrafiltratable and were resistant to heat up to a specific degree. They were not attacked by the various body ferments, therefore did not have a protein structure nor were they bound to protein. Repeated investigations showed that these in serum occurring substances were found in increased amounts in pathologic events, and that they had to be boundary layer active substances, since changes in permeability were caused by them. Eppinger connected the occurrence of these metabolic serum products with the functioning of the vegetative nervous system. It was Pischinger, however, who was successful in determining these humoral effective factors which take action in vegetative basic events, and who recognized their properties and mode of operation.

6. THE FACTOR M AS HUMORAL ACTIVE SUBSTANCE

Pischinger conducted his investigations, which revealed to him the humoral effective factors, with a protein-, carbohydrate- and glycerin-free watery serum preparation. The serum was derived from animals which were put in a particular vegetative condition. The broadly effective spectrum of this substance (it was the preparation called ELPIMED) in many and various disease symptoms led to the clear recognition that therapeutic effects could not be organ-specific, but needed to be categorized into a comprehensively-oriented, i.e. nonspecific therapy. Extensive animal

experiments showed the following results:

After subcutaneous injection of ELPIMED into his experimental animals, a highly significant rise in the monocytes (77%) was seen within a day. This same phenomenon could be reproduced equally well in humans. These simultaneous results leads to the assumption that through the specific preparation of a donating animal there arise substances in the serum which cause a monocytosis in a second animal after subcutaneous injection. Pischinger was justified to give this effectiveness the name Monocytic Factor (Factor M). This monocytogenic ability can be transferred by the serum of pretreated animals. By means of extensive histologic investigations regarding the existence and development of monocytes, Pischinger arrived at the conclusion that the ancestral cells of monocytes lastly are the nondifferentiated reticular cells of the reticulohistiocytoid systems and the soft connecting tissues. This fact, as well as the observation in cell cultures that fibroblasts, when subjected to a threatening situation, will change into mobile round cells, i.e. monocyte elements, shows that the monocyte as genuine ground tissue cell will alert us as to the condition in this system. The number of monocytes yields information on the defense condition of the organism.

As a concurrent symptom during his experiments, Pischinger found that simultaneously with the rise of monocytes when animals were given a subcutaneous injection of ELPIMED, an increase of the lysis rate of lymphocytes occurred. In view of the role which

is given over to the lymphocytes in the framework of immune biological events, it appears that this monocytic factor also influences immunological regulations.

As a result of his numerous investigations, Pischinger concluded that the effective substance complexes of the monocyte factors exist everywhere in the organism and most probably descend from cells or cell fragments. The monocyte-increasing factors occur also in man, of course. Their behavior in the blood is especially interesting because we are dealing here with the question whether evidence can be found to show that they are substantial carriers of vegetative functions in the humoral field. It is obvious, a priori, that a pure humoral regulation does not exist as such. Aside from the fact that all regulating areas must work together, i.e. nerval, humoral and the cellular, we are faced with the question from where the specific humoral effective substances originate and how they end up in the blood. Starting from the fact that there are always a not inconsiderable number of leucocytes which dissolve in blood, Pischinger has been able to show that these cells contain above substances, a feat which could be verified with UV spectrography. He could also document the analog substances from fibroblasts.

Since the major substances of factor M could be shown to consist of energetic active conjugated unsaturated oleic acids, serum iodometry helped to reveal a more accurate grasp and analysis of the basal regulations. Essentially, iodometry could document that substances exist which bind with iodine (respec-

tively utilize the unsaturated oleic acids with their conjugated double bindings), and indeed in amounts depending on certain regulations. With this method of Pischinger's, it was possible for the first time to ascertain more accurate details about the zytohumoral regulation. Simultaneously to this, we have learned to identify the neurohumoral (transmission of metabolic effective products from the vegetative endplait) and the angio- or hemo-humoral regulation function (dispensing of hormonal and metabolic active humors from the capillary into the cell environmental system). The common active environment of all these systems is the extracellular liquid.

Friedrich Kraus had already discovered back in 1922 that motion appearances in the vegetative operating sphere can be steered by border area potentials. With other words, a electro-regulation is taking place here. Serum iodometry yields also hints as to electrodynamic events in the vegetative basis system, where besides the iodine usage value through strength as indicator, electrotitration provides valuable details. After this background we understand that recently in increasing numbers vegetative regulation events and their disturbances are being measured by investigators and followed with electrical methods from the body surface. Kracmar is of the opinion that with capacity measurements the function of the nerval, with resistance values the function of the zytohumoral can be read.

II. THE PRICK PHENOMENON

A good example by which above regulatory events can be identified from basic tissue is the Prick Phenomenon by Pischinger.

Pischinger was able to prove with this phenomenon that even the slightest irritation of pertinent tissue, respectively a needle prick, will set into motion the entire reacting system (meant here is the nonspecific ground regulatory system). The prick phenomenon illustrates the total character of the ground system. Pischinger used five parameters in order to prove the reaction of the vegetative ground systems to a prick into the vena cubitalis. These characteristic features concern the following basic functions of the living body:

1. The differential blood picture (rise of monocytes),
2. The leucocyte numbers (increase of leucolysis).
3. The iodine binding values in serum extract (iodometry),
4. The polarization-electrical properties of hand to hand,
5. The oxygen utilization in the periphery, measured on the HbO_2-content of venous blood.

All functions show in a good manner the 1961 by Pischinger first described prick phenomenon, i.e. that the same system is always addressed whose performances, when the irritation exceeds the local defense, run in totality. The threshold of irritation for this is fairly low. This comprehensive arrangement reacts most sensitively, as shown by the prick effect. The investiga-

tions show without a doubt that under a comprehensive function lies a self-owned system, i.e. our vegetative ground system as a foundation, which therefore presents itself as a total biological vegetative ground system and which runs through the entire organism.

This allows us also to understand the effects of acupuncture as nonspecific vegetative reversing therapy, even when we disregard the interconnections of the meridian rules.

The interlacings of these total reactions reach not only across nerves, but mainly also over the named zytohumoral effective factor M, which can be quantitatively recorded in tissue fluids with serum iodometry. Its determination in blood serum forms the basic foundation for judging the reaction situation and the reaction type of an organism. These cytohumoral substances descend from cells (leucocytes, fibroblasts and others) and appear as the basic substances of humoral regulation. They develop not only in the cell environment system, but also in blood, and indeed in reactions between the leucocytes and the blood liquid, resulting in a regulatory-caused, alternating rich lysis of leucocytes, where the above named humoral active substances are freed.

III. BIOLOGICAL GROUND REGULATION LIES PRIMARILY IN THE PERIPHERY

As shown in several investigations by Bergsmann, there is to be noted an asymmetry of vegetative characteristics and the

regulation between right and left portions of the body (significant differences of the number of leucocytes in the right and left halfs of the body in single-sided focus burdens furnish exemplary proof). The basis of this asymmetry is a side-differentiated run-through of the capillary system. This shows the venous blood from the periphery, respectively the capillary blood shows cellular and chemical differences of changing proportions between both halfs of the body and also between various body regions. This fact that this phenomenon is lacking in the arterial area documents that these differences must develop in the periphery; with other words, the focal point of the regulations does not lie in central areas. The vegetative functions have their root therefore in the periphery, expressing themselves in physico-colloid chemical and electrical characteristics.

IV. EXPLANATION OF NEURAL THERAPHY ACCORDING TO HUNEKE

From these connections, this is how Pischinger was able to explain for the first time the neural therapy phenomenon according to Huneke. As we have already learned through the needle prick phenomenon, there is hardly an intervention into the organism which does not reflect itself in nonspecific ground functions. Seen from a common angle, these are all noxae which endanger the ground system, such as injuries or mechanical disturbances, physico-chemical damages and poisons of tissue-active hormons. Depending upon the breached portals, areas of

disturbance are caused which, however, manifest themselves only after the local defense is overcome. With other words, this is a field of disturbance which begins to scatter, i.e., develops a remote effect. This remote effect may be general or local. The seconds phenomenon as well as the entire field of disturbance therapy can only be understood when the total biological ground system with its three helping poles, the nerve diencephalon, the cellular lymph tissue and the hormone pole (suprarenal gland) is taken into account. Each field of disturbance plays primarily in the cellular connective tissue, which is also identical with the ground system and leads to alterations in the tissue potential, thereby causing damages to the nonspecific vegetative system in total.

If we now inject into a "guilty" depolarization center (field of disturbance) a dose of ELPIMED as the remedy, which repolarizes, it will be understood that the entire and general situation can revert to normal. The seconds phenomenon rests on a general reversal of the comprehensive ground system, with the bioelectrical potential in the center and all consequences reflected in blood and tissue. This must also lead to a restitution at the diseased puncta majoris, of course, if anatomically still possible. It is in these areas where the patient will feel a change in his condition.

V. CONCLUSION

If we attempt to look upon the biological basic regulating mechanism on a comprehensive basis, and if we ask:

1. What regulates,
2. Where are the focal points of regulation,
3. What is being regulated,

we arrive at the following results:

1. WHAT REGULATES?

Regulations begin with the correlations between the cells and extracellular liquid, the life medium of the cell. Besides the cell, the regulating factors of the ground system are the nerves and capillaries, with their differentiated permeability. As the regulated element, seen in a basic sense, there are the body liquids, such as the extracellular fluid and the blood plasma, to which we must also add in a wider sense the lymphs and the liquids of the serous cavities as well as the liquor cerebrospinalis. As a rule, for the basic regulation there are always all three factors involved (the connective tissue triad).

2. WHERE ARE THE FOCAL POINTS OF REGULATION?

Although in the higher organisms the thalamo-hypothalamic

system is seen as the dominant and autonomous regulator and is the first reflex organ from and to the periphery as well as the mediator between brain and periphery, there is sufficient evidence for the cytohumoral regulations in the peripheral ground system, which are phylogetenically much older function models.

As commented upon several times by Pischinger, the parenchymal cell does not have an immediate contact with the vegetative nervous system nor does it with the capillaries. It is surounded by the extracellular liquid. The total connective tissue system with its performance is switched ahead of the organ cells and delivers the nonspecific conditions for a differentiated function of the latter. Therefore, the actual arena of biological events is changed from the special parenchymal cell to the total biological ground regulating system.

3. WHAT IS BEING REGULATED?

In conclusion we may state that we are dealing with the basic functions of life itself; these functions are identical with defense or the equalization of imbalances which constantly influence life from the outer environment. This does not mean that such an influence is unnecessary or harmful. There exist sufficient studies showing that tensions to the inner as well as the outer environment are needed for the continuation of life. However, if these exceed the ability of the body's defense mechanism to cope, this means disease or death.