Immunobiological phylogenesis and ontogenesis

The immunobiological differentiation and maturation takes place apparently in the course of the phylogenesis of the living beings. Whereas graftings in the vegetable kingdom and transplantations in the animal kingdom up to the avertebrates homologously are possible, they can be effected only in exceptional cases with mammals.

Customarily, antibodies are believed to form in the vertebrate organism after ingestion of antigenous foreign substances. There is, however, biological evidence (M. KRÜPE) that even higher plants such as cryptogames and phanerogames can form gammaglobulin though immunoreactions as observed in vertebrates are not known. Also proteins of viruses and bacteria can bind specifically with antigenous substances and cause agglutination or precipitation. These specifically reacting proteins are called *«lectines»* (fr. legere = select), as distinguished from the antibodies. The formation of gamma-globulin has been shown in lobsters and caterpillars of certain moths.

Of the poikilothermes studied so far (reptiles: tortoise; amphibia: frogs; fish: carp), agglutinins and lysins against bacteria, eryhtrocytes and sperm antigens have been found (KRÜPE). Quantitatively, the capacity of forming antibodies is lower than in birds, leave alone mammals, and depends on the temperature. Precipitines have so far not been provoked in cold-blooded animals.

Precipitating, agglutinating and lysing antibodies are sparingly formed in rats and guinea-pigs, but readily in rabbits and chicken. Horses are better producers of antitoxins than e. g. sheep or cattle. Gold hamsters and guinea-pigs are standard animals for sensitizing effects and anaphylactic reactions.

Homotransplantations can easily be obtained in coelenterates, planaria, earth worms, insects and echinodermes (CUSHING and CAMPBELL, 1957). Annelides take up homologous implants better than heterologous implants, the time of discharge depends on the mutual genetic distance.

Avertebrates cannot distinguish between autologous and homologous tissues, in certain cases not even recognize heterologous tissues.

Avertebrates do not show the characteristic consequence of the propagation of granulocytes → lymphocytosis → monocytosis when stimulated by foreign substances. The inflammatory process consists of phagocytosis and digestion of the foreign material. Indigestible material is sealed off.

Pigs and horned cattle have no gamma-globulins when born. Lactoglobulins contain high concentrations of antibodies, which are absorbed enterally within the first few days after birth.

The antibodies of the maternal serum in calves, lambs, mice and rats are transferred via the colostrum. The absorption is effected by pinocytosis.

Immunoglobulins in rabbits, guinea-pigs and rats are transferred via the fetal yolk-bag, not via the placenta. This membrane corresponds to the yolk-bag of chicken, which has long been known as the way of the immunoglobulin transmission in birds (Good and Papermaster).

The existing fragments are too scarce for a phylogenetic synopsis. It is, however, certain that the immunological reactions differentiate in the course of phylogenetic evolution and develop fully in mammals.

The topography of the embryonic interrelations between mesodermic and ektodermic derivatives is found in man as a principle in many variations: layers of epithelial cells, which are filled with mesenchymal (lymphatic, reticulo-histiocytary) formations of tissue.

This principle is preserved the purest in the thymus.

The thymus

is an epithelial-lymphoid organ. Beginning from the 10th embryonic week, the epithelial thymus rudiment originating from the 3rd to 4th gill-arch fills with mononuclear (lymphatic) cells of mesenchymal provenance. The epithelial covering is preserved, but epithelial cells build in the lobes roundish formations of pavementlike epithelium, the Hassall's bodies. These epithelial cells have the characteristics of a secretory function.

Differences between the quantities of nuclei distinguish the cortex area from the marrow area. Compact clusters of lymphocytes with their quantitative superiority of nuclei are distinctive of the cortex. The third population of cells is represented by large mononuclears – reticulum cells, macrophages – which partly phagocytise the smaller lymphocytes and their fragments.

From the organogenesis and experimental findings (Ford and Micklem) it appears that mesenchymal parent cells migrate into the thymus and are apparently necessary for the function. The lymphocytes developed in the thymus can live from 3 to 4 days and only a small part of them (about 1%) are eliminated.

The thymus answers autonomously the influences from outside. Sterile breeding of animals does not influence the cell population. Stimulation of antigens makes lymphocytes decrease and activates the macrophages within 24–28 hours. Well-fed babies have usually a large thymus, which dwindles rapidly after infections, doses of cortison and X-ray radiation (the formerly customary radioscopy). Hyperplasia of the thymus in babies is a symptom of a good defence rather than expression of an illness.

Thymectomy in new-born animals causes a loss of cellular immunity, tolerance to foreign tissue antigens, in case even to Runt disease (stunted growth); the effects are small in adult animals, except lymphopenia.

Thymectomy and agenesia of the thymus may provoke regeneration after thymus implantations. Autogenous mononuclear cells colonize the implant and induce the function.

Much as the thymus was neglected in former studies, its importance seems to have been overestimated in recent years; he certainly plays a decisive part for the colonization of peripheral lymph-nodes and in cellular defence. Owing to the increasing numbers of interesting individual findings of recent past, the organismic connections have too much been neglected.

Bursa?

A substantial arsenal of mesoepithelial derivatives is found in the body-cavities of the warm-blooded animals. There is a large reservoir of lymphatic tissues (Payr's plaques, mesenterial lymph-nodes) of the abdominal cavity, besides an extensive net of mesothelial tissues. These mesothelial cells of the omentum, peritoneum, mesenterium have epithelial forms and mesenchymal functions, which originate from a typically reticular unit.

To explain the verbal significance of the B-cells, much has been philisophized on the possible equivalent of Bursa Fabricii of the birds in the warm-blooded animals. In the «bursae» of the body, in its peritoneal, pleural, meningeal and synovial spaces, the human organism has an extensive, functionally efficient system that can react locally (e. g. in perityphlitic abcesses, peritonitis) or generally (e. g. polyserositis).

The reticulo-histiocytary system (RHS)

The mesenchyme develops from the mesoderm. The originally prevailing epithelial units dissolve increasingly and are replaced by loose cellular masses. The latter constitute the rudiment of all organs and formations of the connective tissue and are called mesenchymes (fr. Gr. enchein = to fill in). The *embryonic mesenchyme* (HERTIG, 1881) is a syncitium, whose protoplasmatic cell framework contains a mucous tissue-fluid. It promotes the fetal forms and is the matrix of all supporting and connective tissues (fig. 136).

As an organismic system, the mesenchyme has penetrated into the medico-biological thinking while our knowledge of the morbific agents increased. After the fundamental observations by WYSSOKOWICH (1886) and METCHNIKOFF (1892) on phagocytosis, ASCHOFF (1924) was the first to point with the concept RES (reticulo-endothelial system) to the organismic connections. SIEGMUND (1927) added with the term *«active mes enchyme»* the functional-phylogenetic consideration to the purely morphologico-topographic idea. Largely adopted has been the term *«reticulo-histiocytary system» (RHS)* as the endothelia are mainly predifferentiated elements and do not belong to the mesenchyme proper with pluripotent qualities (FRESEN).

Outside the uterus, the tissular formations originating from the mesenchyme are divided into the shaped and shapeless supporting tissues. While the shaped supporting tissues e. g. bones, cartilage, tendons, muscles, blood vessels have defined functions and perform special tasks, part of the mesenchymal tissue has retained pluripotency, the fundamental property of mesenchymal parent tissue. These mesenchyme derivatives with fetal potencies include the loose and reticular connective tissues and the terminal capillary net (fig. 136).

Main centres of reticular connective tissue are: bone-marrow, thymus, spleen, lymph-nodes, Kupfer's cells of the liver. The loose connective tissue is found chiefly in the peritoneum, omentum, mesenterium, pleura, meninges, interstitium, subcutaneous connective tissue. Of the shaped supporting tissues, only parts (e. g. metaphysis, periosteum

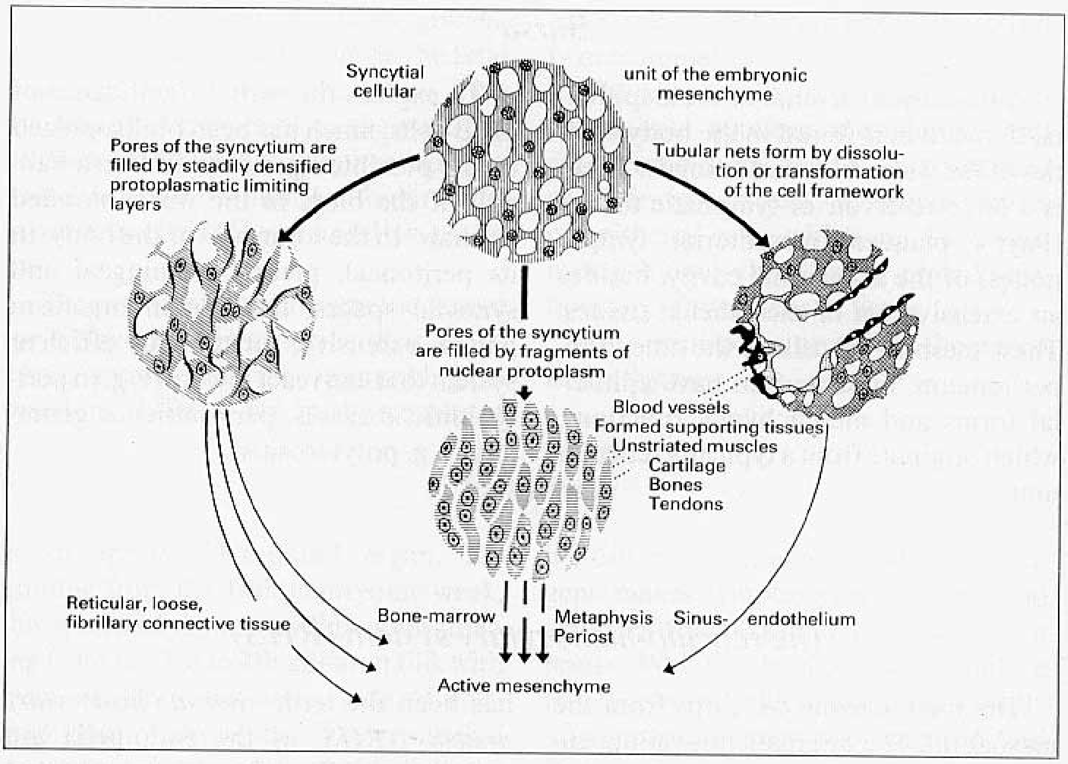

Fig. 136:
The *«active mesenchyme»* of the growing and adult organism.
The embryonic mesenchyme originating from the mesoderm has progressed or changed in 3 directions (see arrow). The active mesenchyme strictly speaking includes the reticular (thymus, spleen, lymph-nodes, bone-marrow, etc.), loose (omentum, peritoneum, mesenterium, pleura, meninges, articular and subcutaneous connective tissue) and fibrillary connective tissue. The formed supporting tissues (cartilage, bones, tendons, unstriated muscles, vessels) have special supporting and conducting functions and preserved only part of the pluripotency of their parent tissues (e. g. bone-marrow, periost, metaphysis).

and bone-marrow on the skeletal system) have physiologically preserved some of the fetal capacities.

The cells of the reticulo-histiocytary system have the following functions vital for the existence of a living being:

1. They are pluripotent. The developmental potencies dormant in them are the more numerous the less the cells are differentiated.
2. They are capable of effecting amoeboid movements.
3. They can take up, disintegrate, rebuild, build up substances and eliminate the products synthetised in the mesenchymal cells. This quality comprises the entire intermediary metabolism, moreover the intake of infectious morbific agents, the storage of organic foreign substances and the formation of proteins including the antibodies (fig. 137).

The intake of solid substances is called phagocytosis, the intake of liquid substances pinocytosis (= drinking).

As to the form and function, the so-called immuno-competent cells comprise 2 categories:

1. Large mononuclears with a comparatively small nucleus and larger space of cytoplasm, which alone by the proportion of space can better synthesize.

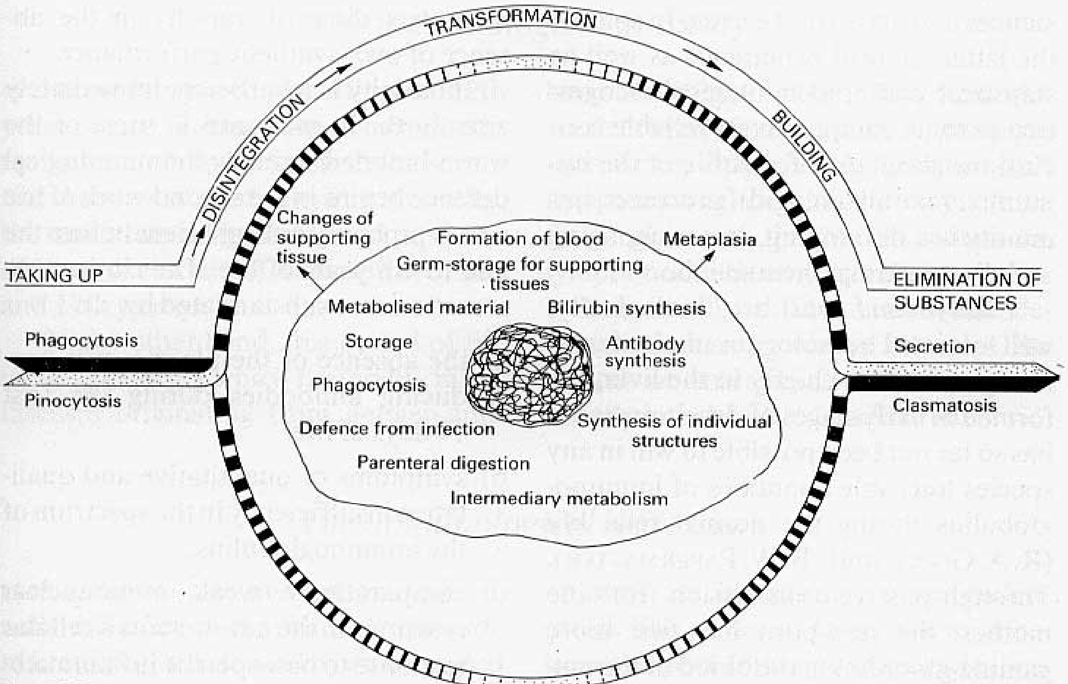

Fig. 137:
Fundamental properties of the pluripotent mesenchymal cell. The capability of taking up substances (phagocytosis, pinocytosis), of disintegrating, transforming and building substances (intermediary metabolism, storage, parenteral digestion, synthesis of proteins, lipoids and carbohydrates as well as their complex formations) accounts for the part that the mesenchyme plays in the germ-storing function of the supporting tissues, in the formation of blood, bilirubin synthesis, defence from infection, formation of antibodies, and for immunity.

The histiocytes, monocytes, reticular cells and mesothelium cells belong to them.

2. Small mononuclears with a comparatively large nucleus and little cytoplasm, capable of migratory and transporting functions rather than of synthesis owing to their small space of cytoplasm and their poor equipments for synthesis; the «small» lymphocytes of the lymphatic tissues belong to them.

The trite term of the B-cells and T-cells has deliberately been dispensed with in this classification. As the cellular form depends on the function rather than on the site of origin, a categorisation as to the origin is more hindering than of didactic use. The flowing functional transitions alone give a clear understanding of the biologically – dynamic connections.