It is of some interest, in connexion with the problem of cellular interactions, to view the affinities between different tissues in various stages of development.

The problem has been extensively investigated by Holtfreter in the early stages of the amphibian egg. Professor P. Weiss has briefly reported on the stimulating observations made by Chiakulas (1952) on grafts of epithelia from various sources to the skin of larval amphibians.

I have performed experiments which bear some analogies to the last-mentioned ones by confronting side by side in situ layers of heterogeneous tissues, which in normal development form distinct constituents of one anatomical region, namely the eye region. Pieces of tissues of various extent were mechanically removed from the eye-forming region of chick embryos of from 2 to 30 somites, and more or less wide gaps created. The organogenetic movements of the intact neighbouring regions reduce the gap rapidly and progressively, so that the fringes of severed tissue layers—which in normal development never establish a material continuity with each other—may be brought into direct contact side by side in the same plane. In this way, presumptive epidermis and retinal tapetum, nervous or pigmented layer of the retina and epithelium of the lens vesicle, &c., can be confronted.

The problem was to test whether in the new conditions the heterogeneous laminae could fuse with each other or whether they were unable to make connexions; and further, whether any changes in the normal course of the histological differentiation of the cells of one of the tissues might take place under influences spreading from the neighbouring cells of the other tissue in the fusion area.

The results can be briefly summarized as follows: the mesenchyme never establishes side-by-side connexions with epithelial layers (epidermis, epithelial wall of the brain, conjunctival epithelium, &c.). At first the mesenchyme covers the gap existing between the free edges of the severed epithelial lamina. Soon, however, the epithelial cells of the borders flatten and slide over the mesenchyme. In this way the cut edges of the epithelial lamina make contact with each other and fuse.

A transitory side-by-side fusion of epidermis and the wall of the anlagen of the brain occurs fairly often; however, each tissue retains its proper differentiation.

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capacities and in later development the epidermis tends to separate from the wall of the brain; mesenchyme slides in between epidermis and brain and proliferates.

On the contrary, the cut borders of presumptive retina and lens epithelium, of tapetum and epidermis, of tapetum and conjunctival epithelium, form lasting and firm side-by-side connexions with each other. In such instances the affinity between the elements of the confronted tissues appears to be strongly positive. However, each of the tissues which at the time of the operation had not yet undergone any apparent differentiation retains through later development its own capacities for differentiation in regard to shape and arrangement of cells, and internal structure of its cellular components. Groups of cells showing transitional morphological characters between the two confronted tissues are never to be found along the fusion line. These facts seem to suggest that no special influence is exerted from one tissue on the other through the narrow area of contact.

Spreading of substances which can determine the fate of cells or change to some extent the course of their differentiation seems to occur in normal development, e.g. in supporting tissues. Many authors in fact maintain that striking examples of infectious propagation of differentiation are to be found in cartilage and bone tissues.

The differentiation of osteoblasts from the perichondral cells when the laying down of the perichondral bone ring of the cartilaginous diaphysis starts has been viewed as the consequence of the spreading from cartilage of an inductive substance (osteogenin, Lacroix). Such a substance determines the progressive differentiation of fibroblasts (assimilatory induction). Evidence was produced that ethanol extracts of bone or marrow (Levander) and of epiphysial plate (Lacroix) can induce the differentiation of fibroblasts of the loose or fibrous connective tissue into chondroblasts or osteoblasts.

An analogous interpretation has been advanced for the results of the following experiment: rib cartilage (and even the elastic cartilage of the ear of the rabbit) freed from its enveloping perichondrium and grafted to the epiphysial plate of the tibia undergoes structural changes similar to those of the epiphysial disk itself, viz. serial alignment and hypertrophy of cells (Lacroix). These processes never occur in normal rib or ear cartilage in situ and represent preparatory steps for the replacement of cartilage with endochondral bone.

Pending experimental demonstration, it might be assumed that also the formation of secondary bone tissue, which is laid down during bone reconstruction, depends on the spreading of substances from the neighbouring bone tissue. These substances might determine the differentiation of fibroblasts, enclosed in the network of the vascular channels of bone, into osteoblasts. Fibroblasts are apparently at rest in the vascular channels where renewal of bone tissue does not occur; but, as soon as bone resorption sets in, the newly formed cavities are filled with fibroblasts and blood-vessels. The fibroblasts which line the wall of resorption cavities gradually become converted into osteoblasts which lay down con-
centrally arranged layers of bone matrix. This process suggests the existence of some inductive agent which diffuses from the freshly resorbed wall of the vascular channels.

REFERENCES