Observations on the development and nutrition of bone and cartilage, and on the relations of connective tissues to each other in health and disease / by Professor Redfern.

OBSERVATIONS ON THE DEVELOPMENT AND NUTRITION OF BONE AND CARTILAGE, AND ON THE RELATIONS OF CONNECTIVE TISSUES TO EACH OTHER IN HEALTH AND DISEASE.[1]

By Professor Redfern, M.D. Lond., F.R.C.S. Eng.

I wish to bring under the consideration of the Society certain conditions of connective tissues, especially of cartilage and bone, which I believe are not sufficiently recognised, and which point to more simple explanations of developmental and diseased actions than are usually offered.

I think it can be proved that every living tissue possesses inherent powers of maintenance; and in diseased states, of active anatomical changes, independent, for their existence at any rate, of the surrounding tissues, or on a supply of vessels and nerves. That is to say, every tissue has a power of its own to do its own work,—to maintain its healthy adult characters, or to change its texture and assume the anatomical characters of other healthy tissues, possibly those of diseased ones. Notwithstanding, when such a tissue forms part of a composite body, such as the human, it influences the other tissues, and is influenced by them, whether for the maintenance of healthy or diseased conditions.

And such tissue-power, manifested, it may be, under normal conditions by changes which go on so slowly as to be observed with difficulty, may, under altered circumstances, be exercised so rapidly, and lead to appearances so startling and different from the original, as to obscure their origin, and to have led to the changed tissues having been described as altogether new, and derived from some extraneous source.

A simple illustration will make this clear. An articular cartilage may be examined repeatedly without definite indications of its continual change, or capacity for change, being observed, but after an injury, or the occurrence of phlebitis

[1] Read at the meeting of the Anatomical Society of Great Britain and Ireland, Dublin, 1897.

after blood-letting, as in cases related by Mr Mayo and Mr Lawrence respectively, complete removal or destruction of such large cartilages as those of the ankle and knee joints has taken place within a month, or, as in Mr Lawrence's case, in 4 days. And in dogs and rabbits I found that in from 3 to 6 days the parts of costal cartilages through which a silk thread had been passed, or such as had been surrounded by a ligature, had become converted into a cellular gelatinous mass, very difficult to recognise as having been formed out of the original cartilage.

In these instances it must be remembered that the irritation was continued for some time, but when the thyroid cartilage is cut, in a case of cut throat, and in instances of fractured cartilage, the changes are so slow that for long it was doubted if such injuries were ever followed by healing. Dr Leidy, in an excellent paper on articular cartilage, in 1849, expressed himself very strongly on this point, saying, "As well almost might the two opposed surfaces of articular cartilage unite in a joint in which there is little motion as for the two broken edges of one to do so."

When I had made incisions in the articular cartilages of dogs, neither microscopic nor visual changes were manifest 7 days after, but abundant proliferation of the cells adjacent to the injured part were found after 49 days (fig. 17), and perfect fibrous union after 24 weeks (figs. 18 and 19). There is now a general admission that wounds in cartilages heal by the formation of fibrous tissue. That is to say, a cartilage like the articular is capable by its own inherent power, and without any assistance from without, of transforming its elements, cells, and hyaline substance into the corpuscles and fibres of that other form of connective tissue which we know as fibrous tissue.

I believe it is neither known nor suspected how frequently many joints in a limb undergo great abnormal nutritive changes in succession. When serious disease in one joint has led to amputation or caused death, the anxiety to determine the characters of the disease by the naked eye and a prolonged microscopical examination often leads to the neglect of the other joints. When these are examined in succession, those near the most diseased one often present structural changes similar to those in the joint first attacked; whilst the distant

ones are often very difficult to open, because of changes of structure producing cartilaginous, fibrous, calcareous, or bony anchylosis. On tearing open such joints, which often requires great force, the opposed cartilages are seen to be the seat of changes in their cells and hyaline substance, which, with intermixture of the elements of the opposed surfaces, and a change of them into a firmer form of connective tissue, explains why they cohere so firmly.

On such surfaces numerous bloody points are often seen. These are the ends of torn blood-vessels which have been formed in the new tissue into which parts of the cartilage have been converted.

Mr Liston, in the xxiii[rd] vol. of the *Med.-Chirurgical Transactions*, described and gave a drawing of loops of blood-vessels which he had injected, and which he looked upon as indicating the vascularisation of cartilage. After the injection of the vessels of such amputated limbs as those to which I have just referred, I found abundant loopings of blood-vessels in the deeper parts of the cartilages. But instead of such vessels being in contact with the cartilage, they are formed in the midst of medullary matter produced out of the cartilage by proliferation of its cells. The changed action of the non-vascular cartilage has transformed it into a vascular cellular or medullary mass, destined for further changes.

In many parts of such joints the uniting matter of the opposed cartilages is fibro-cartilage, in which, as well as in the deeper parts of the hyaline cartilage, calcification leads to the formation of primary bone, and subsequently to the true laminated bone of bony anchylosis.

Thus it appears that when an altered and healthy nutritive action can be secured in a diseased joint, it is possible that perfect bony anchylosis may happen by indirect transformation of the articular cartilage into bone,—a much more advantageous result than the very rare union of bones deprived altogether of their articular surfaces by the destructive action of disease, and no longer held firmly in contact by the ligaments, which are then too long for their purpose.

The suspension of the increase in length of long bones by ossification at the line of junction of temporary and permanent

cartilage, and the rare ossification of permanent or articular cartilage, suggests the existence of a marked difference in the vital action of these two forms of cartilage, and makes it desirable to have positive evidence that articular cartilage can be transformed into bone.

This can be got by examining eburnated or porcellaneous parts of articular surfaces. I believe it has not been noticed that the free surfaces of such parts are nearly on the original level of the articular cartilage, and that, in general, the level of the other parts of the cartilage, greatly changed in structure, is considerably below that of the porcellaneous parts; indeed, frequently very little of those parts of the cartilage remains on the bone.

Sections of porcellaneous parts show them to be formed of excessively dense bone, such as is never formed where the bone has been preceded by ordinary temporary cartilage. Enclosed in the bony tissue, here and there, are small blocks of easily recognisable articular cartilage, as yet free from ossification, and giving positive evidence that the position of the porcellaneous part was once occupied by articular cartilage. When two surfaces of such newly formed ivory-like bone move on each other, they become highly polished, and often, especially in ginglymoid joints, ground into mutually fitting ridges and grooves. The polish of such surfaces is such as cannot be given by any amount of friction to ordinary bone.

The vital power of temporary and permanent cartilage is widely different, and it is only when the general conditions have become greatly changed that permanent cartilage is transformed into very dense bone, and an ivory-like polish is ever given to the part.

The suggestion that a porcellaneous surface is the result of friction of an articular surface which has been deprived of its cartilage has probably arisen from an imperfect appreciation of the level of such surfaces, in comparison with the original level of the whole articular surface.

Permit me now to direct the attention of the Society for a few moments to the exquisitely adapted anatomical structure of articular surfaces, and to the cause of the terrible suffering which often occurs when these parts become diseased.

The blood-vessels of bone, covered by their porous Haversian layers, end in a series of arches under the cartilage, giving, like the series of arches of a railway viaduct, very great resistance to pressure on the summit of these arches, by a very small amount of material. The intervals of adjacent arches are occupied by nearly solid calcified cartilage, as the intervals of the arches of railway viaducts are filled by ballast; and the surface, now presenting only slight inequalities, is covered by highly elastic articular cartilage, in direct contact with the porous bone only here and there, at the summit of the arches of occasional bony layers.

The bone, largely supplied with blood in its Haversian canals, is freely irrigated throughout with nutritive fluid by its canaliculi;—the cartilage, whether traversed everywhere by lymphatic canals or not, is capable of taking up coloured fluids into all its parts, and is deeply coloured by bile-stained blood-plasma in jaundice, whilst the nearly solid calcified cartilage between the bone and the elastic cartilage, both so completely saturated with nutritive fluid, is only just able to transmit sufficient nutritive fluid through its solid mass to keep it alive. It discharges an admirable mechanical function on the articular surface, but cannot be expected to manifest active nutritive changes.

Let us now follow these tissues when a limb suffers seriously from abnormal nutrition. One or more joints are seriously destroyed, their cartilages are softened, and almost entirely converted into a soft, semi-fluid mass, in which it is difficult to recognise the structure of disintegrating cartilage;—what remains of the articular cartilage tears easily from the bone where this has become transformed into a soft cellular mass; and the synovial membrane has participated in the general disintegrating change.

We look at the other parts of the limb,—needles pass readily into all except the dense parts of the shafts of the bones. On looking into the joints, many of them seem at first sight but little changed; but on looking more carefully, the free surface of the cartilages is seen to have lost much of its substance, and to have become softened, roughened, and thinned, especially near the edges of the surfaces. On inserting one blade of a pair

of forceps under the edge of the thinned cartilage, it tears from the bone with great ease, frequently in a single piece. The bone is softened, and more or less converted into a soft granulation mass, which has broken up in the tearing off of the cartilage.

If it be a lower limb, such cartilages as those on the upper part of the astragalus may be torn off from the lateral and upper articular surfaces in one piece, whilst in some of the smaller joints of the foot various stages of cartilaginous, fibro-cartilaginous, or osseous anchylosis may be observed.

Let us now take one of these detached cartilages between the finger and thumb. Its deep or attached surface is as rough as a piece of sandpaper, for its calcified articular lamella, moulded on the rounded ends of the Haversian systems and their interspaces, has come off from them unchanged, though the bone has lost its lime salts, and has become converted into a soft granulation mass, the superficial surface of the hyaline cartilage having at the same time undergone considerable change, and lost greatly in substance, whilst its continuity with its deep calcified lamella has remained unaffected.

It is plain what has happened. The parts most under the influence of nutrition—the bone and the elastic cartilage—have yielded to the destructive influence of the abnormal nutritive action, whilst the nearly solid calcified cartilage has resisted any change to the last, and retained even its lime salts and its hardness.

What is the effect of this in the living body? In the state of health, the vessels and nerves of the Haversian canals of the bone are preserved from injury by the hard layers of the Haversian systems covering them in, but in the diseased state these layers have become resolved into a soft cellular mass, which allows the sharp edges of the projections on the lower surface of the calcified cartilage to tear both blood-vessels and nerves, and produce small extravasations of blood, and terrible agony from laceration of the nerves.

In these states pressure of the articular surfaces against each other compresses the nerves and vessels, producing but little pain; but when rotation is added to pressure, the spicules of the deep surface of the calcified cartilage are dragged through the nerves and vessels, producing the terrible agony which has

so long been noted as indicating disease of the cartilage and bone, and which occurring repeatedly from spasms of the limb on attempts at sleep, exhaust the sufferer, and compel resort to amputation.

Let us turn now very briefly to the evidence that tissue changes are the results of the vital activity of the tissues themselves; that tissues do their own work, and are not indebted to others outside them; that new forms of tissue are produced in the places where we find them out of the materials previously existing in those parts.

I believe if this be established it will greatly simplify our conceptions of many physiological and pathological processes.

An articular cartilage, previously smooth and compact, often presents irregular cavities, as the result of softening, and molecular disintegration, ulceration, without the aid of any other tissue or visible change in its own deeper parts.

The instances in which it had been supposed that pits on cartilaginous surfaces had been produced by the agency of a new vascular and cellular membrane with nipple-like processes occupying the pits, and easily drawn out of them (figs. 3, 4, 5, 7, 8, 9, 10, 13, 18, 19), were cases of increased proliferation of cartilage cells, with accompanying softening and fibrillation of the hyaline substance, leading to the production of a fibro-cellular layer out of the original tissue, firm enough to be torn off, with its nipple-like processes, from the cartilage, and not unfrequently forming a permanent fibrous cicatrix.

In perfectly healthy cartilages, wounds heal in this way, the uniting fibrous membrane presenting projections, and the cartilage corresponding pits, where enlargement and proliferation of the contents of the original cells form a soft cellular mass, which in its turn becomes a firmly adherent fibrous membrane, with corpuscles on its fibrous bundles (see figs. 17, 18, and 19).

The so-called Howship's lacunæ, and their contained cells, are similar instances on the surface of bones and the fangs of teeth, believed to be in process of absorption. As in many another instance, an exalted action, enlargement, and multiplication of the contents of certain cells has taken place, and these soft masses, lying on the bone yet unsoftened, separate readily

from it during their examination, and leave the hollow cavities called Howship's lacunæ. Their subsequent destination varies in different instances. Because of their frequent presence when bone loses its calcareous matter and its structure changes, they have been said to be agents in absorption of bone; but they are not always present, and are not therefore essential in this process, the greatest amount of bony disintegration taking place in the presence of small succulent cells, possibly the result of a want of cohesion of the elements which elsewhere make up these giant cells.

It is difficult to see the consistency of the view that myeloplaxes, when called osteoclasts, should be regarded as agents in absorbing bone; and on other occasions, when called osteoblasts, should be regarded as agents in forming bone.

I am not aware of any one but Mr J. Greig Smith [1] who has hitherto ventured to suggest doubts whether giant cells are agents connected with the absorption of bone. And I think a careful consideration of the continual production of Haversian spaces to be in their turn converted into new Haversian systems in the normal nutrition of bone, as was suggested and demonstrated by Messrs Tomes and De Morgan, points to entirely different views on the process of absorption. The lime salts may be removed and the structure changed, so as to be no longer recognisable as bone, without the presence of giant cells at all.

During the formation of bone which had been preceded by cartilage and calcified cartilage, there is an almost insensible removal of the parts of the calcified cartilage no longer necessary for support, whilst the cells which constitute the medullary material formed out of the contents of the cartilage cells are engaged in the production of true laminated bone.

This is another instance in which the original tissue transforms itself into different adult tissues by its own vital power, into calcified cartilage, bony layers, blood- and lymph-vessels, nerves and marrow.

Heitzman has well described and figured the transformation of cartilage into medullary cells, and traced the formation of blood corpuscles and blood-vessels at individual parts of the

[1] *Journ. of Anat. and Phys.*, vol. xvi., Jan. 1882.

tissue forming bone from cells which he calls hæmatoblasts; whilst the medullary cells surrounding them are engaged in the formation of the tissue of truly laminated bone. He explains the formation of myeloplaxes as due to the coalescence of medullary corpuscles in a territorial form, and refers to Ziegler's demonstration of their formation by cells migrated between two glass plates as the probable explanation of their occupation of the cavities produced in ivory pegs and dead bone by decalcification and liquefaction.

The appearance of blood-vessels in bone in the early stages of its formation has been usually described as due to intrusions or ingrowths of vascular periosteum or of periosteal vessels, without, I think, any sufficient evidence that such things occur at all. That blood and blood-vessels form out of the cells of medullary matter, the result of development of cartilage cells in spaces more or less closed in by calcified trabeculæ, can, I think, be satisfactorily demonstrated. This method of development is consistent with the mode of development of blood and blood-vessels in the embryo, and adds to the instances showing that tissues are capable of effecting their own changes.

In conclusion, let me submit the following considerations :—

The fibro-nucleated membrane, with its nipple-like processes, which has been supposed to cause ulceration of cartilage, is really formed by a change of the structure of the cartilage itself into cicatricial fibrous connective tissue.

The cells of Howship's lacunæ are the results of the increased development of the corpuscles of the tissue in which we find them, not new structures introduced from without.

Bone enclosed in its case of periosteum and cartilage changes into the cartilage of enchondroma.

Ziegler, in treating of metaplasia, pointed out that cartilage can be transformed into mucoid tissue or areolar tissue; cartilage, into osseous tissue; fibrous tissue, into mucoid tissue and bone; and osseous tissue, into fibrous tissue or cartilage,—one form of connective tissue being changed into another.

Ziegler, Dr Woodhead, and others have abundantly shown that blood- and lymph-vessels are produced by the junction and hollowing out of the branching processes of newly-formed cells,

which are subsequently united with protoplasmic endothelial processes of older vessels to form continuous channels for the circulation of blood.

And I think we cannot but conclude that each individual tissue has power to do its own work in the position which it occupies,—of maintaining its own structure and life,—or of changing itself into another kind of tissue, which may be so different from the original that the transformation is not easy to demonstrate.

DESCRIPTION OF FIGURES, pp. 106–108.

Figs. 1*a* and 2*a*. Softening, swelling, and loosening of the tissue of the free surface of the cartilage of the patella.

Figs. 3 and 4. Great enlargement and change in the contents of the cells, and discharge of their contents.

Fig. 5. Soft nucleated mass produced on the free surface by intermixture of the contents of different cells.

Fig. 6. Calcification of deeply seated cells.

Figs. 7, 8, 9, 10. Formation of fibro-nucleated membrane by the contents of the cells on the superficial surface.

Figs. 11 and 12. Comparison of the healthy perichondrial surface of the costal cartilage of a dog, with the same surface 5 days after a seton had been passed through it.

Fig. 13. Membrane with nipple-like process in costal cartilage of dog.

Fig. 14. First appearance of fibres in hyaline matrix of costal cartilage 40 days after insertion of a seton.

Fig. 15. Effects of actual cautery to femoral trochlea 49 days previously.

Fig. 16. Effects of pressure due to a partial luxation.

Fig. 17. Enlargement of cells and multiplication of their contents near the surfaces of an incision into the cartilage of the patella of a dog 49 days previously.

Figs. 18 and 19. Firm fibrous union by a fibro-nucleated membrane with nipple-like processes after a similar incision to that in Fig. 17, but after the lapse of 24 weeks and 5 days.

Fig. 20. Molecular disintegration—Ulceration.

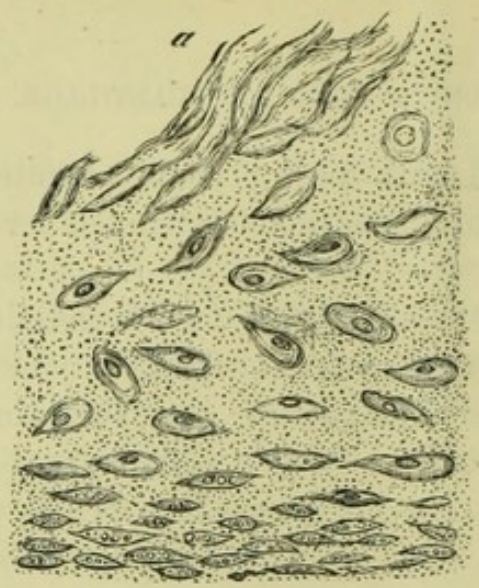


FIG. 1.

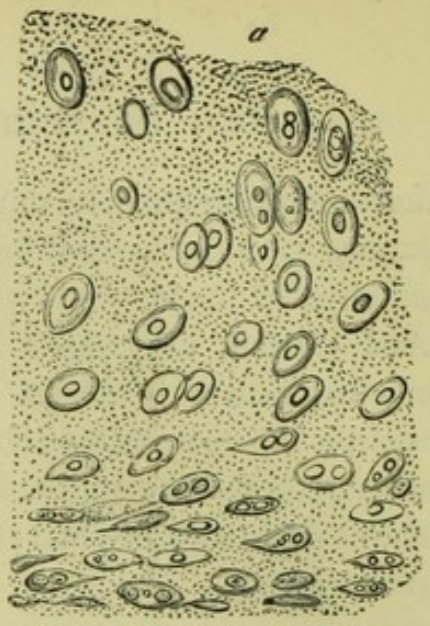
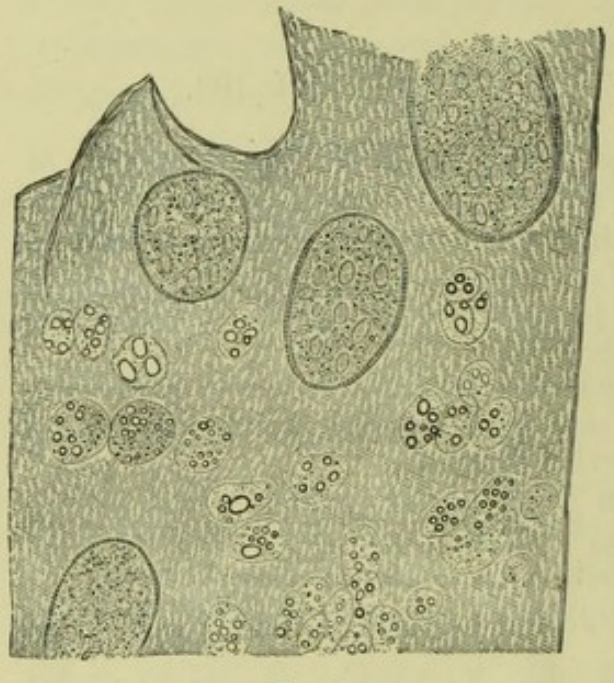


FIG. 2.



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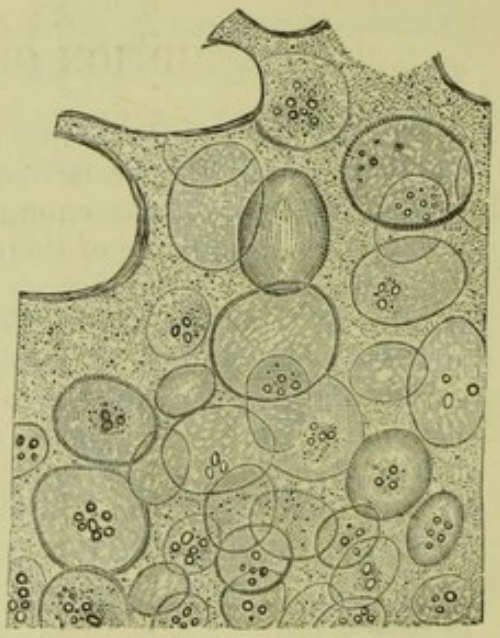

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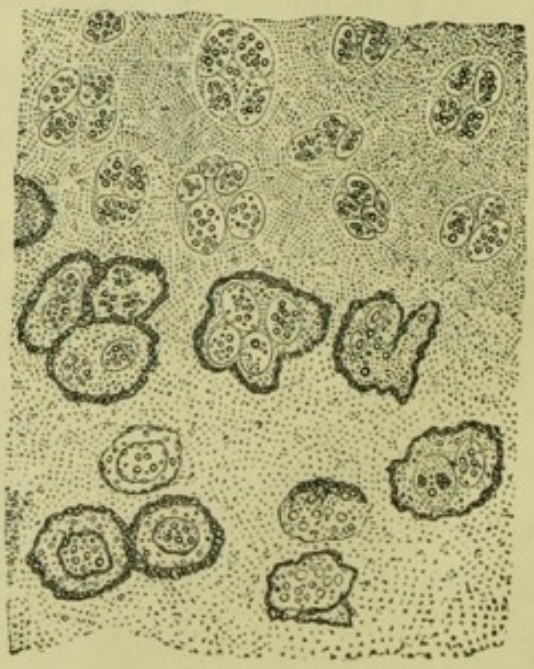
FIG. 5.



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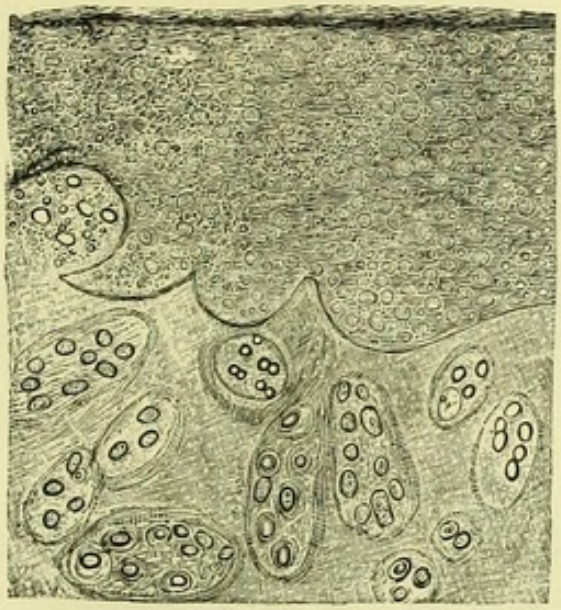

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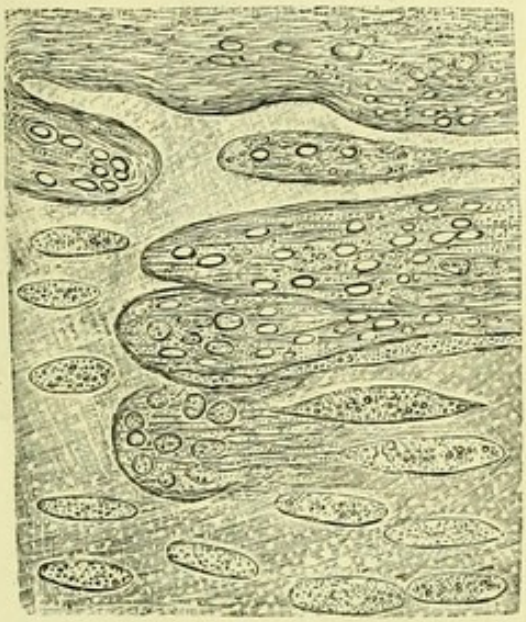

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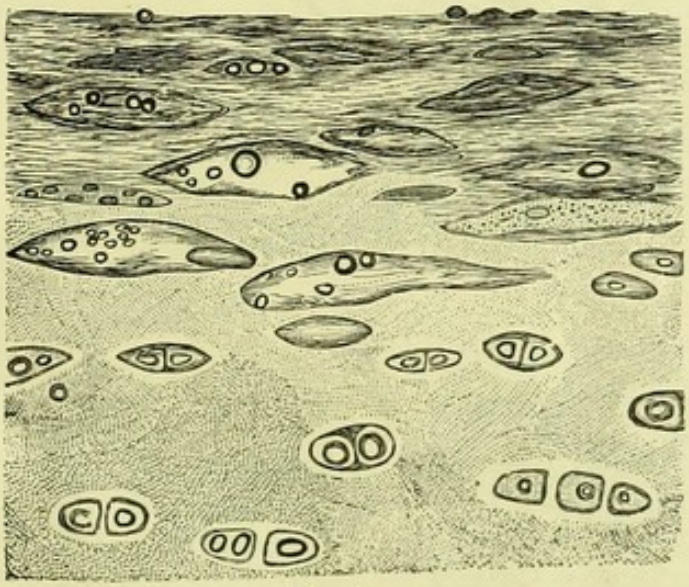

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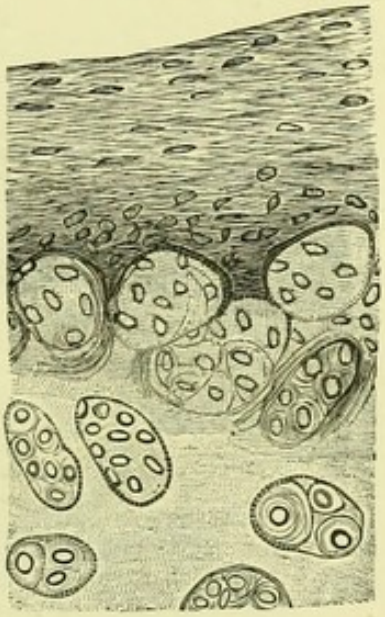


FIG. 10.

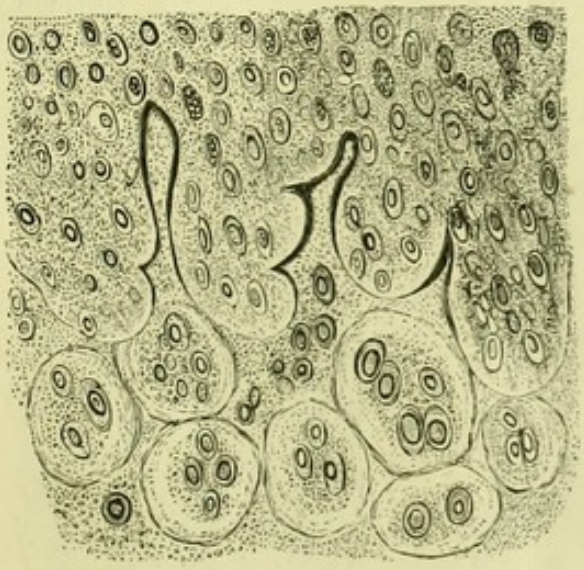


FIG. 13.

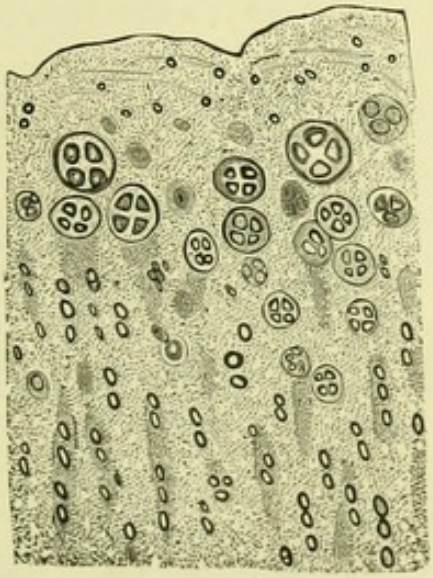
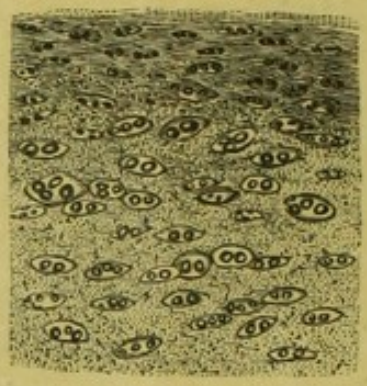


FIG. 16.

FIG. 11.



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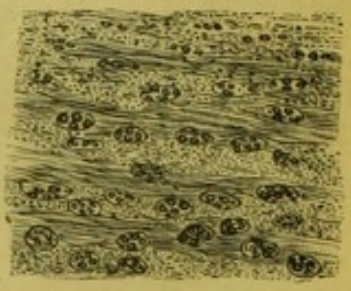


FIG. 14.

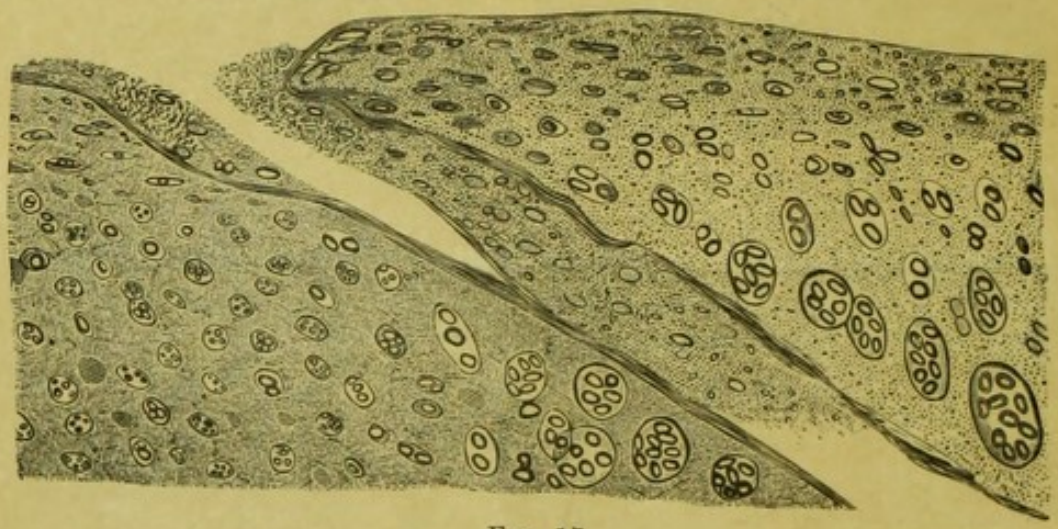
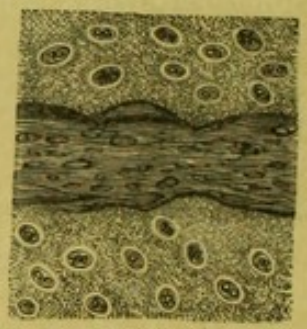


FIG. 17.

FIG. 18.



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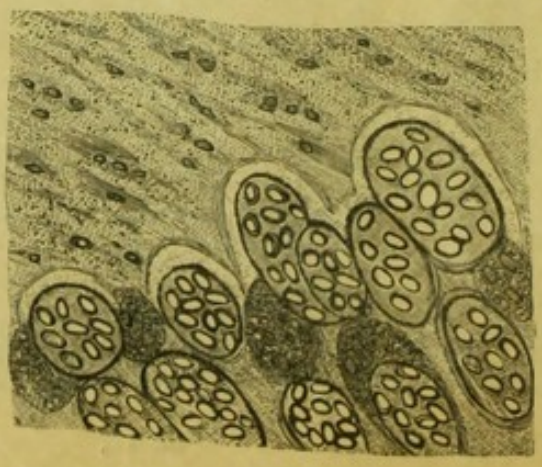

FIG. 15.

FIG. 20.

Unsere Aufgaben auf dem Gebiete der Diätetik.

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