The histology of granular kidney [with plates V and VI] / by Robert Saundby.

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The histology of granular kidney.

By Robert Saundby, M.D.

[With Plates V and VI.]

Bright recognised three well-marked pathological types of diseased kidney, associated with albuminuria, but was ignorant of the intimate nature of the morbid process. In accordance with current pathological doctrines he regarded each variety as a stage in the development of a deposit or growth giving rise to granulations, and hence he called the whole process "granular degeneration." At present we restrict the term "granular kidney" to what Bright regarded as the third stage, and it is believed by many to have pathological and clinical characters which distinguish it altogether from the other two. This separation was not effected early in the history of Bright's disease, nor was it completed without opposition; indeed, it cannot be said that at the present time the points of distinction are generally agreed upon. The naked-eye appearances are sufficiently characteristic. It is only when we attempt to determine the intimate nature of the changes which have occurred that differences of opinion arise. Bright's doctrine of a morbid deposit soon gave way to the theory of an inflammatory process, first taught by Rayer, and confirmed by the histological researches of Johnson, Frerichs, and Reinhardt. According to Frerichs, the three varieties or types described by Bright corresponded to three stages of an inflammatory process, characterised respectively by:—1, hyperæmia with exudation; 2, fatty degeneration of the exudation; 3, absorption of the degenerated exudation and atrophy of the organ. Nothing could seem more apt than this description, but it soon had to yield its place to the doctrine of parenchymatous inflammation brought forward by Virchow, according to which the seat of the lesion was the epithelium of the kidney. Dr. Johnson adopted this view with slight modifications, as he believed that the, so-called, second and third stages often occurred independently of the first, or at least that they were not preceded by an acute inflammatory attack. He drew attention to several points in the histology of these changes, especially to the small cells occupying the tubules and the hypertrophy of the walls of the blood-vessels as characteristic of the small red kidney, which he

regarded as quite distinct from the small kidney which may follow an acute attack.

Traube was the first to lay down clearly the proposition that granular kidney is a distinct disease, separable by clinical and pathological features from all other varieties of Bright's disease. He maintained that the seat of the inflammation was not in the parenchyma, as in the other two forms, but in the interstitial tissue.

Grainger Stewart has brought forward evidence that the small contracted kidney may result from an acute attack, but he recognises the existence of a distinct variety, to which he gave the name of the "cirrhotic kidney," as he formerly regarded it as the consequence of a non-inflammatory hyperplasia of the connective tissue; but in 1878 he announced that he had abandoned this opinion and accepted Traube's view.

Gull and Sutton also support the doctrine of the independent nature of the lesion in granular kidney, and have described it as consisting in the deposit of a hyalin-fibroid material in the intertubular parts including the vessels, and in atrophy of the tubular and intertubular structures.

In 1874 Kelsch published a very minute account of the histology of granular kidney, in which he supported Traube's opinions. According to Kelsch, the seat of the lesion is in the intertubular tissue around the convoluted tubes which occupy the peripheral portions of what are known as the pyramids of Ferrein, the centres being formed by the straight tubes, a disposition of the lesion which he regards as explaining the granular appearance of the surface of the kidney. In 1878 Prof. Charcot endorsed these views, and insisted more especially on the appearance of the small cells within the tubules, already described by Johnson, as the fundamental characteristic of the changes in the small red kidney.

The views of Johnson, Traube, and Gull and Sutton have each the great merit of bringing into strong relief one side of the process, and their fault is that while insisting upon one point they ignore or deny others. If we take them together we may regard the first as emphasising the changes in the tubules, the second the changes in the stroma and Malpighian bodies, and the third the changes in the blood-vessels.

Traube's view of the pathology of granular kidney is widely accepted, and we need no better proof of this than the almost

universal adoption in all foreign countries of the synonym "interstitial nephritis." In this country Traube has many followers, but, either from caution or conservatism, the old names are more popular than this more precise term. We may congratulate ourselves upon our caution in this matter, as the tide of opinion seems to have turned, and several writers have shown indications of their belief that these hard-and-fast distinctions based on the supposed anatomical seat of the lesion cannot be maintained. Thus, Rosenstein has said that there cannot properly be said to exist either strictly parenchymatous or strictly interstitial nephritis, both tissues being affected, and both the large white and the small red kidneys resulting from *diffuse* inflammation. This latter statement is confirmed by the experiments of Grawitz and Israel, who found that after temporarily clamping the renal artery a diffuse nephritis occurred, which passed indifferently into either the large white or small red kidney. In the latter case they noticed particularly the absence of any nucleation in the stroma. Another writer, Dr. Carl Weigert, has stated that both the parenchyma and the stroma are affected in all cases of chronic Bright's disease, and that pure parenchymatous nephritis is only seen as an acute disease. Bamberger has announced his entire concurrence in these views.

My own observations have led me to similar conclusions. The small red and large white kidney, and all the intermediate varieties, are the result of inflammation which affects all the tissues, but varies very greatly in intensity. The parenchyma being the most highly organised tissue, suffers most in proportion to the intensity of the inflammation. The large pale kidney is the result of prolonged or repeated severe inflammation; on the other hand, the small red kidney indicates an inflammatory process of prolonged duration but of minimum intensity; and the intermediate varieties correspond to all the different degrees of intensity possible between the two extremes. The fact of the existence of an indefinite number of intermediate or mixed forms between the two typical varieties of the large white and the small red kidney is a strong argument in favour of the doctrine of unity.

Dr. Greenfield regards the "large, pale, granular kidney," the "small, red, granular kidney," and the various intermediate, forms as a series in which the first is "typical of origin by essentially interstitial growth," the second by "atrophic change," and the intermediate forms by combinations of these two processes

In the small red kidney he states that the disease commences in the vessels and glomeruli, the affection of the latter being fibrous transformation with adhesion of the capillary tuft to Bowman's capsule, as a consequence of which, "*or of an associated inflammatory process*," the tube wastes. "In the larger form there is much more true interstitial growth or exudation."

The "associated inflammatory process" which Dr. Greenfield throws in, by the way as it were, to eke out his hypothesis, constitutes, in my opinion, the link which binds the whole together in one pathological series.

The preparations from which the drawings illustrating the descriptions I am about to give, were taken from two cases, of which abstracts of the *post-mortem* appearances are subjoined:

Case 1.—J. W—, male, æt. 49. Ascites and œdema of lower limbs. Heart, 21 oz., valves competent, muscular fibre healthy. Liver weighed 54 oz., appeared healthy, but under microscope showed commencing cirrhosis (specimen shown). Spleen enlarged and rather hard. Kidneys together weighed 7 oz., small, lobulated, with many cysts on surfaces; capsules thickened and opaque; cortices about one line thick, dark coloured; cut surfaces showed open mouths of dilated vessels.

Case 2.—M. H—, female, æt. 50. Ascites and œdema of lower limbs. Arteries of pia mater thickened and pigmented. Heart weighed 9 oz.; muscular fibre pigmented; valves healthy. Liver large, smooth, soft, yellow on section; old peritonitic adhesions compressed portal vein. Spleen small and dark coloured. Kidneys together weighed 7oz., surfaces granular and lobulated; capsules thickened and adherent; no cysts; cortices only one line thick,

I shall deal with the histological details in the following order: α, the convoluted tubes; β, the straight tubes; γ, the Malpighian bodies; δ, the vessels; ϵ, the connective tissue.

α. *The convoluted tubes.*—The cortex of the wasting organ presents the convoluted tubes in varying degrees of destruction. The changes may be best considered as they involve—1, the epithelium; 2, the basement membrane.

1. *The epithelium.*—As already mentioned, the changes in the epithelium vary with the intensity of the inflammatory process. In the more acute cases the epithelium proliferates rapidly, and the tubules become filled with fattily-degenerated cells. This is too well known to need further remark, but it is not generally understood

that, even in the typical small red kidney, the epithelium also proliferates, although to a comparatively small extent. Plate V, fig. 1, shows a mass of epithelium from the cortex of the kidney of Case 1, undergoing proliferation; its protoplasm is *clear; the nuclei stain strongly with carmine; they are enlarged* (*a*), *oval or hour-glass shaped* (*b*), *or there are two nuclei* (*c* and *d*), and finally the tubules become filled with young cells (*e*). These changes are seen better in figs. 2, 3, 4, 5, and 6. This appearance of small cells filling the tubules was first described by Johnson, as already mentioned, and has been confirmed by Cornil, Ranvier, Kelsch, Charcot, and others, but I am not aware that any one has previously satisfactorily explained their origin. Kelsch imagined them to be due to the proliferation of the endothelia of the basement membrane. Moreover, none of these authors have followed the further changes in these young cells. One of the subsequent transformations is well seen in fig. 7, which represents a group of tubules like those seen in fig. 6, undergoing conversion into fibrous tissue by the elongation of these young cells into spindle cells, and their gradual metamorphosis into a hyaline connective tissue containing a few stellate and spindle elements.

Another mode in which the destruction of the tubules is completed is shown in fig. 8, which represents a comparatively early stage of the process. The drawing shows cross sections of several convoluted tubules filled with round cells, which are not so closely packed as in fig. 6. The sections vary very much in diameter, some of the tubules being evidently dilated. In some there are very few cells, in others none, the whole lumen being filled with a hyaline material, staining very feebly with carmine. These appearances, which may be very readily seen, were first described by Mr. Simon, more than thirty years ago, as "cystic degeneration of the kidney," but have not received due attention. They are, in fact, due to the formation of a myxomatous or gelatinous connective tissue from the young cells filling the lumen, by which the basement membrane is distended, and a cyst is formed.

Besides these two definite changes a great deal of the epithelium appears to be undergoing simple fatty degeneration and wasting.

2. *The basement membrane* becomes swollen and hyaline, and is lost in the new formation of connective tissue, or forms the wall of a cyst.

β. *The straight tubes.*—The medullary parts of the kidney present,

to the naked eye, much less appearance of alteration than the cortex. This is, in the main, due to the fact that the bulk of the cortex is made up to such a great extent by the large secreting epithelium of the convoluted tubules, that its destruction causes a very marked decrease in the thickness of the cortex; but the medullary part is made up of rows of narrow tubules lined with a comparatively small epithelium, and of numerous arteries and veins, so that the destruction of the straight tubules does not produce a very striking difference in the size of the pyramids. But the lesions are essentially the same as those I have described in the convoluted tubes. Fig. ~~10~~, shows rows of straight tubes filled with young cells (*a*), lying between the convoluted tubes, the epithelium of which is very fatty. This drawing is from Case 2. One of the tubules is seen to be dwindling to a simple row of spindle cells.

These appearances are so plain that I can conceive no other interpretation being put upon them by any one who studies the original preparations or the drawings with a mind free from prejudice. The objections that have been urged against this interpretation are (1) that it controverts Remak's law, and (2) that the new formation of all connective tissue arises from leucocytes. As to Remak's law, it may be said that all biological laws have exceptions, and, as Dr. Creighton has remarked, a physiological law may not hold good in pathology. But, by the concurrence of most authorities on embryology, the Wolffian ducts and the Wolffian tubes and glomeruli are formed from the mesoblast, so that Remak's law does not touch this particular case. At the same time I consider that this process is quite analogous to the formation of fibres from the hepatic epithelium in cirrhosis of the liver, described by Dr. Hamilton, and from the epithelium of the mamma in breast tumours, maintained by Dr. Creighton. I possess preparations and drawings which confirm the statements of both these observers. I have, moreover, little doubt that the same process may be seen in the lung.

As to the origin of the connective tissue in the healing of wounds, that is a point which may be fairly considered as *sub judice*. True, Tillmanns asserts that pieces of liver or kidney hardened in alcohol, when introduced into the peritoneal cavity, have breaches in their surfaces healed by wandering cells from the blood-vessels, but on the other hand Von Wyss showed long ago that non-penetrating wounds of the cornea heal by proliferation of the epithelium at the edges of the wound, without any immigration of leucocytes

or proliferation of the cellular elements of the true corneal substance.

γ *The Malpighian bodies.*—We know that the Malpighian bodies are very early affected in this disease. Thoma has shown that they are abnormally ~~favorable~~ not only to fluids but to colloids and small solids, such as crystals of cinnabar, and this in places where no changes can be detected with the microscope. Moreover, we meet with many cases corresponding to Traube's division of capsular nephritis, in which the lesions in these structures are much more advanced than elsewhere, and sometimes, as in one of the present cases (Case 1), not a single Malpighian body appears in a section of kidney nearly a quarter of an inch in diameter.

That the changes would manifest themselves very early in these structures is what we might conclude *à priori*, if we regard the morbid process as a chronic inflammation. In all inflammations as well as in other affections of the connective tissue, the arterial coats, especially the adventitiæ, show the first signs, and are the most advanced seats of the change, whatever it may be. These changes in the Malpighian bodies, so far as they can be followed with the microscope, consist in proliferation of the endothelium lining the capsule and covering the tuft, and the formation of a mass of cellular tissue by the blending together of the growth from the two sources. Fig. 10, Pl. VI, shows one stage of this process, the capsule and tuft being covered with young cells.

The further stage is seen in fig. 11, in which the cellular mass has become converted into a delicate gelatinous tissue, containing stellate elements. Still later the contents may be quite hyaline and stain feebly with carmine, forming a little mucous or colloid cyst, the whole process being quite analogous to that which I have described in the tubules, with this exception, that these Malpighian bodies are not enlarged, or at least not to any notable degree; often, indeed, they are small. The drawings illustrating these changes were taken from Case 2.

δ *The blood-vessels.*—We owe to Thoma the careful measurements which demonstrate, contrary to the statements of many observers, that the arteries of the kidney substance are absolutely *dilated*, in spite of the increased thickness of their walls, and that narrowing of their lumina is exceptional. He showed besides, by careful injections, that fluid runs well into the Malpighian bodies, but that the efferent artery is often destroyed and the capillary plexuses upon the tubules are to a large extent obliterated. The

main point at issue is as to the histological details of the changes in the coats in the vessels.

Johnson, in his original papers, described hypertrophy of the circular and longitudinal fibres of the coats, meaning by the longitudinal fibres the inner coat. Gull and Sutton speak of the change as affecting the outer coat mainly, and deny that any true hypertrophy of the muscular wall is present. Figs. 12 and 13, Pl. VI, taken from two vessels of the same kidney from Case 1, are sufficient to show that both these descriptions are correct, and that Gull and Sutton err only when they deny the hypertrophy of the muscular wall, which though not constant is quite common. Fig. 13 is a vessel much dilated, with little or no hypertrophy of the muscular coat. The internal elastic lamina (*a*) is swollen, its layers are separated and interspersed with nuclei; within is the much thickened endothelial layer converted into a delicate fibrous tissue; outside the elastic lamina is the muscularis, showing widely separated spindle-shaped nuclei, and looking as if it were œdematous. Outside this, again, is a cellular connective tissue, in which no adventitial coat can be distinguished from the surrounding connective tissue. Fig. 12, on the other hand, represents a vessel which is made up almost entirely of muscular fibres. Near the inner margin some fibres of elastic tissue can be recognised on closer inspection, and some of the cells in the neighbourhood are more like connective-tissue spindle cells than muscular fibres, while a few are round or oval, so that probably a transition is taking place, and we have to do with a new formation of muscular fibres. This is analogous to the growth of vessels by concentric layers of spindle cells, which may be readily seen in granulation tissue.

Some of the drawings of Gull and Sutton suggest the notion that they were actually made from vessels such as this (fig. 12), but that some imperfection in their histological manipulation preventing their recognising anything more than the blurred and indistinct structures they have represented in their plates.

e. The connective tissue.—There is so little connective tissue in the normal kidney apart from the structures we have been considering that it is open to question whether this title is correct. But in the diseased kidney the intertubular spaces are so much more easily seen, and are so obviously occupied by connective tissue of some sort, that it is necessary to refer to it. The changes in the capsules of the Malpighian bodies, the adventitial tunics of the vessels, and the basement membranes of the tubes consist mainly in

swelling and hyaline transformation. There is no appearance of interstitial nucleation,[1] such as may be seen after ligature of the ureter, or in the early stage of surgical kidney. The absence of this is due simply to the essentially chronic nature of the process, such changes as take place partaking more of the character of growth than inflammation.

So far as can be seen, the changes are confined to those of swelling or broadening, and hyaline transformation, the results of simple œdema or surplus of plasma from the blood-vessels. The connective tissue suffers little from the abnormal state of the organ on account of its low organisation, though it tends to be reduced, as we have seen, to the gelatinous type, which is one of the lowest in the series of connective substances.

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March 16*th*, 1880.

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[1] Since writing the above, a case has come under my notice which has convinced me that the kidney in this disease is liable to transient inflammatory attacks, in which the intertubular stroma becomes filled with lymphoid cells.

DESCRIPTION OF PLATES V & VI.

Illustrating Dr. Saundby's paper on the Histology of Granular Kidney. From drawings by himself.

PLATE V.

FIG. 1.—A mass of proliferating epithelium from the cortex of the kidney. *a*. Enlarged nucleus; *b*. hour-glass nucleus; *c* and *d*. cells containing two nuclei; *e*. tubules filled with young cells. Hartnack, oc. 3, obj. 8.

FIGS. 2, 3, 4, and 5 represent semi-diagrammatically the stages of cell proliferation observed in the epithelium in Fig. 1.

FIG. 6.—Convoluted tubules filled with small round cells, derived as above described. Hartnack, oc. 3, obj. 8.

FIG. 7.—Transformation of a group of tubules, filled with young cells, as seen in Fig. 6, into connective tissue, by the conversion of the round cells into spindle and stellate cells. Hartnack, oc. 3, obj. 8.

FIG. 8.—Cyst formation within the convoluted tubules, by the myxomatous degeneration of the cellular tissue produced by the proliferation of their lining epithelium. Hartnack, oc. 3, obj. 8.

FIG. 9.—Straight tubes undergoing transformation into connective tissue. The epithelium has proliferated and filled the tubes (at *a* and *a*) with young cells. At *b* the tubule is seen dwindling to a row of spindle cells, and becoming lost in the connective tissue around it. Hartnack, oc. 3, obj. 8.

PLATE VI.

FIG. 10.—A Malpighian body, showing proliferation of the endothelium covering the tuft and lining the capsule, with swelling of the fibrous tissue of the capsule. Hartnack, oc. 3, obj. 8.

FIG. 11.—A Malpighian body, degenerated by myxomatous transformation of the cellular tissue, resulting from the proliferation of the endothelium of the tuft and capsule. Hartnack, oc. 3, obj. 8.

FIG. 12.—A small blood-vessel from a part of the kidney in which the fibroid degeneration was much advanced, showing its walls composed of concentric layers of smooth muscular fibres, with some elastic tissue and a few small spindle cells. Hartnack, oc. 3, obj. 8.

FIG. 13.—An arteriole from the same part of the same kidney, showing (at *a*) the swollen elastic lamina with its layers separated and interspersed with nuclei. Next to the lumen is a broad band of lowly organised connective tissue, derived by proliferation from the endothelium. Outside the elastic lamina is the muscular coat, looking œdematous and containing a few muscular fibres. Outside the muscular coat is a cellular coat, which cannot be separated from the connective tissue in which the vessel is embedded. Hartnack, oc. 3, obj. 8.

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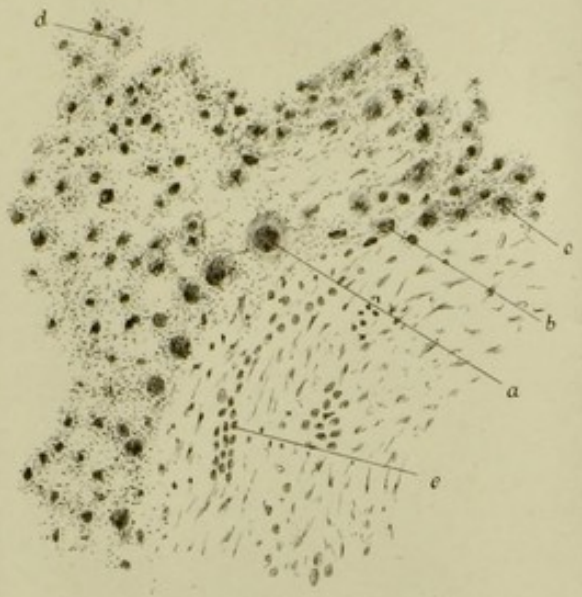

Fig. I.

Fig II.

Fig III.

Fig IV.

Fig V.

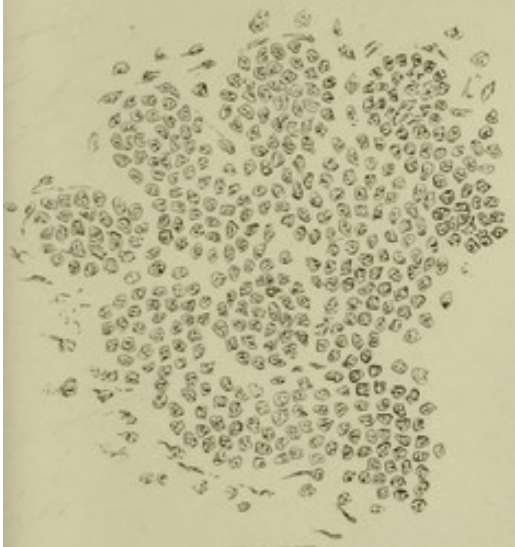

Fig. VI.

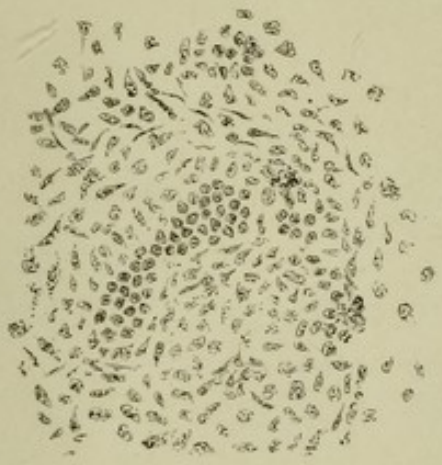

Fig. VII.

Fig. VIII.

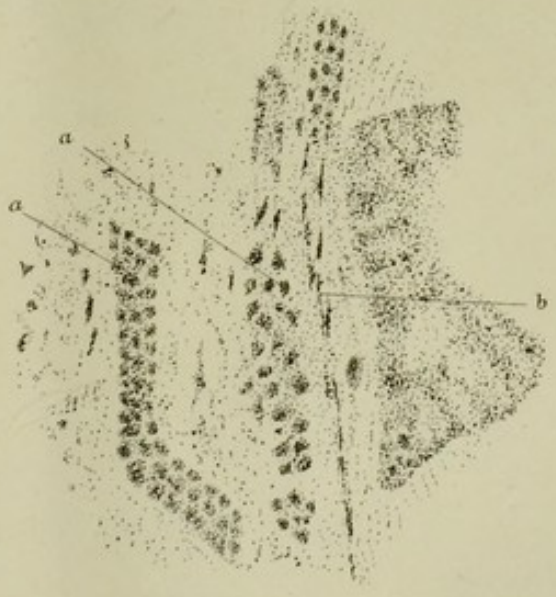

Fig. IX.

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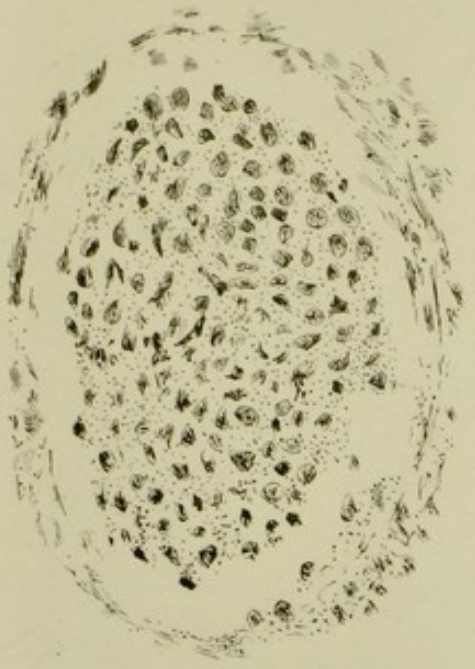

Fig. X.

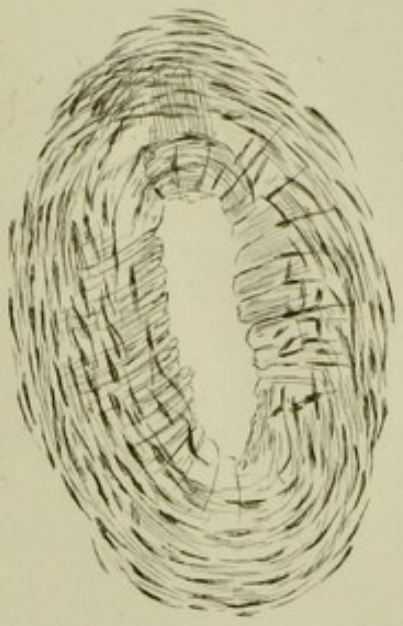

Fig. XII

Fig. XI.

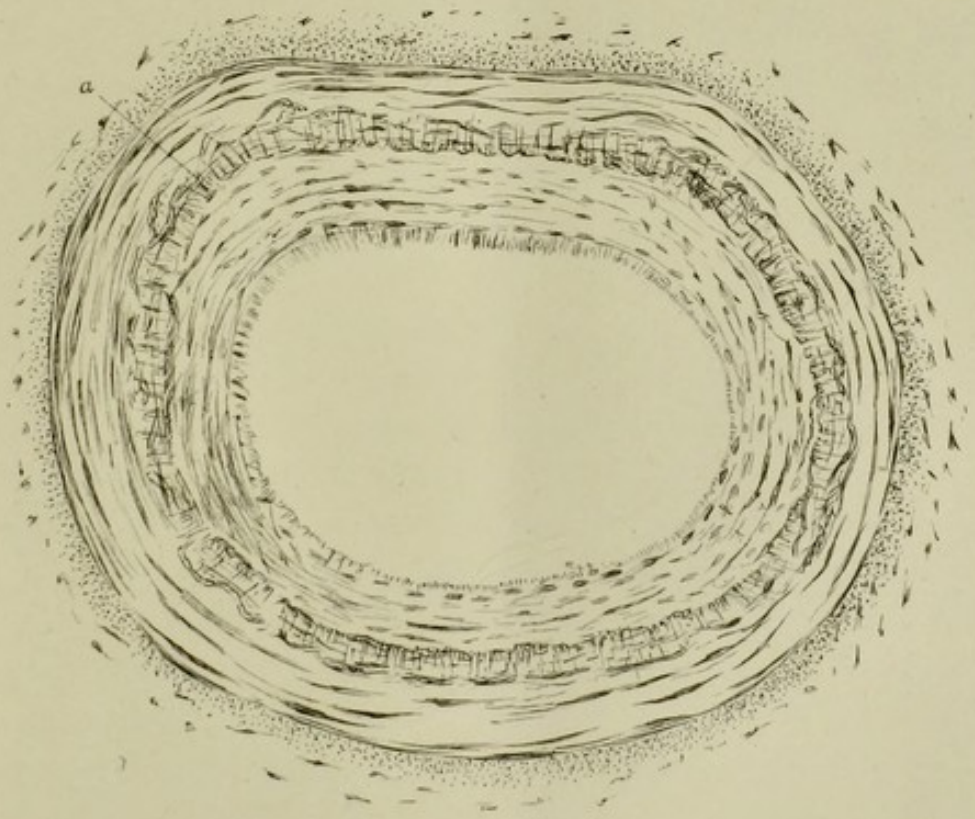

Fig. XIII

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