ON THE MORBID ANATOMY OF CERTAIN FORMS OF POST-SCARLATINAL NEPHRITIS, IN RELATION TO THEIR BEARING ON THE HISTOGENY OF GRANULAR KIDNEY.

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UNTIL a comparatively recent period, post-scarlatinal nephritis was generally thought to belong exclusively to the parenchymatous variety. It was considered that the kidneys were subjected to abnormal irritation by the scarlatinal poison, and also to vicarious overwork consequent on the deficient action of the skin, and the necessity for the elimination of large quantities of waste products. The brunt of the lesion was supposed to be borne principally by the secreting cells of the uriniferous tubules, which became cloudy, granular, and fatty, and were loosened from their basement membrane and cast off in the urine.

Without doubt, in a considerable percentage of cases, these older views are perfectly correct. The clinical symptoms are those of ordinary acute Bright's disease, the urine is diminished and albuminous, and contains renal epithelium, blood corpuscles, and tube casts in abundant quantity; and the condition runs the ordinary course of acute Bright, frequently terminating in recovery more or less complete, according as the renal inflammation subsides, or passes into the chronic form.

Yet though parenchymatous or intratubular nephritis is a frequent sequela of scarlet fever, it is by no means the only form of nephritis liable to supervene upon this disorder. A variety of other morbid appearances have been chronicled from time to time by different observers, among whom may be mentioned Drs Wilks, Bristowe, Cayley, and Coats, Arnold Beer, Biermer, Wagner, and others. The cases recorded by these authorities differ materially from ordinary parenchymatous inflammation, for in those of Biermer, Coats, Wagner, and Cayley the morbid changes were interstitial, while in those of Beer, Bristowe, and Wilks the glomeruli were the parts specially affected.

Klebs, however, was the first to make prominent mention of a post-scarlatinal nephritis leading to peculiar and remarkable changes in the glomeruli (*Handb. der Path. Anat.* lief iii. pp. 644–647). To this he gave the name of glomerulo-nephritis. He describes the interior of Bowman's capsules as occupied by a number of small angular nuclei imbedded in a finely granular mass (see figs. 1 and 2, and Klebs' engraving, *loc. cit.*). These nuclei he evidently considers as springing from a proliferation of the normal corpuscles of the connective tissue of Axel Key, which binds the capillaries of the Malpighian tufts into compact balls. In normal kidneys these corpuscles are not difficult to demonstrate, especially in specimens of cats' kidney stained with logwood after successful injection with carmine and gelatine. A glomerulus is carefully picked out whole, and placed on a separate slide with a drop of water; a moderately thick cover-glass is then pressed firmly down upon it, and moved slightly from side to side so as to dissociate the capillary loops, or these are carefully separated from one another with fine needles under the dissecting microscope. Either of these processes, if properly conducted, will afford a ready demonstration of the glomerular connective tissue. Its corpuscles stain deeply with logwood, and are therefore easily identified. They are seen to be situated in the substance of the glomerular ball, between its component capillaries. Their anatomical site is consequently different from that of the epithelial cells forming the glomerular investment, from which they further differ in form and size.

In glomerulo-nephritis Klebs describes an enormous increase in the number of these corpuscular bodies, which completely fill Bowman's capsules, obscuring the glomeruli, compressing and emptying the capillaries, and thus seriously interfering with renal circulation and excretion (see figs. 1 and 2). According to Klebs, the corpuscular accumulation inside Bowman's capsules is the only morbid condition noticeable in these cases. Clinically glomerulo-nephritis may be recognised by the occurrence of sudden and complete suppression of urine, followed by acute dropsy and uræmic symptoms. The prognosis appears to be very unfavourable, as, indeed, might be conjectured from the anatomical characters of the morbid changes.

Of this variety of post-scarlatinal nephritis I have seen several typical specimens. So far as regards the condition of the glomeruli, they corresponded closely with the description given by Klebs; but there were besides a number of other interstitial changes, and some intratubular changes of minor import, which I shall presently describe.

In my specimens the cell-accumulation inside Bowman's capsules was of the nature of a granulation tissue rich in small cells. The capsules themselves were thickened, and their substance was infiltrated with round cells, while outside their periphery was a dense interstitial accumulation of cell structures similar to those occupying their interior. Sometimes a whole Malpighian body was entirely hidden by an accumulation of multitudes of these small cells (see fig. 8). The epithelium of one or two tubules in the immediate neighbourhood of each affected Malpighian body was generally fatty, staining deep black with osmic acid; but the fatty changes were strictly limited to the tubules in these situations, the epithelium of the great majority being still normal, both in the cortical and medullary portions of the kidney. A few leucocytes and red blood corpuscles were, however, occasionally visible in the lumen of the convoluted tubules.

Around many of the veins and arterioles of the kidney there were copious accumulations of small round cells, which were evidently of a migratory nature (see figs. 2 and 5). These, after passing through the vascular wall, had collected in large numbers in the perivascular connective tissue immediately outside it, the structure of the kidney preventing the majority of them from wandering further (see also paper by Klein, *Trans. Path. Soc.* 1877, pl. xxxii. figs. 2, 3, and 4). This migration of leucocytes points to an interstitial nephritis, affecting not only the connective tissue between the loops of the glomeruli and around Bowman's capsules, but also that of the general kidney stroma, though in a somewhat minor degree. In this respect my specimens differed from those described by Klebs, in which there were no evidences of general interstitial nephritis, and resembled those of Klein (*op. jam. cit.*), in many of which similar interstitial changes were observed.

The cellular accumulations inside Bowman's capsules, between

the individual capillary loops and on the surface of the glomeruli were very general and exceedingly abundant. The effect of the pressure of so large a number of cellular bodies inside the inelastic and but slightly distensible capsules must necessarily be to render the arterioles of the glomeruli well-nigh impervious, and thus to interpose a serious obstacle in the way of the passage of the blood stream and the excretion of urine. Indeed, the gravity of the clinical symptoms is fully explained by the histological characters of the affected kidneys. Dr Klein (*Trans. Path. Soc.*, 1877, pp. 435, 436) is disposed to doubt the accumulation of cellular bodies inside Bowman's capsules in sufficient numbers to interfere with the circulation. But, as we shall presently indicate, and, indeed, as he himself admits, his cases were in all probability not true, or at least not typical examples of glomerulo-nephritis. Dr Klein considers the nuclei as being of an epithelial nature. In all of my specimens, save one to which I shall presently allude, this hypothesis appears to be negatived by the fact that the intercapillary situation of many of the nuclear bodies was proved by repeated experimental crushings and teasings out of the glomeruli. The corpuscular bodies were found *between* as well as upon the surface of the capillary loops, a circumstance which, in my opinion as in that of Klebs, must be allowed due weight in determining their nature.

In my cases there could, I think, be no reasonable doubt that the glomerular circulation must have been seriously obstructed by the large nuclear aggregations inside Bowman's capsules. Were further corroboration of this conclusion required, I should be disposed to recognise it in the fibrous state of some of the glomeruli. In two of my specimens a number of glomeruli presented appearances similar to those figured by Dr Klein in plate xxxiii. fig. 7, *Trans. Path. Soc.* 1877. The impervious capillary loops were transformed into a fibrous texture, more or less completely united with the thickened Bowman's capsules. Their lumen was evidently entirely abolished (see figs. 3, 4, 6, and 7). The nuclei on the surface and in the substance of these fibrous glomeruli were much diminished in number, as represented in the above drawings. Their attraction for vegetable colouring matters was also materially diminished. They were stained much less deeply by

logwood than those upon the surface of other glomeruli in the same section, whose capillaries, though compressed and emptied by the pressure of the cell growth, were still apparently capable of renewed distention in event of the removal of the compressing mass. It appears reasonable to suppose that the fibrous change is due partially, and indeed mainly, to abolition of function by compression, but partly also, perhaps, to direct fibrous metamorphosis of the compressing cells, which, as already stated, appear to be of the nature of a granulation tissue.

I am disposed to consider the cell-accumulations inside Bowman's capsules as originating from two sources. Firstly, many of them are probably derived from direct proliferation of the intercapillary connective-tissue corpuscles of the glomeruli, which they resemble in size, general outline, and behaviour with colouring reagents. Indeed, in the earlier specimens of glomerulo-nephritis, where the intracapsular cell accumulations are seen in their initial stages, the appearances are simply those of moderate increase in the number of these bodies (see fig. 1). Their anatomical situation, as previously stated, is between and not on the surface of the glomerular loops,—in the substance of the Malpighian tufts, and not in the interspace between the glomeruli and their investing capsules. But as the morbid process proceeds, this interspace is usually entirely filled with cellular bodies, which are now seen, not only between the capillary loops, but likewise on their free surfaces, occupying the space between the periphery of the glomerular balls and the inner circumference of their investing capsules. So far as their anatomical position is concerned, the cells thus situated might, of course, be derived, as Klein supposes, from an increase in the epithelial elements investing either the inner surface of Bowman's capsules, or the circumference of the glomeruli. But, on the other hand, they differ from epithelial cells in form, size, contour, and attraction for colouring matters; while they are identical in appearance with the intercapillary corpuscles, and are therefore presumably of the nature of leucocytes or connective-tissue cells. I am, accordingly, disposed to consider many of them as migratory leucocytes, and to regard the intracapsular cell accumulations as composed partly of proliferated connective-tissue corpuscles, and partly of migrated blood cells,

which have passed through the walls of the glomerular capillaries. This idea receives confirmation if we direct our attention to the abundant cell-accumulations outside Bowman's capsules, and around the arterioles and small veins of the cortical substance (see figs. 1, 2, and 5). The cells in these situations, and especially the latter, are clearly migratory, while they exactly resemble those in the interior of Bowman's capsules. Further, in pencilled preparations, the lumen of the cortical capillaries is seen to be occupied by numerous leucocytes, which are often so closely aggregated as to show that the circulation through them during life must have been either materially retarded or reduced to a condition of complete stasis. This cramming of the vessels with leucocytes, apparently ready to emigrate, affords additional evidence, if such be needed, of the migratory nature of those cells which have accumulated in quantity outside the cortical vessels. If, therefore, this process of emigration be observable in the case of the ordinary vessels of the cortex, why should not the same conditions produce the same effects in the case of the vessels of the Malpighian tufts? Indeed, the mechanical conditions of these tufts, lying as they do in the midst of a free space, are more favourable to the outward passage of leucocytes than those of the ordinary vessels of the cortical substance; for whereas in the latter the escaping leucocytes must encounter the outside pressure of the surrounding tissues, they find free exit in the former, and pass directly into the unoccupied spaces intervening between the glomeruli and their capsular coverings. The corpuscular as well as the fluid constituents of exudations tend to escape and accumulate where there is space for them; and it is accordingly not surprising that they should select the interior of Bowman's capsules as the site of their lodgment. Normally the glomeruli do not entirely fill up the interior of the capsular expansions of the uriniferous tubules, a space being left for the escape of the fluid urinary constituents as fast as they are exuded from the capillary loops. This space, empty save for the escaping urinary fluid, offers a favourable situation for the diapedesis and accumulation of the migratory cells which expel the fluid and occupy its place, at the same time compressing the glomeruli and producing the characteristic clinical symptom of suppression of urine. The migration of leucocytes

from the glomerular capillaries, assisted by the proliferation of the corpuscles of the interglomerular connective tissue, proceeds until the interior of Bowman's capsules is filled as full as it can hold with small-cell structures. The capsules themselves are dense, tough, fibrous, and practically inelastic, while the Malpighian capillaries are compressible; and, accordingly, the increasing cell-accumulation presently abolishes the lumen of the vessels by outside pressure, and renders them impervious to the passage of blood. Hence the excretory functions of the kidney are interfered with, and anuria, uræmia, and acute dropsy begin to develop themselves.

In my cases the coats of the vessels of the general kidney stroma were quite normal. No germination of muscle nuclei in the tunica media, or hyaline degeneration of the intima, as recorded by Dr Klein (*Trans. Path. Soc.* 1877), was observed in any of them. The outer coat also appeared perfectly unchanged (see fig. 5).

Parenchymatous changes were limited to those tubules in the immediate neighbourhood of the Malpighian bodies, and consisted chiefly in fatty degeneration of the tubular epithelium, though cloudy swelling and granular disintegration were also observed in a few instances.

It will be seen that the specimens included in the foregoing description approximate more or less closely to the glomerulo-nephritic kidney of Klebs. In all of them the salient feature was the excessive cell accumulation inside and around Bowman's capsules, an accumulation which was evidently responsible for the peculiar clinical symptoms. But in one kidney from the body of a boy eight years old, who died in the Aberdeen Infirmary after a three months' illness from supposed parenchymatous nephritis, the morbid appearances were found in many respects analogous to those described by Klein in his paper on the morbid anatomy of scarlatina, to which I have previously referred in the course of the present article. During his residence in hospital the patient suffered from albuminuria and a variable amount of renal dropsy. I am not aware whether cells or casts of any kind were present in the urine. The albuminuria was supposed to have been consequent on scarlet fever; but the history previous to admission was doubtful. The autopsy was

made by my friend, Mr Rodger, Pathologist to the Aberdeen Infirmary, to whose kindness I am indebted for the specimen. The liver was enlarged, yellowish, and highly fatty. The kidneys were heavier than normal, enlarged, pale in colour, and somewhat dense in consistence. Their surface was smooth, and the capsule stripped off easily. The other organs of the body presented no remarkable changes.

On microscopical examination with a low power (Hart. oc. 3, × obj. 3), the Malpighian bodies were seen to have absorbed the colouring matters (carmine and logwood) with great avidity. Their capsules were thickened, and the intertubular septa in their neighbourhood were increased in width.

Examination with a high power (Hart. oc. 3, × obj. 7), showed general fibrous thickening of Bowman's capsules. The interstitial tissue was increased, especially around the Malpighian bodies, and included tubules more or less empty, compressed, and atrophied. The Malpighian bodies themselves had undergone extensive fibrous alterations. Most of them were reduced in size, the vessels of the glomeruli being impervious, fibrous-looking, and wholly or partially united with their thickened capsules into a solid fibrous mass (see fig. 3; see also Klein, *Trans. Path. Soc.* 1877, pl. xxxiii. fig. 7). Where this blending was incomplete, the vascular loops were shrunken and fibrous, occupying considerably less of the intracapsular space than those of normal glomeruli. The interval between the shrunken glomeruli and their capsules was occupied by a few nuclear bodies, but the number of nuclei inside Bowman's capsules was not by any means excessive (see fig. 7). Indeed, in proportion as the fibrous changes in the glomeruli become more complete, the number of cellular bodies inside their capsules appears constantly to diminish,—a phenomenon noticeable alike in the kidney now under discussion, and also in the others previously described, and, as before stated, probably partly due to direct fibrous transformation of the cellular accumulations (see also figs. 4 and 6).

Individual glomeruli here and there were seen in various stages of colloid or hyaline transformation. Others, together with their capsules, were completely converted into fibrous masses, interspersed with a few round cells, and only distinguishable from

patches of increased interstitial tissue by the preservation of an obscure concentric arrangement. These completely metamorphosed Malpighian bodies were only slightly tinged by colouring matters. Few glomeruli were even approximately normal; and the prolongation of life for three months under such conditions is, therefore, the more noteworthy, as proving what serious structural alterations may sometimes occur in the kidneys without inducing an immediately fatal result. The youth of the patient, and the skilled treatment to which he was subjected, probably operated materially in retarding the eventual untoward issue.

The increased intertubular stroma was principally of a finely fibrous character, though in some situations there was a good deal of small-cell infiltration still remaining around the Malpighian bodies. Indeed, the whole aspect of the changes, both inside Bowman's capsules and in the general interstitial tissue, seemed to point to the fibrous transformation of a previous small-cell formation. This consideration would lead us to regard the case as a later stage of the glomerulo-nephritis of Klebs. In all my other specimens the greatest cellular increase was found inside and around Bowman's capsules; and in this kidney the fibrous increase was greatest also in these situations, and still contained a variable number of unaltered round cells, which had not undergone the fibrillar transformation.

Many of the uriniferous tubules, more especially the convoluted tubes communicating with the Malpighian bodies, were the seat of intratubular changes, which were evidently mere secondary consequences of the primary glomerular affection. We have already stated that many of the tubes were compressed and atrophied by the pressure of the fibrous interstitial increase around the glomeruli. Others were more or less completely denuded of their epithelium; in others, again, the epithelium was in a state of fatty or granular disintegration. On the whole, however, when compared with the changes in the Malpighian bodies, these intratubular alterations were comparatively insignificant.

If this description be compared with that in Dr Klein's paper (*Trans. Path. Soc.* 1877), the many points of close resemblance will be sufficiently obvious. In fact, I have little doubt of the substantial identity of this case with those comprised in Dr

Klein's series; the only point of material difference being in the condition of the coats of the small veins, arterioles, and capillaries of the stroma, which in my specimen were perfectly normal. I am, consequently, at present unable to concur with Dr Klein in the importance which he attaches to the vascular alterations in relation to the development of the clinical phenomena. These latter, I am persuaded, are due firstly to compression of the glomeruli by the cell-aggregations inside Bowman's capsules, as supposed by Klebs; and secondly, to the subsequent fibrous degeneration with which these compressed and empty glomeruli are presently affected. Both processes tend, firstly to obstruct, and subsequently to abolish the glomerular circulation, whose special functions are connected with the separation and elimination of the urinary fluids, and probably also of a certain proportion of the solid constituents likewise. Granted the accuracy of Klebs' description of glomerulonephritis, and the feasibility and sufficiency of his explanation of the cause of the symptoms during life can hardly be questioned. My specimens convince me of the correctness of the one, and I am therefore prepared to accept its corollary also.

The information derived from the study of such specimens as the foregoing is not without significance, as bearing on that much debated cognate subject—the histogeny of interstitial or granular kidney. The great diversity of opinion among pathologists with respect to its origin arises principally from the fact that early specimens are very rare, because the disease in its early stages is very seldom fatal. But when the glomeruli are affected, the condition is one of immediate danger to life, and in such kidneys the general interstitial lesions are often seen before sufficient time has elapsed to allow of the masking of the essential process by subsequent changes. They are therefore peculiarly instructive, since they act as it were as the grammar or key to a complicated and difficult language.

In ordinary specimens of granular kidney the indications of the primary source of the interstitial increase are so doubtful as to admit of a number of conflicting interpretations. Thus,

Dr George Johnson considers the intratubular lesions as the primary and essential elements in the process, and regards the increase in the stroma as merely apparent, and produced by a shrinking together of the normal framework consequent on the destruction of the tubes and their epithelium. Sir W. Gull and Dr Sutton are of opinion that granular kidney is but part and parcel of a general morbid change in the system, characterised by the deposition of a hyalin or hyalin-fibroid material in the adventitia of the arterioles, and a hyalin granular change in the walls of the capillaries. MM. Cornil and Ranvier attribute the renal changes to a chronic arteritis. Again, a numerous section of British and Continental pathologists advocate the theory of a true interstitial nephritis, consisting in an infiltration of the kidney stroma with migratory leucocytes, and their subsequent transformation into a more or less completely formed fibrillar tissue.

To these theories yet another has been lately added by Dr Robert Saundby. At a meeting of the Pathological Society of London, held on Tuesday the 16th of March of the present year, this gentleman exhibited a number of specimens tending to prove that the changes in the granular kidney begin by an active proliferation of the tubular epithelium and a filling of the tubules with free nuclei. He further supposes that the nuclei of the proliferated epithelium become converted into spindle cells and connective tissue. (See reports of the above meeting in *Lancet* and *British Medical Journal*, March 27, 1880.) So far as I understand the report of his statements, he is of opinion that the proliferated epithelial nuclei traverse the basement membrane of the tubules, and thus migrate into the stroma, where they undergo fusiform and fibrillar changes leading to true fibrous increase of the interstitial tissue.

This supposed fibrous histogenesis from proliferated epithelium is so remarkable that it appears to merit a few words of independent consideration, before we proceed to discuss the question as to how far it may coincide with the early interstitial appearances of the stroma as seen in glomerulo-nephritis. The idea, though strange, is by no means new. Holm (*Wiener Acad. Sitzungsb.* 1867), Dr Wickham Legg (*Barth. Hosp. Reports*, 1872), MM. Kiener and Kelsch (*Arch. de Phys.* 1879), and Mr D. J. Hamilton (*Journ. Anat. and Phys.* Jan. 1880), have attempted to

establish an analogous origin of the fibrous tissue of cirrhotic liver from the nuclei of the hepatic cells, and Dr Creighton has also recorded certain indications of a like process of connective-tissue formation in the mamma. Mr Hamilton, more especially, expresses himself with great confidence respecting the origin of the fibrous tissue in hepatic cirrhosis, for he says:—

"The absurdity of tracing the origin of the cirrhotic fibrous tissue to exuded leucocytes, as has been affirmed but never demonstrated by a certain school of pathologists, only requires for its detection a little unbiassed observation."

Accordingly, he thus summarises the results of certain observations conducted by himself:—

"(*a*) The liver cells are one of the main sources of the fibrous tissue developed in the organ.

"(*b*) The first visible change in their transformation is the enlargement of the nucleus, and the development of a nucleolus and intranuclear plexus. The enlarged nucleus then divides, and this is almost simultaneously followed by transverse fission of the whole cell.

"(*c*) Two smaller cells thus arise, each having a nucleus, and these nuclei soon grow to as large a size as that from which they sprung.

"(*d*) The periplast, however, does not increase in size *pari passu*, but at each successive division becomes smaller and smaller, until finally nothing but a free nucleus remains.

"(*e*) This free nucleus now enters upon a new existence. It becomes oval, and from its free border a fresh periplast is generated, which assumes a fusiform shape.

"(*f*) The fusiform or spindle-shaped periplast now splits into a number of fibrils, and becomes more elongated and tapering at the extremities. The ultimate result is the formation of a bundle of white fibrous tissue out of these fibrils, the nucleus remaining on the surface as the nucleus of the bundle."

I regret that it is somewhat foreign to the scope of the present paper to enter into a detailed examination of the grounds on which Mr Hamilton relies in support of his theory. One or two points, however, seem to call for passing remark, in order that

we may clearly comprehend all the issues involved in the question.

Firstly, It is a recognised fact that the nucleus of a disintegrating cell is by far the most resistant of the cell constituents; hence, long after cells have become disintegrated, the nuclei remain behind in a free state, and are apparently but little altered, save that in many instances their capacity for absorbing vegetable colouring matters is materially increased. This fact is observable in the kidney, as well as in the liver, and in the former organ is sometimes extremely characteristic, much more so, according to my experience, than in the latter. For instance, in a section of kidney we often meet with tubules in transverse section, whose lining epithelium has entirely disappeared save for the still persistent nuclei, which are yet visible, clinging to the inside wall of the basement membrane. Their power of absorbing staining fluids is remarkable, and at times perfectly diagrammatic.

The same appearance is observable in the nuclei of the epithelial investment of the glomeruli, more especially in those glomeruli which are becoming homogeneous, hyaline, or colloid, from incipient degenerative changes. This last fact is very significant, and seems to point to commencing degeneration as a cause of the heavy coloration, and not, as Mr Hamilton supposes in the case of the liver cells in which he has observed a similar phenomenon, to the entry of the nucleus upon a new stage of existence. On the contrary, it seems rather to herald the approach of impending dissolution.

Further, after an examination of many hundreds of sections taken from an extensive series of specimens of interstitial nephritis, I have never seen an instance of any approach to fusiform or fibrillar transformation in the deeply-stained nuclei adherent to the inner surface of the basement membrane of tubules whose epithelium has become disintegrated. The nuclei were invariably found to retain their pristine form, nor did they ever exhibit the least appearance of formative activity. Surrounded by the intact and much-thickened basement membrane, they seemed to be quietly awaiting their euthanasia. In the similar process of hepatic cirrhosis, the liver cells become disintegrated and disappear in the same way, and from very much

the same causes as those at work in the interstitial kidney, namely, interference with blood supply, and direct pressure, leading to impairment of vitality and function. Just as in the kidney, their nuclei are the last elements to undergo disintegration; and, consequently, we frequently meet with aggregations of free nuclei in the midst of surrounding cirrhotic bands as figured by Mr Hamilton (*Journ. Anat. Phys.* Jan. 1880, pl. viii. fig. 1), these nuclei being identical in nature and appearance with the nuclei of other cells whose protoplasm is still more or less intact. They also somewhat resemble the elements of the small-cell infiltration in portions of cicatricial tissue which have not yet become fusiform or fibrous, but differ from them in the crowded manner in which they are huddled together by the surrounding process of contraction, and also in their larger size, denser appearance, and greater depth of coloration. They are, in fact, the few survivors of the once numerous army of liver cells, and are quite insignificant in numbers compared with the total bulk of new cicatricial tissue, whose final and fatal contraction upon them they are passively awaiting.

Sometimes a very few of these nuclei appear to have been mechanically compressed into an approximate spindle shape, but of these I have never seen more than perhaps a dozen at the most liberal computation. When isolated they appear to be destitute of protoplasm, mere naked nuclei with no indication of intranuclear plexus, so far as my observations extend.

In the liver, however, a certain dubiety as to the nature and condition of these nuclei may possibly be feasible, on account of the identity of their anatomical site with that of the small-cell infiltration; but in the kidney this doubt is removed, for the basement membrane of the denuded and atrophied tubules containing them is not disintegrated but thickened, and they are thus unmistakably marked off and separated from the surrounding intertubular round-cell infiltration. The cells of the latter evince formative and differentiative activity, whereas the nuclei exhibit no changes of shape, and are evidently inert and passive.

Secondly, A strong inferential argument is afforded against the hypothesis of the histogenesis of a new pathological tissue from the nuclei of a disintegrating normal one, if we consider that adherence to this doctrine must perforce necessitate the

alteration of all our now well-established ideas as to the active portion of the cell constituents. It is no mere hypothesis that the protoplasm and not the nucleus is the active element of the normal animal and vegetable cell; nor is it less certain that the phenomena of disease involve no new vital processes, either structural or functional, which are distinct in kind, and have not their antitype and analogue in certain corresponding normal ones. This is, in fact, one of the fundamental laws of modern pathology; so that the admission of the histogeny of a diseased tissue from the nuclei of a disintegrating normal one implies the inevitable corollary of the histogeny of new normal tissues from the nuclei of previously existing disintegrating ones. There is not a single process of abnormal tissue formation which is radically and essentially distinct in kind from all normal ones, for both normal and diseased processes are alike manifestations of the vitality and functional activity of the tissues; the only difference being that the former are indications of life under favourable conditions the latter under unfavourable. If this be not so, the principles of modern pathology are radically false. Those principles, however, will hardly be overturned by the presumptive evidence of a few isolated specimens. Probability would rather incline towards a possible erroneous interpretation of the appearances observed in the specimens in question.

Thirdly, In the case of the liver, the histogenesis of fibrous tissue from the hepatic cells would appear to involve a breach of the embryological law of Remak. Mr Hamilton attempts to overcome this objection by assigning a mesoblastic origin to the liver cells. He considers it probable that the branching cylinders of cells in the embryonic organ are developed from the mass of the mesoblast which gathers around the sac-like offshoots from the primitive duodenum. This is, of course, possible, for I am fully aware of the difficulties attending the discovery of the exact embryonic source of the tissues of the abdominal organs. Of course nothing save renewed embryological investigations of the most careful nature can definitely settle the question; but, in the meantime, Mr Hamilton's hypothesis, though agreeable to the conclusions of Schenk, runs counter to the researches of the principal modern embryologists. Among these we may cite the authority of Foster and Balfour, who state that the cellular

elements of the liver are derived from the hypoblast, the mesoblastic portions being mainly differentiated into the blood-vessels, and the fibrous tissue of the ducts. This objection does not, of course, apply to the kidney, in favour of whose mesoblastic origin there is a general consensus of opinion on the part of the principal modern observers.

Let us, however, see how far the supposed origin of the fibrous increase in the interstitial stroma of the granular kidney from the nuclei of the tubular epithelium agrees with the facts observed in my early specimens of interstitial lesions. Patches of interstitial cell-infiltration were observed in their initial stages in all my specimens of glomerulo-nephritis. In the one last described the round-cell infiltration was in process of conversion into the familiar fibrous tissue of interstitial nephritis, so that, by the help of this transitional example, I am enabled to trace with tolerable certainty the course of the changes which result in the development of the ordinary forms of granular kidney.

In the common forms of this lesion we observe that the fibrotic substance is most abundant around the Malpighian capsules, along the path of the vessels of the general stroma, and immediately under the capsule, where it forms cicatricial bands running into the cortical substance and firmly binding the capsule to its periphery. Now, *it is precisely in these situations that abundant accumulations of unmistakable leucocytes* are seen in glomerulo-nephritis. In the delicate perivascular tissue around the vessels of the stroma, numberless leucocytes are seen aggregated in dense masses, immediately outside the vessels from which they have migrated. When we add that the general tubular epithelium is quite normal save for the sporadic foci of fatty and granular change in the immediate neighbourhood of the Malpighian bodies to which we have already alluded, the conclusion appears inevitable that the fibrous patches of the later stages of interstitial kidney are the lineal descendants of these masses of leucocytes,—nay, the very leucocytes themselves, which have undergone fibrous differentiation.

Therefore the "absurdity of tracing the origin of the cirrhotic fibrous tissue to extruded blood leucocytes" does not, at least in the case of the kidney, appear so very glaring.

Explanation of Plate XXVII.

Fig. 1 (× 300). A Malpighian body from the kidney, in the early stage of glomerulo-nephritis. The glomerulus is obscured by a small cell accumulation. Bowman's capsule is thickened at one portion of its circumference, and contains a few round cells. A similar cell-infiltration is beginning in the stroma immediately around it. The uriniferous tubules and their epithelium are still normal.

Fig. 2 (× 50). Glomerulo-nephritis as seen with a low power. The Malpighian bodies appear enlarged and prominent, and look as if sprinkled with fine sand. The tubules are normal, but the small arteries are surrounded by a dotted margin of migrated cells. An accumulation of these cells is beginning in the stroma immediately under the general capsule.

Fig. 3 (× 400). A glomerulus which has undergone complete fibrous transformation. The capillary loops are blended with their investing capsule, and are completely impervious. The small cells on the surface of the glomerulus are much diminished in number. The epithelium of the uriniferous tubule communicating with the fibrous Malpighian body is fatty. A neighbouring tubule contains leucocytes, and its epithelium is undergoing granular disintegration. The whole Malpighian body is shrunken and diminished in size.

Fig. 4 (× 400). A Malpighian body with thickened capsule and shrunken semifibrous capillary loops. The round cells on the surface and in the substance of the glomerulus are diminished in number, though not so much as in fig. 3. Outside the thickened capsule are a number of round cells.

Fig. 5 (× 250). An arteriole from the stroma of the cortex, surrounded by a dense accumulation of migrated leucocytes. The coats of the vessel are normal. A capillary communicating with it contains a number of leucocytes.

Fig. 6 (× 400). A fibrous glomerulus, impervious, and united with its thickened capsule. To the outside of the capsule is a dense accumulation of round cells, while those on the surface of the glomerulus are not numerous. Three tubules, close to the affected Malpighian body, contain fatty epithelium which is stained deep black with osmic acid. Another tubule is completely denuded of its epithelium.

Fig. 7 (× 300). A Malpighian body from the kidney of the boy who died in the Aberdeen Infirmary. The glomerulus is much shrunken, occupying not more than half the space in the interior of its capsule, which is thickened and fibrous. A few epithelial-like bodies are seen in the otherwise empty space inside the capsule. The interstitial stroma around the Malpighian body is thickened and fibrous. The uriniferous tubules are denuded of epithelium, and a few are compressed and shrunken.

Fig. 8 (× 300). A Malpighian body entirely hidden by a dense accumulation of small cells.

Fig. 1.

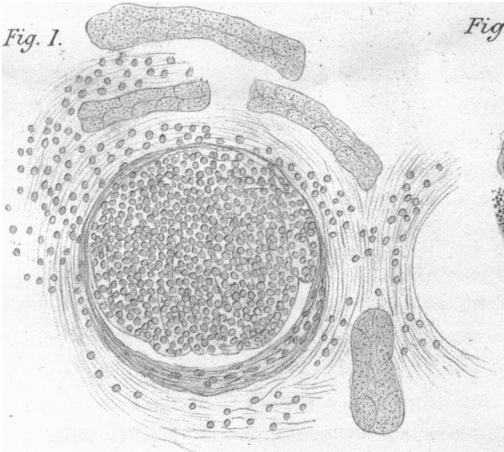


Fig. 2.

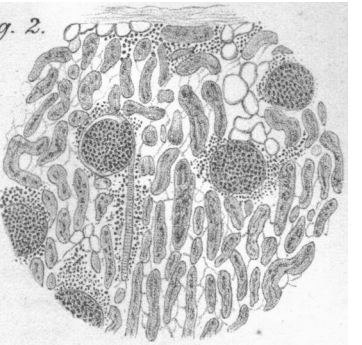


Fig. 3.

Fig. 4.

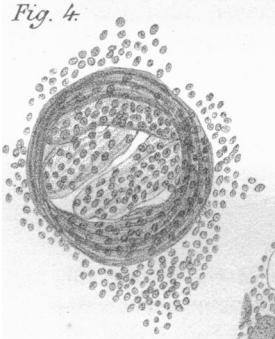


Fig. 6.

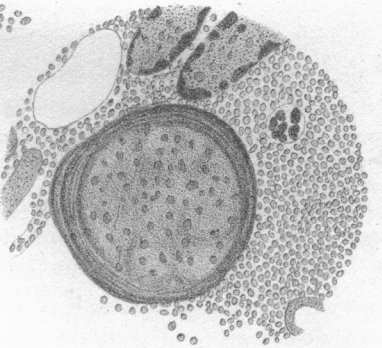


Fig. 5.

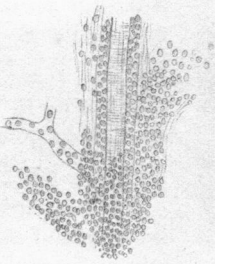
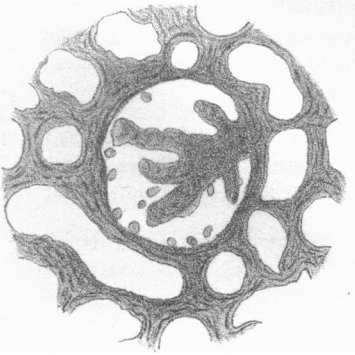


Fig. 7.



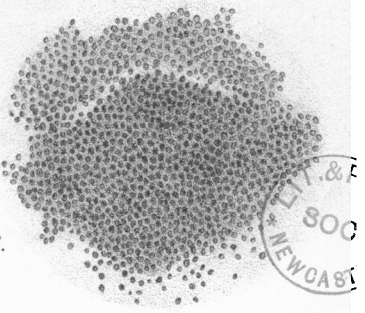


Fig. 8.