NB.

This Thesis is accompanied by a Cabinet containing 253 Microscopical Specimens, a packet containing 55 Coloured Drawings, and a small book containing a description of the Drawings and Specimens.
An Investigation into the Microscopic Anatomy of Interstitial Nephritis

With a Note on Glomerulo Nephritis

by Bryan Chas Waller

M.B. C.M. L.R.C.P. M.R.C.S.
An Investigation
Into
The Microscopic Anatomy
Of
Interstitial Nephritis,
With a Note On
Glomerulo-Nephritis
Illustrated By
Two Hundred And Fifty Three
Microscopical Specimens
And
Fifty-Five
Coloured Drawings:
Being A Graduation Thesis For
The Degree of M.D.,
In The
University Of Edinburgh.
By
Bryan Charles Waller, M.B. C.M.

Αἶλινον αἴλινον εἴπε τῷ ᾿Ιρύ νικέτων,
Arch. Agam. 121, 159.
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To the Memory of
Thomas Lovell Beddoes M.D.,
Poet and Physiologist,
This Work is Dedicated by
The Author.
Chapter I. Introductory.

Many and various have been the views which from the days of H. Bright down to our own time, have been broached respecting the Morbid Anatomy of the "Small red Granular" Kidney. Theories "near the mark or further from the mark, or even altogether far away from any mark; of these," as Carlyle says, "there has been enough." The literature of the subject is extensive, and includes papers of all degrees of merit, some of them chiefly noticeable on account of the daring and poetic imagination evinced by their authors, who with the eye of faith behold appearances otherwise invisible to mortal ken; some on the other hand rich in observation and research, and bearing that unmistakable imprint which long and careful study never fails to bestow. Other writers again, probably with a view to the conservation of energy, have adopted at second hand one or another of the plentiful stock of ready-made theories, dressing and bedizenning the Changeling in accordance with their several fancies, without troubling themselves in the least with superfluous inquiries into the legitimacy of its parentage; these in many cases are blind men led by the blind, and it is to be feared that the delusion is too often their ultimate, and perhaps not altogether uncongenial resting-place. Thus it is not to be wondered at if a large percentage of these dissertations are worth precisely the paper they are printed on, and
valuable chiefly to the butterman as envelopes for his sanctimonious wares. How would it be for students if being worthless they were also harmless; — but such is not the case. for the bewildered learner or busy practitioner with no opportunities for actual observation, is swept away by contending currents of opinion, into a whirlpool of conflicting authorities, and there abandoned “in purgatory wide” like a ship without a rudder, tossed about by every wind of doctrine. For the student too there is yet another lurking danger in the Sunken rocks of Examinations; and as examiners are but men, and for the most part strive, pilot-like, to steer the Medical aspirant into their own pet harbour of theory, it is sometimes more good luck than good guidance if the victim’s ribs and heel are not grazed from theoretical reefs capable of doing very practical damage. Fully aware of the harm done to the cause of Science by those who add to its literature without just cause, due thought, and assiduous labour, — who build upon its foundations a superstructure of wood, hay and stubble, when gold, silver and precious stones lie ready to their hands, — it has been the author’s earnest endeavour throughout the present investigation to form no crude opinions, to promulgate no hollowless theories, and to rush into no hasty and ill-digested generalisations. How far he has succeeded, must now be determined by the arbitration of others, to whose judgment the author hopefully yet somewhat diffidently
commit, the results of the constant work of about two years. One thing, however, he can confidently aver, that whatever the value of his conclusions they have at least been arrived at independently; for though not overweeningly confident in the light of his own lantern, he has at any rate had the satisfaction of knowing that in following its guidance he has been pursuing no Will-o'-the-Wisp. Throughout, the whole research he has.striven to think for himself, and to direct his mind of any previously acquired predilections in favour of one theory or another; and though necessarily obliged to cultivate an acquaintance with the works of others, he has never consciously adopted their views save when in accordance with the testimony of his own experience, and the evidence of his own eyesight. It has been his object in fact to take nothing upon trust, and to adopt as his own the motto of Grudige and Cultivated Storace, who preferred to manufacture his ideas at home and to be "nullius addicere juris advera majestas," rather than save himself the trouble of independent reflection by accepting those so assiduously yet so fruitlessly instilled into him by the worthy "plagiosus Orbilios." — 

The chief microscopical powers employed in the examination of the unjointed specimens have been Hartnack's objectives 3 & 7 (wide angle) and his oculars 3 1/2: Bakers 1 inch, 1/2 inch, and 1/4 inch objectives, with oculars A & B: or for very high powers Hartnack's objectives 8 & 9 (wide-angle) and Ross's 1/5 inch. Two stands have been used, a full-sized
one of Roe's pattern, and a small and extremely convenient one made by Bayson of Edinburgh after a design by Swift. The latter has been in constant use, and is one of the best the author has ever worked with.

A word or two seems advisable on the subject of the accompanying drawings. Great pains has been taken to render them accurate; this result has we believe been attained. They are as nearly as possible facsimiles of the magnified original. The outlines of one or two of the earlier ones were sketched with ordinary lead pencil, but this medium was speedily discarded in favour of Indian ink and colours, which possess all the advantages of pencil without any of its concomitant drawbacks. Etching with the crowquill is a little difficult at first, but the result amply repays the extra labour, as the sharp clear line thus produced is especially adapted to microscopic drawing & nearly approaches, if it does not actually equal the effect obtained by copperplate engraving. In addition to this there is far less fear of injury by rubbing, while of need be, good Indian ink is to some extent erasable.

Most of the microscopic sections accompanying this Thesis, have been cut with the freezing microtome, and are in some instances of a size which may well be termed enormous, often including the whole of the kidney substance from capsule to papilla. The continuity thus obtainable is as will be easily seen of immense advantage to the histologist in that it enables him to direct his attention to a large
connected area, and thus to appreciate more accurately the
distribution of the pathological changes over different portions
of the organ under examination. Sections so cut, though
looking like tracts of country seen under a high power, are
surprisingly uniform in thickness, thus affording a flat field,
instead of one full of hills and hollows as is the case with
even the best sections cut for other means. The introduction
of the freezing microtome has created a revolution in histology,
and the present author is more fortunate than many of
his predecessors in having been able to avail himself of its
aid. Now, by any other method, could sections be cut measuring
an inch and a half across, and of mathematically regulated
thickness; — sections in fact absolutely perfect for the purpose,
for which they are designed? And yet the author has quite
recently seen a book or article he forgets which, in which this
freezer was condemned as useless. May he be pardoned the
suspicion that the fault lay perhaps not so much with the
tool as with the workman? Like most other things worth
doing, section cutting cannot be learnt by the light of
Nature; but a little practice will soon render any one
not intolerably clumsy an adept in the art.

Almost all the subjoined specimens are mounted
with thin cover-glasses, to admit of the use of high powers.
Chapter II. On The Preservation, Preparation, Staining and Mounting of Specimens.

As certain methods of preparation and the use of various reagents have been sometimes not unreasonably credited with the production of pseudo-pathological appearances, the author proposes in the present chapter, to give a short account of the different processes to which his preparations have been subjected in order to eliminate as far as possible, all chance of error in this direction.

In most cases the fresh specimen after having been cut into pieces of suitable size, has been placed to harden first in Müller's fluid or in a solution of Bichromate of Potassa mixed with Spirit, after remaining in which for a fortnight or so it has next been transferred to ¼ per cent solution of Chromic Acid, and there kept until satisfactorily hardened. Better results are obtained by this method than by placing the fresh specimen directly in Chromic Acid, for the Acid does not penetrate so well as the Bichromate, and is apt, especially if the pieces are large, to cause hardening of the circumference while the centre remains nearly unaffected. This untoward result is entirely obviated by the previous use of Müller's fluid which saturates the tissue completely, and acts as to speak as a pioneer for the Chromic Acid. On the other hand it is not advisable to trust to Müller's fluid alone, as Kidney is prepared to receive ever sufficiently hardened, and almost invariably cuts badly, the epithelium being disturbed in the
tubules and the microscopic appearances thus rendered
unsatisfactory. Thus we learn that in histology as well as in
less technical matters, it is sometimes advisable to have two
strings to one's bow.

Chromic Acid specimens often evince a great tendency
to resist the effects of Carmin staining. Though left for an hour
or upwards in strong Carmin solution, it will generally be
found that almost the whole of the dye comes off on washing.
This, were there no means of obviating it, would of itself be
an almost fatal objection to the employment of Chromic Acid
as a hardening agent; for experience has convinced the
author that preparations containing Carmin are by far the
most suitable pigments for the staining of kidney substance.
Fortunately, however, the remedy is easy and effectual. The
water in which the sections are washed after staining, should
be slightly acidulated with dilute Acetic Acid in the propor-
tion of from ten to fifteen drops of 1/8 solution to an ordinary
bowlful of water. This admixture prevents excessive washing
out of the Carmin, and at the same time brightens the colour
and renders it more pleasing to the eye. But while avoiding
the Sphærae of washing off too much of the dye, the histologist
must be careful not to fall into the Charybdis of acidulating
the water not wisely but too well, in which case his
sections will be too deeply and coarsely coloured to admit
of examination under high powers. Diffuse colouring is to be
avoided; the Carmin should stain only the protoplasmic structures.
leaving the general stroma comparatively untouched. Under
a low-power objective stained sections do not perhaps look so
distinctive as those which have retained more of the colouring
matter; but with a power of 300 diameters or upwards,
such as that given by Hartnack's obj 5, or by a good English
5th inch, these specimens come out beautifully, whereas the
heavily coloured ones are well-nigh entirely useless.

The staining reagents which the author has
principally employed during this research are Carmine, Picro-
carmine, Logwood Solution and ½ per cent Osmic Acid solution.
We shall say a word or two about each of these.

Osmic Acid besides serving a useful purpose in
blackening fat, is also a general staining agent of great value
from its extreme delicacy. It tinges the outlines of cells, and
defines the boundaries between different structures. When he
first began to work on the kidney, the author was accustomed
to see it alone; but afterwards seeing how admirably sections,
previously stained with Osmic Acid bore further colouring
with Carmine, he has lately had recourse largely to this method
of double staining, which he believes to be one of the best
modes of demonstrating kidney substances whether normal or
diseased. The sections are left for an hour in ½ per cent
Osmic Acid solution, then taken out and washed, floated
upon a slide, and covered with strong Carmine solution
in which they are allowed to remain for from 15 to 20 minutes.
They are then washed in acidulated water, again placed on a slide, and
mounted. It has been said that Chromic Acid can only be satisfactorily employed when working with fresh specimens, but this is a mistake, for even tissues preserved and hardened in Chromic Acids are stained with great beauty and certainty. The staining, slight at first, deepens and improves after the specimen has been mounted and exposed to the light.

Strong solutions of Carmine and Logwood have been used throughout this investigation. The author has had some experience of weaker fluids, but has not been compensated by any appreciably more satisfactory results for the extra expenditure of time and trouble entailed by their employment. The following is the formula of the strong Carmine solution:

Take of Carmine (purest) $3^\circ$

Strong Ammonia $3^\circ$

Water $3^\circ$

Make the Ammonia hot, the Carmine into a paste in a mortar and then add the water.

This solution stains most tissues in from five to twenty minutes. Chromic acid preparations requiring the longer time. If the Carmine tends to precipitate owing to the evaporation of the Ammonia, the fluid should be filtered, or the pigment may be deposited molecularly on the sections, an accident which renders them nearly useless. After filtering, the solution answers its purpose apparently as well as ever. Carmine also
gives a good demonstration of kidney tissue, but objects thus prepared are as a rule inferior to those previously stained with Cinnabar.

Logwood staining answers very well for sections of kidney, and is especially useful for low power objects; though at times from some unknown cause the colouring is extremely delicate and beautiful, and shows well under a magnifying power of 300 diameters or upwards. Such a specimen is that numbered Series G. 9, from which Drawing No. 11 has been made. The author had previously tried to stain this section with methyl-aniline, but the attempt proving a failure, probably because it had been previously placed in Cinnabar Acid, he re-stained it with Logwood, when it turned out extremely well, and is now an exceedingly characteristic specimen, the nuclear tissue being coloured with exceptional distinctness, while the general oblongs is but slightly tinted.

The chief difficulty with Logwood is to procure a good pulp; Martindale of London sells one of superior quality, but the following receipt for which the author is indebted to the kindness of Mr. S. P. Hamilton, FRCS, Pathologist to the Royal Infirmary, Edinburgh, is so satisfactory that one might go a good deal farther and fare worse. It keeps well, stains rapidly and permanently, and if properly made, is very agreeable to the eye, and less fatiguing than the more glaring Carmine. Much however depends upon the quality of the extract with which it is prepared.
Take of
Friseh Extract: 34 oz. (in case) 3
Sulphate of Alum 1 1/4 lbs.
Put these into 20 ounces of water, and let the mixture stand
for a week, shaking well every day. Then filter, add ten ounce
of Glycerin, and evaporate down to 3/4 of the original
bulk; if during evaporation the colour tends to precipitate,
add a few grains more Alum. While still hot add 3T of
Pure Refined Carboxyl Acid.

This solution stains in from three to seven minutes; but a
much better result is obtained by allowing the tissue to remain
in the fluid for a quarter of an hour or twenty minutes, and
afterwards removing the excess of colouring matter with Glacial
Acetic Acid, which washes out the diffuse staining leaving
only protoplasmic structures affected by the reagent. After being
dried, the section should be washed in water, floated out
quite flat upon a slide, and covered with a dropper two of
Glacial Acetic Acid by means of a glass rod, until its deep
purple colour changes to a sort of dirty brown, when it
should again be thoroughly washed before mounting. If the
staining fluid be weak or of inferior quality, dilute Acetic Acid
(1:8) should be used instead of Glacial, as in this case the
strong acid is liable to remove the colour entirely.

Picrocarmine, when well prepared, is a reagent
yielding results unsurpassed by any other. It may be used either
alone, or after staining with Acetic Acid. Many of the subjunc
preparations thus treated are beautiful in the extreme. A
Picrocarmine fluid of very variable quality is sold by
Macfarlane, Chemist, North Bridge, Edinburgh. The first
sample obtained by the author was excellent, but all subsequent
supplies have proved very disappointing. Picrocarmine is
especially useful in determining the aortic valves as to
which coat of the renal arteries is hypertrophied in Interstitial
Nephritis.

The fluid in which most of the specimens are
mounted is ordinary Tannant's solution, carefully, prepared with
picked Gum Arabic, though Glycerine jelly has been used
in some instances. That made by Rimington answers its
purpose well, and is not liable to be spoiled by the growth of
a troublesome fungus which frequently affects inferior varieties.

One or two sections of injected Cat's kidney, and one of
colloid matter from the Thyroid body, are mounted in
Dammar but this medium is not suitable for the demonstration
of kidney as it renders the tubules too transparent. But one
section is mounted in pure Glycerine and this only with a
view of showing how misleading are the effects produced by
this preservative. Indeed the author believes as will be stated
in an ensuing chapter, that had Dr. Jull and Sutton used Tannant
solution instead of Glycerine and Camphor water in the mounting
of these preparations which gave rise to the formation of the
well known Arterio-capillary fibrotic theory, a serious
modification not to say radical change might have been
affected in their views.

Every specimen has been prepared and mounted with the author's own hands. The utmost care has been taken over to tear or otherwise alter the appearance of the sections through and careless manipulation. Needles have been employed as little as possible and the sections floated on and off the slides by means of a bowlful of clean water.

A few sections of injected cat's kidney, illustrative of certain points in normal anatomy, have been made by hand with a long sharp thin bladed knife, as the kidney in question having been preserved in alcohol was too brittle to cut satisfactorily in the freezing microtome. The usual pattern of hand section knife much resembles the so-called Share Knife in an ordinary Port Morton case. Such an instrument is far preferable to the clumsy razor still in general use, the blade of which is far too short and heavy for such delicate work. The blade of the section knife should be well moistened with alcohol, and the tissue to be cut imbedded in some suitable substance, waxy liver answering the purpose admirably. If however this not omnipresent substance is not to hand, a mixture of paraffin and oil of cloves or in default of this a piece of common carrot will yield an available substitute. The carrot must not be stringy or the knife will suffer. Hand Section Knives should be made of special temper, very thin in the edge and flat on both sides. The blade, which should be of sufficient length, perfect, straight.
and rather more than half an inch in breadth. Special care should be bestowed on their setting, as if blunt they not only waste the tissue to be cut but seriously damage the good temper of the operator. They are favourite with surgical instrument makers, for they cost a small fortune to keep in order. What is sharpness in any other knife is bluntness in them; as Pers. Swift said of servants they are necessary evils. But necessary, they are and will be, for all the more delicate and fickle tissues until Time, Chance, or Ingenuity discover some new and improved method of hardening.
Chapter III. On Certain Points Relating to
The Anatomy of The Normal Kidney.

It would serve no useful purpose to devote much space
in the present dissertation to a consideration of the histology of
the normal kidney, as this subject has been already amply and ably
treated by many competent authorities whose writings are easily
accessible. Among these, the author may mention the
following works which he has himself had occasion to consult:

1. Breeck, Die Bindegewebige der Mensehlichen Nie.-
2. Bowman Phil. Trans. 1842.

There are however one or two points of special interest
to the Modern Anatomist, which seem to demand some little
notice, at this stage of our inquiry, as ignorance or disregard of
them has proved a fruitful source of all kinds of errors in the
study of pathological conditions, in that some writers have
been thereby betrayed into the mistake of attributing strictly
normal appearances to the results of disease. And here it may
not be thought out of place to listen a word of condemnation
on the practice which is so fear but too prevalent, of attempting
to master the pathology of an organ without any previous
acquaintance with its healthy structure. A practitioner
so the fortunate owner of a large and expensive microscope
fitted up with costly lenses and apparatus procured regardless
of expense, is not too apt to think that the mere possession
of such an instrument is of itself sufficient to render him
an accomplished histologist. One might as well suppose
that the difference between an artist and a dauber lay in
the completeness and excellence of their respective pictorial
armamentaria. A long and careful apprenticeship of strenuous
is imperatively required of the histologist who would do work
worth the performance. With heart and soul, with strength
and purpose he must address himself to his task; the normal
anatomy of an organ must be mastered before proceeding to the
pathological; the eye as well as the mind must be trained
to observe and discriminate. No amount of simple reading and
listening to lectures will make a pathologist who will repay the
cost of manufacture. Actual contact with fact is the one
and only means of arriving at a true interpretation and
appreciation of their significance.

"Legimus animo demissa per aures
Quam grave sunt oscilia specta fidibus."
There is probably no more deplorable exhibition than that made by the book-crammed student, when brought face to face in the examination room with the pitiless realities of the dissected body. Up to the ceiling, down to the floor, from side to side, anywhere away from the face of his examiners, under his meaningless gaze; his flimsy knowledge edges out of his fingers, he stammers, he stammers, he flounders hopelessly, over the most simple questions until at last down goes the bed mark on the fatal paper, and the misdirected labour of months is bestowed in vain. If therefore a practical familiarity with naked-eye Anatomy is considered so essential a qualification in the candidate for a licence, is it not absurd to suppose that a like practical acquaintance with microscopic Anatomy is a thing of little or no consequence in the practitioner who aspires to be a pathologist? Ignorance in a would-be teacher is surely worse than ignorance in a learner, for in the first case the ignorance of the student's negligence simply, recall upon himself individually, whereas in the latter it is the profession at large which suffers from the erroneous results of slipshod and unscientific investigations.

Nor is it to be supposed that because a man is an excellent physician, he is also necessarily a competent pathologist. He may be so, and indeed ought to be so; but proficiency in the one branch cannot be taken as evidence of corresponding attainments in the other. We must be normal anatomists first, and pathological anatomists afterwards; there is no royal
road; the scientific fledgling cannot christen like run almost.
ere his beak has chipped the shell; he must crawl first; and
crawl very slowly sometimes. But to resume.

We shall glance very briefly, at a few facts connected
with,
(1) The Renal Tubules
(2) The Renal Connective Tissue
(3) The Renal Vessels.

(1) The Renal Tubules.

In almost every drawing seen by the author, the
calibre of the seminiferous tubules has been represented as
being far too wide. Normally it is but small in comparison
with their external circumference, and is often only apparent
as a kind of three-cornered star on the end of a seemingly
solid cylinder. This is well shown in an engraving on page
789 of Professor Turner's Introduction to Human Anatomy.
But the greater portion of the interior is occupied by
epithelium, and if the lumen appears wide, it is simply
due to the partial falling out of the epithelial cells during
the preparation of the section. This is a fact of which any one
can easily convince himself. Almost any one of the subjoined
preparations of normal kidney will serve to demonstrate it;
and it is indeed generally admitted, but as generally we
fear ignored. Some little time ago, this narrowness of the
calibre of the seminiferous tubules formed the topic of a
conversation between the author and a clever pathologist who
cultivates a somewhat rude and dogmatic style of assertion. Pooh, said the gentleman "it is a well-known fact." True, replied the author "but why then is it not a well-remembered fact?"

If we consider for a moment the issues which depend upon it, we shall not be disposed to underrate its importance. It vitally affects Dr. George Johnson's theory, which we shall frequently have occasion to allude to in the ensuing pages, and it has continually led to mistaken ideas as to the blocking up of healthy tubules. We would also call attention to another appearance which it is of no less importance to recognize as normal, namely the very considerable granularity of healthy renal epithelium.

(II) The Renal Connective Tissue.

The existence of the renal connective tissue, which was first described by Bowman and Goodson, has been denied some writers but is now generally admitted by all the best authorities. (See Beer, Rudolph: Path. Anat. Syll. Soc. Trans. vol 2 pp 148, 9: Klats, Hals: Path. Anat. Lieff, p. 630; Stricker's Histology Art. Kidney, etc.)

The renal connective tissue is distributed with the vessels in the same manner as in the liver. (See Drawing I.) It contains fibre, cell-elements, and according to Ludwig lacunae spaces in connection with the lymphatic system. Rindowsi also mentions lymphatics with complete endothelial walls (Centralbl. 69.S. 145). Delicate connective tissue processes, pass inward from the capsule into the cortical substance, which become much enlarged on the intervention of interstitial changes. Connective tissue is likewise...
present in the glomerulus binding together the capillary loops, as first noticed by Axel Key. It is owing to this connective tissue that the glomerulus does not collapse on being picked out from the surrounding structures, but retains its pristine form. Among the connective tissue, and between the capillary loops, are a number of rounded cell-elements, which in the Glomerulo-Nephritis of Klebs become greatly multiplied. (See Drawings 2 + 3). These bodies are not merely cells from the epithelial covering of the glomerulus but true connective tissue corpuscles, as proved by the fact that they are found not only on the circumference of the glomerulus but also in its substance, between the individual capillary loops. A demonstration of their anatomical site may be obtained by placing an injected glomerulus on a slide with a drop of water and then squeezing it out (pressure under a rather thick cover-glass). Logwood stains them a deep violet. (See also Klebs, Hand. d: path. Anat. 1895. p. 126)

(iii) The Renal Vessels.

As already stated on the previous page, the artery of the kidney are accompanied by processes of connective tissue, distributed in a manner similar to that observed in the liver. A kind of fibrous adventitia is thus formed external to the adventitia proper which is very thin. (See paper by Dr. Ringrose Atkins British Med. Journal April 3rd 1875 in the course of which this normal thinness of the adventitia is alluded to). On picking out a normal renal arteriole from its
the opurious adventitia adheres to it as a shabby, ragged, investment. It is this opurious adventitia and not the real outer coat of the arteries, as supposed by some, which is primarily enlarged on the occurrence of interstitial changes. This point will be fully dealt with hereafter, and need not therefore occupy our attention at present.

In the normal kidney the glomerulus never entirely fills the space inside Bowman's capsule.

The accompanying series of preparations of Cat's Kidney, most of which are injected with material of two colours, are useful as affording a general idea of the normal structure of the vessels. Those mounted in Damar display the vessels to the best advantage, owing to the transparency of the tubule in sections thus treated. Instead of the coloured injections the author has made many attempts to avail himself of the far more delicate silver process, but never hitherto with much success. Thinking the failure might be due to the action upon the silver fluid of the urine, Cat's more especially the chloride, he in several instances carefully washed out the vessels with distilled water, and with distilled water acidulated with Nitric Acid, previously to the introduction of the ⅛ or ⅜ per cent Nitrate of Silver solution. This, however, did not answer the desired purpose, and although he has not abandoned the idea, he has not as yet been able to carry it out successfully.

(Specimen No. 1) of this series illustrates one of these failures. The larger arterioles are blackened here and there, but the smaller one
are for the most part entirely unaffected, though the injection was very carefully made & could scarcely have failed to find its way into them.) Perhaps the non-success of these experiments may have been partly due to the circumstances that the animals (chief cats) were all killed under chloroform before injecting the silver salt; for although the injection was always performed with the utmost expedition, and with every precaution such as placing the body in warm water, there may yet have been times for the loss of some of that furtive vitality in the absence of which experience has shown the invariable futility of attempts at injection with silver. Were he free to follow out his own ideas, the author would be inclined to try again on the living animal; but considering the present state of the law in this country, it is not likely that the opportunity will be afforded him for some time to come. It is true that by flight into Germany or France distressed seekers after forbidden knowledge may find countenance and refuge at the price of temporary expatriation; but unfortunately now as of old it is equally true that “Non cuivis homini contingit adire Corinthium”. A little rest, a little clamber, a little folding of the hands to sleep, - this is the dealing to which English Science is now consigned. So, to alter Longfellow’s line, her votaries must learn to wait, if they are not allowed to labour. Probably they may have ample leisure to cultivate the virtue of patience. Charles Lamb has shown in his delightful Essay on Rossetti, how many hundreds of years elapsed before the
pigtailed Celestials became convinced that a general domiciliary conflagration was not absolutely essential to the proper culinary preparation of that savoury animal; the form and fashion of whose caudal extremity they have so industriously copied in their own persons since the days of Confucius; how much longer then will it take before the elimination of the perennial porcine and acinice elements from our British House of Parliament is at last successfully accomplished? We will leave the reader to muse on this distant contingency.
Chapter IV. Historical Resume.

The compilation of a complete bibliographical record of all the theories and descriptions good, bad, and indifferent, which have been placed before the medical world on the subject of Interstitial Nephritis, would be a task alike beyond the range of the author's reading, and the limits within which he would fair confine the proportions of the present treatise. It has, however, occurred to him, that a short exposition of the views of a few of the leading British and Continental authorities, past and present, might not only prove interesting from a historical point of view, but instructive also, as evidencing the very different conclusions drawn by different observers from the same facts. These theories are of course all more or less coloured by the different pathological systems predominant at the time of their first promulgation; but many of the older ideas have displayed a curious vitality, and at the present day still continue to be firmly held notwithstanding the manifold changes which later discoveries have wrought in the complexion of pathological science. The new light thrown of late years upon the process of inflammation, has however induced many to adopt explanations of the morbid appearances very different from those which would have been considered tenable before the researches of Virchow, Lister, Cohnheim, Stricker, Ludwig, Recklinghausen and many other modern investigators.

We shall omit all mentions of these authors who without committing themselves to any particular theory, have been...
content with the mere enumeration of macroscopical appearances, as the differences between their several descriptions are so slight and unimportant, as not in any way to affect the question of the true nature of the process. For instance, some authorities describe the colour as red, others as pale, whereas in point of fact, like the disputants who quarrelled over the colour of the chamber, both are right and both wrong, the colour being a matter simply dependent upon the presence or absence of mechanical hyperaemia. The essential pathological conditions become visible only by the aid of the microscope, which alone reveals those minute structural alterations of the kidney substance wherein they consist. Upon these alterations two distinct interpretations have been put, and it is possible therefore to make a primary subdivision of the theories into two classes. Firstly, those who hold that the primary and essential lesion has its seat inside the miniferous tubule, and Secondly, those who consider that the primary alteration are to be referred rather to the interstitial tissue, all intra-tubular changes being secondary to and consequent on certain primary interstitial changes. Among those who hold the former opinion may be mentioned Johnson, Simon, Freichs, Niemeyer, Todd, and Sebert; whilst of those who advocate the latter, Beer, Rindfleisch, Klebs, Dickinson, Stainer, Stewart, Green, and Jones and Leriche (in their latest edit. by Payne) are the most conspicuous.

Besides these two very distinctly opposed schools, there is another and smaller one, the members of which are disposed to consider
the diseased state as originating in the bloodvessels:—Sir William
Hall and Dr. Sutton on the one hand, and M.M. Cornil and
Rauvier on the other, may though differing widely among
themselves, be grouped together under this last head.

(i) The Intratubular School.

Dr. George Johnson's Views.

Dr. Johnson maintains that the primary change which
lead to the formation of the "small red granular" kidney, which
by the way is often more pale than red, and in the early stages
is enlarged instead of diminished in size) consist in destructive
alterations of the epithelium of the renaliferous tubules, due to
the circulation in the blood of various morbid products.

for 1877: On Diseases of the Kidneys 1852: Lectures on
Bright's Disease, &c.

We quote his own words, as taken from the Pathological Society's
Transactions for 1877, page 390.

"The primary and essential structural change in the granular
kidney consists in disintegration and destruction of the glandular
epithelium of the convoluted tubes; the products of this disinte-
grating process appearing in the urine during life, in the
form of granular casts of the tubes, and the result is that
when sections of the kidney are examined microscopically, while
some tubes retain the normal lining of epithelium, others are
filled, and rendered opaque by epithelium in various stages
of disintegration, and others are more or less denuded of epithelium.
a few granular particles only adhering to the inner surface of the basement membrane. Then as a result of this destruction of their gland cells, many tubes are seen in different stages of atrophy and contraction, and between these contracting tubes are seen wide spaces more or less hyaline or fibrous, which are mainly occupied by the atrophied remains of other wasted tubules and capillaries. In some tubes the normal epithelium is replaced by a lining of delicate transparent rounded cells, each with a single nucleus. Again other tubes may be seen in various stages of dilatation into cysts. This process of dilatation goes on until cysts more or less numerous may be seen by the naked eye. The explanation of this cyst formation is probably to be found in the fact that some tubes continue to secrete an aqueous fluid, while their lower portions are plugged by epithelial debris, and thus they become distended by their own secretion. He further says that though there may be a little increase in the fibrous othema, he agrees with Dr. Wilkie and Moxon in saying that it is not much.

This, though called from one of his latest utterances, is substantially the opinion first maintained by Johnson in 1847, in a paper read before the Royal Medical-Chirurgical Society. On the same evening, his then colleague Mr. Simon read an independent paper on the same subject, the results of his investigations leading him to adopt substantially the same opinions, though Mr. Simon “believed the transparent portions of the kidney to be microscopic cysts” while Dr. Johnson “interpreted them to be denuded tubes, as they are generally admitted to be” (Johnson, op. loc.)
As we shall presently consider at length these views of Sir John, we shall pass them by for the present without further comment.

**Views of Ferrie, Niemeyer, &c.**

Ferrie (Die Brightsche Nierenkrankheit, 1851) considers the "small red granular" kidney to be merely the last stage of a parenchymatous nephritis, passing through the three stages of (i) hyperemia and incipient exudation; (ii) changes in the exudation, and (iii) atrophy. Niemeyer (Text-Book of Practical Medicine, Humphreys and Hackett's Translation) agrees practically with Ferrie, though he allows that there is a secondary or concurrent proliferation of the interstitial tissue. He also mentions a primary interstitial nephritis leading to increase in the fibrous stroma, but this he dismisses in few words as apparently of rare occurrence, and comparatively unimportant.

Lebert, (Traité d'anatomie pathologique, vol. 2, page 336) though a general follower of Ferrie, seems to be in doubt whether the atrophy and contracted kidney is not rather a separate form of Bright's disease than a subsequent stage of the parenchymatous variety. He says, (as quoted his ponderous work, as it is not particularly easy of access) "Nous avons surtout confirmé les doctrines que professe Ferrie sur ce sujet." His description of the atrophic form is as follows:

"Dans la troisième forme les canaux et les capsules s'affaissent, le tissu cellulaire de nouvelle formation autour des canaux se contracte et devient cicatriciel; tout l'organe diminue notablement de volume et de poids, la capsule est adhérante, la surface est..."
irrégulières, lobulée, creusée de sillons; les granulations sont nombreuses. La consistance devient coriace, la substance corticale est surtout notablement réduite de volume... Le for du Food, but what follows is rather curious in part. "Les canaux minipés renferment des épithéliums granulo-fraiseux, des figures de fraise et des granules; les cylindres sont également injectés de fraise. Les contours des canaux sont irréguliers, plisseés, fibres; les capsules de Malpighi sont remplis de soutelettes de fraise; beaucoup de capillaires, dans les flammules, ont disparu. La substance est pâle anémique; on trouve également beaucoup d'éléments fibroplastiques, autour des capsules, mêlés de fibres, qui leur donne un aspect concentrique; le tissu fibreux est parsemé de soutelettes de fraise."

Even in the second form, which corresponds to Treich's second stage, he allows some amount of increase in the connective tissue et al. -"Dans la seconde (forme) l'écoulement se trouve dans les capsules, dans le parenchyme, dans les épithéliums, sous formes de granules, mêlés de fraise. Une partie des matières exsudées s'organise en tissu cellulaire." (See also Lebert, Pates, 140, 141, 142.)

Todd, (Clinical Lectures on Diseases of the Urinary Organs, 1867) is more or less a disciple of Johnson, "though the evidence of an inflammatory process having any share in the production of this state of kidney appears" to him "to be very unsatisfactory." He considers that certain abnormal materials contained in the blood are conveyed to the kidney for elimination, and that
in their passage through these glands the poisonous elements create a highly disturbed state of their nutrition, a state partly in some degree inflammatory but chiefly atrophic, the tendency of which is to cause the organs to waste and shrink.

(II) Intertubular School

Bartels, Arnold Beer, (Die Bindegewebe der menschlichen Jiere); Rindfleisch, Path. Histology, 2nd ed.; Los: Kraus; Dickinson, (On Albuminuria, 2nd Edition); Klebs, Handbuch der path. Anat.; Spren (An Introduction to Pathology and Moticul Anatomy); Jones and Keating (Pathology 2nd edit. by Payne); and Aitken, (Practice of Medicine, Vol II), though differing on some minor points are all entirely at one as to the essential nature of the mobid process, which they refer to an interstitial nephritis, or inflammation of the connective tissue stroma, leading to increase of the intertubular tissue owing to the presence of a small cell growthe analogous to granulation tissue; which growth present undergoes a more or less complete transformation into fibrous tissue. This newly formed fibrous tissue next proceeds to shrink, and by its contraction compresses the secreting elements, thereby leading to secondary intratubular lesions. Dr. Grainger Stewart, (A Practical Treatise on Bright's Disease of the Kidney, 2nd Edit. 1871) while maintaining that the changes are due to increase in the amount of fibrous stroma, is of opinion that there is no proof of the inflammatory origin of this fibrous increase, and considers it rather in the light of a connective tissue hyperplasia unconnected with inflammation both.
regards origin and course. Dr. Stewart distinguishes between this primary interstitial overgrowth, and that secondary hypertrophy of the stroma sometimes consequent on parenchymatous nephritis. This last he considers to have its origin as stated by Johnson, Frerichs and Niemeyer, while in the case of the true primary interstitial kidney, which he denominates "cirrhotic", he believes in accordance with others of his school that the intratubular change, are secondary to the interstitial overgrowth. As this stands in the same relation to the Interstitial Theorists, as Dr. Todd's doc, to the Intratubular ones.

(iii). Theories of Primary Vascular Lesion

Of these there are but two: (i) The Theory of Sir W. Gull and Sutton; and (ii) The Theory of M. M. Cornil and Dauvres.

The theory of Sir William Gull and Dr. Sutton we shall presently discuss in a separate chapter; it is however shortly this, that the kidney change are but part and parcel of a general circulid state consisting in the deposit of a "hyalin" or "hyaline fibroid" material in the adventitia of the arterioles, and of a "hyalin-franular" alteration in the walls of the capillaries (see Med. Chin. Trans. vol. LV)

M. M. Cornil and Dauvres attribute the change to a chronic arteritis.

There is thus as we have seen no lack either of theories or of investigators; on the question of the contracted kidney it is almost a case of tot hominem gnot centerique; and besides the prominent pathologists above mentioned, there is a
short of followers on either side, some of whom we shall now very briefly indicate.
Dr. Tanner (Practice of Medicine 6th Edit) appears to endorse the opinions of Dr. Johnson, as does also Sir Thomas Watson in the latest edition of his Elegant and Classical Work. Dr. Bristow (Practice of Medicine), does not commit himself to any distinct opinion, though he allows the reality of the connective tissue hypertrophy, and further remarks that the origin is chiefly inflammatory in certain cases. Dr. Wilks and Moxon (Pathology) also give forth an uncertain sound. They say (op. cit. page 80), "The term 'chronic desquamative nephritis', rests on a supposition as to the origin of the disease, of which there is no sufficient proof. The pathological nature of the change is probably analogous to cirrhosis of the liver, or sclerosis of the nervous centre. Some regard the epithelium as the special seat of the disease, others the interstitial tissue which is supposed to increase and compress the tube, but no sufficient evidence of this is given. From having been often able to trace the choledecal tube up to necessed Malpighian corporacles, we are inclined to believe that closure of these corporacles, may be the starting point of the disease. But all that can be certainly said is that the tube waste in the manner above described." Respecting the occurrence of a third atrophic stage of the parenchymatous kidney, they say that though there is no proof of its existence, they do not absolutely deny its possibility. These sentiments also inform me that the consistance of the interstitial kidney (whereb
they mean the contracted kidney of Bright) is not tough! Had they the ill fortune to be fed on meat of the same consistence, for a fortnight or so, they might find cause to attach their opinion, unless indeed some beneficent fairy compassions their last plight, were to endow them with a strength of jaw equal to that of Old Father William in Lewis Carroll's racy piece of nonsense, Alice in Wonderland.

Dr. W. J. Roberts (Practice of Medicine) says, "Most English writers are of opinion that the true cirrhotic kidney is the result of chronic interstitial nephritis, attended with proliferation of the intertubular connective tissue, which becomes much increased and compresses surrounding structure. He does not however express any positive leaning towards one side or the other, and ends by remarking that "the whole question is at present in a state of great uncertainty." Dr. Ringrose Atkins of Brit. Med. Journ. 3rd April 1875, and Dr. T. J. Maclean of Dundee, in a paper read before the Medical-Chirurgical Society of Edinburgh (for a short epitome of which see Brit. Med. Journ. June 26th 1875), uphold Dr. Johnson's conclusion, while in Virchow's Archiv; for 1877 are two excellent papers, the one by Thomas and the other by Uberoth, in which the opposite theory is advocated.

In the midst of such a cloud of conflicting witnesses, it is perhaps no easy matter for the independent observer to keep his head cool, to preserve a judicial frame of mind, and to form and maintain an unbiased opinion. The eye is very
prone to see what it is led to expect, and the reason is often apt to be unduly influenced by the spirit of partizanship, or by one or another fashionable pathological system. As some sort of safeguard against this possible untoward influence of precept, the author consulted his specimens first, and the voluminous literature of the subject afterwards; - not until he had carefully examined many dozens of sections, and had begun as he thought to see in his own mind the dawn of a well-grounded conviction, did he seek in the works of other writers, extracts, upon or facts and arguments in support of the conclusions at which he had thus, in a manner independently, arrived. From that time forward however he has made constant reference to a great mass of writings, and he trusts that while on the one hand he has endeavoured to see and think for himself, yet that on the other, he has not been heedless or unmindful of those rich stores of information so lavishly garnered up at the expense of the labours of others.
Chapter V. On Granulation Tissue, with Reference to the Nuclear Tissue of Interstitial Nephritis.

As stated in the preceding chapter, Dr. George Johnson and those who agree with him, attribute the appearance, seen in the "small red granular" kidney, to the breaking down and disintegration of the sinusoidal tubules and epithelium, which are in his opinion alone and entirely responsible for its production. He denies the reality of the apparent fibrous increase in the later stages, and asserts that it is merely due to the approximation of the normal amount consequent on the shrinking occasioned by the inevitable disintegration and wasting. Dr. Wilks and Moxon (Path. Anatomy, page 509) lend a partial sanction to this assertion, stating that there is very little fibrous increase except in the neighbourhood of the vessels. Dr. Johnson's theory is considered at some length in Chapter VII. infra, and we shall accordingly content ourselves meanwhile with endeavouring to show the absolute identity of the so-called "nuclear tissue" of interstitial kidney with that known as "embryonic," "indifferent," or "granulation" tissue, and seen for example in the first stage of new formations, and in the reparative process in wounds, ulcers, etc. Fortunately, the author is able to submit for comparison a very rare and beautiful series of preparations of healing ulcers from the human subject, in which typical granulation tissue is shown, better perhaps than he has ever before seen it. If one of these specimens be set side by side with a tract of interstitial kidney, where the cells still retain
this rounded form, - that is where differentiation into fibrous tissue has not proceeded far, - the resemblance is so striking as to arrest immediate attention. Compare Drawing No. 34 which represents a portion of one of the annexed specimens of healing ulcer with Drawings 8, 27, 28, 29, 37, 439; also with Drawing No. 16 Series Glomerulo-Nephritis, and with Diagram No. 4 which is slightly altered from Rindfleisch. [4] From these drawings it will be seen that the round-cell tissue in the interstitial kidney is practically identical with the granulation tissue of the healing ulcer. We shall now proceed to consider the possibility of ascribing to both a common origin.

On Page 22 passing mention was made of the lymphatic spaces and vessels discovered by Ludwig and Rindowski in the connective tissue of the kidney. In this as in all connective tissue there are two kinds of cells, stable and mobile, the stable being the ordinary well-known connective tissue corpuscles, while the mobile are in all likelihood lymphocytes which have migrated through the vascular walls, passing through the capillaries and entering the lacunar system of lymphatics. (See Art: on the Lymphatic System by Recklinghausen in Stricker’s Histology: Klein - On the Lymphatic System Vol. 1 and Recklinghausen.)

[4] Note. For the copying of this Diagram, as well as for several other artistic and accurate drawings from original specimens, the author is indebted to Mr. James Ryan, Student of Medicine, to whose facile brush the illuminated title page likewise owes its existence.
On the Lymphatics in Relation to Connective Tissues, Birkhe 1862.

Note on The Lymphatic System.

It may be perhaps useful before proceeding further to recapitulate very briefly one or two of the most important points relating to the Lymphatic System. The regular lymphatic vessels merge into and arise from an irregular system of spaces, diagrammatically represented in Drawing No 5 and known as the lymph-canicular system. In the drawing a lymphatic is seen arising from a series of these spaces. The lymph canicular system is easily demonstrable either in the cornea or in the pincelled centrum tendineum of young rabbit, cat, and guinea pigs by means of Nitrate of Silver. Two such preparations accompany the present Thesis. They were made a long time ago, and are now far too dark, owing to reduction of the Silver from exposure to light; nevertheless in the ink marked corners they still show the lymph-canicular system very fairly under a 4 inch objective. In these lymph canicular spaces lies a system of branched corporcles, demonstrable by means of Chloride of Gold; the author submits one very beautiful illustrative preparation from the Cornea of the Cat. He has also succeeded in demonstrating them by means of the same reagent in pieces of fascia, such for instance a thin strip of fascia lata from the thigh of the Frog. These branched bodies are the permanent connective tissue.
corpuscles. The lymph-canicular system is in communication with the lymph vascular system both by direct origin of the latter from the former, and also by means of openings in the walls of the lymphatic vessels which are known as stomata. These are well seen in the subjoined beautiful preparation of the septum cystostome lymphatici magnoe of the frog. This preparation is stained both with Wohrle of Silver and Carmine and shows these stomatic openings surrounded by a ring of protoplasmic bodies, deeply stained by the Carmine and considered by Klein to be of the nature of germinating endothelium.

The bloodvessels also communicate with the lymph-canicular system by certain small openings in their walls called stomata, and well seen in the accompanying preparation of Frog's Rectum, the vessels of which have been injected with silver. Through these openings leucocytes pass into the lymph-canicular system, in which they are often seen and recognised as the mobile cells of connective tissue. — Drawing No. 6 illustrates the communication between bloodvessels and lymphatics. Whether the two systems ever directly communicate with one another without the intervention of a system of lacunar space, is a point which has not been yet satisfactorily elucidated. The lacunar spaces, demonstrated by Ludwig in the
connective tissue of the Kidney form a lymph-vascular system like that just described; and the existence of these spaces is of the very utmost importance with respect to the proper comprehension of the phenomena of interstitial inflammation.

On the occurrence of interstitial changes in the Kidney, the number of mobile connective tissue cells is largely increased by the plentiful emigration of white blood corpuscles through the walls of the vessels. These in a formative inflammation like the interstitial, give rise alone or in conjunction with the fixed corpuscles, which by their division may take some share in the process, to embryonic, indifferent or granulation cells, which are after a time differentiated into more or less fibrillated connective tissue. The nucleus becomes oval, the cell elongates, takes on a lanselot or fusiform shape, and is presently completely metamorphosed into a fibre. Thus a greater or less amount of wavy fibrous tissue is formed, the process of fibrillation being traceable from stage to stage in the interstitial Kidney with as much ease and certainty as in the case of cicatricial tissue from a wound. Indeed, the two processes are precisely analogous, nor is there more room for scepticism in the one than in the other. See preparation No. 12 of Healing Ulcers. Examine especially the ink marked corner just under the epidermis where the process of cicatization is somewhat advanced, and note the wonderful resemblance to nuclear tissue in the kidney when undergoing a similar transformation.

The assertion that the cells of the nuclear tissue do actually
differentiate into spindles and fibres is founded not upon conjecture but upon positive fact, and of this fact no satisfactory explanation has ever been given consonant with the acceptance of Dr. Johnson's pathology, for flat rejection is not argument, nor will it, we think, in many cases, suffice to make those of the adverse party distrust the results of their own observation.

In the latest stages of interstitial change, coarse wavy fibrous tissue is to be found in abundance, — in far greater quantity than can be accounted for on the supposition of the shrinking together and approximation of that met with in the healthy organ, which is altogether so little as to have led some writers into the error of affirming its entire absence. It should be further remembered that the normal connective tissue is in great part cellular, though there is without doubt a certain admixture of fibres. Perhaps Dr. Johnson may be inclined to go so far as to admit, or at any rate not actually deny the fibrillar transformation of the normal cellular connective tissue (See Path. Soc. Trans. 1877, page 301), but even this concession would be very far from sufficient, for were the appearance of fibrous increase in reality due solely to contraction consequent on the destruction of the tubule, and other secreting structures, the diminution in size of the interstitial kidney-grass though it be in extreme cases, would neverthless be inadequate to account for the large tracts of fibrous tissue so evident over the greater portion of the atrophied cortex. Series & of the accompanying microscopic preparations exhibit a typical example of extreme atrophy, and in this kidney there must
have been fibrous tissue enough to supply at least half a dozen normal ones with their necessary framework.

Since then the fibrous increase is not merely apparent but real, how according to Dr. Johnson's theory can this increase be accounted for? It is not merely the descendant of disintegrated tubule and epithelium, for even allowing these to be responsible for the round-celled appearances at the earliest stages, it is altogether too much to be asked to accredit them with the power of forming fibrous tissue. Nor indeed does Dr. Johnson intend to attribute to them any such power; his way of meeting the difficulty is easy, though it is scarcely satisfactory, for he simply denies the existence of any fibrous increase. If the fibrous increase he as we venture to think it is, an evident matter of fact, it is entirely inexplicable from the standpoint assumed by Dr. Johnson. True, Riedelstein intimates that he has never met with actual fibrous tissue in the intestinal kidney, but since seeing is in a manner believing, the author refers the reader to his preparations for the settlement of this point, and notably to those of Lexer, &c., which, under a good microscope may be trusted to speak with a voice far more eloquent and convincing than that of mere words.

Again it may be argued that the round cells of intestinal kidney are smaller than those of granulation tissue. This objection however is not worth much. Granulation cells exhibit great difference in relative size, the largest (excluding giant cells) measuring from about $\frac{1}{1600}$ to $\frac{1}{1800}$ of an inch in diameter,
while the smallest are not more than the $\frac{1}{2500}$ of an inch, or even less. This size will differ greatly according to the amount of fluid present in the tissues containing them; and in the kidney, owing firstly to the chronic or subacute nature of the interstitial process, secondly to the density of the kidney substance, and thirdly to the drain afforded by the ureiniferous tubules, fluid in any appreciable quantity is never met with. Nothing but the nuclei of disintegrated renal epithelium could in any other way account for the round cells in question; and if we take into consideration the fact presently to be mentioned that in the early stage of interstitial change there is positively no intratubular affection observable, there is in the author's opinion no way of escaping from the inevitable conclusion, in favour of which so many valid arguments are forthcoming, while those against it prove on close examination to have no sufficient basis offact.

The following is a list of the principal arguments in favour of the interstitial theory. Those which have not been already discussed will be considered in the Subsequent Chapter.

(i) In the first stage of the lesion, the kidney is enlarged.
And the process been merely one of wasting and disintegration of the tubular structures, we should expect diminution rather than increase.

(ii) In the early stage the intertubular septa are greatly increased in width by the presence of a small-cell infiltration precisely resembling granulation tissue, which in many parts forms large tracts, very
conspicuous even under low powers.

(iii) In the early stages, the tubules if not actually perfectly normal, in that they are often compressed, are at all events easily recognizable, so that there is little fear of confusing the products of intratubular disintegration with those of intertubular cell-infiltration. And even in later stages the outlines of the tubules are nearly always to some extent recognizable by the skilled observer, so that the danger of mistaking their broken down contents for round cell tissue is even at this advanced period more imaginary than real.

(iv) The round cells of the new tissue may be seen elongating into spindles, and differentiating into fibres. They are therefore in a stage of growth, not of decay.

(v) Owing to this differentiation there is in the later stages an abundant fibrous increase, this increase being far greater than could be accounted for by the approximate of the small amount of fibrous tissue normally present in the healthy kidney.
Chapter V. Authors Own Views.

From what has been said in the previous chapter it will by this time be pretty evident to the reader that the views of the author are in accordance with those of that School of Pathologists which ascribes the appearances constituting the "small red granular" or interstitial kidney to the results of a sub-acute or chronic inflammatory process affecting the intertubular tissue and leading ultimately to its fibrous increase. This is the opinion of those writers who on page 38 were grouped together as members of the Intertubular School: and the results of the author's investigations will be found essentially corroborative of the conclusions expressed in the works of these authorities. Briefly then he believes that the origin of the morbid process is to be referred to an inflammation causing emigration of leucocytes through the walls of the vessels, which leucocytes either alone or more probably aided in some degree by the proliferation of the permanent connective tissue corpuscles, give rise to a small cell formation of the nature of granulation tissue, the cells of which being at first round, become subsequently spindle shaped, and are finally more or less completely metamorphosed into fibrous tissue. This process is strictly an Intestinal Nephritis, and by this name he prefers to designate it.

For descriptive purposes it will be convenient to divide the process into two stages, though it must be understood that there is no definite boundary line between the two, but that the one merges imperceptibly into the other, all sorts of
intermediate appearance, being so or rude met with in the same specimen. This insensible gradation of changes from initial to advanced, enables the observer to trace with certainty the connection between the apparently very dissimilar lesions constituting the two ends of the chain.

These two stages are,

(i). A stage of Cell-Infiltration.

(ii). A stage of Cell-Transformation.

In the first an embryonic tissue is formed, in the second it is differentiated into connective tissue, cellular, and fibrous.

We shall first describe these two stages somewhat shortly, and afterwards consider in detail those points which possess special features of interest or interest. By this arrangement the author trusts to attain as great an amount of pertinacity as is possible in a somewhat difficult subject.

Stage I. Cell Infiltration.

A Naked Eye Examination.

Kidney generally heavier than normal; enlarged, sometimes very appreciably; colour pale, whitish; surface smooth.

Capsule easily detached, congested veins being often noticeable on the surface; consistence soft and doughy nearly resembling that of the Parietal, Kidney; contours normal.

Section: cortex enlarged; its consistence is doughy and its colour yellowish white (some observers deny the yellowish tinge. It is of course not due to fat) and bloodless; it has sometimes been described as resembling a section of raw turnip; the Malpighian
bodies are red and prominent.
Medulla congested, otherwise unaltered.

Modifications. According to the process has been more or less chronic, the new tissue is more or less fibrous, and the kidney may be either enlarged or reduced in bulk. The capsule may be also to some extent adherent, and the surface slightly granular. Some specimens are red owing to passive congestion.

This stage is analogous to the corresponding one in cirrhosis of the liver - Smooth Intestinal Hepatitis. This stage of Intestinal inflammation is only distinguishable from the parenchymatous variety by the aid of the microscope.

B. Microscopic Examination. See Drawings 12, 17, 8, 27, 28, 29.

The capsule of the kidney is seen to be thickened and sometimes more firmly adherent than in the normal organ, though not so as to be separable with tolerable ease. Stretching inwards from the capsule into the cortical substance, are bands of new matter consisting of small cell or granulation tissue. These bands are due to an enormous thickening of the delicate connective tissue processes, which normally pass from the capsule into the substance of the kidney. Tubules and vessels are included in the new tissue, which embraces and constructs them. On examining this "nucleus tissue" with a high power (x 300) it is seen to contain multitudes of round cellular bodies, of the nature of leucocytes, in which under a very powerful lens a nucleus is sometimes discernible. These cells may also be seen in process of
conversion into spindle (See Drawings 28, 10), and the spindle, again undergoing incipient transformation into fibrous tissue. The round cells are sometimes rather ill-defined, as in Serie A of the microscopic preparations, (See Drawing 8, from the kidney) but in most specimens they are distinguishable with ease. (See the tract of interstitial cell-infiltration in the preparation of Glomerulo-Nephritis; see also Drawing N° 15 Serie Glomerulo-Nephritis.) The connective tissue along the path of the renal vessels is increased by a similar formation. This condition is also well shown in specimens of Glomerulo-Nephritis, the interstitial cell-infiltration around the renal vessels being very evident in this form of interstitial nephritis. (See Drawings 11 a 17, Serie Glomerulo-Nephritis.)

These changes are not uniform, some parts of the kidney being much more affected than others.

Changes are also visible in the renal arteries. Their adventitia is in the first instance perfectly normal and unthickened, though the connective tissue following the path of the vessels is already just slightly increased in amount. The middle of muscular coat presents an appearance of thickening even at this comparatively early stage. (See the preparations in Serie A; also Drawing 13.) While the intima is often affected with that condition described by Heubner[1], under the name of Arteritis Obliterans which consists in a proliferation of the inner coat, leading to ultimate...

[1] Note. Wilks, Bristowe, Huglings Jackson, and others, made passing mention of this lesion before the date of publication of Heubner's monograph; but up to that time the subject had excited little attention or interest.
clusion of the vessels affected. A somewhat early stage is figured in
Drawing 13.

The seminiferous tubule are normal with the exception of those
constricted by the new material, which forms a ring around them,
lessening their calibre and leading to subsequent obliteration. See
Klebs. Colloid matter is often present in the tubules, and the glomeruli
also are not infrequently similarly degenerated. (See Drawings 8 and
31) Some writers speak of the colloid material as being of a waxy
nature. This however is not the case, for it is stained neither by
iodine nor by methylenblue, while on the contrary it stains with
carmine in precisely the same manner as colloid found elsewhere.
(See specimen of colloid from the Thyroid body is subjoined for the
sake of comparison.) It is derived from the renal epithelium,
which after a time degenerates, owing to the pressure exercised
on the tubule by the new material. Globules of colloid form inside
the epithelial cells (See Diagram No. 30) which presently burst,
letting free the colloid in the interior of the tubule. The epithelial
nuclei long resist the colloid change, and are often seen imbedd
round the inside wall of a tubule filled with colloid, adhering
more or less closely to the basement membrane, and contrasting
markedly with the colloid which absorbs colouring matter much
more faintly (See Diagram No. 30 figure 2). In the same manner
and from the same cause the glomeruli become converted into
colloid masses. Bowman’s capsule is much thickened, and new
material is generally especially abundant in the neighbourhood
of the Malpighian bodies; the glomeruli consequently become
Klebs, Traube, Virchow.
compressed, and its vessels are presently rendered impervious; degeneration thus ensues, and nothing but a mass of colloid remains inside Bowman's capsule towards the situation of the capillary loops (See Drawing 31). The medullary portion of the kidney is generally but little affected.

This stage is identical with that described by Rehn as "corporeal overgrowth." The new material, which is at first composed of lymphoid elements resembling those of granulation tissue, presently undergoes that fibrous transformation which constitutes the second stage of the interstitial process; but even at this early period especially if the process of the change has been slow and chronic, fibillation more or less advanced may be here and there apparent— a fact which conclusively establishes the connection between the enlarged kidney of this stage, and the shrunken atrophic and granular one of the second. Rindfleisch as before mentioned (page 44) makes the remarkable statement that "even in extreme cases of contracted kidney no appearance of delicate tissue or of fibillation can ever be detected in the surrounding connective tissue" (Syd: Soc: Trans vol. 2, page 151). This assertion is the more inexplicable, as even in the earliest stages observed by the author some amount of fibillation has as a rule been recognizable. We must except however the cases of Glomerulo-Nephritis, in which (the process being more acute) there has been no time for differentiation, the cells consequently retaining their rounded form.

Stage II. Cell Transformation.

This stage corresponds to the "small red granular," "irritated contracted" or "gouty kidney of other authors. The granulation
Tissue the formation of which constitute the first stage, become in this stage differentiated into more or less completely formed fibrous tissue, which shrinks and by its compression cause atrophy of the other renal structures with great diminution in the size of the organ.

A Naked Eye Examination.

Weights diminished, often excessively; size visibly smaller, sometimes very much atrophied and shrunken; contours altered, irregular; surface rough, uneven, granular or lobnailed; capsule thickened opaque and very adherent, so much so that on fail of tearing off portions of the kidney substance come along with it; colour pale, unless red from passive congestion, the granular projections being light coloured "like parched peas" (Dickinson), while the depression between them are red from the presence of the superficial vessels which run in these vallae; (See coloured Plate Dickinson on Albuminuria; also Bright Reps on Medical Cases 1827 Plates 1-3) Cysts are often seen on the surface. The consistence is tough and leathery, somewhat like cartilage. On section the cortex is observed to be tough and diminished in size, being in extreme cases reduced to not more than two or three lines in thickness; its colour is pale yellowish, uniform or mottled with red. The convoluted tubule and Malpighian capsules are frequently dilated into cysts. There are sometimes very numerous, some being visible to the naked eye, while others are microscopic. The Malpighian bodies are small and atrophied and so approximated by the general shrinking as to appear abnormally
numerous.

The medullary substance is generally but little altered, though occasionally cystic; the pyramids are sometimes hyperaemic, sometimes pale yellowish, like the cortex.

B. Microscopic Examination. (See drawings 25, 26.)

The cell infiltration of the preceding stage is now in process of differentiation into fibrous tissue. Many of the cells are seen elongating and assuming a spindle shape; and the spindles in their turn are here and there undergoing metamorphosis into fully formed fibrous tissue. True wavy fibrous tissue is most abundant in the sporuous adventitia of the vessels (see drawings 14, 15, 19) and around the Malpighian capsules and convoluted tubules; that is to say, the increase is most marked in those situations where fibrous tissue is normally present. The Malpighian capsules are greatly thickened, leading to compression of the vessels of the glomerulus. In this stage the small cell formation is very distinct. Its elongation into spindles is perhaps best seen in dogwood preparations, as this reagent stains the cells more deeply than carmine, and while inferior for general purposes, affords a somewhat cleavage demonstration of this particular fact.

The importance of the fusiform change in the shape of the infiltrated round cells is very great, as it affords one of the strongest arguments against Dr. Johnson's theory of their origin from epithelial debris. The dispute as to the nature of the new tissue is to all intents and purposes settled by the fact of the cells assuming this fusiform shape, for it is seen that they are in a stage not of depression but of
growth, not of disintegration and decay, but of progression
and differentiation.

The arteries of the kidney also present many noteworthy
changes. Many of them are obliterated by the pressure of the new material.
Their increase of the connective tissue which accompanies them in
their distribution is now very evident. [See Drawings 11, 15 and 19]. The
adventitia proper does not at first share in the thickening,
but in many cases the process involves it secondarily, and it
becomes blended with the surrounding new formation,
making as it were common cause with the general fibrous
increase. [See Drawing 15]. It is however often distinguishable as a
separate structure even in very advanced specimens of interstitial
change, nor is there ever according to the author's now well
established experience, any material of a “hyaline-fibroid” nature to be found
in connection with it. When thickened, its thickening is
secondary, and consequent on an extension of the general inter-
stitial change. The tunica media is unquestionably hypertrophy.

Of this there can be no doubt, as in well-stained specimens
there is little fear of even a comparative tyro's mistaking one
coat for another. On this point the author cordially agrees with
Johnston, and is prepared to support his statement with a
large mass of drawings and preparations. (See especially Drawings
9, 12, 14, 19, 22 and 38 figs. 12+3). The hypertrophy appears to be a
true one, the nuclei of the muscle cells being multiplied, accord-

The tunica intima is frequently affected with Arteriitis Obliterans,
The presence of this condition, which passed unnoticed and almost unknown until the publication of Heubner's monograph on Syphilitic Diseases of the Arteries of the Brain, may formerly have given rise to mistakes as to which of the three arterial cells was hypertrophied. Now however it need no longer prove a source of fallacy. It is well marked in interstitial kidneys taken from syphilitic subjects (See Series I) but is by no means confined to these. Series A, B, and C, which all exhibit it more or less, were obtained from patients who neither from their history nor from the results of the subsequent autopsy could be considered as ever having been affected with the venereal taint. Endocarditis obturans may therefore be considered as a common though not invariable factor in the interstitial process. This condition is figured in Drawings 9, 11, 12, 13, 14, 16, 17, 18, 22, 23 and 24.

Extensive changes consequent on the pressure of the new material are now evident in the prininorous tubules. The epithelial cells become detached, and the tubes demided of their lining. In some cases the pressure leads to distortion of the epithelial cells as figured by Dr. Dickinson, more rarely to fatty change, and again very frequently to the formation of colloid. It must not however be supposed that all the empty tubules which strike the eye in a mounted section, are stripped of their epithelium solely as the result of the morbid changes. Especially in thin sections much epithelium will fall out during preparation in spite of every precaution; in
determining, therefore how much has been destroyed as the result of disease alone, it is advisable to examine some of the thicker sections in which it is more readily retained.

Many tubules are entirely obliterated by pressure. Their basement membrane like the adventitia of the vessel, appears to take a secondary share in the interstitial process; it becomes thicker and fibrous and is ultimately blended with the new formation. Owing to the unequal pressure exercised on the tubule at different points of their course, cysts and dilatations are very common. (See Drawing 26). Colloid degeneration of the epithelium may also act as a cause of cystic formation. Thus a tubule may be constructed at two points, and the epithelium between them consequently undergo colloid degeneration; the colloid may then be carried away through the very narrow yet still pervious opening, and escape in the urine, as hyaline matter, a cyst remaining behind. Again cysts may be formed by the vis a tergo of the urine acting upon a constricted point in the lumen of a tubule; and as many points in the same tubule are sometimes simultaneously narrowed, a tubule sometimes is often found to present a series of moniliform dilatations. Perhaps also the contraction of the new material may to some extent further the cystic change, by drawing asunder the walls of the tubes as supposed to be the case in Drueckpacchen. The thickening of Bowman's capsule leads to obliteration and colloid degeneration of the contained glomerulus, and on the disappear-
ance of the capillary loops, the interior of the capsule may be (dilated.
into a cyst. Those glomeruli which have not undergone the collapse change are diminished in size and much compressed, while the general shrinking greatly diminishes the distance between them. The pressure often leads to rupture of the capillary loops, and small hemorrhages are consequently not infrequent.

The processes of new materials which have been before alluded to, as passing from the capsule into the substance of the cortex, are now seen to arise opposite the depressions between the hornail projections visible to the naked eye on the kidney surface: these depressions being caused by the shrinking of the new tissue, while the hornail protuberances are due to the bulging of portions of kidney substance surrounded and strangled by its tightening grip.

The interstitial changes and shrinking above described are for the most part confined to the cortex. As a rule the medullary portions of the kidney are but slightly altered even in advanced stages. Occasionally there is some increase in the fibrous stroma, and cysts sometimes form in the straight tubules, as figured in Drawing 32; with these exceptions however there is but little noticeable change in the medulla, even though the cortical portion may be almost entirely destroyed. See Thomas, Virch Arch Band 17/figs 1897 or page 48.

It should be noticed that these cases are very few and far between in which the whole or nearly the whole of the small-cell formation takes on a truly fibrous type. In most granular kidneys even in the very last stages of shrinking and atrophy, round cells and spindles are still visible over large areas of the new formation. Series E of the accompanying
preparations exhibits the most extensive fibrous metamorphosis which the author has hitherto encountered. In this remarkable kidney interstitial changes are seen carried to their furthest stage, and as examples of the latest stage of extreme fibrosis, the sections taken from it are consequently highly valuable. (See Drawing 21 from a specimen of this series. Drawing 20 also exhibits very complete fibrous change.)

Having thus given an account as succinct as possible of the principal morbid appearances met with in the two stages of interstitial nephritis, it now remains to consider in a little more detail some of the results at which we have arrived.

Firstly then, there occurs the question, is the interstitial cell-infiltration to be referred to a nephritis, or is it simply the consequence of a hyperplasia of the normal connective tissue altogether apart from inflammation? Dr. Grainger Stewart in his excellent work on Bright's Disease, argues in favour of the latter mode of origin, and quotes Dr. Sandfield Jones in support of his position. On page 184 of the latest edition of his work, he states that the evidence in favour of the inflammatory nature of the interstitial changes appears to him to be defective. (See also article by Dr. Stewart Brit. Med. Journ. Nov. 15th 1873; v Report of Discussion before Brit. Med. Assoc. ibid Septr. 6th 1873.) He further says: "I know of no observation which warrants the assertion that in the earliest stage, free exudation is to be found among the elements of the stroma, and as we shall presently see, there is much reason to think that there is no such exudation. In the absence of direct evidence, this view (as to the inflammatory origin) appears to rest upon two considerations, 1st That the formation of connective tissue is
result of inflammation; and 2nd, that the analogous disease of the
liver is supposed to result from inflammatory action."
From this statement it is warrantable to conclude that the presence or
absence of "exudation" conclusively settles, according to S. Stewart's opinion,
the question as to the presence or absence of inflammation, or at least throws
such a weight into the wavering balance, that the unfortunate nephritic
theory is obliged then and there to kick the beam. But is exudation
necessary to inflammation? This will depend largely upon what that rather
indefinite word is taken to signify. If understood to mean merely the leum
of the blood, the phenomena observed in non-vascular structures, at once
negative the conclusion that its presence is a sine qua non of the
inflammatory process. If on the contrary the emigration of white blood
corpuscles be included in the term, there is abundant evidence of the
outpouring of a vast number of these in the stage of nephritic cell-
infiltration. We shall assume however that it is the liquid exudation
the absence of which inclines S. Stewart to reject the inflammatory interpretation.
Now the exudation in a formative inflammation like the interstitial, is
always at a minimum. And even in certain exudative inflammations
proper, as for instance in Dry Pericarditis, the quantity of fluid is at times
very insignificant. But taking into consideration the structure of the
kidney we should far from wondering at its absence in that organ, be rather
at a loss to account for its outpouring in quantity or long continued presence.
In the first place the interstitial inflammation is chronic or subacute,
and in an inflammation of this character, fluid exudation is always
inconspicuous or absent. Further for aught we know, some slight fluid
exudation may be present in the earliest stages; but these are rarely
seen in the Post Mortem room, for the simple reason that they are seldom attended with any fatal result. Moreover, the density of the kidney substance, and the drain afforded by the cortical tubules, militate strongly against the effusion or long persistence of any fluid exudation. Green (Path. 2nd edit. page 191) well remarks, "In dense organs as the liver and kidney, owing to the compactness of the structure, a large amount of effusion is impossible, and what there is, is so intermingled with the structural elements of the organ, that it does not appear as an independent material." Again in those rare cases in which a kidney comes under the observation of the pathologist in the very earliest stages of the interstitial process, it is actually enlarged, soft and doughy, the capsule is thickened and juicy, and the general appearances present a remarkable resemblance to those induced by parenchymatous inflammation. Surely this is a strange state of matter if due to other causes than inflammation! Further, be it remembered, that the small cell infiltration is not in the first instance, fibrous or even of the nature of differentiated connective tissue, but consists of cells precisely identical with leucocytes, the emigration of which in such numbers seems to point conclusively to a causal inflammation.

Dr. Handfield Jones whose authority I. Stewart quotes, describes the occurrence of fibrous patches in serous membranes such as the pericardium, pleura, peritoneum, cardiac valves &c., and in the substance of organs, as the liver, lungs, testicles, and uterus. These he rightly argues are not all due to inflammation. But further he says, as quoted by I. Stewart: "that the hypertrophy causing the increase and thickening of fibrous tissues goes on and on, as a substantially independent process, totally unassociated with any trace of inflammation, ..."
even though it may by possibility have originated in it. Now this last is a rather naive admission, and seems in fact equivalent to a total abandonment of the positions previously joined at the cost of so much argument. If a fibrous increase is originated by an inflammatory process and due to the migration of lymphoid elements consequent on inflammation, then the overgrowth is unquestionably inflammatory, even though it proceed after the subsidence of the inflammation. The cicatricial tissue of wounds is generally acknowledged to be inflammatory, although we do not expect to meet with the phenomena of inflammation in a scar after old. The inflammation simply supplies the material, which is afterwards utilized at leisure. It is the mason who conveys the blocks of stone to the site of the future building, not the mason who with mallet and chisel hews them into shape. If then inflammation is in the first instance the provocative agent of a fibrous hyperplasia, providing the round cells which are presently to be differentiated into fibres, the fibrous overgrowth when complete is assuredly inflammatory even though the inflammation has long ago disappeared.

We must not be understood as wishing to refer all fibrous increase to the result of antecedent inflammation. The simple overgrowth described by Deer in the Kidney, milk spots on the pericardium and other kindred fibrotic changes are in all probability not only carried on, but initiated, totally apart from inflammatory action. But so-called "irritative hypertrophies", trench so closely upon the province of inflammation, that in many cases, such as those where the tissue elements are numerically increased, the author believes the distinction to be one without a difference, and dependent rather upon...
the degree than upon the nature of the changes included under the term. The "copious ulceration" of Beer, corresponds to interstitial inflammation, and this he is in accord with the present writer in attributing to the results of inflammation.

It is a common fallacy to say that where there is no lymph and exudation, there is or has been no inflammation; the lymph and exudation may have vanished, whereas the consequences of the inflammation may remain.

One can understand the non-inflammatory origin of such fibrous increase as that constituting a milk spot on the periosteum. The normal tuberculous connective tissue is excited to increased activity of growth by the continued friction. It enlarges, and after a time, not finding its quarters sufficiently spacious, provide itself with elbow room at the expense of its next door neighbours. But it is the same connective tissue after all; it has grown larger and become a bill, but it has received no numerical additions. In short its elements are enlarged, but their number remains unaltered. Such an increase need not perhaps be accounted inflammatory. But if the connective tissue elements are increased numerically, the cause must be sought in something more than mere hyperplasia. Connective tissue is a peculiar structure, and statements as to its non-inflammatory hypertrophy require at least to be carefully sifted. It may be thought that according to this view, for great a prominence is assigned to inflammation of connective tissue structures. Yet how general, how universal, a process is this same inflammation! The labourer would doubtless be not a little
surprised and incredulous if told that his horny hands were provided with their pachydermatis covered at the expense of a process which he regards with as much terror, as the ancients did the dreaded name of Osmogon. Yet such is the case; a little more of the exciting cause, and not epidermal increase but a blister would be the consequence. So it not their perfect nonsense to ascribe such an epidermal thickening to irritative hypertrophy when inflammation and inflammation alone is responsible for it, as amply evidenced by the redness and heat of a delicate hand when subjected to some unaccustomed attrition? To be sure the inflammation goes no farther than congestion, but though slight in amount its nature admits of no question. If the connective tissue elements of a part are increased, the new elements must have originated from some pre-existing ones, and whether they originate from emigration of leucocytes, or from division of the already existing connective tissue corporacles, both these processes must, according to the present state of our knowledge, be alike referred to an irritative and causatory inflammation. Of course the transformation of already existing cellular into fibros tissue does not of necessity involve the agency of inflammation, and thus come appearance of numerical non-inflammatory hypertrophy may sometimes be caused; but if the increase be greater than can be accounted for in this way, it appears to the authors that the inflammatory theory can alone adequately explain the position of affairs. The advocates of "irritative hypertrophy" may say that this view is merely theoretical and incapable of proof. True it is theoretical,
but so is their own, and the onus probandi lies with them, not with us, for before proceeding to separate these numerical hypertrophies from inflammation proper, it is but reasonable that something more than mere supposition should be alleged in favor of such a divorce.

Irritative numerical hypertrophy then, unless used as the equivalent of nascent inflammation,—to borrow a term from Chemistry,—is a name likely to mislead, and expressive of a purely hypothetical condition.

The arguments pro and con, as to the inflammatory or non-inflammatory nature of the interstitial increase, may be shortly tabulated as follows:

Dr. Stewart: Con.

(i). There is no free exudation.

The Author: Pro.

(i). Free exudation is not to be looked for, because,

(a) The inflammation is chronic and formaotive.
(b) The density of the kidney substance prevents its effusion.
(c) The uriniferous tubules drain it off as fast as it is formed out. Against this it may be argued that the urine contains little or no albumin in the earliest stages. But as shown by (a) & (b), there is little or no albuminous exudation poured out, so that its absence in the urine would occasion no astonishment.

(ii). There is direct evidence, namely,

(e) The enlarged, soft, doughy, and succulent condition of the kidney in the earliest stages.
(f) The abundant infiltration with lymphoid cells.

(iii). Fibrous increase is often met with totally apart from inflammation.

(iii). Increase in the size of the original elements is often so met with, but increase in their number is very seldom, perhaps never, somethi
In conclusion it occurs to the author that Dr. Stewart's reasons for rejecting the inflammatory theory may perhaps be due to his being holding at the time of the publication of the last edition of his work, some of the older ideas as to the nature of the inflammatory process. In this case we may look for some alteration of his views in subsequent editions. Dr. Stewart's conclusions are invariably marked with such care and accuracy, and are in the main so consonant with the results of the author's observations, that he has thought fit to discuss at some length, this their almost only point of material difference.

Dr. Sandfield Jones also appears to have modified his opinion as to the origin of interstitial kidney; for in the last edition of Jones and Trenching's Pathology, by Payne, its causation is clearly ascribed to a Nephritis.


One of the most noticeable changes in the interstitial kidney is the thickening and adhesion of the capsule. This thickening is of a densely fibrous character, with here and there a few fibulating spindles, and occasional round cells; small vessels and lymphatic spaces also, are to be seen in its substance. The normal delicate bands of connective tissue passing between it and the surface of the kidney are enormously increased, and penetrate far into the substance of the cortex, as shown in Drawing No. 7. So firm is the adherence caused by this thickening of these processes, that in advanced cases large portions of the cortical substance are torn off on forcible evulsion of the capsule. The author has never seen a specimen sufficiently early to exhibit typically the stage of cell infiltration, which doubtless occurs here, as
in the substance of the kidney proper. Indeed interstitial kidneys are
tended long allowed to retain their capsular investment. The difficulties
experienced in separating the capsule, seems to be provocative of attempts
to do so; and these are generally so unfortunately successful that by
the time the specimen reaches the hands of the histologist there is
rarely any capsule left to separate. Of course if we make our own
preparations it is within our power to exercise some restraint over our wild
ambitions; but for students in private practice this care. When it came
into the author's possession not an atom of capsule was left on the
kidney which furnished the accompanying series. A.

In order to determine whether or not the apparent new tissue
form really a something superadded to the normal elements of the
kidney substance, or simply an appearance produced by the
destruction of the tubules and epithelium, we should examine rather
those specimens which exemplify the early stages, than those in which
there has been great destruction of the secreting structures. Although the
tubular epithelium is often but little altered even at later periods,
and by thus directing our attention to specimens in which came
from the results of compression it is to all intents and purposes
normal, we do much to eliminate sources of confusion and fallacy.
At the outset however we have to confront the difficulty caused by the
extreme rarity of such early specimens, though the accompanying
sections illustrate of glomeruli. Pyelitides afford also excellent instance
of early general interstitial change. In these, the round cell infiltration
is abundant, while owing to the comparative integrity of the tubules,
its nature is unmistakable. Only a very few tubules are affected, and the
only in the neighbourhood of the Malpighian bodies. Here there is slight Parenchymatous change, which is to be considered as secondary to the interstitial lesion. Glomerulo Nephritis is in fact simply an interstitial nephritis differing only from the common variety in its anatomical site of greatest intensity, is attacking not merely the general interstitial tissue but also that which binds together the vascular loops of the glomeruli. In consequence of this peculiar anatomical situation, it is a dangerous and fatal disorder; and such cases afford perhaps the most typical examples of early interstitial change which ever find their way into the hands of the pathologist (see Chapter on Glomerulo Nephritis).

Of the ordinary variety Series A is the earliest the present author could procure. He has seen earlier and better ones, but the fortunate possessors of these if aware of their value are naturally very loth to part with them, and if ignorant of the worth of their windfall, either consign them to the refuse box, or preserve them as naked eye specimens of parenchymatous kidney, which to the unaided eyesight they very much resemble. In Series A, the Small cell infiltration is rather ill-defined, but is seen to consist of the ordinary roundish lymphoid cells, imbedded in a homogeneous or dimly granular matrix. In many places the cells are seen elongating into spindles, and in some parts of the sections are more or less fibrillated. Had sections of this kidney been mounted in Glycerine without previous hardening in Chromic Acid, they would doubtless owing to the homogeneous appearance of the matrix have furnished typical example of "elastic fibroid" change. This artificial appearance
which Sir P.outh and Suttow wrongly suppose to be of a truly pathological nature, will be discussed in the ensuing chapter devoted to the consideration of their theory. In Series A the normal connective tissue septa are much increased in width, and as the tubules are pretty normal, and even when much compressed are still recognizable, there is the less danger of mistaking connective tissue for disintegrated tubules and epithelium. Indeed the fear of a practised observer’s falling into this error need be but slight; it may be argued that the epithelial nuclei stain with eosin in precisely the same manner as the lymphoid cells of the new tissue: granted—but for all that there are ways and means of appreciating a difference considerably greater than that between tweedle-dum and tweedle-dee. The epithelial nuclei are sharply defined, round in shape, never fusiform or ovalate, though they may be oval; they are larger, denser, and more opaque than the round lymphoid cells, and they always lie in relation to portions of compressed tubules which afford a ready means of identifying them.

As to the tubules themselves, it is the author’s belief that their basement membrane never becomes disintegrated. If it enter into the processes going on around it, and undergoes fibrillation with perhaps even greater readiness than the new material itself. If warrant for this assertion be demanded, the author would direct attention to the fact, that around an atrophied tubule a constraining ring may be observed almost invariably; which, as in the case of the thickened Bowman’s capsule, is distinctly more fibrillated than the surrounding small-cell tissue. [See Wilks & Moxon, Path. Anat., p. 301; Klebs, Path. Anat., 4th ed. page 641;]
also Niemeyer Practice of Medicine, Humphrey and Hackley's Texts, 1876, vol. 2, page 23). In these constricting rings and in the thickened Bowman's capsules, spindle cells are often very apparent; and in these situations as also in the increased connective tissue in the neighborhood of the vessels, the process of round-cell transformation first into spindles and subsequently into fibres may be very satisfactorily observed. Not that it is at all difficult to recognize the same thing elsewhere, but in these places it is often very plainly and beautifully exemplified.

Later on, the same thing occurs in the adventitia of the renal arterioles; this coat becomes thickened, and is presently blended with the surrounding new material. It should however be totally understood that this is a secondary change. The fibrotic process, far from beginning in the adventitia, involves it only when the alterations elsewhere have become very evident. Drawing No. 1 represents an artery from a specimen in Series G, which at first sight seems to offer some support to the theory of fibrosis of the outer coat. A closer inspection however, however, reveals this apparent confirmation into a fallacy; the adventitia, which is represented by a thin, well-defined dark line, is at one point separated from the surrounding increased connective tissue, and is seen to be wholly unthickened, and but slightly attached to its fibrous surroundings. That the thickened connective tissue is not the real adventitia is abundantly evidenced by the fact that two tubules filled with colloid are visible amongst it. (For another excellent example of the adventitia remaining unthickened in the midst of extremely advanced fibrous change, see Series E, prep. 7, inside the ink ring.)
Picrocarmine (1 per cent solution) gives a very good demonstration of the coats of the arterioles. The adventitia and intima are stained yellow, while the muscular coat is coloured red. The newly-formed tissue around the adventitia is coloured red if not far advanced in fibrillation; if fibrous it is yellow also, but the adventitia being denser is easily distinguishable by its deeper coloration. Double staining with Carnine and Osmic Acid answers the same purpose extremely well, and the importance of the aid afforded by these reagents in enabling us to recognize and distinguish the several coats can scarcely be overestimated. All doubt, all uncertainty vanish with their use. Dr. Galabin (On the Connection of Bright's Disease with Changes in the Vascular System, page 14) says it is somewhat difficult in a transverse section to distinguish between the circular muscular fibres and the fibrous tissue outside them. The intelligent use of Picrocarmine obviates this difficulty at once and entirely. Of course the possession of a bottle or regiment of bottles full of staining fluids, will not render an ignorant man a competent histologist, for microscopic reagents require to be used as Opie mixed his colours—with brains—but in the hands of a practiced observer and dainty manipulator they are capable of affording the most absolute evidence as to which is which in the matter of the arterial coats.

The middle or muscular coat is, as has been before stated, hypertrophied. This hypertrophy is noticeable at a comparatively early period in the history of the interstitial changes; indeed the author has scarcely ever seen an instance of undisputed, intestinal
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The middle or muscular coat is, as has been before stated, hypertrophied. This hypertrophy is noticeable at a comparatively early period in the history of the interstitial changes; indeed the author has scarcely ever seen an instance of undoubted interstitial
kidney (of the ordinary variety) the arteries of which did not show it in a greater or less degree. He is therefore led to consider it as a very frequent, if not constant, change; though all parts of an artery are not equally affected by it, as is easily seen in longitudinal section embracing any appreciable length of the vascular coats. The hypertrophy appears to be a true one; that is, today the enlargement of the middle coat is in all probability due to increase of the non-stripped muscular elements. In three the author has seldom observed any notable structural alterations; according to his experience they colour normally with carmine and other reagents, the nuclei are normal in shape, nor has he ever seen them fatty degenerated. (Drawing 22 represents the muscular coat as being very faintly coloured, but the whole section from which this drawing was made is but very faintly, though delicately stained.) So Hull and Sutton allege that the nuclei do not absorb carmine so readily as in healthy vessels.

The occurrence of thickening of the middle coat in the early stage of interstitial kidney may perhaps be advanced as an argument against the true muscular character of the increase, since muscular hypertrophy is a slow and gradual process. But, as has been often mentioned in the present treatise, the very early stages of interstitial nephritis rarely come under clinical, far less under pathological observation.

What therefore the morbid anatomist recognizes as an early stage, may be in reality the product of a morbid process which has lasted for months or even years. Interstitial nephritis is essentially chronic, or at most subacute; the fatality of its initial stage is almost nil, and a sufficient time consequently elapses between its supersession.
and its recognition at the autopsy, showed of even the tarry development of true muscle cells. The absence of hypertrophy of the muscular coat in the author's acutely fatal cases of Glomerulo-Nephritis, also tended to strengthen these conclusions. Dr. Dickinson in his work on Albuminuria (2nd Ed.) while admitting the existence of the muscular hypertrophy says that degenerative changes also occur in the middle coat of the vessels. His illustrations are taken from the arteries of the Dia Mater. Traube and Ludwig also hold similar views. The author has pretty frequently met with this apparent atrophy. It is figured in Drawings No. 23, and No. 24. At times it appears to him to be not so much atrophy as an absence of hyper trophy, three parts of the muscular coat which still retain their normal thickness appearing wasted, by contrast with the adjoining greatly hypertrophied portions. At other times he must confess, it looks very much like atrophy proper. The muscular coat appears more homogenous than natural, and is in some places unquestionably reduced in thickness. (See Drawing 24.) This condition of the tunica media is almost invariably accompanied by considerable thickening of the intima consequent on Endoarteritis Obliterans. The occasional atrophy is however no argument against the coexistence of the abundantly evident hypertrophy. (See Paper by Dr. Johnson, Path. Soc. 1877, page 385.)

In a monograph like the present, which deals solely with the "Microscopic Anatomy of interstitial Kidney, it would be out of place to propound or endorse any theory as to the cause of this muscular hyperplasia; suffice it to say that the author is convinced of its
existence, and that the accompanying preparations especially
Series B and 2, render the fact abundantly evident. Hypertrophy
of the tunica media is represented in Drawings 9, 11, 12, 13, 14, 15, 19, 22,
and 38 figs 1-3. It is far too great to admit of being explained away on
the ground of Post Mortem contraction analogous to the so-called
Concentric Hypertrophy of the heart, for the middle coat is frequently
two, three, and even four times its normal thickness, an appearance
with no possible amount of mere contraction could suffice to
occasion. Confirmatory evidence of its true muscular character
is given by Sir Granville Stewart, (Brit. Med. Journ. Sept. 1st and
November 15th 1873); by Dr. Atkins (Brit. Med. Journ. April 3rd 1875);
rather hesitatingly by Dr. Galabin, (On the Connection of Bright's Disease
with Changes in the Vascular System); by Dr. T. J. MacLagan of Dundee
in a paper read before the Medico-Chirurgical Society of Edinburgh (see
Report, Brit. Med. Journ. June 3rd 1876); and in the last edition of
Jones and Sidgwick's Pathology, by Payne.

Again on examining the arterial coats in longitudinal section,
the muscular nuclei are seen present in greater numbers than in
unaffected vessels, a fact which not only goes far to prove the true
nature of the hypertrophy, but at the same time negates the theory
of Post Mortem contraction. Sir William Gilly and Dr. Sutton say the
muscular layer varies in thickness, and that it is difficult to say
what are or are not its normal dimensions. Well, do do men
vary in stature, yet if we meet with a man eight feet high
and proportionally stout we call him a giant. - How much more
Drotdajnian then should we consider him if he reached as much.
as twice or thrice the ordinary maximum stature of humanity—
that is to say, if instead of eight feet of longitude, he towered above
our diminished heads at the height of twelve or eighteen? Yet
this disproportion is no more than actually exists between the
muscular coat of healthy arteries and that of the hypertrophied
vessels of interstitial nephritis. "Si magna lieet composere parvis,"
would Sir William Full if set side by side with Chang the Chinese
Giant, entertain any lingering doubts as to whether his own riches
equalled those of the native of Sericana? The truth is, why then
this uncomfortable suspicion as to normal and gigantic muscular
coats?

We subjoin a few measurements, showing the relative increase in
the muscular coat as compared with the thickness of the whole arterial
wall.

<table>
<thead>
<tr>
<th>Normal.</th>
<th>Interstitial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adventitia</td>
<td>Media</td>
</tr>
<tr>
<td>Nearly 3.</td>
<td>4.</td>
</tr>
<tr>
<td>4.</td>
<td>3 1/2</td>
</tr>
<tr>
<td>3</td>
<td>3 1/2</td>
</tr>
<tr>
<td>2 1/4</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>2 1/4</td>
</tr>
<tr>
<td>Nearly 3</td>
<td>4 1/2</td>
</tr>
<tr>
<td>3 1/2</td>
<td>4 1/2</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1/2</td>
<td>about 2</td>
</tr>
<tr>
<td>Normal.</td>
<td>Intima</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>Adventitia</td>
<td>Media</td>
</tr>
<tr>
<td>$3/4$</td>
<td>1.</td>
</tr>
<tr>
<td>$1 1/2$</td>
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<td>$1 1/2$</td>
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<td>1.</td>
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<tr>
<td>$1/2$</td>
<td>1.2.</td>
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<tr>
<td>2.</td>
<td>$2 3/4$.</td>
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<tr>
<td>2.</td>
<td>2.</td>
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<tr>
<td>3.</td>
<td>3.</td>
</tr>
<tr>
<td>Much disorganized about 3.</td>
<td>4.112.</td>
</tr>
<tr>
<td>Disorganized</td>
<td>5.</td>
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<tr>
<td>2.</td>
<td>3.</td>
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<tr>
<td>$1 1/4$.</td>
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<tr>
<td>1.</td>
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<td>1.</td>
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<tr>
<td>1.</td>
<td>$1 1/2$.</td>
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<tr>
<td>2.</td>
<td>2.</td>
</tr>
<tr>
<td>Nearly 2.</td>
<td>2.</td>
</tr>
<tr>
<td>$1 1/4$.</td>
<td>2.</td>
</tr>
</tbody>
</table>

Some arteries at $3/4$.
It will be seen from this table, that the intima is also very generally thickened, by the "Arteritis Obliterans" of Kuntner.

For the awkward and cacophonous word "Arteritis," we prefer to substitute the term "Endoarteritis," which is sufficiently euphonic to merit exemption from the category of,

"Words which should only be said on holidays when one has nothing else to do."—

Atheroma is already known by the term Endoarteritis Deformans, and there appears to be no valid reason pane the German nationality of its discoverer for the introduction of an extra i into the name of the unfortunate Kuntnerian lesion, whereby its back is lost for all purposes of utterance. Our nomenclature is ameliorating enough already, without going out of the way to make it worse.

The author is acquainted with a gentleman who is ambitious of the sponsorship of such words as Pericarditis, Myocarditis, etc., maintaining empirical principles that we are bound in the manufacture of these potentious designations, to slide only the last syllable of the pseudo-classic appellation, and then to add to the remainder the termination it is as a sort of compensation for the abstracted caudal extremity. Now were any principle of linguistic correctness really involved, the present writer might be found as ready as any one to run the risk of sharing the fate of the man who would insist on pronouncing hard names, and whose pathetic tale is told in a rather clever song by a present alumnus of Ondina;

"Where the orator swallowed his tongue And finally ended the learned debate."
The author he repeats, would manfully face this violent risk, if by so doing he could lay the flattering sanction to his soul, that he was assisting to preserve in its pristine purity the glorious language of Homer and Smaetenes,—that most mellifluous yet most expressive of all human tongues. But "Myocardium" is classically as bad as "myocarditis" and only a shade less execrable than "myocarditis". Now the hero of Homeria would stare at "thangirclusis"! Even Aristophanes, that polysyllabic prince of comedy, might pull a long face under his mask, if compelled by insuperable Milo the turlesque a nineteenth century medical lecture for the amusement of the shade of Asculapius, His Majesty's Court Physician. — But what nomenclature is canines, so of two evils let us choose the least, and discarding all pretense of classic correctness in what is so undecently modern and barbarous, adopt that form of terminology which is least trying to our much abused organs of speech. But to return.

For anatomical purposes the inner arterial coat may be divided into three layers, exhibiting distinct structural differences. The inner surface of the tube is lined by a layer of irregularly shaped epithelial cells, the outline of which is often lanceolate. Preparations of the Rectum and Bladder of the Frog, injected with Nitrate of Silver, afford a very beautiful demonstration of this epithelium, the cement substance between the edges of the cells being stained by the reagent, while the cells themselves are unaffected. A few such preparations are included in the subjoined collection. (See Index to Preparations.) Immediately underneath this epithelial layer is one of greater pathological importance consisting of connective tissue containing branched corpuscles lying in lacunae spaces similar to
the plasma canals in the cornea. The corpuscles are demonstrable by chloride of gold, which, though a somewhat uncertain reagent, gives occasionally very beautiful results; while the lacunae in which these cells lie are rendered visible by the action of Nitrate of Silver which stains the ground substance a dark colour, leaving the lacunae visible as irregular patches of a lighter hue. The ground substance is for the most part homogeneous, though it may sometimes present an appearance of titration or even of fibrillation. A longitudinal elastic meshwork is also said to be occasionally present in this layer. The last and thickest portion of the inner coat consists of elastic layers superimposed on one another as a varying number of longitudinal fibrous networks, which not infrequently assume a membranous form with perforations constituting the "fornitute membrane" of Finle.

Having thus glanced briefly at the normal structure of the inner coat, we shall be in a position to appreciate the morbid alterations induced by the obliteration changes above alluded to. These are probably initiated and have their chief seat in the middle or connective-tissue layer of the inner coat. The microscopic appearances are shortly as follows. The inner coat becomes thickened, and assumes a sort of fibrous character, the sides of the lumen of the vessel being in the advanced stages rough, ragged, and splintered, much resembling coarse cocoa-nut matting. (See Drawing No. 16). The fibrous filaments have a concentric arrangement around the axis of the vessel, and obscure spindles are often noticeable among them, together with large, roundish, oval, or irregularly spherical bodies of the nature of connective-tissue corpuscles. No trace of epithelial lining is in most instances discoverable.
In the earlier stages the sides of the narrowed lumen (see Drawing 13) are still smooth, but present no appearance of epithelium, unless some irregular cells close to the inner edge may be considered as such. The elastic coat of the intima appears to be separated more or less completely into its component layers. Small vessels may sometimes be seen in the proliferated inner coat. These appearances require high power for their satisfactory demonstration in the smaller arteries of the kidney, and a Hartnack’s wide angle 9 objective, a very beautiful and wonderfully cheap lens, has been used by the author for this purpose.

The thickening of the intima goes on, until at last the affected arteries are completely occluded by a fluffy ragged material (see Drawings 16, 17 and 18) which, when obliteration is entire, becomes denser and more fibrous, and assumes the appearance of more or less perfect concentric fibrillated rings. Dr. Jull and Sutton have noticed this condition of the arteries (Med. Chir. Trans. vol. IV, page 275). Dr. Grainger-Stewart also makes mention of a thickening of the intima in the arterioles of the Dia Mater, but says that he has “never seen evidence of diminution of the lumen” (Ibid. Med. Journ. Nov, 1873).

The author has never seen the proliferated elements arranged in distinct layers of different morphological type as represented by Dr. Greenfield (Path. Soc: Trans. 1877, Plate XIII), the appearances as seen by him in the kidney being more comparable to Dr. Barlow’s drawing (Ibid. Plate XV fig. 1); though in the author’s specimen spheroidal cells were more abundant than spindles, fibres more abundant than either, and epithelium rarely and doubtfully present. Something of this difference may however be due to the difference in size and
situation of the arteries examined, as those examined by Dr. Greenfield and Barlow were taken from the brain, where the author has not infrequently encountered very similar appearances. The arteries examined by the author in the kidney were also much smaller. The highest power used by Dr. Greenfield was 90x or 3 x obj 7 tube out, while the highest amplification employed by Dr. Barlow is specified at 150 diameters. The arterioles observed by the author were on the contrary so small, that 90x or 3 x obj 9 wide angle, tube out, were requisite in order to obtain anything like a precise idea of the structure of their intima.

The nature of the process seems to consist in a proliferation of the connective tissue corporcles of the middle layer of the inner coat, with subsequent fibrillation of the connective tissue. Such a theory is in accordance with the behavior of connective tissue elsewhere, under like inflammatory conditions, and is in the author's opinion a satisfactory explanation of this interesting lesion. The preparations in Series I show this condition markedly. This kidney was waxy, as shown by the three iodine preparations, and the very imperfect history conveyed a suspicion of syphilis; but as before stated, obliterative arterial changes are met with in many nephritic kidneys, when during life there was no reason whatever for supposing the existence of any constitutional disease. Nevertheless it must be confessed, that on such a subject it is difficult or impossible to obtain anything like positive evidence, owing to the little reliance to be placed on the history as given by the patient. If, however, at the autopsy there was a well marked absence of other syphilitic lesions, it would be altogether unjustifiable to assume the existence of syphilis simply because the
arteries of the kidney were found affected with Endocarditis Obliterans. (This condition is depicted in Drawings 9, 11, 12, 13, 14, 16, 17, 18, 22, 23 and 24). For further information on this subject see Leeb's monograph On Syphilis, Diseases of the Arteries of the Brain; also Deblais on Visceral Syphilis Path. Soc. Trans. 1877, cases by T. Greenfield, Darlow, Ver.

It is evident that this narrowing and obliteration of arteries must materially contribute towards the causation of secondary intratubular changes, for owing to the direct obstacle thus interposed to the sufficient supply of blood, the nutrition of the tubules and their contained epithelium must be even more seriously impaired than by the presence and pressure of the increased interstitial tissue, which in the first instance may even give rise to the formation of new vessels as in the case of granulations. Indeed if the lymphoid infiltration be very abundant, it is hard to understand how the life of the cell-elements can be maintained without more or less vascularization. Klebs appears to consider that some of them may degenerate Sattely, and Lebert also says, "le tissu fibreux est interose de fontelettes de graisse", but this condition has never come under the author's observations. The new vessels, however, if actually formed cannot long remain perversions. As in the case of cicatricial tissue, the subsequent shrinking will serve to obliterate most of them, together with many of the normal vessels. Remembering then these two factors of interference with blood-supply, namely, occlusion of arteries from within by Endocarditis Obliterans and from without by cicatricial contraction, it is no wonder if after a time intratubular changes follow in the wake of the intertubular
increase, even apart from the pernicious influence exercised on the tubes themselves by the pressure of the mass material. Accordingly we find that the secreting structures undergo various forms of degeneration. The epithelium is compressed and loosened from the basement membrane of the tubes; sometimes it breaks up into a finely granular mass; sometimes it undergoes colloid degeneration; less frequently it becomes fatty; in other cases a few epithelial cells seem to have vanished altogether, their remaining neighbours being nearly normal, though this may be partly due to the falling out of the abscesses during the preparations and mounting of the section. The author has noticed that the protoplasm of the epithelial cells occasionally stains with Carmine and other reagents in an apparently capricious manner, probably due to incipient degenerative change. In a few instances he has remarked a similar deep colouration of the connective tissue corpuses in the substance of the glomerulus, and this he regards as the herald of impending colloid degeneration. (See Drawing 36.) Sometimes also from some unknown cause the lymphoid cells of the nuclear tissue are stained with a clearness perfectly diagrammatic (See Drawing 10). The nuclei of the epithelial cells are sometimes variable in the extent to which they absorb the colouring matters; but this inconsistency cannot be looked upon as an indication of actual abnormality, as the same thing occurs in normal specimens, and is very likely due to unimportant chemical changes. The epithelial nuclei are the most persistent of all the intratubular elements, and a tube is often seen in transverse section with this.
nuclei still clinging to its inner wall, from which all trace of the
cells themselves has vanished. Altogether considering the immense
interference with function which the presence and shrinking of the
new material cannot fail to induce, the intratubular change, though
great, are not more than might be expected from a like
cause. In the later stages some epithelium is fatty, much is simply
destroyed, and much also converted into colloid; many tubules
are dilated and cystic; the denuded basement membrane is
thickened, fibrous, and blended with the new tissue, the glomeruli
become impervious and finally degenerate into colloid masses;
Bowman's capsule is thickened, and fibrous like the basement
membrane of the tubules; many tubules are compressed and atrophied,
and others are entirely obliterated. But while we recognize the
importance of these intratubular alterations, we cannot agree with
Dr. Johnson in regarding them as the primary and essential part
of the morbid process. They occur as a consequence and not as
a cause; and are subsequent not antecedent to the primary
small-cell increase of the kidney stroma.

Before closing this chapter it will be necessary to say a few
words on a form of renal disease closely resembling true primary
interstitial nephritis, namely, that increase of the fibrous stroma sometimes
met with in the later stages of Chronic Parenchymatous inflammation
and consequent on a secondary irritation of the connective tissue
occasioned by the primary intratubular affection. The clinical
history of such cases, and more especially the marked appearances
of intratubular change, together with the much less evident granular

of the kidney surface, the less firm, adhesion of the capsule and the
much smaller amount of fibrous increase, alike concur to separate
this condition from that consequent on true primary interstitial
inflammation. This secondary fibrosis has been well described by
Dr Grainger Stewart in his treatise on Bright's Disease, (3rd edit. p. 16)
and great credit is due to him for clearly establishing the distinction
between it and that true primary one which forms the subject of
the present treatise. Johnson, Niemeyer, and many other writers have
fallen into the manifest error of regarding all interstitial alteration
as secondary to intratubular changes; but not the less is it erroneous
to rush into the opposite extreme, and suppose that all intertubular
changes are of necessity primary.

In the present treatise we shall not enter into a detailed account
of this secondary form, which belongs rather to the domain of the
parenchymatous inflammation upon which it is consequent; but
shall refer our readers meantime to Dr Stewart's very accurate
description, (op. cit. p. 16); also to a discussion on Bright's Disease,
held during the 41st annual meeting of the British Medical
Association (see Journal Sept 6th 1873), in which Dr Grainger Stewart
again affirms and expounds his views on this subject.

Overleaf we append a tabular summary of the principal
contents of the preceding chapter.
Summary

(1). The "small red granules", "contracted", "shrinkage", "interstitial", or "gouty" kidney is the result of a true interstitial inflammation attended with increase of the normal stroma owing to the formation of a tissue composed of indistinct or embryonic cells, which new tissue is presently transformed into more or less completely developed fibrous tissue.

(2). For purposes of description two stages may be distinguished in the history of the morbid process, namely (i) a stage of Cell-Infiltration, and (ii) a stage of Cell-Transformation.

(3). The original lesion is essentially intertubular, and all subsequent intratubular changes are secondary to and consequent on the primary intertubular change.

(4). The adventitia of the renal arteries is not at first hypertrophied, but may subsequently become so by an extension to it of the hyperplastic process affecting the connective tissue which normally accompanies and is distributed with the vessels.

(5). The tunica media of the renal arteries is hypertrophied sometimes very greatly; this hypertrophy being due in all probability to true muscular increase.

(6). The tunica intima of the arteries is frequently thickened and proliferated, as a consequence of Endo-arthritis obliterans.

(7). The already familiar designation Interstitial Nephritis, is pathologically correct, and fulfills all the requirements of an accurate and scientific terminology.
Chapter VII. Views of Dr. Johnson.

Criticisms.

"I find myself once more called upon," remarks Dr. Johnson in a paper published in the Pathological Society's Transactions for 1877, page 389, "to maintain that the small red granular kidney is not the result primarily and essentially of an interstitial nephritis, or of an arteriolopilosis, or any other form of fibrosis as Sir W. Gull and others believe."

I still maintain the view that the primary and essential changes in this form of renal degeneration are intratubular, and consist of degeneration and disintegration of the glandular epithelium."

He quotes Dr. Wilks and Morson who say (op. cit. 509) "Some authors especially Dr. Dickinson describe an increase of fibrous tissue; we think there is a little increase round the vessels, but not much. The patches of fibrous tissue figured in Dr. Dickinson's excellent drawings we have always seen, but high powers resolve these patches into the remains of tubes, as indeed would probably follow from consideration of the drawings themselves." "We have found that a fibrillated condition prevails in the tube walls which become coarse looking; but all large patches of apparent fibre we have always found to be chiefly made up of apparently wasted tubules."

"Dr. Johnson goes on to state that the opinion expressed in the above quotation, is substantially, that which he maintained in 1847 (Med. Chin. Trans. vol. xxxi), and which he has subsequently seen no reason to alter; save that in the 33rd volume of the Med. Chin. Trans. he made mention for the first time of the muscular hypertrophy of the arterioles."

We have quoted Sir Johnson's own words, in order to avoid all chance of misrepresenting or over-colouring his ideas.

In our former chapter on granulation tissue, we spoke of the identity of the interstitial process with that which provides for the repair and healing of wounds. This we shall not again discuss. Sir Johnson may deny, but he cannot alter the fact of this analogy. As to the presence or absence of fibrous change we are obliged to join issue with him; and as facts are more convincing than words, we will, if necessary, engage to meet him with specimen for specimen, (See especially, p. 10) before a committee of unpurjudiced and properly qualified observers. When Dr. Wilks and Brown admit a little increase of fibrous tissue around the vessels, they admit an appearance glaring and patent; for the increase is oftentimes not a little, but goes as far as the formation of patches or cases of coarse, unmistakeable fibres (Drawings 8, 15 and 19.) See also Article by Thomas, Virchow's Archiv: Bd. 15, Hft. 1 in the course of which he remarks: "Es liegt somit offenbar eine pathologische Bildung von fibres vor, welche zuerst weich und zellreich, später derb und hartig wird, und sich in Gänge der Gefäßverzweigung anschliesst." — But let us not be misunderstood; by this statement we afford no support to Sir Wm. Gull and Dr. Sutton's theory of arterial-capillary fibrosis; for it is not the arterial adventitia, but the connective tissue distributed with these vessels, which is thus hypertrophied. In these situations, as before mentioned fibrillation is most conspicuous, namely, around the vessels sternal to their adventitia, in Bowman's capsule, and around wasted tubules. (See Klebs, Virchow, Traube, Thomas, and Ringrose Atkins Brit. Med. Journ. April 3rd, 1879.)
but it is not about elsewhere, far from it. Neither is the fibrous appearance due merely to thinning of the connective tissue normally present, for reasons which we have already discussed.

On Page 390 Path.Soc. Trans 1877 Dr. Johnson gives a detailed account of his interpretation of the appearances met with in the small nodular kidney. To that account as the latest exposition of his views we shall now refer. In it he affirms that the primary and essential change consists in disintegration and destruction of the glandular epithelium of the convoluted tubules. Here again we arrive at a direct conflict of evidence, for on the question as to the state of the epithelium in the early stages the present writer is entirely at one with Dr. Dickinson. Thoma also in the excellent paper above cited says, "Nirgendwo zeigen die Epithelbekleidungen in unverglichenen Fällen selbständige Erkrankung, wenn im Bereiche der bindewebsigen Wucherungen, noch auch in den relativ intakten bliebenen Abschnitten der Rinde." Dr. Johnson talks about tubes being filled and rendered opaque. (See also his Work on Kidney Diseases.

Before asserting that tubes are actually in this condition, much care is required, for normal epithelium is opaque, and normal tubes present but little appearance of lumen. (See Page 21 supra). "Other tubes" says Dr. Johnson "are more or less completely denuded of epithelium, a few granular particles only adhering to the inner surface of the basement membrane." Perfectly correct; but this is a secondary change, occurring only in the later stages, and consequent on the presence and pressure of the interstitial increase. In some cases, Pursues Dr. Johnson, "the normal epithelium is replaced by a lining of delicate transparent rounded cells, each with a single nucleus." (See also Brit. Med. Journ. Feb 15th 1879).
The author has frequently observed these "cells," but he has seldom further observed the fact of their nucleation. If nucleated, as they are sometimes, though rarely, they are lymphoid cells which have escaped into the tubules via the capillary loops of the glomeruli. Such are more frequently seen inside the tubes in Glomerulo-Nephritis (see Chap. 9, p. 187; also Klein, Data, etc.: Trans. 1877, page 436). Now the presence of these lymphoid elements inside the tubules would be well calculated to occasion secondary intratubular changes, such as compression, loosening, and shedding of epithelium, so that this fact acts both ways. Dr. Johnson may of course state in return, that their presence is due to a primary intratubular epithelial change, but in that case we should expect to find the epithelium in a state much resembling Parenchymatous inflammation. More frequently these "cells" are in reality not cells at all, being nothing more or less than the nuclei of the cells of the tubular epithelium, which being more persistent than the other cell constituents remain after the secondary intratubular changes have caused disappearance of the epithelial cell-wall and protoplasm. (See Diagram No. 30, Fig. 2.)

Again why is it that cysts are so frequent in the small red granular kidney, and so infrequent as a consequence of Parenchymatous Nephritis, either acute or chronic, where the intratubular changes are undoubted? Why should one form more than another of intratubular change lead to cystic formations, and dilatations of the tubules? On the hypothesis of intertubular increase the presence of these cysts is easily accounted for; but how does Dr. Johnson account for them? Let us see what his paper says: "The explanation of this cyst formation is probably to be found in the
fact that some tubuli continue to secrete an aqueous fluid, while their lower portions are plugged by accumulated epithelial debris, and thus they become distended by their own secretion, (op. cit. p. 308). According to this explanation, cystic formation should be at least as common in parenchymatous inflammation as in interstitial). We cannot help wishing that Dr. Johnson would "explain his explanation."

Dr. Johnson attributes the primary destruction of intratubular structure, which according to his theory constitutes the principal factor in the development of small red granular kidney to the circulation of a blood poison, producing irritation and destruction of the delicate epithelium, while the basement membrane of the tubules, and the renal capillaries, remain much longer in accordance with the law of the "survival of the fittest." The author agrees with Dr. Johnson as to the blood poison (that is, in the case of bilateral interstitial nephritis), but differs from him altogether as to its effects on the kidney structures. The irritation being chronic and not very intense, is just as likely to give rise to interstitial as to intratubular change. The nature of the irritation then affords no argument for Dr. Johnson's theory, though it may perhaps by its chronic character furnish a slight presumption against it.

In some parts, pursue. Dr. Johnson, the basement membrane and the Malpighian capsule, appear to be thickened, and assume a fibrous texture, so that an examination of the granular kidney without reference to the normal structure and especially to the appearance of the fibrous network

(11) Note. Gout, rheumatism, alcoholism, lead poisoning, chronic dyspepsia (Porcheron), syphilis, are the chief known causes of Interstitial Bright's Disease.
which is seen on examination of a section of normal kidney after washing away the gland cells might lead to the belief that the tubules are surrounded by an abnormal fibrous tissue. Now it is precisely a want of acquaintance with the appearances of the normal kidney, which constitute one of the principal charges which the author is afraid must be found relevant against Dr. Johnson. Of course, after the gland cells are washed away, Dr. Johnson sees a fibrous network in the normal organ;—that is to say, speaking roughly, about one tenth part fibre, and nine tenths vessels; but if this fibrovascular stroma be found in the small red granular kidney, it is, as is very commonly, is increased in amount fifteen or five times its normal dimensions, where is the argument in favour of Dr. Johnson's conclusions afforded for existence in normal quantity in the normal organ? Dr. Johnson should not be content with washing the gland cells from a section of healthy kidney; let him take also an advanced stroma and granular kidney, and wash them out of this, too; when in spite of the superior vascularity of the former, he will find the fibrous network far more evident in the nephritic. As to the basement membrane of the tubules, and the Malpighian capsule, "appearing" to be thicker, they appear to be no much in the same manner as the sun appears to shine, or as day and night appear to an unprejudiced and minute observer to succeed each other. So evident is the thickening of Bowman's capsule, that Trunke has mentioned a variety of nephritis which he calls "capsular" and endeavors to distinguish by clinical and anatomical characteristics as a distinct and separate form of disease.

Dr. Johnson continues, "The remarkable changes within the seminiferous tubes receive no explanation from the theory in question (i.e., the theory of..."
interstitial nephritis) they are therefore left unexplained and of course unaccounted for." The author trusts that should the present treatise ever come under the eyes of Dr. Johnson, it may be fortunate enough to escape a like condemnation at the hands of that veteran disputant, to whose labours so much of our present accurate knowledge of renal disease is due; for according to the best of his ability he has neither shirked nor shunned over the question of intratubular changes, but while fully acknowledging their presence and importance, has striven to show that they are explicable in a far more easy and satisfactory manner on the theory of intertubular increase than on that of primary intratubular inflammation.

Dr. Johnson next proceeds to point out a few amongst the insuperable objections to the theory of interstitial fibrosis which is so confidently maintained by some pathologists. The first of these is the red colour of the granular kidney. This is held to be "quite inconsistent with the doctrine of an intertubular deposit which must inevitably obliterate the capillaries and render the cortex more or less pale and anaemic." To tell the truth, this does not sound very insuperable. The contracted kidney is often more pale than red. If red, the colour is due to passive congestion; but so frequently is it pale and anaemic that in Chapter VI paleness has been stated as the rule, and redness as the exception. In the first stage of interstitial nephritis, it is that of cell infiltration, a red colouration of the kidney is extremely rare, and if present due only to the above-mentioned cause. Thomas (op. cit. page 47) says "Die Farbe des Organs schwankt je nach dem verschiedenen Blutgehalt von einem schwachgrünen Weisssgrau bis zu blasrothen und matt dunkelrothen Schattierungen." (See also Rindfleisch, Kloeb, Dickinson, and others.)
But Dr. Johnson assumes that an intertubular deposit must have an obliterating influence on the intertubular capillaries, vastly in excess of that which the author is disposed to allow or ascribe to it. He compares the anemia which would result from such a deposit to that 'visible over a circumscribed spot when arteries and capillaries are obstructed by embolic patches of fibrin.' But surely it is one thing to plug up an artery completely, and another to exercise pressure upon its outside, pressure which may perhaps reduce its lumen to one-half, but which it is quite unwarantable to assume to be severe enough to cause immediate and total occlusion. Such anemia he says is visible in the large white kidney. Surely not; otherwise if at all comparable to that induced over a limited bit by an embolism it would affecting the whole kidney soon produce, not anemia merely, but strangury. Again he says that we should expect fatty transformation of the epithelium consequent on the pressure of the intertubular deposit. Well, to a limited extent we have it, especially in glomerulo nephritis; but why should the degeneration be necessarily fatty and not colloid? Degeneration of some kind we should both expect and do actually meet with, but the author quite fails to see why it must of necessity be fatty. He agrees with Dr. Johnson in saying that fatty intertubular changes are comparatively rare and insignificant, but he accepts in their stead the extensive colloid transformation which Dr. Johnson has "left unheeded and of course unaccounted for." There are also changes of a disintegrative nature which point to a loosening of the attachment of the epithelium to the basement membrane and compression of the cells one against another in the narrowed tubule. Recently we find a stage in which the tubules
are in parts altogether denuded of their lining. There is no need to go over
again in this place the history of changes which we have before minutely
particularized; suffice it today that these changes are quite consistent
with the hypothesis of interstitial increase, which presents no
difficulties save to an observer who comes to the work determined to
discover them whether they exist or not.

The next "insuperable objection" is the following.
"On examining a section of kidney the characteristic intratubular
changes may often be seen in various stages of progress while the
intraglomerular capillaries surrounding these morbidly changed tubes are
infected with blood and evidently quite normal." Here again Dr.
Johnson is harping on his foregone conclusion of complete circulatory arrest
as a consequence of intratubular deposit. The consequence, we repeat, of
such complete arrest would be gangrene. Indeed, the author does not
believe in the complete stoppage of the circulation even in very small
capillaries as a consequence of the first stage of cell-infiltration. He
could even conceive, as he has before hinted, the formation of new vessels for
the nourishment of a large exuded mass of lymphoid cells. The process of
vascular obliteration takes place in the stage of cell transformation and
shrinking of the kidney, not in that of cell-infiltration and enlargement.

But we have yet to account for the intratubular changes being seen in
various stages of progress while the intratubular capillaries surrounding the
morbidly changed tubes are infected with blood and evidently quite
normal. "First of all then, the author differs from Dr. Johnson in the question
of facts. Where the intratubular change were most marked, there he
likewise remarks the consequent intratubular alterations, but where he,
interstitial changes have been insignificant or absent, there is no longer found the intratubular structures normal also. But even granting the accuracy of Dr. Johnson's statement, is there no way of accounting for intratubular changes as consequent upon interstitial inflammation, even though the parts in the immediate neighborhood of the affected tubules may be comparatively normal? Already in this chapter we have mentioned the occasional presence of leucocytes in the tubules. May not their presence be sufficient to account for the occasional occurrence of this phenomenon? The escape of blood into a tubule, from rupture of the capillaries of a glomerulus connected with it, might also produce the appearance or even the reality of intratubular change.

The fact that interstitial changes may be induced in a kidney by obstruction of its vessels, appears to the author to have no significance either way, though mentioned by Dr. Johnson in the present article in support of his own theory. Subacute or chronic irritation from any cause may induce interstitial inflammation, and to the author it seems a matter of little moment whether this irritation arises from a blood poison or from a local cause.

While entirely agreeing with Dr. Johnson as to the hypertrophy of the muscular coat of the arteries, the author differs from him on an anatomical point respecting the structure of this coat. In the Med. Chir. Trans.; vol. 33 page 114, and vol. 56 pp. 449-50; also in the Path. Soc. Trans. vol. 28 page 384, in criticizing a drawing illustrative of Sir W. Harvey and Dr. Sutton's paper in the 55th vol. of the Med. Chir. Trans. (Plate W. fig. 6) he avers that the muscular coat consists of two layers on inner longitudinal and an outer circular, which he figures in the
first of the above references. This statement is at variance with all modern anatomical teaching, and directly opposed to the results of the present author's investigations. If the curious drawing criticized by Dr. Johnson we shall have occasion to speak later, and shall therefore more fully state our conviction that if it be a true and faithful representation as it presumably is, if a specimen in the possession of Dr. Gull and Sutton, the inner ring which they account muscular is in all likelihood the tunica intima thickened by endoarteritis obliterans, while the enlarged circular layer is as stated by Dr. Johnson the hypertrophic muscular coat. The author believes in common with all accepted anatomical authorities, that the muscular coat of the arteries is arranged in concentric direction, and that a circular one (see Klein, Path. Loc. Trans. 1877 pp. 33-4). If this hypertrophy of this circular layer in interstitial nephritis, there is in his opinion ample and convincing evidence. The longitudinal muscular layer figured in Dr. Johnson's drawing on page 114 of the 33rd vol. of the Med. Chir. Transactions, is beyond a doubt the thickened and proliferated intima in a state of endoarteritis obliterans (see also Thoma, Archiv 1877 B. 71). The author has seen the same appearance of hypertrophy of the muscular coat in arteries from the tongue of a cat; but he is quite ignorant of the state of the animal's kidneys.

With regard to the view that the muscular hypertrophy is simply the result of post mortem contraction of the muscle cells, while perfectly convinced in his own mind that no amount of contractions could produce so marked an appearance of thickening and multiplication of muscle nuclei, it was nevertheless the author's intention to perform a series of experiments which he was in hopes would conclusively settle the question. It was his purpose to certain
the amount of apparent thickening; if any, of the tunica media in the arterics of animals poisoned both by a single large dose and by small doses of some drug causing contraction of the arterics, such for instance, as opium. Unfortunately, however, for the completeness of his researches they had not reached this stage before the passing of the recent prohibitory enactments, so that he was presently compelled to apply to the Home Secretary for a licence authorizing him to proceed. This was curtly and peremptorily refused, without the assignment of the slightest reason. If however it be a consolation to have company in misfortune, the author was soon able to avail himself of this petty crumb of comfort, for he speedily learnt that he was but one out of many sufferers from a piece of legislation, which if it continues to be enforced will have the effect of so retarding the flood of scientific progress in this country, that in the course of a decade or so, our legislators may proudly reflect upon the fact that during that period the world has been preserved from some hundred of useful discoveries, and the advancement of knowledge in these islands hindered not a little by the ingenious disposition of a very formidable and effectual stumbling block, planted in the way of the pioneers of science and humanity. A Government which, despite its pretentious oligarchical tendencies, has proved itself but too ready to hand over the control of the educated, free to the ignorant many, and to purchase evanescent popularity at the price of lasting folly. Truly if the intellect of the nation is to be thus hedged about with contumelious restrictions, we shall come at last to exclaim with Sophocles in the Aegisthids: µεν δ' εν ἀκοντίον ἀξίων χαίρειν. 

To a happy thing to be a drum-skull. —

Metaphorically speaking a dose of eurora has been given to British Science, and its members formerly so active now hang paralyzed and passive.
Better paralyse the limbs of a frog than the brains of a nation. But we disagree somewhat.

On page 117 of the 33rd volume of the Med. Chir. Trans., Dr. Johnson makes the curious statement that in consequence of the destruction of the gland cells and arrest of the process of secretion, the circulation in many vessels of the small red granular kidney ceases, and oil globules collect in the canals of the blood vessels. Such a collection of oil globules the author has never seen, nor is he without grave doubts as to its even occasional existence, for in spite of the constant use of Bninie Acid he has in no single instance detected any sign of intravascular fatty change. Dr. Galabin (On the Connection of Bright's Disease with Changes in the Vascular System) says 1837:

"As to the state of the capillaries, or minutest arterioles, I have found a granular or apparently fatty condition common in cases of granular kidney." He does not say in what situation, whether inside the lumen or in the coats; and the present author thinks it not improbable that the numerically increased muscular nuclei of the tunica media have been mistaken by Dr. Galabin for fatty granules, an error not quite so improbable as might at first sight appear. Dr. Gall and Sutton Med. Chir. Trans. vol. 65, page 281, describe groups of fat granules aggregated together in the wall of the smaller arterioles of the Pia Mater. Todd also (Colin: Lect. on Dis. of the Urinary Organs 1857, Lect. 11, p. 109) says that the canals of the minute afferent arterioles of the Malpighian bodies are sometimes blocked with oil. We suspect however that with the improved methods of microscopical observation now becoming general, the discovery of oil in the vessels of the kidney in interstitial nephritis will become less frequent, day by day.
In the 55th volume of the Med. Chir. Trans. was first published the now well-known paper by Dr. Gull and Sutton on what they denominate "Arterio-capillary fibrosis," a supposed general morbid state of the vascular system, of which as they maintain, the lesions occurring in interstitial nephritis are but part and parcel.

We quote verbatim the following summary of the results of their observations: (Med. Chir. Trans. vol. IV page 283).

"(i) That the arterioles throughout the body in that condition usually called Chronic Bright's Disease, with contracted kidney are more or less altered.

"(ii) That this alteration is due to a "hyalin fibroid formation" in the walls of the minute arteries, and a hyalin granular change in the corresponding capillaries.

"(iii) That this change occurs chiefly outside the muscular layer, but also in the tunica intima of some arterioles.

"(iv) That the degree in which the affected vessels are altered, and the extent to which the morbid change is diffused over the vascular system in different organs, varies much in different cases.

"(v) That the muscular layer of the affected vessels is often atrophied in a variable degree.

"These facts show that there is a morbid state in which the kidneys are contracted, the heart hypertrophied, and the minute arteries and capillaries altered by a hyalin fibroid formation. Further, that the kidney changes are often but not always a part and parcel of this morbid state.
The absence of such lesions of the kidneys proves that they do not constitute an essential and indispensable part of the general process. (p. 286)

We will further allow Dr. Bull and Sutton to describe their "hyalin-fibroid" substance in their own words.

"A fine hyalin or hyalin-fibroid substance was seen between the convoluted tubules, which made the tubules appear wider apart than normal. In some parts this substance had a homogeneous appearance; in others it had a striated or fibroid appearance like a network, and contained minute indistinct nuclei; and in others it had a coarser and more defined fibre-like character. This substance was seen in considerable quantity round the Malpighian bodies and in still greater amount in and around the walls of the minute arteries." (page 274)

In the first place we would ask attention to the fact that this description answers almost equally well for granulation tissue; (see Tissue of Healing Ulcers) and in point of fact it is simply and solely the granulation tissue deposit between the convoluted tubules to which Dr. Bull and Sutton apply the term of "hyalin-fibroid" substance. It is, in the main, an alteration in name, and that for the worse; since such terms as "necrotic tissue," "granulation," "indifferent" or "embryonic tissue," "small cell infiltration," "infiltration with lymphoid cells" and the like, convey a correct notion of the etiology of the new formation, whereas the appellation "hyalin-fibroid substance" points to a pathology, which, as we shall presently see, is but slightly corroborated by facts.

Further, this "hyalin-fibroid" alteration is said to be seen in the walls of the minute arteries outside the muscular layer, and also in
the tunica intima of some arterioles. In the early stages of granular contraction, Dr. Gulbrand Sutton says (p. 275), "In the walls of some of the minute arteries, and also outside and around them there appears to be an excess of fibroid tissue, and the artery in consequence seem thicker than normal. In making this observation we are well aware that there is normally more or less of areolar tissue around the minute renal arteries, therefore it is difficult with any degree of certainty to appreciate any slight increase in such tissue, but after careful observation it seemed to us that the outer coats of the arterioles even at this early stage were thickened by increase of fibroid tissue. The muscular tissue did not appear increased."

According to the present author's experience, the "areolar tissue around the minute renal arteries," is the seat of small-cell infiltration at an early period in the history of Interstitial Nephritis, as might be expected from the presence of the lymphatic spaces before alluded to as being demonstrated by the injections of Ludwig. As to the adventitia however, it is for otherwise. In a great number of instances it remains normal and unthickened even in very advanced stages of granular contraction, and if thickened at all, this thickening is due to a secondary extension of the process of hypertrophy going on in the connective tissue surrounding it. This connective tissue is both early increased and early fibrillated, and on casual observation might convey to a not very thoughtful or practised histologist the idea of thickening of the adventitia, though this coat is distinctly visible as a narrow, dense, finely fibrillated ring, quite normal, and but loosely connected with its hypertrophied surroundings, as may be
proved by picking it out with needles. This fact even alone and unsupported is, if established, almost absolutely fatal to the "intercapillary" fibrotic theory; and in support of it the author is prepared to appeal to almost every preparation in a series numbering considerably over two hundred. In these specimens thickening of the adventitia proper is only seen in a very few; and those, the most advanced; and in these is simply due as just stated, to an extension of the processes going on around. Primary and early thickening of the adventitia, whether hyaline or fibrinous, the author has absolutely never seen; hyaline changes in the adventitia he has never seen in any stage of the disorder, if we except that thickened and translucent appearance sometimes observed in the loops of the glomerules, which is probably the harbinger of impending colloid change. Fibrinous thickening of the adventitia he has only seen late in the disease, and as a secondary consequence. This is a strong and decided standpoint to assume; but the author is confident of his facts, and these conclusively negative the statements of Sir C. Yell and Sutton. He does not however in the least impugn the absolute correctness of the description given by these gentlemen of the appearances seen by them in their own specimens; but he does strongly maintain that if such a state of matters as that described by them be visible in their preparations, it is simply, owing as stated by Dr. Johnson, (Med. Chir. Trans. vol LVI.) to the methods of manipulation and mounting to which they were subjected. Sir William Yell and Sir Sutton admit that their specimens were not mounted by themselves, but by assistants; and they could therefore have this
no opportunity of observing any changes which might ensue in consequence of the use of reagents and mounting fluids. Now the author on the contrary has mounted every one of his specimens with his own hand, and can state with perfect confidence that they are in no way altered by the treatment they have undergone. In this opinion Dr. Gall and Sutton might look long before they found anything confirmatory of their theory. He has likewise appended the following chapter on Preservation, Preparation, &c, in order to furnish the reader with a minute account of every step in the preparatory process, and to enable him if so inclined, to check the author's conclusions of the adoption of the same methods with specimens of his own. Certain mounting media, especially Glycerine, are very prone to alter specimens preserved in them. Dr. Saladin (On the Conn. of Bright's Six with Changes in the Vascular System pp. 132-144), and also to Some Extent Dr. Granger Stewart (Brit. Med. Journ. Nov. 1815 and 1873), confirm the statements of Dr. Johnson as to its untrustworthy character, especially if acidulated. These allegations the author has verified, and he thoroughly concurs in the condemnation of pure Glycerine as a mounting medium. Well-made Gunther's Solution, and Rimmington's Glycerine Jelly, though both containing Glycerine in some form or other, are free from these objections. Arteries of the Pia Mater mounted in Glycerine alone, or in Glycerine and Camphor water (the fluids used for the preservation of Dr. Gall and Sutton's specimens) rapidly present appearances of hyaline change, and still more so if acetic acid be added. With care and pains also, "hyaline fibroid" substance may be largely manufactured in the Kidney; that is to say if the
Specimen has not been hardened in Chromic Acid, which seems
inimical to its development. Fresh Kidney mounted in Acetic acid
and glycerine readily assumes this guise; Kidney hardened in
Bichromate Solution or Müller's Fluid less readily, though the
author has had some success even with specimens so treated. He
subjoins one excellent example, for the fictitious nature of which he
can vouch, for he carefully followed its transformations from one
stage to another. It was taken from a normal kidney hardened in
Müller's Fluid, and was before undergoing the treatment presently
to be detailed, as healthy looking an artery as one might wish
to see. First of all it was stained in the usual manner with
Picroic acid, being left for about an hour in a ½ per cent. solu-
tion of this reagent. It was then allowed to remain all night in a
bowl of clean water, a procedure which did not affect it in the
least, for when examined in the morning it appeared quite natural
both under low and high power. It was then spread out on
a slide, and covered with Glycerine acidulated with a few drops of
1 to 8 solution of Acetic Acid. After remaining thus about two
hours, a cover glass was put on to it, and on examination, it
presented the remarkable appearances which it still maintains.
No distinct muscular coats and no intima are distinguishable.
The whole wall, the thickness of which is very irregular is composed
of hyaline fibroid material, surrounded by somewhat denser ring,
which represents the adventitio proper. Around this is some
connective tissue pretty normal in general appearance, though
rather “hyaline,” and swollen to twice its size before the
addition of the glycerine and acetic acid. Curiously enough, close to this strangely metamorphosed artery, is another and smaller one, much less altered, for though its three coats are so blended together as to be practically indistinguishable, they are not swollen out as in the case of its neighbour, thereby affording a striking example of the capriciousness with which these spurious appearances develop themselves. They are at times very easy, and at others very hard to produce. We annex a drawing (No. 35) of this interesting specimen of the arts and manufactures. Both specimen and drawing are very like the arteriole from the muscular tissue of the heart "greatly thickened by the fibroid material," figured by Dr. Gull and Sutton Plate VI fig. 6. Med.Cirr.Sans:Vol.IV. [See also fig. 4 of the same Plate, Arteries from the Choroid. In this last figure we are much puzzled to think what can be the nature of the globular bodies inside the lumen, though possible they may be due merely to swelling of the intima under the action of Glycerin.

Anything like Fig. 4 of the same plate, it was never our good fortune to behold; but we conjecture that it may perhaps be considered as representing an artery the intima of which is thickened by endo-arteritis obliterans, while the middle circulus coat is greatly hypertrophied, and the adventitia either fused with it by the action of the glycerine fluid, or left altogether reconfigured by the artist owing perhaps to its having lain outside the field of the microscope, which last alternative is quite possible as the power used was a high one (x 750). Or again the inner ring may be composed of the intima and media much confounded altered and blended
together of the glycerine, and so charged that their best friends
would not recognize them, while the outer coat is swollen by
the action of the glycerine, and presents a false appearance of
hypertrophy. But at least this drawing is an enigma, nor do we
pretend to be able to explain it satisfactorily. D'avi nonimus on Edips,
but at least it is perfectly certain that glycerine often renders it
almost impossible to distinguish one arterial's coat from another.

Were it permitted me, we should advise S't Elliott and Sutton
to harden their next specimens of kidney in Chromic Acids
(1 to 400), letting them remain in this at least four weeks; a
preliminary soaking in Müller's fluid of about three weeks
duration being advisable, especially if the pieces of tissue are large.
Let them then be cut in the freezing microtome, a strong solu-
on of gum Arabic being used for embedding. Before cutting, they
should remain for a night in plenty of clean water, to allow the
Chromic acid to soak out. After cutting, let them be mounted,
not in glycerine, but in thick Tannin prepared with a
saturated solution of gum, or in good Glycerine Jelly. Specimens
so treated will pass through the ordeal unaltered, and find
their evidence in an eminently trustworthy manner. Should Sir
William Elliott and S't Sutton thus prepare their next series, the
author ventures to predict that it will not prove rich in "hylia-
fibroid" material. He would also venture to make another
suggestion to S't Elliott and Sutton, which is that it is hardly
advisable to trust to assistants for the preparation of specimens;
as errors in manipulation are exceedingly apt to give rise to the
most perplexing pseudo-pathological alterations, a statement amply confirmed by the startling metamorphosis perpetrated by the author. The histologist who relies on others for the preparation of his objects, and only inspects them himself when they have been neatly mounted and finished off, is like a father who sees his son for the first time when the latter is already middle-aged, and trusts to the mere fact of his paternity to afford him an insight into the character and antecedents of his offspring.

Mr F. J. Hamilton FRCS, Pathologist to the Royal Infirmary, Edinburgh, once told the author that in Dr Gull and Sutton's specimens, which he saw at a meeting of the British Medical Assoc. there appeared to him to be as much "hyalin fibroid" material in the healthy as in the abnormal ones. If this were so, doubt, for normal arteries mounted in glycerine present very much the same appearances as diseased ones.

Plate V Fig 1 Med. Chir. Trans. Vol. IV represents some Malpighian bodies as seen by Dr Gull and Sutton. Bowman's capsule is with perfect correctness represented as thickened and fibrous, but in place of the glomerulus a number of "fat and other granules," are figured inside Bowman's capsule. The author has never seen any such appearance in any specimen of interstitial nephritis examined by him; though J. Wilks (Path. Soc. Trans. Vol VI p. 264) describes a case of fatty degeneration of the Malpighian bodies. Lebert (Traité d'Anat. Path. Vol 2, page 336) says "les capsules de Malpighi sont remplies de gouttelettes de graisse," but his description refers probably to the third or atrophic stage of parenchymatous inflammation.
Some of the "fat granules" in Dr. Full & Sutton's drawing somewhat remind
the author of the nuclei visible in the same situation in glomerulo-
nephritis; but altogether this representation is nearly as puzzling as
that of the arteries, criticized on page 706 supra. The author would
not say that a glomerulus never becomes fatty in ordinary uncom-
pli cated interstitial nephritides; but he can affirm unhesitatingly
that among hundreds of specimens he has never remarked a single
instance of fatty change. Dr. Full and Sutton's specimen was taken
from the body of a girl nine years old, an unusual, though by no
means unprecedentedly early age for the occurrence of interstitial
changes. Dr. Barlow Lancet Aug. 1st & 8th, 1874 describes the case of
a child 5 years and 8 months old, in which the kidneys were
granular and the heart hypertrophied. But on the other hand
out of 79 cases of contracted kidney the histories of which were
collected by Dr. Galpin from the Post Mortem records of Guy's Hospital
during the four years 1869-72, there was none younger than 10
years of age. Extreme youth of the patient cannot however be held
incompatible with the existence of contracted kidneys. Perhaps
Sir W. Full & Dr. Sutton's case may have been one of those in which
the interstitial changes seem as the secondary consequence of chronic
parenchymatous inflammation. There is yet another conjecture
which we may hazard respecting these "fats," Malpighian bodies,
glycerine sometimes causes healthy glomeruli to assume a very
extraordinary appearance, especially if the vascular loops be partially
filled with red blood corpuscles. (See some glomeruli in the preparation
of Artificial Hyalin fibroids.)
Altogether, the drawings illustrative of Dr. Gull & Sutton's paper, afford room for free speculation, "not too fine a point on it," as Mr. Squeers by would say.

On page 177 of the same paper Dr. Gull and Sutton allude to the granularity of normal renal epithelium in terms which seem to call for some brief notice. They attribute the granularity to mechanical congestion, and consider it as a part of Post Mortem phenomenon. It is however equally evident in the kidneys of cats which have been rapidly bled to death, either by cutting the throat, or by complete decapitation, though in the case of these animals, PM or direct anti-mortem venous congestion was from the manner of death impossible. The conclusion therefore appears to be inevitable that granularity is a natural and typical condition, though it may of course be indefinitely exaggerated as the result of disease. Still the normal granular appearance should always be remembered in determining whether the epithelium of any given kidney is altered as the result of disease.

In the present monograph the author is not prepared to follow Dr. Gull and Sutton into their elaborate paper on "Arterios capillary fibrosis" in the spinal cord. Should he have the opportunity, he will gladly do so at some future time; nor is he altogether unprepared to begin the prosecution of such investigations; but he refrains to say that up to this time material to work upon has been entirely wanting. Yet though diseased spinal cords have found their way but very sparingly into the author's hands;—though these which he has hitherto possessed have been as few and far between...
as angelic visits, or as the currants in a confectioner's bun, there are a few observations which from his acquaintance with the normal structure of the cord, he may perhaps not unnecessarily venture to make. First, then, he begs to congratulate Dr. Gull and Sutton on their enforced abstinence during this investigation from the use of the staff of that broken reed, glycerine. Canada Balsam is an excellent mounting material for nervous tissue, and second, perhaps only to well prepared Sammar Fluid,- in either of these media specimens may be mounted with ordinary care, without the least fear of adventitious change.

Secondly, he would allude to the fact that in the cord, as in the kidney, more or less connective tissue is distributed with the vessels, which connective tissue cannot in any sense of the word be said to constitute their adventitia. In interstitial inflammations it may be taken as a rule, that the greatest increase of connective tissue will be met with in those situations which contain the most normally, and as a consequence, it is not surprising if, as mentioned by Rindfleisch, the so-called fibrous thickening in inflammatory induration present a red spot or line in their centre, which is in fact a distended blood vessels. Rindfleisch, however, speaking of inflammatory induration of the cord, says that the adventitia of the vessels is made up of concentric layers of round cells, (Path. Hist. Syd. Soc's Trans: vol 2 page 350) and further states that the vessels are in a condition which he would not compare elsewhere to call one of chronic inflammation. Dr. Gull and Sutton (Path. Soc's: Trans: 1877) quote this passage in support of their...
conclusions; for Rindfleisch's inflammatory induration is in their opinion simply arterio-capillary fibrosis as seen in the cord. The statement of so accurate an authority as Rindfleisch must always have great weight, especially when corroborated as they now are by the results which Dr. Gull and Sutton have embodied in their careful and beautifully illustrated paper. We will not therefore attempt to deny that the arteries and capillaries of the cord, which last, as Stricker believes, have a continuous layer of protoplasm on their outer surface, are really involved in the process of inflammatory induration; indeed, we deem it highly probable that the observations of Rindfleisch are correct on every material point. What, however, we entirely fail to see is that this state of matters in the cord has anything more than an incidental connection with the very dissimilar kidney lesions. That most of the renal vessels, analogous to that above-mentioned, has ever come under our notice in the course of our researches into the morbid anatomy of Interstitial Nephritis, we can confidently affirm. The two pathological states appear to the author to be quite different. Assuming with Rindfleisch that the first anatomical element of inflammatory induration, or as Dr. Gull and Sutton would doubtless prefer to call it, arterio-capillary fibrosis of the cord, is the recognised in alterations of individual vascular tufts, the present author can only say that no such alterations were ever visible in any example of interstitial kidney, which has as yet come under his notice. In the kidney he has never under any circumstances seen an adventitia "made up of concentric layers of round cells"
often fine deep," (Rindfleisch). Thickening of the adventitia he has seen, but it was not the first anatomical element of the disease, nor the second, nor the third, but a very late and entirely secondary one.

With regard to the influence of reagents in inducing an appearance of thickening of the outer coat in the case of vessels from the Pituitary, a very accurate and reliable observer F. Grainger Stewart says (see Brit. Med. Journ. No. 15, 1873.) "The conditions which I have observed are — first a more or less marked thickening of the coats of the small arteries. This is in some cases so distinct as to attract attention by its wavy fibrous appearance, and the sinuous outline of the vessel, where no reagent has been applied. But these appearances become much more distinct when the specimens are placed for a short time in water or in glycerine, or when a little dilute acetic acid is added. In many cases the application of these reagents produces an appearance of thickening, certainly, of increased prominence of the external coat, even when the vessel without reagent appeared natural. But the appearance thus artificially produced differed from that of the true thickening in that it was never watery or fibrous looking. I found no evidence of free exudation, or of the presence of any solid material in connection with the outer coat.

The condition thus described corresponds exactly to the appearance of the specimens of so-called hyaline fibroid disease which I examined." He also found evidence of thickening of the tunica media, and in some cases of the intima. The tunica media was never atrophied, nor was the lumen of the vessels diminished. No
thickening or exudation was seen in the walls of the capillaries. These
facts were gathered from the examination of a series of 23 cases, in 12
of which the vessels were normal. But here ends all that is in
any way favourable, in Dr. Stewart's testimony, to the "arterio-capil-
laris fibrosis" hypothesis; for out of 10 cases in which the outer coat
was thickened, there was no Bright's Disease at all in 6.

Dr. Stewart is nevertheless clearly of opinion that some of his
cases presented a thickening of the outer coat of the arterioles which
was not traceable to the use of glycerine or other reagents. But
Dr. Pull and Sutton are not much advantaged by this admission;
for Dr. Stewart's statistics go to prove that the thickening (which in
might be the result of many other causes) was altogether
unconnected with Bright's Disease, either as cause, effect, or
necessary concomitant. In the walls of some of the vessels there were
small aneurisms, due probably as we may conjecture, to that
diseased state generally known as Chronic Periarteritis, which
might quite satisfactorily account for the thickening, unless Dr.
Pull and Sutton would include this condition also in their "arterio-
capillary fibrosis", despite the entire absence of connection between
it and nephritis of any kind. Now the author has seen Chronic
Periarteritis in plenty, but he has never seen anything of the
nature of "arterio-capillary fibrosis", either in the vessels of the Pia
Mater or elsewhere, save and except as a consequence of the use
of reagents. Not that he would ever in the face of Dr. Stewart's
statements that the adventitia is never thickened; - it maybe so
from many causes; but he simply states that so far as he knows,
there is not a grain of the ghost of a grain of evidence to connect this thickening with interstitial nephrites, while on the contrary there is strong proof in favour of a relation existing between thickening of the tunica media, and this variety of renal lesion. Such evidence is afforded in the course of Dr. St Beitrag to the paper above-mentioned, as well as by many other authorities already quoted. Finally, in the Dia Mater as in the kidney, care should be taken not to mistake one arterial coat for another, a confusion which the use of glycerine is here as elsewhere extremely liable to occasion.

The thickening of the inner coat of the arterioles is due, not to "arterio-capillary fibrosis", but to Endoarteritis Obliterans, a condition which we have already described.

Much praise is due to Dr. Gull and Sutton, not only for the careful manner in which they have sought to collate facts in support of their theory, but also for having by their example afforded, a powerful incentive to others to prosecute researches in the same direction, thereby conducing greatly to the wider and more thorough ventilation of the whole question. But while sensible of the benefit they have thus rendered to the profession, the author is unable to accept the conclusions, his own investigations having led him to believe that they have fallen into certain errors already stated, which may be epitomized under the following heads. (See next leaf)
Summary

1. In the interstitial kidney Dr. Reed and Fulton have probably in many instances mistaken the middle for the outer coat of the arterioles, and have thus been misled by a factitious appearance of thickening of the latter. Their use of glycerine as a mounting fluid has probably done much to further this confusion.

2. In other instances, though well aware that there is normally more or less of areolar tissue around the minute renal arteries, they have fallen into the error of confounding this with the adventitia proper. This mistake may be also in some measure traceable to the use of glycerine.

3. In the Spinal cord, Pia Mater, and other organs, they have observed certain pathological and pseudo-pathological states, which in consequence of their ideas as to the nature of the kidney lesions, they have been led to consider anatomically identical with those lesions, whereas the great differences exist between them.

In conclusion then, there appears to be no evidence of the existence of a general morbid state of the vascular system, characterized by "Arterio-Capillary fibrosis," and "hyalin fibroid" changes, for such a state of matters does not exist in the kidney, and there are ample reasons for doubting its existence elsewhere.
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\text{Nov 15th 1878.}
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Note On Glomerulo-Nephritis.

The materials of the following Note have been gathered from an examination of the kidneys in three cases of Post Scarlatinal Nephritis. From the first case the author subjoins one microscopical preparation (labelled A), from the second case one also (labelled B), and from the third case ten, which are distinguished as Series J., and numbered from 1 upwards. - Twelve preparations in all.

Klebs (Handb. p. 594. p. 14. p. 14.) was the first to direct special attention to a Post Scarlatinal change in the glomeruli, to which he gave the name of Glomerulo-Nephritis. Arnold Beer, J. Brislowe (Patt. Soc. Trans. vol VIII p. 235), and J. Wilks (Patt. Soc. Trans. vol VI p. 266), had previously remarked conditions more or less similar, but to Klebs belongs the credit of first accurately describing the microscopical anatomy, and of clearly distinguishing this variety from others previously recognized. Until very recently Post Scarlatinal Nephritis was generally considered to be of the Parenchymatous variety, though Biermer, Lato Wagner and Ogley have described cases in which the changes were interstitial.

We shall first give a translation of Klebs' description, and then proceed to a consideration of the appearances as seen by ourselves.

"On Mr. examination the kidneys are seen to be slightly or not at all enlarged, firm to the touch, the capsule easily separable, the surface smooth, and the parenchyma very hyperemic. On careful inspection, the glomeruli appear pale like small whitish spots. The uriniferous tubes are often unaffected, though occasionally the convoluted tubules are somewhat cloudy. On microscopical examination, we find neither interstitial changes, nor that proliferation of epithelium known as Renal Balanx, a state of matters often supposed to exist in default of other perceptible derangements; so that with the exception of the condition of the glomeruli there seems to be nothing beyond the congested state of the kidney to account for the
symptoms (ammonia, uraemia, and acute dropsy). This (is the congestion) however, is palpably insufficient, since complete retention of urine, and acute uraemia have never been observed either in acute or passive hyperaemias of equal intensity, such for example as those consequent on poisoning by Carbonic Acid, or on mechanical congestion.

If a thin section of the fresh kidney be made with a Valentin's knife the anaemic condition of the glomeruli becomes still more evident; and if the sections be washed in water the glomeruli stand out in their substance as objects darker and denser (darker) than the urino-erous tubules, while in direct light they are visible to the naked eye as white spots. In microscopic examination the whole interior of the capsule (Bowman's) is seen to be filled with small somewhat angular nuclei, lying imbedded in a finely granular mass, while on the inner surface of the capsule the epithelial lining is seen in profile as a row of flat multibody projections. The vessels of the glomeruli are almost entirely obscured by the nuclear mass. It is somewhat difficult to ascertain accurately the real anatomical situation of the manifest nuclear increase, and this can only be done by careful isolation of the glomeruli --- and picking it topieces with fine needles, whereby one learns that the epithelial lining of the glomeruli is still visible, and indeed as a general rule, even more closely adherent than normally. The epithelial cells are for the most part polygonal or ovalate, with large oval bladder-shaped (blaschenformigen) nuclei, and very often adhere by one corner to the surface of the glomerulus: in certain cases I have seen them feebly degenerated, but as a general rule their substance has a clearer and denser (feller und fester) appearance than under normal conditions. By carefully separating these epithelial cells we recognize in the fragment of glomerulus, around and between the unchanged and empty capillary loops, the same small angular nuclei already so conspicuous on a general view of the glomerulus. The difference of these elements from those of the epithelium both in respect of form and situation,
shows quite clearly that their origin is due to a multiplication of the connective tissue corpuscles of the glomerulus, owing to the presence of which (cell multiplication) the vascular loops are subjected to compression." (Klebs: Handb. d. pathol. Hist. ii p. 845-6)

On the question of naked eye appearances the author is entirely at one with Klebs, so that there is no occasion for a reiterated description. He will therefore confine himself to an enumeration of the changes observed by him on microscopic examination of the three kidneys already alluded to. Specimen f affords an example of the earlier, and Series j of the more advanced lesions, while Specimen B occupies an intermediate position between the other two. On examining with a low power (chart: oc3 x ob3) a section of kidney affected with glomerulo nephritis, we remark appearances similar to those figured in Drawing No. 1 Series Glomerulo Nephritis. The attention is principally arrested by the dense appearance of the glomeruli, which occupy almost the whole of the interior of Bowman's capsule, and colour deeply with reagents such as Carmine and Levkos. With this power especially if the tube of the microscope be elongated, small bodies like grains of sand can be seen covering the loops of the glomerulus. These small bodies are also seen in the interstitial tissue, scattered here and there about the kidney substance and arranged in foci around the vessels. (See Drawing) Most of the uriniferous tubules are unchanged, but here and there especially in the neighbourhood of the Malpighian bodies, a few tubes are noticeable the epithelium of which is granular cloudy or fatty. The capsule of the kidney is more or less thickened. The interstitial tissue generally appears more abundant and more distinct than in the normal organ.

On examining with a high power, (chart: oc3 x ob7) a most interesting series of lesions becomes visible. Let us first direct our attention to the Malpighian bodies. Figures 2 and 3 represent their condition in the earlier stages. Bowman's capsule
is thickened and infiltrated with round cells. These round cells are also met with outside the capsule, their numbers varying according to the intensity of the process and the stage at which the specimen comes under observation (see Drawings 2, 3, 4, 5, 6, 7, 8). The epithelial lining on the inside of Bowman’s capsule can be recognized without difficulty, and is quite unchanged. Great numbers of the small, round, oval, or angular bodies like leucocytes are seen lying on and between the capillary loops of the glomeruli. As previously mentioned in the present treatise, a certain number of corpuscular bodies are normally found imbedded in the connective tissue binding together the loops of the glomerulus (see page 23); but in this affection the number of these bodies is very largely increased. In early examples, such as those figured in Drawings 2 and 3, there may be perhaps speaking roughly, six or eight times the normal number; while in extreme cases such as that represented in Drawing 7, the whole Malpighian body may be entirely obscured by them. The new cells resemble the healthy ones, but are perhaps a trifle larger. As to the question of their nature, the author is disposed to regard them as leucocytes which have migrated through the walls of the capillaries. Some of them may have their origin in the proliferation of the normal connective tissue corpuscles, but their number is in the author’s opinion too great to warrant the supposition of their entire derivation from a multiplication of these elements. When present in excessive quantity, they may, as before mentioned, more or less completely obscure the vascular loops. Drawing 7 shows an enormous accumulation of these cells, in and around a Malpighian body. The vascular loops are entirely concealed, and Bowman’s capsule is so infiltrated filled and surrounded by the round cells as to be indistinguishable as a separate structure. In fact, in and around the Malpighian body, nothing is visible but a dense congeries of roundish cellular
elements like leucocytes. The compression exercised on the vascular loops by the large accumulation of cells must be enormous, and in marked cases amply sufficient to occasion serious obstruction to the renal circulation.

This cell-infiltration in and around the Malpighian bodies, is perhaps the most noticeable feature in the whole morbid process, as it certainly is the cause of the exceptional clinical symptoms which follow on the development of this variety of renal lesion, and on this account the name "glomerulo-nephritis", appears a descriptive and suitable one. While Klebs, however, the present writer cannot say that this is the only lesion he has been able to discover.

As a consequence either of the compression exercised on the glomerular loops by the round cells just mentioned, or of other conditions which we shall presently discuss, fibrous degeneration of the glomeruli and the proliferated cellular contents of Bowman's capsule, is by no means infrequent. When this occurs the number of round cells inside the capsule becomes much diminished (see drawings 80, 81). The transformed capillaries are converted into a more or less dense fibrous mass, continuous here and there if not entirely with the inner circumference of the thickened capsule. (See also Plate 33 fig. 7, Klein on Anat. of Scarletina Path. Soc. Trans. 1877.) Drawing 10 represents extreme fibrous degeneration of a glomerulus, with granular and fatty changes in the tubule connected with it. Comparatively few round cells are visible on the surface of the degenerated glomerulus, and the dye (g民国) has scarcely at all coloured the fibrous mass, which consequently contrasts notably with the deeply stained capsule surrounding it.

Dr. Klein in the paper just referred to, speaks of having encountered emboli in a case of 18 days duration accompanied by very intense interstitial
inflammation. He thinks it "not impossible that also in his other cases embolism of arteries stands in a causal relation to the interstitial inflammation which in this disorder attacks not only the glomeruli but the general intertubular tissue," in precisely the same manner as in the ordinary variety of interstitial kidney. Dr. Klein states no grounds for this theory, which appears rather hasty, considering that emboli were met with in but one case out of his series of 23. As the author has only observed a doubtful embolus in a single case, he is unable to concur with Dr. Klein in ascribing the interstitial changes to this curious and apparently very unusual cause.

These general interstitial changes we shall now shortly discuss. In all the author's specimens, in addition to the glomerular affection, there were evidences of more or less intense and widespread interstitial nephritis. We have before remarked (p. 67 and 68) that these cases afford excellent examples of early interstitial changes. The small cell infiltration is so abundant and so evident, and there is such an entire absence of any chance of its confusion with the products of intratubular change, that in our humble opinion these specimens might serve to convince even Dr. Johnson of the reality of an interstitial nephritis. In these cases the round cells cannot possibly be confounded with epithelial debris, and thus the intertubular nature of the lesion is placed entirely beyond dispute. Glomerulo-nephritis is in fact nothing but an interstitial nephritis specially affecting the glomeruli, and in consequence of this special anatomical site, proving fatal in the early stages with a rapidity and constancy fully equal to the parity of a like result in the initial stages of the ordinary variety. Around the arterioles there are large accumulations of migrated leucocytes (See Drawings 11, 12, and 13: also Klein op. cit. Plate 32, fig. 14). The intertubular capillaries are much dilated, and contain great numbers of white blood corpuscles. (See Drawings}
3, 11, 12, 13. 7th). Sometimes the leucocytes accumulated outside a vessel have the appearance of lying in a sort of adenoid pectinum (Klein), but this the author is disposed to attribute to underlying capillaries, the walls of which are more or less visible through the superincumbent mass of lymphoid cells. The author has not seen any formation of nuclei of the middle coat of the arteries (Klein), neither has he ever observed any hyalin degeneration of the intima (ibid). All the arterial coats have been found so far as his researches extend in a perfectly normal condition. Drawing 15 represents an area of advanced interstitial cell infiltration. The intertubular tissue is greatly increased by the presence of lymphoid cells, so that the spaces between the tubules are many times their normal thickness, while the tubules themselves are compressed but otherwise pretty normal (See also Klein, op. cit. Plate 32 figs 2-4.)

Small interstitial haemorrhages evidenced by the presence of red blood corpuscles, and hemorrhages into Bowman's capsules from rupture of the glomerular loops are by no means infrequent.

Intra-tubular changes are present to a greater or less degree in all the subjoined specimens. These changes are not uniform but sporadic, a few tubules here and there being affected, while others in their neighborhood remain perfectly normal. The tubules thus altered, are few in number compared to those which remain unchanged. The convoluted tubules are more frequently affected than the straight, though the latter are by no means exempt. Those tubules in the immediate neighborhood of the Malpighian bodies seem especially liable to alterations of their contents. These alterations consist of cloudy swelling and granular degeneration of the epithelium, the cells breaking up into a mass of small dark granules which occasion
more or less blocking up of the lumen. Talty, degeneration also, is a change of
still more frequent occurrence. (See Drawing B). It often appears to begin in the
nucleus of the epithelial cells, (see Drawing H), and is rendered very evident by
staining with Osmic acid. Red blood corpuscles and leucocytes are frequently
seen inside the tubules. Their presence may have something to do with the
causation of the intratubular alterations, which are to be regarded as secondary
to the interstitial changes, and may be accounted for both by the entry of
blood cells into the tubules, and also on the score of deficient blood supply
due to the pressure exercised by the small cell tissue both on the glomeruli
and also on the intertubular arterioles and capillaries. Direct pressure
on the tubules themselves, must also not be lost sight of in estimating the
causes of secondary intratubular alterations.

Dr. Klein agrees with the author in regarding the intratubular changes as
secondary, for he says, "This (i.e., the parenchymatous change) becomes distinct
after the interstitial changes have reached a certain degree, and they (i.e.)
are quite insignificant before this degree of interstitial nephritis is attained."
And again, "The more intensive (i.e.) the degree of interstitial change, the
more marked is the enlargement of the kidney, and the more distinct is the
parenchymatous nephritis, the number of urinary tubules which either contain casts or are in process of destruction by being flooded
with the inflammatory products (especially cells) increasing gradually.

It follows from this that the intensity of the parenchymatous change
is dependent upon the degree of the interstitial nephritis." (op. cit.)

In the author's three cases he has not noticed any deposit of lime in the
epithelium or lumen of the urinary tubules (Klein).

The changes just enumerated are most conspicuous and widespread.
in the cortical portion of the kidney, though the medulla is by no means exempt.

Dr. Klein considers the nuclear increase on the surface of the glomeruli
tobe due to a proliferation of epithelial nuclei; but as mentioned by
Klebs, these bodies differ from epithelial cells or nuclei alike, in form and in
anatomical site. They are situated between the vascular loops as well as
on their surface, a fact which is alone sufficient to negative the
supposition of their epithelial nature. Dr. Klein also states that in the course of
his investigations he has never seen any accumulation of these cells within the
Malpighian capsules in such numbers as to be likely to cause compression of
the vessels of the glomerulus and consequent interference with the circulation.

He admits however that his cases were probably different from those described
by Klebs. Of this there can be no doubt; for a very cursory inspection of the
authors specimens will suffice to confirm the accuracy of Klebs description,
and to demonstrate beyond doubt the immense obstacle which the excessive
nuclear proliferation must of necessity occasion to the free passage of blood
through the capillary loops. Indeed a more favourable condition for the
development of amenia, pyemia and acute dropsy could scarcely be imagined.

The principal changes just described may be thus summed up briefly:

...
Summary

A. Special Changes

1. Increase of nuclear bodies, probably leucocytes and proliferated connective tissue corpuscles inside Bowman's capsule on the surface of the glomerulus, in such quantity as to be likely to cause serious circulatory obstruction from pressure on the vascular loops.

2. Thickening and nuclear infiltration of the substance of Bowman's capsule.

3. Great accumulation of nuclear bodies in the immediate neighborhood of the outside of Bowman's capsules.

4. Fibrous degeneration of the vascular loops of the glomeruli, probably consequent on pressure and obstructed circulation.

B. General Interstitial Changes, etc.

1. Appearances consequent on general interstitial nephritis, namely, dilatation of capillaries with accumulation of leucocytes in their interior; migration of leucocytes through the vascular walls, and interstitial increase from small cell infiltration.

2. Small hemorrhages, interstitially, into the interior of Bowman's capsule.

3. Embolism of an artery in a single instance.

C. Secondary Intratubular Changes

1. Sporadic Parenchymatous Nephritis, chiefly in those tubes in the immediate neighborhood of the Malpighian bodies, with (a) cloudy swelling, (b) granular degeneration, and (f) fatty degeneration of the tubular epithelium.

2. Presence of leucocytes, red blood corpuscles in the interior of the unisierous tubules.
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Gayley, " " Vol. 21 page 250.


Klein, " Soc. Trans. 1877.

Wilks, " " Vol. 6, page 264.
- Additional Note On a Fourth Case of Glomerulo Nephritis.

Since the above note was written, the author has received another specimen of Glomerulo Nephritis from his friend, Mr. James Rodger, Pathologist to the Aberdeen Infirmary. A series of sections from this kidney are included in the accompanying collection (Series D). They will be found very interesting and rather curious, especially when considered with reference to the history, which though somewhat scanty and meagre is as far as it goes authentic being extracted from the Post Mortem Record of the Aberdeen Infirmary.

A boy aged 8 years was admitted into Hospital in the acute stage of Parenchymatous Nephritis. His previous history was doubtful and unsatisfactory though it was supposed that the attack occurred as a consequence of Scarlatina. The boy remained in Hospital for 3 months, during the whole of this time his urine was albuminous, and he suffered from more or less renal dropsy. At the end of that time he died. On post mortem examination the liver was found highly fatty and yellowish, and the kidneys enlarged and pale. There were some other remarkable changes. Dr. Rodger described the kidneys as examples of "Nephritis, parenchymatous as well as interstitial perhaps," a guarded opinion beyond all nothing more could be said with certainty without a further microscopic examination.

The author received this kidney a month ago, among a number of other specimens, for microscopical examination. It was then almost fresh and far too soft to admit of cutting in the freezing microtome. He was therefore compelled to place it in...
Gromic Acid for a month. Previously, however, he cut a few small hand sections which enabled him to make out the general condition, and from these he at once ascertained beyond doubt that the specimen was one of glomerulo-nephritis, though in a somewhat unusually advanced stage.

The foregoing history is peculiar and a little puzzling. It appears that the boy lived three months after an attack of supposed parenchymatous inflammation. The clinical symptoms of his disease would be extremely interesting, and the author has written to inquire particulars. According to his experience, glomerulo-nephritis is not a common disease, which is fortunate, as it appears generally to end fatally, the immediate precursor of death being anuria, azoemia, and acute dropsy. Indeed the anatomical features plainly show the gravity of the disorder. Most of the glomeruli are compressed by an abundant cell infiltration inside Bowman's capsule, which interposes a serious obstacle in the way of renal circulation and secretion. But further, if we take into consideration the chances of an ultimate restoration of the glomeruli to their normal condition, our prognosis cannot fail to be very guarded. A large quantity of granulation or embryonic material occupies the interior of Bowman's capsule and compresses the vascular loops, in a varying degree in different Malignant bodies, but to such an extent as to render the majority of them well-nigh impermeable. Now when the lesion is thus far advanced, it is an open question whether the glomeruli would ever again become perfectly normal and
even if the obstructing materials were quickly and entirely removed; how much more so then, is their restoration doubtful, when such a speedy removal is as far as we can see impossible?

We may reasonably conjecture that the mass of granulation tissue inside Bowman's capsules follows as a rule one of two courses. The author's observations incline him to think that in those cases where the fatal termination is delayed long enough the compressed and impervious glomeruli generally become fibrous as stated on Page 123, the number of granulation cells on the surface of the fibrous capillary loops becoming at the same time greatly diminished. (See Drawings 8, 9 & 10, Series Glomerulo Nephritis). Dr. Wilks however (Path. Soc. Trans. vii, 264) describes a curious case in which the Malpighian bodies were totally degenerated; and it is possible that fatty degeneration may occasionally supervene in the excised cells of the nuclear tissue, involving also the impervious and functionally necrotic glomeruli. The author is inclined to think that the entire removal of the nuclear proliferation through the urine, tubules, is a result, by no means the least of its problems. If therefore the patient survives long enough, it appears reasonable to suppose that the nuclear tissue inside Bowman's capsule will undergo change either fibrous or fatty, neither of which in the case of such important secreting structures as the Malpighian bodies are favourable to the chance of ultimate recovery. In this case, we shall presently see, there was very general fibrous change, though the patient continued somehow to exist in spite of it for the comparatively
long periods of three months.

The author has scarcely sufficient experience to warrant his regarding an opinion as to the mode in which recovery is affected from an attack of Glomerulo-nephritis. He may however state his present belief that recovery from an undoubted attack is very rare. One supposed case within his knowledge did certainly escape for a time the payment of the universal debt, but in this case the accuracy of the diagnosis was in his opinion open to question. - Further evidence on this point, culled from an extended series of clinical and pathological observations is much needed. Even the condition itself has as yet attracted but little attention; though eight years have elapsed since the publication of Klebs' description. - The author believes that it is quite capable of being diagnosed during life. In those cases seen by him (two in number) the invasion of the symptoms was sudden and characteristic, and in one case he was enabled to predict a fatal result, a prophecy which unfortunately proved only too accurate. If after an attack of Scarletina we meet with albuminuria, accompanied with suppression of urine more or less complete, purulent symptoms, and acute dropsy, the medical attendant may be pretty sure that he has to do with a case of this nature.

Why the Scarletinal poison should especially affect the connective tissue of the Glomeruli, which is exempt in the ordinary variety of interstitial nephritis, we can only conjecture, though this fact seems to confirm the old view of an attempt at elimination.
of the poison through the medium of the Kidneys. The subject offers a wide and promising field for future investigation.

The accompanying sections were cut in the freezing microtome on the 26th April in order to admit of their being sent in on the 30th, with the rest of the specimens illustrative of this Thesis. The Kidney was not at that time quite sufficiently hardened, and as a consequence the Epithelium is in some places disturbed in the tubules and loosened from the basement membrane, a fact which must be remembered and allowed for in estimating the character and extent of the intratubular changes.

The first noticeable alterations visible on examination with a low power are the readiness with which the glomeruli about the colouring matter, the thickened appearance of their capsules and the increase in width of the intertubular septa in their neighbourhood.

On examination with a high power Bowman's capsule are seen to be very generally thickened, the thickening being in the majority of instances of a character rather fibrous than cellular. The interstitial tissue around the outside of the capsule is as a rule increased, and includes tubuli more or less compressed. The glomeruli are variously altered. Very frequently the whole Malpighian body is much reduced in size, the vessels of the glomeruli being immensely fibrous looking, and united with the thickened capsule into a solid fibrous mass. Sometimes, the glomeruli consist...
a tendency to become colloid. Again the vascular loops are often reduced in size, shrunken, and fibrous, not only not filling up the whole interior of the capsule as in the other three cases, but occupying less space than the normal glomerulus. The interval between the shrunken glomerulus and the inner surface of the capsule is usually occupied by a few nuclear bodies, though the number of nuclei inside the capsule is not nearly so large as in the cases before described. In the preceding chapter it was stated as probable that in proportion as the fibrous change proceeds in the vascular loops, the number of nuclear bodies on their surface and between them diminishes, and confirmation of this opinion seems to be afforded by the present case.

It is highly probable that this specimen is similar to some of those described and figured by Dr. Klein (Path.: Doc. Trans. 1877). The number of nuclei inside Bowman's capsule is not very great; and were it not for our knowledge of the more typical condition, they might be easily thought to be of an epithelial nature as Dr. Klein considers them. After dissection of this kidney Dr. Klein's statement that he never saw nuclei present inside Bowman's capsule in sufficient quantity to produce compression of the glomerular vessels becomes quite intelligible.

There is a good deal of small-cell infiltration around the Malpighian bodies, but the increase in the neighbourhood is as a rule more fibrous looking than in the three former
series. Indeed the whole aspect of the changes seems to point to the fibrous transformation of a previously edded small cell formation, an interpretation which is constant ly the history.

Some glomeruli are converted together with their capsules into a fibrous mass interspersed with a few round cells, and blue slightly with reagents. These are only distinguishable from a patch of interstitial tissue by the preservation of an obscure concentric arrangement.

Few glomeruli are even approximately normal, and it is rather surprising considering their condition, that life should have been prolonged for three months from the first occurrence of the attack. The youth of the patient probably operated in his favour.

As before stated, the interstitial stroma is increased, especially in the neighbourhood of the Malpighian bodies. The tubules included in the interstitial tissue are somewhat compressed as in the ordinary variety of interstitial kidney. Of the precise nature of the intra-tubular change, the author would not like to speak positively, as he considers that the tissue is not quite sufficiently hardened to yield perfect trustworthy results. The number of empty tubules does however appear greater than could be accounted for by the falling out of the epithelium from insufficient hardening. Scattered parenchymatous changes are noticeable here and there, and a few tubules contain colloid matter.
The vessels appear to be perfectly normal. There is but little interstitial increase around them; their adventitia is natural, the muscular coat is not hypertrophied; and the intima is normal in thickness, and presents no hyaline or other changes.

With the preceding rather hurried synopsis of the morbid appearances visible in this interesting kidney, the author now begs to conclude his Thesis. He cannot flatter himself that he has at all times done sufficient justice to a subject which affords scope for half a dozen monographs like the present;—but where he has failed he can only crave indulgence in the words of the famous historian of the Canterbury Pilgrimage

"For every word men may not chide or praise,
For in this world certain me neither there is
That he ne doth or sayth sometime amis."

29th April 1879.  Finis.