Nicholls (A. G.)

A CONTRIBUTION TO THE STUDY OF BRIGHT'S DISEASE WITH SPECIAL REFERENCE TO THE ETIOLOGICAL RELATIONSHIP OF THE BACILLUS COLI.

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A CONTRIBUTION TO THE STUDY OF BRIGHT'S DISEASE WITH SPECIAL REFERENCE TO THE ETIOLOGICAL RELATIONSHIP OF THE BACILLUS COLI.

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There is scarcely any subject in the realm of medical pathology which has been more carefully and persistently studied than Nephritis. Yet there is no disease, unless it be cirrhosis of the liver, which is more obscure.

From Bright onward, careful observers like Rokitansky, Ziegler, Weigert, Klebs, Ewald, Grainger-Stewart, and Wagner, have investigated the subject. Valuable experimental studies have been made by Grawitz and Israel, Ponfick, Aufrecht, Litten, Roberts, V. Kahlden, Pernice and Scagliosi, which have materially increased our knowledge. But while the histological features of the disease are well known, and have been accurately described, and the clinical features of the various stages are in a general way understood, the ultimate nature of the process is still a mystery.

With regard to acute nephritis, upon which there have been multitudinous studies of late years, we have probably attained something like the truth—the whole series of "infections" and mineral or other toxins being the etiological factors concerned in the vast majority if not in all the cases. The origin, however, of the chronic forms and their relationship or otherwise to the acute stage, may be said to be largely unknown.

The clinical symptoms, the character of the urine, give us merely the roughest sort of information, and every pathologist knows how difficult it is to predict the actual condition of the kidneys from the clinical ex-

amination in any given case. Indeed the confusion of the whole subject may be inferred from the numerous attempts at a rational classification of the various forms of kidney inflammation, which have been proposed, all of which differ more or less in important particulars.

This, I am inclined to think, is the result of too limited a view, and the failure to realize the different factors in the problem. To have any degree of comprehension of the disease, clinical studies, histological examinations, bacteriology, and experimental work, must be laid under contribution.

Acute inflammation of the kidneys is now said to be the result of the following conditions:—

1. Intoxication, e.g., from bacterial toxins, alcohol, lead, cantharides, phosphorus, chlorate of potash, salicylic acid, etc.

2. Complication of :—(a), The acute infections, as, scarlatina, smallpox, pneumonia, acute rheumatism, erysipelas, endocarditis, typhoid, diphtheria, septicæma, cholera, epidemic cerebro-spinal meningitis, gastro-intestinal disorders, etc. (b), Chronic diseases and cachexias:—arterial sclerosis, diabetes, syphilis, pulmonary phthisis, carcinoma, etc.

3. So-called "idiopathic" cases.

In prosecuting the study of such a subject it is well to remember that the kidney is not the sole field of observation, but that the participation of the blood, the vessels, and other organs, in the process should be taken into account. We should too, I think, separate from true "nephritis" or inflammation of the kidney, that whole group of cases classed under the first divison which are really "degenerations" of the kidney epithelium, and are not properly inflammations at all.

There is abundant evidence to prove that the toxic substances above mentioned do bring about degenerations of the nature of cloudy swelling, fatty degeneration, or even necrosis, in the epithelium of the secreting tubules.

Moreover, it has been established by experimental studies, notably those of Wandervelde (Act. d. pois sur les cell. epithél. n. canalicules contournées, Brux., 1894), that toxins such as those of cholera, cholera nostras, tuberculosis, diphtheria, pneumonia, influenza, and chemicals, such as chromic acid, lead, phosphorus, mercuric chloride, when injected into animals exert through the blood-stream a harmful influence upon the secreting epithelium bringing about changes identical with those found in the human subject.

Still it must be emphasised that such changes do not constitute nephritis, and since inflammation in the organism is so rarely dissociated from bacterial invasion, it may well be doubted whether when inflammation does supervene, it is not of the nature of a direct infection.

In the case of true acute nephritis, the trend of the investigation of the past 15 years points strongly to the unity of the process as a result of various microbic infections. The varieties of these are numerous.

Bouchard, (Des néphritis infectieuses, Rév. de Méd. 1, '81), in nine cases of typhoid with nephritis that came to autopsy, found the specific bacillus in every one and in several other living cases found the germ so long as the albuminuria persisted. But since this investigation was six years before the full studies of Gaffky on the bacillus, there may be some little doubt as to the value of the results.

Letzerich, (Untersuch. u. Beobacht. ueber Nephritis bacillosa interstitialis primaria. Zeitschr. f. klin. Med. Bd. 13, '87, S. 33.) described an epidemic of acute intersitial nephritis with the ordinary clinical symptoms which was due to a bacillus resembling the B. tuberculosis, but shorter. Injected into animals it produced nephritis.

Mannaberg (Zeitschr. f. klin. Med. '90), in fourteen cases of acute Bright's in acute endocarditis, found streptococci in the urine which he was unable to find in the urine of other cases after a prolonged investigation.

That acute nephritis could be epidemic apart from any relationship with scarlatina, was shown by Fiessinger (Ga. Méd. de Paris. Oct. 10,'01). Acute nephritis has also been known to follow infected wounds of the skin, impetiginoid eczema, pemphigus, vaccination, acute tonsillitis and various lesions of the alimentary tract. Among the bacteria which have been recently shown to produce acute nephritis, are the B. Typhi, the diplococcus lanceolatus, meningococcus intracellularis, B. Friedlanderi, streptococcus pyogenes, staphylococcus albus and aureus, and the B. Coli.

The condition is to be regarded as an attempt on the part of the kidneys to eliminate the toxins and micro-organisms of the various diseases. That the kidneys do excrete bacteria even in the absence of gross lesions of the organs is amply proved. Weichselbaum (Wiener med. Woch. No. 41, 1885), in a case of ulcerative endocarditis found streptococci and staphylococci in the urine; the B. Typhi is found in the urine in quite a large percentage of cases, and numerous other germs have been found in various diseases.

The best statistics on Bright's disease are those of Agnes Bluhm (Ueber die Aetiologie der Nephritis, D. Arch. f. klin. Med. Bd. 47, '90.) Of 140 cases of acute Bright's disease, 70 per cent. could be traced to acute infections. Only 2.85 per cent, were directly traceable to cold. One of the cases followed acute ileus.

The acute nephritis of the infections is of various types. At one time, degenerative processes in the secreting epithelium predominate, such as extreme cloudy swelling, fatty degeneration, desquamation, and imperfect nuclear staining. At another, the brunt of the toxin falls upon the glomeruli bringing about effusion into the Bowman's Capsules, congestion of the glomerular capillaries and shedding of the capsular epithelium; or occasionally small-celled infiltration into and about the Bowman's capsules. Or at still another, an acute interstitial infiltration of

leucocytes with œdema of the boundary layer (the "lymphomatous" nephritis of Wagner). Lastly, all three may be combined. The first form is most common, but the type seems to depend upon the nature of the infection. The tendency of scarlatina for instance, to cause a glomerulonephritis or an acute interstitial inflammation is well known.

Occasionally the primary infectious diseases are ushered in by an acute nephritis, which may predominate the clinical picture, as in the so-called "renal typhus." Generally, however, the cases occur late on in the course of a specific infection, and are to be regarded as complications due to the effort at elimination. They are probably exaggerations of the common conditions of cloudy swelling, between which and true inflammation, no hard and fast line can be drawn. Again, some of these cases may be the result of a mixed infection.

Further, all grades of severity exist, from a mild inflammation up to a true local suppurative condition. The infection may be in some cases an 'ascending' one from the bladder, but more commonly a 'descending' one from the blood-stream. Only on the latter supposition can we explain the nephritides which occur in skin affections, anginas, and intestinal disorders.

It should not be forgotten than an acute attack may be grafted upon a chronic nephritis which was unsuspected, thus simulating a primary attack. ("Acute recurring nephritis" of Wagner.)

The idiopathic cases are those which occur in previously healthy persons; often the only causes that can be assigned are chilling of the body, or excessive exercise in the cold. This form is especially apt to occur in alcoholics. That there is some relation between the skin and the kidney seems clear.

The etiology of these and the forms occurring in chronic disease will be discussed later.

When we come to consider the production of chronic nephritis the task becomes more difficult. It is usual to teach that the acute cases may become chronic, and that the cirrhotic kidney is an end-stage of the chronic parenchymatous nephritis, or is due to arterial disease, or again, to certain poison, as alcohol, gout, and lead. (The "primare Schrumpfniere" of the Vienna School.) This does not, however, explain all the cases; cases of contracted kidney occur where there was no history of any acute attack, and run an insidious course. And again, cirrhotic kidneys may occur in children, where there could be no question of arterio-selerosis or chronic intoxications from mineral substances.

Further, the cirrhotic kidney has been known to result from infective diseases, as pneumonia (diplococcus), and influenza. The etiological elements in this form then seem to be very various, and the course apparently without any fixed rule.

While it is generally admitted that acute nephritis is in the immense majority of cases, due to some infective agent, as yet, I believe, no one

has ventured to say that chronic Bright's disease is due to the direct action of bacteria.

Holst, indeed, is inclined to support the view that microbes by their toxins are able to produce nephritis without being present in the kidney *per se*, and that the action may appear late or after the primary infection has disappeared, thus producing the chronic disease. But this view does not seem consistent with the facts. Recent investigations, almost without exception, go to show that in acute nephritis microbes are present in the kidney. In the case of pneumonic nephritis, Massalong and Klebs frequently found the diplococcus lanceolatus in the kidney. Michelle, too, (Morgagni, Aug. 1896), in 19 cases found the pneumococcus in 18. In six cases of acute nephritis, and acute nephritis grafted upon chronic in pneumonia, I have found the diplococcus in every one.

Councilman (Trans. Assoc. Amer. Phys. Vol. xiii., 1898.), records the following results:—

42 cases of acute interstitial nephritis were examined bacteriologically post mortem.

In 24 diphtheritic cases the kidney was sterile in six.
- In 11, the B. Coli was found.
- In 5 the streptococcus pyogenes was found.
- In 1 the streptococcus aureus was found.
- In 8 the diphtheria bacillus was found.
- In 1 the B. Foetidus was found.

In 5 cases of scarlatinal nephritis.
- In 3 the streptococcus.
- In 2 the B. Coli.
- In 1 the staphylococcus.

In 8 of mixed infection of diphtheria with scarlatina or measles.
- 2 cultures were sterile.
- 3 the streptococcus.
- 3 the B. Coli.

In other six cases:—
- 3 the B. Coli.
- 2 the staphylococcus aureus.
- 4 the streptococcus.
- 1 the pneumococcus.
- 1 sterile.

He does not regard the presence of the colon bacillus found under such conditions as of much etiological value. He obtained the same results in the kidneys in the same diseases, in which no interstitial nephritis was present.

Thus he concludes that no weight could be laid on the presence of

bacteria in the kidneys as a causative factor in the acute interstitial lesions.

This conclusion does not seem to me to be warranted for it is amply proved that in these specific diseases germs are to be found in the urine where no gross lesion of the kidneys exists, at least clinically, and the production or not of nephritis depends on the correlation of several factors, outside of the mere presence of bacteria.

With a view of gaining further information and ascertaining whether bacteria were present or not in the various forms of Bright's disease, I have availed myself of the pathological material of the Royal Victoria Hospital from about 325 autopsies and also the clinical notes of all the cases of nephritis in the Wards for the past four years.

In approaching this investigation, I have thought that more valuable information would be attained by examining sections of kidneys which presented evidence of nephritis microscopically, in addition to those which were taken from cases which were recognised clinically. For by this means one gets a wider view of the subject, inasmuch as the study embraces all grades of the disease from the incipient forms up to the most advanced stages. Particularly valuable is the study of the early stages since it is only thus that a true appreciation of the process can be formed.

Sections were made from 105 kidneys presenting the varous forms of nephritis. All cases in which there was cystitis or any evidence of an "ascending" infection, or local tuberculosis, were excluded as unnecessarily complicating the subject.

Some of the material of the early years was hardened in Müller's fluid, so that many kidneys presented evidence of post mortem growth of bacteria, these were excluded in drawing conclusions. The material, however, which was hardened in Formol-Müller was satisfactory. All cases in which there was clearly a terminal infection as shown by plugs of bacteria in the capillaries were also excluded.

The method of staining was as follows:—

Celloidin sections, cut as thin as possible, were placed in carbolthionin for from 12 to 24 hours in the incubator. The formula of the stain was:—

Solution of carbolic acid, (1—40) 100 cc.
Thionin,..... 1 gramme.

Filtered as used.

The sections were then decolorised in weak acetic acid, dehydrated in aniline oil, washed in xylol and mounted in balsam.

Those sections in which pus cocci, or micro-organisms positive to Gram, were suspected, were also prepared by the Gram-Weigert method. The results were very satisfactory. Carbol-thionin is certainly the best

stain for bacteria in tissues that I have employed. The sections were examined by 1-18th Reichert oil-immersion lens and No. 4 eye piece.

The classification that I have adopted of the various forms of the disease, is purely a histological one based mainly upon my own investigations, but is practically that of the German School. The division is as follows, it being premised that is somewhat arbitrary, the various forms passing imperceptibly one into the other, the predominant feature being taken as the guide.

1. *Acute Parenchymatous Nephritis,* in which there was degeneration of the epithelium of the secreting tubules as evidenced by cloudy swelling, desquamation of cells, exudate, and imperfect staining of the nuclei, often with casts. It includes hæmorrhagic cases.

2. *Acute Interstitial,* in which there was an acute leucocytic infiltration about the glomeruli or in the lining cells of the Bowman's capsules tween the tubules, without grave degenerative changes in the tubular epithelium,

3. *Acute Diffuse,* where the first two forms were combined.

4. *Acute Glomerulitis,* evidenced by congestion of the glomerular capillaries, desquamation of the lining cells of the Bowman's capsules with effusion and exudation into the capsules.

5. *Chronic Parenchymatous,* in which there were marked degenerative changes in the secreting cells, but with a tendency to connective tissue proliferation; haemorrhagic cases included.

6. *Chronic Diffuse,* where the fibrous hyperplasia had progressed still further, bringing about atrophy and dilatation of the tubules with sometimes hyaline degeneration of glomeruli with periglomerular fibrosis.

7. *Chronic Glomerulitis,* a sub-variety in which the glomeruli showed predominantly, degeneration, atrophy and periglomerular fibrosis.

8. *Chronic Interstitial,* the terminal stage of the chronic diffuse, where the secreting cells were extensively atrophied with cystic dilatation of the tubules, sclerosis of the glomeruli and extreme fibrous proliferation.

9. *Arterio-Sclerotic and Senile,* where the process was most marked in certain vascular districts.

10. *Amyloid Fatty Kidney,* a combination of amyloid disease and parenchymatous degeneration.

11. *Amyloid Contracted Kidney,* amyloid disease in a cirrhotic kidney.

This classification is intended merely to afford a convenient division for the purpose of the present study.

In all, 105 specimens were examined and classified as follows, 28 being excluded for the reasons mentioned :—

Acute parenchymatous	26	Chronic glomerulitis	1
Acute interstitial	3	Chronic interstitial	10
Acute diffuse	4	Arterio-sclerotic and senile	13
Acute glomerulitis	0	Amyloid fatty kidney	2
Chronic parenchymatous	8	Amyloid contracted kidney	0
Chronic diffuse	11		

The results were very striking. Analysis of the different classes gave the following:—

Disease.	No. of Cases.	Bacteria Found.	Negative.
Acute Parenchymatous:			
Typhoid	5	B. Typhi 2, B. Coli (?) 2	1
Ulcerative Phthisis	5	Diplococci and Bacilli 2	3
B. Aërogenes Capsul	2	B. Aërogenes 2	0
Diabetes	1	Diplococci with halo; very small, 1	0
Lobar Pneumonia	2	" Lanceolatus 2	0
Mitral Stenosis	1	" with halo, 1	0
Diphtheria	1	B. Löffleri and Cocci 1	0
Pyemia	1	Staphylococci, 1	0
Eclampsia	1	Long B. with rounded ends, B. Coli (?) 1	0
Puerperal Septicæmia	1	Staphylococci and B. 1	0
Epid. Cerebro-Spinal Meningitis	1	Diplo. Intracellularis, 1 (Weichselbaum)	0
Acute Interstitial:			
Lobar Pneumonia	1	Small Diplo. (?) Diplo. Lanceolatus;	0
Pyemia	1	Cocci and Bacilli	0
Puerperal Septicæmia	1	Cult. gave Streptococci	0
Acute Diffuse:			
Cancer with septic peritonitis	1	Diplo. in cultures. 1	0
Typhoid	2	B. Typhi in areas of infiltration,	0
Lobar Pneumonia	1	Diplo. Lanceolatus 1	0

Of the 32 acute forms of various kinds, bacteria, generally the specific germs of the disease, were found in 28. The overwhelming proportion of positive results leads me strongly to the conclusion that in the vast majority of cases, if not in all, acute nephritis is due to the presence of specific microbes. That there were four negative results does not invalidate the conclusion, for the infection being embolic it is very probable that in such kidneys there are sporadic areas of inflammation surrounded by comparatively healthy tissues. Indeed, this sporadic form is recognized by several of the recent French observers, and is quite analogous to embolic suppurative nephritis.

It is suggestive that minute diplococci with halos were found in one case of pancreatic diabetes, and in one of mitral stenosis with passive congestion of the intestines, while in an eclamptic patient, bacilli were found strongly resembling the B. Coli. The significance of this will be seen later.

In the eight examples of chronic parenchymatous nephritis, four showed minute diplococci with a delicate halo mostly between the lobules in the cortical area. Of these one case, which was associated with *Atrophic Cirrhosis* of the liver, showed a few well marked minute diplococci with a halo. In two, one an alcoholic kidney, bacilli of doubtful nature were seen. Two others gave negative results.

The chronic glomerulitis case showed a slight acute interstitial in-

flammation as well, and a few rare diplococci were seen. The primary disease was septic peritonitis.

The amyloid fatty kidneys showed no germs.

Still more interesting and suggestive were the results found in the chronic diffuse, chronic interstitial, and the arterio-sclerotic type of the disease.

In the chronic diffuse nephritis, bacteria were found in all 11 cases. In two there were rather large diplococci, which might be the diplococcus lanceolatus as a lobar pneumonia was present. In five, small diplococci; in four short stumpy bacilli were seen with polar staining closely resembling the B. Coli. These were situated in the areas of round celled infiltration, beneath the basement membranes of the tubules, and in one case within the lining cells of the secreting tubules.

One case, in which the small diplococcus form was seen, was associated with atrophic cirrhosis of the liver.

There were 10 cases of chronic interstitial nephritis. In all were found the minute diplococci with a halo, mainly in the areas of round-celled infiltration, some few within the Bowman's capsules, and in one case within the cells of the tubular epithelium.

Figs. I. and II., Plate 1, show very well the diplococci in the small celled infiltration. In the 13 arterio-sclerotic and senile forms, three gave negative results, but the specimens were very poor; nine showed small diplococci with a halo, chiefly in the areas of round-celled infiltration, and also in one case in a glomerular capillary, in another. within a Bowman's capsule, and in a third with the lumen of a secreting tubule.

In two of the cases besides there were noted bacilli of varying forms. These were diplo-bacilli of small size, very short bacilli with rounded ends, a slender form with polar staining and others, large and curved conforming well to the usual appearance of the B. Coli.

To sum up, in the 45 cases of chronic nephritis of all forms, minute diplococci, as a rule with a distinct halo, were seen in 29, and bacilli having the ordinary appearance of B. Coli in 4 more. In only six were no bacteria seen, but this might easily be due to poor sections or errors in technique, for it is difficult in a large series of sections to get perfectly even results.

These diplococcus forms were very minute and might easily be overlooked with an ordinary 1-12th immersion. Sometimes it could be made out that they were really very short, fine bacilli with polar staining the intervening substances being almost colourless. They were generally in the areas of interstitial round-celled infiltration. Rarely I have seen them within the Bowman's capsules, and within the secreting cells of the contorted tubules ; on one occasion within a lumen. The halo was probably not a true capsule, but due to the effects of refraction.

As to the nature of these diplococcus forms, it may be said that they are identical in appearance and size with the diplococci which Adami has found recently in the liver, associated with progressive portal cirrhosis, and which he has proved to be a variant of the colon bacillus. His very important investigations appeared in the MONTREAL MEDICAL JOURNAL in July, 1898, the British Medical Journal for October, 1898, and the Lancet of August 13th, 1898. He found diplococcus forms in all livers which stained a brownish hue and were probably dead forms, while in atrophic cirrhosis of the liver they were increased in number and stained well. He has, I think, established the fact that these forms are really a modified colon bacillus, and that the liver in health, is constantly excreting them, thus constituting a chief barrier of defence against bacterial infection from the gastro-intestinal tract. In experimental animals he found that in 15 minutes after intravenous innoculation with a pure growth of the B. Coli, the endothelium of the capillaries had enclosed the germs, and in two hours the bacteria were to be found within the parenchymatous cells of the liver. The germs which were of the ordinary colon type presented also diplococcus form. The diplococcus isolated from cirrhotic livers formed very minute colonies on nutrient agar and produced relatively little gas, but in other respects conformed well to the colon type.

With a view to discover if the colon bacillus is to be found in the urine of nephritis cases, I have examined the urine in one case of acute hæmorrhagic nephritis, and in one of chronic interstitial. The method employed was to sterilise the meatus and glans penis then to allow the patient to pass several ounces of urine and collect the residue in sterilised flasks. These were then sealed and placed in the incubator for 48 hours. In the first case I obtained the colon bacillus, but it died out rapidly, and I was not able to study it very closely.

In the second case, the chronic interstitial, various forms were found as seen in Fig. I., Plate II. These were stout bacilli, either straight or curved with rounded ends, some with polar staining ; they all resembled the ordinary colon forms. Besides these there were small ovate bacteria, and shorter more delicate bacilli with polar staining. There were also short chains composed of very short bacilli with rather blunt ends showing polar staining. All were negative to Gram. A broth transfer was made and after 48 hours all the usual forms of the B. Coli were seen with the addition of minute diplococci with a halo. These, owing to the crescentic form of the stained portions resembled gonococci. Small diplococci with halos were seen exactly resembling those seen in the sections, also a similar diplococcus, but larger.

When transferred to agar for 48 hours, a thick tallowy growth was produced, and microscopically the germs were short oval bacteria, very small, with the 1-12th oil immersion exactly like cocci ; also numerous

minute diplococcus forms. No bacilli were seen. (Vide Fig. II., Plate II.) This was transferred to a Bouillon made from kidney reacting, 1.5 per cent acid to phenolthalein ; this showed minute diplococci with halos, diplobacilli, a slender bacillus with polar staining and besides these, the ordinary typical colon. (Fig. I., Plate III.)

Cultures from the coccus and diplococcus forms were made on broth, milk, potato, glucose, agar and litmus agar. They showed that in all respects the organism reacted like the B. Coli, with the exception that indol was not produced. Unlike Dr. Adami's diplococcus, this one produced a very heavy growth on agar.

When grown with sterilised bile on agar, the cocci and diplococci seen, were even smaller than those produced on plain agar.

With regard to the presence of B. Coli or other germs in the urine of chronic nephritis, information is lacking, and my investigations on this point are still going on, being hampered at present for want of enough clinical material. Still, in the cases I have examined I have found the colon bacillus, although as is well known, it is also present in other conditions, notably cystitis, nephrolithiasis and pyelonephritis suppurative. *Fernet* (Bull. et Mém. de la Soc. des Hôp. Paris, Dec. '92), in a case of acute interstitial nephritis occurring two months after an abortion, found the B. Coli in great numbers in the urine.

Several observations have been made on normal urine to discover if it usually contains germs. The best studies are those of Enriquez, (Recherches bact. sur l'urine normale, Sém. Méd., No. 57, 1891, p. 468,) This author collected the urine in the way which I have employed, and concluded that normal urine was aseptic.

In the urine of 11 healthy people, and five cadavers, the cultures in 10 were sterile, in five staphylococci, and in one, non-pathogenic bacilli were found. These last cases, however, were taken from tuberculous wards, and in two there was a history of previous infection. The urine of seven healthy rabbits was sterile. In the post mortem records I have studied, as a rule, there is no note of cultures taken from the kidneys or urine.

In three cases of tuberculosis of the intestine, the B. Coli was found in the kidney once and in the urine once ; one case sterile. In two cases of typhoid fever, B. Coli in one ; one sterile.

One case of tubercular pyelonephritis gave B. Coli.

One case of nephrolithiasis gave B. Coli.

One case of chronic mixed nephritis with amyloid disease gave the colon bacillus.

The presence of the colon bacillus so generally in the kidneys, which I have studied, receives additional importance from the fact that in this study I have been careful to exclude all cases in which there were cystitis, suppurative pyelonephritis, and tubercular abscesses—conditions

in which there is apt to be an 'ascending' infection with the colon bacillus. We must then conclude that the infection is a 'descending' one by way of the blood stream. That the presence of the colon bacillus is to be explained as a terminal infection or a post mortem overgrowth, I do not believe, for it is easy to eliminate cases of this kind as I did very freely, for the differences are quite distinctive. In ante-mortem terminal infections, the germs are largely in the capillaries, often forming large plugs, and consist of large fat bacilli, short bacilli, or sometimes diplococci, but always much larger and staining more deeply than the diplococcus forms I describe. Further, there is no evidence of inflammatory reaction about these large bacteria, while in the case of the diplococcus, they are enclosed by an inflammatory round-celled infiltration. Neither is it a post-mortem growth, for in this case, the germs are in the superficial cortical layers, and are always much larger and different in appearance and staining powers. Such germs can be seen with an ordinary No. 7 objective, while the diplococcus requires the 1-12th oil immersion at least, or better the 1-18th. Then again, the diplococci are always very few in number, perhaps only five or six in a section.

It is almost impossible to get perfectly normal kidneys in the post mortem room, but I have examined a few for diplococci in which microscopically the tissue showed no abnormality. In 10 such sections, 7 showed no germs; three showed rare diplococci similar to those in the nephritis cases, but on further examination I found that in one case there had been a hernia operation, and there was an acute local enteritis ; in the second there had been a gastrotomy performed, and there was local peritonitis ; and in the third a spina bifida had been removed. Thus in two there could have been infection from the intestinal tract.

That the process in chronic nephritis with productive inflammation is due to an embolic infection, is strongly supported by the histological features in the sections I have studied. The lesions in the chronic forms are identical with those in the acute interstitial as to their anatomical distribution.

In the great majority of the acute interstitial and acute mixed varieties, the areas of round-celled infiltration are to be found around the glomeruli or around the afferent vessels, and interlobular arterioles exactly as would be expected in an embolic infection. The same holds good for the chronic cases. In the arterio-sclerotic type, that the infiltration and proliferation is mostly confined to vascular districts needs only to be mentioned. In the early stages of the chronic diffuse nephritis one sees the inflammatory exudation in the same way about the afferent blood vessels, associated with connective tissue hyperplasia. The cells of the Bowman's capsules proliferate causing atrophy and hyaline degeneration of the glomerular tuft, or we get small fibrous patches about the vessels between the contorted tubules.

In both acute and chronic forms the vessels of the affected areas often show marked congestion. Later on, in the chronic interstitial type (contracted kindey), the fibrous tissue overgrowth is so generalized that this relationship to the blood vessels can no longer be made out. In my series, the process could be accurately followed out.

What is the starting point then of this colon bacillus invasion? The most obvious is the intestine. We have ample evidence that intestinal discorders can cause acute nephritis. It occurs in gastro-enteritis and in Cholera Asiatica, for instance.

Ebstein, (Deut. Med. Woch., June 15th, 1897), discusses acute nephritis as a complication of chronic gastro-enteritis. In a case he records in a woman of 27, there was a history of diarrhœa for nine months previously, pain in the epigastrium and anorexia, for six. The nephritis came on most acutely, and was fatal in a few days from eclampsia, coma and collapse. At the autopsy acute nephritis was found, a tape-worm in the intestine, acute follicular ulcerative enteritis and enlargement of the mesenteric glands. The spleen was normal. Influenza and all other infections as a cause were excluded and Ebstein concluded that the condition was due to an intoxication from the intestine.

Dupeu, (Acute Nephritis in Children.—Journ. de Méd., July 10, '97), states that acute nephritis may be a result of ordinary gastro-intestinal intoxication, particularly when there is dilatation of the stomach. It has been observed in children as young as 11—16 months fed by the bottle, and in whom vomiting and diarrhœa were prominent symptoms. In these cases it may last 2—4 weeks and present all the usual features of Bright's Disease.

With a view to determine the relationship, if any, of various gastro-intestinal disorders to nephritis, I have examined carefully the clinical records of the Royal Victoria Hospital for the past four years, having access to these through the courtesy of Prof. Jas. Stewart. In making the estimate I have been careful not to accept as an etiological factor the nausea, vomiting, and diarrhœa, which so often usher in or complicate an uræmic attack, but I have endeavored to find out if there was any history of such disorders existing for lengthened periods which might reasonably be regarded as of etiological moment.

There were 71 cases of nephritis of various forms divided according to the reports as follows:—

Acute Parenchymatous Nephritis	10
Sub-acute Parenchymatous	15
Chronic Parenchymatous	17
Chronic Interstitial	29

The etiological factors were:—

Chronic Alcoholism	15 times
Dyspepsia, (Gastro-enteritis, nausea, Vomiting, etc)	15 times

Infectious Diseases, (Influenza, Acute Rheumatism, Diphtheria, Typhoid).....	11 times
Exposures to wet and cold or to extremes of temperature	5 times
Appendicitis..	Once
Puerperal Eclampsia..	Twice
Gastralgia	Once
Acute Gonorrhœa	Once
Chronic Gonorrhœa..	Once
Insidious, (No definite cause)..	22 times

Thus it will be seen that of the 71 cases studied, 29 were subsequent to gastro-enteric disturbances, assuming as one fairly may that such would be present in the chronic alcoholics. This is a percentage of 40.84 per cent. of all cases. Excluding the acute cases due to the various infective fevers in which the etiology is quite established, the proportion becomes 50 per cent. In 30.98 per cent., the onset was insidious, and no cause could be assigned.

These facts go far to show that there is a definite relationship between nephritis and disorders of the alimentary tract, for when we consider that there were in the records no special investigations made to establish such relationship, but merely the ordinary routine investigation, the above figures become invested with even greater importance. Further, there were very few of these gastro-intestinal disorders acute in character, but in most there was a history of such symptoms extending over periods of months or years.

It will be interesting to examine the cases divided according to their clinical types in relation to previous lesions of the gastro-intestinal tract.

In the 10 cases of acute parenchymatous nephritis, no cause could be assigned, in 3, there was a history of :

Acute Tonsillitis (Rheumatic) in..	1
Extremes of Temperature, etc., in..	1
Acute Rheumatism, in..	1
Acute Infections, in..	3
Gastro-Intestinal Disturbances, in....	1

In the 15 sub-acute parenchymatous nephritis, the causes were:—

Acute Gonorrhœa, in..	1
Exposure to wet and cold, in..	2
Alcoholism (1 case with hernia)	3
Mild Dyspeptic Symptoms, in..	2
Insidious Onset, in	4
Unknown, in..	1
Puerperal, in.....	1
Catarrhal Appendicitis (?), in..	1

As would be anticipated, the acute infections are the most common causative factors in the acute and sub-acute forms, but in 7 out of the 25. some gastro-intestinal disturbance existed previously.

The etiological factors in the 17 chronic parenchymatous nephritis were :—

Infective Diseases, as Measles, Diphtheria, Mumps, Scarlatina, etc	2
Chronic Alcoholism	5
Wet and Cold	1
Gastro-intestinal Disturbances, (Diarrhœa, Dyspepsia, etc.	5
Unknown	4

In the chronic interstitial types, 29 in all :—

Wet and cold	1
Alcoholism	7
Gastro-Intestinal Disturbances, etc	6
Infections, (Influenza, Typhoid, Diphtheria, Chronic Gonorrhœa, 1 each)	4
Insidious	5
Unknown	6

Clinical evidence then strongly supports the view that Chronic Bright's Disease, and indeed Acute, may be a result of some long-standing gastro-intestinal disorder, 50 per cent. of cases giving this history. thirty per cent. of cases are insidious in onset, all the usual causes being absent; such might be called " Cryptogenetic forms." Can these be due to an infection from the intestine ? It is very probable, but the clinician must further elucidate this point by a more careful study of the history. I certainly have found the diplococcus form of the colon bacillus in several diseased kidneys, where no cause could be assigned for the chronic nephritis, also in the kidneys in one case of cancer of the pancreas, and in one of passive congestion of the intestines.

That albuminuria occurs as a complication of acute gastro-enteritis, chronic diarrhœa, dysentery, and the like, is well known. In 21such cases taken at random from the records, I have found albuminuria in five. Whether this fact is of much significance or not remains to be proved, although certain recent observers insist that all albuminurias are pathological.

But to afford a point of entrance for the B. Coli, a lesion of the intestinal tract is not all. There must be an increase in virulence of the bacillus, and this is the usual condition.

Macaigne, (Arch. Gén. de Méd., Dec., 1896,) has published some important experimental observations. He has found that B. Coli derived from the healthy intestine is harmless in the abdominal cavity, but it

becomes virulent if there is some disorder of the intestinal tract as diarrhœa, constipation, strangulation, etc. He could produce nephritis in animals by intravenous innoculation with B. Coli but usually obtained a suppurative form.

Klecki produced artificially, compression of a loop of intestine in the dog, and found that the virulence of the bacillus taken from this part was greater than that of the germ taken from an uninjured portion.

Sanarelli, (Ann. de l'inst. Pasteur, 1894, pp. 193 and 353), found in guineapigs suffering from typhoid fever, that the virulence of the colon bacillus in the intestine was greatly increased.

Anything then which causes a loss of the lining epithelium of the intestine with increased virulence of the germ, provides the starting point for a systemic infection. That this often happens is beyond doubt. The occurrence of pneumonias due to colon infection is well recognized in strangulated hernia, and in septic peritonitis due to the same germ, the bacillus coli has been found in all the organs of the body including the kidneys.

The usual line of infection is through the mesenteric glands and liver, which thus constitute the first barrier of defence, either through the portal blood or by the bile ducts or both ; further, it may take place through the abdominal lymphatics. Prof. Adami, in his work referred to, has shown that the liver normally contains the colon bacillus, but apparently in a dead state, and this agrees very well with what we have found in post mortems, where we very frequently fail to get germs from the liver. His investigations show that the cells of the liver take up the germs and excrete them in the bile thus rendering them inert.

This view, however, is in seeming opposition to that of Roger, (Sém. Méd., Oct. 19, 1898) who hold the view that the liver is powerless against the colon bacillus, and even assists its growth. His observations, however, were made on experimental animals, with virulent cultures so that the case is not the same as that with which we are dealing. Should the condition mentioned exist so that we get a relatively virulent germ introduced into the liver, then we get local results on the liver leading to parenchymatous degeneration, perhaps cirrhosis, and even to invasion of the systemic circulation. This invasion of the blood stream would, a priori, be more likely to take place the more severe the lesion from which the liver was suffering.

To determine whether there is any connection between hepatic disorders, as for instance, cirrhosis of the liver, and the various forms of nephritis, I have consulted the post mortem records of the General Hospital from 1883 to 1898, to which I have had access through the courtesy of Dr. Wyatt Johnston. In addition I have made use of the Royal Victoria records from 1895 to 1898. In the aggregate there were 1547 autopsies.

Atrophic cirrhosis of the liver, or atrophic cirrhosis with fatty infiltration, occurred 24 times. Associated with these :—

Acute Parenchymatous Nephritis was found.. ..	Twice
Chronic Parenchymatous Nephritis..	Twice
Chronic Diffuse Nephritis..	Once
Chronic Interstitial Nephritis..	15 times
No special abnormality to gross appearance..	4 times

This was a total percentage of 83.30, or Chronic Nephritis only in 75 per cent. Conversely, the proportion of chronic interstitial nephritis in all diseases other than cirrhosis of the liver, was 242 cases or 15.64 per cent.

In three cases of hypertrophic cirrhosis, acute parenchymatous nephritis was present in one ; chronic interstitial in one, and no change in one. These figures speak for themselves.

Further it has been mentioned by several observers that fibrosis of the pancreas often goes with cirrhosis of the liver, facts pointing to a common cause. In the five Royal Victoria Hospital cases, this condition was present in every case. Of course the same infection that would attack the one would be likely to affect the other, the excreting ducts opening so close together. I have also frequently observed that there is a similar relationship between the kidneys and the pancreas in a large proportion of cases.

But while in the case of the liver and pancreas, the infection could be through the ducts, in the case of the kidneys, of course, it must be through the circulatory system. Moreover, it needs only to be mentioned that the toxins which are supposed to bring about nephritis act in a similar way upon the liver. This is seen in the case of chronic alcoholism, and it is far from uncommon to find in the infective diseases such as tuberculosis and typhoid, at one and the same time, an acute infiltration in the portal sheaths and in the interstitial substance of the kidney.

The disease must then be regarded as an attempt on the part of the kidneys to eliminate the bacteria which reach them. Much information on this point may be gathered from experimental work.

As early as 1874, Franke and Gscheidlen, and in 1879, Watson-Cheyne, were investigating the fate of bacteria injected into experimental animals. Their investigations together with those of Cohnheim, proved conclusively that such bacteria were excreted by the urine.

Wyssokowitsch, (Zeitschr. f. Hygiene u. Infectionskr., Bd. 1, '86), after a long series of experiments with various germs concluded that bacteria were only excreted by the kidney when there was some local lesion of the organ, in other words, that a physiological excretion does not exist.

Schweizer, (Virch. Arch. Bd. CX., 1887), on the other hand was of

the opinion that bacteria could pass the kidney epithelium in the absence of any lesions which it was possible to recognize by the ordinary methods.

The majority seem to think that some degeneration of the secreting parenchyma, be it never so slight, is necessary to permit the passage of germs into the urine. Such primary lesions would be afforded by the condition of congestion and cloudy swelling which is such a constant accompaniment of the acute infection.

Pernice and Scagliosi, (Beitrag. zu. Aetiologie der Nephritis. Arch. f. path. Anat., cxxxviii, 3.), injected various pathogenic and non-pathogenic bacteria beneath the skin such as, anthrax, B. pyocyaneus, staphylococcus, and B. prodigiosus. In the kidney they produced hyperæmic endarteritis, and haemorrhage into Bowman's capsules.

These lesions lead to the passing of the bacteria into the tubules and hence into the urine. The presence of the germs in the tubules caused swelling, fatty and hyaline degeneration of the epithelium, later, exudation and casts. The contorted tubules were chiefly affected, but also the straight tubules. Later there was desquamation of cells, collapse of the tubules and hyperplasia of the connective tissue. These authors got the same results with filtered products of growth.

Through the kindness of Professor Adami, I have studied the kidneys in the case of the rabbits inoculated intravenously with pure growths of B. Coli, which he employed in his studies on cirrhosis of the liver. These animals were inoculated in the auricular vein, and then killed at regular intervals.

Rabbit A., killed 15 minutes after intravenous inoculation with pure growth of typical B. Coli.

Microscopically, there were relatively few bacilli found, which were confined to the vessels of the cortical region and the neighborhood of the glomeruli. They appeared as fair-sized bacilli.

Rabbit B., killed 30 minutes after.

The bacteria were found in great numbers in the capsule and as large embolic masses in the arteriæ rectæ of the pyramidal portion. The glomerular tufts contained relatively few. Many could be seen in the perivascular lymph-spaces between the contorted tubules and between the collecting tubules in the medulla. These had the typical appearance. Bacteria could be seen in the endothelial cells of the capillaries, within the secreting cells of the cortical tubules, and in the lumina. When enclosed in cells they were, as a rule, smaller, often appearing as slender bacilli with polar staining, and sometimes as a diplococcus form with a distinct halo. In the cells they stained badly, and seemed to be in a state of absorption. Fig. II., Plate IV.

Rabbit C., killed one hour after.

Bacilli were much fewer in number, being mainly confined to the interlobular and straight vessels, but also being seen as shadows in the parenchymatous cells of the convoluted tubules.

Rabbit, D., killed four hours after.

The bacteria were seen largely in the interstitial substances between the convoluted tubules; many were within the excreting cells showing as faint diplococci or short bacilli with polar staining. Some were also seen beneath the basement membranes of the tubules, and with the lumina.

The glomerular capillaries contained very few. The diplococcus form was noted to be much smaller than the usual colon type. Cultures from the urine were sterile.

Rabbit E., killed 24 hours after.

Marked parenchymatous degeneration of the secreting cells; very few bacteria could be seen, mostly in shadows beneath the basement membrane of the contorted tubules.

These simple facts are in accordance with the observations of Chiari, Adami and others. After the intravenous inoculation of an animal, bacteria are found in all organs, principally the liver, kidneys, spleen and bone-marrow, but after a short time, chiefly in the liver. It is important to note that the endothelial cells of the capillaries and the secreting cells of the convoluted tubules in the kidney, have the power of ingesting bacteria, rendering them for a time, at least, inert. The same thing has been shown by Adami in the liver, when within 15 minutes after inoculation, he observed bacteria within the endothelium, and in two hours within the liver cells themselves. I have seen the same ingestion of germs by the secreting cells of the contorted tubules of the kidney in the case of acute nephritis in lobar pneumonia, and in septicæmia. (Fig. 1, Plate IV.) The tendency of the bacillus to assume a diplococcus form is noteworthy.

Thus the liver and kidney parenchyma are shown to play an important part in the resistence of the organism against bacterial invasion. This resisting power on the part of the parenchyma, however may be diminished in many ways, particularly by chemical and bacterial toxins, thus permitting the more rapid passage of germs through the organs.

Cavazzani, (Ueber die Absonderung der Bakterien durch die Nieren. Ctbl. f. allg. Path. u. path. Anat., iv. ii., 1893), found that after the injection into an animal of toxic substances such as cantharides or pyrogallic acid, the kidneys permitted the passage of bacteria through their substance much more quickly than in the case of animals which were not so treated.

That the kidneys are a most important factor in the elimination of germs from the body is beyond question; they may do this when least

suspected. Enriquez found streptococci in the urine, of a person whom he thought healthy. On more careful examination, however, a minute abscess was found on one finger ; this gave a pure growth of streptococci.

Whether a normal kidney will allow germs to pass through it is a moot point. Orth thinks that it may do so, when no gross esion can be made out.

Neumann and Konjajeff, on the other hand assume that there must be a local kidney lesion. However, this may be, certainly the kidney does permit the passage of bacteria where one cannot find a lesion more severe than cloudy swelling.

It is certain, however, that for a time at least, the kidney cells are able to attack the bacteria, apparently digesting them, and rendering them inert. Later, when the vitality of the excreting cells is sufficiently lowered, living germs are to be found in the urine.

This view is in accord with that of Sherrington, (Journal of Pathology and Bacteriology, Feb., 1893), who found that the escape of bacteria tended to occur in the late stages of a communicated disease, and not immediately upon the introduction of them into the circulation. This means that only after the tubular epithelium has been depressed by soluble toxins, do the cells become pervious to the germs. He, however, concludes that his experiments do not support the suggestion of Cohnheim, that the body protects itself against bacterial action by the excretion of living germs through the kidney and liver.

In the light of the present study we get an entirely new conception of the process at work in the case of Bright's Disease. All cases, acute and chronic, are brought into the category of 'infections.' The nature of the infecting germ varies; in the acute forms it is usually the specific germ causing the primary disease, although in some cases it is the colon bacillus. In the chronic cases, in the great majority, it is the colon which is the infective agent, but there is some evidence to favor the view that a few germs like the bacillus Pfeifferi and the diplococcus lanceolatus are capable of producing fibrosis. Two processes are at work, parenchymatous degeneration and productive inflammation. Parenchymatous degeneration alone is not to be regarded as a true nephritis, but is the result of chemical and bacterial toxins, bringing about injury to the secreting epithelium. Whether inflammatory infiltration occurs in addition or not depends on several factors.

1st, the number and size of the infecting germs.

2nd, the degree of virulence.

3rd, their specific qualities.

If the germs are few in number and of small size, they may pass through the glomerular capillaries, and merely produce degeneration and necrosis without further change. If they be sufficiently numerous to

block the vessels or get into the capillary endothelium, then we get local inflammatory reaction with acute leucocytic infiltration.

A germ of low virulence brings about a low grade of infiltration, but if of high virulence, and in sufficient numbers, extreme degeneration is brought about, and interstitial abscess formation. The inherent quality of the germ is of importance. Thus some germs nearly always bring about suppurative inflammation, while others are more apt to bring about a reparative fibrous hyperplasia. This has been shown recently by Von Wunscheim, in a study of pyelonephritis. When the infection was due to streptococci or staphylocci, suppuration resulted, but when it was due to the B. Coli, he saw distinct evidences of connective tissue production. However, these differences probably have something to do with the virulence and abundance of the bacteria concerned.

In the chronic cases where fibrous hyperplasia is beginning to make its appearance, just as in the leucocytic infiltration of the acute cases, we see the fibrous change beginning about the afferent and interlobular vessels associated with vascular dilatation, followed later by compression and degeneration of the glomeruli, atrophy of the tubules, and the formation of casts. Interstitial proliferation then is the key-note of the process. This proliferation is the more readily brought about since there is present a germ which tends to produce fibrous hyperplasia ; present too, in very small numbers in an infective process probably extending over years. And further, the progressive nature of the lesion is due to continuous action of a germ which has been shown to be present in all stages. I consequently cannot believe as Holst does, that a toxin can go on acting so as to bring about a fibrous hyperplasia, long after the original infection has disappeared. That an infective agent, like the B. Coli, for instance, can be shown to be the corpus delicti, in all the stages of Bright's, explains the anatomical distribution of the lesions, the pathological process, and the etiological momenta, in a way that none of the usual theories have been able to do. We must, I think, assume that before the germs can act there must be a lowering of the vitality of the epithelium through toxins or otherwise.

To explain the nephritis that occurs in a chronic disease in the case of the constitutional diseases, diabetes, tuberculosis, etc., we have mostly a degenerative process from toxic influences, or a mixed infection. In carcinoma we must look for secondary infection or an intestinal lesion.

The idiopathic or 'cryptogenetic cases, are most likely to be of the nature of infections from the alimentary tract, a mere congestion of this tract being sufficient.

To sum up, my conclusions are as follows:—

1. The different forms of Bright's Disease are to be regarded as

various stages in the same general process, there being a unity prevading the whole pathological picture.

II. All forms of nephritis are due in the immense majority of cases to infective agents ; the acute, to the usual specific germs of the primary disease, and the chronic, as a general rule, to the bacillus coli, though other germs may, sometimes, be concerned.

III. Acute interstitial inflammation and subsequent connective tissue hyperplasia are the key-note of the process; this is, however, preceded by parenchymatous degeneration.

IV. The point of invasion by the B. Coli is the gastro-intestinal tract; for other germs it may be various.

V. The liver and mesenteric glands are the first barriers of defence ; and the endothelial cells of the capillaries and secreting tubules of the kidney have the power of ingesting bacteria, this being an attempt at inhibition and elimination.

PLATE I. FIG. I.

Reichert oil-immersion $\frac{1}{18}$th. Without eyepiece.

Kidney. Area of round-celled infiltration showing minute diplococc at A. and B.

Patient, a male, aged 27 ; clinically a chronic nephritis of one year's standing ; there was a history of repeated exposure to wet and cold. The kidneys were of the large white variety passing into the contracted stage ; microscopically a chronic diffuse nephritis.

PLATE I. FIG. II.

Reichert $\frac{1}{18}$th.

Kidney. Area of round-celled infiltration showing a diplococcus at C

Patient, a female, aged 21 ; clinically a chronic nephritis of 8 months standing ; onset insidious.

Kidneys were extremely contracted ; microscopically extreme interstitial nephritis.

PLATE II. FIG. I.

Reichert, $\frac{1}{18}$th.

Original growth of B. Coli from the urine of a patient with advanced chronic interstitial nephritis.

Shows colon bacilli of the ordinary type, bacilli with polar staining, cocci and diplococci ; also chains of minute bacilli with polar staining. Taken from a flask in which the urine had been allowed to stand for 3 days at 37°C.

PLATE II. FIG. II.

Reichert $\frac{1}{18}$th.

The same organism as last transferred to 1.5 per cent. acid agar for 48 hours.

Now single cocci and diplococci.

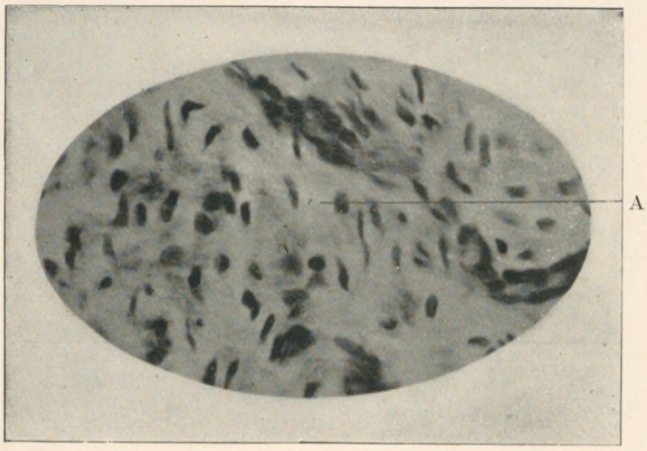

PLATE I, FIG. I.

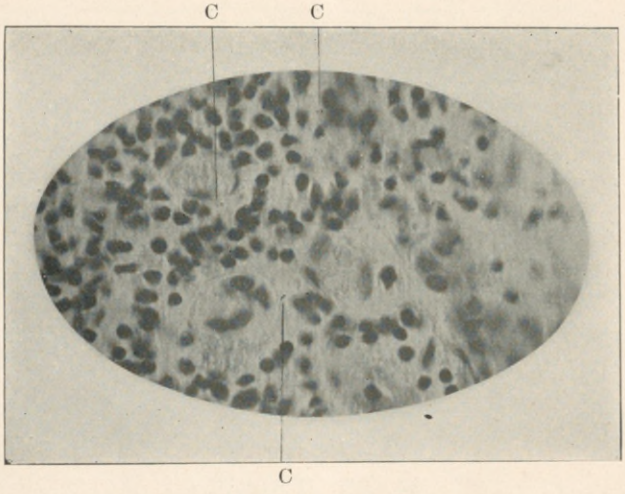

PLATE I. FIG. II.

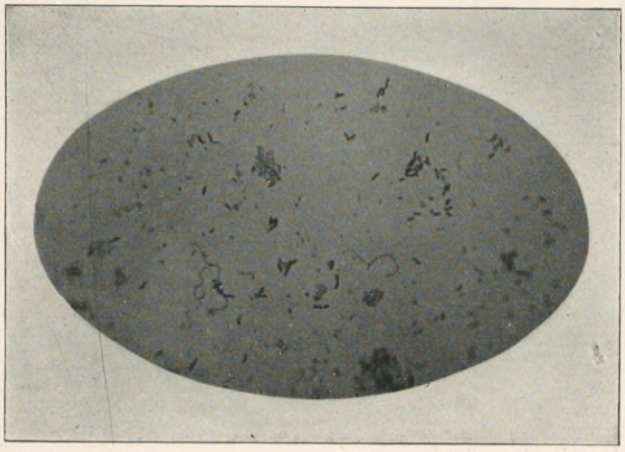

PLATE II. FIG. I.

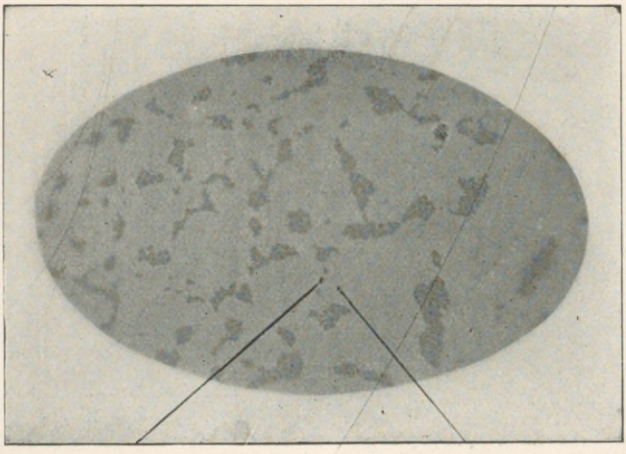

PLATE II. FIG. II.

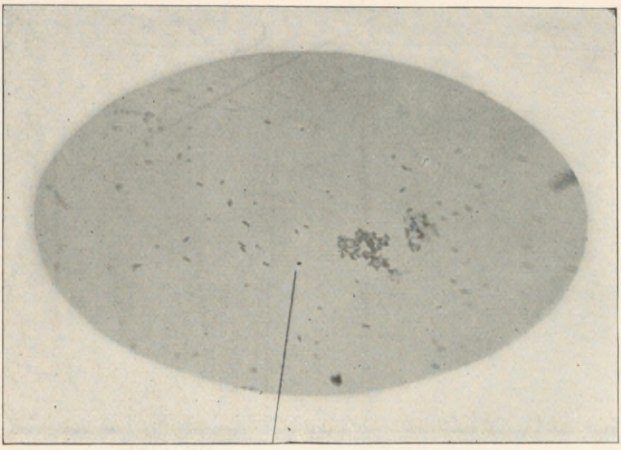

PLATE III. FIG. I.

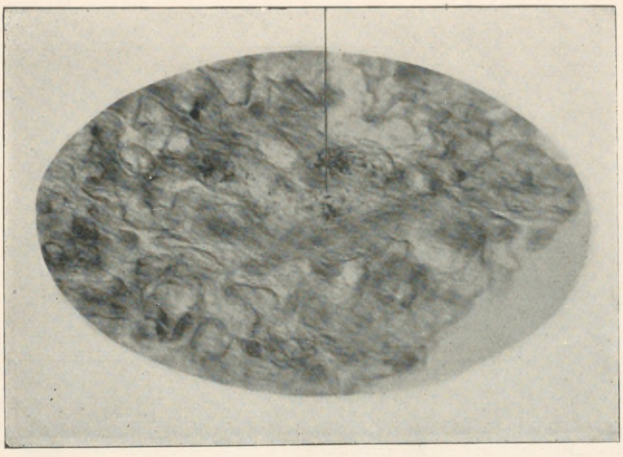

PLATE III. FIG. II.

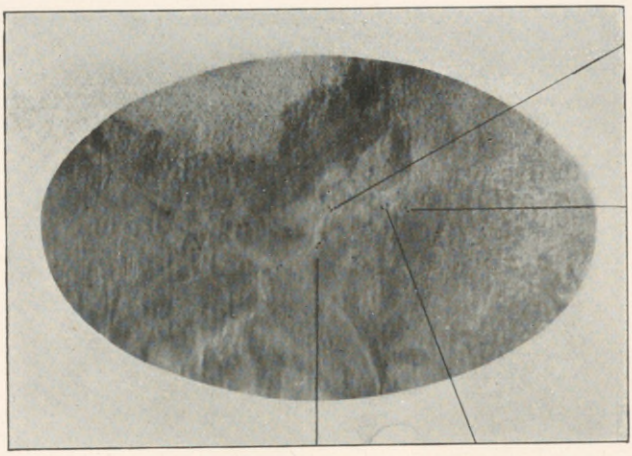

PLATE IV. FIG. I.

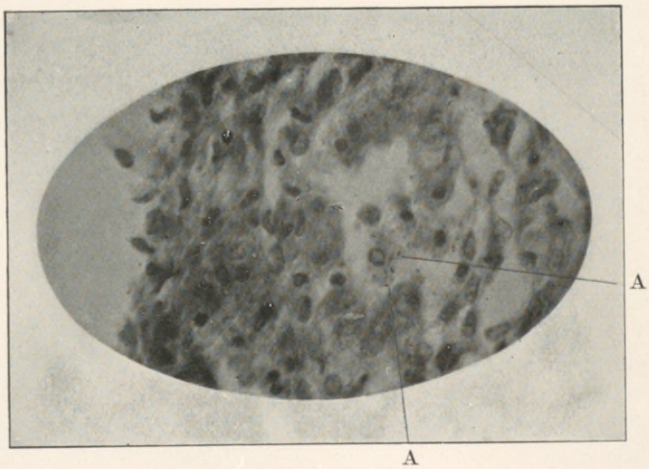

PLATE IV. FIG. II.

PLATE III. FIG. I.

Reichert $\frac{1}{18}$th.

Same as last on kidney bouillon 1.5 per cent. acid. Ordinary colon forms and minute diplococci.

Note.—The diplococci in the sections and in the slides from the cultures when viewed by transmitted electric light were seen to be really minute short bacilli with polar staining.

PLATE III. FIG. II.

Reichert $\frac{1}{18}$th.

Acute parenchymatous nephritis in acute lobar pneumonia.

Figure shows part of a glomerulus with numerous diplococci of pneumonia in a capillary.

PLATE IV. FIG, I.

Reichert $\frac{1}{18}$th.

Acute parenchymatous nephritis in acute lobar pneumonia.

Diplococci of pneumonia in the lumen of a contorted tubule. Under the microscope, however, the diplococci could be seen as shadows within the secreting cells.

PLATE IV. FIG. II.

Reichert $\frac{1}{18}$th.

Kidney showing secreting tubules from an experimental rabbit half an hour after inoculation with pure growth of B. Coli.

The bacilli are seen as diplococcus-like forms within the secreting cell shown at A.

NOTE.—For the above photographs I am greatly indebted to Dr. David Patrick who has admirably succeeded in a difficult task.