

THE EXPERIMENTAL EFFECT OF THE
COLON BACILLUS ON THE
KIDNEY *

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The following experiments were undertaken without any preformulated theories and with no attempt to prove anything. My previous work on the colon bacillus stimulated a desire to know more about this organism in its pathogenic rôle within the kidney.

This work is represented by one hundred animal experiments wherein a comparative action between the colon bacillus, the typhoid bacillus and the staphylococcus is shown under different conditions, and these bacterial invasions compared with the effect of a soluble toxin made from each.

In the first series 1 c.c. of a twenty-four-hour bouillon culture of various strains of colon bacilli was injected into one ureter just below the pelvis. These infected kidneys were removed at varying intervals along with the opposite kidneys. Most of the injections were made without producing any obstruction in the ureter, and some with obstruction by either narrowing with a ligature or a small pebble placed within the lumen.

As has been so often shown, the obstructed ureters produced the typical pathology of a pyonephrosis, varying in extent in direct proportion to the extent of the obstruction. The picture produced by the simple injection was consistent in each case, showing a glomerular nephritis. The cellular infiltration was of the polynuclear type in the infected organ, and mononuclear in the opposite one. In some areas there were interstitial hemorrhages, but no extensive involvement of the tubules was found in any instance. No focal necrosis or miliary abscesses, and in no instance in which the kidney remained for longer than twenty-four hours could bacteria be demonstrated in the tissue or by culture from the urine. No specimen showed a limitation of the pathologic condition to the pelvis even as soon as twenty-four hours after the injection, but each picture was that of a pyelonephritis, with the glomeruli the seat of the inflammation. The opposite kidney in every instance showed a similar change, but much less pronounced. In those cases in which the opposite kidney remained *in situ* for some time after the removal of the infected one, a complete restoration to normal is shown. This fact is borne out clinically very frequently. A surgical kidney on one side will produce a toxic nephritis in the opposite organ, which recovers spontaneously on removal of the seat of the infection. That it is a toxic condition is shown in some of the subsequent experiments.

The typhoid bacillus produced a more generalized parenchymatous nephritis, which was emphasized by obstructing the lumen of the ureter, but did not produce a pyonephrotic change. The opposite kidney showed similar changes. Blood-cultures and urine-cultures were positive in each instance.

The staphylococcus produced either focal necrosis or a complete pyonephrosis. Cultures from the urine were positive; from the blood negative.

The next step was the injection of cultures of these three organisms, singly, into the sheath of the ureter, extraperitoneally, at about its middle third; and in another group of animals subcapsularly at the cortex. The histologic pictures were practically the same as when the organisms were introduced through the ureter. The typhoid bacillus produced a general parenchymatous nephritis; the staphylococcus focal necrosis, with inflammatory processes throughout the kidney. The colon bacillus still showed the glomerulitis predominating, and, in addition, when the injection was made at the cortex, a pyelitis secondary to a nephritis. Blood-culture was positive for typhoid, urine-cultures positive for staphylococcus and typhoid.

In the next series of experiments soluble toxins in varying strengths were made from the three organisms and injected at the locations just described. The histologic picture changed somewhat. The typhoid toxin showed an intense parenchymatous involvement, with areas of granular degeneration. The opposite kidney was involved to about as great an extent. The staphylococcus toxin gave a similar picture, but not nearly so marked. The colon toxin gave a very pronounced picture of a generalized parenchymatous nephritis. The type of cellular infiltration with each toxin changed from the polymorphonuclear to the lymphocytic, a rather significant change. The opposite kidneys were involved equally as much, and all became normal from three to four weeks following the injection of the toxin. When too great a concentration of the toxin was used, the animals died very promptly. No attempt was made to ascertain very accurately the minimum lethal dose.

If any conclusions are to be drawn from this work, three facts stand out prominently:

1. A non-traumatized kidney in the absence of ureteral obstruction will overcome spontaneously the invasion of virulent micro-organisms.

2. It appears that our recently slighted blood-stream is the means of extension of these infections from the pelvis to the cortex, from the cortex to the pelvis, and in all probability from the periureteral tissue to the renal parenchyma. This is based on the fact that the glomeruli are the structures mostly involved. Though, in the face of the recent very interesting work of Hess,¹ later verified by Eisendrath, whose specimen showed a predilection for the lymph-tract as the route for ascending infections, my renal specimens show only the glomeruli involved.

3. The pathologic changes are due to a direct toxic action and the soluble toxins of the organisms are carried to the opposite kidney, where a similar picture is seen.

In no instance does any specimen show the changes found by Hess, who asserts that cultures of colon injected into the pelvis will produce pus foci and areas of necrosis within from thirty-six to forty-eight hours, and if the bacteria act longer the changes become more marked. The very convincing work of Francke² leads one to believe that the colon bacilli pass from the mesenteric lymphatics into the right kidney, seldom into the left, yet left-sided pyelitis is almost as fre-

* Read before the Section on Genito-Urinary Diseases at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

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1. Hess: Deutsch. med. Wchnschr., 1912, No. 30; Mitt. a. d. Grenzgeb. Med. u. Chir., 1912, No. 26, p. 135.

2. Francke: Arch. f. Anat. u. Physiol., 1910, p. 191; Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1911, xxii, 623; Berl. klin. Wchnschr., 1911, p. 1973.

quent as right, and if we are to ascribe to gastrointestinal disturbances the rôle for the production of colon bacillus pyelitis, then the blood-stream must be at least as important as the lymph-stream in carrying the bacteria to the kidney.

Most of the experimental work done along this line has been with narrowed or completely obstructed ureters, which, of course, gives an exaggerated pathologic picture. My object was not to imitate a clinical state, but to ascertain how far the kidney could overcome a simple bacterial invasion, since we see so often a bacteriuria without any clinical manifestation.

Mueller³ concludes that a pelvic infection spreads to the cortex along the lymphatic channels upward, but all of his experiments were performed after first obstructing the ureter. Kumita⁴ has traced the lymphatic capillaries in the cortex, where he says they communicate with the lymphatics of the capsule and surround in a most intimate manner all the convoluted tubules. The meshes of this network are circular and surround in a parallel manner the blood capillaries. From the capillaries, lymphatic vessels arise which surround Bowman's capsule and penetrate the glomeruli. This finding confirms the work of Mueller, although it does not prove that infections in non-obstructed ureters extend along the lymph-channels. All of my specimens show the glomeruli the seat of the cellular infiltration, rarely any interstitial or tubular involvement. This, of course, speaks for a blood-stream extension. One would expect to find thrombi or emboli in hematogenous infections, yet none could be demonstrated. If the extension were urogenous, that is, along the secretory current, the entire epithelial lining of the corresponding tubules, from the papillae to the point to which the inflammatory process has ascended, would show a corresponding damage, which certainly has not been seen in any of the specimens.

In justification of my conclusions, so widely differing from such reliable observers, whose work has been quoted, it must be remembered that this piece of work was not begun to prove any clinical picture or trace the origin of any pathologic process. The technic employed, therefore, differs markedly from that of other experimenters along this line, and the results necessarily are different.

My sincere appreciations are due Dr. James W. Jobling and Dr. Edwin Kirk for their many valuable suggestions.⁵

TECHNIC

Preparation of Bacterial Cultures.—Pure cultures of colon bacilli isolated from the human and rabbit feces. Also stock cultures used. Quantity injected, 1 c.c. of twenty-four, forty-eight and seventy-two-hour bouillon cultures. *Staphylococcus pyogenes albus* and typhoid bacillus obtained from stock culture. Same quantity used.

Preparation of Toxins.—The toxins were made by washing off in normal salt solution a twenty-four-hour agar-slant. This was allowed to stand twenty-four hours. Toluene added to kill the bacteria, which required from twenty-four to forty-

eight hours; this toluene then pipetted off. They were then centrifuged and the supernatant solution (the soluble toxin) pipetted off and stored in the ice-box until used.

Preparation of Tissues.—Cut tissues immediately fixed in Zenker's solution and in 10 per cent. liquor formaldehydi. All embedded in paraffin.

Stains Used.—Hematoxylin eosin; Unna's eosin methylene blue; Loeffler's methylene blue and Gram stain for bacteria in the tissue; carmin for fibrin.

Urine cultures made from bladder. Blood-cultures made from renal vein or heart, if at necropsy. Cultures from urine and blood made in bouillon.

Operative Technic.—Twenty-five rabbits and seventy-five dogs used. Anesthetic, ether. Typical lumbar incision. Great care was taken not to traumatize either the kidney or surrounding structures. Whenever possible, the injections were made without tearing the organ from its fascial and fatty bed. Injections into the periureteral tissue were all made extraperitoneally. The kidneys were removed from one to thirty days following injections.

ABSTRACT OF DISCUSSION

DR. LOUIS E. SCHMIDT, Chicago: Work of this kind brings out a great many clinical observations. When we know work of this kind to be true, naturally our clinical point of view may differ from what it was from the former facts at our command. When a disease condition, obstruction and infection, exist on one side it is well worth our while to study the opposite kidney; there can be no question that the toxic action on the opposite kidney is just as important as in the kidney in which the disease really exists. In the experimental work which Dr. Koll has done, of which the details are not given, how long after the beginning of obstruction and infection were the kidneys removed? From the clinical point of view when we have a renal stone possibly obstructing the lower end of the ureter, how long are we permitted to wait before we consider operative interference on that side and before the so-called sound side becomes involved? That is a matter of great importance. There is no question that all of us see patients with ureteral stone that we do not operate on because the stone is at apparent rest and there is practically no infection present, but we must take into consideration the condition that exists on the other side. Naturally, from the circumstance that there are more infections on the right side, we could wait longer on the left side than on the right. Furthermore, the question of bacteriuria exists. That question is still under discussion. It is often stated that bacteriuria arising from the kidney cannot exist unless there are changes in the renal epithelium; that in individuals suffering from tuberculosis there are tubercle bacilli found in the urine without any renal changes. That is doubted more and more at present. It is believed that the intoxication has caused changes in the kidney which permit this condition to exist. I am under the impression that the colon bacillus, which is the one we most frequently deal with in bacteriuria, produces some changes which permit this condition to exist. I have yet to see cases of renal bacteriuria which clear up without any treatment. I have seen prostatic cases clear up from time to time. They would be macroscopically clear one week and the next week they would show the typical characteristics of bacteriuria. Another important point, clinically, is that we should always take notes of cases, for instance, of chronic appendicitis that exist for long periods of time, in which the condition is not acute but the patient has pains in the right lower quadrant. This condition undoubtedly produces some obstructive condition, and naturally infection can easily occur, and in that way may produce renal conditions similar to those described in the paper.

DR. H. W. PLAGGEMEYER, Detroit: One case has bothered me a great deal of late, and I want to ask Dr. Koll what he thinks about it. This patient gives no history of pain, but the phthalein on the right side was merely a trace at the end of thirty minutes. On the left side there was 16 per

3. Mueller: Arch. f. klin. Chir., 1912, xevii, 44.
4. Kumita: Arch. f. Anat. u. phys. Anat. 1909.
5. In addition to the references already cited, the following will be found of interest:
Asch: Mitt. Centralbl. f. d. Krankh. d. Harnorg. u. Sexualorg., 1902, xiii, 690.
Bauereisen: Ztschr. f. Gynäk. u. Urol., ii, No. 5.
Schnitzler and Savor: Fortschr. d. Median, 1894, No. 23.
Von Kleckli: Arch. f. exper. Pathol., xxxix.
Münich: Arch. f. klin. Chir., 1912, No. 98.
Wildbolz: Cor.-Bl. f. Schweiz. Aertze, Jan. 1, 1912.
Venus: Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Sept. 16, 1911.
Cuturi: Ann. d. mal d. org. genito-urin., xxix, 514.
Brewer, G. F.: The Present State of Our Knowledge of Acute Renal Infections, THE JOURNAL, A. M. A., July 15, 1911, p. 179.
Koll: Tr. Am. Urol. Assn., 1911; *ibid.*, 1912.

cent. in the first fifteen minutes and 7 per cent. in the second fifteen minutes, making a total of 22 per cent. The blood urea was 0.2 per cent., the urinary urea on the right side was 0.7 per cent., and on the left side 0.8 per cent. by the Marshall test. On the right side there was a profuse colon infection in the urine and also on the left side. What would Dr. Koll think about operating in a case like that with a distinctly low phthalein on the opposite side?

DR. A. J. CROWELL, Charlotte, N. C.: Some five or six years ago I prepared a paper on the rationale of traumatic nephritis. I had no proof except clinical proof that such was the case but this was really positive of a right-side nephritis following severe traumatism to the left kidney. In Dr. Koll's experimental work I think I see further proof that such a condition can occur. He speaks of the removal of an injured or diseased kidney preventing a diseased condition of the opposite kidney. Dr. Squires and I have lately been doing some experimental work on traumatizing the kidney and injecting the various fresh bacteria, but we are not yet ready to make any report further than the macroscopic appearance. We have operated on about fifty rabbits up to the present, traumatizing the kidney with and without injecting various bacteria into the veins thereafter. I hope, later, to make a report of this work. Macroscopically, the traumatized kidney followed with intravenous bacterial injections, with the exception of a few cases, showed but little of interest.

DR. I. S. KOLL, Chicago: One big mistake that experimenters frequently make is to lay down the laboratory findings as a dogmatic control of clinical findings. There is a long range between the test-tube and the patient, and I am convinced that while our experimental work may pave the way for our clinical deductions, nevertheless we must be careful in applying laboratory findings to clinical manifestations. Now, as to the length of time that it is safe to allow a stone or an infection to remain before urging operative interference, the point is an arbitrary one, because if a calculus is obstructing either the pelvis or the ureter, in the absence of infection, of course, the kidney is not going to be destroyed as rapidly as if there was an infection. How long before the kidney will be infected when there is obstruction to the ureter also cannot be foretold. The infection in the kidneys removed in my experimental work varied from twenty-four hours to four weeks. I found that within twenty-four hours after the injection of colon bacilli into an obstructed ureter there were very marked changes in that kidney. In some instances in which there was a high degree of virulence of the organism there was a marked tendency to total destruction of the kidney in twenty-four hours. In the absence of obstruction—and by obstruction we must consider that due to edema or inflammation of the ureter, because that certainly is an obstruction—I was not able in twenty-four hours to recover the organism in the urine taken from the bladder. This widely differs from the work of other experimenters, but I tried it over and over. I was careful not to bring the kidney up out of its bed. I went into the ureter and injected my organism extraperitoneally, and thereby produced less traumatism. In those cases I could not recover the organism after twenty-four hours. I do not believe there is a bacteriuria without renal changes. Within twenty-four hours there is a distinct nephritis. I do not

believe that a pyelitis exists as a pathologic entity. In twenty-four hours the glomeruli show changes, but of course the changes are more marked in the pelvis. Answering Dr. Plaggemeyer's question concerning the involvement of both kidneys, if he found involvement indicated by the low phthalein output, the question is, What is the type? By a toxic condition in the opposite kidney I mean that there is no infection, but the toxins are producing an irritation of the parenchyma that is manifested, not by pus-cells in the urine, but by casts, albumin and red corpuscles in more or less abundance. So I should say that if in one kidney he found practically no pus cells present and that great quantities of pus were in the opposite side, that is certainly a case for operation. The toxic condition is manifested not by leukocytes but by hyaline and granular casts, by albumin and by erythrocytes.

EXPOSURE OF APPENDIX BY CULLEN'S METHOD

A SIMPLE WAY OF REMOVING AN ADHERENT RETROCECAL APPENDIX THROUGH THE ORDINARY GRIDIRON INCISION

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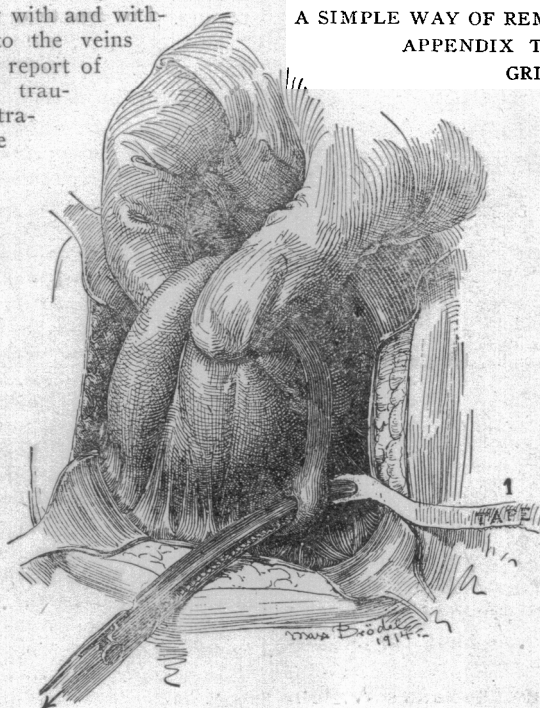


Fig. 1.—Pushing a blunt Kelly forceps through the meso-appendix at the cecum.

For at least seven or eight years Dr. Thomas Cullen, one of the attending surgeons at the Church Home and Infirmary, has been employing such a simple and easy device for exposing retrocecal and densely adherent appendices that I feel its general adoption would not only shorten the time taken in these operations, but also render the surgeon's work much easier.

One of the most important points for the operator to decide when commencing an appendix operation is what kind of an incision to make. In those cases in which the abdominal pains are rather vague, it is usually wiser to make a right rectus incision, as either the gall-bladder or appendix or both may be diseased. With the right rectus incision it is possible to lengthen the wound upward or downward as may be desired. In this manner the entire field can be most satisfactorily exposed.

Again, when a gangrenous appendix is suspected, a right rectus incision may be made and if drainage be necessary then a small gridiron incision can be made near the anterior superior spine just where the drain is to be inserted directly down to the cecum.

It is not my desire to discuss the general subject of appendix incisions but to refer to the method Cullen and those associated with him have found eminently satisfactory in those cases in which the diagnosis of appendicitis was relatively certain and the pain localized to the appendix region—those cases in which one would naturally make a gridiron incision. Not infrequently in these cases after the incision has been made it is next to impossible to expose the appendix, as it is