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Urinary tract infections

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"SENIOR THESIS"

"URINARY TRACT INFECTIONS"

BY

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"INTRODUCTION"

Urinary tract infections play an important role in nearly all branches of medicine. It is a type of infection which has its focus in various parts of the body. In order for an individual to be cured of his urinary tract infection, he has not only to go to the Urologist but also to the Dentist, the Rhino-Laryngologist, the Internist and the Surgeon.

The Dentist claims the primary focus is that of the teeth, the Rhino-Laryngologist claims the tonsils and the sinuses, the Internist claims the general run down condition of the patient and the Surgeon states that the appendix and gall-bladder ought to be removed before the infection of the urinary tract will clear up.

The Internist finds many individuals who have a bacturia. This bacturia may not give symptoms relative to the urogenital tract; but the toxins may poison his body to such an extent that the patient is not himself and needs medical treatment. Such a patient, if their resistance becomes to such a low point would develop very severe urogenital symptoms.

The art of treating of urinary tract infections is a very difficult problem; because there are so many obstacles to overcome, which makes the problem so baffling.
"HISTORY"

(I) "Medical treatment for Urinary tract diseases was first recorded in the Papyrus of Ebers, written 1550 B.C. and from this time the present various remedies have been used both internally and externally.

"The first operation spoken of in the time of "Ayurveda of Sucrutu", the great work of the Hindus in India, was perineal lithotomy which was performed about the same way as to day. They also were treating stictures by gradual dilatation with sounds of metal or wood and treating diseases of the urethra and bladder by injections.

"Hippocrates (400 B.C.) was interested in vesical calculi, and described accurately how a stone grows gradually from a nucleus. He was interested in the surgery of the kidney. He was the first to point out the change in the urine in diseases of the kidney and bladder.

"Cornelius Celius, the great Roman medical writer (Christian era) wrote on urethrotomy for impacted urethral stone; catheterization for retention of urine, vesical calculus and lithotomy.

"Salen wrote upon incontinence and retention of urine and described an S-shaped or curved catheter which was to be used for diagnosis of vesical calculus.

"Medicine at this time fell in the hands of barbers and charlaton, and the advances along urological times wasn't heard of until the discovery of the movable kidney in 1497 by Mesure of Paris.

"During the heyday of the Saleinian Scholl, near Naples, all the physicians were practically urologists, as they depended largely upon the urine for the diagnosis and prognosis; and the
urinal became the ensignia of the physician and the emblem of medicine.

"Boerhaave was the first to discover the specific gravity of urine. In the eighteenth century Catugno discovered albumine in the urine of diseased kidney by boiling it. Roulli and Cadet discovered urea and isolated many salts of the urine and Schule discovered uric acid.

"Modern urological history is divided into two parts, the first half of the nineteenth century was confined to improving and elaborating urethral and bladder work, urinary examination and study of pathology.

"Bright was the first thoroughly to consider diseases of the kidney from the point of an internist.

"The laboratory men were principally engaged in the work of urinary analysis until Pasteur's discovery of bacteria and microbic infection, followed latter by the discovery of the gonococcus, the tuberculosis, streptococcus, colon bacillus and others of the important forms of infection."

The great urological problem today is the discovery of a suitable urinary antiseptic. One of the chief drugs used today is acriflavine. Dr. Edwin Davis, instructor of Urology in our University, was the first to experiment with this drug in the United States.

With the improvement of technic and instruments, the Urologist has risen high or higher than any specialist in the history of medicine.
Determining the etiology of urinary tract infections is a big problem. With the many routes of invasion it is very difficult in placing your finger on the focus of infection.

Modern methods of blood culture have abundantly proved that the circulating blood frequently contains living bacteria. Hidden foci of infection, teeth, tonsils, sinuses, appendix, gall bladder, seminal vesicles and prostate are often the sources of a bacteremia. Every living adult must at some time have had a bacteremia from some one of these causes. This bacteremia is often, perhaps usually, symptomless, the normal resistance of the body being sufficient to conquer the infection.

We find many patients who were perfectly healthy and their urine on examination was free from bacteria; but suddenly and without demonstrable cause become thoroughly infected by the colon bacillus. By going into their history we find the etiological factor of these cases, of being, unusually run down. We know that the organisms pass through the kidney, in many cases without producing any lesions; but given a bacteremia of sufficient virulence and of sufficient duration the resistance of the kidney must eventually be so lowered as to succumb in some degree to the continued onslaught, with resultant pyelitis, pyelonephritis, pyonephrosis or septic infarct.

"In many severe cases of kidney infection due to colon bacillus, we may get a complete recovery without operative interference, while in other cases infection once established in the kidney may continue almost indefinitely, in spite of all effort to relieve it; and without any demonstrable harm to the organ or individual. These latter cases immunized themselves to the
infection. A careful search for a focus of infection of these patients with colon bacillus, usually fails to reveal any infection. Although these patients are most generally below par.

"There are many factors which lead to an infection of the bladder. The types of cystitis under consideration depends, on their etiology upon a local inflammation, the exciting causes of which are due to pathogenic organisms which have gained entrance into the bladder from without, through the urethra or from contiguous organ.

"A normal untraumatized bladder, primary bacterial cystitis rarely, if ever, occurs; an a bacterial cystitis is caused by injury to the bladder with an easily superadded infection from without. The most common predisposing factors are:

"I. Traumatisms such as during instrumentation, following hysterectomies, fracture of pelvis and pressure from fetal head. That of pregnancy is usually not with in about the sixth month, is acute as a rule and is sometimes severe.

"2. Congestion such as exposure to cold, dampness. Saturated urine, excessive alcoholism. Transparital infection through the lymphatics from the intestine to the bladder as observed in appendicitis, dysentary and internal hemorrhoids."

"The bladder, which is one of the most vital physiological functioning organs of the body, is most frequently abused.

(4)."Most of the ordinary things of life are done poorly by a surprisingly large number of individuals and it will not due to assume that such a frequently performed act as emptying the urinary bladder is always done properly. Some time in life the majority of our patients develop habits in this regard, which, if continued over a long period of time would, at least,
produce symptoms, if not true pathology. Fortunately these habits are usually of short duration and might be said to belong to the various phases of mental and physical development.

"The bladder having both a voluntary and an involuntary role to fulfill, with its emptying entirely dependent upon an attitude of mind, with minds varying so greatly in poise as they do, its career is one fraught with many hazards. With the countless interference of one kind or another it easily may be caused to develop habits. It is made to hold a larger quantity of fluid than it was intended to hold; its owner insults it by increasing his intra-abdominal pressure to force a sphincter that was intended to be opened otherwise; and it is also damaged by pelvic congestion of constipation and menstruation.

"Thus the bladder develops certain pathology and we are treating many cases according to our commonly false etiological assumptions through the urogenital tract and not the constant mental and physical buffetings.

"By cystoscopic examination of the bladder we may observe pathological findings of which the etiology is not infection but is due to "habit bladder".

"The particular habit causing this vesical change is becoming less common as society gradually erases, what we have known as false modesty. It is becoming generally realized that the bladder should be emptied from time to time and it is no longer vulgar to be seen going into places where this can be done. There are still some individuals, usually young women, who made it a practice to empty the bladder only when it cannot possibly hold more urine. The result of this habit is a large pale, apparently thin walled viscus.

"Another form of habit is that of habit pseudocontracture."
These patients are generally a nervous, introspective young men, who has a pet phobia, the dread of being caught somewhere with a full bladder without any opportunity to empty it. For this reason he always voids every time he imagines this could happen. The trigone "flush button of the bladder", becomes more and more sensitive and the summons to void occurs on the least dilatation, the patient finds it necessary to void more frequently and to arise several times at night. The diagnosis is very baffling in these cases, the doctor consulted runs the scale of all diseases causing frequency, and finally tells the patient he is uncurable. The diagnosis does not need a cystoscopic examination but can be made from the history. The amount of urine passed in twenty-four hours divided by the amount passed at each urination will show the cause of frequency to be a lessened bladder capacity. The real cure with these cases is with the patient himself. He should wait until the third or really urgent summons before he voids.

"There are many patients who strain to force the vesical sphincter open instead, of waiting for its normal relaxation. There are millions of vesical sphincters too modest to dilate in company, or, perhaps, more correctly hampered by mental inhibition. Many persons carry out his same tactics when alone, so that every act of urination is accompanied by and enormous increase in intravesical pressure.

"The result of this practice over a number of years is to produce a back pressure bladder. In some cases it may show trabeculation and succulation. The diagnosis is made from the history, the absence vesical neck and urethral obstruction and
any evidences of a spinal cord lesion. These patients can be cured by teaching the patient to relax and not contract in the re-establishment of urination. (The latter deals with persistent sinus of suprapubic fistula after post operative prostatectomy.

"Unmarried women show a vesical picture of very marked trigonal injection with the absence of any pelvic or urogenital lesion. Its annoying symptom is great frequency of urination, burning and tenesmus. This is most generally associated with excessive sexual indulgence, and it is also observed in unmarried women exhibiting the prudery and vulvar appearances commonly attributed to digital masturbation.

"Great prolongation of the normal sexual act causes a dilatation and tortuosity of the trigonal vessels, a convexity of the surface of the trigone as far back as the plica enteruretivica and great broadening of the rim of the vesical outlet.

"Frequent masturbation causes enlargement of the verumontanum, injection of posterior urethra and redding of trigone. Coitus interruptus only cause enlargement of verumontanum. Many cases of obscure etiologic factor, can usually be traced to the patients habits, and changing these habits one may find gratifying results."

The relative toxicity and clinical significance of the bacteria known to be pathogenic for the urinary tract is by no means clear. Each may establish mild infection or severe ones. However, the infections due to the pyogenic cocci seems to be less pertinacious than those due to the Bacillus coli; and more likely to result in cortical and perinephritic suppuration.

(3)."The comparative frequency of the organisms as the exciting causes are:
Bacillus coli communis
Bacillus typhosus
Gonococcus
Bacillus tuberculosis
Bacillus lactis aerogenis
Streptococcus
Staphylococcus group
Micrococcus urae
Bacillus proteins volgaris group
Salmonellae ammoniae
Bacillus pyocaneas
Surcinae

In cystitis with acid urine.

In cystitis with alkaline urine.

Either alkaline or acid.

The routes in which the urinary tract becomes infected is not very well agreed upon. In all bladder infections there are three avenues open by which the organisms may gain access to the kidney. As to which avenue the infection takes, is very hard to decide; as many noted research men have very good theories on each one. Some authors deny emphatically that an ascending renal infection by way of the lumen of the ureter from the bladder can occur. Other investigators staunchly maintain that tuberculosis of the bladder is always a descending process, the result of a primary kidney infection, and at no time is it a primary infection of the bladder with as ascending process involving the kidney secondarily.

(5)" The spread of the infection may take place through the blood stream. The organisms gain entrance to the blood stream and are either excreted by the kidney without damaging it, or they or their toxins or both set up an inflammatory process
within the organ. The excretion of bacteria by the kidney after injection of the organisms in the blood stream was noted by David, McGill, Helmholtz, Young, and others. Others believe that the kidney only excretes only those organisms which cause lesions within the organ itself.

"The second theory concerning the avenue of ascending infection to the kidney from the bladder assumes that there is a close relationship in the lymph supplies of the bladder, ureter and kidney. The lymph supply and anastomosis have been studied by a host of observers. Some state that the lymph vessels from the middle third of the ureter pass to the glands in the lumbar region which lie both beside and anterior to the aorta and the inferior vena cava, and internal to the common iliac artery. From the lower third of the ureter, the vessels go directly to the hypogastric glands which also receive the lymph from the bladder wall. These vessels from the upper third of the ureter go to some lymph glands lying along the aorta and vena cava and then communicate with those of the kidney hilus and kidney proper.

"Judging from the above observation, it seems that the possibility of a direct communication between the bladder and the kidney through the lymphatic system, is quite remote, though a rather circuitious route may exist. If there are some connection it must be remembered that much of the way the organisms would have to travel against the flow of the fluid within the lymph vessel. Many investigators believe that this is the main avenue of infection and practically all workers in urology admit its possibility. David, McGill and others on experiment animals came to the conclusion that the lymphatic system is important in
the infection in the kidney following primary bladder involvement.

"The third theory is that of ascending infection of the kidney from the bladder by infected urine, this is admitted by a large number of workers.

"A partial obstruction or stagnant urine in the bladder will cause a hydro-ureter which may assist the bacteria in reaching the kidney.

"Reflux of urine from the bladder into the ureter takes place with ease in some cases. After the urine reaches the ureter it may readily be carried into the renal pelvis by the antiperistaltic contractions of the ureter."

The majority of urologists consider all three possible avenues of travel of infection from the bladder to the kidney.

(5)"Gruber and Rabinovitch experimented on 15 healthy dogs, they produced a pyelitis in 14 of the dogs who where operated upon and who had been injected with a virulent bacillus coli in the bladder. They attributed the pyelitis due to an ascending infection, the organism gaining entrance to the ureter through the patent orifice, (which was fixed by an operation) and being carried by antiperistalsis or by the active motion of the organisms themselves upwards along the ureters into the kidney pelvis and perhaps later into the kidney substance proper."

(6)"Interference with any part of the excretory motor mechanism of the urinary tract results in stasis of urine and this stasis is by far the most important factor in favoring the incidence of urinary infection in the first place. In order not to have stasis we must have adequate contraction of the wall of the renal pelvis with its suction action of the papillae, the peristaltic waves of the ureter, increasing in rate and force
as diuresis occurs, and the complete emptying of the bladder under adequate stimulus of distension. Any mechanical or functional factor in the urinary tract from the external meatus to the smallest renal calyx may hinder the normal flow of urine and produce stasis.

"Some of there complications are as follows:

1. Phimosis in the male, contracture of the external urethral orifice in women.
2. Stricture of the urethral; congenital inflammatory or traumatic.
3. Calculi or foreign bodies in the urethra and their resulting scars.
4. Hypertrophy of prostate.
5. Congenital valves of the prostate urethra.
6. Contraction of the vesical outlet and "median bar" formation.
7. Faulty innervation of the bladder musculature interfering with urination, due to lesion or disease of spinal cord (tabes, fracture of spine, spina bifida occulta etc.).
8. Vesical calculus.
10. Diverticulum of the bladder.

In the ureter and above.

1. Stenosis and subsequent cystic dilatation of the intravesical end of the ureter.
2. Abnormalities of insertion of the ureter into the bladder through defective development.
3. Interference with or entire destruction of the ureterovesical valve accompanying stricture of the urethra or
the hypertrophied prostate.

4. Primary neoplasm of the ureter.

5. Ureteral calculus.

6. All conditions interfering with ureteral motility from without.

7. Congenital dilatation of the ureter.

8. Renal dystopia and movable kidney.

9. Congenital abnormalities, such as horse-shoe kidney, and renal dystopia, duplication of the ureter and kidney pelvis.

10. Renal tumors both pelvic and parenchyma.

11. Renal calculus.


The diagnosis of such cases is very important. Patients may complain of indefinite pain, and unknown cause for rise of temperature, nausea and vomiting with or without blood changes; these symptoms can frequently be accounted for by stasis of urine in the upper urinary tract.

(7)"Pyelonephritis with the colon bacillus as the infecting agent following attempts at coitus, probably occurs with greater frequency than reports indicate. Young women recently married may complain of frequency, dysuria and pain in renal area. On examination of the urine, which is cloudy and contains many pus cells and colon Bacillus.

"The infection may start from small wounds consecutive to rupture of the hymen and then developing an ascending infection. Many of these cases are overlooked, the patient only giving symptoms of cystitis. These latter patients may only have a mild
dysuria and transient frequency. On the other hand they may have violent urinary symptoms together with high temperature, severe pain and marked prostration.

"In the mild cases of young women, the organisms may remain latent for a number of years, and then may play an important role in the production of the pyelonephritis of pregnancy. Any stasis of the urinary tract caused by a stone or pregnancy may cause the infection to flare up. Cases are on recorded where the Colon Bacillus urinary infection persisted for 12 years without any evidence of harm, but which finally caused a severe suppuration pyelonephritis following the production of a ureteral kink by a mobile kidney.

"The type of urinary infection occurs in women who have a perineum, which is tense, a narrow rigid orifice, and a urethral outlet somewhat behind the vaginal orifice, these women are rebellious to the painful manipulations of examination just as they are to coitus.

"The pathogenesis of ascending urinary infections following coitus, is largely due to trauma. The urethra orifice may be brused which favors entrance for colon bacillus. The bacillus may be present in the vagina, especially in constipated women, and this trauma during coitus is a very favorable media for the bacillus if present to cause it to get a foot hold and along with an infected bladder cause an ascending urinary infection. (Rovsing states that infection may possibly spread from a ruptured hymen to the kidney). It is probable that in the majority of cases the bladder is primary infected, the infection being then carried up the urinary tract by way of one of the three avenues of infection."
There is no constant route of infection, as previously stated, but there must exist an infected bladder before there develops a pyelonephritis in these cases of ascending urinary tract infection after traumatic coitus.

The condition is the same no matter the route of infection. Once the infection is established, post nuptial pyelonephritis of this type assumes the properties of chronicity and resistance to treatment usually obscured in the more common types of pyelonephritis.

Dr. Braasch states that such cases should be interested to us all, because acute pyelonephritis may result also from trauma following cystoscopy or urethral catheterisation.

(8)"In any instrumentation of the genito-urinary tract the operator should combine gentle manipulation with a most rigid aseptic and antiseptic technique. Severe reactions occasionally follow instrumental or operative manipulations. Some attribute the cause of urethral fever to a reflex nervous influence, poisoning of the wound and system due to a changed condition of the urine and the ascending extension of inflammation to the kidneys. A retention catheter for drainage purposes is badly tolerated by certain individuals and one should resort to suprapubic drainage in such cases before it is too late."

(9)"Parasitic infection of the urinary tract is exceeding rare. Only one case has been reported, a case of trichomonas vaginalis found in the pelvis of both kidneys, bladder and vaginal secretion.

"In this case the patient was in bed with fever, chills, and constant pain in left side radiating down thigh and groin.

"Urine was clear, pyelograms revealed no pathology. But
by laboratory work, the parasitic organism trichomonas which was about five times the size of a red blood cell was found in the centrifuge urine. By frequent lavages of the kidney pelvis with 2% mercuriochrome and silver nitrate 1:1000 the parasite was destroyed and the symptoms subsided."
"SYMPTOMS"

Patients who have an infection of the urogenital tract usually complain of certain specified symptoms. Yet some of these symptoms, the patient ignores and many cases escape diagnosis during the period when they are most amenable to treatment.

(10) Pain is a symptom of great importance because it, more than anything else, impels patients to seek assistance from the physician. The pain characteristic of urologic diseases can be divided broadly into renal and ureteral pain, vesical pain, urethral pain, prostatic and perineal pain and scrotal pain.

"Renal and ureteral pain may occur as constant pain or in paroxysms of renal or ureteral colic. The pain is referred usually to the surface of the body, and according to the peripheral distributions of the nerves, the visceral branches of which supply the kidney and ureter. The constant renal pain is usually described as an achining pain, and is less apt to be referred to distant areas than the colic. It is usually appreciated in the loin of the affected side, and, therefore, directly over the kidney region. It may simulate pain from intra-abdominal lesions. Pathological kidney may remain painless for long periods of time. Occasionally compensatory hypertrophy of a sound kidney is associated with some aching pain, so that if the diseased kidney is painless, the only pain experienced by the patient may be on the healthy side.

"Renal colic is due to spasmodic contractions of the ureteral or pelvic muscles. These contractions are due to some foreign substance in the ureter. The severity of the colic depends upon the individual and the amount of muscular contraction.
It is very often characterized by definite radiation, which is usually along the course of the ureter, extending to the external genitalia (penis and scrotum in men, vulva in women) or down the homolateral leg, or upward from the groin to the kidney region, or it may extend across the body or to the scapular region.

"Colic is often accompanied by nausea, vomiting, constipation, distention and retraction of the testis.

"Vesical pain may be divided into that felt directly in the hypogastric region, and referred pain, which is usually felt along the course of the urethra or at the end of the penis. Emptying the bladder may relieve the pain for a time, but if the bladder is very irritable, spasmodic contractions may occur while it is empty, causing pain, which may be relieved after a small quantity of urine enters.

"Bladder pain depends upon an infiltration, inflammatory or neoplastic of the vesical wall. Bladder pain is most always accompanied by frequency of urination. The mildest type of bladder pain is described as a burning on urination. As the condition grows worse spasmotic contractions are produced which are extremely painful, this is known as tenesmus or strangury. These violent contractions may cause bleeding of the inflamed areas.

"Urethral pain is usually burning stinging, or lancinating. It may be only present during voiding and it is hard to distinguish from referred bladder pain. The point of greatest intensity often seems to be situated in the glans penis.

"The prostatic pain is usually felt in the perineum or
rectal region. It is burning, aching, lancinating, or throbbing. Referred pains from prostatitis is often increased in the morning.

"Dysuria another specific symptom is defined as painful and difficult urination. This is a general symptom in cystitis cases. Difficulty of urination, accompanied by more or less pain, occurs when there is a true infravesical obstruction. Obstructions lower in the urethra usually give the following symptoms:

1. There may be little or no frequency associated.
2. Marked diminution in the size of the stream.
3. Voiding is followed by a dribbling of urine from the meatus for some little time.

"Hematuria, while sometimes neglected by the patient, usually alarms him and sends him to the doctor; Women are most apt to ignore hematuria than men, since they are accustomed to see blood mixed with the urine during menstrual periods.

"Some idea of the source of the blood can be gained by examination of a three glass specimen of urine.

"Blood coming from above the vesical sphincter is usually thoroughly mixed with the bladder urine, whether its source be in the kidneys, the ureters, or the bladder. This type of hematuria can only be established by cystoscopic examinations.

"Bleeding from the kidney or ureter always indicates a lesion of importance.

"Frequency of urination may occur in three quite different ways:

1. The capacity of the bladder may be reduced by muscular hypertrophy, cicatrical contractions, calculi or tumors, so that
it cannot contain the normal quantity of urine, and must be emptied more frequently.

2. A partial obstruction below the bladder may produce a residual urine. The bladder may then contain, over and above the residual, only a small quantity, and must be emptied more frequently than normal.

3. The irritability of the bladder may be increased by inflammation or neoplastic infiltration, so that the desire to void arises more frequently and more imperiously than normal.

"The beginning of frequency may be difficult to determine exactly. Individuals vary as to the number of times a day they empty their bladder. The most important point in these cases to measure the quantity ordinarily expelled. As frequency increases, it may be accompanied by urgency, precipitancy or tenesmus.

"Frequency is often the first sign of urologic disease, and while mild forms may be ignored, the severer grades incapacitate patients completely, and cause the greatest distress.

"Pyuria is of great diagnostic significance, but is often ignored by patients. In other cases they are alarmed by mistaking a cloud due to phosphates or carbonates for pus. In the case of a turbid urine the presence of pus should always be confirmed by microscopic study.

"The three glass test tube is of special value in helping to determine the source of pus in the urine.

"Pyuria indicates an inflammatory condition, but it must not be forgotten that this inflammatory condition is often complicated by some other lesion, especially stone, neoplasm, or obstruction."
"DIAGNOSIS"

(11) "To know and recognize the symptomatic possibilities of urinary tract infections is a long step toward the diagnosis of secondary infection of the upper urinary tract.

"The responsibilities of medical diagnosis do not rest with establishing the existence of an upper urinary tract infection, but the infecting organism must be determined; possible primary foci sought out and the patient as a whole evaluated."

(12) "The urethra is the habit of numerous organisms. The fossa navicularis and the pendulous urethra are habitied by various diploccoci and staphylococci predominating, but the colon bacillus and other bacteria are commonly found. The Smegma bacillus is found in the lower portion of the anterior urethra but never back of the external sphincter. The urethra is easily sterilized by various antiseptic solutions and the Smegma bacillus can be eliminated by irrigation even with sterile water so that no difficulty is experienced in being sure that acid fast organisms are really the bacilli of tuberculosis."

By a simple laboratory test which requires very little time, one can determine the organisms causing the infection of the urinary tract.

(13) "A positive nitrite reaction in an infected urine depends upon the presence of nitrites formed from nitrates normally present, by the action of certain nitrite forming bacteria (Bacillus coli, staphylococcus, pyocyaneus etc.) the cause of the majority of infections of the urinary tract. Those that will not form nitrites are gonococcus, streptococcus and Bacillus tuberculosis. The latter two being rare as infective agents of the urinary tract."
"The reagent used is as follows:

1. Dissolve 0.5 grams of sulphanilic acid in 150 cc of 10 per cent acetic acid.

2. Dissolve 0.2 grams of alpha-naphthylamine in 20 cc of boiling water, and filter into 150 cc of 10 per cent acetic acid.


"The urine must be freshly voided into a sterile chemical clean container (because a non-sterile container may contain nitrite forming bacteria). Take 2 cc of urine and an equal quantity of reagent. If there is nitrite forming bacteria present, a pink color develops immediately.

"The reaction of the urine makes no difference to the test. In phosphaturia the cloudiness of the urine disappears as the precipitated salts dissolve, and no interference is found with the test.

"These cases with bacteria in the urine that are non-nitrite forming bacteria, may easily be determined by other methods. The presence of gonococcus is easily determined by smear in most cases, as the infection is rare in the upper urinary tract and a urethral discharge is usually present. Infection by streptococcus is rare in the urinary tract.

"The urine may show a negative test, and yet contain pus; one should always then look for tuberculosis bacillus.

"The urine may show a negative test, may not contain sufficient nitrite to give a positive test, due to a very great urinary frequency, not allowing time between urination for the conversion of nitrates into nitrites. Badly infected urine may
give a negative result, because the fermentation may go beyond the nitrite stage. In these latter cases add a few drops of a 10 per cent sodium nitrate solution and this mixture incubated for one half hour; if there is nitrite forming bacteria present you should get a positive reaction.

"From a clinical consideration, the greatest diagnostic importance of a positive test is in a case suspected of renal infection, such as an acute fibrile condition with pain in the right side of the abdomen. In such an instance one must always consider a colon bacillus pyelitis, especially in females. In these cases by the use of the nitrite test, one may quickly prove his diagnosis. This test is also valuable in pyelitis in children. The urine in this type of infection may contain no pus; but the presence of organisms can be determined within a few minutes with the nitrite test."

The appearance of an infected urine depends a great deal on its pH. We find that the colon bacillus occurs only in an acid or neutral urine, producing a peculiar odor, described as that of a dead mouse. The pyogenic cocci establish an alkaline media and thus aid in the formation of phosphatic calculi.

(3)"In acute bacterial cystitis with an acid urine, the pus forms a yellowish, or greenish-white, mobile deposits, not unlike that due to amorphous phosphates. The supernatant urine being fairly clear, and on agitating the vessel, the pus tends to distribute itself throughout the urine. In acute bacterial cystitis, with an alkaline urine, the pus appears as a tenaceous, gelatinous mass, which clings to the walls of the containing vessel and cannot easily be detached by shaking it, the bulk of the urine keeps permanently turbid.
The pus in the acid urine is due to one type of organism and that in an alkaline urine to another, as shown on page 9.

"Under certain conditions unexplained, an acid cystitis may supervene an alkaline cystitis and visa versa. When such is the case the prognosis is not so favorable, as the prospects of ridding the bladder of the infection without entering into the chronic stage, are rather poor. Resolving cystitis should under careful treatment terminate within the third day period."

(14)"Diagnosis of cases of urinary stasis, due to obstruction can easily be determined by an accomplished urologist. By a pylographic study of the urinary tract one can determine if any pathology is present. A normal kidney, pelvis, calyx, and ureter emptying time is from three to seven minutes. By fractional ureteropyelography one can determine, in any of the pathological conditions, present, the amount of stasis of urine; and how long the infected urine remains in the urinary tract. In any of the obstructive cases the emptying time may be delayed from seven minutes to four hours or more."
"TREATMENT"

Our knowledge as to the exact etiology and mechanism of urinary infections remains rather meager, and the treatment of such cases is still more baffling. If we were only to have to treat the urinary tract alone it would not be so difficult, but bacteria penetrate into the periurethral glands and other outpocketings of the urinary tract, which make it very difficult for drugs to reach the glandular structures.

One may for a short period be able to produce a steril urine; but that is not the primary problem.

(15) "In the infection of the lower urinary tract, the prostate, seminal vesicles, vas deferens and epididymis may be constant sources of re-infection. Besides that we generally have some outside sources of infection, such as teeth, tonsils, sinuses or colon, contributing to the re-infection of the urinary tract.

"Every portion of the urinary mucosa has been made accessible for the application of antiseptics, yet this has not been accompanied by equally satisfactory results in the treatment of all urinary infections."

(16) "In treating a case of urinary tract infection we must study the case as to the:

(a) Infecting agent.

(b) The source and portal of entry of this infection and its character and degree of extension.

(c) The abnormal conditions of the genito-urinary tract which may be accessory to the prolongation or spread of the infection."

The problem is to stop the infection at its source. That means thorough investigation of the lesion outside the urinary tract first, then proper methods to remove the lesion and so head
off the source of infection.

(12) "In cases of inflammatory infections of the urethra, the bacteria have usually penetrated into the periurethral glands and difficulty is experienced in obtaining sterility. We find that penetrating dye antiseptics are of particular value owing to their ability to go more deeply into the glandular and enterstitial structures along the urethra; the same is true to chronic prostatic infections.

"Sterilization of the bladder is usually not difficult. An infected bladder due to stasis will quickly clear up as soon as the obstruction is removed. It may throw off the infection spontaneously.

"When the kidneys are involved, a lavage is very benificial. The intravenous application of mercuriochrome has proven in many cases of kidney infections to be very benificial."

In attempting to treat urinary tract infections with drugs, we find that many complications arise.

(12) "As has been stated that fresh supplies of active living organisms are constantly contributed from the deeper tissues of the infected urinary passages, or from the prostate or seminal vesicles or from other places to which the drugs may hardly penetrate, and thus the infection may be kept up and renewed indefinitely. Once the urine is infected it forms a favorable culture medium which is continually being reinforced by the blood, pus and general organic debris, usually present, and these elements may in addition absorb and decompose a considerable part of the remedy and thus further diminish its effective action on the bacteria. The formation of ammonia from urea in some
cases and the obscure chemical interchanges alway going on among the urinary salts must also constitute a disturbing factor, which frequent emptying of the bladder may leave from time to time a quite inadequate supply of the drug to cope successfully with the bacterial growth."

(18) "At the present time there is no known drug which can be given by mouth which would prevent the growth and development of bacteria within the urinary tract. One of such nature would have to be defined as a chemical stable compound, comparatively non-toxic, and non-irritating to the lower urinary tract, which is eliminated, unchanged, by the kidney and which exerts a definite antiseptic action in high dilution in urine of any action. Up to date we have chlor-mercury fluorescein, acriflavine, and hexyl resorcinol which meet the requirements. We find that the elimination of any of these compounds from a normal individual will kill bacteria in a test tube, yet the same compound given to an individual with chronic bacteriuria over a given length of time, is likely to have no appreciable effect upon the bacteria in the freshly voided urine. Thus are urinary antiseptic must also have the power to produce proven clinical value. This latter property is one of great difficulty, because each individual is a clinical experiment in itself. We find each individual with bacteriuria varies day by day in the pus and bacterial content of the urine. The urine which is cloudy today may be clear and sparkling to-morrow.

"We must also consider the case in trying to prove whether or not a certain urinary antiseptic has produced a clinical value; because there are numerous so-called accessory or predisposing
causes of urinary infection which must first be eliminated.
There are certain well defined and well recognized, "intra urinary," predisposing factors which may be grouped under the main headings, urinary retention, calculus, new growth and tuberculosis.
In trying to prove the value of a certain drug in the above cases would be very hard to do. Whether our predisposing or underlying cause of infection be intra-urinary or systemic, to disregard this primary cause and to attempt a cure by merely rendering the urine antiseptic is obviously ridiculous.

"To prove a certain drug is a antiseptic value in urinary infection, we must first select are cases, and then do a complete general physical examination. Thus the clinical efficiency of a given "experimental" urinary antiseptic must be determined by the average opinion of a number of competent, unprejudiced observers, each of whom has tabulated accurate results, proving clinical value."

As Dr. Edwin Davis stated, one can only determine the value of a urinary antiseptic drug by ite clinical value and its benifical results. In some of the following articles I have tried to show the value of some of the antiseptic drugs used to-day showing both experimental and clinical results.

(19)"In 1917, with the assistance of Dr. H. Young, Dr. Edwin Davis obtained a small supply of acriflavine from Browning of (Bland Stutton Institute of Pathology, Meddlesex, Hospital, London). This was the first sample of this drup to be used in America.

"It was found that acriflavine in test-tuble experiments inhibits the colon bacillus and the Staphlococcus in high dilution in urine of and alkaline reaction. It was also determined that
the drug rapidly appears in the urine after intravenous and oral administration and is excreted in large quantities. It was also possible to conclusively prove that acriflavine in small dosage (.01 grams) administered orally to a normal individual, will cause the secretion of antiseptic urine, provided the reaction of the latter is alkaline. This drug should therefore theoretically be of clinical value in the treatment of various infections of the Urinary Tract, including pyelitis of infancy, chronic pyelitis of adults, acute pyelonephritis and in acute and chronic cystitis. During the treatment of acute gonorrhea urethritis it should be administered internally as a prophylactic against developing posterior urethritis.

"In treating acute urinary infections with acriflavine, Dr. Davis found a large proportion of these cases to have shown a prompt improvement, characterized by a drop in temperature, a disappearance of bladder symptoms, a macroscopic clearing of the urine and a disappearance of bacteria from the urine. In cases of chronic urinary infection 60 per cent showed an improvement.

"In 30 per cent of the patients there was a slight nausea, this was part due to the bicarbonate.

"In local treatment of acute anterior urethritis, acriflavine should be used in a solution of 1:8000, made up in normal saline solution, and this solution should be injected several times. On daily injection of 1:4000 solution is given if tolerated without urethral irritation.

(20)"The most recent contribution to the legion of the urinary antiseptic is S. T. 37 or Hexylresorcinol, by Leonard. It has a far more powerful germicide than any substance ever before described as possessing and equal degree of toxicity to
animals and man, it meets the qualifications of an ideal urinary antiseptic. It is administrable by mouth, chemically stable, non-toxic, and non-irritating to Urinary Tract, bactericidal in high dilutions in urine of any reaction and is excreted by the kidney unchanged in sufficient percent to impact active bactericidal properties of the urine."

We know that by lowering the surface tension of a germicidal solution we increase its bactericidal properties. By experimental procedures it has been discovered that a dilution which may be quite inert will become active when the surface tension of the solution is reduced.

(21)"The surface tension of pure water is 77 dynes per centimeter; Hexylresorcinol can lower the surface tension of urine to an average of about 50 dynes per centimeter. Lenord found by the administration of sodium bicarbonate increased the surface tension to about 66 dynes per centimeter, thus making the hexlyresorcinal almost inactive. It has also been found that by force fluids, which is one of the chief therapeutic measures in Urinary tract infections, also raises the surface tension.

"The use of Hexylresorcinol for urinary tract infections must be under strict observances and the following precautions must be taken:

1. The dosage must be adequate (.6 gram t.i.d.)
2. The fluid intake must not be increased.
3. Sodium bicarbonate must be avoided.
4. The course of treatment should be uninterruped and sufficiently prolonged."

(16)"Hexylresorcinol is bactericidal for all usual organisms
infection the Urinary tract.

An average of 63.5 days for Bacillus coli

" " " 18 " " Staphlococcus aureus
" " " 94.5 " " Bacillus proteus
" " " 91 " " Bacillus lactis aerogenes
" " " 133 " " mixed infection
to sterilize the urine.

The duration of the disease apparently has no bearing on the length of time necessary to affect a cure providing the renal parenchyma has not been damaged.

"S.T. 37, by thorough disinfection of the Urinary tract is an aid in preventing recurrent stones.

"In post-operative urological cases S.T. 37 is an aid in healing wounds in streptococcosis infections."

I have used this drug on post-operative urological cases, which I was taking care of for a Doctor this summer. We obtained very satisfactory results,

(22)"The French state that bacteriophage is a therapeutic agent of exceptional value in combatting certain types of infections of the urinary tract. Some authors have isolated particularly active races of anti-coli bacteriophage from sewage and employed them in treatment of chronic cysto pyelitis in females and obtained very good results.

"D'Herrils states that spontaneous recovery from an infectious disease is brought about by sudden activity of a natural bacteriophage, normally in symbiosis with members of the intestinal flora and capable of suddenly adapting itself to pathogenic invaders."
"In dealing with chronic urinary infections one is far more often confronted with bacteriophage resistant organisms. It is known that the resistance of the causal organism may vary some from day to day, and if one assumes that contact of the organism with a fully active bacteriophage should theoretically at least, lead to a therapeutic result. But as yet no one has been able to isolate bacteriophage of such polyvalency and virulence for different strains of bacteria.

"Theoretically at least, bacteriophage suspensions may exercise a therapeutic effect in two different ways.

(a) By direct action of the lytic principle on the usual microbe.

(b) By a stimulating action which the dissolved bacterial proteins in the suspension may exercise on the defense mechanism of the host."

(23)"It has been shown that a strain of bacteria exposed to the action of a given germicide may develop an increased resistance to the action of that germicide. If this is true may not the certain phenomena occur in certain local infections, such as the urinary mucosa in which the offending organism may be exposed to the action of various local and internal urinary antiseptics for long periods of time. It has been shown in cases where after a period of weeks on a certain urinary antiseptic, a sudden change of reaction of urine with a change of antiseptic cleared up the case within 48 hours."

It has been proven that the organism only gains and increased tolerance to only one germicide which it is exposed, and I believe that in a chronic urinary infection a logical plan is to apply the drug rotation."
Another drug that is being used a great deal to-day is Mercurochrome. 'It is one of the most efficient agent for intravenous chemotherapy. It is particularly effective in cases of acute and subacute infections of the urinary tract and it has also been of great value in occasional cases of acute general sepsis of various types. In chronic infections involving the urinary tract and the tissues it is not of great therapeutic value."

Dr. H. Young has found that mercurochrome given by mouth gives a valuable germicidal or antiseptic effect, and it might have a very beneficial effect upon local foci in the intestinal tract which were presumably responsible for certain colon bacillus infections of the genito-urinary tract."

We know that the Ph control: the growth of bacteria in the urine. In order to treat a primary acute bacterial cystitis successfully we must first identify and recover the organism. This way we can establish a correct bacteriological diagnosis and make preparations for an autogenous vaccine.

We find that acid cystitis is milder than alkaline cystitis, unless it is tubecular. Alkaline cystitis, is usually severe and serious, the urine extremely dirty and fowl, and frequently contains calcareous material.

"While it is easy to make the urine alkaline by saline drugs, it is extremely difficult to reverse the action and make it acid.

"It is essential to render the urine bland during the first two weeks of the onset of the cystitis. Copious drafts of alkaline water and the administration of sodium bicarbonate in one drahm dose four times daily will promptly relieve the
tenesmus and pollakauria. Sodium bicarbonate also possesses a slight diuretic and antiseptic properties. After a period of two weeks, the hyperacute symptoms will have sufficiently subsided and a return to an acid urine and the administration of antiseptic is advisable. Calcium chloride or ammonium chloride are very efficient acidifiers when given in 30 gr. doses four times a day. At this time urotropin given hypodermically in 15 grain doses daily should be commenced and continued for eight days. At the end of which time all symptoms will have subsided and a return to alkaline for six days is recommended. (Urotropin should be given hypodermically at this time because Urotropin and acid given at the same time by mouth causes gastric irritation.)

"The patient should be in bed during this time for a period of three weeks, caution should be taken so as not to cause patient to have a chill.

"Small doses of urotropin should be given for at least a month after the disappearance of all symptoms, like-wise small doses of calcium chloride. (Urotropin causes a temporary increase in discomfort and urinary frequency).

"Forced diuresis is important one up to the point of giving Urotropin.

"Elimination of infection from and alkaline urine.

(1) First move is to get urine acid to diminish urinary decomposition and hinder the growth of the organisms.

(2) Give ammonium chloride in doses of 30 grs. at three hour intervals and continue for two weeks. At the end of this time the urine will obtain a moderately acid reaction. The symptom of tenesmus and frequency will have subsided to allow patient out of bed for short intervals."
In many cases of staphlococcus cystitis the condition may be cleared up by the control of the reaction alone. In those cases of chronic infection probably due to mixed infection, vaccine therapy should be used.

"Under no circumstance should instrumentation be attempted in cases of acute primary cystitis. In females after symptoms have subsided a view of the bladder can be had, but must be done quickly and without trauma. Do not attempt to catheterize ureters at this time for fear of causing an ascending infection.

"Instillations do very little in these cases and never should be performed when patient has acute symptoms. At end of first week 5% argyrol may be used, once a day, they should be retained for at least one-half hour if possible."
"CONCLUSION"

Once the urine is infected it forms a favorable culture medium which is continually being reinforced by the blood, pus and general organic debris. These cases may become chronic and we find that there occurs almost complete local immunity so that the patient experiences no discomfort and complain of no symptoms; these cases are frequently overlooked.

Such cases who become secondary infected with some virulent organism, such as pneumococcus would be in a very dangerous condition. With the lowered body resistance the infection of the urinary tract would become active, and the body would have a double burden to overcome. These patients should be under treatment.

The Urologist has a great problem in treating urinary tract infections. He finds many bearers which must be treated first, before he is able to obtain satisfactory clinical results in treating the infection of the urinary tract. At times he must try varies antiseptic drugs in order to gain any results. This switching of drugs and treatments, causes one who doesn't understand the necessity of combating the infection in this manner to think that the Doctor doesn't know his stuff. Consequently after a few weeks of treatment, without gaining any satisfactory results, he goes to another Doctor; who must again start at the beginning. He administers the same drug as the first Doctor. But the organism has become immune to this drug, and so the infection becomes more chronic.

The problem is to educate the patients at the beginning. Explain to them the chronicity of the infection, and that the
treatment is a long drawn out procedure. Only in this way are we able to gain satisfactory results.

In the treatment of any infection the Doctor plays only a minor part, in curing the patient. The administration of drugs is only a small factor, nature has to overcome most of the burden.
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