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## Trigonitis

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TRIGONITIS

A Thesis Offered in  
Partial Fulfillment of  
the Requirements for  
the Degree of  
Doctor  
of  
Medicine  
by  
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College of Medicine  
University of Nebraska

1936

## TRIGONITIS

The condition which I shall treat of is one which is both little known and little appreciated by the general practitioner and indeed, even the urologist, in whose field it lies has of it, at best, only a hazy conception. I shall deal with infections of that small portion of the urinary bladder bounded by the two openings of the ureters and the vesical orifice called, because of its shape, the trigone. I shall attempt to limit my writings to those forms of trigonitis which are primary in that small area of tissue and are not merely extensions of pathology from neighboring structures such as the kidney or posterior urethra. The medical writings concerning infections of the trigone are exceedingly few in number. Louis Orr, in 1933, states that in a search of the literature dating from the last half of the Eighteenth Century the condition is described less than a dozen times. Ryall, in 1929, discussing the most frequent trigonal lesion, says that he is (13) unaware of any illustrated description of the

condition in urologic literature. According to  
(16)  
Hammond, as late as 1924, "English urologists were  
practically unaware of the disease and knew abso-  
lutely nothing of the pathology involved. He gives  
credit to Knorr, a German, for first describing  
the condition in 1900. In this connection Howard  
(6)  
Lindeman states, "Trigonitis was first described  
as a clinical entity by Knorr in 1900 and subse-  
quently verified by a host of observers. There  
have been some who have denied that this condition  
exists as a clinical entity, but there seems to be  
a preponderance of evidence in favor of the exist-  
ence of this condition as such." It should be noted  
(11)  
that the "host of observers" evidently failed to  
have their verifications printed. One author states  
that in the period from 1900 to 1924 several articles  
have appeared in America, where the condition has  
been called cysyitis localized to the neck of the  
bladder or cystitis colli. Because trigonitis is  
(6)  
found predominantly in women, much of the work done  
has been by gynecologists. It is still further  
significant that in the urological texts of the

present day only a few paragraphs are devoted to this topic. Considering then, the scant attention that has been accorded infections of the trigone it is not strange that there are many conflicting ideas in the writings; indeed, the differences of opinion are nearly equal in number to the men who write on the subject. Still, upon several cardinal principles there is some definite agreement. With these amicable points, then, as a foundation, and with others which are disputed and with considerable practical information outlined to me by practising urologists, I shall build my discussion.

Rather than to plunge the reader headlong into a discussion of the disease itself it might be better to familiarize him with some important embryological and anatomical considerations of this trigonal region. These points may serve to explain why certain pathological processes limit themselves to the region in question, and show no tendency to involve the rest of the bladder.

The bladder is entodermal in origin, being derived from the urogenital division of the cloaca within the

first two months of embryonic life. At a very early period in the growth of the embryo, there occurs an evagination from the ventral surface of the caudal end of the primitive gut. This structure, the allantois, gradually reaches out into the belly-stalk and becomes with further development an integral part of the umbilical cord. The portion of the allantois between the gut and the umbilicus is called the allantoic duct. That part of the gut which lies caudal to the allantois expands to form the cloaca which is at first a blind sac separated from the ventral surface of the embryo by the cloacal membrane. This membrane consists of the entoderm of the gut, a thin layer of mesoderm and the ventral ectoderm. Later, by a partition which grows in from its lateral walls, the cloaca is divided into a smaller dorsal portion which becomes the rectum, and a larger ventral portion-- the urogenital sinus. A constriction in this sinus then, at about the eleven millimeter stage of the embryo, differentiates a proximal vesico-urethral anlage which gives rise, as its name denotes, to the bladder and urethra. In the female, practically

all of the urethra is derived in this manner; in the male, the prostatic and membranous portions.

The ends of the mesonephric ducts and ureters are taken up in the developing wall of the vesico--urethral aulage and so include a mesodermal constituent in the bladder structure, which persists as trigone and proximal urethra. It is clear, then, that the bladder has a dual origin, partly mesodermal, partly entodermal,. The trigone is mesodermal of common origin with the urinary portion of the prostatic urethra, from the primary excretory ducts. The rest of the bladder and of the urethra is derived from the urogenital sinus and is entodermal.

Regarding the bladder mucosa; it is smooth when the bladder is filled and, except in the trigone, lies in loose folds when the bladder is empty. It varies also in thickness depending upon the degree of distension of the viscus. Over the trigone, it is always smooth and relatively thin. The epithelium is of the transitional type. The epithelium of the trigone does not differ in its essentials of structure from that of the remaining portions of the bladder.

In the bladder the submucosa is quite thick allowing the epithelium to be thrown into folds when the bladder is empty. In the trigonal region the amount of submucosal tissue is very slight, so that the epithelium is virtually fixed to the underlying muscle. Because of the fixation the surface of the mucosa is always smooth and velvety even in the contracted state. At the most under normal conditions in this region, there may be very fine longitudinal wrinkles or tiny epithelial papillae. The firm attachment of the trigonal mucosa prevents its prolapse into the urethra during micturition. The lining of the bladder appears to be a delicate salmon pink when viewed through a cystoscope. An irregular fine tracery of scattered venules show through from the submucosa. The trigone usually appears darker because of its greater vascularity.

The shape and size of the trigone vary considerably. Roughly speaking, it is approximately an equilateral triangle with sides from 2.5 cm. to 5cm. long. In the female the trigone is less distinct than in the male.



The frequency with which trigonitis is met may be only estimated. I have been unable to find any adequate statistics regarding its incidence. Knorr found eighty cases in four hundred cases in his clinic complaining of bladder symptoms. Furniss says,  
(11)  
"It is one of the most frequent bladder lesions in females; thirty per cent of the cases in the gynecological department have bladder symptoms and fully ninety per cent of these have cystitis colli, or trigonitis." Orr feels that the condition is  
(5)  
much more common than has been reported. Ryall  
(13)  
states that the pseudomembranous type of trigonitis is not infrequently met with in the female.  
(16)

As regards sex distribution, there is some difference of opinion. The majority of writers state that trigonitis occurs predominantly in the female. Ryall and Pelouse state that pseudomembranous trigonitis occurs exclusively in that sex. Louis Orr  
(16 & 15)  
reporting five cases of the pseudomembranous type, two of which were in males. Hammond states that the  
(13)  
condition is more common in women.  
(6)

Other factors in the etiology are even less definite.

Lindeman admits that the exact cause of trigonitis is unknown. He thinks that the condition is a little more common in women near the menopause but on the whole, age seems to be of little significance. Hammond has seen the disease most often in women between forty and fifty-five and it is his opinion that involutionary changes in the neighboring sexual organs may have some relationship. In one series of cases reported by Pelouse the age range is from twenty to sixty years and in another series the ages varied from twenty-one to seventy-one.

According to Lindeman, parity seems to be of no account. He states that the condition is relatively as frequent or more so in nulliparous as parous women. Also, that of the parous women it seems to occur proportionately no more frequently in those with cystocele than in those with normal bladder support. In Pelouse' first series single women predominated, while in his second, and larger, the reverse was true.

Pilcher says that a chronic cystitis frequently resolves itself into a chronic trigonitis, but in

the experience of Cary and Lindeman, the converse, that trigonitis is frequently the result of cystitis, is certainly not true. The two last named writers (3 & 11) claim that trigonal infection generally begins insidiously without any preceding bladder or other disease. Kelly and Byford have ascribed the condition to a hyperacidity due to improper metabolism but others have reported cases with alkaline urine. Garceau and Walther believe that it may be an infection from the start or be an infection grafted on a hyperemia due to pelvic engorgement from accompanying pelvic disorders. Hammond states that the condition may arise during pregnancy, but is more common (11) after labor, particularly if there has been some infection of the urinary tract. Also, that it follows inflammations of the neighboring organs--e. g. salpingitis and appendicitis-- but is not common in uncomplicated tumors of the uterus and ovary and such conditions as cystocele. Pelvic operations, he says, are common precursors, especially if they set up retention of urine.

(6)  
Regarding the offending micro-organism in trigonal

infections, there is considerable controversy. Young ascribes certain cases of trigonitis to an ascending Neisserian infection and states that in some cases pure cultures of gonococcus have been obtained.

(18)  
Hammond admits that trigonitis may follow gonorrhoea but states that in his cases a history of gonorrhoea is not common. Hammond states that trigonitis in women is frequently postgonorrhoeal. Lindeman states (6) that there is no satisfactory evidence that the gonococcus plays any important role and most cases show no evidence of recent or ancient gonorrhoeal infection.

(11)  
Hammond cites several cases of trigonitis which arose after acute infectious diseases such as influenza. Colon bacilli and staphylococci have been (11) found in the catheterized urine by Carey, and many others, but these offenders are frequently found in (3) the urine of perfectly normal bladders. Pure cultures of the colon bacillus have been reported. It is doubtful if any truly exhaustive bacteriological studies have been made in this condition. Regarding urine cultures Thomas Moore states that it has been

his experience that little is to be learned by them unless special cultrual methods are employed, with due regard for the oxygen tension and hydrogen ion concentration. He states that many times such bacteria as staphylococci and streptococci have been found in large numbers in direct smears of the urine sediment, although a culture of the same specimen, using ordinary culture media, will reveal no trace of the organisms, but only a luxurient growth B. coli. Rosenow described a case, in which, he demonstrated the presence of pseudodiphtheria bacilli in company with colon bacilli. Townsend also cultured pseudodiphtheria bacilli from some of his cases. In 1917 Nelken and Langford corroborated Rosenow's findings. Ryall made no mention of of any bacteriological findings other than the colon bacillus.

(13)

Young states that an acute localized cystitis is rare since an acute process tends to involve the entire bladder and it is his opinion that it is only mild, indolent, infections which remain circumscribed. Heitz-Boyer feels that trigonitis is due to organisms insufficient in number or virulence to set up a severe

(16)

(18)

infection, excreted by the kidney and poured out over the area between ureteral and vesical orifices. Rosenow has attempted to apply his theory of elective (18) localization, and using a strain of streptococcus, succeeded in reproducing trigonal lesions in rabbits. Other workers, however, have not been able to duplicate his findings.

There has been very little written of the microscopic pathology of trigonitis. Of gross appearance there are many detailed accounts which will be dealt with later in describing the cystoscopic picture. In a case of chronic trigonitis in a woman, curetted by Garceau, the curettings were submitted to "a Harvard pathologist" of unknown name, who gave the following description of the specimen, "Situated immediately beneath the stratified epithelium of the bladder are numerous lymphocytes massed together in an area to form an area similar to lymphoid tissue. A few lymphocytes are seen in the stratified epithelium, but these are very few. The stratified epithelium is well preserved in the specimen; it shows an occasional mitotic figure, but there is little

evidence of inflammation in the stratified epithelium. In some areas the aggregation of lymphocytes is situated immediately beneath the bladder stratified epithelium, and this epithelium is intact. This shows chronicity of the process. The trigone is on the whole, smooth. There is abundant evidence of subepithelial inflammation." (11) Veit says; "There is round-celled infiltration, vascular proliferation, epithelial hyperplasia, desquamation and cyst formation." Legneu describes it as follows; "Vascularization of the mucosa, (11) epithelial cyst formation, and even leucoplastic transformation of the epithelium. At first there is a local hyperemia contrasted with the normal bladder mucosa, later a thickening of the mucous membrane even to proliferation and formation of papillae and warts." Young says, "The usual picture is that of (11) a rather superficial congestion and edema. There is some cellular infiltration, both round and polymorpho-nuclear, though the reaction may not be severe enough to cause pus cells to appear in the urine. \*\*\* If this condition persists, chronic changes supervene, consisting of polyps, small masses of granulations,

sometimes covered by epithelium and with a raspberry appearance, and fibrosis. In the pseudomembranous (18) types the membrane is on the order of an exudate.

So far as I can find no one has had the opportunity of performing a post mortem examination on any case of trigonitis.

The symptomatology of the infections of the trigone is described differently by various writers. Lindeman says, speaking of chronic trigonitis in the female, that generally speaking, the onset is insidious with gradually increasing frequency of urination, especially by day, but somewhat also at night. He states that there is usually no pain, but at the end of the act of urination there is generally a sensation of incompleteness and a desire to pass more. Some patients are obliged to relieve themselves as often as every five minutes during the day, voiding only a few drops each time. As this condition progresses the patient becomes more and more miserable, all work, meals, and even sleep are interfered with and the patient is obliged to devote her entire time to emptying or trying to empty her bladder. In these later stages



there may be some pain, but it is rarely very severe, and, occasionally, there may be a slight terminal hematuria. Hammond says that while the onset is usually <sup>(11)</sup> insidious, it may be very acute when an infection of the urinary tract is probably the primary cause. He also notes frequency during the day, followed later by increasing nocturia. This symptom is more pronounced after exercise, exposure to cold, or any indiscretion in diet. He states that pain referred to the neck of the bladder, to the perineum, or to the external meatus is common. It sometimes radiates to the sacral and lumbar regions. It is not relieved by rest; while sometimes most intense before and during micturition it is generally most marked at the end. It may be extremely severe, and there may be acute paroxysms unrelated to micturition. In some cases only a slight burning pain or a feeling that the bladder has not been emptied is present. There may be urgency of micturition and also a little difficulty in starting the stream. Sometimes, he states, there is a history of hematuria.

(6)

Of the course and prognosis of the chronic type

Furniss says that it may last for years, and Sommers,  
(5)  
"With remissions it may last indefinitely." Garceau  
(11)  
mentions a case that continued for ten years, and the  
patient was in a pitiable state from loss of sleep.

Hammond says that though the symptoms may remain  
stationary for years and years, and periods of complete  
remission may occur, the course is gradually progressive,  
and sooner or later the general health becomes under-  
mined.

(6)  
Ryall, Orr, and Pelouse, discussing pseudomembranous  
trigonitis are in fair agreement on the symptoms,  
course and prognosis of that type of infection. The  
former states that, as a rule, the symptoms set in  
suddenly without premonitory complaints. He lists  
frequency present both day and night as the primary  
symptoms. Regarding pain, he states that it usually  
occurs at the end of micturition. In other cases it  
sets in at the commencement of the act, lasts through-  
out and becomes more severe directly the bladder is  
emptied. It may last but for a few minutes or persist  
until the next call to micturition; as a rule the more  
severe the pain the shorter the duration. Its seat is

at the external urinary meatus, and has been described, when severe, as agonizing. Its severity varies from time to time. The pain at the onset of an attack is less severe; it develops in intensity, reaches its acme, and, after variable time, wanes, leaving a soreness or uncomfortable feeling. Intermissions of days or weeks may elapse. In addition to the pain referred to the external meatus, dull aching in the legs or groins may be present. The pain, as a rule, is exaggerated for about a week before the catamenia appears but is relieved when the flow is on.

In some cases, according to Ryall, there may be tenesmus. In his opinion the tenesmus, the pain and its severity, together with the urgency, depend on the mischief extending into the neck of the bladder and some distance down the urethra. He states that urethral involvement may in some cases be beautifully demonstrated by the irrigating urethroscope. Pelouse (16) lists as the most frequent symptom frequency, and as the next most frequent vesical tenesmus. Like Ryall, (14) he attempts to explain the variance of symptoms in different cases. "The severity of symptoms," says

Pelouse, "varied to some extent with the nervous make-up of the patient, as would be expected, but their character bore a more direct relation to the trigonal location of the lesion. Patients in whom the lesion was confined to the posterior portion of the trigon had frequency of urination alone, whereas those in whom the lesion approached or passed into the vesical outlet experienced the more severe symptoms of burning or tenesmus and, at times, the appearance of a few drops of blood at the end of urination. At times there was not a true vesical tenesmus in these cases but a period of vesical discomfort lasting for some time after urination."

(14)

Concerning the hematuria just mentioned Pelouse found it in five out of forty-two cases. According to Ryall hemorrhage is rare; he has seen it on but one occasion, and it lasted six day. Hammond merely states that hematuria is sometimes found. Cabot says that blood cells are found occasionally in the urine, due to diapedesis.

(16)

(6)

(2)

Orr points out that the mode of onset is somewhat different in different cases. Often times patients

consult a physician a year or more after the beginning of the trouble, the only symptom being, in most cases, frequency, or perhaps a slight terminal hematuria.

In one of Orr's patients the first symptoms were those of a typical acute cystitis with frequency, urgency and tenesmus without chills or elevation of temperature.

Rosenow reported one patient who was seized with a sudden attack of chills and fever with frequent painful and bloody urination. Nelken reports a patient with a history of two months terminal hematuria without distress before he was seen.

(13)

As for the duration, all agree that, untreated the condition may persist, with remissions, for months and years. Ryall says that the symptoms have a tendency to recur. Peiouse states that, as regards the clinical course, there are obviously two types of pseudomembranous trigonitis. The first, he says, and vastly more common type, is characterized by a sudden onset, a duration varying from a few weeks to several months, and a cessation as sudden as the onset. These seemingly self-limited attacks show a definite tendency to recur at varying periods ranging from a

(16)

few months to several years. The less usual type of the disease presents a long history of urinary frequency, in some cases as high as twenty years.

(14)

The diagnosis of trigonitis is not easily made.

The symptoms, to be sure are, in many cases suggestive, but certainly none of them are peculiar to this condition. Perhaps most characteristic is diurnal frequency. Appropos of diagnosis Dr. Thomas D. Moore states, "The chronicity of this disease and its severity approach those of urinary tuberculosis and advanced panmural fibrosis. In addition to leukoplakia these two conditions might well be considered in the differential diagnosis." Bacteriological studies of the urine and pyelography may be used to advantage in excluding tuberculosis. Because in the majority of cases the urine is repeatedly free from pus, many cases are classified as neurotics, and their symptoms thus explained. At any rate the certain diagnosis of trigonal involvement rests entirely upon the use of the cystoscope. Several excellent descriptions of the gross pathology, as viewed through this instrument have been written.

(13)

Ryall's account of the findings in the pseudo-membranous type is classical. Quoting him, then, "The condition is characterized by the appearance of a somewhat translucent veil or cloud of grayish pink color in the trigonal area, either completely covering the trigone and sometimes extending into the urethra or merely present as scattered patches. (The latter effect is well seen in the healing stages of the trouble.) This veil or opacity of the superficial layer of the trigonal mucosa is thickest and most marked at the periphery, where the edges are well defined and irregular, being raised above the surrounding area. It is thinner and more transparent in the center. The color varies; in some cases it resembles a cloud in the sky in its heaped-up whiteness, in others it presents a pinkish hue and may exhibit a granular effect at the periphery, like sago grains enmeshed in a silken veil." He goes on to add that the veil may be so transparent that it is missed by the unskilled cystoscopist, and this is in accord with the opinion of Pelouse, who advises the operator to look at the trigone

obliquely, lest he fail to observe it looking directly. He says that the membrane looks exactly as though the surface had been touched with the weakest solution of silver nitrate that possibly could make a slight blanching of the tissue. He claims that the lesion is always confined to the trigone and it is singularly almost always on the right side in front of the right ureteral orifice, extending for varying distances toward the vesical outlet. Rarely, he states, is the lesion found on the left side, and even more rarely does it cover the entire trigone. Dr. Thomas Moore describes an injected (14) trigone upon which are irregular areas of a thin grayish membrane, resembling wet tissue paper.

(13)  
Hammond's cystoscopic findings are somewhat different. He describes the trigone as congested and thickened, and compares its appearance to red velvet. The line of demarkation from the surrounding healthy bladder is usually very distinct. He states further that edematous patches are not uncommon especially in the neighborhood of the uternal sphincter, and that the papillae may be much swollen



and hypertrophied, resembling true polypi. Scattered red spots like petechiae and small shallow ulcers may be seen. Lindeman's description of chronic trigonitis is similar. He describes the trigonal mucosa as swollen, dark red, intensely angry looking, and cloudy. Blood vessels may be seen but their contour is far less distinct than in the remainder of the bladder. The normal yellow mucosa cannot be seen between the vessels as in simple hyperemia, states Knorr. Garceau has described scattered red spots resembling ecchymoses, as has Lindeman. Carey claims that the trigone bleeds easily at a slight touch of the cystoscope but Lindeman finds it particularly resistant to trauma and states that it can be made to bleed only with difficulty. Lindeman states that in his cases of chronic trigonitis whitish or yellowish white areas in the congested region due to cellular metaplasia are rare, but that when they do occur, the cases are particularly intractable to treatment. Furniss and Carey are in agreement with the finding. Whether these areas of cellular metaplasia are similar to the membrane or pseudomembrane

described by others is a matter of conjecture, but I think that in a part of the cases this may be true. It is my opinion that the membranous and the non-membranous types are not two distinctly different conditions, but are more probably different stages of, or different reactions of the individual to the same disease. The fact that the treatment, course, and prognosis of the two varieties of trigonal infection is very similar seems to bear out this conclusion.

Various methods of treatment of trigonitis have been advocated. Ryall advises rest in bed for a week if the symptoms are very acute. Nearly all authorities agree that the common urinary antiseptics, such as Urotropine and the analine dyes are of no value. Ryall suggests the use of sandal-wood oil in ten minim doses, or preferably, creasote in five minim doses to relieve the distress, but makes no curative claim for these drugs. In connection with this he also uses potassium salts and large doses of tincture of hyoscamus. Hunner has advised the continuous bath, and others have instilled various drugs but without marked success.

Ryall says that locally, the application of silver nitrate to the trigone gives the best results. This may be done by injecting one dram of a solution into the previously emptied bladder, through a soft catheter, the medication to be voided at the next micturition. Ryall uses this method at five to seven day intervals, starting with a one percent solution and increasing the strength up to as high as a six percent concentration. Knorr introduces an endoscope (16) after previous installation of a eucaïne solution, and through it passes a sterile cotton wound applicator treated with a silver nitrate solution from one to five per cent. The endoscope is then withdrawn and the bladder contracts in a spasm on the applicator squeezing out the silver solution over the bladder floor. The applicator is withdrawn after thirty seconds, thus at the same time medicating the urethra. Pelouse advises injections into (11) the bladder of a half ounce of one to three percent silver nitrate leaving the solution until the next urination. In the more severe cases he advises evacuation of the silver solution after a few moments

and injection of a half ounce of one of the sedative oils, such as oil of gomenol. He says that all but a comparatively small number of patients are quickly rendered symptom-free by this treatment. Garceau advocated the formation of a vesical-vaginal fistula and scrubbing the trigone with a short fivered brush, or curretage, in stubborn cases. Most urologists consider this procedure ultraradical and avoid it.

Lindeman having tried silver nitrate application and various other treatment but with very little success, devised an injection method, similar to the ones used in the treatment of hemorrhoids, which he believes holds great promise. He uses a Brown-Buerger cystoscope and a self-devised injecting device. The solution used consists of a sterile two to three per cent concentration of quinine and urea hydrochloride in normal saline. It is colored rather deeply with methylene blue. It is advisable, he states, to add a small amount of adrenalin. Only two or three drops of the solution are injected, or enough to form a small blue weal. The needle

is then withdrawn and entered elsewhere until as much of the trigone as is desired is infiltrated. Lindeman generally begins close to a ureter and works across the trigone in a line, and then back across the trigone a short distance in front of this line. This is continued as far forward as desired. It is advisable not to make the injections too close together; each new weal should just abut on the one preceeding it. Several sittings are usually necessary to cover a large trigonal lesion. Lindeman states that he has treated several patients in this manner and that there have been no bad results and no failures. His patients have unaminously stated that they have been greatly relieved for consideral periods of time; some apparently have been permanently cured. Cystoscopy of patients previously treated showed that the areas of injection were plainly discernable for long periods of time after. The areas where the weal had been stood out as pale yellow spots, resembling almost normal bladder wall, surrounded by the diseased, angry looking mucosa. Hammond admits that the injection treatment has given <sup>(11)</sup>

good results but he complains that it is difficult to carry out in women and impossible in men.

(6)

Ryall and Hammond have employed diathermic fulguration through a cystoscope with promising results.

(16 & 6)

The current is applied directly to the trigone in lines radiating from the internal meatus. The current should be sufficiently strong to cause the area to which it is applied to take on a whitish appearance. Hammond thinks that undoubtedly a superficial necrosis occurs but he has never seen any harm follow this method. Subsequent cystoscopy, he says, shows that the congestion has largely disappeared and the trigone has a more normal appearance.

(6)

Thus we find that trigonitis is resistant to all those remedies that are beneficial in chronic cystitis. Ryall stated that unless local treatment is administered the chances of getting well are not hopeful. The treatments recommended by the various writers, as set forth above, have, each one, some merit. The reader has probably noted that they are all rather similar in principle if not in technique. The underlying principle seems to be that of cauterizing or

necrotizing the involved area. No single method is favored, since it is easily seen that the choice depends largely upon the skill and ingenuity of the operator as well as upon his prejudices and those of his patients.

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