MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

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URINARY TRACT SYMPTOMS AND INFECTIONS IN THE ADULT

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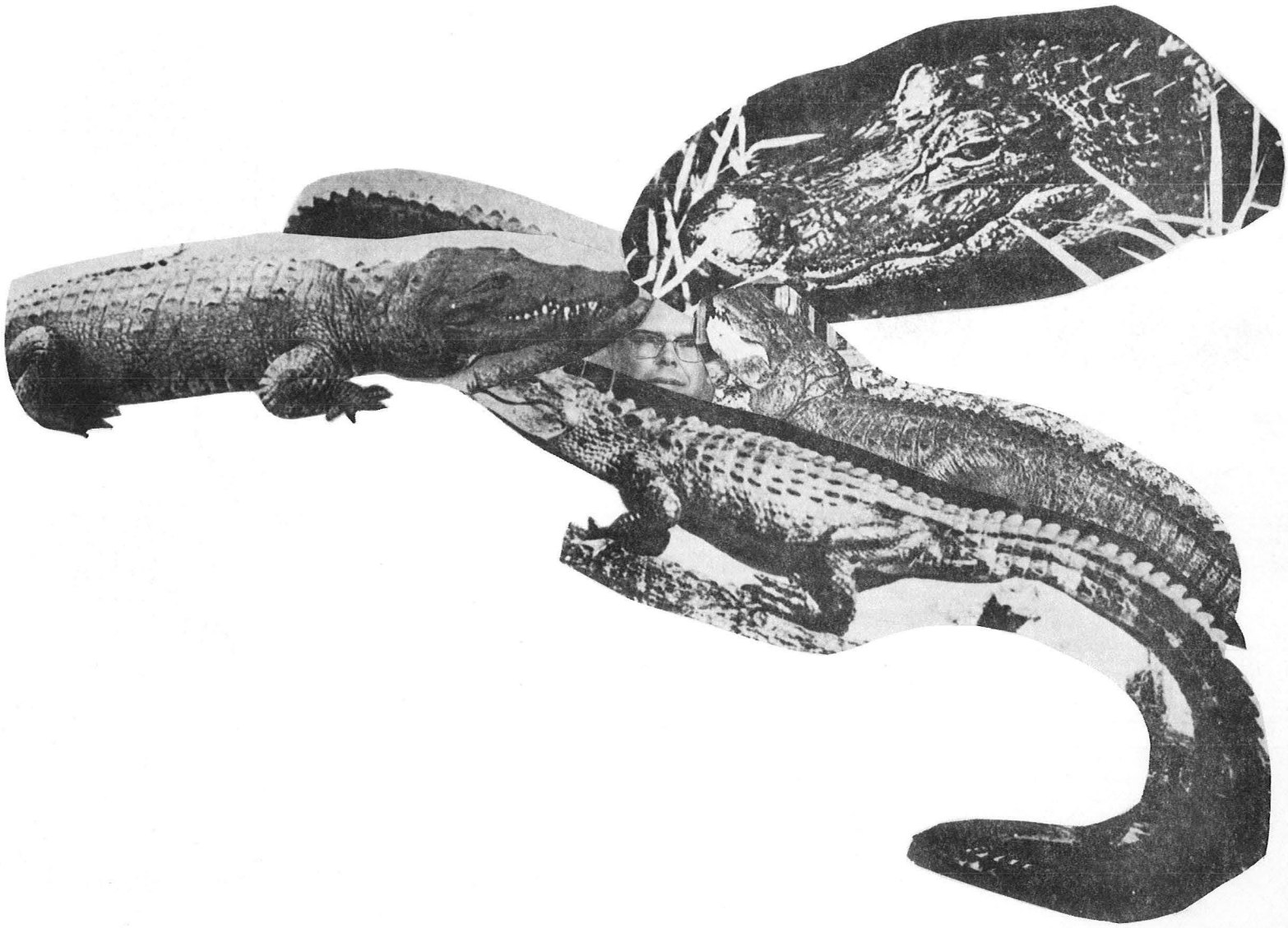


URINARY TRACT SYMPTOMS AND INFECTIONS IN THE ADULT

Case: 34-year-old [redacted]

[redacted] *1972:* awakened with urgency and terminal dysuria. Symptoms intermittent. No antimicrobial therapy.

[redacted] noted appearance and progressive increase in left CVA tenderness and fever. Urinalysis at 11:00 p.m.: 50-200 WBC/hpf, loaded with gram-negative bacilli. Culture: 44,000,000 cols/ml of *E. coli*. Treatment began with sulfisoxazole (1.0 gm q6h) and continued for 14 days.

[redacted] completely asymptomatic

Jo[redacted] urine culture "sterile". IVP normal.

[redacted]*:* urine culture "sterile".

Problems:

1. What should the acute management include:
   a. Sulfonamides, antibiotics, or other agents? For how long?
   b. Should an intravenous urogram and voiding cystogram be done?
2. If the initial urine culture were negative, what would you do? Stop antimicrobial therapy or continue?
3. Should the urine culture be repeated? If so, when? If positive upon repetition but the patient is asymptomatic, what should be done?
4. What is the anticipated course and ultimate prognosis?

Recent progress in the prevention and control of many infectious diseases has brought to the fore those infections which are caused primarily by the indigenous bacterial flora and those which represent hospital associated infections. Infections of the urinary tract occupy a major position among these types of infection.

The sensation of discomfort on passing urine is experienced by large numbers of patients at some time or other during their lives. In a survey of 2933 women, aged 20-64 years (over 86% of all such women in the survey area of South Wales), 21.8% of women said that they had had dysuria during the previous year (*1*). Age had no significant effect on this proportion. Nearly 10% of all women had consulted physicians during this time, with the proportion being significantly higher in the younger age group. Dysuria is encountered in approximately 1% of patients seen by primary care physicians, with marked variations between women and men and at different ages (*2,3*) (Figure 1, Table 1).

FIGURE 1

Urinary Infections in Males and Females in a General Practice Between 1955 and 1957: Incidence per Thousand

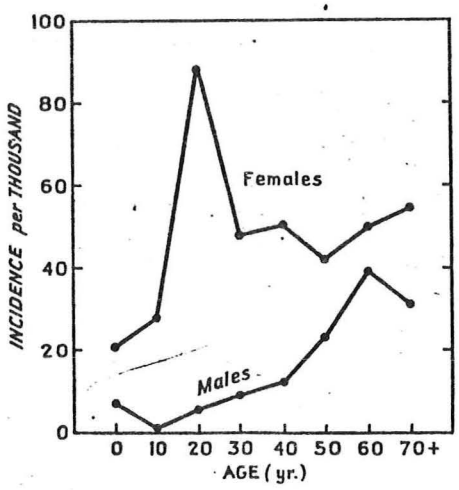


TABLE 1

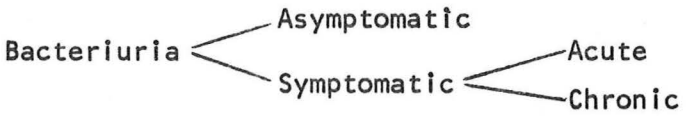
Prevalence of Urinary Tract Infection (3)

Age in Years	*No. pts/1000 pop./year*	
	Females	*Males*
16-19	14	0
20-29	26	1
30-39	22	2
40-49	16	4
50-59	12	2
60-69	26	8
70-	30	18
Average	20	3

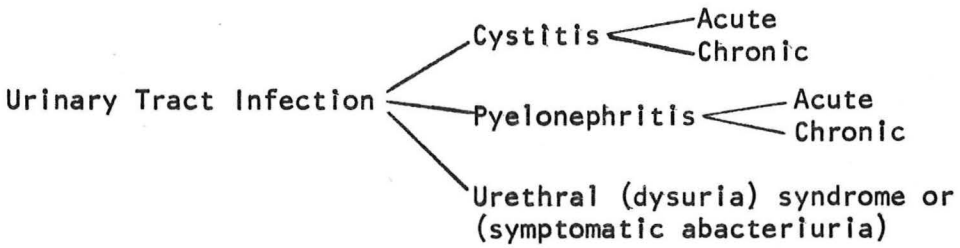
In addition to this large group of symptomatic individuals, at least one half of whom seek medical advice, there is an additional group of individuals with infection in the urinary tract which has received much attention, i.e., women with asymptomatic bacteriuria. Population surveys have shown significant bacteriuria in from 3 to 7% of adult women. Sussman et al. have studied the same general population in South Wales as Waters studied and determined the prevalence of bacteriuria to be 3.0% (*4*). In followup studies, Asscher et al. demonstrated that bacteriuria cleared spontaneously within one year in 11% of this group of bacteriuric women, while 5% of a group of non-bacteriuric women developed bacteriuria during the same interval (*5*).

In attempting to analyze the significance of such observations, it is essential to define terminology. Unfortunately, terminology in the field of urinary tract infections has become somewhat of a morass. Following is an attempt to define and interrelate some of the terms:

Bacteriuria: the presence of a "significant" number of microorganisms in urine. The number to which "significance" is attached depends upon the method of collection; for suprapubic aspirations any bacteria are of significance, for catheterized specimens the figures of $\geq$ 10,000 or 100,000/ml have been used, and for "clean voided" specimens "significant" bacteriuria requires at least two specimens containing the same bacterial species (or serogroup of *E. coli*) with both $\geq$ 100,000/ml. Bacteriuria may be either symptomatic or asymptomatic. Even the term asymptomatic doesn't mean the absence of symptoms on direct interview, but rather the absence of symptoms of sufficient severity to bring the patient to a physician; thus,

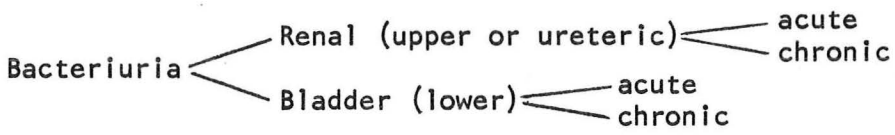


Other terms include:



From the operational standpoint, the term *pyelonephritis* is applied to bacterial (non-tuberculous) infections involving the renal parenchyma and/or renal pelvocalyceal system. The designation *urethral syndrome* will be defined subsequently.

Finally, the term *bacteriuria*, which is too loose, can be further defined as to localization of the site from which bacteria are shed into the urine:



These latter may or may not be symptomatic.

ACUTE URETHRAL SYNDROME (Dysuria syndrome or symptomatic abacteriuria):

It has long been recognized but has not been discussed in the literature until recently that many patients seen with complaints of frequency and dysuria have "negative" urine cultures. In the now classical study, Gallagher, Montgomerie and North studied a group of patients seen in the offices of eight physicians in Auckland, New Zealand (*6*). A qualified nurse obtained a catheterized specimen of urine which was immediately refrigerated and examined and cultured within one hour of collection. During eight months, 130 patients were studied (Table 2).

TABLE 2

Quantitative Bacterial Counts of Urine (6)

No. of Bacteria/ml	*No. of Patients (130)*	
	With Infection	*"Without Infection"*
$> 10^5$	56	-
10^4-10^5	8	-
$< 10^4$	-	12
Sterile	-	41
Quantitative culture not done	13	-
Total	77 (59%)	53 (41%)

The interesting finding is the many similarities between the group of patients with bacteriuria and those without (Table 3):

TABLE 3

Presenting Symptoms

Symptom	*Patients With Infection (77)*		*Patients Without Infection (53)*	
	No.	*%*	*No.*	*%*
Fever	28	36	8	15
Dysuria	71	92	38	72
Hematuria	18	23	7	13
Frequency	70	91	50	94
Loin pain	26	34	17	32
Lower abdominal pain	49	64	34	64

Significant pyuria (> 5 WBC/hpf) was present in 10 of the 77 urines from patients with bacteriuria (13%), as compared with 7 of 53 (13%) of patients without bacteriuria.

The physicians were asked to assess the sureness of their diagnoses (Table 4):

TABLE 4

Clinical Assessment of Diagnosis of Infection of the Urinary Tract

Clinical Assessment	*Patients With Infection*		*Patients Without Infection*	
	No.	*%*	*No.*	*%*
Certain	27	35	10	19
Highly probable	34	44	22	41
Probable	13	17	12	23
Doubtful	3	4	9	17
Total	77	100	53	100

Gallagher et al. felt that many cases were due to infection confined to the urethra and surrounding glands, especially since bacteriuria subsequently appeared in 13 of 46 of the patients who were initially abacteriuric. These overall observations have been confirmed in subsequent studies; Steensberg et al. (*3*) found 23% of their women and 14% of men with symptoms of urinary tract infection did not have bacteriuria and Fairley et al. (*7*) found 23 of 66 (35%) of women presenting to general practitioners with symptoms of acute urinary tract infection had $\leq$ 10,000 bacteria/ml of urine. In the group of 23 patients studied by Fairley, 9 had pyuria (> 2000/ml) (39%) and 5 had gross pyuria (> 15,000/ml). Patients with renal infection invariably showed > 20,000 WBC/ml, whereas 5 of 22 with bladder infection had counts within the normal range (< 2000/ml).

O'Grady et al. have shown that patients with frequency and dysuria in the absence of bacteriuria fall into two groups: those who were symptomatic and always abacteriuric and those who were symptomatic but sometimes bacteriuric *(8A)*. Urinary white cell excretion also fell into two patterns: patients who never had pyuria or had < 20 WBC/mm^3 (Figure 2) and those who had higher levels of pyuria (Figure 3). In this latter group, significant pyuria was seen with symptoms but without infection. In 28 of 91 patients, treatment for various conditions outside the urinary tract cured (or strikingly improved) their symptoms (Table 5).

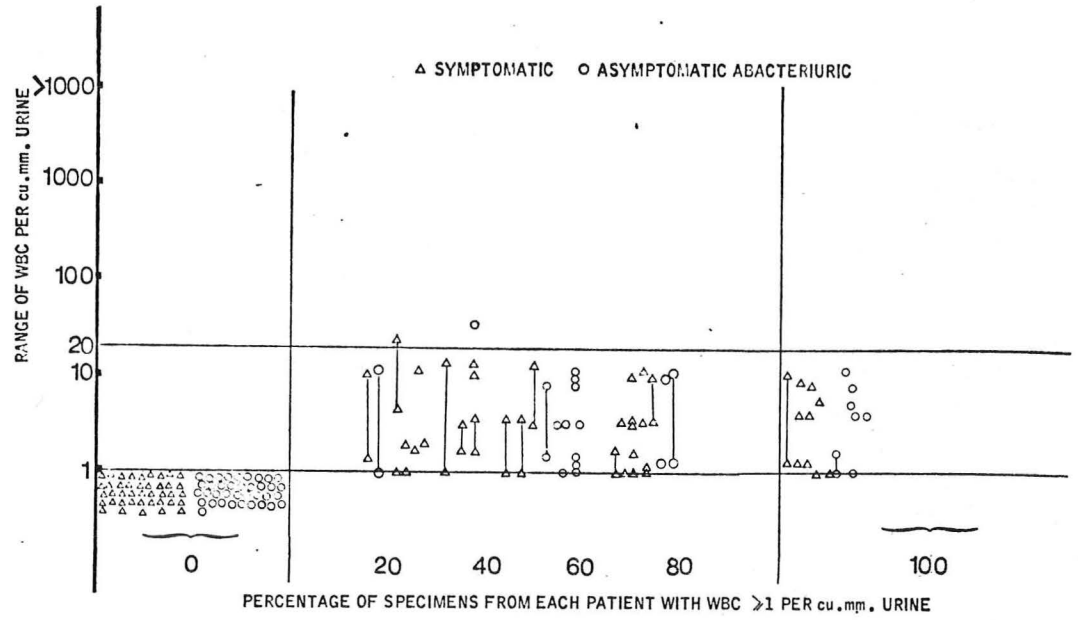


FIGURE 2
White cell excretion patterns of patients with abacteriuric "urethral syndrome" with o asymptomatic and Δ symptomatic

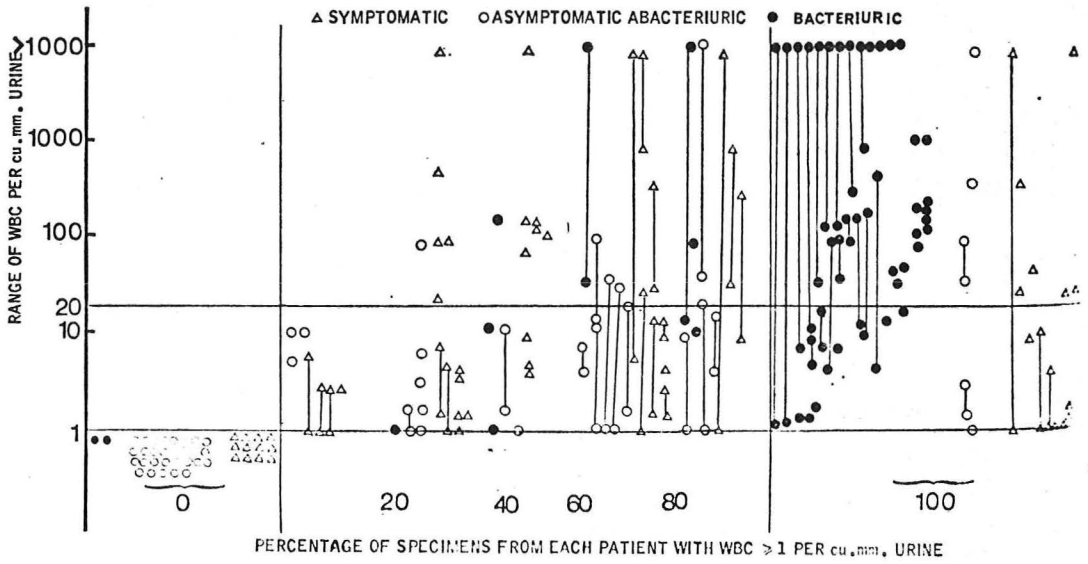


FIGURE 3
White cell excretion patterns of patients with intermittently bacteriuric "urethral syndrome", when o asymptomatic, Δ when symptomatic and abacteriuric, ● when symptomatic and bacteriuric

TABLE 5

Nature of Successful Treatment in Patients With Abacteriuric "Urethral Syndrome"

No. of Patients Whose Symptoms Were Controlled:			
by appropriate treatment		*by*	
Inflammatory disease of bowel	4	Pregnancy	2
Gynecological surgery	4	Chlordiazepoxide	2
Vaginitis (Senile 9)	12	Bellergal	2
"Pill" upset	1		
Self-medication	1		
Total:	22		6

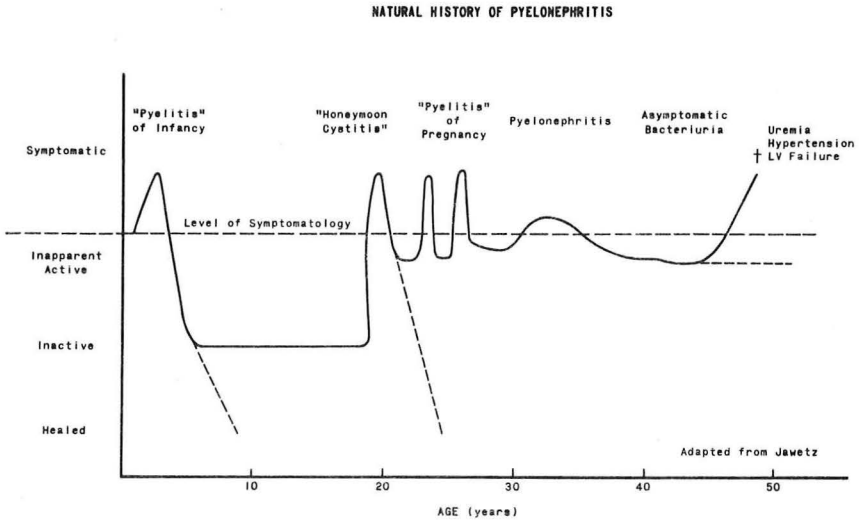
The etiology in many of the patients with the urethral syndrome without pyuria remains unknown. Studies in progress have included searches for viral agents, chlamydiae (TRIC agents), gonococci, wall defective bacteria, etc. In the patients with pyuria, symptoms and sterile cultures, it is essential to include tuberculosis, fungal disease of the kidneys and calculus disease in the diagnostic considerations. It remains to be proven but it is likely that patients with abacteriuria but pyuria would benefit from antibacterial therapy, while those without pyuria will not.

The importance of recognizing this syndrome(s) rests in that many of these women do not have bacterial urinary tract infection, will be studied extensively, often treated with costly and/or toxic antimicrobial agents, be subjected to various invasive urological procedures, be carried as "chronic pyelonephritis", etc.

BACTERIURIA (Symptomatic and Asymptomatic)

Since the classic work of Longcope and Winkenwerder and Weiss and Parker, the occurrence of chronic renal disease as a consequence of pyelonephritis has been well recognized in the United States *(8B,9)*. Weiss and Parker asked, are cases of "silent bacteriurias" benign or can they cause subsequent hypertension or renal failure? Should they be treated as intensely as those associated with the clinical picture of pyelonephritis (*10*)? Based upon numerous observations such as those of Weiss and Parker as well as those of many others, it was postulated that pyelonephritis might be considered as a disease continuum rather than as a series of apparently unrelated episodes (*11*) (Figure 4).

FIGURE 4



This sequence of events can be well documented by individual patient summaries, as illustrated by the following:

28-year-old [redacted] ([redacted]), admitted to the hospital for the last time in [redacted] 1957. There was a history of hypertension in the patient's mother and two aunts. Her present illness is sketched as follows:

1941: Delivery stillborn at home
1952, [redacted]: Antepartum second pregnancy. Blood pressure 118/70-140/90
1952, [redacted]: Admitted postpartum. Blood pressure 168/100. Urine: 80-90 WBC and trace albumin
1953: 3rd pregnancy. Blood pressure increased. Followed in [redacted].
1954: 4th pregnancy, delivered at home.
1955, [redacted]: Antepartum (last trimester) 5th pregnancy. Blood pressure 150/108 to 170/105. Urine: no albumin, 3-5 WBC. Blood uric acid 3.9 mg.%. Treated as pre-eclampsia with fall in blood pressure to 134/88.
1955, [redacted]: Postpartum admission blood pressure 140/92.
1957, [redacted]: Postpartum admission, 6th pregnancy. Blood pressure 220/110. Ocular fundi showed vasospasm, heart was enlarged. Urine: 4+ albumin, 1+ sugar. BUN 17 mg.%. Treated as pre-eclamptic, blood pressure decreased to 180/120.
1957, [redacted]: Seen in hypertension clinic. Blood pressure 220/140. Ocular fundi: old bilateral macular retinitis and arteriolar spasm, no A-V nicking. Heart enlarged.
1957, [redacted]: Admitted [redacted] for sterilization. Blood pressure 230/150. ECG: left ventricular strain. Urine: 12-16 WBC/hpf. Urine cultures: 7/23

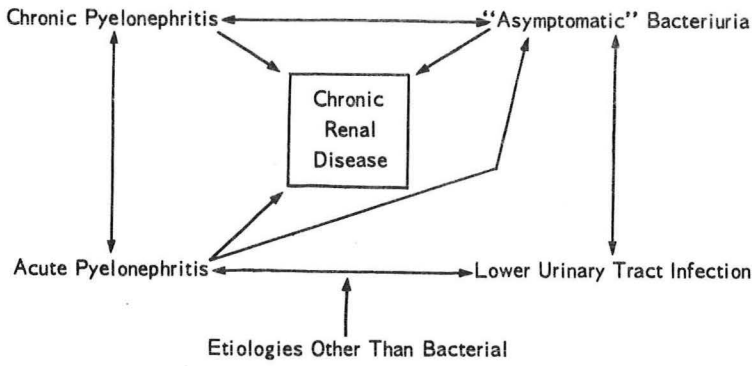
sterile, 7/31 > 500,000 *Staphylococcus aureus* (coagulase positive)/ml. [redacted] sterile. BUN 21-69 mg.%. Treated with streptomycin, tetracycline and novobiocin. Blood pressure decreased to 150/100.

1957, [redacted]: Seen in emergency room several times for nausea, vomiting, diarrhea, fainting and "convulsions". BUN 146 mg.%. Readmitted [redacted]/57. Blood pressure 180/120, other findings as before. Developed acute pulmonary edema and died within 36 hours of admission. Laboratory findings at that time: BUN 114 mg.%, CO_2 12 mM/liter, creatinine 8.8 mg.%, WBC 54,000/mm^3 with 98% PMNs. Urinalysis: 3+ albumin, rare WBC, gram-positive cocci seen on smear. Culture: *Streptococcus fecalis*. Postmortem examination revealed extensive bilateral acute and chronic pyelonephritis.

The concept of a disease continuum reflects a retrospective approach which may be applicable to individual experiences. The problem may be better approached from the epidemiological standpoint, as illustrated in Figure 5.

FIGURE 5

KINETIC RELATIONSHIP OF ACUTE AND CHRONIC BACTERIAL PYELONEPHRITIS TO CHRONIC RENAL DISEASE



The anatomical changes designated as "pyelonephritis" can be produced by a number of non-infectious etiologies; Freedman presents a list of 14 such causes *(12A)*. These will not be considered in this disussion. There is general agreement that both acute and chronic pyelonephritis can lead to the development of chronic renal disease; the unanswered questions relate to the kinetics of these interrelationships, definition of these relationships being paramount in quantifying the problem.

As an initial approach, the assumption that infection limited to the lower urinary tract would not directly cause chronic renal disease, except as a potential source for ascending infection or as an etiology in the genesis of obstructive uropathy, would seem justified. Yet the majority of patients seeking medical care for urinary tract infections do so because of lower urinary tract inflammation, hence these patients represent a group which is seen without screening programs. How frequently do such patients have evidence of renal parenchymal involvement?

In their review, Reeves and Brumfitt state: "We consider that a major advance in the understanding of urinary tract infection will occur when a simple and reliable method is available for the localization of infection within the urinary tract of the individual" *(12B)*. Analysis of Tables 3 and 11 clearly indicates that clinical features including fever and cortovertebral angle (loin) tenderness are inaccurate and misleading. In addition, these are of no value in the asymptomatic individual.

The methods available for *localization* of the site of urinary tract infection are summarized in Table 6:

TABLE 6

Methods Available for Localization of Infection in the Urinary Tract

Direct	*Indirect*
1. Ureteric catheterization	1. Serum antibodies
2. Renal biopsy	2. Urine concentration test
3. Bladder washout technique of Fairley	3. Urinary enzyme excretion
	4. Antibody coated bacteria in urine

The most reliable method for the localization of the site of involvement has been the recovery of bacteria in ureteral urine obtained from the affected kidney. This technique has been used since the resurgence of interest in the quantitative bacteriology of urine (*13*). Stamey, Govan and Palmer have extensively utilized the technique of ureteral catheterization to enable differentiation between pyelonephritis and lower tract infection (*14*) (Table 7).

TABLE 7

Compilation of Localization Studies Utilizing Ureteral Catheterization

Technique	*Ref. No.*	*Author*	*(Date)*	*Type Patient*	*No.*	*Sex*	*Bladder (%)*	*Renal (%)*	*Uncertain (%)*
Ureteral Cath.	14	Stamey	1965	Referred	95	F	40	60	
					26	M	62	38	
Ureteral Cath.	15	Whalley	1965	Postpartum bacteriuria	23	F	26	74	
Ureteral Cath.	16	Fairley	1966	Bacteriuria pregnancy	50	F	46	44	10
Ureteral Cath.	17	Fairley	1967	Recurrent infection	70	F	36	64	
Ureteral Cath.	18	Turck	1968	Recurrent infection	51	F	49	51	
					3	M	0	100	
Ureteral Cath.	12*B*	Reeves	1968	Chronic bacteriuria	24	(21 F)	46	54	
Ureteral Cath.	19	Eykyn	1971	Referred recurrent	187	(85% F)	36	64	
Ureteral Cath.	20	Whitaker	1973	-	26*	(25 F)	73	27	

* children

Because of the patchy distribution of lesions, renal biopsy is an unreliable tool for estimation of the frequency of pyelonephritis; for example, Freedman performed renal biopsies at the autopsy table on 20 patients with proven pyelonephritis and in only 6 did the biopsies reveal pyelonephritic changes (*21*).

The indirect method which has been used most widely is that of measurement of antibodies in the patient's serum against the O antigen of the bacteria causing the infection. When the infection involves the renal parenchyma, antibodies appear but are absent when infection is confined to the lower urinary tract. While useful in groups of patients, in individuals there often are exceptions. An example of the correlation is as follows *(12B):*

Site of Infection	*No. of Patients*	*Antibody Titer*	
		< 1:320	*≥ 1:320*
Bladder	11	8	3
Renal	13	2	11

Other investigators have defined renal parenchymal involvement on the basis of impairment of renal function. Winberg reported that 17 of 20 children (77%) with acute non-obstructive urinary tract infections had diminished capacity to produce a concentrated urine (*22*). This defect repaired in 4 to 6 weeks following the response to treatment. In these same children, acidification in response to an acid load and endogenous creatinine clearances were normal in all but 3 and 2 children, respectively. Subsequently, Kaitz and Norden and Tuttle reported that 45% and 42% of pregnant women with asymptomatic bacteriuria were unable to concentrate their urine above 700 mOsm/kg of water (*23,24*). Recovery of ability to concentrate their urine returned with successful antibacterial therapy.

While there is a correlation between these indirect methods (Table 8, ref.*12B)*, neither is sufficiently predictive to be useful on an individual basis.

TABLE 8

Relation of Urine Concentrating Ability to Hemagglutinating Titer

Hemagglutinin Titer	*Maximum Urinary Osmolality (mOsm/kg)*	
	< 750	*> 750*
≥ 1:320	12	4
≤ 1:160	5	39

More recently, Fairley et al. have developed an ingenious technique for obtaining ureteric urine without the need to pass ureteric catheters (*17*). Their method involves insertion of a triple lumen Foley catheter and collecting a specimen of bladder urine. The bladder is then emptied and 100 ml of sterile saline containing 5 mg of gentamicin (or 2 mg of neomycin) and 125,000 units of topical streptokinase-streptodornase is injected into the bladder and allowed to remain for 45 minutes. The bladder is then emptied and washed with 3 liters of sterile saline. The bladder is again emptied and the last few milliliters saved for post-washout culture. Urine collections are made every 10 minutes until five additional specimens are collected. Bacterial counts are done on all specimens. Patients are classified as having only lower tract infection if all cultures following the bladder washout are negative. Patients are classified as having upper tract infection if both of the following criteria are met: (1) bacterial counts greater than 10^2 organisms/ml are present in four of specimens 3 to 7; (2) there is at least a 10-fold increase between specimen 2 and specimens 3 through 7 (*25*). Typical results of the bladder washout (BWO) procedure are illustrated:

Site of Infection	*Spec #1 Bladder*	*#2 immed. post BWO*	*#3 0-10 min*	*#4 11-20 min*	*#5 21-30 min*	*#6 31-40 min*	*#7 41-50 min*
Bladder	>100,000	0	0	0	0	0	0
Renal	>100,000	1000	10,000	80,000	80,000	90,000	90,000
Equivocal	>100,000	400	3,600	2,800	2,000	2,400	1,800

The BWO procedure has been used quite extensively and correlates well with the results of ureteric catheterization (Table 9).

TABLE 9

Compilation of Localization Utilizing the Bladder Washout Technique (Fairley)

Technique	*Ref.*	*Author*	*Type Patient*	*No.*	*Sex*	*Bladder (%)*	*Renal (%)*	*Equivocal (%)*
BWO*	17	Fairley 1967	Recurrent UTI	29	F	17	69	14
BWO	26	Bremner 1969	-	150	-	41	59	
BWO	7	Fairley 1971	Acute UTI, gen.practice	48	F	46	44	10
BWO	25	Boutros 1972	Prenatal screening	194	F	40	52	8
BWO	27	Gower 1972	-	48	F	38	54	8
BWO	28	Jones 1973	Misc.	26	15F	31	58	11

* Correlated with ureteral catheterization. The 4 equivocal results were in patients with bladder bacteriuria

Unfortunately, BWO procedure is invasive and too cumbersome for routine use.

Thomas, Shelokov and Forland have described a simple technique for the detection of antibody coated bacteria in urine sediment which appears to correlate with the site of infection (*29*). Steve Jones and Jim Smith have just completed a study comparing the BWO of Fairley with the detection of antibody coated bacteria (Table 10).

TABLE 10

Direct Localization by BWO	*Antibody Coated Bacteria (ACB) Present*	*Absent*	*Total*
Upper (renal)	17	1	18
Lower (bladder)	0	8	8
Total	17	9	26

$p < 0.002$

From these data, the detection of ACB in urine sediment appears to be a sensitive, reliable non-invasive technique for localization of the site of urinary tract infection. The technique is applicable to the hospital diagnostic laboratory and results can be made available early in the patient's management.

It is standard academic dogma to admonish that knowledge of the natural history of a disease is essential to its rational diagnosis and management. Yet at this time data relevant to the natural history of symptomatic urinary tract infections are both scanty and conflicting. Review of some of the available data will emphasize the necessity for a simple reliable method of localization of infection.

In a study of 66 women who presented to general practitioners with symptoms of acute urinary tract infection, Fairley et al. performed cultures and BWO localization studies in those with bacteriuria (*7*). The results are summarized in Table 11:

TABLE 11

Acute Urinary Tract Infection in General Practice

Manifestations	*No Bacteriuria or 10,000 organisms per ml (23 patients)*	*Renal Bacteriuria (21 patients)*	*Bladder Bacteriuria (22 patients)*
Symptoms suggesting lower urinary tract infection:	%	%	%
Frequency	95	98	70
Burning	70	68	70
Suprapubic pain	70	68	51
Symptoms and signs suggesting upper urinary tract infection:			
Loin pain	50	48	19
Temperature	35	44	4
Rigors	15	32	15
Nausea and vomiting	25	24	8
Hematuria (macroscopic)	25	20	12

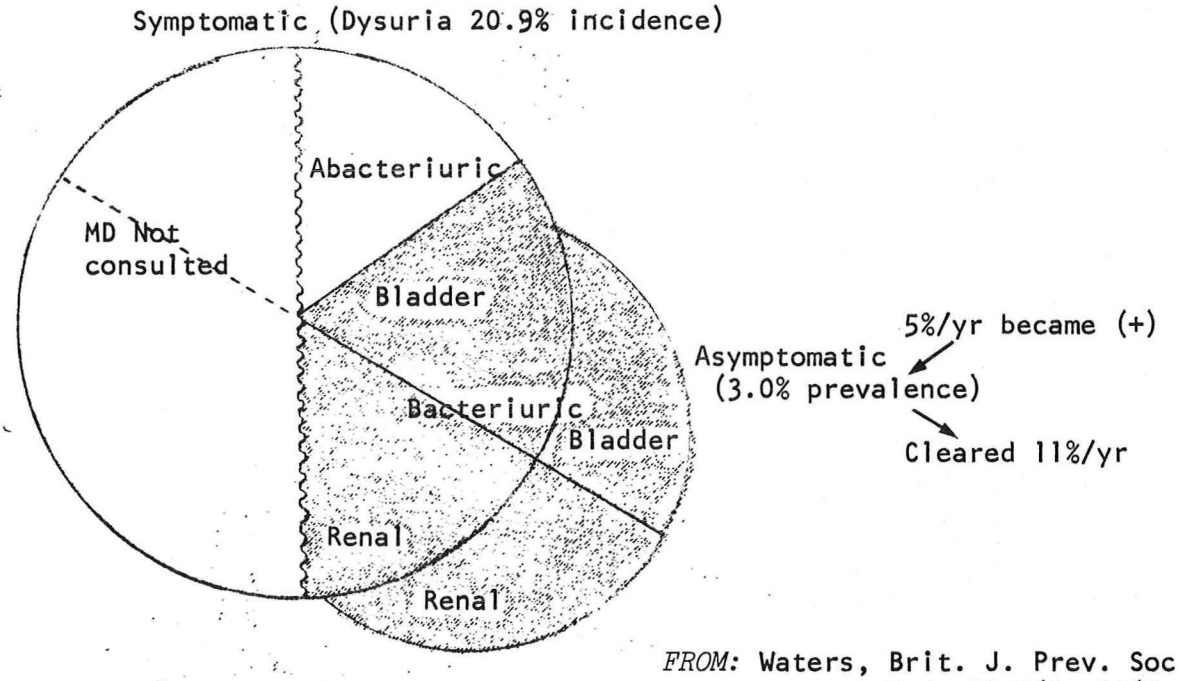
Note that one-third of patients had the acute urethral syndrome; in this group, one half had CVA tenderness and 15% actual rigors. Of those with bacteriuria, one half had renal bacteriuria and one half had bladder

bacteriuria. Again, differentiation on clinical grounds in any individual patient isn't possible.

From these observations, as well as those reviewed previously, the clinical problem of urinary tract symptoms and infection in adults can be depicted as follows (Figure 6):

FIGURE 6

Urinary Tract Symptoms and Infection in Adult Women



FROM: Waters, Brit. J. Prev. Soc. Med. 23:263, 1969
Asscher, Brit. Med. J. 1:804, 1969

Dysuria occurs in approximately 20% of women each year, half of whom seek medical attention. Of these, one third will have the acute urethral syndrome (symptomatic abacteriuria), two thirds will have bacteriuria. Of the two thirds with bacteriuria, one half will have bladder bacteriuria, while one half will have involvement of the renal parenchyma. At the same time, the prevalence of asymptomatic bacteriuria is approximately 3%, with 11% clearing each year and about 5% becoming positive. It is against this background that the available data on the natural history and management of urinary tract infections must be assessed.

Observations on the prognosis of urinary tract infections (bacteriuria in some instances) are summarized in Table 12:

TABLE 12

Prognosis of Urinary Tract Infection (Adults)*

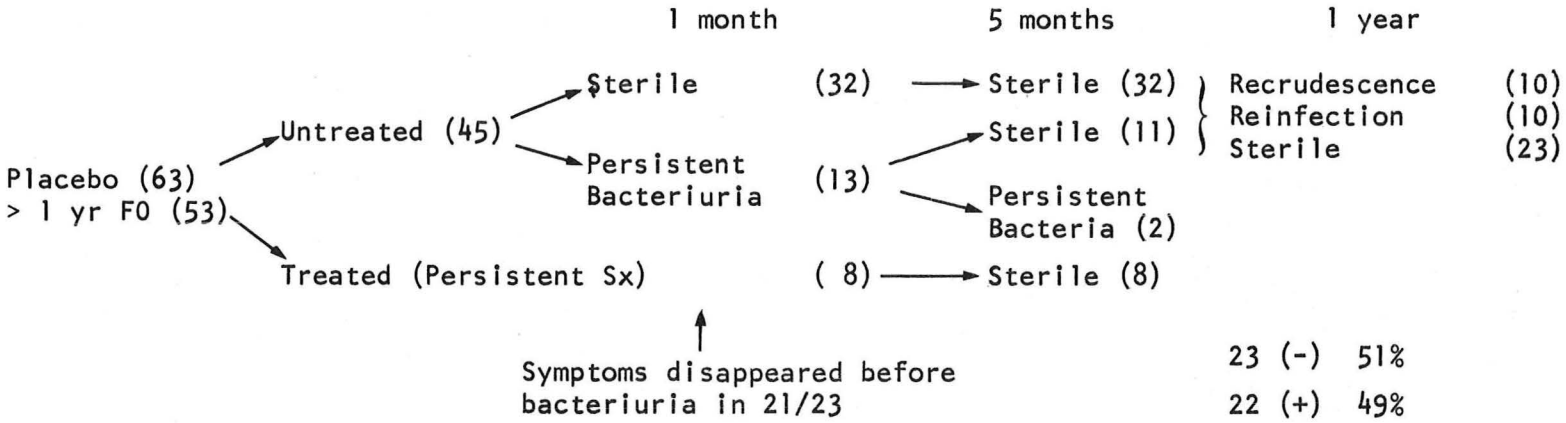
Senior Author (Ref.)	*No. Patients*	*Followup (yrs)*	*Comments*
Freedman (21)	111	1/2-3	47% Rx failure, 0 progression
Pinkerton (30)	50 (B.P.)	5	21% WBC and bact., 21% IVP C.P.
Jackson (31)	-	-	10% of patients with 1+ culture develop C.P.
	10	6	Active infection throughout 50% C.P.
Fry (32)	125	4-6	2.4% C.P., 7.2% cystitis
Prat (33)	84	1-6	12% had progressive decrease in GFR
Little (34)	16	1/4-2	75% had smaller renal outlines
Whalley (15)	131 (B.P.)	1/6-1	81% + culture, 27% IVP C.P.
Johnson (36)	47	3-6	41 "pyelonephritis", 21 uncleared infection ΔC_{Cr}-12.6, 26 cleared infection ΔC_{Cr}-18.8
Bryant (35)	36	> 2, av. 3.2	36 hypertensive-bacteriurics matched with 36 hypertensive non-bacteriurics. No difference.
Zinner (38)	134	10-14	36 (27%) bacteriuric, + → +: C_{Cr} nl (18): 793 mOsm/kg; IVP-C.P. 9/32 + → -: C_{Cr} nl (15): 889 mOsm/kg; IVP-C.P. 3/9
Parker (39)	74	10-20, av. 15.5	11 (15%) had fatal or serious sequelae (unilateral nephrectomy in 8 patients)
Asscher (40)	96	4	BP, urea, renal size - no progression
Freeman (37)	47	25-49 mos.	6 renal failure - 3 infection (2 unrelieved obstruction) 41 no ↓ in renal function

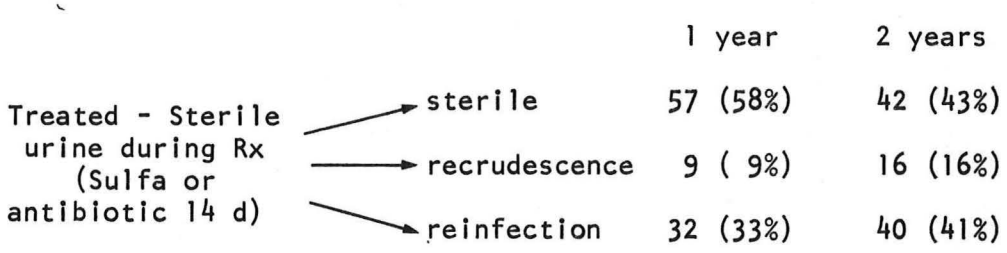
* B.P. - bacteriuria during pregnancy, C.P. - chronic pyelonephritis

Close review of several of these prospective clinical trials is of major interest (Table 13) (41). All of the patients in this study had 3 or more cultures with > 10^5/ml of the same organism on voided urine or a suprapubic aspiration. Treatment included sulfa 2.0 gm/day or ampicillin 1.0 gm/day, oxytetracycline 1.0 gm/day or chloramphenicol 1.0 gm/day for 14 days, with the agent selected on the basis of susceptibility tests.

TABLE 13

Treatment of Acute Symptomatic Uncomplicated Urinary Tract Infection in Nonpregnant Women





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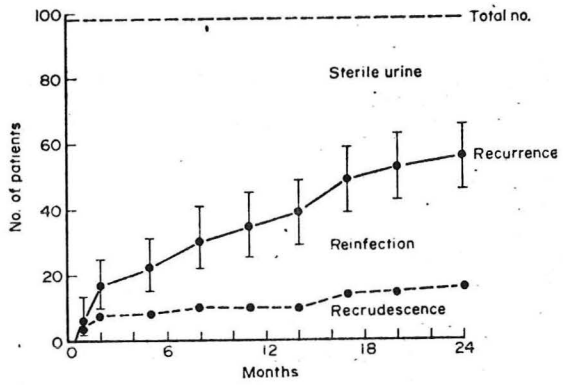
Note that 43 of 45 patients with placebo had sterile urines at 5 months, and also that symptoms disappeared before the bacteriuria in 21 of 23 patients on placebo. In the treated patients, recrudescence was detected in 16 patients and reinfection in 40 patients (Figure 7).

FIGURE 7

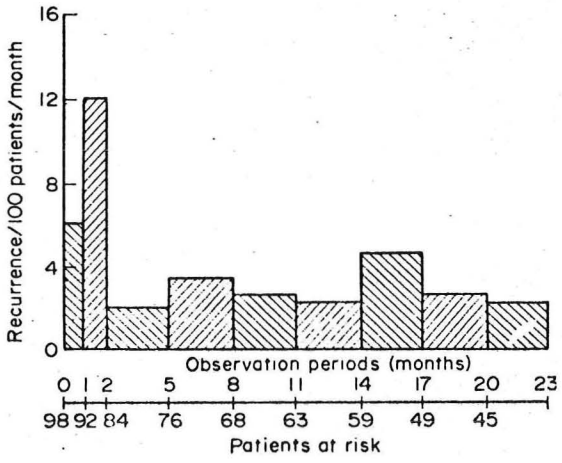
Reinfection and recrudescence during 2 years' followup of 98 women with uncomplicated urinary tract infection who attained sterile urine during treatment (95% confidence limits are shown)



The rate of recrudescence was highest during the first two months after treatment (Figure 8).

FIGURE 8

Recurrence months in % of patients with sterile urine after treatment during 2 years' followup of 98 women with uncomplicated urinary tract infection

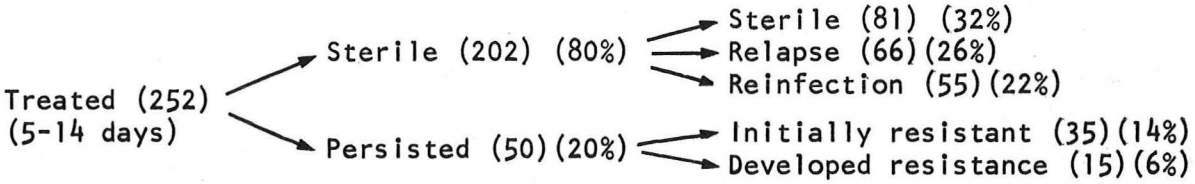


In this study, 1/6 of the patients accounted for 70% of all recurrences. The majority with many recurrences had their first within 5 months after initial treatment. Followup means culture of urine at regular intervals because 39% of recurrences were asymptomatic.

McCabe and Jackson have published similar observations in a group of patients with chronic bacteriuria, all of whom were treated (Table 14) (*42*).

TABLE 14

10.3 months



In a longterm prospective study, Asscher and associates have assessed the longterm results of the treatment of asymptomatic bacteriuria in adults (Table 15).

Although symptomatic infections developed more commonly among the bacteriuric than the control women, treatment suitable for use on a large scale did not prevent the emergence of these symptoms. Furthermore, there was no evidence that bacteriuria leads to rise in blood pressure, serum urea concentration or kidney scarring.

Since the classic concept of the pathogenesis and cause of pyelonephritis is based on the assumption that continuing infection may result in renal failure, longterm therapy has been used by some. The studies of Freeman and associates provide the only data as to the efficacy of continuous chemotherapy (Table 16).

TABLE 15

Longterm Results of Treatment of Asymptomatic Bacteriuria (5,40)

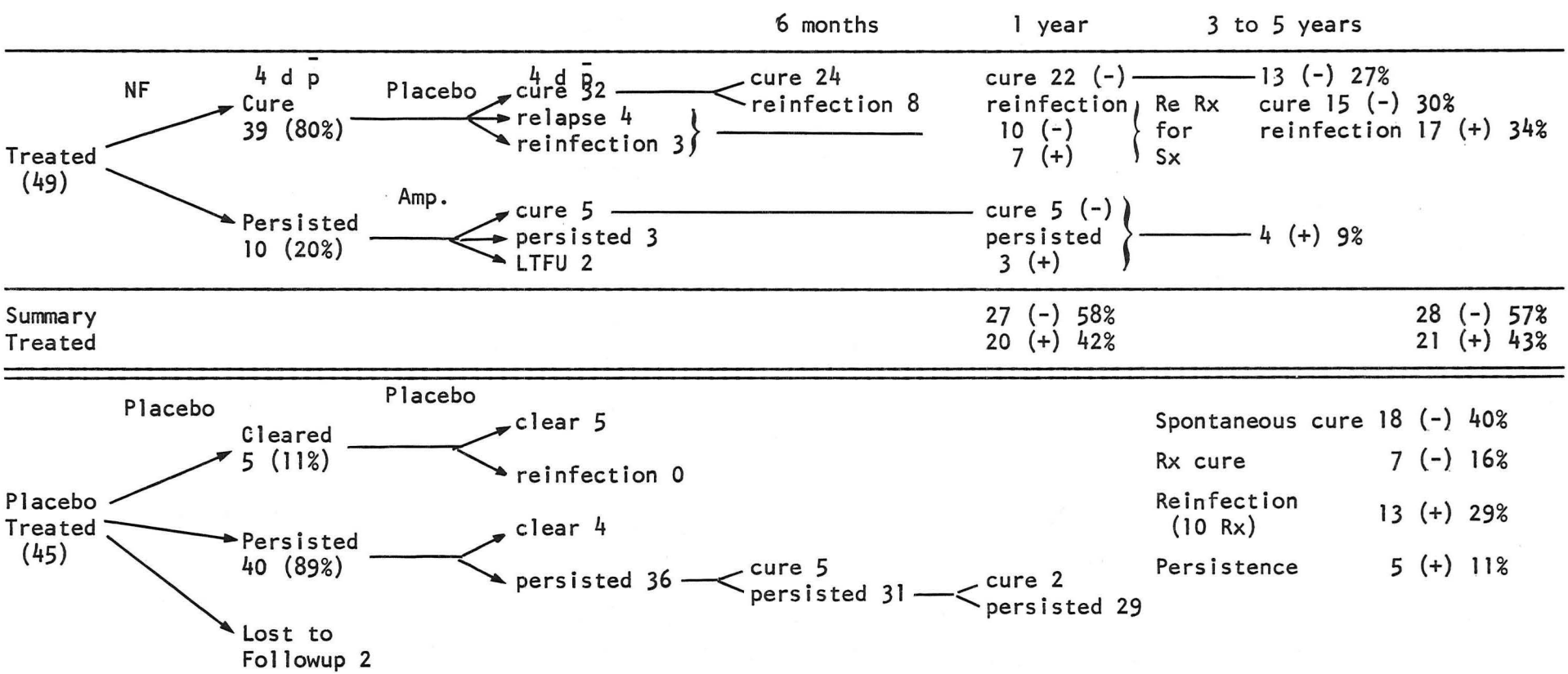
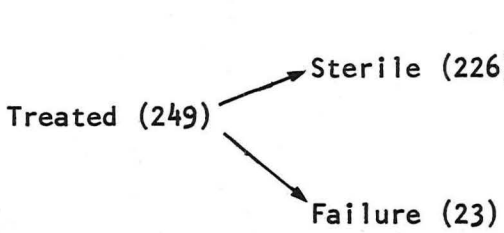


TABLE 16

Prevention of Recurrent Bacteriuria by Continuous Chemotherapy



	Recurrent Bacteriuria Cumulative %		*Cumulative % of Pts. With Acute Symptoms*
	13 months	*25 months*	*25 months*
Placebo (41)	73% (+)	73% (+)	48%
Nitrofurantoin (38)	54% (+)	57% (+)	22%
Sulfamethizole (38)	45% (+)	55% (+)	7%
Methenamine mandelate (31)	39% (+)	53% (+)	34%

At 13 months (*43*) there was a significant diminution in bacteriuria in persons treated with chemotherapy. However, by 25 months, there was no significant difference in the frequency of bacteriuria, although the proportion of patients who developed acute symptomatic exacerbation was less on sulfamethizole. Even the slight gains at 13 months must be balanced against significant drug toxicity in each group.

From these studies, it is apparent that if broad concepts are to emerge regarding management of urinary tract infections, localization will be essential. Preliminary studies suggest its value. Turck, Ronald and Petersdorf studied the patterns of recurrence in relation to the site of infection and found that bladder bacteriuria was associated with reinfection, while renal bacteriuria was associated with relapse (*18*) (Table 17).

TABLE 17

Chronic	*Site of Infection*			
	Bladder ⟵ ⟶ *Renal*			
	No. Pts.	*Rate/Pt.*	*No. Pts.*	*Rate/Pt.*
Total	25	-	29	-
Relapses	11	10.4	52	1.8
Reinfection	27	1.1	13	0.4

Finally, the importance of localization to therapy is illustrated by the observations of Boutros et al. that the instillation of 100 ml of 0.2% neomycin in the BWO procedure eliminated the organisms in 20 of 36 patients (55%) with no recurrences (*25*). Observations such as these suggest that the management of bladder bacteriuria may be reduced to single dose therapy while that of renal bacteriuria may require intensive therapy.

In summary, there is general agreement that interrelationships exist between lower urinary tract infection, acute pyelonephritis, chronic pyelonephritis and chronic renal disease. The kinetics and modifying factors which determine the frequency with which these conditions produce chronic renal disease have been only partially defined. Rational programs directed toward alleviation and control must include longitudinal evaluation based upon adequate localization of the site of involvement.

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