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URINARY INFECTIONS:

A New Diagnostic Technology

by: Paul Fugazzotto, MSPH, Ph.D.*

Urinary Research Center

Rapid City, South Dakota

- * Recent Director of the Nevada State Health Lab (1970-1981)
50 years experience in research/diagnostic microbiology*

It is a well known fact that many thousands of the people afflicted with urinary infection have been plagued with it for extended periods of time. This situation came to my attention about twenty-five years ago as chief microbiologist in a clinical laboratory when I was faced with the problem of pinpointing the etiologic agents in such cases.

The practice at that time, and still in vogue today, was the universally adopted procedure of direct agar plate culture, stressing colony counts and Gram negative organisms. In the light of strictly classical bacteriology, I was soon convinced this could not possibly be an adequate procedure for reliable diagnosis. Moved by this conviction, I initiated research into technical aspects of the tests to attain a dependable diagnostic procedure, accumulating results in more than 8800 clinical specimens, tested in parallel, using variations in the so-called "Standard Procedure". (collaboration with local hospitals)

In the early studies, I introduced increases in incubation periods (beyond the usual twenty-four hours) to three and four days. This resulted in two- and three-fold numbers of significant findings. (Table 1) (Even with no other factor change, the findings of "significant counts" proved to be a function only of incubation time.) Furthermore, addition of a broth culture resulted in eliciting significant organisms in addition to those recovered on agar culture.

Table 1. Effect of increasing incubation time and of adding broth culture. Phase I.

	24 hours	48 hours +
Agar plate culture growth	19.7%	41.2%
Colony counts of 100M/ml.	6.4%	12.4% ^a
	Recovery from culture	
	Agar	Agar-Broth
Cath. bladder urine	41.4%	77.3%
Cath. kidney urine	26.3%	78.1% ^b
Beta hemol. strep.	1.9%	4.7%

^a 6562 specimens (1864-4698)

^b 625 specimens (228-397)

Then, to compare the results of agar versus broth culture in my own hands, I searched my own records and found that in parallel test, my agar cultures missed 16 to 17 + % of the cases which harbored significant bacteria. (Table 2) This compares rather closely to the differences found between my results (with broth cultures) and those of hospital laboratories (culturing on agar only). (Table 3) I had learned many years before starting these studies that etiologic agents in deep-seated infections convert to the "hydrophilic state" they do not emerge on agar culture; they require liquid medium for growth. What this tells us is that using today's "standard procedure" fails to take

into consideration as possible etiologic agents those organisms which do not average in routine testing. (This is about 25% of active infections). — Easily confirmed in your own lab if you do comparative tests.

Table 2. Research lab results on primary inoculation, agar vs. broth.

Agar	No Growth	Growth	No Growth	No Growth	Growth	Total
Broth	No Growth	Growth	Growth	Growth*	No Growth	
Phase II						
Number	434	498	109	70	7	1118
Percent	38.8	44.5	9.7	6.3	0.6	16.0
Phase III						
Number	121	169	39	22	1	352
Percent	34.4	48.0	11.1	6.2	0.2	17.3

* Column represents no growth overnight, but growth on the following day.

Let us shift our attention to another facet of urinary tract bacteriology. It is readily realized, and admitted, that there is rarely any assurance that the laboratory receives the ideal "clean voided" specimen for culture; that is: specimens completely devoid of urethral contaminants, such as coli, klebsiella, proteus, pseudomonas, and other Gram negative enterics. Is it any wonder, then, that these same organisms are most often reported as the etiologic agents in routine testing, and have been so reported for many years?

Table 3. Culture results of research lab versus collaborating clinical labs, Reno, Nev.

Lab Results		No. of specimens from Clinical Lab				
Research	Clinic	A	B	C	D	Total
Neg	Neg	120	40	110	107	377
Pos	Pos	132	197	66	129	524
Neg	Pos	4	8	1	5	18
Pos	Neg	71	56	142	17	286
	Percent	21.7	18.6	44.5	6.6	24.4

* 104, or 73% were Gram positive organisms

† Discrepant results

In the textbook "Diagnostic Microbiology" by Bailey and Scott (page 283), there is a paragraph that says: "...sixty to eighty percent of all urine specimens received for culture by the average hospital laboratory may contain only contaminants or no etiologic agents of infection". This is not exactly true: it should read "MAY FIND AND REPORT only contaminants, or the etiologic agents of infection ARE NOT FOUND". Needless to say, then,

the logical conclusion must be that reports issuing from these laboratories cannot possibly be diagnostically valid.

The less than ideal specimen, reflecting essentially urethral contaminants, is no doubt the source of the common concept that UTI's are Gram negative infections, fixed in the minds of doctors and laboratorians since 40 to 50+ years ago. There has been no indication of any significant improvement in the receipt of the "ideal specimen" by the laboratories through time. In a recent review of the sections on UTI as described in a dozen recently published microbiology text books, I found all of them propagating the legend of the Gram negative bacillus as the predominant infecting agent; and all of them reciting the colony count as the device to establish diagnosis. There has been no research in the literature to support by comparative (parallel) testing the value of the colony count and its specific application for pinpointing etiologic agents. Also, there is no research in the literature directed toward the role of Gram positive organisms as possible etiologic agents. Such organisms are only rarely reported by clinical laboratories. Only Fugazzotto's work has researched this possibility.

There is still another facet to UT bacteriology nowhere discussed in the literature: urine is the catch-all of body waste chemicals, reflecting the patient's intake of antibiotics, other drugs, food, drink, as well as products of katabolism. These substances coat the bacterial surfaces, and interfere with their metabolism when carried over to artificial culture medium. This is well known and accepted mechanism for action of drugs (especially antibiotics) on bacteria. Furthermore, in the infectious process, the organisms exist in a fluid environment, under reduced oxygen, affected by products of host defenses. They cannot be expected to emerge, typical and uninhibited, when transferred along with urine waste products to artificial solid (agar) medium; and they don't.

In view of the above, it was obvious to me that the organisms in the bladder urine must be freed of the interfering inhibiting urine components in order to provide them with the best conditions to emerge and be evaluated. After considerable preliminary testing, I did devise a washing procedure for removal of the urine chemicals, leaving cleaned organisms to emerge in their normal metabolic state. The result was a new diagnostic technology.

In mid-April 1986, I initiated clinical studies, as the function of my Center for Urinary Infection Research, whereby patients are admitted to the program from any source, to be tested and monitored on a continuing basis. After determining the suspected etiologic agent, its sensitivity to a series of antibiotics is also determined; and a report of the results is prepared for transmittal to the patient's doctor. On the first visit of the patient, I obtain as complete a history as I can regarding length of time infected and symptoms regarding urinary functions, treatment history, and other pertinent information. I also give them an instruction sheet along with detailed verbal

explanation as to how a proper specimen is taken. Since the opening of the Center, I have admitted more than 480 patients to the program; and on these I processed more than 2,300 urines. The data accumulated to date are as follows:

1. All but two of these patients were initially treated repeatedly for years as Gram negative infections, just as is the practice today. (The two exceptions were acute cases.)
2. All have gone from doctor to doctor, to clinics, to hospitals, receiving the very same treatment in all cases, and repeatedly for years.
3. In all cases, when laboratory tests were done, the results were reported with a Gram negative etiologic agent, or "no significant organisms", "possible skin contaminants", or "no growth".
4. Some of these patients have travelled to distant parts of the country, to be processed by the most prestigious hospitals and clinics, to no avail. (From NY to California)
5. All of these patients gave the same history of treatment and diagnostic failure.
6. On testing with my new diagnostic technology, I found all but the two mentioned above, to have a Gram positive infection — the predominant organisms being the *Enterococcus* and *Gallkya*. In fact, with a few exceptions (of *Pneumococci* Group B Strep, *Micrococci*, etc.), these were essentially the only etiologic agents found in more than 96% of the patients.

The fact that cures of more than a year were attained in the less chronic cases, treated with specific antibiotic, represent proof to me that my new diagnostic technology is valid, with no reservations. Furthermore, all the chronic cases of extended duration that remained consistently on the program, are experiencing drastically reduced or complete loss of symptoms. In the past months, I have been receiving specimens from patients of Interstitial Cystitis in California, and elsewhere in the country; and even at this early date after only short courses of treatment, these patients are also experiencing distinct reductions of symptoms, in response to specific therapy.

Considering the above, and other issues not mentioned in this report, I have to conclude that UTI's are not predominantly Gram negative infections, but rather Gram positive. It appears most likely that my patients and all chronic cases have had a Gram positive infection from the very beginning; that Gram negative infections are a distinct rarity, reported on the basis of urethral contaminants, so easily recovered by the elementary procedures widely used today
