It’s a common perception that urine is sterile; the only time microbes are ever recovered is when there’s a urinary tract infection (UTI), or when the sample has been contaminated with normal vaginal or skin flora.

*Escherichia coli* is by far the most common cause of UTIs and is implicated in 80-85% of all urinary tract infections, while *Staphylococcus saprophyticus* causes 5-10% of UTIs.

Diagnosis often involves culture on blood agar and MacConkey agar, with a positive culture defined as $10^5$ CFU/mL of a single species of bacteria.

However, the recent research from Paul C. Schreckenberger, PhD goes against the grain. Dr. Schreckenberger has spent the last few years studying urinary tract infections, their culture and diagnosis, and has discovered some interesting results. Recently, Dr. Schreckenberger presented a four part seminar on urine culture in which he discussed his findings. This article is based on his presentation and the results of his study.

Dr. Schreckenberger found that the $10^5$ CFU/mL “golden rule” didn’t always apply to the diagnosis of UTI. He wondered, if a patient had obvious symptoms of a UTI, why did the culture often come up negative? He believed there must be something else, something that the traditional culture methods were not catching.

To prove his theory that traditional methods often do not detect or correctly identify the infectious agent, Dr. Schreckenberger and his lab performed a study. The team collected urine from participants with symptomatic acute cystitis via a clean catch method and through a straight catheter.
As predicted, the results varied considerably. Some patients had a concentration of 10^5 CFU/mL from the voided clean catch, while the urine taken from the straight catheter had none. This indicated that the organisms recovered from the voided urine were not, in fact, the causative agent, but were instead contaminants such as *E. coli* and *S. saprophyticus* that could incorrectly direct treatment. But what, then, was causing the infection? Dr. Schreckenberger and his team decided to find out.

In a follow-up study researchers collected urine from healthy, asymptomatic female patients who were free from known UTI in three different ways: voided clean catch, trans-urethral catheter, and suprapubic aspirate. All three specimen types were assessed with culture, light microscopy, and 16S RNA gene sequencing.

The researchers found that all samples contained bacteria that could not be routinely cultivated using traditional methods. Samples collected through the straight catheter and the suprapubic aspirate had nearly identical bacterial identities, while the voided sample also contained vaginal organisms.

To determine whether or not the sequences represented a population of live bacteria, the researchers set up growth media to cultivate these obscure organisms, with stellar results. The battery of media included incubation in fluid thioglycollate, culture on blood agar, chocolate agar, and CNA, all of which were grown at room temperature, 30°C, 35°C, in CO2, and under anaerobic conditions. With these expanded tests, 52 out of 65 patient samples grew bacteria, while traditional culture methods deemed 95% of them negative.

These results led the researchers to conclude that the urinary tract does, in fact, have normal flora and that urine is not sterile.

Further evidence of this ground-breaking claim came when Dr. Schreckenberger and his team investigated the rate of infection after botox-injection surgery in patients with overactive bladder. The patients were deemed free of infection prior to surgery, but then acquired an infection after the surgery. Thorough examination of the procedure indicated no opportunity for introduction of the microbes. Therefore, the team of researchers decided to look at the abundance of microbial flora in the urine of these patients. Interestingly, those...
with low bacterial load in their urine prior to surgery had a higher rate of infection than those who had a heavy bacterial load. The researchers concluded that the normal flora found in urine protects the urinary tract against pathogens and infection.

This brought to light the issue of treating urinary infections with antibiotics: while antibiotics reduce the prevalence of pathogens, they will also rid the bladder of its protective normal flora. This provides an opportunity for other organisms to establish an infection, which would then be treated with another bout of antibiotics and result in a possible overuse of treatment.

These studies remind us once again that there is still much to be learned about the intricacies of the human microbiome.

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Comparison of the total bacterial communities in (A) TUC Transurethral Catheter (blue) and SPA Suprapubic Catheter (red) samples. Numbers of genera in each sample type were totaled, and the percentage of that total was calculated for each genus. Only the most abundant genera are shown. Error bars represent standard deviations.