# Study of antibody-coated fungi in patients with funguria and suspected disseminated fungal infections or primary fungal pyelonephritis[1]

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**Summary:** The direct immunofluorescence method for the detection of antibody-coated bacteria in urine sediments has been used by investigators to distinguish invasive bacterial disease of the renal parenchyma from noninvasive bladder bacteriuria. The purpose of the present investigation was to test the usefulness of the demonstration of urinary fungal immunoglobulins and complement in distinguishing patients with fungal cystitis from those with suspected disseminated fungal disease. Twenty-one patients with microscopic funguria were suspected clinically of having disseminated fungal infection. Urine specimens from these patients were tested for the presence of antibody- and complement-coated fungi by direct immunofluorescence with the use of specific goat antisera to human immunoglobulins and complement. No unexpected frequencies of combinations of urinary yeast staining by specific antibody were noted. Urine specimens demonstrating funguria from 12 patients with uncomplicated illnesses were also examined for the presence of antibody- and complement-coated fungi; no unexpected frequencies of combinations of urinary yeast staining were noted in this group and no differences in frequencies of specific antibody staining were noted when compared with results in patients with suspected invasive fungal disease. Thus, no difference in the occurrence of specific antibody or complement adsorbed to urinary yeasts was observed between patients suspected of having invasive fungal disease and a small group of control patients.

## Introduction

The direct immunofluorescence method for the detection of antibody-coated bacteria in urine sediments has been used by previous authors to distinguish invasive bacterial disease of the renal parenchyma from noninvasive bladder bacteriuria (Thomas *et al.* 1975, Pearsall & Sherris 1966, Thomas *et al.* 1974, Jones *et al.* 1974, Lehmann *et al.* 1968). This method of distinguishing upper from lower urinary tract infections has proved a valuable adjunct to the accurate diagnosis and prognosis for patients with significant bacteriuria, whether symptomatic or not. The usefulness of direct immunofluorescence for the detection of antibody-coated urinary fungi and the relationship of adsorbed urinary fungal immunoglobulins to invasive renal fungal disease has been evaluated in two instances (Harding & Merz 1975, Everett *et al.* 1975). Harding & Merz (1975) demonstrated no apparent relationship between urinary fungal antibodies and invasive renal disease; however, these workers studied only 25 patients and did not assess the presence of adsorbed fungal complement (C3). Everett *et al.* (1975) also attempted to assess immunofluorescence of urinary yeasts using a polyvalent equine antihuman globulin. Although only 18 patients were studied, the authors were able to demonstrate no correlation between the presence of urinary yeasts with adsorbed immunoglobulin and invasive renal fungal disease. The purpose of the present investigation was to test the usefulness of the demonstration of urinary fungal immunoglobulins and complement in distinguishing patients with fungal cystitis from those with presumed disseminated fungal disease.

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## Methods

Urine specimens from patients hospitalized in the Special Care Unit and having funguria demonstrated microscopically were brought to the attention of the author by the staff of the routine microscopy laboratory. Freshly-voided urine obtained from Special Care Unit patients with indwelling bladder catheters, whose urine specimens showed yeast or pseudohyphal forms during routine urinalysis, were obtained and cultured on routine mycological media, and fungal isolates were identified by standard procedures. An aliquot of the freshly-voided urine specimen was simultaneously brought to the protein research laboratory (Foundation for Blood Research, Scarboro, Maine) where, after not more than 4 hours refrigeration at 38–40 °F (3.3–4.4 °C), each urine specimen was tested for the presence of antibody- and complement-coated fungi by direct immunofluorescence with the use of specific goat antisera to human immunoglobulins and complement.

The clinical presumption of disseminated fungal infection was based on the following characteristics: hospitalization in a special care unit for more than one week; indwelling urinary bladder catheter for more than one week; endotracheal intubation or tracheostomy and mechanical ventilation; concomitant administration of two or more antibiotics; treatment with corticosteroids; use of at least one indwelling arterial catheter or the use of an intravenous hyperalimentation catheter; prior surgery of an unsterile site or extensive trauma or major thermal burn wound; and demonstration of new funguria upon routine urine microscopy.

## Results

Twenty-one patients satisfied criteria for inclusion in the group of patients with presumed disseminated fungal infection. Sixteen patients had urinary yeasts identified (13 Candida species, 2 *Torulopsis glabrata*, and one unidentified yeast) and 6 patients had fungaemia with a microorganism identical to their urinary fungus. No unexpected frequencies of combinations of urinary yeast staining by specific antibody were noted in either group. Thirteen of 21 patients with suspected disseminated fungal disease died: 5 post-mortem examinations were performed but in no instance was invasive fungal disease of the kidney, brain, lung, gastrointestinal tract or myocardium noted.

Urine specimens demonstrating microscopic funguria from 12 patients hospitalized in nursing units other than the Special Care Unit (and who were discharged from the hospital after uncomplicated hospitalizations) were also tested for the presence of antibody- and complement-coated fungi by direct immunofluorescence. No unexpected frequencies of combinations of urinary yeast staining by specific antibody were noted in this group and no differences in frequencies of specific antibody staining were noted when compared to results in patients with presumed invasive fungal disease (Table 1).

*Table 1. Specific antibody coating of urinary fungi*

| | IgG | IgM | IgA | C3 |
|---|---|---|---|---|
| Patients with suspected infection (21) | 13 | 6 | 13 | 6 |
| Control patients (12) | 6 | 3 | 7 | 0 |

Thus, no difference in the occurrence of specific antibody or complement adsorbed to urinary yeasts was observed between patients suspected of having invasive fungal disease and a small control group of patients.

## Discussion

The present investigation suggests that the demonstration of urinary fungal immunoglobulins and complement is not helpful in distinguishing patients with suspected invasive renal fungal disease or disseminated fungal disease from those patients with uncomplicated urethral or bladder funguria. Despite the absence of certainty in identifying patients with invasive fungal

disease, the present findings are clearly in agreement with those of Harding & Merz (1975) and of Everett *et al.* (1975), who also found no clinical usefulness in the fluorescent antibody demonstration of urinary yeast immunoglobulins.

Serological tests of host immunoreactivity to fungal antigens (Glew *et al.* 1978, Kozini *et al.* 1978) and serological demonstration of fungal antigenaemia itself (Weiner & Yount 1976) continue to provide the most sensitive (but suboptimally predictive) indicators of disseminated or locally invasive fungal disease.

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