globulin containing cells. We do not understand the processes involved, but this seems to be a useful procedure.

References


Technical methods


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Letters to the Editors

Antibody-coated bacteria in urine

A simple, reliable, non-invasive test to differentiate between infections of the upper and lower urinary tract would be of great value, and in the February issue Mengoli and co-workers\(^1\) repeated the claim that a test for antibody-coated bacteria in the urine can differentiate these infections. However, their evidence is not based on direct localisation of the infection by a method such as bladder washout.\(^2\) In addition, they have explicitly studied highly selected groups of patients, discarding, for example, some patients thought to have non-obstructive pyelonephritis.

We have found only three published studies that correlate the site of urinary tract infection, localised by a direct method, and the presence or absence of antibody-coated bacteria in the urine. Jones *et al.*\(^3\) studied 29 adults with urinary tract infections, many of them with known underlying disease such as nephrolithiasis. They found good correlation between upper tract infections and the presence of antibody-coated bacteria. A German study\(^4\) found similar results in 26 patients, some known to have renal disease. Hellerstein and others\(^5\) carried out a prospective study in children. They found antibody-coated bacteria in the urine to have no correlation with the site of urinary tract infection in 45 children.

We also performed a prospective study but in women on general medical wards, selected only by the growth from a urine sample of a coliform organism in a count of at least \(10^5\) per ml. Sixteen women were studied, with a mean age of 70 years. Their medical problems included heart failure, stroke, and uncontrolled diabetes mellitus. The site of infection was determined by a direct method\(^6\) that involved drainage of the bladder through a catheter and instillation of an enzyme preparation followed by an antibiotic (we used 125,000 units of streptokinase-streptodornase in 10 ml water followed after 15 minutes by 40 mg gentamicin in 50 ml of 2·74% sodium bicarbonate, left for 30 minutes). The bladder was then drained and irrigated several times with saline. Samples of the last part of the washout fluid, and at 10, 20, and 30 minutes after the washout, were taken for viable counts. Criteria for diagnosing upper or lower urinary tract infections from these counts have been given.\(^7\) Antibody-coated bacteria were looked for in the patient’s urine using sheep anti-human globulin conjugated with fluorescein.\(^6\) Controls were overnight subcultures of bacteria from the same urine treated in the same way.

We found eight infections of the upper urinary tract. Of these, five had antibody-coated bacteria. There were five lower tract infections, four having antibody-coated bacteria. Three bladder washout tests gave equivocal results, including two in which the infection was due to a mixture of a coliform and an enterococcus. The other equivocal test was associated with antibody-coated bacteria.

We concluded that the test for antibody-coated bacteria was of no value in determining the site of infection in our patients, selected not because they were known to have long-standing urinary tract disease (as were many of those of Mengoli,\(^1\) Jones,\(^3\) and Kohnle\(^4\))但 only because they had bacteriuria (as were those of Hellerstein\(^5\)). Any explanation for the discrepancy between the results of these studies must be speculative at the moment but may include factors such as duration of infection, number of previous infections, and immune competence of the patient. How the patients were selected for study is the most important factor.

We suggest that the test for antibody-coated bacteria by itself is misleading in the investigation of an individual patient with urinary tract infection.


\(^{6}\) Disbrey BD, Rack JH. *Histological Laboratory Methods.* Livingstone, 1970.


References
Letters to the Editors

The authors reply as follows:

We agree with Howie and Burdon that the criteria for selection of the patients can influence the outcome of a study on the differential incidence of antibody-coated bacteria (ACB) in upper and lower urinary tract infection (UTI). However, they state that we 'repeated the claim' that a test for ACB in the urine can differentiate between pyelonephritis and cystitis. This is not true since we limited ourselves to report a clinicopathological correlation on statistical grounds.

In our opinion, the phenomenon of ACB is due to secretory antibodies in urine. These are produced by plasma cells which have accumulated in the lamina propria, and this process can become operative at any level along the urinary tract. The local immune response in lower UTI is qualitatively similar to that which can be found in upper UTI, although it is less frequently detectable. The higher frequency of ACB detection in the group of patients with pyelonephritis may be explained by a stronger antigenic stimulation in this condition. Accordingly, elevated urinary levels of specific antibodies have been found in 22 of 23 episodes of pyelonephritis and in 15 of 47 episodes of cystitis by means of sensitive radioimmunooassay.

Bearing these considerations in mind, the number of false-positive results depends on two main factors. The first is the heterogeneity of the lower UTI group, which includes subjects with asymptomatic bacteriuria and subjects suffering from a long-standing symptomatic UTI associated with demonstrable urological abnormalities. In fact, the percentage of ACB detection in the latter condition in our study is approximately three times higher than in the asymptomatic bacteriuria subgroup.

The second factor is the sensitivity of the assay procedure. In this regard, the quality of the fluorescent antibody is important. To obtain the best diagnostic discrimination between upper and lower UTI, every batch should be tested and appropriately diluted. In connection with these arguments, one problem encountered in analysing the data from various investigative groups is the lack of uniform criteria for what constitutes a urinary sediment that is positive for ACB.

The proportion of false-negative results in the pyelonephritis group seems less prone to be influenced by minor variations in the sensitivity of the assay. This is probably due to the greater uniformity of the local antibody production, provided that the members of this group are selected on the basis of stringent criteria (definite evidence of urographic supravesical obstruction, persistent significant bacteriuria, chronic clinical course). In a study made in a large, unselected population with bacteriuria, an abnormal intravenous pyelogram was the single most common finding in the ACB-positive group.

Direct invasive methods to localise the site of UTI are attended by increased risks and discomfort to the patients. In addition, the bladder washout test provides a substantial number of indeterminate, equivocal results.

The functional and anatomical integrity of the renal tubule can be evaluated indirectly by assaying various urinary proteins (muramidase, N-acetyl-β-galacosaminidase, LDH isoenzyme V and β2-microglobulin). Upper and lower UTI can be discriminated by these assays, and there is a fairly good consistency with the ACB test. Nevertheless some degree of overlap was observed for every protein marker studied.

A simple, reliable, non-invasive test to differentiate between infections of upper and lower urinary tract is still awaited. In this context the search for ACB could play an important role.

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