THE DETECTION OF ASYMPOTOMATIC BACTERIURIA IN GENERAL PRACTICE

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As long ago as 1881, Roberts drew attention to the existence of asymptomatic bacteriuria and postulated that this condition might prove to be a forerunner of frank urinary tract infection. Dodds (1931) suggested that this condition had particular significance in pregnancy, though Baird (1936) whilst agreeing that symptomless urinary infection occurred in pregnancy was unimpressed both by its frequency and its contribution to maternal ill health. Using quantitative bacteriological urinary counts, Kass (1956) showed that it is possible to distinguish between urinary tract infection and contamination in voided specimens of urine. Infected urine contains organisms in a concentration greater than 100,000 per ml., usually consisting of a single species of recognized urinary pathogen. In contrast to this, contaminated specimens of urine have a bacterial count less than 10,000 organisms per ml., often consisting of several species. With the development of this technique various population groups were studied in order to define the extent of the problem, the natural history of bacteriuria and also to determine whether other conditions are associated with the presence of asymptomatic bacteriuria. During these studies it has become apparent that pregnant women are particularly liable to asymptomatic bacteriuria and that this can influence the health of the expectant mother.

A number of surveys of bacteriuria of pregnancy, including those of Kass (1960), Kaitz and Hodder (1961), Turner (1961) and Sleigh et al. (1964), reveal an average incidence of about 5 per cent. These bacteriuric women have been shown to be at particular risk of developing frank pyelonephritis, hypertensive disease of pregnancy and, less certainly, premature delivery.

Frank pyelonephritis develops in 40 per cent of bacteriuric women in pregnancy and Kincaid-Smith (1965) regards this as being sufficient reason for detecting and treating bacteriuria. Indeed, Le Blanc and McGanity (1964) and Little (1965) have shown that pyeloneph-

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Ritis of pregnancy is virtually a preventable disease. Further support to the view that bacteriuria of pregnancy should be identified is given by the convincing studies of Stuart et al. (1965) and others who have demonstrated that hypertensive disease in pregnancy occurs more frequently in bacteriurics than in non-bacteriurics, the frequency rising with maternal age. Although there have been conflicting observations upon the association between prematurity and bacteriuria of pregnancy, Kass (1962), Sleigh et al. (1964) and Le Blanc and McGanity (1964) have all recorded an increased risk of premature delivery in bacteriuric women when compared with non-bacteriuric women.

In a recent discussion on screening tests in general practice the opinion was expressed that, at present, it is only worth while attempting to detect asymptomatic bacteriuria in pregnancy. Criticism of a different character has been made by those who feel that the search for asymptomatic bacteriuria in general practice is impractical because quantitative counts are costly, time consuming and rarely available to the general practitioner. It is for this reason that there has been a wide search for an acceptable alternative technique suitable for use as a screening procedure both in general practice and in hospital departments. As yet no single screening test has proved universally acceptable. All represent, to some extent, a compromise between acceptable accuracy and simplicity; the individual choice of a screening test depending largely upon local facilities.

Each of the many screening tests for asymptomatic bacteriuria has been described in favourable terms by those closely associated with its development, whilst comparative studies of screening tests have been conducted with attention focused upon the accuracy of the method in hospital conditions. Procedures that are suitable for large scale use in hospital practice are not necessarily suitable for use in the differing circumstances of general practice. For this reason this commentary upon available screening procedures is made from the viewpoint of use in general practice.

Methods for recognizing bacteriuria

Quantitative bacteriological methods
1. Pour plate techniques.
2. Surface viable counts.

Semiquantitative bacteriological methods
3. 'Standard' loop.
5. Routine methods.
6. 'Swab' plating.

Chemical screening tests
7. Griess nitrite test.
Stain techniques
11. Methylene blue stain.

Cellular deposit

These techniques vary both in their accuracy and their ease of execution. It is necessary to examine them in greater detail for features which are of value to the particular circumstances of general practice.

1. Pour plate quantitative count. This method relies on the supposition that, in dilution, a single bacterium or aggregate on culture will produce one colony. Though accurate, it is a laborious, time consuming and expensive technique that requires full laboratory facilities. It is an impractical method for the general practitioner, but because of its high degree of accuracy it serves as a yardstick with which to judge other methods.

2. Surface viable counts. There are several variants of this technique which consists of spreading a known volume of urine on a suitable solid culture medium. It is less tedious than the pour plate method, but to some extent the time gained in not having to prepare serial dilutions of urine is lost in counting the colonies after incubation. This method also requires full bacteriological facilities; even where this is available it is expensive in time and materials and thus is not suitable for use as a screening test in general practice.

3. 'Standard' loop semiquantitative method. This entails inoculating surface media with a 2, 3 or 5 mm. loopful of uncentrifuged urine and subsequently counting the number of colonies grown. Studies have established a fair degree of correlation when this technique is compared with a pour plate method. Although Randolph and Greenfield (1964) recommended the adoption of this procedure as being suitable for use in the North American consulting room it is not suitable for the general practitioner in Great Britain.

4. Filter paper strip method. Ryan et al. (1962) developed a technique using strips of filter paper, whereby small aliquots of urine could be distributed uniformly on the surface of an agar plate. A standard curve is plotted, relating the number of bacteria per ml. to the number of colonies per filter paper strip area, by contrasting standard plate counts of dilutions of pure cultures of various organisms with the filter paper strip readings. A variant of this method using a measured area of blotting paper has since been described by Leigh and Williams (1964) and found by Brumfitt and Percival (1964) to be accurate, rapid, economical and suitable for routine laboratory use. Equipment to enable practitioners to
perform this technique in their consulting rooms is marketed in North America and it has been found quite easy to perform the test in general practice in Great Britain. The method has the advantages of being economical, requiring little skill and is a direct observation on the infecting organism. Apart from some means of incubation, the technique requires only a supply of McConkey agar plates, suitable paper and a simple means of heat sterilization.

5. Routine bacteriological methods. These have little place, as screening techniques in general practice. Even if the facilities are available, in most hands the technique is insufficiently accurate to differentiate adequately between significant bacteriuria and contamination. Although Guttmann and Stokes (1963) showed that their routine methods gave results comparable with more laborious techniques it would be better to describe their method as 'semi-quantitative' as they appear more precise than the routine procedures followed in many laboratories.

6. 'Swab plating'. Bradley et al. (1966) have described a simple plating technique using commercial swabs to inoculate urine directly on to a McConkey plate.

This method is apparently sufficiently accurate to differentiate between urinary contamination and infection. It has proved easy to use in general practice but awaits further evaluation in order to establish its accuracy.

7. Chemical tests—Griess Ilosvay nitrite test. This test depends upon the reduction of nitrates in the urine to nitrites by actively respiring bacteria. The recognition of the nitrite is effected by a chemical spot test giving an immediate colour change. Though not all bacteria are able to reduce nitrate it is fortunate that this ability is possessed by all the Gram-negative urinary pathogens. The test depends upon the presence of at least 100,000 organisms per ml. of urine and also upon their being an adequate supply of nitrate as substrate. For this reason, Sleigh (1965) modified the test so that urine is incubated with excess nitrate for 4 hours at 37°C, before adding the reagent. By this means the accuracy of the test has been increased so that he was able to identify 97 per cent of significant bacteriurias with only 2 per cent of false positive results. Other studies have not obtained this degree of success but it has proved to be a sound screening test with much to commend it for use in general practice.

8. The triphenyl tetrazolium chloride (T.T.C.) test. Colourless triphenyl tetrazolium chloride is reduced by actively respiring bacteria to red insoluble formazan.

Simmons and Williams (1962) developed this observation into a practical test for the recognition of significant bacteriuria. The test
gives 94 per cent correlation with quantitative counts on urine containing more than 100,000 organisms per ml. Gram-negative bacteria such as Escherichia coli and Proteus give uniformly positive results but there is a lack of correlation with mixed infections, staphylococci and streptococci. Fortunately, when these organisms are found in urine it is usually indicative of contamination of the specimen. The disadvantages of the technique are that the reagent is rather unstable, requiring extensive laboratory facilities for its preparation. Furthermore the method involves incubation of the reagent with the urine specimen for 4 hours at 37°C. The test has, however, many of the characteristics which make it suitable for use in general practice. No expensive apparatus is required other than a simple water bath and it is easy to perform and interpret. It is at least as accurate, if not more so, as other chemical screening tests and has been found by Constable (1966) to be easy to integrate into the routine of antenatal care in general practice.

9. Detection of urinary catalase. The enzyme catalase occurs in most bacteria that attack the urinary tract and can be detected by observing the release of oxygen resulting from its action on hydrogen peroxide. Gagnon et al. (1959) developed a rapid method of catalase determination by impregnating a paper disc with a solution of the substance under test and observing its speed of flotation in a column of hydrogen peroxide.

Unfortunately catalase is also present in kidney tissue and white and red blood cells, thus accounting for the high proportion of false positive results that have been found to occur during evaluation of this technique.

10. Gram stain of urinary deposit. This has been described as "the poor man's colony count" and Kass (1956) found this simple technique identified 80 per cent of specimens with significant bacteriuria. Few studies have been as enthusiastic as this and in unskilled hands its accuracy falls steeply. Certainly in my experience it has proved an unsatisfactory means of identifying bacteriuria, moreover a centrifuge is an essential piece of equipment.

11. Methylene blue stain of urinary sediment. This simple staining technique has been described as useful by some American authorities but has not gained wide acceptance.

12. The detection of bacteriuria by the presence of pyuria. The urine may be examined microscopically for the presence of white cells; an increased number of cells indicating inflammatory change somewhere in the renal tract. This inflammation need not be infective in origin. The assessment of pyuria may be made either qualitatively or quantitatively. The main criticism to the use of this method is that a large proportion of bacteriuric patients fail to show
pyuria. Kass (1956) found pyuria occurring in less than 60 per cent of patients with asymptomatic bacteriuria and this finding has been confirmed by subsequent studies.

Discussion

Two distinct problems arise in the detection of bacteriuria in general practice. First, whether the identification of asymptomatic bacteriuria is of value in this field of medicine and secondly, if search for bacteriuria is to be made, which of the screening tests are most suitable for use in practice.

There are two aspects of general practice in which detection of bacteriuria extends the range of the practitioner's care, namely in antenatal supervision and as a research study of asymptomatic population groups. This latter study, which is suitable for investigation from general practice, would assist in defining the extent of the problem and form questions concerning this finding which then may best be answered by other disciplines of medicine. The arguments for the detection of asymptomatic bacteriuria of pregnancy have already been outlined. The object of antenatal care is the prevention of maternal and foetal ill health and when there is evidence of a means of reducing this toll it is incumbent upon the obstetrician, whether in hospital or domiciliary practice to extend the scope of antenatal care as necessary. This screening has the added value that not only may the incidence of pyelonephritis of pregnancy be reduced but a number of patients with previously unsuspected renal tract abnormalities may be detected. The value of recognizing bacteriuria of pregnancy is especially pertinent in general practice where, if a new concept or technique is introduced into antenatal supervision, care must be taken that decline in emphasis of another aspect of antenatal care does not unwittingly follow.

Butler and Bonham (1963) have drawn attention to the too common failure to record the blood pressure in general practitioner antenatal care and such simple observations must be followed diligently before more sophisticated techniques are adopted.

In considering the methods available for identifying bacteriuria it must be borne in mind that the criteria for a satisfactory screening test are not necessarily the same as for a standard biological investigation. It is useless introducing complicated and time-consuming techniques into the surgery, for after the initial enthusiasm wanes the hurly-burly of general practice will cause them to be used less frequently, thus rendering them valueless.

At present the screening tests which can be most readily used by general practitioners are the T.T.C. test, the modified nitrite test and the filter paper strip semiquantitative bacteriological method. The chemical tests differ in their individual advantages. The T.T.C.
test is, in most people's hands, rather more accurate than the nitrite test but the relative instability of the tetrazolium salt may prove too great a handicap in some circumstances. Both techniques require incubation and apart from a water bath the only apparatus needed is sterile pipettes and clean glassware. The advantages of the filter paper strip method are that it is accurate and it is a direct observation on the infecting organism. The culture is then available on the agar plate for subsequent studies if required. The technique is a little more sophisticated than the chemical methods and requires a supply of McConkey plates, an incubator and previous correlation with quantitative counts with the particular paper used. It is however rapid, economical, easy to interpret and can with little difficulty be used with advantage in general practice.

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