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Bacteriuria in pregnancy

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BACTERIURIA IN PREGNANCY

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Bacteriuria in Pregnancy

Since the early 1900's investigators have noted that pregnant women are more likely to have bacteriuria.[4,5] This condition is often asymptomatic, and a very detailed history is necessary if one is to establish prior urinary tract infection. Seventy-six per cent of the pregnant patients in one study gave no history of difficulty involving the urinary tract at the time their infection was diagnosed.[19]

Work by Kass (1956, 1960) has demonstrated that pyelonephritis during or immediately following pregnancy develops in 40 per cent of women with untreated bacteriuria. He also noted that pyelonephritis was unusual in those women who were treated successfully or who had no demonstrable bacteriuria.[14] With early detection and adequate treatment the risk of pyelonephritis can be decreased.

Using plate dilution cultures, bacteriuria has been defined as at least 100,000 or more bacteria per cubic centimeter of urine, discovered on two consecutive examinations.[16]

Using this definition, the prevalence of bacteriuria in pregnant women has been stated as 6 per cent with a range of 2 - 10 per cent.[16,33,35,38] The difference in prevalence depends partially on socio-economic factors, the highest income and social scales having the lowest rates. There is convincing evidence that in many instances bacteriuria antedates conception. Various authors,

including Kunin, et al, determined the prevalence of bacteriuria in school girls to be 1.2 per cent, rising to 3.5 per cent in 15 - 19 year old Negro school girls.[18] Sleigh, Robertson, and Isdale observed that 8 per cent of 397 nulliparous married women had bacteriuria, compared with 6.6 per cent of 1,684 pregnant women living in the same area. These findings would indicate that the incidence of bacteriuria rises in the years immediately prior to marriage and has little to do with pregnancy.[31]

Kaitz and Hodder also studied the relationship between bacteriuria and socio-economic status, and they stated that Negro women, who in their series came from a lower socio-economic group, had a higher prevalence of unrecognized urinary tract infections than Caucasian women.[12] However, Whalley, Norden and Kilpatrick, in comparing gravid Caucasian and Negro women of the same socio-economic group, found no significant difference in the incidence of urinary tract infection.[25,35] A host factor which seems to influence the frequency of bacteriuria in Negro women is sickle cell trait. The incidence of bacteriuria in pregnant Negro women with sickle cell trait is twice as high as a comparable group of women without the trait, 13.9 and 6.4 per cent respectively.[37]

In the gravid patient, Kass felt that fewer than one-fourth of the women with bacteriuria had acquired the infection after the second month of gestation. Whalley is of the opinion that trauma to the urethra and bladder, incidental to coitus, is a significant

factor. Other contributing factors, especially noted after the second month of gestation include: 1) slowing of the urine flow in dilated and distorted ureters, perhaps made atonic by the increased secretion of progesterone, and 2) pressure on the lower urinary tract caused by the enlarging uterus. Trauma associated with parturition will also contribute to post partum bacteriuria and to bacteriuria associated with future pregnancies. Little felt that the incidence of bacteriuria decreased with increasing age, in contrast to the experience of Kass (1962), and was higher in primipara and grand multipara.[19] Williams, et al, noted no definite relationship of bacteriuria to age or parity.

Symptoms are not volunteered by patients in many obstetrical clinics. One author noted in questioning 157 women with confirmed gram negative bacteriuria, that only 50 per cent had symptoms referable to the urinary tract, and complaints were primarily of increased frequency of micturition, a symptom also common in pregnancy.[38] Monzon, et al, and Pion, et al, writing in the American Journal of Obstetrics and Gynecology, stated that only one-third of pregnant women with bacteriuria have symptoms.[24] Asymptomatic patients may find they did indeed have vague symptoms once infection is cleared. Symptoms usually attributed to the gastrointestinal tract, such as nausea, vomiting and reflex ileus, may be caused by urinary tract infections as the innervation of other abdominal organs and the kidney is the same.[21] Failure to

find large numbers of bacteria in the urine of a patient with the classic symptoms of urinary infection should raise questions of 1) antibiotic therapy prior to collection of specimen, 2) ureteral obstruction, 3) excessive hydration, 4) urinary pH under 5.0, or 5) slow growing bacteria such as anaerobic Bacterioides organisms.[21]

Urinary tract infections in pregnancy are usually caused by gram negative organisms. One author reported only three gram positive infections in a series of 3,000 patients. He suggests gram positive infections are usually misdiagnosed and caused by contaminants.[38] "Clean catch" or catheterized specimens are reliable, if special techniques are used and if the specimens are examined within one hour of collection, or are refrigerated for not more than 24 hours. Investigation should include microscopic examination of the urinary sediment and plate dilution cultures.

In attempts to further study the pregnant patient with bacteriuria, other methods have been used to localize the site of infection. An excretory pyelogram, with minimal radiation exposure has been helpful. Hanley's method, one full-sized abdominal film taken 20 minutes after injection of 40cc of Hyopaque, has not proved harmful to mother or fetus.[9] In screening a series of pregnant patients with confirmed bacteriuria, other authors noted approximately one-half of the women had urinary tract

anomalies, as revealed by a single film intravenous pyelogram. The most frequently found abnormality was dilatation of the ureters and kidney pelves. A high percentage of patients with chronic pyelonephritis was found in those with ureteral involvement radiologically, whereas, those with no changes demonstrable radiologically or merely bladder involvement did not have this disease. The true significance of a high urinary bacterial count in assessing bacteriuria as a result of pregnancy, is debateable. Kass' (1960) observations, confirmed in Melborne by Kincaid-Smith and Bullen (1965), demonstrate underlying chronic renal disease in the majority of gravid patients with bacteriuria. In their studies, intravenous pyelography revealed a very high incidence of radiologic abnormalities in the kidney.

Impaired urinary concentrating ability has been demonstrated in pregnant women with asymptomatic bacteriuria. Slight, but statistically significant differences in renal function between bacteriuric and non-bacteriuric women have been noted. Kaitz (1961) noted that pregnant women with bacteriuria cannot achieve normal levels of urine osmolality after dehydration. Thus, obtaining specimens by ureteral catheterization and measuring urine osmolality, an indirect method of indicating unilateral kidney involvement has been found. [10,30]

Fairley, Bond and Adey used bladder aspiration techniques as well as cystoscopy and ureteral catheterization to pinpoint

the site of asymptomatic infection. They found bacteriuria localized in the bladder in 23 patients and in the kidney in 22 patients. In only 10 per cent of 50 consecutive patients were they unable to accurately determine the site. The finding of bacteria in ureteral urine is highly significant in that bacteria obtained in this manner can only be found in pyelonephritis.

Brumfitt and Percival (1965) found elevated titers of serum antibodies in 32 per cent of women with asymptomatic bacteriuria of pregnancy. Antibody production is believed to occur only within the kidney. Elevated titers discovered at first prenatal visits suggest that renal involvement occurs early, even in the absence of symptoms. Pregnant patients with bacteriuria usually will show an elevated serum leukocyte count, especially if the kidney is involved.[22] Although most pregnant women have leukocytes with normal phagocytic activity, in one study approximately 9 per cent had leukocytes with decreased activity. This figure, which is nearly the same as that quoted for the incidence of urinary tract infection in pregnancy, would tend to suggest a correlation between the two, i.e., decreased phagocyte activity may be associated with urinary tract infections in pregnant women.[14,16]

Urinary protein commonly has been associated with urinary tract infections, especially in young people. However, it has been stated to be an unreliable indicator of urinary tract infec-

tion in pregnancy. In one study, it was absent in 59 per cent of confirmed infections, present in trace amounts in 31 per cent, and definitely present in only 10 per cent.[38]

Pregnancy may create a situation where catheterization with slight trauma may contribute to the establishment of infection. Tuch and Petersdorf note a 0.5 per cent incidence of urinary tract infection after a single catheterization in non-pregnant ambulatory patients.[34] It would be expected that gravid women would have a higher incidence of infection after catheterization.

Endotoxins elaborated by E. coli (the most common etiological agent of urinary tract infection) may lead to subplacental hemorrhage with resulting prematurity.[11] Mackay's study of chronic pyelonephritis noted fetal deaths in 8 of 33 case pregnancies. No infant survived if the maternal BUN was greater than 50 mg%.[20]

A number of authors have found the prematurity rate and fetal mortality to be associated with bacteriuria of pregnancy.[9,10,15,17] Kass, writing in Biology of Pyelonephritis, reports an increased risk of prematurity and fetal loss in pregnant women with persistent bacteriuria, and stated the risk is significantly reduced by antimicrobial agents throughout gestation. Kincaid-Smith suggests that underlying chronic renal disease accounts for a higher percentage of premature deliveries, fetal loss and pre-eclamptic toxemia. She notes a high frequency of middle trimester abortions, as well as a high rate of fetal loss after 28 weeks

gestation.[14] The number of patients with toxemia was higher in women with bacteriuria.[17] This agreed with the study of Kass; but unlike Kass they did not note a decreased incidence with long-term antibiotic treatment as Kass reports.

As of early 1967, only four articles have appeared which do not document an increase in prematurity among women with persistent asymptomatic bacteriuria.[16] Other authors have stated that bacteriuria in early pregnancy did not seem to increase the likelihood of prematurity, neonatal death, stillbirth, fetal anomalies, abortion, essential hypertension or eclampsia.[3,19]

Children born of mothers with bacteriuria have not been extensively studied, but Zilliacus and Totterman report a greater susceptibility to all kinds of infections in neonates of mothers with bacteriuria of pregnancy, indicating lowered resistance in these particular infants.[21]

Thus, the relationship of bacteriuria to other problems of pregnancy, except pyelonephritis, is open to debate. Other authors did not feel there was an increased maternal morbidity or mortality associated with bacteriuria in pregnancy - only that which is associated with the disease itself separate from pregnancy. It was stated, however, that an increase in renal dead space and a decreased drug tolerance make management more difficult in pregnancy.[8]

In the management or treatment of urinary tract infections in pregnancy, difficulties with therapy are manifold. It is

not the purpose of this paper to discuss the individual treatment regimen for each etiologic agent. It is, however, within the scope of this paper to note the types of chemotherapeutic agents used, the duration of treatment, some of the body defense mechanisms which are important in pregnancy, and the hazards to the fetus. Leukocytes and phagocytosis have previously been discussed.

In discussing drug reactions which have an adverse effect on the obstetric patient, we recognize that the same drug idiosyncrasies may occur here as in the non-pregnant patient. Most, if not all, drugs are capable of crossing the placenta from mother to child and, therefore, cannot be given to one without affecting the other. In-vitro sensitivity studies, therefore, usually are helpful in deciding the best treatment methods. The effect of a drug upon the embryo or fetus may differ quantitatively or qualitatively from its effect on the mother.

From the first missed period to about the third or fourth month of gestation must be regarded as critical in the development of the fetus. Therefore, agents which can affect the fetus during this time should be used with caution. Exogenous teratogenic factors in humans produce effects at the time of placental crossing rather than after a time lag.[29] Antibiotics and other chemotherapeutic substances are capable of interfering with the normal multiplication of cells. Antibiotics can cause fetal abnormalities in animals, but whether or not they have a similar

action in humans is yet unresolved.[29] The effect of Penicillin G and allied drugs used for respiratory infections may so decrease the gram positive flora of the lower urinary tract that overgrowth of gram negative bacteria may occur. The use of drugs which depress gram negative bacteria, e.g., tetracyclines, may lead to invasion of the urinary tract by gram positive organisms.[21]

Sulfonamides, Novobiocin, Chloramphenicol, Tetracycline, and other drugs do have reported toxic or unusual side effects. Sulfonamides reportedly cause increased susceptibility of premature infants to kernicterus at relatively low levels of serum bilirubinemia. Novobiocin has also been associated with hyperbilirubinemia. Chloramphenicol in large doses produces the so-called "grey baby syndrome" in premature infants. In view of its free transfer across the placenta, it should be used with considerable caution during pregnancy.[21]

Streptomycin likewise crosses the placenta readily. In view of the known effect on hearing, it would seem advisable to limit it only to selected cases. Erythromycin has been questioned regarding liver damage. Nitrofurantoin can cause hemolysis. Finally, Tetracycline has been noticed to discolor the deciduous teeth and may affect bone growth. From this information, it would be important to select the most effective antibiotic and limit its use to the minimum dosage and duration necessary to treat that infection.[21]

The time for eradicating maternal bacteriuria is not known. Actual value of continuous drug administration for 20 to 30 weeks during pregnancy with associated risks of toxicity to fetus and mother has not been determined.[35] Short course therapy (5 - 7 days) was found to be relatively ineffective by McFayden and McCallum.[22] Longer term therapy, i.e. three weeks and more, was found to be much more satisfactory, and persistent bacteriuria recurred in only 6 of 30 patients treated in this manner.[16] Early recognition, aided by specific questioning of the patient early in pregnancy and rational treatment for at least three weeks is beneficial in controlling bacteriuria and preventing pyelonephritis.

Following pregnancy, a complete evaluation should be carried out in any patient with a urinary tract infection. Kass, in checking untreated patients, found recurrent bacteriuria in 80 per cent of patients post-partum.[16] Whalley found 81 per cent have positive cultures two months post-partum if bacteriuria persisted until delivery.[35] Certain women, i.e., those who had infections prior to pregnancy, those who had clinical infections and bacteriuria during pregnancy and those who are catheterized either before or after delivery, have the highest incidence of urinary tract infections post-partum. These women should routinely have urinary cultures following delivery with intravenous pyelograms performed on all those who had infections which were

difficult to clear. McFayden and McCallum declared that one-half their patients with a primary urinary tract infection had abnormalities detected by intravenous pyelography following pregnancy.[22]

Careful analysis and evaluation of all pregnant patients with urinary symptoms or bacteriuria, however vague, is extremely important. If the number of women with pyelonephritis, toxemia, and chronic renal failure is to be decreased in the future, follow-up of all urinary tract infections is mandatory.

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