

## GRIESS' TEST AND PROPHYLACTIC FURADANTIN THERAPY@

by

MIRU SHIVDASANI,\* M.R.C.O.G., D.Obs. R.C.O.G.

SHOBHA JOGLEKAR,\*\* M.D.

A. ACHARYA,\*\*\* B.Sc.

An association of bacteriuria with maternal and foetal morbidity has now been definitely established. Various reports indicate a significant incidence of bacteriuria ranging from 2 per cent to 7 per cent. About one-third of these will eventually develop urinary tract infection before or soon after delivery. Bacterial colony counts in the urine are time-consuming and expensive for the purpose of routine screening of all antenatal patients; therefore, a simple test known as Griess' test can be performed to detect bacteriuria. The test was discovered by a German scientist, Griess, who developed a reagent for the detection of nitrites in a solution. When urine contains bacteria, nitrates are converted into nitrites, which could then be detected by this reagent.

The results of evaluation of Griess' test have been variable. Smith *et al* (1961) found that 97% of Griess' positive urine specimens had bacterial

colony counts of more than 100,000 per cmm; but only 50% of urine specimens with significant bacterial colony counts had a positive Griess' test. Smith and Schmidt (1962) got no false positive tests, but reported that the test was effective and reliable for screening outpatient women for bacteriuria. They felt, however, that Griess' test is not satisfactory for hospitalised patients as the latter group is likely to have a nitrate deficient diet. Deshan *et al*, (1966) found that the test had an overall accuracy of 89.8% and Merit *et al* (1967) found that 80% of their patients with significant bacteriuria gave a positive Griess' test. This indicates that the test is of some value, if limited, in the screening for bacteriuria.

### AIMS

We undertook the study with the following aims:-

(1) To find the incidence of asymptomatic bacteriuria in apparently normal patients and in pregnancies complicated by toxæmia or anaemia.

(2) To evaluate the results of Griess' test in cases with a positive finding.

(3) To compare the results of patients treated with Furadantin (Nitrofurantoin) with those of the untreated group.

@From the Dept. of Obst. and Gynec., K. E. M. Hospital, Bombay.

\*Pool Officer.

\*\*Hon. Asst. Gynecologist & Obstetrician, K. E. M. Hospital and Hon. Asst. Prof. at Seth G. S. Medical College.

\*\*\*Research Assistant.

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### Material and Methods

Our report comprises a study of:-

(1) Two thousand cases of apparently normal pregnancy.

(2) One hundred cases of toxæmia the criteria for the selection being the presence of any of the two following conditions:- (a) oedema, (b) albuminuria, (c) blood pressure above  $\frac{140}{90}$  mm Hg.

(3) Fifty cases of anaemia (Hb below 8 Gm. per 100 ml.) complicating pregnancy.

Mid-stream urine specimens were obtained in sterile test tubes from the patients at the antenatal clinic. None of these patients actively reported any urinary symptoms, although on direct questioning, 15 patients were found to have mild urinary symptoms.

Griess' test—The reagent was prepared by dissolving 1.5 gm. of sulfanilic acid (chemically pure) in 450 ml. of 10% acetic acid. This mixture was added to a solution of 0.6 gm. of alphanaphthylamine dissolved in 60

ml. of a pink colour. The urine was tested by adding 1 ml. of reagent to 1 ml. of urine in a clean test tube. Development of a pink or red colour indicates a positive test.

Where the test was positive, the urine was saved for further examination and the following tests were performed:—

(1) Microscopic examination of the centrifuged sediment.

(2) Colony count on blood agar plate by serial dilution method 1:100,000.

(3) Isolation and study of the organisms by standard methods.

(4) Sensitivity test for Furadantin by dried disc method.

All the above tests were repeated at each antenatal visit till the Griess' test was negative on two consecutive occasions. Griess' test was, however, repeated even subsequently till delivery.

### Results

Table I shows that the incidence of positive Griess' test is 3.25% in nor-

TABLE I  
Incidence of positive Griess' test

	No. of cases.	Positive Griess' test		False Positive
		Total No.	Percentage	
Normal pregnancy	2000	65	3.25%	5
Toxaemia	100	10	10%	0
Anaemia	50	3	6%	0

ml. of boiling distilled water. The resultant colourless reagent remains stable for several months if stored in a stoppered amber-coloured bottle in the refrigerator. Deterioration of the reagent is detected by the develop-

ment of a pink colour. The urine was tested by adding 1 ml. of reagent to 1 ml. of urine in a clean test tube. Development of a pink or red colour indicates a positive test.

*Culture*—The urine was cultured in the cases with positive test and the results were as shown in Table II.

TABLE II  
Results of culture

Causative organism	No. of cases	Percentage
1. Coliform group	54	73.9
2. <i>B. pyocyaneus</i>	6	8.2
3. <i>Proteus</i> group	6	8.2
4. Staphylococci	10	13.6
5. Streptococci	5	6.9
6. Intermediate	2	2.7
7. <i>Kl. Ozanaea</i>	1	1.3

The commonest organism grown was *E. coli* in as many as three fourths of the total number. One fifth of the total positive cases showed gram positive cocci, staphylococci being double the number of streptococci. *B. pyocyaneus* and *B. proteus* were equal in number. Another significant finding was that 85% of the cases showed only one organism. The remaining 15% showed more than one pathogen.

#### Colony counts

Excepting 2 cases, all had colony counts of greater than 100,000 organisms per cm. Of these two, one had a count of 12,000 per cm. and the other had a count of 10,000 per cm.

#### Treatment

Of the 2,150 cases, the first one thousand, apparently normal pregnant women, were selected for the treated group. No treatment was given to the remaining patients, constituting 1150 women of the untreated group.

Furadantin, 50 mg. 6 hourly, was given for five days. If the test was positive again during any time of pregnancy, the course of treatment was repeated.

#### Effect of therapy

Thirty-three patients with "true" positive Griess' test (confirmed by bacteriological and cultural investigations) were given treatment. Of these, 3 did not return to the follow-up clinic. Thus 30 patients comprised the "treated" group.

Of these 30 women, 3 cases showed *B. pyocyaneus*. This is almost always resistant to Furadantin and, therefore, this group is excluded.

Twenty patients, out of the remaining 27 cases (74%), reverted to a bacteriologically negative status during pregnancy; 14 (51.8%) of these responded to one course of treatment, 6 required one more course. The other 7 (25.9%) grew pathogens resistant to Furadantin.

In the 'untreated' group, 40 women of 1150 patients had a positive test. Seven (17.5%) of these reverted to a bacteriologically negative status; 2 (5%) were found to have a negative test on the following visit and 5 (12.5%) became abacteriuric within 4-6 weeks.

#### Follow-up

At the postnatal clinic, 17 of the 20 patients treated were found to have no bacteriuria, 2 patients did not return to the postnatal clinic and 1 patient had a colony count of 12,000 per cm. In the untreated group, 30 cases (75%) were still found to have bacteriuria and 4 patients did not return to the postnatal clinic.

A follow-up was especially directed to detect the development of pyelonephritis during pregnancy and the puerperium. Table III shows the result of follow-up of these patients.

TABLE III  
Results of follow-up

	No. of cases	Incidence of pyelonephritis			
		Antenatal		Puerperal	
		Cases	%	Cases	%
Treated group	30	1	3.33	0	0
Untreated group	40	5	12.5	12	30

Pyelonephritis was absent in 29 of the 30 patients in the 'treated' group. One patient (3.3%) who grew resistant *E. coli* developed clinical pyelonephritis during pregnancy. Seventeen of the 40 patients (42.5%) in the 'untreated' group developed clinical pyelonephritis, 5 in the antenatal period and 12 in the puerperium.

#### Discussion

Although asymptomatic bacteriuria has been recognised for many years, interest in this condition regarding the prognosis of such patients arises mainly from the observations of Kass (1962). He suggested that early detection of bacteriuria will decrease the incidence of subsequent pyelonephritis and premature deliveries. Detection of asymptomatic bacteriuria is, therefore, extremely valuable from the point of view of treatable nephropathies.

Kass observed that acute pyelonephritis occurred during pregnancy only in those women with bacteriuria present from early pregnancy or before. It has also been corroborated elsewhere that a few patients without bacteriuria will also develop pyelonephritis. Therefore, acute pyelonephritis may not be eradicated completely by treating all women with bacteriuria, but its detection and treatment early in pregnancy will take care of at least two-thirds of the

cases of pyelonephritis. In our study, excepting for one patient who grew a resistant organism, none other developed pyelonephritis in the 'treated' group.

The relationship of bacteriuria to prematurity is still debatable. Kass (1962), LeBlanc and McGanty (1964), Kincaid-Smith and Bullen (1965), have found an excess rate of prematurity in bacteriuric patients, whereas Norden and Kilpatrick (1965), Bryant *et al.* (1964), Sleigh *et al.* (1964), and Whalley (1969), have found an equal incidence of premature deliveries in patients with or without bacteriuria. Whatever be its effect on prematurity, bacteriuria will affect the foetal outcome because of the increased incidence of pyelonephritis and hypertension.

An increased incidence of asymptomatic bacteriuria in patients with hypertensive disorders is reported by Kincaid-Smith and Bullen (1965), Norden and Kilpatrick (1965), and Devi *et al.* (1967). On the other hand, Low *et al.* (1967), and Monzon *et al.* (1963), have noted no relationship between the two conditions. Similarly, an association between asymptomatic bacteriuria and anaemia of pregnancy is also a matter of dispute. Giles and Brown (1962) noted a higher incidence of anaemia in patients with bacteriuria. Kaitz and Hodder (1961), and Whalley

(1967), found no significant difference in the haemoglobin concentrations of patients with and without bacteriuria. In our study, a higher incidence of bacteriuria was detected in cases of toxæmia and anaemia, and thus our results are significant.

The risks of bacteriuria associated with pregnancy can be appreciably reduced by treatment with antibacterial agents like Furadantin. Continuous antibacterial treatment has been advocated by Kass (1962), Kincaid-Smith and Bullen (1965), and Little (1965). This treatment involves risks of toxicity of the drug in both the foetus and the mother. It is our opinion that bacteriuria should be treated with a short course of Furadantin. We found this method effective in 66% of the patients, who were abacteriuric at the follow-up clinic, compared to 16.6% of untreated patients. The incidence of pyelonephritis in pregnancy or puerperium was only 3.3% in the treated group, whereas it was 42.5% in the untreated group. No side reactions, which warranted withdrawal of the drug, were noted in our study. Where pre-treatment sensitivity tests cannot be carried out, Furadantin should be the treatment of choice. It is effective in the majority of cases because it has broad-spectrum chemotherapeutic action. It is relatively free from toxic manifestations, and has the advantage that drug resistance does not develop, as with the antibiotics.

### Summary

1. Griess' test was performed to detect asymptomatic bacteriuria in the antenatal patients.

2. Two thousand cases of 'apparen-

tly normal pregnancy', 100 cases of toxæmia and 50 cases of anaemia were studied.

3. Quantitative urine culture was done where the test was positive.

4. A controlled trial of short term Furadantin therapy was carried out.

5. Furadantin was found effective in the majority of patients with asymptomatic bacteriuria.

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