THE GUTERMAN TEST FOR PREGNANCY

BY

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Guterman (1944) described a comparatively simple test for pregnancy which depends on the colour developed when pregnanediol extracted from the urine of pregnant women is treated with sulphuric acid. Because of its rapidity and the fact that it does not involve the use of animals it appears to have certain advantages over the more commonly used biological procedures for pregnancy diagnosis. It was therefore decided to give it a trial, the results of which are recorded below. The technique of the test is described in full by Guterman in his paper of 1944, to which he has added certain essential modifications in a later publication (Guterman, 1945).

Briefly, conjugated pregnanediol in the urine is hydrolysed by acid in the presence of toluene to give an extract of free pregnanediol, as described by Astwood and Seegar Jones (1941). When free pregnanediol is treated with concentrated sulphuric acid an orange-yellow colour is produced (Talbot, Berman, MacLachlan, and Wolfe, 1941), and the appearance of this colour indicates a positive result. Actually, colours ranging from the palest straw to brownish orange may be obtained, and while the former is to be regarded as negative, the pale yellow colour given by a weakly positive urine requires considerable experience of reading the test to differentiate.

Results of Investigation

In all, 107 tests were made of 105 patients in whom a diagnosis of pregnancy was entertained on clinical grounds; of these, 79 subsequently turned out to be pregnant. Table I shows that in the positive diagnosis of pregnancy the Guterman test was only 57% accurate.

TABLE I

Clinical Category	Number of Patients	Guterman Test Results	
		Positive No.	Negative No.
Pregnant	79	45 (57%)	34 (43%)
Non-pregnant ..	26	4 (15%)	22 (85%)

The earliest at which a correct positive test was obtained was 8 days from the end of the last menstrual period, and in this case it is known that the test was done on the 15th day after a known single coitus. The latest correct positive result was obtained on the 270th day of pregnancy. The accompanying Chart shows the proportion of correct positive tests to the total number of women tested at each month of pregnancy; it suggests that the test was never more than 65% accurate in the first four months of pregnancy, when it is most likely to be of use, and it was not until the fifth month that any degree of accuracy in diagnosis was obtained.

Of the tests giving an incorrect result 34 were negative, their distribution being shown in the Chart. Four tests gave false positive results, and brief clinical particulars of these are given in Table II.

Another group of women have been tested to determine the usefulness of Guterman's reaction in predicting the outcome in cases of threatened abortion. In this group 47 tests were carried out on 33 patients. In 20 cases the tests

TABLE II.—Four False Positive Results

Case No.	History
31	Period within 25 days before the test was carried out. Com- plained only of enlargement of the breasts, which has since subsided. Definitely not pregnant.
45	Admitted with irregular too frequent menstruation and sal- pingitis. Also mentally deranged. Last menstrual period within 25 days before the test. Not pregnant.
84	Found to have a blood-stained pleural effusion six months after childbirth: ? chorion epithelioma. Urine sent for Aschheim-Zondek test, but Guterman test done as well. Aschheim-Zondek negative, Guterman positive. Not chorion epithelioma; not pregnant.
74	Single woman, about a week overdue with period. Period began two days after test reported positive. Definitely not pregnant.

were positive or became so on repetition, and 17 of these patients continued their pregnancies, one of them being treated throughout with "proluton C." The 3 patients who aborted in spite of persistently positive tests did so at 4, 5, and 28 days after the last positive result; the last-mentioned patient had been treated throughout with progesterone, and, although she aborted 28 days after the last test, the size of the foetus suggested that intrauterine death had occurred at about the time of that test.

Negative tests, or those which became negative on repetition, were given in 11 women, and subsequently they aborted at periods ranging from 1 to 70 days after the last negative result.

Two women gave negative tests after the onset of the symptoms of abortion, but pregnancy continues to the time of writing; one of these patients had a positive result

42 days after her last menstrual period, but when she was tested again 14 days later the result was negative in spite of the fact that she was being treated with progesterone.

Chart showing results with the Guterman test. The black and white areas represent patients giving positive results and negative results respectively.

Discussion

Browne, Henry, and Venning (1939) and Bachman, Leekley, and Hirschmann (1940) have shown that from 5 to 10 mg. of pregnanediol is excreted daily during the last half of the normal menstrual cycle. As a rule this output ceases one to four days before the onset of the flow (Venning and Browne, 1937). If conception occurs the menstrual daily rate of excretion is maintained or slightly increased (Jayle and Libert, 1946) for the first 70 to 100 days of pregnancy, after which the amount excreted begins to increase rapidly, reaching a maximum of from 60 to 105 mg. daily at about the 266th day. From then until parturition the quantity of pregnanediol excreted falls, though Dahle (1946) throws doubt on this, and no pregnanediol can be recovered from the urine after the first 48 hours of the puerperium.

Our experience with the Guterman test as a method of diagnosis of early pregnancy is at variance with that of other workers. Guterman (1945) in an account of 248 cases, of which 133 were described in his first paper (Guterman, 1944), claims that it is accurate in 92% of cases if sufficient care is taken over the technique. Morrow and

Benua (1946), using Guterman's technique slightly modified and reading the results against an artificial standard in the photo-electric colorimeter, find that the test gives a large number of false positive results in the latter half of the menstrual cycle in non-pregnant women. They confirm the statements of Venning (1937), Hain and Robertson (1939), and Tien (1941) that the colour values for the pregnanediol excreted in early pregnancy may overlap those found in the latter half of the menstrual cycle. They point out that the test is usually positive in early pregnancy but may be negative in pregnancies which progress quite normally. MacCormack (1946), using a slightly modified technique but reading her results with the naked eye, finds an absolute correlation between the Guterman and Friedman tests.

The results presented in this paper do not support the view that the test is reliable enough for adoption as a routine clinical laboratory technique. When it is considered that the total daily output of pregnanediol in the urine in the first three months of pregnancy is only from 10 to 25 mg., and that only 100 ml. of urine is used in the test, it is clear that the amount of pregnanediol present in any given specimen must be very small, and it follows that the colour developed will be correspondingly weak and difficult to differentiate from the straw colour which Guterman regards as negative. In a recent preliminary communication Somerville *et al.* (1947) describe their modification of the methods of Astwood and Jones (1941) and Talbot, Berman, MacLachlan, and Wolfe (1941), which essentially seems to consist in controlling the cooling of the precipitation mixtures to give more regular and exact quantitative recoveries of pregnanediol. They have found that rapid cooling of precipitation mixtures results in low and irregular recoveries; and since rapid cooling is a feature of Guterman's qualitative technique it seems not unlikely that the variability of the results obtained may be at least in part ascribed to that. It is interesting to note that Somerville and his co-workers use for their method one-fifth of a 24-hour sample of urine, which is likely to be more than the 100 ml. prescribed by Guterman.

In view of the very small differences between the amount of pregnanediol excreted in the latter half of the menstrual cycle and that excreted in the first two or three months of pregnancy careful consideration should be given to the question whether any test based on the pregnanediol excretion is likely to be of much value in the accurate diagnosis of early pregnancy.

Guterman (1945) stresses the importance of using freshly prepared alkali dissolved in methyl alcohol for the precipitation of impurities, in order to prevent the occurrence of false negative results. This reagent is freshly prepared every three days in this laboratory.

Cope (1940) has pointed out that toxæmia of pregnancy and chronic nephritis can interfere with the excretion of pregnanediol, but there is no evidence that any of the patients giving false negative results in this series were not completely healthy, with the exception of two. Cases 46 and 49 were both suffering from hyperemesis gravidarum at the time of testing. Case 46 gave a positive result 69 days after the last menstrual period. Case 49 was negative when tested 66 days after the last menstrual period, at which time the Aschheim-Zondek test was also negative; and she was again negative by Guterman's test seven days later. Both these women have proceeded to term.

When the test has been used to predict the fate of threatened abortion our results appear at first sight to agree well with those of Guterman (1946), who was able to predict accurately the outcome in 68 out of 73 cases of threatened abortion; he states that the continuing excretion of pregnanediol in threatened abortion indicates that the

pregnancy will be retained, but that if excretion falls or ceases altogether abortion will become inevitable. In this series loss of the pregnancy was foretold successfully in 11 out of 13 patients who gave negative tests, but it is felt that this may well be due to chance in view of our experiences with the test in the diagnosis of pregnancy.

Our finding of three patients who aborted in spite of persistently positive tests is supported by MacCormack (1946): two out of her 30 patients with threatened abortion were positive by both Friedman's and Guterman's tests up to 24 hours before they aborted. She found the Guterman test negative in 30 of her patients, of whom 22 proceeded to abort. Cope (1940), using Venning's (1937, 1938) method for the gravimetric assay of pregnanediol, reports three cases of inevitable abortion in which the urinary pregnanediol excretion was high; and Browne, Henry, and Venning (1939) record a similar case.

In general it seems that if positive results, or tests which become positive when repeated, are obtained from patients with threatened abortion the likelihood is that they will retain the pregnancy, though it is not by any means certain. It is such a common event in normal pregnancy for the test to be or to become negative that little weight can be attached to it as a finding where the continued life of the ovum is in the balance.

Summary

A report is given on the Guterman test for pregnancy.

Tests were made of 105 patients; 67 gave correct diagnoses, 34 gave false negative results, and 4 gave false positive results.

Investigations of 33 patients with threatened abortion showed that the test foretold the outcome within rather wide limits.

The literature is discussed briefly, and the question is raised whether any test based on pregnanediol excretion has any useful part to play in the diagnosis of early pregnancy.

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The Annual Report of the Pasteur Institute of Southern India, Coonoor, includes some information on antirabic treatment. At the Institute itself 370 patients received a complete and 59 an incomplete course. The mortality rate among these patients was 0.5%. There were 11 deaths among the 12,922 patients who received complete or incomplete courses at the various subsidiary centres, giving a mortality rate of 0.08%. The total number of patients treated at the subsidiary centres over the 25-year period 1922-46 was 208,481 with 716 deaths, corresponding to a mortality rate of 0.34%. Of the 11 deaths in this group in the year 1946-7 10 followed dog bites and one followed a jackal bite.