

THE USE OF THE MALE FROG TEST AS AN AID IN THE DIAGNOSIS OF RETAINED PLACENTAL TISSUE

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In a previous article (1) we pointed out the value of the male frog, *Rana pipiens*, as a *new test animal* for early pregnancy. As the number of tests increases, it still is nearly one hundred per cent correct in the first trimester of pregnancy. The more recently published work of Robbins and Parker (2) substantiates our results and clinical laboratories throughout the United States are using this test in increasing numbers. Information regarding the storage, handling and feeding of the frogs has been published in another article (3).

A New Use For the Test

During the experimental work on the male frog pregnancy test we *discovered a fact which is of great clinical importance*. It was suggested by the following history.

Case History: Mrs. R. W.—On January 5, 1948, Mrs. W. awoke at 2:00 A.M. and found that she was bleeding per vaginam. After some cramp-like pains she passed several large clots. The clots were examined and one was found to contain a small foetus measuring about 4 Cm. in length. There was no more bleeding. The first specimen of urine the next morning (January 6, 1948) was injected into two male frogs. The test was positive even though the foetus had been passed. The patient was treated conservatively; bed rest, soft diet, sedatives and Ergotrate tablets (gr. 1/320 tid). The pulse and temperature remained normal. Bleeding was slight, patient remained in bed.

On the morning of January 8, 1948 cramps and vaginal bleeding, which was more than normal in amount, occurred. The patient was hospitalized. Vaginal examination revealed a soft uterus, the cervix was dilated two finger tips and the placenta, though partially extruded, *was still adherent to the posterior wall of the lower uterine segment*. Digital removal of the placenta was not attempted. Intravenous Ergotrate did not cause the expulsion of the retained placenta. On January 9, 1948, the first morning specimen of urine was injected into two male frogs. *The test was still positive*. At noon on January 9, 1948, the patient was sent to the operating room and a dilatation and curettage was performed. A placenta measuring 7 cm. in diameter was removed, the uterus carefully curetted and packed with sterile gauze. The first postoperative urine specimen, voided at 8:00 P.M. January 9, killed two male frogs before the test could be completed. The first morning specimen voided January 10, 1948, *eighteen hours after the placenta had been removed*, was injected into four frogs. *All four frogs were negative*. The first morning specimens of urine for the next two mornings were injected into frogs and the test were *negative* on both days. The uterine pack was removed at the end of twenty-four hours. Recovery was uneventful. The patient was discharged in good condition.

From this case we inferred that:

- 1) The pregnancy test on the male frog (*Rana pipiens*) is *positive as long as there is live placental tissue still adherent to the uterine wall*.
- 2) The hormone which is responsible for the positivity of the male frog test is *produced only by the live attached placenta* and, therefore, should be called the "gametokinetic placental hormone". Such a hormone may prove to be useful in cases of infertility.

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Due to the ease, accuracy, and rapidity of the test we assumed that it could be used clinically in obstetrics as well as for the diagnosis of pregnancy. Consequently, one of us (Pickett) undertook the testing on male frogs of a series of cases at White Cross Hospital, Columbus, Ohio. While the number is not large, the results consistently demonstrate the fact that the above inferences were correct.

Investigations Undertaken

1. Every case of therapeutic abortion was to have a male frog test run both preoperatively and twenty-four hours postoperatively.

2. If possible every dilatation and curettage was to have a male frog test run preoperatively and postoperatively.

3. All cases of threatened abortion, inevitable abortion and missed abortion which were admitted to the Department of Obstetrics were to have a male frog test performed on admission and repeated, if it was suspected that there was retained placenta either attached to the uterine wall or unattached.

This procedure was followed in a series of nineteen cases.

Conclusions

1. There was only one case of therapeutic abortion in the series. The patient was hospitalized, the urine was tested on male frogs both before and after surgery. The frogs tested *positive* preoperatively and they tested *negative* twenty-four hours postoperatively.

2. There were eighteen cases of known pregnancy in which there were signs, such as nausea and vomiting, associated with cramps and vaginal bleeding or "spotting" either continuous or intermittent. Male frog tests were run on these cases. Four of them were inevitable abortions. The frog tests were *negative* before the foetus aborted. Six were "missed abortions". The frog tests were *negative* and the patient either was subjected to a dilatation and curettage or, if clinically improved, they were treated conservatively. *There were six cases of this kind in which the frog tests turned out positive.* These cases were considered to have the *placenta still attached* and all six were subjected to supportive treatment and bed rest. All six are *still pregnant* and in good condition. These were diagnosed *threatened abortion*. Without this test some of these surely would have been subjected to surgery and the baby lost.

3. The *missed abortion* cases, many of which would have been kept in bed for several weeks and treated expectantly, were curetted and were discharged improved in several days. The pathology reports on all such cases showed that an abortion had taken place.

4. It is believed that these cases show that the original inferences were correct and that the male frog test can be used to diagnose the detachment or death of the placenta thereby putting the differential diagnosis between "threatened abortion" and "missed abortion" on a much firmer basis and saving many babies which would have been lost through surgery.

REFERENCES

- (1) Wiltberger, P. B., and D. F. Miller. The Male Frog, *Rana pipiens*, as a New Test Animal for Early Pregnancy. Science, Feb. 20, 1948, Vol. 107, No. 2773, p. 198.
- (2) Robbins, S. L., and F. Parker. Endocrinology, April, 1948, Vol. 42, No. 4, pp. 237-243.
- (3) Miller, D. F., and P. B. Wiltberger. Some Peculiarities of the Male Frog Test for Early Pregnancy. The Ohio Journal of Science, May, 1948, Vol. XLVIII, No. 3.