mole, and one as a chorionepithelioma of the testis. Of the 27 negatives, 26 were subsequently proved clinically not to be pregnant. The one false negative was an early pregnancy of less than six weeks which a few days later became a threatened abortion.

Discussion

A suitable quantity for injection was 1 ml. of first morning urine, this being the most concentrated specimen of the day. Positives could then be obtained when afternoon specimens gave negative results. Some of Klopfer and Frank's (1949) false negatives may be due to this, despite the injection of 2 ml. a toad. Cerquiglini's (1948) injection of 10 ml. a toad is far too much for toads around 20 g. in weight.

The weight of the toads should be over 15 g. This was shown by analysis of the first 25 positive tests (see Table). Of the toads heavier than 15 g. 97% were positive after six hours, while only 75% of the lighter toads were then positive.

TABLE.—Difference in Response Between Light and Heavy Toads

Time in Hours	No. of Toads First Giving Positive Result	
	Over 15 g.	15 g. or Less
After 2	24	5
" 4	7	6
" 6	2	1
" 24	1	2
Not in 24	0	2

Pairs of toads are used for every test, and the result is regarded as positive even if only one responds. Thus in our series of 53 positive tests (that is, 106 toads), three toads gave a negative result. With single toads the accuracy would then have been 97%, but the use of pairs brings it to over 99.9%.

In considering the stage of pregnancy after which the toad test becomes positive one has to realize that this, as well as the Aschheim-Zondek, Friedman, and Hogben tests, is essentially a test for gonadotrophins; so the result will depend on the concentration of gonadotrophins excreted in the urine. In normal pregnancy the urinary gonadotrophin level shows a marked rise about the fourth to sixth weeks; before this time it is generally too low for there to be sufficient gonadotrophin in the injection mass to produce a positive result in the various biological pregnancy tests.

As the thresholds of different test animals—mice, rabbits, *Xenopus*, *Bufo*—are not the same, and as in various tests different amounts of urine are injected, it is obvious that not all of the pregnancy tests will become positive at the same time. It has been tentatively put forward (Frazer and Wohlzogen, 1949), and since confirmed (Frazer and Wohlzogen, 1950), that in the British toad the threshold (ED 50) is about 8 i.u. for standard chorionic gonadotrophin. Despite the results of Bach and Szmuk (1949) on frogs, this threshold in *B. bufo* has not varied significantly at different times of the year in toads kept in a warmed animal-house. Use of the same standard gonadotrophin has shown a threshold for the Friedman test of 15 i.u. approximately; for the Aschheim-Zondek 10 i.u. approximately, and for the *Xenopus* 70 i.u. approximately (Frazer and Wohlzogen, unpublished). With the usual amounts of urine injected in these tests—namely, Friedman 15 ml., Aschheim-Zondek 2 ml., *Xenopus* 7 ml., and *B. bufo* 1 ml.—this means roughly that the gonadotrophin levels above which positive results are obtained with unconcentrated urine will be: Friedman, 1 i.u./ml.;

Aschheim-Zondek, 5 i.u./ml.; *B. bufo*, 8 i.u./ml.; and *Xenopus*, 10 i.u./ml.

From this it becomes apparent that the Friedman test will give a positive result earlier in pregnancy than the others. The toad test, however, can be brought up to the same level of sensitivity as the Friedman test by concentrating the urinary gonadotrophins eight times by the method of Scott (1940).

Conclusion

The series of positive results with unconcentrated morning urine were obtained from cases ranging from the fourth week (eight cases) to the seventh month of pregnancy. Over this period there would seem to be no bar to the use of the toad test; but when negative results are obtained in what may be the third to sixth weeks of pregnancy it would be advisable, for 100% accuracy, either to concentrate the urine eightfold or tenfold and repeat the test, or to perform a Friedman test. If neither is feasible the test should be repeated after a fortnight. Which alternative is adopted may depend upon the laboratory facilities available.

Summary

The use of the male British toad (*Bufo bufo*) for pregnancy tests is described. In a series of 80 consecutive cases no false positive and only one false negative result was obtained.

The results are discussed, and suggestions are made for the assessment of the results of pregnancy tests in what may be the first six weeks of pregnancy.

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Medical Memoranda

Inversion of the Uterus

Inversion of the uterus is a very rare condition. The incidence is variously estimated at figures varying between 1 in 16,000 and 1 in 200,000 deliveries. The most searching article on the subject is that written by P. Das (1940). He studied the literature from the earliest times and found records of 391 cases, of which 297 were puerperal. I have found references to a further 122 cases in the journals available to me, while many more are to be found in the *Index Medicus*.

CASE REPORT

The patient, aged 34, was in her fourth pregnancy. Her last menstruation was on October 10, 1946, and her expected date of confinement was July 28, 1947. Her three previous pregnancies had gone to term and her labours had been rapid—the longest three hours. All the children are alive and in good health. Throughout pregnancy she was very well and had no abnormalities of any kind.

Two weeks before her expected date she felt crampy pains which she attributed to indigestion. These persisted for about 24 hours, when they became stronger and were followed by a "show," after which delivery was accomplished in about 50 minutes. The perineum was intact. The third stage was completed in 20 minutes, with a total blood loss of about 10 oz. (284 ml.).

One hour after delivery the uterus was firmly contracted, and as there had been no loss of blood I left the house. The nurse was called away to another case about an hour later. When she left, the uterus was still firm and no bleeding had occurred. About 30 minutes after her departure the patient felt the need to micturate, and having no bedpan raised herself on to the chamber pot. During the act she "felt something come down" in the vagina, and, finding a mass at the vulva, lay down and sent for me.

On arrival about 10 minutes later the inverted fundus was visible at the vulva, the tubal ostia showing clearly. Only slight oozing was occurring from the placental site. Her pulse was 92. The vulva and fundus were liberally swabbed with "dettol" (20%). Vaginal examination confirmed that the uterus was inverted. The loose cuff of the dilated cervix was palpable. The uterus was reinverted by gentle pressure with a sterile pad. Morphine, $\frac{1}{4}$ gr. (16 mg.), and ergometrine, 0.5 mg., were given and a course of sulphathiazole was ordered. Her pulse rate was now 80.

Throughout the puerperium her temperature did not rise above 98° F. (36.7° C.) nor the pulse rate above 88. The patient was allowed up on the twelfth day and has been free of symptoms since. She carries out her household duties every day.

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Acquired Sensitivity to Thiopentone

The following case illustrates how individual requirements for thiopentone can vary from time to time.

CASE REPORT

A woman aged 64 was to be operated on for acute intestinal obstruction. Her general condition was poor, she was ill-nourished, and had been vomiting for 24 hours, though cyanosis and jaundice were not present and she did not look anaemic. Her blood pressure was 180/100 mm. Hg, and pulse 100. Atropine sulphate, 1/100 gr. (0.65 mg.), and morphine sulphate, 1/6 gr. (11 mg.), were given one hour before operation and she was induced with 12 mg. of curare and 0.3 mg. of thiopentone. Slight respiratory depression for about 10 minutes followed this, but no apnoea. Anaesthesia was maintained with cyclopropane and oxygen, and 3 mg. of curare was given after half an hour. A volvulus of the pelvic colon was found and resected, leaving a left inguinal colostomy. The operation lasted 65 minutes, and at the end the patient had completely recovered her cough reflex.

Failure of the colostomy to close necessitated another operation six weeks later. Her general condition had by now greatly improved. Premedication was given as before. After an initial dose of 0.2 g. of thiopentone she became apnoeic, and artificial respiration with oxygen, using a Coxeter-Mushin absorber, was undertaken. The surgeon at this stage commented on the satisfactory relaxation. The absorber was cut out of the circuit periodically lest the washing out of alveolar CO₂ had been serving to maintain the apnoea. After 20 minutes she was intubated orally and the pharynx packed without any sign of resistance from the patient. Later 3 ml. of nikethamide and 1.5 ml. of picrotoxin were given intravenously with no response.

After 50 minutes' apnoea spontaneous respiration began, and at the end of the operation, which lasted one hour, she was breathing normally. Consciousness was regained an hour later, and apart from mild bronchitis she made an uneventful recovery.

COMMENT

The altered response of this patient to thiopentone points to some change having occurred in her detoxicating powers.

Thiopentone detoxication is imperfectly understood (Hewer, 1948), but the drug is believed to be broken down

quickly in the tissues generally (Adams, 1944). The role of the liver in this process is very debatable, and, while some hold that it plays a major part (Shideman and Kelly, 1947a, 1947b; Shideman, 1948, 1949; Walker and Wynn-Parry, 1949), Richards and Appel (1941), Lundy (1942), and Scheifley (1946) do not believe that liver damage prolongs thiopentone anaesthesia. Liver and kidney function tests done on the day after the second operation revealed gross dysfunction, and there were persistently high quantities of urobilin in the urine.

The patient was also grossly deficient in vitamin C. While this deficiency prolongs pentobarbitone ("nembutal") narcosis, of which thiopentone is the sulphur analogue, Adriani (1946) denies that it plays any part in the detoxication of thiopentone.

Fears that thiopentone administration might have a deleterious effect on patients undergoing sulphonamide therapy were abandoned after the experience gained in the last war (Adams, 1944). Nevertheless, it may be mentioned that in my case 21 g. of sulphadiazine had been administered two weeks previous to the second operation, and that a course of succinylsulphathiazole was started 24 hours before it. The precise bearing of this on the course of events is a matter for speculation.

Shortly before her discharge from hospital the patient informed us of her intention to resume the "injections for the blood," which she had been having thrice weekly prior to admission. Blood examination at that time showed: red cells, 1,430,000; white cells, 2,000; Hb, 40%; the stained film being typical of pernicious anaemia. Her first operation being a night emergency, no pre-operative blood examination was feasible, and her satisfactory post-operative course gave no indication for haematological investigation.

On incubating thiopentone with blood at body temperature, Richards (1947a, 1947b) found a decrease in potency which did not occur when plasma was substituted for whole blood. This suggests that some enzyme in the red cells is capable of detoxicating thiopentone. In my case the deficiency in the red cells due to anaemia at the time of the second anaesthetic would mean loss of this enzyme and could account, at least in part, for the altered response to the drug.

Liver deficiency could have been secondary to the gross degree of anaemia that developed during the six weeks' abstinence from liver extract, and could have been a manifestation of anoxia. Thus the "acquired sensitivity" to thiopentone can be attributed to a combination of gross anaemia and liver damage.

I am indebted to Mr. A. M. Abrahams and Dr. J. B. Hargreaves for permission to publish this case, and I would be interested to hear of any similar cases.

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