A history of diagnostic tests for pregnancy

A recent meeting of the Medical Sciences Historical Society looked at developments in pregnancy testing methods, from the animal-based techniques of the 1940s to present-day immunological methodology. Howard Wingfield reports.

The Spring meeting of the Medical Sciences Historical Society (MSHS) was held in March and took as its theme a history of diagnostic tests for pregnancy. Four members of the MSHS gave accounts of the history of pregnancy tests, from the use of animals such as mice and toads, through to the *in vitro* immunological tests available today.

MICE AND TOADS

Dr Eric Bridson told the meeting how he started his career in 1944 and used the Aschheim-Zondek (A-Z) test, which utilised immature female mice. He described how the test was performed and how it took more than three days to obtain a positive result, which was made by the detection of follicular development in the ovaries of the mice following injection with urine from the subject being tested.

John Fincham, who began working in Watford in 1949, then described the introduction of the Hogben test in his laboratory. This used female South African toads (*Xenopus laevis*) as the test animal, which was not sacrificed, and gave a result in one or two days. The injection of kaolin-treated urine into the dorsal sac of the toad stimulated the production of eggs, which were separated and collected by allowing them to fall through a mesh filter.

Dr David Petts then gave an account of a variation of the Hogben test used in his own laboratory in the 1960s. Here, male toads were used and detection of the human chorionic gonadotrophin (hCG) hormone in the urine was by stimulation of the production of spermatozoa in the toad. Generally, a positive result could be reported the same day but the procedure was labour intensive and only performed when clinically important.

CLEAR BLUE THINKING

The main speaker for the meeting was Professor Paul Davis (Insense; previously Unilever Research) who described the development and impact of immunological tests from the 1970s onward. As with the later animal tests, immunological methods detected hCG. However, in addition to providing benefits in the laboratory setting, these tests increasingly were conducted in the home environment.

The key breakthrough in the 1970s was the production of antibodies against hCG. Agglutination tests in which the antibodies were linked to red blood cells and then freeze-dried were used initially and these were available for both laboratory and home testing from 1978. They took about two hours to perform, needed multiple manipulations, had endpoints that were unstable and were difficult to manufacture.

In 1985 the Hybritech Icon test appeared. This used antibodies immobilised on a membrane with enzyme-linked immunosorbent assay (ELISA) technology to give a coloured endpoint. At this time, the first Clear Blue test system became available from Unilever. This was also an adaptation of a laboratory ELISA method, but it was made simple for home use by its dipstick technology.

> 'In addition to providing benefits in the laboratory setting, immunological pregnancy tests increasingly were conducted in the home environment'

Professor Paul Davis described the development and impact of immunological pregnancy tests from the 1970s onward.

It reduced the number of test manipulations required to three, reduced the testing time to 30 minutes (instead of two hours) and gave a clear result. As a consequence it became the market leader within 12 weeks of its launch.

In 1988 the Clear Blue One Step was introduced. This employed immuno-chromatography – a lateral-flow test system in which the sample flowed through a strip on which the antibodies to hCG and the reagents were immobilised. With the addition of electronics to the test system, it is now possible to advertise the product as being able to give "a clear yes in one minute".

FROGS FROM THE PAST

The meeting concluded with members of the audience contributing their experiences of some of the earlier types of pregnancy test. These included a reminiscence of the time a laboratory's neighbour found some frogs in her garden. She 'returned' them, accusing that "some toads have escaped from your laboratory".

The meeting gathered together recollections from the past from those who were there and 'made' history in laboratories that were very different from those of today. Without such recordings, it is likely that knowledge of past working lives will be lost. All in all, the meeting proved very successful and enjoyable. ■