



SCIENCE

How a Frog Became the First Mainstream Pregnancy Test

In the 1950s, if a woman wanted to know if she was pregnant, she needed to get her urine injected into a frog.

By Ed Yong



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MAY 4, 2017

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The African clawed frog, *Xenopus laevis*, is a palm-sized, greenish-gray animal that hails from the ponds and rivers of sub-Saharan Africa, where it lived for millions of years without anyone injecting it with urine. That unbroken streak changed in the 1930s, thanks to a British scientist with the fantastic name of Lancelot Hogben.

Hogben was a talented but irascible zoologist with strident left-wing politics and penchant for burning bridges. In his early career, he studied hormones by injecting them into frogs, and when he moved to South Africa in 1927, he continued those experiments with the local amphibians. One of them—*Xenopus*—was so abundant and easy to work with that Hogben spent much of his time with the creature, and even named his house after it.

In 1930, Hogben injected *Xenopus* with extracts from an ox's pituitary gland—a pea-sized hormone factory at the base of the brain. In response, the frog started laying eggs. This accidental finding was a fortuitous one. At the time, scientists knew that the urine of pregnant women contained hormones that were made in the pituitary and that affected the development of ovaries. If those same hormones could trigger egg-laying in *Xenopus*, perhaps the frog could act as a living pregnancy test.

Hogben never alluded to this application in his early reports, but it wasn't long before he was working towards it. Disenchanted with racism in South Africa, he returned to Britain shortly after his seminal experiments and brought a colony of *Xenopus* with him. His colleague Charles Bellerby worked out how to raise the frogs appropriately, showed that they would reliably lay eggs when exposed to the urine of pregnant women, and confirmed that when they're not mating, they don't lay eggs spontaneously. Another team from South Africa had been doing similar work, and as academics are wont to do, the two groups developed a bitter feud. It was never truly resolved, although Hogben could be said to have won, since the test that resulted from this work took his name.

And so it was that tens of thousands of frogs were infused with human urine between the 1940s and 1960s.

The “Hogben test” was simple. Collect a woman’s urine and inject it, fresh and untreated, under the skin of a female *Xenopus*. Then, wait. If the woman is pregnant, between five and 12 hours later, the frog will produce a cluster of millimeter-sized, black-and-white spheres. The results were reliable. One researcher reported that after injecting 150 frogs, he never got any false positives and only missed three actual pregnancies. And as one doctor wrote to Hogben’s colleagues: “Thank you for your report on the pregnancy test on Mrs. X. You may be interested to know that of one GP of many years’ standing, one specialist gynaecologist and one frog, only the frog was correct.”

There’s a long history of folk pregnancy tests: As my former colleague Cari Romm once wrote, “a long, long time before women peed on sticks, they peed on plenty of other things.” But the first reliable test was created in 1927 by German scientists Bernhard Zondek and Selmar Aschheim. Their “A-Z test” involved injecting human urine into immature female mice for a few days, dissecting the animals, and checking if their ovaries were bigger than normal.

A later version of this test used rabbits instead of mice. For some reason, people came to believe that the rabbits would die if the test was positive, and the phrase “the rabbit died” became a euphemism for pregnancy. In truth, the rabbits *always* died, because, like the mice, they had to be dissected to check the size of their ovaries. This meant that testing for pregnancy was laborious, expensive, and bloody work. In one Pregnancy Diagnosis Station, run by a friend of Hogben’s, around 6,000 rabbits were sacrificed every year.

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By comparison, the *Xenopus* test was faster, simpler for practitioners, and much easier on the animals. The frogs can live for up to 30 years in captivity, and since the tests didn't kill them, they could be reused. They were also easy to get. At first, doctors imported them from South Africa where, in the words of scientist Edward Elkan, "animal dealers seem to have no difficulty in catching as many as are required." Later, many *Xenopus* colonies were established overseas.

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In the 1960s, scientists developed chemical tests that searched directly for human chorionic gonadotropin (hCG)—the tell-tale hormone that the frogs were reacting to. The frogs were slowly abandoned. But according to medical historian Jesse Olszynko-Gryn, they were the innovation that turned pregnancy-testing into a large-scale activity. He wrote:

Although facilities existed, getting a test was neither a rite of passage for the expectant mother nor an aid to the woman who wanted to terminate an unwanted pregnancy. Rather, laboratory tests were mainly reserved for use in urgent, medical-priority cases that required differential diagnosis – for example, to distinguish the growth of a normal fetus from that of a tumor. Doctors, not women, controlled pregnancy testing and they were not keen on making this laboratory service available to every woman on demand. If a woman sent her own urine specimen to a laboratory it would not be tested, and if she went to her family doctor she might well be told to return in a couple of months when the physical signs of an advanced pregnancy were apparent.

One experiment was disrupted by an audience member who tried to rescue the frog.

If *Xenopus* changed pregnancy testing, then pregnancy testing also changed *Xenopus*. With large stocks of *Xenopus* popping up around the world, scientists started using the animal for other lines of research. It became a “model organism”—one of the mainstays of laboratory research. It has been repeatedly used to study how cells work and how embryos develop. It has flown into space. It was one of the very first back-boned animals to be cloned—a feat that led to a Nobel Prize.

But the frog’s rise to fame may have had an inadvertent dark side. In 2004, Che Weldon from South Africa’s North-West University analyzed hundreds of *Xenopus* museum specimens to show that the frog, in its native African home, is occasionally infected by a fungus called *Batrachochytrium dendrobatidis*, or *Bd* for short. *Xenopus* can tolerate these infections, but most other frogs aren’t so lucky. *Bd* has now spread across six continents and has killed countless populations of frogs in its wake. Weldon and others believe that the international trade in *Xenopus*, for either pregnancy testing or lab research, could have triggered this amphibian apocalypse.

Their case isn't definitive as other species could have also been responsible for carrying *Bd* abroad. But whether or not *Xenopus* is the “Typhoid Mary of the frog world”, it can still act as an invasive pest when released into habitats where it doesn't belong. For that reason, 11 U.S. states have made it illegal to own, transport, or sell these animals without a permit.

New York isn't one of them. On August 29, 2012, anthropologist and artist Eben Kirksey staged a “performative experiment” in Brooklyn, where he re-enacted the obsolete pregnancy test. His subject was Loretta—a frog that he had ordered from a company that supplies the animals to labs (1-800-XENOPUS). Also present were three other people, one of whom had recently gone through IVF and genuinely wanted to know if she was pregnant.

Kirksey has tried to stage several such experiments in recent years, with varying degrees of success. One was cancelled after protests from animal-rights campaigners, and another was disrupted by an audience member who tried to rescue the frog. (“First time stealing a frog, but strangely not my first time fighting a pregnant woman,” she later wrote.)

But on August 29, things went smoothly. Kirksey injected Loretta—and nothing happened. The assembled on-lookers, including 130 people watching on a live webcast, realized they didn't really know what frog eggs looked like. “Is that something?” one person wrote. “No wait, I think that is a smudge on the screen,” said another. Later, the would-be mother peed on three modern pregnancy tests, which turned up negative.

“We had to accept that Loretta had been right all along,” Kirksey wrote.