Thalidomide is a sedative drug introduced to European markets on 1 October 1957 after claims of extensive testing on rodent embryos to ensure its safety. According to Greek, Shanks, and Rice, testing on pregnant animals for teratogens was a common practice at the time, though it is unclear what testing was actually done on thalidomide. Some critics claim that no testing was done on pregnant animals, while others claim that some was done. Based on the record of the time, thalidomide was approved for use in Germany, so doctors prescribed it to treat morning sickness in pregnant women. However, in humans Thalidomide interfered with embryonic and fetal development in ways not observed in rodent tests. Pregnant women who take Thalidomide are at greater than normal risk for spontaneous abortion and for giving birth to children with developmental anomalies such as shortened, absent, or extra limbs, as well as a variety of heart, ear, and internal organ defects. The failure of rodent models to inform scientists of Thalidomide's teratogenicity in humans [3] ignited debate about the proper use of cross-species testing during drug development.

Thalidomide was first marketed on 1 October 1957 by the West German pharmaceutical company Chemie Grünenthal, headquartered in Achen, Germany. Chemie Grünenthal hailed Thalidomide as multipurpose drug capable of treating morning sickness, restlessness in children, loss of vision, and some forms of cancer. By the late 1950s, the company was marketing Thalidomide in forty-six countries. In early 1961 doctors noticed an extraordinary increase in documented cases of children with a variety of birth defects, and they soon hypothesized that maternal exposure to Thalidomide during pregnancy caused these often-severe congenital abnormalities. By March 1962 many countries had banned Thalidomide, however by then greater than 10,000 babies worldwide were born with birth defects attributed to Thalidomide.

Those birth defects mystified researchers and government entities alike, because pre-marketing tests in lab mice and rats had showed no signs of teratogenic risk. Public outrage ensued over the lack of strict regulations in regard to drug testing. That outrage motivated a scientific debate over the efficacy of using model organisms, like mice and rats, in drug development. By 1962, researchers across scientific disciplines began studies on Thalidomide’s teratogenic effects in various organisms. The most commonly used embryological model organisms during this time included rabbits, rats, and mice.

A 1962 study titled "Thalidomide and Congenital Abnormalities," by Victor Knapp, George Christie, and Mary Seller, all working in the UK, looked at the teratogenic effects of Thalidomide on rats, mice, and rabbits, and the study reported no abnormalities in the offspring of these animals after researchers had exposed the pregnant females to the drug. The authors noted that the study provided no grounds to think that drugs containing Thalidomide were safe for human use, and they argued that the only method guaranteed to safely deal with drugs of unknown teratogenicity would be to completely refrain from using them unless absolutely necessary. In 1963, Joseph A. DiPaolo, working in the US, discussed various birth defects found in mice fetoṣus whose mothers were fed Thalidomide daily, but he found only one kind of anamoly called fetal resorption, or the partial or complete dissolution of fetal tissues after some embryos had died in utero.

In 1965, J.D. McColl and colleagues in Canada further illustrated the limitations of animal studies for the use of predicting human responses to potential teratogens. In their study titled "Effect of Some Therapeutic Agents on the Developing Rat Fetus," McColl and colleagues observed in rats an increase in resorption rate but no incidences of phocomelia, the absence or abnormal development of the limbs. In humans limb truncation in offspring is a common congenital abnormality arising from Thalidomide use by pregnant women. This abnormality is caused by exposure to the drug in a short time period in early human embryonic development. Similar to Knapp, Christie, and Seller's statement from three years prior, McColl and colleagues stated that the factors involved in embryogenesis and drug interaction are so complex that straightforward predictions from animal models to humans were not possible.

From these studies, and many others, the scientists formed a consensus about the key feature of rodent embryos that grants them the resistance to Thalidomide's teratogenic effects. Mouse and rat embryos both possess superior antioxidants than those in humans. These rat and mouse antioxidants protected their embryos from the damaging free radicals that Thalidomide introduces into developing embryos.

Studies performed by William McBride in New Zealand, and by Raymond Cahen in France, in 1961 and 1966 respectively, demonstrated that mice given megadoses of Thalidomide didn't exhibit classic toxicity. A 2004 study by Jun Lu, Lai-Ming Ching, and colleagues in New Zealand found that organisms from different species metabolize Thalidomide in different ways. The half-
Sources


Thalidomide is a sedative drug introduced to European markets on 1 October 1957 after extensive testing on rodent embryos to ensure its safety. Early laboratory tests in rodent populations showed that pregnant rodents could safely use it, so doctors prescribed Thalidomide to treat morning sickness in pregnant women. However, in humans Thalidomide interfered with embryonic and fetal development in ways not observed in rodent tests. Pregnant women who take Thalidomide are at greater than normal risk for spontaneous abortion and for giving birth to children with developmental anomalies such as shortened, absent, or extra limbs, as well as a variety of heart, ear, and internal organ defects. The failure of rodent models to inform scientists of Thalidomide's teratogenicity in humans ignited debate about the proper use of cross-species testing during drug development.

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