since 1955, and phocomelia did not appear there until 1961. Almost all the few Swiss cases have been traced to Contergan from Germany.

Little is known about the metabolism of thalidomide, how the body excretes it or how long the deformity-producing factor persists in the body. About all that is certain is that it is insoluble in water and in fat. Obviously the usual laboratory animals metabolize it differently from human beings; it does not induce sleep in the animals. Investigators at the Grünenthal laboratories have tried unsuccessfully to produce phocomelia in rats, mice and rabbits. They have shown that the drug passes through the placenta of rabbits, but the offspring were normal in these experiments. G. F. Somers of the Distillers Ltd. laboratories has fed massive doses to pregnant rabbits. The rabbits did not sleep; they did, however, produce offspring with abnormalities remarkably similar to those in human infants. Since thalidomide makes a horse sleep, it may be that the horse will react in other ways as man does. Experiments with monkeys and apes will also be of interest. When the proper experimental animal is found, thalidomide does offer the possibility of studying the origin of malformations.

It is not yet possible to determine the exact number of infants born with phocomelia in West Germany, but the outbreak was devastating. The records of the Institute of Human Genetics in Münster show three cases of bilateral phocomelia in 1959, 26 cases in 1960 and 96 in 1961. Up to this spring 13 pairs of twins afflicted with phocomelia had been registered. Since twins occur once in every 100 births, the institute estimates that there will be 1,300 cases in the state of North Rhine-Westphalia, where it is located. It is an indication of the prevalence of phocomelia that the state's Ministry of Health has set up a registry for all children with defective hands and arms who will need orthopedic help. As of January, 800 had been registered, 80 per cent suffering from phocomelia, and reports were in from only half the state. By now the total may have reached 2,000. Applying this experience to the population of West Germany as a whole, the country anticipates a minimum of 4,000 cases. I should not be surprised by a total of 6,000. There is every reason to believe that two-thirds of the infants will live for many years; indeed, the children appear to have a normal life expectancy.

In England, alas, the incidence is also high. Reports of phocomelia associated with Distaval appear regularly in *The Lancet*, the British weekly medical journal. Clifford G. Parsons of Birmingham has advised me that almost every physician at a medical meeting in England last spring had seen at least one case. The total for the the country will probably be in the hundreds, however, not in the thousands.

Reports are still coming in from all over the world showing that phocomelia has occurred wherever thalidomide has been used. Sweden has had 25 cases, from Contergan purchased in Germany. Switzerland has had four cases. The Portuguese preparation, Softenon, has caused seven cases in Lebanon. Distaval has produced a case in Israel. In Peru, Contergan obtained by the father in Germany caused a case. Lenz has written me of an outbreak of phocomelia in Brazil. As yet I have received no figures for Portugal.

In September, 1960, when the Merrell Company applied to the Food and Drug Administration for permission to distribute the thalidomide compound, none of these untoward developments could have been anticipated. Clearance was delayed because the initial submission of papers was found to be "incomplete." Over the next few months, while the manufacturer gathered and filed additional material in support of the application, the first indications of the drug's neuropathic side effects were reported in the German medical press. Frances Oldham Kelsey, a physician and pharmacologist at the agency, took note of these reports. She also noted that the proposed label for the drug recommended its use against the nausea of pregnancy. From her work with quinine in connection with the malaria project during World War II, Mrs. Kelsey had become "particularly conscious of the fact that the fetus or newborn may be, pharmacologically, an entirely different organism from the adult." She therefore requested more data from the manufacturer to show that the drug was safe in pregnancy. Before her questions were answered the outbreak of phocomelia in Germany had brought withdrawal of the drug from the market in that country.

If thalidomide had been developed in this country, the story would have been quite different. Almost everyone agrees that with no knowledge of the delayed neuropathic effects of the drug and no appreciation of its dangers in pregnancy, the thought would not have occurred to anyone that it might injure the unborn