causes cancer in animals it will also cause it in humans, which is not actually the meaning of the statement. The statement simply indicated that if an agent does knowingly produce cancer in humans, when this agent is given to experimental animals, they will also develop cancer. The real question is actually the reverse: Do all agents that produce cancer in experimental animals also produce cancer in humans? The answer to that question is that it is not true that all agents producing cancer in experimental animals can be arbitrarily stated to produce these tumors in humans. As a matter of fact, certain agents may apparently produce cancer or tumors under one set of circumstances in a specific group of animals, even of the same strain or breed, while other groups exposed to the same agent may not develop these lesions.

A case very recently in point relates to the production of breast tumors in a group of beagles by one of the hormones present in a particular birth control pill. This agent, known as chlormadinone, was given in one series of experiments to a group of dogs (specifically, beagles) and a substantial percentage of these animals developed breast tunors, which, according to interpretation, may have been malignant. Because of these observations, the United States Food and Drug Administration removed this particular chemical from its list of approved experimental compounds for contraceptive study. This was done at a time when chlormadinone in the same dosage, used as a "mini-pill", had already been marketed for some time in England and, I believe, Canada and other countries. It has also been for several years a constituent of one of the major sequential oral contraceptives on the market in the United States. Of great interest here is the fact that on the basis of dosage in a given menstrual cycle, chlormadinone as a mini-pill, given at a dose of ½ mg. daily for 28 days (the average length of a menstrual cycle), would require a total of 14 mgs. per cycle. At the same time, chlormadinone in the present compound still on the market would provide 2 mgs. a day for 5 days in a sequential preparation for a total of 10 mgs. per cycle. In addition, the marketed preparation also provides .08 mgs. of mestranol daily for 20 days, one of the estrogens used in many contraceptives and an agent which has been accused by those claiming cancer is related to oral contraceptives as being the agent most likely to produce these tumors. In other words, we have a situation now in which 10 mgs. of chlormadinone may be used commercially per cycle by millions of women while in the experimental preparation which was apparently virtually on the verge of FDA approval, a total mini-pill dose per cycle, with no estrogen at all, was 14 mgs. I was told, when I questioned this, that beagles who had been treated with the marketed sequential product containing the estrogen developed no tumors of the breast. It might therefore be deduced that perhaps the added estrogen which some claim causes cancer, might have actually protected the animals against this. Either that, or the daily dose of a mini-amount of the progestogen was more carcinogenic than the intermittent, every fourth week dose of more concentrated amounts of the hormone along with daily estrogen. Here, again, we have an area where facts were obtained on the basis of experimental observations and these facts required interpretation which, despite their seeming lack of logic, led the FDA to remove the experimental drug from further study and permit the marketed preparation to remain available. Thus far, regardless of one's logic, this may seem purposeful in order to protect the public on the basis of observations that were suspicious. Yet, consider one additional piece of information that has just become known. Another company testing a similar hormone for a mini-pill, in addition to using nontreated control beagles also started for its own information another series of what might be termed "controls in therapy" and gave a similar set of their beagles chlormadinone in the same experimental design as described above and which had resulted in withdrawal of chlormadinone from the study. Strikingly, none of the chlormadinone-treated animals in this company's studies developed breast tumors!

These facts are important to note, not because they prove anything, but simply to illustrate how *extremely difficult it is to prove anything.* I would leave it to pathologists and those experts in veterinary medicine to explain why one group of the same animals under the same investigational conditions developed a substantial percentage of breast lesions while another group of the same animals under the same conditions failed to develop any. I would also wonder about the statistical validity of interpretation of positive findings in relatively small groups of animals.