to below. The screenings were essentially free from noxious weed seeds and from ergot sclerotia.

Experiments were initiated to determine the suitability of rats as a means of tracing the causative agent. It was definitely established in July, 1944, that the material in question contained something which is highly toxic to rats. Sixty parts of normal stock ration mixed with forty parts of powdered screenings killed rats in an average of about ten days. Subsequent experiments have involved a study of the symptoms produced at different levels of intake and a search for the causative factor.

The symptoms observed varied with individual animals and with the level at which the toxic material was fed. Frequently observed symptoms in rats were:

(1) Incoordination to complete paralysis of rear quarters.

(2) Extreme swelling and discoloration (dark red) of usually one rear leg only, frequently followed by sloughing of affected tissues.

(3) Dark blue discoloration of tails, frequently followed by tail eating.

(4) Extensive tissue hemorrhages.

Preliminary experiments with 2-week-old chicks indicate that they are even more sensitive to the toxic material than are rats.

No decrease in toxicity has been observed in screenings stored at room temperature since July, 1944. The toxic factor is largely insoluble in ethyl ether and in petroleum ether but is largely, if not entirely contained in boiling alcohol extracts. Results obtained to date with several lots of screenings fed to over 150 rats, strongly suggest a causal relationship between toxicity and the degree of nematode (*Anguina agrostis*) infestation of the fescue seed.

J. R. HAAG

OREGON STATE COLLEGE

SIGNIFICANCE OF NEGATIVE RESULTS IN SMALL SAMPLES

AT the recent Gibson Island Conference on Cancer, reports were made on the failure to cause regression of tumors by the use of various chemotherapeutic agents. It was stated that from 10 to 25 animals were used in each experiment. The question was raised whether such numbers were always adequate to test therapeutic effect, particularly since, in cancer, true effectiveness of as little as 10 per cent. may have practical importance. The reply made was that the types of tumor employed never regress spontaneously and consequently regression in even one animal would be highly significant. During the discussion it appeared that other investigators were following this line of reasoning. It seems desirable, therefore, to point out that while a single positive result in a small group of animals bearing tumors which do not regress spontaneously would be significant, in the sense that it would lead to further testing, the converse is not true, *i.e.*, failure to observe a single regression in 10 to 25 animals does not always conclusively demonstrate the absence of therapeutic power. If a therapy were capable of causing 10 per cent. regressions, then, in samples of 25 animals, no regressions might be observed by chance in $.90^{25}$ or 7 out of a hundred trials. One may question whether a possibility as important as effective cancer therapy should be dismissed with so high a margin of error.

Following the convention of considering a chance probability of over .05 as too great to be reliable, Table 1 states the various sizes of sample (n) for which the probability of no successes would be .05, for various values of true effectiveness (p).

TABLE 1

PROBABILITY OF NO SUCCESSES = .05 = $(1-p)^n$ FOR VARIOUS VALUES OF p AND n

p	.10	.15	.20	.25	.30	.35	.40	.45	.50
n (to nearest whole number)	28	18	13	10	8	7	6	5	4

In experiments with groups of 10 animals one might easily miss chemotherapeutic agents which had an effectiveness of less than 25 per cent. This is, of course, elementary probability, but it is of interest that in this instance the considerations of elementary probability may have been ignored because of failure to distinguish between the significance of a single positive result not noted before and the significance of the absence of this result. The crucial experiment when successful may be conclusive, but, if it is unsuccessful, one must still ask whether the experiment as performed allowed the positive event sufficient opportunity to occur. Since we are about to witness great activity in the field of experimental chemotherapy of cancer, it is to be hoped that none of this work will be rendered inconclusive on such well-recognized grounds.

MORTON L. LEVIN
HYMAN GOLDSTEIN

DIVISION OF CANCER CONTROL,
NEW YORK STATE DEPARTMENT OF HEALTH

THE RUMBLING OF THUNDER

THE rumbling of thunder certainly does not arise from any single cause. Among possible causes Humphreys[1] lists (*a*) inequalities in the distance from the

[1] W. J. Humphreys, "Physics of the Air," McGraw-Hill, ed. 3, pp. 379, 441. 1940.