STATISTICS IN INVESTIGATIONS IN ANIMAL PRODUCTION*

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Mr. President, Ladies and Gentlemen,

I feel deeply the honour of addressing so distinguished a group, especially in view of the great accomplishments of many who have spoken to you before and of those who will speak to you on this occasion. I am especially honoured to speak at a meeting over which the President of India presides.

My subject is research in animal production, with special emphasis on the statistical approaches which have been tried and found useful. I shall not draw a line between mathematics and statistics, since any such line must be somewhat artificial from the standpoint of subject-matter and the needs of the user, although such a division may sometimes be useful for administrative purposes. This is not peculiar to mathematics and statistics. Any classification of subject-matter in universities or research institutes must be artificial and unrealistic at times. For example, is the structure of the atom properly a subject of physics or of chemistry? In my own institution this problem has been solved,..at least in part,..by building the Institute for Atomic Research between the physics building and the chemistry building and connecting it with both, so that workers in atomic research can go all the way from extreme chemistry to extreme physics without even going outdoors! And when we want our graduate students in animal breeding to get a good understanding of the genetic aspects of cytology, we send them unhesitatingly to lectures in departments of botany or zoology or genetics or veterinary anatomy and histology, according to where the best instruction in that topic seems to be at the moment, almost irrespective of the fact that these students are interested mainly in animals. Emphasis on *departments* or on *classification of subject-matter* is always likely to erect unintended barriers to free interchange of ideas among students and, more serious still, among the faculty members themselves. Much truth is in the old adage: "When you lock your laboratory door you lock out more than you lock in." The fact that the locking may have been unintentional does not make the loss any less real.

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Formal research in animal production goes back at least as far as Lawes and Gilbert, of Rothamstead fame, and their work a hundred years ago on the chemistry of the animal body. Some might date it even further back to work on physiology in Germany but, except for many important findings about the chemistry of nutrition, it first got under way on a large-scale after 1890 in the United States. Most of the agricultural colleges there had been founded 20 or 30 years earlier as teaching institutions. The subject-matter taught was the collected and edited experience of those farmers who were thought most successful. This was modified and explained a bit by what was then known about physiology, chemistry and other young sciences. It was also affected a little by the sometimes disconcerting experiences which the teachers encountered in their field and laboratory work. This laboratory work was an important part of the instruction in the agricultural colleges from their very beginning, but it was intended mainly to give the students actual practice and demonstrations. Only to a small degree was it then intended as research in the modern sense.

Emphasis on research began to increase when the federal government just before 1890 passed a law which gave each State each year a small but assured amount of money for the expenses of an agricultural experiment station at the agricultural college. Some of the States had already been appropriating money of their own for agricultural experiment stations but this small supplement from the national treasury enabled and encouraged all to start. This constituted a somewhat undesigned experiment in how to do agricultural research. At least it was a way to learn by trial and error. The federal government did almost no controlling or co-ordinating of the research conducted by the various States, except that it furnished abstiacts of work in that field and made sure that the appropriated funds were spent according to law. In this way the independence so necessary to really successful research was attained to almost the same degree as prevailed in the Universities of pre-1914 Germany. Statisticians well appreciate the need for replication of lots or plots. The need for independent replication of statisticians or other research workers is sometimes overlooked.

The first experiments with animals were done largely according to methods which had already proved fruitful in such sciences as chemistry, physiology and embryology, which bore somewhat directly on problems of animal production and already had accumulated some traditions and experience in research methods. Indeed much of the early research in animal production was done by men who were primarily chemists, but were also interested in animals and feeds.

The advantages of discussing with each other their findings and experiences soon caused these men to organize professional scientific societies. Those doing research in animal production organized such a society in 1908 under the name of The American Society of Animal Nutrition. Later they included other topics and changed the name to The American Society of Animal Production which now has more than 1,200 members and owns and publishes the *Journal of Animal Science.* Separate societies to serve more especially the interests of those working with dairy cattle and with poultry were organized almost as early and had established their own scientific journals by 1921.

From its very inception the Society had a regular committee on methods of investigation. Its recommendations were not binding on anyone, but they were a real help to the beginners. Usually they were followed unless something in the local circumstances made the investigator think it best to do otherwise. Most of those recommendations were based on experiences of the members of the committee or their friends, evaluated somewhat subjectively. Sometimes fragmentary tests of the methods themselves were conducted, although not as systematically as analytical chemists study proposed new methods. For example, long before 1912 Armsby once weighed the steers in his calorimeter experiments for 11 or more successive days to learn that some variation from day to day was characteristic and inevitable. Partly as a result of this, partly because an odd number of days would permit the experimenter to start his rations at noon of the middle day, and partly for other reasons of labour and expense, the committee has recommended for many years that animals be weighed for three successive days at the beginning and again at the end of feedlot trials and that the average of the three weights be used as the true weight on the middle day. The question was re-opened in the 1920's when research of animals under extensive pasture conditions became more common. Some conjectured that driving the cattle and sheep and sometimes long distance from their pastures to the scales for weighing on the two extra days might disturb them enough that the average of the three-day weights would actually be less accurate than the first day's weight. This uncertainty led me to study the accuracy of cattle weights. I used correlations at first but soon heard of the then new and convenient method of computation, known as the "analysis of variance". I completed the study in 1928 with that method. The struggle to understand and explain (in terms of steers and pounds) the near-identity of the results by the two methods helped me understand how the text-books (whose authors are often intent mostly on sampling errors and tests of significance) give to nearly all beginning students an exaggerated idea of the difference between interclass and intraclass correlations. Incidentally, I overlooked then the possibility of cyclical changes in weight extending over periods several days in length.

The general idea of "experimental error" is at least as old as the astronomer's custom of taking several observations or the chemist's habit of running analyses in duplicate and then using the average if the replicates agree closely but discarding one or more of them, or doing it over, if the replicates are widely aberrant. Animal husbandmen in their group experiments usually relied on meeting this need by having several animals per lot. Only rarely did they include actual duplicate lots in experiments with farm animals. The only experimental findings which animal husbandmen generally respect as likely to be valid are differences between two or more lots fed at the same time and balanced to be as nearly alike as possible when the experiment began and with all variables except the one whose effect is being studied kept as nearly alike as the investigator could manage. Even so, they have always known that something unknown to the investigator and not pertinent to the difference being studied might have happened to one lot and not to the other. That is, they have always understood the possibility of experimental error, even though they did not know or use definite methods for measuring that. Naturally, those who do not actually use duplicate lots are likely not to appreciate how large the experimental error is likely to be.

The committee on methods has always recommended that a trial be repeated three times before the results are accepted as valid and are published with any recommendations for the animal producer to act upon them. Three was chosen arbitrarily on the experience of the committee members and their friends. They felt that an aberrant circumstance which could lead to a wrong recommendation might possibly happen twice in succession by rare coincidence, but would never happen three times in a row ! In modern terminology this was a recommendation that each comparison be conducted in three randomized complete blocks, with time being included as one of the variables between blocks. (Animal husbandmen do not generally use this terminology, since the recommendation was routine before the terminology was invented.) This recommendation was not always followed. The investigator often thought it more important to investigate many problems superficially and get at least a hint of the answers, than to investigate a few thoroughly. The number of lots physically and financially possible in any one year was generally so small that, except with such laboratory animals as rats, duplication or triplication within a single year would have reduced drastically the number of questions which could be asked of the animals.

Even when the experiment was duplicated or triplicated and the results varied, as they always did, the animal husbandman had no objective yardstick for measuring how much to doubt that the average which he had found was the true value which he or his clients would find in the future. For that he relied on "common sense" which, one may speculate cynically, is a quality distinguished by its uncommonness ! Yet a man who conducted feeding trials for more than two years and studied his data diligently did, I feel sure, usually come to conclusions rather close to those he would have reached by modern statistical methods. Pre-conceived opinions may often have carried more weight than a man realized in leading him to his conclusion. If the experiment came out the way he had expected from all else he knew about the subject, he accepted it; if not, he hesitated and repeated the experiment again, perhaps with modifications to try to detect any plausible reasons for the difference.

Incidentally, we still have this trobule with us in all research except the negligibly small fraction of cases where we can assign a probability figure to what we think or conclude from combining our general experience, the literature on kindred topics, and what we think can be deduced from the scientific principles governing the case. In the long run this biases us, at least a little, in the direction of having our experiments confirm our preconceived ideas more than they should. Obviously it would be a silly waste of knowledge and effort to ignore all previous experience and experiments, or to make no use at all of what can be deduced from any general scientific principles which seem to apply. Yet trusting these things too much can lead to error. For example, I had a colleague once whose careful statistical analyses led him to conclude that the pigs which gained the most live weight per pound of feed had the fatter carcasses. The correlation was small but it seemed statistically significant. I argued that this conclusion must be wrong, as it contradicted the law of conservation of energy. Since a pound of fat contains something like nine times as much energy as a pound of non-fat live weight, it seemed to me impossible that the pig which added the most fat could do so on the least feed. We argued the matter, from time to time, for about two years. Finally he designed and conducted an experiment with yellow mice, which have the genetic peculiarity that they are fatter than their non-yellow litter mates and have the laboratory advantage that it is feasible to analyze the whole mouse chemically for ether extract. The results proved him right and me wrong, at least as concerns the mice. I am now more willing to concede that he may be right about the pigs also. I had overlooked the importance of differences in physical activity. Those are conspicuous in the mice, the yellow ones being much more lethargic and less active than their non-yellow brothers. I still believe in the conservation of energy, but I believe more strongly than before in the experimental approach as yielding more dependable results than logic !

The trouble was not in the logic itself, in the strictest sense of that word, but that I did not have all of the premises included and correctly stated. But in the real world one never can know whether he does have all the premises included and correctly stated. Therefore, it comes to the same thing practically; namely, that logic is an undependable method of seeking truth. We cannot get along without it and yet we cannot depend on it ! Eric Temple Bell, one of the great mathematicians of my country, once put it tersely thus: "Mathematics is concerned only with the consistency of its deductions and not at all with the 'truth' of its hypotheses. Science, on the other hand, is concerned first and last with facts,..things which can be sifted from human experience, and checked against human experience, in the actual world. Between the first facts and the last there may be long chains of mathematical reasoning, but these are not the concern of science. They are mere conveniences to obviate a welter of grammar and syntax in the common tongue."

To most animal husbandmen the "null hypothesis" and the tests of significance built around it seem an awkward and backward way of looking at a question which doesn't interest them. What they want is the best estimate of what the difference really would be if the experiment were repeated under the conditions they expect to prevail where they may be asked to recommend for or against one of the practices. That comes first and some sort of a reasonable measure of how much that estimate is likely to be wrong (that is; a kind of confidence interval or fiducial limit) comes second. To be told that a difference is not significantly different from zero seems almost meaningless if (as always happens, of course) that difference also is not significantly different from a host of other possible values which may be near zero but are not exactly that. When we want to use our findings as a basis for action in the real world something is artificial about always choosing zero as the point from which significance is to be reckoned. Also the choice of probability levels of ·05 and ·01 at which to call a difference "significant" or "highly significant" is, of course, arbitrary.

Unless the costs of the alternative courses of action differ greatly, there is really little difference in what one would *do* if the probability of the difference having been a chance one is ·10 or ·03 or ·007. Of course, if the costs of making the change were considerable, action on these three outcomes might be very different. But then we should require to balance those costs against the probable gains and for that purpose we require to know not whether the difference is "significant", but *how large* it is. That is, we are back at the central fact that what we really want from the statistical methods is the best estimate of the real size of the difference, *plus* some idea of the confidence we can place in that figure. Our statistical problems are primarily of *estimation*, not of *significance*.

Biometrical methods which resemble modern statistical methods in general, although without the refinements of small sample theory, were brought into animal production research mainly by the geneticists and animal breeders who at first merely adopted what they considered useful among the methods worked out by Galton and Karl Pearson and their associates. Raymond Pearl, who was for many years before 1917 in charge of animal husbandry investigations at the Agricultural Experiment Station of the State of Maine, was perhaps the major introducer of these methods into animal husbandry in the United States but many others contributed. This began at least as long ago as 1907, as can be seen from E. D. Davenport's book on principles of breeding.

So far as I know, the first application of biometric methods to feeding experiments with groups of farm animals was made by Mitchell and Grindley of the Illinois Station in 1917. Until the late 1920's or early 1930's the inflation of the intra-lot standard deviation by balancing the lots to be as nearly alike as possible when the experiment began was overlooked. This is not surprising, since only the rate of gain was studied individually and that by only a few workers. The animal husbandmen looked mainly at the lot average, just as agronomists are generally concerned with lot averages and not with data on single plants.

What we now call "repeatability" was studied on egg, milk, and wool production in several places before the early 1920's. I studied this on wool and mohair production in the 1920's and on dairy qualities in the 1930's.

Efforts to apply small-sample methods to feeding experiments were largely led by Crampton in Canada until after the middle 1930's. Then Yates and some of his colleagues in Britain began to pay attention to this field and Lucas in North Carolina has pushed it far.

In the United States until near the end of the 1920's the use of statistical methods was promoted mainly by two groups who had little else in common...the geneticists (including plant and animal breeders) and the economists. Innovations in method generally arose only out of a specific need in working on a particular problem. Thus, Wright, trying to reduce to fundamentals his findings about the inheritance of size of various body parts in crosses between large and small rabbits, developed and published in 1918 a partitioning of the sums of the squares which, for estimating the size of effects, is much like what we do now with analysis of variance, although he did not call it by that name and he did not take degrees of freedom into account. Later (1921 and 1934) he refined and expanded this into his method of "path coefficients" which, mathematically, is the same as multiple correlation or regression, but has the advantages of representing pictorially the "model" being used and of showing the postulated "dependent" and "independent" relations among what would all be called "independent variables" indiscriminately in the terminology of ordinary multiple regression.

Biologists have always been impressed by the complexity of the problems which they study. They are aware of the tremendous saving in mental effort which might accrue if they needed to remember only a few "basic" or "fundamental" principles, instead of the enormous amount of detail which they see in their original observations. Hence they have always sought ardently for basic or simplifying principles. An example is Wright's theoretical analysis (1921) of the consequences of various mating systems. The subject was already old. Many biologists had had a try at it, either theoretically or experimentally or both, but the generalizations they reached were limited and were mostly confined to a few regular systems of inbreeding such as selfing or mating full brother and sister. Wright became interested in it because his main task in his first major position was to analyze the data from an extensive experiment on inbreeding of guinea pigs. That experiment was already nearly 10 years old when Wright came in charge of it. Trying to interpret his actual data and to guide the experiment in the most profitable direction each successive year made Wright feel the need of knowing the general or most probable consequences of inbreeding which are to be expected if one could assume, as even then seemed almost certain from the evidence, that all inheritance among sexually reproducing organisms followed the basic rules discovered by Mendel. With his path coefficient method Wright succeeded in deducing and describing the changes to be expected in a population under any specified kind of inbreeding or outbreeding, intense or mild, regular or irregular. One parameter of his solution, the correlation between uniting gametes, turned out to be a linear measure of the expected decrease of heterozygosis in the population, and also of the increase in variance expected if the effects of the genes were additive and also with the effects on the population mean with any degree of dominance, although perhaps not with all possible forms of epistasis. This permitted designing and analyzing experiments where the inbreeding system was irregular.

I have mentioned Wright's success in reducing the expected consequences of mating systems to quantitative terms, not primarily because of its intrinsic importance, although this was considerable, but because it illustrates so well the fact that in animal investigations the problem of measuring the character or combination of characters which are the main interest, is so much of the time more important than the problem of testing statistical significance. The measurement of individual growth is a familiar example. Growth curves of animals are generally S-shaped and asymmetrical with the point of inflection at or near the life stage which corresponds to puberty in man. How should one use or code or transform these facts to come nearest to extracting all the information which is in individual differences in growth rates in any experiment? Most of the studies of growth in meat animals in the past have been at ages when the growth curve was almost straight. Hence, most workers have used the straight-line slope as the measure of growth rate, although a few have used the differences between the logs of the weights. In recent years the interest in ways of feeding very young animals has shifted more attention to the accelerating portion of the growth curve. Consequently the problem of whether and how to use logs to extract most of the information has become more acute.

Nearly 30 years ago a vast co-operative study of factors influencing quality and palatability in meat was undertaken in the United States. How does one measure even such a moderately specific quality as "tenderness"? By a mechanical shear test? By some sort of mechanical chewing machine? By chemical analyses for collagen or other fibre? By the subjective opinions of a panel of samplers? And in any event, how many hours and at what temperature should the meat be aged before tenderness is measured? If tenderness is to be rated by the sensory reactions of human beings, how long and in what manner should the meat be cooked? With or without how much salt or other flavouring? And when it comes to more elusive qualities, such as flavour, aroma, juiciness, and the like, these difficulties multiply. Similar difficulties, usually to a lesser degree, attend the whole field of sensory tests for qualities which influence consumer acceptance of all kinds of food products and also of other products, such as textiles.

More than 30 years ago, Laughlin undertook to study the inheritance of racing ability in Thoroughbred horses. But how fast is a horse who wins one race and loses another against some of the same entries? Or one who generally tends to win on a muddy track but not on a dry one? Or at short distances but not at long ones? Laughlin chose to measure racing capacity as the horse's average time in his "fastest 20 races, fairly run on a dry track". This measure contains plenty of subjectiveness, but can you devise a better one for what racing fans really mean when they talk about a horse's speed?

The main changes in animal husbandry research which have come with modern statistical methods and small sample theory are: (1) computing the experimental errors more correctly, especially by taking into account the degrees of freedom actually present; and the effects of such stratification as is incidental to balancing the lots; (2) some increase in the use of factorial designs, especially with pigs and chickens; and (3) the estimation of effects by "fitting constants". The simultaneous comparison of many varieties or strains, which is so conspicuous a part of plant breeding, has little counterpart in animal husbandry. The nearest approach is in random sample egg-laying trials with chickens and in the comparison of inbred lines and crosses among them which, in a few places, is beginning to be complicated enough that making the design efficient is a problem.

Much of the success or failure of agricultural research depends on knowing or guessing what questions to ask of the plants or animals. G. G. Simpson says: "Facts are elusive and you usually have to know what you are looking for before you can find one!" For that reason it is important that the men planning the research and interpreting it be familiar with the chemistry and physiology and the rest of the biology of the case and with the economics and details of management which might have to be changed if practices were changed as a result of the research. It usually happens that putting some change into operation, after research has indicated it to be desirable, will reveal that some other unanticipated details will need rearranging and perhaps may even require some systematic research in order to find out how they should be changed. It is no accident that manufacturers of fine machines, such as automobiles, cannot possibly get along without proving grounds, in which to discover and correct the mistakes of their engineers and designers before the machines are sold in large numbers. This is true, no matter if they have on their engineering staff the best brains in the land. My limited experience in this respect leads me to have generally more admiration and respect for the ability of those engaged in what we call "applied" research than for those engaged in "pure" research. The disdainful attitude occasionally met among the latter merely reveals their ignorance of the complexity of the real world and of the ingenuity often required of a man who is to make a product which will work better in that real world than any product of that general kind has ever worked before.

Sometimes the main obstacle to making research more successful is that the experimenter does not understand the basic principles well enough to ask the right question. For example, more than 30 years ago I was studying the inheritance of cryptorchidism in Angora goats, in which this defect is moderately frequent. When it came time to replace the first cryptorchid sire with another, I chose an unrelated one, thinking that thus I would conform to the principle of one thing at a time and wouldn't be complicating the results with another variable, inbreeding. Had I understood then what was already in print about inbreeding and what I know now about incomplete penetrance, I would have done it the other way around. I think my unwise choice then delayed the results of that bit of research something like two years.

Animal husbandry research contains many events which illustrate that great discoveries are often made while looking for something else. The men who found the vitamins were not looking for them. How could they look for something which they didn't know existed? The direct experimental assault on the nutritive difference between white and yellow maize had failed because of an unsuspected "interaction"; namely the need for the near-absence of vitamin A in the rest of the ration if the difference was to show. The men who found the vitamins were trying at first to balance rations completely with material from one plant only, such as corn or wheat, just to see if it could be done. When they failed (for other reasons it now appears), they set off on the trail of finding whether each different amino acid must be present in the ration. This in turn led to the necessity of feeding chemically purified rations in order to investigate accurately the "biological values" of proteins. Failure of the early attempts at this led to the discovery of vitamins. Then a scientific gold rush into this field occurred, as soon as the field was known to exist. You all know the near-accidental discovery of the antibiotics in medicine. The rush in recent years to test them in nutrition was sparked by the somewhat idle curiosity of men who wanted to know how the antibiotics would affect the activities of the organisms which live in the rumens of animals. Workers at my station have had to do much in an unintended direction in the last six years investigating the toxicity of soyabean meal made by a certain process. The process was devised originally because extractors of soyabean oil understandably wanted a solvent which was not explosive, as was the widely used hexane. The chemist who gave them a non-inflammable solvent didn't find out first, in the few short trials he made, that the resulting meal was poisonous. This is understandable since not all lots of meal are toxic and even the toxic lots need to be fed to cattle in rather large amounts for at least four or five months before the symptoms appear. Moreover it is doubtful that this meal is toxic at all to pigs and chickens; certainly it is not equally toxic to all species. The pertinent fact, for our purposes here, is that some of my colleagues have had to do a lot of research on a problem which wouldn't have appeared on any list of proposed research which they or their administrators might have prepared 10 years ago.

This question of whether we *can* know at all accurately which are the most profitable questions to ask our animals or plants has so many important implications on the planning and administration of research that I would like to quote freely from Professor Phillips, formerly head of Mathematics at Massachusetts Institute of Technology, an argument which is essentially statistical.

"Is it possible to know the direction in which progress lies? In physics there is a principle of relativity which asserts that it is not possible to know which way we are moving nor how fast. Is there a similar principle applicable to progress?

"My first reason for doubting the possibility of a logical conclusion is that rarely, if ever, is sufficient evidence available.

"A second reason for doubting whether the future implications of present events can be foreseen is evidence that the future is not wholly determined by the present and the past. A characteristic of logical determination is what, in mathematics, is called continuity. An indefinitely large result should not be produced by an indefinitely small cause. When such appears to be the case, we say the result is unreasonable. This kind of unreasonableness is common, however, in everyday life. For example, the world was much disturbed in recent years by a man named Hitler. Some 60 years ago Hitler was merely a germ cell. If a few molecules had been removed at that time Hitler would never have existed. When the lives and fortunes of millions of men are dependent on the fate of a single microscopic cell, causality in any worth-while sense does not function.

"All human affairs are thus subject to an indetermination principle. What will happen five minutes from now is pretty well determined, but as that period is gradually lengthened a larger and larger number of purely accidental occurrences are included. Ultimately a point is reached beyond which events are more than half determined by accidents which have not yet happened. Present planning loses significance when that point is reached.

"My reason for making such obvious remarks is that although we admit the fact that no one can prophesy, yet governments are elected and assigned authority which can not be used wisely except by people possessing the gift of prophecy.

"Here is the fundamental dilemma of an advancing civilization. There is serious doubt whether the way forward is known, and doubt even whether beyond a very brief interval any forward direction is determinate.

"Nature faced this problem millions of years ago when it involved the improvement of the species. The problem was to utilize mutation and cross-fertilization to develop the best product. Nature solved it by leaving both processes to chance. If there had been a better way it seems certain that some species would have found it and used it for its own benefit. The fact that after millions of years this remains nature's way is strong evidence that there is no better way.

"Translated into the realm of human affairs this means that progress is made by trial and error. In any process of trial and error the probability of a favourable result is proportional to the number of trials. If we would find the conditions most favourable to progress, the conditions under which the greatest number of things will be tried should be sought. The advances of which I am speaking are all mental. Such advances will be most frequent when the number of independent thought centres is greatest, and the number of thought centres will be greatest when there is maximum individual liberty. Thus it appears that maximum liberty is the condition most favourable to progress.

"Throughout history orators and poets have extolled liberty, but no one has told us why liberty is so important. Our attitude toward such matters should depend on whether we consider civilization as fixed or as advancing. In a fixed society there ought to be best methods of doing things. Experts should be more capable of finding these methods than ordinary people and, for the good of all the people, these methods should be put into effect by collective action. In such a society the practical problem is to obtain the best rulers; there is no need for individual liberty.

"In an advancing society, however, any restriction on liberty reduces the number of things tried and so reduces the rate of progress.

In such a society freedom of action is granted to the individual, not because it gives him greater satisfaction but because if allowed to go his own way he will on the average serve the rest of us better than under any orders we know how to give.

"The greatest misfortunes are the things that don't happen. Take, for example, the First World War, which is estimated to have cost about 8,000,000 lives. At that time we did not have penicillin. I have asked many people how many lives penicillin might save per year. The question is foolish but most people agree a million would be conservative. Assume that it is half that number. Between the First World War and the time penicillin was generally available it would then have saved at least 12,000,000 lives. And to this should be added most of those millions who died of influenza in the epidemic of 1918–19. At the time of the war, therefore, there were two misfortunes. We had the war and we did not have penicillin. Not having penicillin was clearly the greater misfortune. In fact the greatest misfortune the world has ever experienced consists in not having things which never yet have existed. But you are not going to get people much exicted about something which does not exist when you can't even tell them what it is the non-existence of which you are worrying about !

"Many think we are near the final frontier of knowledge. Others think unlimited advances will continue. Our whole philosophy of life depends on whether we hold the one view or the other. One type of advance is unlimited and involves no speculation; namely advance through mere complication of what already exists. A study of science indicates that the structures now used are of two types. First are those which involve only a small number of variables, each of which has an individual function. This includes most of present-day engineering. Second are structures which involve an uncountably large number of variables, but in which only average values are used. Such are the atomic systems of thermodynamics and major fields of economics. Between these extremes are structures which involve a very large number of variables, each of which has an individual assignment. Illustrations are the hereditary units, or genes, in biology. A little consideration of the nature of numbers and combinations of numbers will show that this intermediate domain is indefinitely larger than the two ends. Relative to such matters we are like the builder who might say: 'I know how to make perfect bricks; cities and town are mere piles of brick.' So we know how to make certain elementary combinations. Assembling these into structures of unlimited complexity is a work of the future.

"When I was born the telephone had been invented but was not in use. Electric power, the internal combustion engine, X-rays, moving pictures, the airplane, radio, even central heating, good roads, and a continuous supply of fresh food have all come since I was born. The world into which I was born was more like that of Julius Cæsar than like that of the present day. If individual liberty can be retained, I see no reason to doubt that when my son shall reach my present age he may again say: "Of all we have the better half has been developed during my life-time." But even though this rate of advance should continue forever, the above analysis shows that unlimited further advance would always be possible; that the unknown would always infinitely transcend the known."

We can agree with Professor Phillips that limitless further advance is possible, even though we think that its direction is partially determinate, at least over a short time in the immediate future. New knowledge usually comes one step at a time. Each step is usually connected with something we already know. Borrowing Professor Phillips' analogy, we can say that next year's scientific discoveries are pretty well determined by the current and recently past discoveries although, of course, at least a few utterly unpredictable discoveries will occur next year. The discoveries of year after next and of five years from now and of 10 years from now, however, are increasingly determined by discoveries, in part accidental, which have not yet been made. This poses a central problem in the planning, co-ordinating and administering of research. This year's research can be planned or directed with some assurance that pertinent answers to some of the current problems will thereby be gained, although some mistakes by the planners or administrators will be made and some waste and missed opportunities will ensue. Even for this year, the individual research workers will on the average be more productive for our general good if they are given at least a little freedom to explore whatever questions intrigue them, even when their administrative superiors believe that working at such questions would be silly and wasteful. But planning research for the future becomes less and less useful and more harmfully inhibitory as that future becomes more remote. This is almost irrespective of the wisdom of the administrators or of the individual research workers. It flows out of the indeterminacy of the direction in which progress lies, or at least the partial unknowability of where the most useful research findings may be had.

The administrator's dilemma is how to steer a middle course between such confusion and other waste as might ensue if the administrator were right but did not direct the efforts of the individual workers in the direction which he thinks most profitable, and the sometimes larger waste and lost opportunities for progress which ensue when he does co-ordinate and direct the workers but is wrong about where the major opportunities are. For short-time research into immediate applications, the former kind of waste may be a real enough danger to warrant some concern and efforts at co-ordination. For the long time research which, for lack of better words, we may call "fundamental" or "basic" the latter danger is much the more serious. As in other cases where the optimum policy is an intermediate one and the parameters are known only imperfectly, actual situations leave plenty of room for honest disagreement about whether research activities are being co-ordinated less or more than is really optimum.