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Some Statistical Issues Concerning Allopathic Drugs for Degenerative Diseases

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SUMMARY

This paper considers statistical issues in experimentation for the development of so-called 'modern' (allopathic) medicine, particularly for degenerative diseases. The allopathic approach became popular because of its great successes in controlling epidemics, and also the spectacular advances in surgery. However, in the field of degenerative diseases and prevention of diseases, much further work is needed. It is well known that allopathic drugs have, in general, large numbers of side effects. In this paper, we discuss this field and its statistical aspects.

Key words: Allopathic drugs, Degenerative diseases, Preservatives.

1. INTRODUCTION

It is the experience of most people that allopathic drugs, in general, have side effects. Sometimes, death of the patient could also be a side effect. Due to public uproar or otherwise, we notice that often many drugs and/or procedures that were enthusiastically used before are stopped, recalled, or banned. We are told that these drugs undergo a lot of testing before they are approved, and as a side information, we are told that drugs based on herbs, food supplements, and other natural sources are, generally, not 'scientifically' proven to be sound, and their companies have to write "This product is not intended to diagnose, treat, cure, or prevent any disease." Yet, the fact is that the use of Nutritional Food Supplements, Homeopathy, Western Herbal Medicine, TCM (Traditional Chinese Medicine) and Ayurveda is spreading all over the world. For example, many American companies have started to manufacture Ayurvedic drugs. A couple of years ago, in St. Petersburg, Russia, when I was sick I was given an Ayurvedic drug from a store close to my hotel.

We hear that only the 'traditional' medicine (i.e., the modern allopathic medicine) is really sound, other systems like those mentioned above could be dangerous; this is in spite of the fact of the existence of notorious side effects. Here too, the facts are different. Firstly, we have to notice the simple fact that allopathic medicine came into popular use only since about the 1940's, before which time in the West herbal medicine and homeopathy were mainstream. Indeed, herbal medicine had always been mainstream since the dawn of history. So, rationally speaking, herbal medicine should be called 'traditional'. In any case, I disagree that these systems are dangerous. The proof is that there were about 5 billion people on the earth when the allopathic system came into popularity, and all these people evolved with the help of systems other than the allopathic one.

What to say of humans, even animals learning from experience, seem to have found herbs to be useful. For example, it is well known that, given independence (i.e., being left to themselves in the 'wild'), cattle graze selectively when they are sick; they do graze from certain areas where they normally don't, and they do not graze from some areas where they normally do. However, misled by the 'herbs are not scientifically proven philosophy', I am not sure if all humans have this much of discrimination in their eating habits (particularly in 'developed' countries).

The purpose of this paper is to discuss the general overall situation with respect to the allopathic system, look at some of the 'outrageous' issues, and discuss what can be done. (See also the related paper: Srivastava 2007).

2. THE ALLOPATHIC APPROACH

To fix attention, we shall take a few aspects of this approach one by one.

2.1 Prevention and/or Cure Versus Painkiller and Surgery

Until recently, women beyond a certain age were advised to get a mammogram taken once a year. The philosophy (Call it P2.1a) is that, in case breast cancer is present, it is good to detect it as early as possible so that treatment can begin. Of course, no one could disagree with an innocent statement like P2.1a. But, the point is what is left out in the statement. In other words, the question is: What is to be done until the cancer is detected? So far as I am aware, the answer (P2.1b) seems to be: 'Nothing special'.

An analogy may help here. Suppose we are at the ranch, and we know that there is a danger of robbers coming in. Policy X would be to periodically examine the ranch, see if there are any robbers, and fight with them if there are some. Policy Y would be to make the ranch more secure so that it may be hard for robbers to try to get in. Policies P2.1 a, b would correspond to X. In other words, instead of just waiting until a woman gets cancer and then treating the same, it might be more prudent to do more research to find things that would significantly reduce the chance of getting cancer.

Of course, research is done in the universities in departments such as nutrition, and also in drug research institutes. (For example, in the field of breast cancer, phytoestrogens have been found by the nutritional medicine researchers to have anti-cancer properties.) But, often, these departments and institutes do not have enough money to carry out large scale clinical trials, with the result that there is unnecessary quarrel between pharmaceutical companies (PC's) and the so-called 'alternative medicine', and good and promising work of the latter is condemned by the former as being without scientific evidence. Actually, that work usually does have quite a bit of scientific support.

On the other hand, PC's being private organizations, their research is oriented towards obtaining patents and making profit; they are not and can not expected to be philanthropic organizations. Thus, most of the research at the PC's can not be expected to be oriented towards finding a permanent cure for degenerative diseases. Often, at the best, their medicines require that they be taken throughout one's life. But, this has added dangers. Even a single medicine, if it is taken over a long period of time, is likely to have strong side effects. On the other hand, when a patient takes several of them for a long period, then there is the increased danger of their interacting with each other, and producing a possible catastrophe.

Thus, the fact remains that since prevention is not pursued much under allopathy, the result is that there is unnecessary suffering and pain and enormous expense for most people. It is indeed the duty of the governments to be a little more 'welfare-of-the citizen-minded' and put money into research on how to actually cure people rather than just somehow maintain them (which usually means maintain only those who are wealthy enough) on life long expensive drugs. Even in USA, in a recent election year, one of the important issues was that a large section of the people of that country had to choose between eating meals and eating drugs! In USA, at least the nutritional medicine (vitamins, minerals, nutritional supplements, and other products of research in Nutrition Departments and Drug Research Institutes) is available to some extent at least thus far. India seems to be much behind in this field. Even it is hard to easily purchase 'complete Vitamin B-Complex' (i.e., B-Complex that has all its components, not just thiamine, riboflavin, pyridoxine, and cyanocobalimin). For India, copying the West in allopathy, and not supporting research in Ayurveda, homeopathy, and nutritional medicine, is a great mistake. It is interesting that while Ayurveda got de-emphasized in India in the last few decades, American PC's have started to manufacture Ayurvedic drugs. Some have even gone a bit too far, and tried to patent things like turmeric and neem! Depending on allopathy alone, with its approach of 'pain-killer and surgery without any real curative medicine' (for degenerative diseases), Indians may find themselves in unhappiness even with a seemingly opulent economy. This is indeed true for the rest of the world as well, except that in large-sized rich countries, the problem may seem less acute for most people. But,

even though the economy may seem to be good, large sections of people may still be spending too much of their income on drugs and still living in ill health.

But, even if everyone had enough money to pay for drugs, I still do not see the rationality of the philosophy of painkiller and surgery. When a disease begins, why should it not be treated? I like the other systems because they do treat the disease. Under the painkiller and surgery system for degenerative diseases, the patient is initially given a painkiller. Now, the body does fight with whatever disease is developing; that is how it has been built. In many cases, the body does succeed in putting down the disease, and the patient thinks that the doctor's medicine has 'cured' him. But, as a matter of fact, this is not true. Even the word 'painkiller' is a misnomer; usually, the drug does not actually kill the pain. The drug makes certain parts of our brain or the nervous system insensitive to the pain. So, even though the pain may be raging inside, the body does not know it, and even may unconsciously continue to delight in the excesses which created the disease in the first place.

On the other hand if the body does not succeed in putting down the disease, the patient comes back to the doctor and another stronger painkiller or similar device gets prescribed. This cycle may go on. Eventually, some organ of the body gets damaged enough that the damage gets recorded on a machine. Then, the talk of doing surgery begins.

I do not agree with the above (pain-killer and surgery) philosophy and the culture that it has created. (People, who like to show off their status by bragging how many hundred-thousands they spent recently on medical treatment, will be disappointed with me.) But, I am not in favor of promoting unbridled competition to exploit the resources of this planet, create unnecessary suffering, and then treat the same in expensive ways. Yes, I have heard of capitalism and communism. Both of these are materialistic at the core. But, these are not the only two alternatives available to the world. There is the third alternative of human decency and rationality, of being scientific and spiritual. An approach where we do not treat a disease and let it prolong is none of these. India, which produced people like Gandhi or Tagore should encourage the third alternative. Gandhi taught us to develop freedom of thought, because that was real independence. And, Tagore sang "Where the mind is without fear and the head is held high/… / where the clear stream of reason has not lost its way into the dreary desert sand of dead habit/… / Into that heaven of freedom, my Father, let my country awake." The time has come for India to relinquish copying and to contribute the gems from the core of its own real achievements of 6000 years to the welfare of the world.

2.2 Preservatives

The food industry has enlarged much in the past decades. One basic feature behind this is the use of preservatives. Nowadays, most foods sold in the market have preservatives in them. The average consumer ingests a relatively large amount of preservatives per day. Over years, and decades, this adds up to enormous total intakes. The question (Q2.2a) is: Is the useful life of the average person decreased as a result of this by 10 to 50 years? In other words, if a typical person (without taking preservatives) would been active to the age of 90, would he or she now (under preservatives) be active only to the age of 60? If a woman has consumed preservatives from birth until the age of 35, would the child of this woman start having diseases at the age of 25 which normally people used to get around the age of 75 (a phenomenon that is currently occurring)?

Because of poor planning, and the elementary level of scientific thinking at which clinical trials are usually handled, not much is gained from them. On top of this, all the data collected is supposed to be the property of the company which does the trials. Thus, humanity in general is supposed to look at the results largely through the lens given by the company. Even so, it is easy to see that a trial which really studies the effect of preservatives on humans should go on for 150 years. Why? Because, in order to do an unbiased experiment, you have to take two randomly selected groups (say, group A and group B) of people (say, a hundred thousand in each group), give preservatives to one group (say, A) and no preservatives to the other group (B). You have to make sure that no one in B has any parents or grand parents who took preservatives. (This will be hard to do.) For

each person in each group, the experiment must begin at the moment of his/her birth. After, you have created the two groups you have to watch each person in each group until his death. You should also watch the children of members of each group. Clearly, all this is a very long process, and will require ages to complete. Obviously, it has not been done yet. So, all the approval of the preservatives is based on guess work of scientists. Because of their own negative experiences with preservatives, many people avoid food with preservatives, and for such people companies have to produce food without preservatives and write on their product 'no artificial preservatives used'. This is also going on for decades.

Artificial preservatives are added to food products so as to increase their shelf life; in other words the preservatives increase the usable life of the food (on the shelf), so that it can be eaten for a long time without seemingly getting spoiled. There is, of course, the question of the usable life (on this planet) of the eater of the food. What happens when, in a person's diet, real food gets replaced by preservatives in relatively large amounts and in an ongoing basis? In an intelligent world, I would think that there would be more interest in the life of the eater of the food (for whom the food is created in the first place). Many old-fashioned people still go for fresh foods. But, is it just a matter of fashion? One wouldn't think so if one was asked to explain why since the 1970's a large percentage of women need Caesarian section or why children in their twenties are developing diseases that their ancestors had in their sixties and seventies.

2.3 Live Experimental Units

We discussed two issues related to clinical trials. The moral from the first one is that the approach of pain-killer and surgery is not satisfactory; we should get interested in actually curing the degenerative diseases. Once, in 1990, in Washington, D.C., a group of people were lamenting that there is nothing that can help against arthritis. I pointed out that this is not true; I had cured myself by using alfalfa seed-and-juice tablets. They said their experiments showed that alfalfa did not help. They said they took patients that were severely suffering from arthritis, divided them randomly in two groups (one with alfalfa and one with placebo), and the results were about the same. It turned out that the patients they took were advanced cases and they had been treated before with pain-killer and antiinflammation drugs such as Indocin.

Clearly, their experiment was biased. Natural elements such as alfalfa are good for the human body because the human body (along with those of its ancestors) has grown out of and through an environment where it was in close proximity with plants for a billion years. So, the plants (herbs) are able to help the body if the body is sick in a 'natural' way. But, after the body has been treated (and, therefore, hurt) by chemicals (such as those in pain-killers), then alfalfa has to fight against not only the natural disease but also the artificial chemicals and the damage done by them, and there it may not succeed to well.

The moral is that we should conduct unbiased experiments where people, as they develop arthritis for the first time, are randomly divided in two groups, one with alfalfa (or other appropriate natural factors) and the other with placebo. It seems that one basic difference in the experiments done by natural medicine people and by allopathic people is that the experimental units are chosen differently.

The second point we made above was that some experiments are too long and unwieldy to be performed (such as a possible one on preservatives); and so we take refuge in faith, namely in the guess work of some scientists. While it is true that all scientific results have a subjective element in them, and we cannot entirely get out of guess work, we can and should make a reasonable effort for minimizing it.

We now discuss another issue with clinical trails, namely the fact that here the experimental units are 'live'. To elaborate, consider first an agricultural experiment, such as the one that compares the 27 ($= 3 \times 3 \times 3$) level-combinations formed by taking N (nitrogen), P (phosphorus), and K (potassium) at three levels each (0, 20, and 40 pounds per acre). There are large well established theories for that; we shall not go into that here. Here, we consider another fact, that here the experiment is done by taking a set of plots (called experimental units), treating each unit with one of the 27 fertilizers, and noting, (say) the yield from each unit. In

the analysis of the data, we merely assume that the units have certain patterns of homogeneity within them. We do not know the intrinsic level of N or P or K inside each unit. Since the units are inert (i.e., they are not living creatures), they cannot tell their own condition. A unit here does not speak, and tell (for example) 'I am already loaded with too much of K' or 'I have too little of P and K', etc. In other words, the units are inert. We must give them treatments that we are studying and measure various responses on each unit (like the total crop yield, average leaf area, etc.), but we cannot expect suggestions from them.

Clinical trials, on the other hand, are quite different; here the units are most often human beings, who can speak and communicate. 'Double blind' clinical trials are quite often considered very convincing. There are reasons for that which are well taken. But, there is a more important aspect that usually gets ignored. It is that one could utilize the fact that the units are live to our advantage. In the agricultural experiment, if the units could tell whether there is an abnormality in them with respect to N, P, or K (too much or too little of any of these), we could remove these units from our experiment and get a much more homogeneous set of units, that would in turn lead to much more accurate results. Similarly, in principle, we could gain much from the units in clinical trials because they are live. We cannot go into all the details of how to utilize information from live units; that would be a large subject. Here, a few important aspects of this will be noted.

Ordinarily, in most experiments, there is only one response variable. For example, in an agricultural experiment, the response variable studied is usually the yield of the crop. Sometimes, a few other variables, like the average leaf area, the amount of protein, etc may also be included. However, in all cases, the responses studied are decided upon by the experimenter, and not suggested by the units themselves, because the units are inert. But, in a clinical trial, the units are usually live human beings; and a person who is an experimental unit in the trial would be able to inform us if he or she is having positive or negative experiences which are worthy of mention. Note that some of these experiences may be extremely important, and may throw a great deal of light on what is going on inside the body, leading to insight into how to cure the disease more easily.

In the next section, we shall discuss some statistical aspects of how to handle responses that are suggested by live experimental units.

3. STATISTICAL ASPECTS OF RESPONSES SUGGESTED BY LIVE UNITS

An experiment in which many response variables are studied is called a multireponse experiment. (Roy *et al.* 1970) Usually, in such an experiment, the possible set of responses is known beforehand, and one or more responses are measured on each unit during the course of an experiment. There are various statistical procedures on how to analyze the ensuing set of data so as to answer important questions. But, when we include responses suggested by live experimental units, the number of responses can be potentially very large. Some of these responses may have lots of correlation among themselves, which may not be necessarily linear. Also, the information on some of the responses may be very scanty. Thus, the usual methods of multivariate analysis of variance may not work. Below, we suggest an approach that has been thought out by the author over the years.

Let R denote the set of responses under study; note that to begin with all the elements of R may not be known. Let R1 denote the subset of R which is known and is being actively studied, let R2 be the part of R which contains responses that are known but are not being actively studied, and let R3 be the remaining part of R which contains responses that may be suggested by the live units.

It is suggested that we consider a model for dealing with R which is in the Bayesian framework. Let p denote the total number of elements of R; note that p may be not be known. However, we can try to approximate the stochastic process which determines the change in these p variables. At any time, the value of these variables is a p-dimensional vector. It is proposed that we try to lay down a model of the distribution of this p-dimensional vector by using an appropriately parameterized multivariate gamma distribution. An initial value of these parameters (for variables in R1 and R2) can be used from previous studies or by an educated guess (as is common in the Bayesian approach). Since R2 is not being studied,

there will be no posterior distributions studied for R2. For R1, posterior distributions will be found as observations are obtained.

However, the variables inside R1 and R2 may also be connected with each other by appropriate differential equations, which may even be stochastic. Using these, new knowledge concerning R2 could be obtained.

Our main concern here is with R3. Let y denote a response included in R3. Clearly, y will come into picture if its value is abnormal, either too high or too low. For example, in gastro-enteritis, the value of y (blood pressure) may suddenly fall. In some case, a particular pain may be experienced, which could also be characterized as an abnormal value of some variable.

Thus, we can say that a response y under R3 will get measured (*i.e.,* will get attention) if its value is too low or too high. In other words, we have a multivariate gamma distribution in which some variables are censored (either above or below), i.e., these responses get observed only if their value is too low or too high or both. (The last case could arise, for example, if the response is heart rate.)

In order to do clinical trials whose purpose is to find actual cures for disease, a basic infra-structure of statistical theories and approaches is needed, and the above ideas could be very helpful in the same.

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