EDITORIAL

PLANNING THE DERMATOLOGIC SERVICES IN A COUNTRY-III

In order to deal with the diseases that occur in a country, it is important to know what to do in each case. Most of this information is available from the textbooks and the medical journals, but a large proportion of this technology is developed in the countries of the West. It must be realized that indiscriminate adoption of foreign technology can be hazardous. Therefore, before adopting any foreign technology, one must ask, whether it is really needed and whether it is safe for our people. In deciding whether a drug or a technique is needed, it is important to consider first of all if this drug/technique is more effective than those already available, because it is no use importing drugs if these do not bring in distinct advantages.

The crucial question to ask would be, will the profession be less efficient in dealing with diseases if we did not bring in the new drug. Let us explain it with a few examples. There is a large variety of corticosteroids, antibacterials and antifungal agents available for treatment. If we had only a fewer of these corticosteroids for systemic use, would it not be as good. The same thing can be said about the topical antifungal agents. The introduction of miconazole as an antifungal agent was a welcome addition because this agent is effective against candida as well as dermatophytes, and it came at a time when this range of activity was not available, but several other similar agents which followed were probably not necessary. Anti-acne preparations also belong to the same category. Most patients who do not obtain a good response from anti-acne treatment are the ones who do not use the drugs properly. Introduction of new drugs or formulations in such areas is not likely to help the situation. The reverse however, is true of antibacterial and systemic antifungal agents. The high incidence of resistance to the antibiotics and the hypersensitivity reactions make it imperative that alternative drugs are available for substitution. If we did not have rifampicin for leprosy, ketoconazole for fungi and the other antibiotics for pyogenic infections, the profession would certainly be handicapped.

The second important aspect to consider before adopting a new drug/technique is to see if it is safe for the population. The pharmaceutical which develops a drug, is expected to conduct toxicity studies before a drug is approved for clinical use. Such toxicity studies are as a rule conducted on laboratory animals but safety in animals cannot be extrapolated in its entirety to the human beings, though these preliminary studies do ensure that the drug is not too toxic. Human studies are therefore, a natural sequence and this is carried out along with the studies to evaluate the therapeutic efficacy. The systems which must be checked during human safety evaluation studies should include the haematologic system for anemia, leucopenia, thrombocytopenia and hemolysis, the renal system for nephrotoxicity manifesting as albuminuria, hematuria and raised blood urea and creatinine, liver for hepatotoxicity as raised levels of serum bilirubin, SGOT, SGPT and alkaline phosphatase, diabetogenic effects manifesting as raised blood sugar and glucosuria, and also safety during pregnancy for teratogenicity. There are however, many other side effects which may be minor but still interfere with the continuation of therapy in some patients. Such effects should be looked for and recorded during the first few years after the drug is released for

commercial use. Hypersensitivity to the drug is another important side effect which is detected only after the drug has been in use for some years. Above all, it is important to note that a drug which has been found to be safe in one community, may not be as safe for another ethnic community. The example of the toxicity caused by the mexaform group of drugs in the Japanese is well known. It is also equally important to realize that all the adverse reactions, both clinical as well as laboratory parameters, that are recorded during the treatment period, may not be due to the drug itself. During these studies therefore, it is essential to record all the new signs and symptoms that appear during this period and to ensure that these were not present before the administration of the drug. Any sign or symptom produced by the drug should not have been present before the drug was started, and it should disappear within a reasonable period after the drug is withdrawn. Similarly, the laboratory investigations must be undertaken before the drug is started, these should be repeated after the completion of the treatment and also 2-4 weeks after the withdrawal of the drug, to ensure that any changes which are likely to be attributed to the drug were not present earlier, and that these appeared only after the drug was administered. Even then, it is quite possible that the observed changes were entirely co-incidental and not produced by the drug.

The therapeutic efficacy of the drug is the most important aspect which needs evaluation. It is generally taken for granted on the basis of the data provided by the pharmaceutical, and the country of adoption may not undertake any such trials. In case however, the data is not convincing, a clinical trial may be undertaken to have a first-hand knowledge of the therapeutic effects. There are several methods of evaluating a drug. The easiest and the most commonly used method consists of an open trial, which means that the drug is given to the patients in a fixed dosage schedule for a fixed duration and the results are recorded at appropriate intervals. The main drawback of such a study is that the patient as also the doctor can get biased for or prejudiced against the drug and the recorded results may be entirely incorrect. Open trials are nevertheless still useful for pilot studies during which the daily dose, the frequency of administration and the duration of treatment are experimented with to find out the optimum schedule.

For more critical evaluation of the drug, single or double blind studies which incorporate comparison with placeboes are necessary. A placebo is an inert chemical which is prepared in tablet/capsule form to look exactly similar to the active drug. In single-blind studies, the patient is given a fixed number of tablets/capsules in a fixed dosage to cover a specified period of treatment. Some patients are given the active drug while others are given the placebo but the patient does not know whether he is receiving the active drug or the placebo. In this system, the bias of the patient is taken care of, but that of the doctor can still villify the results. In the double-blind study, neither the doctor, nor the patient knows whether the patient is receiving the active drug or the placebo. Packets are prepared containing the total number of tablets/capsules required for the fixed period of treatment. Some packets contain the active drug, while others contain the placebo. Each packet is given a number and a list is prepared to record which packet numbers contain the active drug and which contain the placebo. The assignment of the numbers to the active drug and the placebo has to be random and irregular, but the total number of packets containing the active drug must be equal to the number of packets containing the placebo. The list is kept aside unknown to the treating physician who would dispense one of the packets to each of his patients, record the number of the packet and the results against the number of the packet used. After the

completion of the entire study, the list of code numbers is consulted to separate out the effects produced by the packets containing the active drug, in comparison with those containing the placebo. The drug is considered to be effective only if it produces significantly better results compared to the placebo. This is a fairly fool-proof method unless the number of patients included in each group is too small and the severity of the disease in the patients in the two groups is not equal.

In a double-blind cross-over study, every patient is treated with two packets one after the other. Thus, some patients will receive the active drug during both the periods, others will receive the placebo on both the occasions, a third group will receive the active drug during the first period and the placebo during the second period and the reverse will happen to the fourth group. Such a study has the advantage of comparison of the placebo and the active drug in the same patient, but the number of patients has to be much larger.

Similar methods are applicable to topical preparations as well; one may use an open study, a single-blind study, a double-blind study, or a paired-comparison study. In the last named method, two different ointments are applied on the two comparable lesions or on the two respective sides of the body and the results are compared directly. This method takes care of the spontaneous regression that most lesions are likely to undergo.

Apart from importing the drugs/technology from abroad, a stage must come when the scientists of the country must take up the challenge of solving their own problems. An indigenously developed know-how not only saves a lot of foreign exchange, but it is also a reassuring step towards self-sufficiency and national prestige. The scientists should ensure that they pick up the national problems and use national resources and materials as far as possible, while the country must encourage this effort by preferring the local products over the foreign-made preparations.

Whereas research should be the pride of the nation, it must be realized that bad research is worse than no research, and every person cannot be a good research worker. A bad research worker may succeed in getting his data published in some journal, but for every wrong data published, it requires at least 5 good studies to uniformly contradict the results before that bad research is discarded and forgotten. The author calls this as *literature pollution* and considers it as the worst kind of disservice to the humanity, because it misleads the profession. When research is forced on unwilling students or if it is given weightage for further promotions, every one is forced to resort to research and sometimes even clandenstinely pile up the data to swell up the list of their publications. Most of such work however, is undependable, meaningless and a sheer waste of scant precious resources. Since every one cannot be a gifted research worker, research should remain the domain of only those who enjoy research.

Research is generally divided into two categories, (1) fundamental research which looks into the basic mechanisms and is chiefly concerned with answers to the *hows* and *whys*, and, (2) applied research which is undertaken to solve a particular problem. Applied research has the charm of being immediately useful, though fundamental research is the key to all knowledge and ultimate progress.

Before embarking upon a project, the research worker must survey the relevant data already available on the topic and then plan the project. The research worker should be clear about the aims of his study, and the various possible outcomes of the study. It will be helpful if the worker also gives a thought to the interpretation of the results likely to be obtained and incorporate studies which will support the conclusions drawn from the study. It is always preferable to

undertake a few pilot experiments before launching the entire project, to know the possible results and plan the methodology accordingly. A review of the data obtained at an early stage of the project also helps to modify the techniques if necessary—the mid-course corrections. But the early results should not bias the investigator for the entire project; there is no place for bias in research. After the entire data has been obtained and the conclusions drawn, it is better to evaluate the validity of the conclusions by applying the conclusions on the next set of patients or by repeating the same experiments. This reconsideration helps one to tone down the conclusions and statements if the earlier claims happen to be exaggerated. For the sake of accuracy, it is better to hold back the publication of the results till it is confirmed by the author himself. The first and the most severe critic of one's own work should be the research worker himself.

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