DRUG PROVING AND CENTRAL COUNCIL FOR RESEARCH IN HOMOEOPATHY

V.M. Nagpaul*

Introduction

The systematic procedure of testing drugs on healthy subjects in order to elucidate the symptoms reflecting the action of drugs is called "DRUG PROVING". Ever since the dawn of Homoeopathy "Drug Proving" has played a very crucial role in its development. The therapeutic application of Homoeopathic Drugs is based exclusively on this. Hahnemann reasoned that in order to know that what healing properties are contained in a given substance, we must know what the substance is capable of doing in a healthy person. The law of similars states that any substance which can produce a totality of symptoms in a healthy human being can cure that totality of symptoms in a sick human being. Proving of drugs, therefore, is a technique for ascertaining the curative powers of a drug.

Historical Development of the Concept

Hahnemann gave credit to the physician Albrecht von Haller for observing before him the method of proving (testing) drugs with reference to their pure and peculiar effects by altering the sensorial condition of man. Yet the fundamental theoretical basis for the proving of drugs on healthy persons was originally enunciated by Hahnemann himself, inspite of the fact that there still are stray instances on record where provings have been done earlier such as:

William Alexander, surgeon in Edinburgh, had made a proving on his own body. He nearly lost his life by taking two scruples of camphor, after which he desisted from drug proving.

Samuel Crumpe, an Irish physician, published "An Inquiry into the Nature and Properties of Opium."

Hahnemann studied different languages compulsively and was competent in German, Latin, Greek, English and Spanish, with a smattering of other languages. His eight translations from English, French and Italian into German included a work of considerable significance. A Treatise on Materia Medica by Dr. William Cullen who was a leading teacher, chemist and physician in Edinburgh and was considered to be an authority on medicinal substances. Hahnemann was given the task of translating the second edition of this book in two volumes consisting of 1170 pages from English into German in 1790.

While translating this work Hahnemann succumbed to the temptation of experimenting with one particular drug, Cinchona bark (Cortex peruvian) on himself. This drug had been used by the indigenous natives of South America for the treatment of malaria and had been brought to Europe by missionaries. It was given its name by the Swedish Botanist Linnaeus, after the Duchess of Cinchon, Vice Queen of Peru, who was cured by it. The statement made by Dr. Cullen in this book regarding the action of Cinchona bark in the cure of ague appeared unsatisfactory to Hahnemann and he was prompted to try this drug on himself.

"For the sake of experiment I took for several days four quentchen (drachms) of good Cinchona twice a day. My feet, the tips of my fingers, etc. first became cold, and I felt tired and sleepy; then my heart began to beat, my pulse became hard and quick, I got an insufferable feeling of uneasiness, a trembling (but without rigor), a weariness in all my limbs, then a beating in my head, redness of the cheeks, thirst; in short, all the old symptoms with which I was familiar in ague appeared one after the other. Also, those particularly characteristic symptoms which I was not to observe in ague–obtuseness of the senses, a kind of stiffness in all the limbs, but specially that dull disagreeable feeling which seems to have its seat in the periosteum of all the bones of the body, these

*Assistant Director (Hqr.) Central Council for Research in Homoeopathy, B-1/6, Community Centre, Janakpuri, New Delhi-110058.

all put in an appearance. The paroxysm lasted for two or three hours each time and came again afresh whenever I repeated the dose, not otherwise, I left off, and became well".

Thus Hahnemann recorded the effects of a medicine administered to a healthy person which foreshadowed his enunciation of one of the first principles of his new method of treatment–Homoeopathy. This led him to a six year study of different drugs on himself and others. The results of the laborious, painstaking work of proving homoeopathic medicines was published first in Hahnemann's work Fragmenta de Viribus Medicamentorum Positivis in 1805 and later in his Materia Medica Pura in six parts, between 1811-1821. Several thousand symptoms were recorded in an index covering sixty six individual medicines.

Hahnemann conducted repeated experimental drug studies on himself and sixty four volunteers whose names are listed in his Materia Medica Pura. In total he investigated 101 remedies over a period of about half a century, establishing the method which has come to known as "provings" (or testing) medicines.

His immediate followers, Hering, Stapf and others, carried out their own provings but continued to turn to Hahnemann for advise. The first generation of Homoeopathy continued this tradition. During the 19th century provings multiplied in Germany, France, England and above all in the United States under powerful influence of Hering whom we are indebted for his heroic personal proving of Lachesis. His other provings are Apis, Glonoine, Benzoic acid, Aloes, Allium cepa, Millifolium, Natrum sulph, Flouric acid, Oxalic acid, Kalmia, Podophyllum, Eupatorium and Sanguinaria.

In Australia from 1842, the Homoeopathic Society of Vienna undertook numerous reprovings as well as establishing new pathogenesis including Argentum nit., Kali bichromicum and Coccus cacti.

Aims and Objectives

To discover the positive characteristics of the action of the drug on the vital energy of the human beings; to obtain a full knowledge of its action (i.e. the totality of morbid symptoms produced by that drug) so that its powers can be readily distinguished from any other drug for the lawful application of the remedy in states of disturbed vital energy which is called disease. At the present time, there are literally hundreds of drugs derived from minerals, plants and diseased tissues whose characteristics have been fully delineated through carefully conducted provings and thousands more which have at least been partially proven. As homoeopathy continues to advance, it is necessary to perform provings of new remedies so that the therapeutic armamentorium can be further expanded.

Planning and Protocol

There is a lot to think about and arrange before commencing a proving so that no vital piece of preparatory work is overlooked. Planning of the whole operation of the study should be done before any steps are taken to execute it. Of these the most significant are:

PERSONNEL

There are some forms of experimentation which are a one man enterprise, but this is not true in the case of provings. Every proving is a co-operative enterprise which consists of:

Trial leader or project director

He initiates and takes an overall view of the whole proving programme, decides upon the drug and the potencies in which it is to be proved. He ensures that the methods used during the experiment confirm to the highest standards. He also decides according to routine randomization techniques as to which subjects will receive the experimental drug and which will receive placebo. He decides as to what should be the test substance. He is the person knowing the actual drug being proved as well as the codes governing who receives the drug and who receives placebo. In the CCRH this function is performed by an Asstt. Director.

Pharmacological adviser

He assists the trial leader or project director and provides him with information regarding toxicity in connection with the drug to be proved both in toxic and hypotoxic doses. The toxicity of a drug is determined at DSU at HPL, Ghaziabad.

Panel of investigators

They monitor the responses, inquiring in detail into each symptom recorded in the Prover's Day Book Proformae. In CCRH this job is done by Research Officers/Asstt. Res. Officers posted at different Units at Ghaziabad, Lucknow, New Delhi, Midnapore, Gudivada and Calcutta.

Subjects or provers

They receive the drug or placebo. They also maintain careful records of symptoms experienced by them. The value of choosing human subjects for our provings is that subjective symptoms—the sufferings—caused by a drug as well as the phenomena caused by a drug can be ascertained.

Selection of variables

The study is to be undertaken on a sample of healthy persons selected on the basis of biological, environmental, social and nutritional variations and there are clear-cut rules for the inclusion of persons to be selected as provers or subjects.

Rules for inclusion

— The subject must be between 18-45 years of age, so that the natural bodily degeneration that comes with age will not be a serious factor.

— The person should be reasonably healthy by orthodox standards and is well balanced in body, soul and spirit.

— The subject must be well acquainted with homoeopathic methodology and above all he or she must have a good knowledge of the symptomatology found in homoeopathic materia medica. This is necessary for the subject to fully appreciate the particular deviations that may manifest during the experiment or proving.

— The subject must be able to lead a life which is as normal as possible during the course of the experiments. This means that the life circumstances of the individual must be such as to allow a definite time for sleep, for walking and for eating etc.

— The subject must be intelligent enough to properly appreciate and record the subjective symptoms as deviations from his normal condition of life as these subjective symptoms are of utmost value.

— Honesty is a pre-requisite of a good prover for he must be very careful to record all phenomena as facts that can be produced repeatedly in others; therefore facts must be carefully recorded from the very beginning of experiment.

Rules for exclusion

The subjects categorized below should be excluded from the provings.

— The subject should not be hysterical or anxious person. This is necessary because such individuals display a high incidence of 'placebo effect'.

— Those who note down a lot of emotional symptoms. Too many symptoms in these realms confuse the final results.

— Those who obviously omitted to recall symptoms or who exhibited superficially in reporting. These tendencies indicate either a lack of mental clarity or lack of sincerity.

— Those who suffer from hypersensitivity diseases such as asthma, hay fever, allergies, food hypersensitivities etc.

DETERMINATION OF DOSAGE

The determination of the dosage depends on the nature of the drug to be proved. However, there are certain considerations which are sufficiently stable for guiding rules. These are:

— Any drug which in its natural state affects the vital energy but little will develop in proving should be proved only in high potency.

— Any drug which in its natural state disturbs the vital energy to functional manifestations only may be proven in a crude form.

— Any drug which in its natural state disturbs the vital energy to destructive manifestations should be proven only in a potentised form.

Rhythm of administration of dose

If the first dose of medicine produces no effect, and enough time has been allowed to be sure that the prover is not sensitive to it, the next best thing to do is to create sensitiveness to it, which may be attempted safely by administering a dose 4 times daily for a period of fourteen days unless the symptoms arise earlier.

Time scale

Proving trials take time. If proving results are worth having, they are worth waiting for. Therefore no fixed time scale can be prescribed. In CCRH proving of a drug normally takes 6-9 months.

NATURE OF THE TRIALS

The nature of trials on proving should be:

— Double blind technique where neither the investigator nor the subject knows what drug is being proved and in which potency also which subjects are being subjected to the drug being tested and which are being subjected to placebo.

— Multicentre trials are undertaken for the proving of a drug. The studies are conducted at least at two different centres under the same protocol before publishing or releasing the data for professional use.

NUMBER OF SUBJECTS REQUIRED

The higher the number of subjects the better would be the accuracy of the results. However, it may not be possible to go for a big number of subjects for practicability and availability reasons. Hence an optimum number should be selected so that it may yield the information with precision. In CCRH 15 candidates (10 males and 5 females) are employed at one centre which include 30% controls who receive only placebo in a randomized fashion. This is known as "Fixed control" method. There is another method where each subject or volunteer who has been subjected to active drug at one stage of proving becomes control in another stage. This is known as cross over system.

NEED FOR CONTROLS

Influences and bias on the part of the provers and the investigator can significantly modify drug responses and interfere with the interpretation of the therapeutic efficacy of a drug. To avoid such complications, test responses to drugs require the use of a dummy preparation or substitute drug referred to as 'placebo' which is of the same

colour and texture as the test substance and is administered to the control group in the same way as that of the experimental group.

PRECAUTIONS

— Care is taken that nothing which may ruin the health be proposed for proving.

— Administration of the drug is halted at the earliest indication of symptoms.

— Avoid any extraneous influences which may distort the results such as stress situations like anxieties & major arguments etc. if the subject is not used to them as these interfere with the drug trial.

— Avoid tea, coffee, wine or brandy, spices, strong condiments or strongly salted foods; avoid all green vegetables, roots, and all kinds of salads and pot herbs. All of these retain some disturbing medicinal properties, even if most carefully prepared. Hahnemann did not encourage even games or work which might disturb the concentration or judgement of the prover. Moderate exercise may be undertaken.

Ethical considerations

— The subject or prover should be in such a mental, physical and legal state as to be able to exercise fully his or her power of choice.

— Consent should, as a rule, be obtained in writing from the subject. However the responsibility always remains with the investigator or investigating team. It never falls on the subject even after consent has been obtained.

— The nature and purpose of the drug proving must be explained to the subject or prover.

— Provings should never be done in toxic doses: for toxic symptoms we must rely solely on the reports of accidental provings recorded in toxicological literature.

— The investigator or the investigating team should discontinue the provings if in his, her or their judgement, the proving, if continued, be harmful to the subject.

REPORT FORMS

It is certain that, for each prover a large amount of information will be accumulated. In the first place there will be relevant data to be collected in the pretrial period. As it is nearly impossible nowadays to find perfectly healthy people, therefore, a format is designed to minimise recording of any pre-existing pathological symptoms. This is known as PRE-TRIAL MEDICAL EXAMINATION REPORT FORM.

Secondly there will be drug response data originating in the proving trials after the administration of the drug. Such data has to be recorded in two different documents such as:

(a) Prover's Day Book Proforma: For the subject or prover to record the subjective symptoms or deviations from his normal conditions of life.

(b) Symptoms Elaboration Proforma: For the investigators to monitor the responses of the subject, enquiring in detail into each symptom recorded by the prover.

Lastly there is a Proforma for recording the state of health of the subject after the proving trials are over which is known as POST-TRIAL MEDICAL EXAMINATION REPORT FORM.

RECORDING

The information collected during the study is recorded on predesigned documents, as already mentioned. While doing so the following instructions are followed for the purpose of scientific validity of the work. The Pretrial Medical Report and Post-trial Medical Report is produced by a team of investigators consisting of persons having specialized knowledge in psychiatry, otorhinolaryngology, ophthalmology, gynaecology (in case of female subjects only), general medicine, dermatology and pathology.

— Adherence to the protocol, honesty and sincerity are pre-requisites both on the part of investigators and the subject.

— Diary entries must be made by the provers at least three times a day to prevent even minor memory lapses etc.

— Each entry should record even the slightest deviation from the subject's normal state.

— Intensity and duration of the symptom should be carefully recorded.

— Possible exciting causes should be recorded meticulously.

— A detailed record of the order of appearance of all the symptoms should be made.

— Analysis of the symptoms such as location, sensation, duration and the modifying characters of the symptoms, together with concomitants or apparently unrelated symptoms, should be properly recorded.

— Recording should be done without prebiased ideas about the outcome of the provings.

SOURCES OF ERROR

Sources of error which are likely to enter into the proving trials are:

Non-response errors are mainly due to lack of cooperation from the subject, or illegible entries in day book reports.

Response errors-description of the same symptoms by different subjects.

Ways of minimising errors

There are several ways of minimising these errors. The following are important:

— The subjects are assured that the information will be treated as confidential.

— There are frequent meetings between investigators and subjects to record elaboration and clarification on each symptom.

— The subjects are provided with allowances for attending the proving centres.

SYSTEM OF DATA COMPILATION AND INTERPRETATION

When the proving trials conclude, all daily records of the subjects and the panel of investigators from each of the two centres are collected at the Asstt. Director's office at CCRH Hqr. and all symptoms which represent deviation from the subjects normal state are listed and the experiment is 'unblinded'. Symptoms generated by the placebo subjects are deleted from the records, all remaining symptoms collected and the results published.

Drugs Proved Under CCRH

1. Abroma augusta folia
2. Aegle folia
3. Atista indica
4. Bartya iodata
5. Boerrhavia diffusa
6. Cassia sophera
7. Cassia fistula
8. Cuprum oxydatum nigrum
9. Cynodon dactylon
10. Embelia ribes
11. Formic acid
12. Hydrocotyle asiatica
13. Kali muriaticum.
14. Thea chinensis
15. Aranea diadema
16. Mygale
17. Tarentula cubensis
18. Tarentula hispanica
19. Malaria officinalis (short proving)
20. Curcuma longa (short proving)
21. Aranea scinencia (short proving)
22. Aegle marmelos
23. Chelone
24. Tela aranea
25. Holarrhena antidysenterica
26. Tylophora indica
27. Azadirachta indica
28. Thymol

Data Obtained During Provings and Verified Clinically

ABROMA AUGUSTA

Location	*Symptom*
Head	Dull frontal headache with heaviness < in the sun < motion > open air > pressure
Nose	Coryza-profuse thin watery
Rectum	Stool – Hard – constipated – stool – brown black
Urinary	Urine – frequent – profuse < 4-8 p.m. Burning during & after urination
Female Genitalia	Menses Dark Clotted With pain in abdomen Delayed

KALI MURIATICUM

Head	Vertigo < walking in sun light Heaviness – forehead
Ear	Earache Thin watery discharge < night thick whitish < winter
Nose	Coryza – thick yellowish < morning Obstruction nose < night Discharge white Discharge – post nasal thick, white

Throat

Pain with soreness
< swallowing
Tonsils inflamed

Female Genitalia

Leucorrhoea
thick
white

Respiratory

Cough with expectoration
< night
Cough Dry
< night
Cough followed by vomiting

CASSIA SOPHERA

Nose

Coryza with discharge
Bland
profuse
obstruction < night

Respiratory

Cough with difficult breathing
Cough dry
< morning
Cough with expectoration
thick
yellowish
Chest-pain during cough
< inspiration

CYNODON DACTYLON

Eyes

Conjunctivitis

Stomach & Abdomen

Flatulence
< after eating
pain before stool

Rectum

Watery stool
Bleeding piles with pain in rectum

AEGLE FOLIA

Head

Forehead
< 4-8 p.m.
> pressure, with bodyache
> cold

CUPRUM OXYDATUM NIGRUM

Stomach & Abdomen

Appetite, diminished, aversion to food, with
Discomfort and uneasiness in the abdomen with pain in abdomen, occasional.
Stool loose, 2-3 times in a day.
Itching over whole body agg. warmth, night amel. scratching, undressing.
Body weight, loss of
Cuprum Oxydatum Nigrum when prescribed on these indications, improved the appetite and also the body weight.

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