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The Network's NEWSLETTER Rx

Association for Rational Use of Medication in Pakistan

Clinical trials: value and Problems

A clinical trial is done to give definite answer(s) to questions about the management of health problems. A large number of trials tell us nothing of any value because they have been badly designed, poorly done or wrongly analyzed.

Most of the clinical trials done in Pakistan fall in this category. Almost all of them are sponsored by the pharmaceutical industry and most of them are non-randomized, non-controlled and are open. The only idea behind these so called clinical trials is to increase the sale of these drugs.

On the other hand good trials give us important information about one of several treatments used for a particular condition.

In the present issue of the newsletter Professor Andrew Herxheimer has eloquently discussed the ways the clinical trials should be done and what these trials tell us illustrating it with an example from recent literature.

Most of our readers are not familiar with the methodology of clinical trials as nowhere in their medical or pharmacy training are they exposed to it.

A checklist has also been provided which will help in scientific appraisal of clinical trial reports, so diligently passed on to doctors by the representatives of the industry.

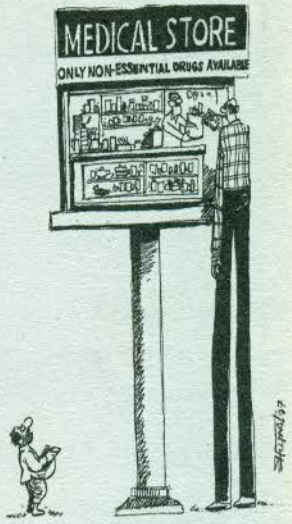
The use of this checklist will reveal that most of these so called clinical trials are worthless and will help the prescribers to critically evaluate the evidence of effectiveness of the products provided by their promoters. This would also help the medical practitioners to make better and rational treatment choices for their patients.

Unquestioned acceptance of the results of clinical trials and then prescribing these drugs in other words mean exposing patients to in-efficacious, dangerous and expensive products.

The Network s mission is to promote rational use of medication and essential drugs concept in Pakistan in order to optimize the usefulness of drugs and help bring equity in their access.

Diminishing essential drugs

While we have been raising concerns regarding the total disregard of the health authorities about non-availability of a large number of essential drugs in the country, there are more and more such drugs going off the shelves, perhaps never to come back again. That is unless there is a drastic change in the present attitude of the authorities and the manufacturers. But these possibilities, we believe, exist only if the sufferers - the people of this country start pressurizing the Government.



The Drug Act 1976 stipulates that "Every drug shall be produced in sufficient quantity so as to ensure its regular and adequate supply in the market". What kind of implementation of law exists in this country and how irresponsible is the drug regulatory which can ensure the availability of essential drugs like Penicillin and Digoxin in the market.

Conditions for registration

1. The Drug(s) must be marketed within 6 months of receipt of this communication.
2. The registration Number, Maximum Retail Price and other particulars shall be provided as per Drugs (Labeling & Packaging) Rules, 1976.
3. Every drug shall be produced in sufficient quantity so as to ensure its regular and adequate supply in the market.
4. The manufacture of any drug shall not, without the prior approval of the Registration Board, be discontinued for a period which may result in its shortage.
5. Colour Scheme of the labels / labeling should not resemble with any of the drug(s) which has / have already been registered.
6. One of the complete method of testing of the finished drugs containing full details of all minor & major steps and protocols alongwith specifications (lower & upper limits) shall be submitted to the following institutions within a period of one month:
   a. Chief Drugs Control & Research Division, National Institute of Health, Islamabad.
   b. Director, Central Drug Laboratory, 7th Street, Defence Housing Society, Karachi.
   c. Director, Drug Testing Laboratory, 1-Birdwood Road Lahore.
7. One copy of the master formula (of all registered drugs) containing the names of active and inactive materials along with the quantities shall be furnished to the Assistant Drugs Controller concerned within a period of one month for which a receipt shall also be obtained.
8. The import of raw materials will be made in accordance with the Import Trade Control Order.

This list of conditions for registration of drugs is from the back page of registration letter provided by MoH to the manufacturer at the the time of registration of the drug!

It is quite interesting how this disappearing act typically takes place in the market. First, the company introduces a new "research product" which is priced many times higher with hyperbolic claims and starts promoting it for the same indication side by side with the old product in order to maintain the franchise and goodwill of the prescribers. Once the new product takes root, marketing push for the old product is gradually withdrawn, sales are let to dwindle and the product eventually dies off. Another point of view is that even meager price increases are not approved by the authorities for these essential drugs which even after increase in the price will remain far cheaper than their substitutes.

Few important non-available essential drugs

Phenoxymethylpenicillin
(PenicillinV Syrup®) by Glaxo Welcome is not available in the market for quite some time now.

Digoxin
Cardiac Glycoside by Lahore Chemical & Pharmaceutical Works (Pvt.) Ltd. This life saving drug is absolutely not available.

Thyroxine
by Wellcome for hypothyroidism is not available.

Amitriptyline (Tryptanol®)
by MSD used for agitated depression is also missing.

Phenytoin Sodium (Dilantin®)
by Parke-Davis used for epilepsy is not available.

Niclosamide (Yomesan®)
by Bayer for tapeworm infections is in severe short supply.

Methotrixate
for childhood acute lymphoblastic leukaemia by Lahore Chemical & Pharmaceutical Works (Pvt.) Ltd., Cynamid and Lederle. This important drug is also not openly available in the market and is being black-marketed at a very high cost.

Chlormezanone - criminal neglect

As mentioned on these pages of the April '97 issue, chlormezanone use has fatal side effects. The leading manufacturer of chlormezanone, Sanofi Winthrop, has been reported by SCRIP (No. 2176, p. 16, 1996), to have decided to withdraw this product worldwide. This withdrawal has taken place in many developed countries including USA since many months now. In France manufacturers of four chlormezanone containing products decided to stop marketing these products in October last year. In fact the clean up action there was so drastic that all the stocks available in the market were immediately recalled by the manufacturer.

This lethal product is still freely available in the Pakistani market in any quantity one may wish to buy. Some brand names of chlormezanone and their manufacturers include: Baserol (Sanofi Withthrop), Muscerol (Pharmatec), and Samerol (Sami).

The Ministry of Health's best response in this regard during the last 3-4 months has been a clarification in the newspapers that a new rule has been made according to which any drug banned in USA, Canada, European Union, Japan, Australia, China, Switzerland or in the country of origin for safety reasons will be banned in Pakistan "automatically". What does "automatically" mean? Has the Ministry de-registered these products, the news report is silent about it. The Ministry's announcement carried by national dailies of April 4 claimed that the concerned companies had already complied with Ministry's directives to refrain from manufacturing and importing this product. Now, the ground reality shows that either the Ministry officials are so naive or else they just do not care a hoot whatever happens to the people of this country. This is potentially a case for suo-moto action by the Supreme Court or Federal Ombudsman. Our past experiences tell us that the MoH will continue to look busy but do nothing in the public interest.

Latest drug registration spree

During a Drug Registration Board Meeting on 16 June 1997 the number of new applications for registration was around a staggering 550 and more than 300 new products were provided registration. How the board members were able to look into the efficacy and safety of these "new products" is any body's guess. Most interesting to know is that the board can also reject applications! How efficient! In the same meeting three new manufacturing licenses were also approved.

Quality assurance drive in the Punjab province: a commendable start

Serious concern has been shown by the Chief Minister , Punjab over the availability of spurious/sub-standard drugs. He has directed the health department to take immediate steps to ensure the delivery of quality drugs to the people. In response, Provincial Quality Control Board in its meeting held on 22nd April 1997, decided to refer the cases of 15 firms who are habitual manufacturer of sub-standard drugs to the Federal MoH with strong recommendations to suspend their manufacturing and registration licenses. These manufacturers have been prosecuted on more than five cases from 1995 to date. We congratulate the provincial authorities on this bold step and expect that the same line will be taken by the Federal MoH. To caution our readers we are producing the name of these dubious manufacturers.

Name of Firm	Total Prosecutions
1. Orient Labs, Lahore	22
2. Iphco International,Lahore	17
3. Flacon Pharma, Gujranwala	15
4. Hydro Pharma, Lahore	19
5. Albro, Lahore	06
6. Anglo Pak, Karachi	09
7. Bentlay Pharmaceutical, Lahore	10
8. Multi Pharama, Lahore	06
9. Cyrus Pharma, Lahore	06
10. Ankaz Pharmex, Karachi	06
11. Venus Pharma, Lahore	09
12. Country Cotton, Lahore	11
13. Shah Brothers, Faisalabad	14
14. Whitesun, Gujranwala	08
15. Warya Brothers, Faisalabad	08

Dr Andrew Herxheimer is a world renowned clinical pharmacologist. He is founding editor of "Drugs & Therapeutics Bulletin" from the UK and remained associated with this fortnightly for more than 30 years. These days he is spending an active retired life.
He is one of our valuable international advisers and we are extremely grateful for his contributions, especially for this feature on clinical trials.
-Editor

WHAT DO CLINICAL TRIALS TELL US?

Clinical trials are done to give clear answers to questions about the management of disease. It is necessary to restate the basic ideas that underline clinical trials because if these are unclear it may be difficult to understand some of the other issues surrounding trials.

Whenever we are ill we have to decide whether to do anything about it - to treat ourselves or to consult someone else. Whatever we decide we then make further choices, often a whole series of them, based on what we estimate will be the likely consequences - the benefits, disadvantages and costs in terms of convenience, time and money. And, if we consult somebody, they will use their knowledge and experience of disease and its treatment to help us make such estimates. But making good choices requires reliable information about the outcomes of the relevant treatments for a particular condition. This information is best obtained from clinical trials.

Controlling clinical trials

A clinical trial is done to give a definite answer to a question about the management of a health problem. This is not as straightforward as it sounds. It is not enough simply to give a new treatment to some patients and see what happens. The answers that this would produce would often be wrong and always be unreliable, partly because the course of an illness is so variable and partly because of biases in favor of or against one or other treatment. Many illnesses get better even when no treatment is given and a treatment is of value only if the patients receiving it do better than those not receiving it. A comparison group, called the control group, is therefore needed to control conclusions.

Randomization

To make sure that any differences in outcome between the test group and the control group can be attributed to the treatment being tested, everything else about the two groups should be as similar as possible. The most reliable way of making sure of this is to determine by chance which group each participant will be in, that is, to allocate them to the groups at random. The larger the groups the more alike will they be in all their various characteristics. This is usually done by using random number tables, or an electronic random number generator. Randomized controlled trials enable us to make the most reliable comparisons between treatments or treatment packages, including management without any specific treatment, and to reduce bias.

Cross-over trials

In some trials it is possible to compare the test treatment with the control in the same patients, by giving them one treatment for a certain period then the other for a similar period, often with an interval in between - a cross-over trial. It is quite possible that patients do better on whatever treatment is given first, so in such a cross-over trial half the patients (selected at random) start on each treatment to cancel out any difference due to the order.

Blinding trials

Bias can arise from people's beliefs and preconceptions about treatments. If a doctor, nurse, patient or investigator knows what treatment the patient has had, their expectation can influence what they observe or experience. Ideally, everyone involved in a trial should be blind to which treatment the patient is getting, that is, the trial should be a double-blind trial.

What do clinical trials tell us?

A large number of trials tell us nothing of any value because they have been badly designed, poorly done or wrongly analyzed. But good trials can give us important information about one of several treatments used for a particular condition.

To establish the value of a trial we need to know: what condition was studied; what the diagnosis was and what it was based on; how it was confirmed and how certain it was; what sort of people were included and excluded; what the setting of the trial was; what interventions were compared. If a drug was tested, the dose used and the duration of treatment is very important, and also the pharmaceutical formulation and even the source of the drug. If it was a therapeutic apparatus or an operation being tested, sufficient detail must be given in the report to relate it to other things that have been published and to clinical practice. The report must also state what outcomes were looked for, how they were observed, how they were recorded, the particular measurements that were made, what techniques were used and when that was done in relation to the treatment, and how long people were followed up. Once the validity and usefulness of the trial has been established then the results can be considered - did the effectiveness of the treatments differ? In what way did they differ and by how much? There are many aspects to effectiveness, for example, greater survival, speed and degree of recovery, relapse rate, duration of recovery and relief of various symptoms. When evaluating a clinical trial one has to look at whether there are any important endpoints that have not been considered. Scientists and investigators design trials to ask questions that they think are scientifically important. Until now, consumers (patients) have had little influence on the design of trials. But there are things that matter to patients that trials need to address. One of these is obviously unwanted effects. Also it is important to know how representative trial patients were of all patients with the condition being treated.

Subgroups

Subgroups can only provide useful information if the trial was designed to examine them. The best that can be said about a subgroup pulled out at the end of a trial is that the result raises an interesting question that may deserve further investigation in a trial

An example of a good clinical trial

A randomized, prospective, double-blind, placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure

Background

Anal fissure is most commonly treated surgically by internal anal sphincterotomy. However, there is some concern over the effects of this procedure on continence. Nitric oxide donors such as glyceryl trinitrate (GTN) have been shown to cause a reversible chemical sphincterotomy capable of healing fissures in a small series of cases. This study reports a prospective, randomized, double-blind, placebo-controlled trial to test the hypothesis that topical GTN is the best first-line treatment for chronic anal fissure.

Methods

80 consecutive patients were randomized to receive treatments with topical 0.2% GTN ointment or placebo. Maximum anal resting pressure (MARP) was measured with a constantly perfused side-hole catheter before and after the first application of trial ointment. Anodermal blood flow was measured during manometry by laser Doppler flowmetry. After initial treatments, patients were given a supply of ointment (either GTN or placebo) to be applied to the lower anal canal twice daily. Patients were reviewed 2-weekly. At the initial and follow up visits patients were asked to record pain experienced on defecation on a linear analogue pain score. Endpoints were healing of the fissure or condition after 8 weeks of treatment.

Findings

After 8 weeks, healing was observed in 26/38 (68%) patients treated with GTN and in 3/39 (8%) patients treated with placebo ($pC0.0001x2$ test). Linear analogue pain score fell significantly in both groups after 2 weeks of treatment. This fall was maintained in those treated with GTN but pain scores returned to pre-treatment values by 4 weeks on treatment with placebo. MARP fell significantly from a mean of 115.9 (SD 31.6) to 75.9 (30.1) cm H_2O ($p<0.001$, Student's paired t-test) in patients treated with GTN but no change was seen in MARP after placebo. Anodermal blood flow measured by laser Doppler flowmetry significantly increased after application of GTN ointment but was unaffected by placebo.

Interpretation

Topical GTN provides rapid, sustained relief of pain in patients with anal fissure. Over two-thirds of patients treated in this way avoided surgery which would otherwise have been required for healing. Long-term follow up is needed to assess the risk of recurrent fissure in patients with GTN.

Lancet 1997; 349: 1 1-14

The Cochrane Collaboration

In 1979 Archie Cochrane pointed out the need for "... a critical summary, by specialty or subspecialty, adapted periodically, of all randomized controlled trials". In response to this challenge, The Cochrane Collaboration has developed as an international network whose mission is to prepare, maintain and disseminate systemic reviews of the effects of health care.

For further information see The Network's Newsletter, Vol.5, No.2, page 16 or ask for more relevant references.

designed to answer that specific question.

Cost versus benefit

It is important to consider how treatments compare in convenience and cost. Most trials do not give direct answers to these questions. However, it is possible to tell from what happened to the patients: how convenient, pleasant or unpleasant a treatment was and what happened to the people in the two comparison groups. It is also possible to make some estimates of costs, in terms not only of money but of time spent by patients, people doing the trial and people caring for the patients.

Reliability of results

The question of the reliability of results can only be approached by statistical evaluation of data. Could the results in a trial have come about by chance? Something might be statistically significant but not clinically significant. It is very common for a clinical trial to give an uncertain result. The difference between the active treatment and the control may be in the predicted and hoped-for direction, but could easily have arisen by chance. This happens especially in trials that have included relatively few patients, or when the real difference between the treatments is small, or when there is great variability among patients. It is important to decide beforehand what strength of evidence is needed to be convinced that the treatment effect is real and then to combine the results from all the relevant trials in a systematic and reproducible way.

Meta-analysis

One method for combining data is meta-analysis. It is not appropriate to add the results of trials unless they are sufficiently similar. When meta-analysis is justified and possible, the combined results can give a clear answer that could not have been obtained from any of the individual trials. The methods of performing such systematic reviews of clinical trials have now been well worked out.

CLINICAL TRIALS

AT DIFFERENT PHASES OF DRUG DEVELOPMENT

Drugs develop in many pre-clinical and clinical phases. The objective of the pre-clinical phase is to find out the efficacy and safety (teratogenicity, carcinogenicity & mutagenicity) of the test compound in animals. If permitted, clinical trials are then conducted in human beings.

Phase I study

Carried out on about 100 healthy human volunteers. Pharmacokinetics, pharmacodynamics and metabolic effects of the drug are observed.

Phase II study

Involves administration of the drug in about 500 patients to find out the optimum dose and pharmacological effects in a particular disease.

Phase III study

Multi-centric clinical trial: The candidate drug is administered in 1000-3000 patients to check efficacy and adverse drug reactions (ADRs). Data obtained is submitted to authorities and if they are satisfied license is granted to manufacture and market the drug.

Phase IV study

Post marketing Surveillance: the objective is to find out the long-term safety as well as any new indications. This is done by monitoring ADRs of the new drug being used by millions of patients. If several reports of any unacceptably serious effect are obtained, the authorities may ban the drug.

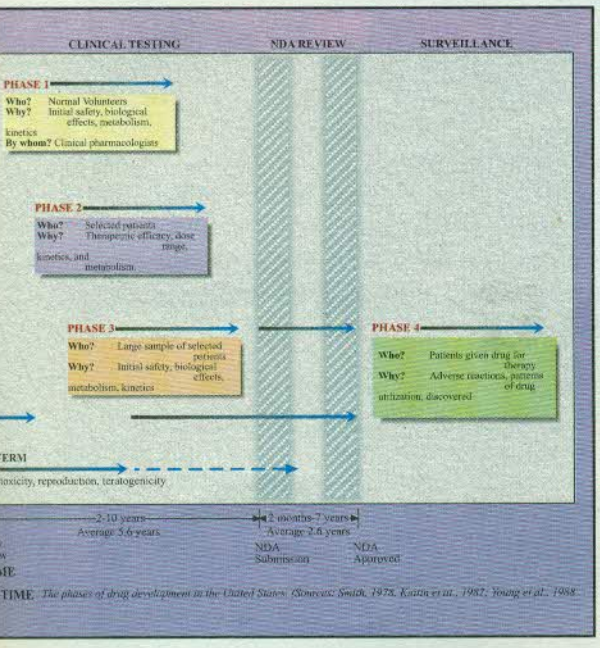
No "new drug" development takes place in countries like Pakistan. The companies sponsor few clinical trials but their aim is more promotional than evaluative. Most disturbingly, Phase IV studies, which are also statutory requirements in Pakistan, do not take place. This coupled with absence of any effective ADR monitoring system, one never knows what harm drugs are causing to the people. Post marketing surveillance in developing countries mean only marketing surveys by companies to grab wider market share.

Reasons for a trial

Finally, it is important to elicit the reason(s) that, made the authors choose the questions asked in a particular trial and to decide whether the questions matter to patients and/or doctors. Many trials are done by pharmaceutical companies to provide evidence of effectiveness for their drugs so that they can give the trial results to the regulatory authorities to obtain a license and market the drugs. That does not mean that the questions those trials ask are medically important. In fact, the drug may be duplicating something for which a good treatment already exists.

Conclusion

Clinical trials should give us clear answers to questions about the management of disease. Randomized controlled trials are the best way of making reliable comparisons. The art of designing and performing trials is to ask questions that are important for patients and that can be answered. Trivial or unanswerable questions are not worth investigating. A single trial can provide definite answers to no more than one or two questions, so the results of related trials need to be combined whenever that can be done.



The phases of drug development in the United States. (Sources: Smith, 1978; Kuhn et al., 1982; Young et al., 1988)

Check List for Appraising a Clinical Trial Report

Methodology of Clinical Trial

1. Whom is the study about?
- ✓ how were the subjects recruited?
- ✓ who was included and who was excluded from the study?
- ✓ were the subjects studied in "real life" circumstances?

2. Was the study design sensible?
- ✓ what intervention was being considered?
- ✓ what outcome(s) were measured and how?

3. Was the study adequately con trolled?
- ✓ If a "randomized" trial, was randomization truly random?
- ✓ Were the groups comparable in all important respects?
- ✓ Was assessment of outcome "blind"?

4. Was the study large enough and continued for long enough, and was follow up complete enough, to make the results credible?

Questions about Material Provided by Medical Reps.

1 Does this material cover a subject that interests me and is clinically important in my practice?

2 Has this material been published in independent peer reviewed journals? Has any significant evidence been omitted from this presentation or withheld from publication?

3 Does the material include high level evidence such as systematic reviews, meta-analysis, or double-blind randomized trials against the drug's closest competitor given at optimal dosage?

4 Have the trials or reviews examined a clearly focused, important and answerable clinical question that reflects a problem of relevance to patients? Do they provide evidence on safety, tolerability, efficacy, and price?

5 Has each trial or meta-analysis defined the condition to be treated, the patients to be included, the interventions to be compared, and the outcomes to be examined?

6 Does the material provide direct evidence that the drug will help my patients to live a longer, healthier, more productive, or symptom free life?

7 If a surrogate outcome measure has been used, what is the evidence that it is reliable, reproducible, sensitive, specific, a true predictor of disease, and rapidly reflects the response to therapy?

8 Do trial results indicate whether (and how) the effectiveness of the treatments differed and whether there was a difference in the type or incidence of adverse reactions? Are the results clinically as well as statistically significant?

9 If large amounts of material have been provided by the representative or company, which three papers provide the strongest evidence for the company's claims?

Adapted from: Trisha Greenhalgh. How to read a paper: the basics of evidence based medicine. London: BMJ Publishing Group, 1997.
ISBN 0-7279-1139-2

Rational use of drugs in Diabetes Mellitus

Lt Gen (R) Mehmud Ahmad Akhtar, HI(M)

Non-Insulin Dependent Diabetes Mellitus

Most of the patients suffering from Non-Insulin Dependent Diabetes Mellitus (NIDDM) are overweight. The rational treatment is to reduce weight by prescribing appropriate diet and taking regular exercise. This should be given adequate trial for a couple of months before prescribing drug therapy. Of course, if diabetes is severe, then drug therapy should be started immediately. Following is the description about the important oral hypoglycemic agents and their rational use:

Biguanides Metformin may be prescribed to overweight diabetics who suffer from mild diabetes and particularly those who find difficulty in controlling their appetite. These may cause gastrointestinal disturbances, therefore, should be given before meals and not on empty stomach. It should be started in small doses and gradually increased. Its advantages include: no significant hypoglycemic reactions, no rise in blood insulin levels and generally, decrease in blood cholesterol levels (unlike sulphonylureas). It is contraindicated in patients suffering from Congestive Cardiac Failure, significant liver and renal decompensation as it may cause lactic acidosis.

Sulphonyl-Ureas There are a number of sulphonyl-ureas in use. They have the same mode of action but different pharmacokinetics i.e. half life. Tolbutamide has the shortest half life, chlorpropamide the longest and others in between. BNF, 1995 has rightly commented that all the sulphonyl-ureas are the same and the selection depends upon personal preferences, experience and the cost.

All of these also have the same hypoglycemic reaction which occurs after four hours of their ingestion, but is uncommon. This can be avoided by splitting the large dose into two or three doses a day and arranging carbohydrate content of the meals in such a way that hypoglycemia reactions are avoided. For example if hypoglycemia occurs in the morning after breakfast then one can increase the carbohydrate content of the breakfast or take extra-mid-morning carbohydrate or shift the pre-breakfast dose of sulphonyl-urea. In old age the principle of drug therapy is to use drugs of short half life. In this age group, Tolbutamide or Glipizide may serve the purpose well. Tolbutamide has the shortest half-life but it is not available in Pakistan though it is included in our National Essential Drug List.

Rational therapeutics mean use of effective, safe and cost-effective drugs. One day therapy with full dose of Glibenclamide (Glicon®) costs Rs 2.31 and a years treatment with full dose costs Rs 843 while with Gliclazide (Diamicron®) a day's treatment with full dose costs Rs 23 and a years treatment, Rs 8400. It means that money spent on one patient's treatment with commonly used Gliclazide can be used to treat nearly 10 patients with Glibenclamide. On the institutional level, the difference assumes astronomical proportions. If one has to use Gliclazide which should be rare if at all, one can choose other less expensive Gliclazide preparations which are relatively inexpensive as compared to the commonly prescribed one.

The claim that it has anti-platelet effect is baseless. It is pertinent to note that the Gliclazide is not even registered in the USA. None of the sulphonyl-ureas has this effect, rather a University Group report on sulphonyl-ureas has accused these of having caused more heart attacks. One can prescribe acetylsalicylic acid for patients needing anti-platelet therapy. It should be kept

in mind that WHO Expert Group on Essential Drugs, diabetic experts all over the world and the books of medical sciences do not attribute any advantage to any sulphonyl-urea compared to each other.

Which insulin, human or beef should be used and why?

In Pakistan insulins are available from human and beef sources. Human insulin is very expensive in Pakistan. A vial of 10ml (40 units/ml) human insulin costs Rs 170 while that of beef insulin with same quantity, costs around Rs 60. It has been aptly stated in the text book for Clinical Medicine (edited by Parveen Kumar) that the practice of use of human insulins in the UK is the result of market forces. This means that the consideration is not scientific but commercial. Insulin from the animal source is as effective as the human insulin and furthermore, it has better shelf life and stands better physical disturbances like shaking etc., so that it withstands carriage in bag or purse, better and also has a longer half life and thus longer duration of activity. It has now been proved that the production of antibodies is not a problem with the animal source insulins and human insulin is no exception to the production of antibodies. Therefore the so called advantage claimed with human insulin does not exist. In even transient situations like NIDDM patient, during emergencies and in pregnancy etc., insulin from animal sources can be used with equal efficacy and no more untoward effects and at a much lesser cost and better stability.

Market monitoring reveals that Beef Insulin is in severe short supply these days.

Keeping in view the Hippocratic oath, moral and ethical obligations to the patients and the country; doctors should not waste patients and country's meager financial resources and should use cost-effective beef insulin and not human insulin in the management of insulin dependent Diabetes Mellitus and also for emergencies in NIDDM as well as during pregnancy. Human insulin has a specific indication i.e. if the patient is allergic to beef insulin, which is a very rare situation.

Most of the Pakistani patients are very poor and the life long disease puts too much burden on their families. Public hospitals do not provide even life saving medicines to the poor. It is indeed very painful to see that these very hospitals waste their funds in buying human insulin for rich undeserving patients with point blank refusal to help the poor, with the usual answer that "the funds are not available". A beef insulin can treat three patients for one patient treated with human insulin. It is high time that the medical profession should realize its obligations to the patients and the nation. It is a pity to note that the so-called pseudo-specialists and super-specialists are the major culprits in this regard. They serve the commercial interests of the multi-nationals at the peril of the poor patients of their own country. They set bad examples and misguide the junior members of the medical profession and promote irrational therapeutics.

Latest Costing of Oral Hypoglycemics

Name of the drug	Strength	Daily dose	Cost/tab (Rs)	Cost/year (Rs)
Glicon® (Glibenclamide)	5 mg	1 to 3 tabs.	0.77 [a]	281 to 843
Diamicron® (Gliclazide)	80 mg	1 to 4 tabs.	5.75 [b]	2100 to 8400[c]

a: pack of 60 tabs for Rs 46, b: pack of 20 tabs for Rs 115.20, c: rounded figures

Insulin

Human	40 units (10ml)	Rs. 170 / vial
Beef	40 units (10ml)	Rs. 60 / vial

Dialogue

A letter full of zeal

We have decided to join the campaign against irrational use of medication. Following are our proposals to strengthen and enhance the movement:

1 Our Department would like to hold a symposium "Role of Medical Professionals and Mass Media in Rational use of Drugs" with your help. This will be a starting point for rational drug use campaign in this part of the country.

2 Establishing a counter-detailing unit in the Department which will serve as a resource center for rational drug use activities in the College.

3 Organize monthly tour program for educating doctors throughout the Sindh province.

4 Launching a rational drug use campaign for general public through media has already been started as we have contacted editors of some leading newspapers and periodicals.

Promotion of rational drug use is a difficult task. It needs concerted efforts from all concerned quarters. We look forward to The Network's help and guidance.

Prof Abdul Rahim Memon, Head, Pharmacology Department, L M C, Jamshoro

Although we are contacting you separately also, your letter deserved to be shared with other readers of the newsletter for the excellent ideas you have come up with and also for the proactive spirit of your group.

Guide to Good Prescribing

I am interested to have *"Guide to Good Prescribing"* published by the WHO which was reviewed in your Sep. '96 issue.

Dr Mahmooda Abdal, Hayatabad, Peshawar

Those who require this book should send us a money order or crossed postal order for Rs 150/- and we'll send a plastic ring-bound photocopy by registered mail.

For informed consumer

Yours is perhaps the only organization in the country looking after the interest of the consumers. In the absence of effective legislation, it is crucial that the consumer is well informed about goods and services in general and drug use in particular. In this regard I have the following to suggest:

Network's newsletter should be sent to EVERY doctor in the country, Network's decision to start a monthly for general public is very welcome but I would suggest that each issue should be pre-tested with a sample of the target readers.

Dr Imran Iqbal, Nishter Medical College, Multan

As a country unfortunately we are abysmally late in enacting a law for safeguarding the rights and interests of the consumers.

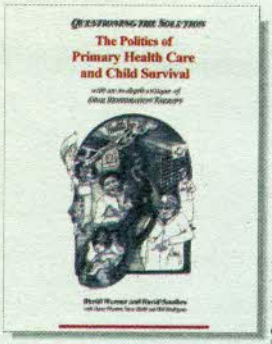
Presently the newsletter has a circulation of around 12000. As you can well appreciate it is an expensive undertaking but we are trying to increase its readership as much as we can. The idea about pretesting the urdu newsletter is well taken.

Useless liver tonics

As hepatitis spreads in the country at an alarming speed so does the most unethical prescription and use of "liver tonics" like Jetepar®, Hepa-Merze®, Liverjin®, Silirex®, Litrison® and so on. It has been pointed out time and again that these drugs are not even mentioned in any text book of repute and they are not only useless but potentially harmful and cost a lot to the poor patient.

Dr S Manan Hangu, Kohat

BookReview



Questioning the Solution,

The Politics of Primary Health Care and Child Survival. *By David Werner and David Sanders.*

Samina Chunara reviews the latest masterpiece from the gurus of Primary Health Care: David Werner and David Sanders.

Paulo Freire died three weeks ago in Sao Paulo, Brazil, where he had spent a lifetime working as a philosopher, revolutionary, and educationist of change. He is seen by many as the third world visionary who recast the image of the poor not as passive recipients of developmental aid but as active participants in re-imagining their lives.

"Questioning the Solution", written by two men who have spent years of dedicated work in underdeveloped countries, is a book inspired by Friere's methodology and applied to the health care system. Like education, they link the issues of health with the problems of inequity. It is not about the statistics of doctors, hospital beds, or medicines but involves putting health in the context of the kind of nutrition to which people have access, the quality of water, sanitation, education, the vocation of family members and thereby the purchasing power of the household, and a social infrastructure that prevents the undue commercialization of health services.

The authors illustrate this by taking the case of primary health care and child survival. According to WHO estimates, 13 million children die each year of preventable diseases in developing countries. To deal with this disease of poverty that affects thousands of children each year, the medical industry first came up with an intravenous saline solution. The next option was the discovery and marketing of ORS, that are basically a mixture of table salt, a simple sugar like glucose, and baking soda to which orange or lemon flavoring may be added.

An informed mother can make an equally effective mixture at home while encouraging the child to eat because what the medical profession left out of its diagnosis for years was the fact that the children who die of dehydration are often also undernourished and that food helps the body to absorb water. Simple foods available in the poorest of households like, sweetened tea, yogurt based drinks, rice water, plain water, and mother's milk if the child is still of suckling age, are equally important and effective and much more practical than either intravenous solutions or oral rehydration salts. Then the question is: why one of the commonest and deadliest of diseases attacking children was medicalized to this extent?

Donor agencies protect the multinationals including pharmaceuticals and infant food manufacturers and force governments to "open their markets to healthy competition" while stipulating that governments cut subsidies on health and education so that international loans can be reserviced. In effect, this means riding roughshod over the majority of the poor and the vulnerable in order to strengthen local elite in collusion with international capital. Countries that resist such incursions are severely penalized.

In the broad analysis, authors contend that only in raising the questions of social justice and equity can the issue of health care be truly addressed. All other strategies would be merely helping people survive a miserable life a little longer by dressing up the wounds. To them, this means striving to establish stronger, stabler, popular governments which are responsible to the people and not to donor agencies or to the international market. "Questioning the Solution" encourages the reader, whether health worker, medical professional, or policy maker to read carefully into his or her own situation making links with larger political contexts and to find their own solutions.

Health care of the people is a responsibility of the state

From the speech of Chief Justice at the conference of Medicines for the Nation on 30 Nov,1996.

The Chief Justice of Pakistan Syed Sajjad Ali Shah said in his inaugural address that you may be surprised to know that the right to health is not listed in our constitution in the chapter on Fundamental Rights. By way of interpretation of the words "right to life" by Supreme Court of Pakistan , however, this right now stands in the list of such rights. Article 9 of the Constitution reads "No person shall be deprived of life or liberty save in accordance with the law".

In the case reported as Shehla Zia vs. WAPDA under human right jurisdiction, while dealing with Article 9, the Supreme Court observed that the word "life" in the Constitution has not been used in a limited manner. A wide meaning should be given to enable a man not only to sustain life but to enjoy it." The Chief Justice added that "under our Constitution Article 14 provides that the dignity of man and subject to law, the privacy of home shall be inviolable. The fundamental right to preserve and protect the dignity of man under Article 14 is unparalleled and could be found only in a few Constitutions of the world. The Constitution guarantees dignity of man and also ' right to life' under Article 9 and if both are read together the question will arise whether a person can be said to have dignity of man if his right to life is below bare necessity living without proper food, clothing, shelter, education, health-care, clean atmosphere and unpolluted environment." His Lordship further stated that the word 'life' has to be given an extended meaning and can not be restricted to vegetative life or mere animal existence. The learned Chief Justice further added that thus the right to health has indirectly been added to the Chapter on Fundamental Rights.

In the Chapter on principles of policy in the constitution Article 38(d) guarantees that: "the state shall provide basic necessities of life such as food, clothing, housing, education and medical relief for all such citizens irrespective of sex, caste, creed or race, as are permanently or temporarily unable to earn their livelihood on account of infirmity, sickness or unemployment." He said that in the health sector the provision and availability of quality medicines at affordable prices is an important objective of the government policy. This objective has been pursued by successive governments through various policies. The National Drug Policy addresses this issue fairly comprehensively. The results however have not been very successful. The Chief Justice observed that it appears the drugs market is flooded with spurious adulterated and sub-standard medicines. There are complaints of old and expired medicines being sold to innocent people resulting in financial loss and at times danger to and loss of human life. The cost of medicine has gradually increased making it impossible for people to buy. It is also stated that unlike our neighbors Bangladesh and India the cost of medicines in Pakistan is very high. Why it is so and what is the way out. The Chief Justice thought that the main reason of high cost of medicines in Pakistan is because we can hardly manufacture less than 10% of the raw material used for drugs. The balance of raw material is imported from abroad at a very high cost. I understand that under the National Drug Policy there should have been a gradual increase in the manufacture of indigenous basic raw material but this has not happened.

"the state shall provide basic necessities of life..." Article 38(d)

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