

## Clinical Research and Health Care Delivery in Developing Countries

### Recommendations of the Conference

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*The three-day Symposium, characterised by impassioned presentations and a high degree of interactive participation during the panel discussions of each session, put forth a number of salient points worthy of consideration by those involved in, and responsible for, various aspects of Health Care Delivery in Developing Countries. The major issues which emerged during the discussions and exchanges and seemed to be of great concern to the speakers and the multidisciplinary audience are summarized hereunder.*

#### CLINICAL DRUG DEVELOPMENT

**T**he basis of clinical drug development is the double-blind, randomized, controlled clinical trial. Designed and executed properly, clinical trials can prove to be excellent models for initiating medical students and practising doctors into the art of scientific investigation. Hence, they deserve much greater attention from senior clinicians.

- The principles and practice of clinical trials should be included in the section of therapeutics of the undergraduate and postgraduate medical curricula.
- The importance of ensuring Good Clinical Practice (GCP) as a necessary adjunct to Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP) must be reiterated to medical students and young medical graduates at various appropriate stages of their education and training.
- Clinical trial requirements (including clinical trial protocols, case record forms, institutional ethical committees, informed consent, etc) must be standardised to ensure better quality of clinical data on medicines, both old and new.
- Herbal medicines should be subjected to systematic and scientific evaluation, both in the pre-clinical and clinical settings, with the use of modern methods of assessment of safety and efficacy.
- The framework for collecting and monitoring clinical data on adverse drug reactions and initiating Post-Marketing Surveillance (PMS) should be outlined and put to the test.

- Pharmaceutical companies which do not fulfil Good Manufacturing Practice (GMP) and Quality Assurance (QA) requirements should not be granted licences for the development and production of drugs, particularly life-saving drugs.

#### EPIDEMIOLOGY AND HEALTH POLICY

Epidemiology is the basis for health care planning and evaluation but is neither taught in medical schools nor practised properly even by national agencies. Enlisting the co-operation of practising physicians could help gather good epidemiological data using available resources. In addition, the following proposals emerged during the deliberations.

- Epidemiology should be made a major compulsory subject of learning in medical curricula.
- A thorough review of present methodology for epidemiology studies with the specific objective of suggesting methods of standardised data collection should be undertaken.
- Epidemiological data generated from properly executed epidemiological studies should be put to better and more optimal use for health care, health policy planning and implementation.
- Epidemiological information must be properly disseminated to medical schools, policy makers and planners and a system to ensure this must be introduced.

- Periodic review of health policies and regular evaluations of their impact on incidence of diseases in the community, morbidity and mortality must become a built-in safeguard for health care planners.

#### NEW DRUG APPROVAL, DRUG REVIEW AND 'OLD' DRUGS

Pre-registration clinical trials required in the developing countries, including India, should be more purposeful so as to utilise the available meagre resources to maximal advantage. At the same time, efforts need to be made to develop the required resources. Other recommendations:

- Investigators, i.e. clinical trialists, should be trained in Good Clinical Practice (GCP), persuaded to accept the concept of Clinical Audit, made responsible for quality of data generated by them and subject to inspection by appropriate regulatory authorities.
- Strengthening of Central Drugs Standards Control Organisation so that it could competently discharge responsibilities assigned to it. Mandatory scientific review of existing drug products should be part of the aforesaid responsibilities without political connotations and pressures, which unfortunately is the case today.
- Rational therapeutics and drug evaluation should be taught at both undergraduate and postgraduate levels in the medical curricula and in Continuing Medical Education (CME) programmes.
- Untapped potential of existing drugs (old drugs) needs to be assessed to widen indications, improve dosage forms and minimise cost. Academic clinical pharmacology units must be strengthened to work in conjunction with drug regulatory authorities and the pharmaceutical industry to achieve these goals.

#### ALTERNATIVE MEDICINES

It is an accepted fact that alternative medicines have a role to play in an integrated approach to health care in both developed and developing countries. However a *code of practice* should be drawn up to encompass the following critical issues which affect the quality of health care and the genuine options available to the consumer:

- Clinical evaluation by modern scientific methods should be applied to assess safety and efficacy of medicines, and ongoing monitoring of these parameters.

- Delineation of a rationale for the use of a particular product or combination of products for a specific ailment or group of ailments must be a requirement for regulatory approval and marketing.
- Ethical approach to therapeutic claims and proof of efficacy before claims are made must be mandatory.
- Ongoing development of methodology for standardization of methods of manufacture, principles of Good Manufacturing Practice (GMP) and Quality Assurance (QA) should be actively encouraged, undertaken and, if necessary enforced.

#### DRUG RESEARCH IN THE CONTEXT OF DEVELOPING COUNTRIES

Lack of financial, infrastructural and manpower resources make it extremely difficult to do basic research on potential new medicines in the developing countries. Equally important, the lack of respect for intellectual property, i.e. lack of protection of inventors' rights, and the reality of limited markets, make probable return on investments low and unattractive.

The participants at the Symposium proposed that carefully selected disease areas and therapeutic segments should form the basis of catering to the acute medical needs in developing countries. The consensus was that the following suggestions merit active consideration.

- National laboratories are necessary and should be set up to include research sponsored by private enterprise (industrial conglomerates) on new medicines for endemic diseases which plague the developing countries.
- Pharmaceutical companies should, when necessary, pool resources, apportion responsibilities and work towards reasonably assured returns.
- Specialised laboratories should be set up with international financial and technical aid to tackle already defined problems of developing countries.
- Evolution of a fair system of rewards for innovation (patents, inventors' certificates or their equivalents), both to the innovator and the organisation, is a measure that deserves active government support.
- Most importantly, it is desirable to develop a culture for clinical research work on existing drugs, not merely to reformulate and sell, but to seek new indications, new dosage forms, reduction of costs of treatment, better compliance and convenience, better monitoring of efficacy and safety in various ethnic groups.

## MEDICAL EDUCATION

Unless the instructional objectives in the undergraduate medical education are based on the recognised and defined needs of primary health care, the present system will only churn out doctors preoccupied with high technology tertiary care medicine which is full of glamour but devoid of the time-honoured, well-tested and inexpensive methods of clinical medicine.

- Changes should start right at the undergraduate level where medicine must be taught with a community bias.
- Medical students should be given a clear perspective of the important but limited role of modern gadgetry in health care delivery.
- The meagre resources of developing countries must be spent to improve the lot of the rural and urban poor and underprivileged, and the young doctor should be trained to care for the patients as part of the community.
- The interface between clinical pharmacology and primary health care needs strengthening in the interest of rational therapy, optimal drug utilization and cost-effectiveness.
- Family medicine should be developed as a specialty at medical schools.
- Clinical pharmacology should be an intricate part of the medical curriculum and all major teaching institutions must have academic clinical pharmacology units.
- The importance of Good Clinical Practice (GCP) and the initiation of patient care with a research outlook so that clinical research methodology enhances clinical medicine should be brought to the attention of the medical undergraduate.
- Formal elements in our curricula and examination systems should be less important than the quality of those who enter medical schools as students, and those who staff them as teachers.
- Serious final examinations in all subjects must have the additional safe-guards of being inspected and assessed by an autonomous body.
- The examiners need to be trained and regular participation of 'competent external examiners' is advisable, with a maximum tenure of three years. Re-assessment of the competence of examiners (the established generalist or specialist for continued competence to practise and examine in a particular field) must be mandatory.
- The 'internal component' of the examining process to allow the student's past record to be taken into account as a possible corrective to an unrepresentative performance 'on the day' is desirable and must be instituted.

- The minimum academic standards for recruitment of students to undergo training in medical school must be standardised for *all* medical schools in the country. The influence of monetary power to 'buy' a medical seat must be eradicated. Merit should be the principal criterion followed by aptitude. Both these should be evaluated by standardised procedures.

## HIGH TECHNOLOGY IN HEALTH CARE

The high cost of sophisticated instruments and equipments used in current medical practice and the high rate of obsolescence of these devices and gadgets, make it imperative that their procurement is judicious and their optimal use is ensured.

In the four-tier health care system comprising Primary Health Centres, District Hospitals, Teaching Hospitals/Referral Centres, and Private Institutions, the importance of defining need-based high-technology diagnostic tools for each type of unit and prioritization cannot be overemphasized. Expedient cost-effective analysis and time-scheduled budgetary reviews to ascertain the concordance of allocations and requirements should also be mandatory. Technology has a role to play at every level of health care but its indiscriminate use is unethical and unjustified. It is an adjunct to clinical diagnosis, not an alternative. Good clinical medicine has to be the corner stone of health care. Technology should be used with compassion and understanding to enhance the accuracy of diagnosis, to ensure better prevention and treatment, not to dehumanise health care and commercialise it.

## TECHNOLOGY TRANSFER

The transfer of technology from the developed to the developing countries is an essential ingredient of progress in the developing world. As this is a fact of life, it is worth establishing an international technology cell or institute which could be a research centre and evaluate the multifarious needs and limitations of the developing countries. There is a parallel in the Food and Agriculture Field.

At present, the obstacles to technology transfer of the right kind and at the right time are:

- Lack of awareness of availability and source.
- Inadequate social, economic and physical infrastructure.
- Lack of financial resources.
- Inability to appreciate and absorb modern technology.

## INDIGENOUS MEDICAL DEVICE DEVELOPMENT

In some developing countries such as India where skilled manpower is in abundance, the scope for the development of indigenous medical devices is ample and should be actively and systematically explored. Furthermore, a planned strategy which comprises training technical graduates in the finer nuances of medical devices technology and creating a better nexus between institutes of technology and commercial organisations will result in optimisation of skills for the needs of the country. Alternate technologies, if required, can thereby be evolved to make the device cheaper and generally more applicable both at centres with adequate and limited facilities. Regrettably, in spite of a large potential for indigenous production of health care devices, Indian industry has not yet taken to this area wholeheartedly because of current policies and restrictions. Concerted efforts are required to establish norms for Good Manufacturing Practice for each category of devices and to enforce them. The implementation of policies which permit Indian devices to be used provided they conform to international standards of GMP cannot be overemphasized.

## PLANNING, STRATEGIES AND RESOURCES FOR HEALTH CARE

Planning consists of fixing priorities, outlining strategies, mobilising resources, periodic monitoring and, if and when required, making mid-course corrections. Health care strategies involve not only medicines, doctors and hospitals but also public health, sanitation, nutrition and shelter. Of these, medicines, hospitals and doctors constitute the most visible and short-term parameters. The Health Policy of 1982

has defined goals and delineated Primary Health Care as the key strategy for achieving Health for all by 2000 A.D. Regrettably, financial resources and achievements have not matched the stated goals. First and foremost, the allocation of around 3.5 per cent of GNP for health care including family welfare is woefully inadequate. The participants at the Symposium expressed resentment at this miniscule allocation of funds for health care and family welfare and reiterated the view that health care expenditure should be increased to at least 10 per cent of GNP, as per the recommendations of various review committees of the last three decades or more.

The other points made were:

- Total revamping of planning for health care, including decentralisation and reversal of the top to bottom approach with active community involvement.
- Re-examination of the essential drugs list, keeping in mind local needs rather than perceived national needs.
- Introduction of branded generics to ensure quality and lower prices and to meet the essential drugs need.
- Drug regulatory agencies to be provided financial, and infrastructural manpower support to fulfil their tasks and meet their obligations as the conscience keepers of the country for medicines.
- Matching inputs of resources and better co-ordination between planners of production, investment and licences with those responsible for health care delivery.
- Integration of the preventive as well as the curative measures of modern scientific medicine.
- Recognition of the importance of accountability both in prospective financial plans and allocation of priorities.

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### **Clinical Diagnosis of Alzheimer's Disease**

Contrary to the prevalent belief amongst the lay public and many physicians, Alzheimer's disease can be diagnosed accurately in over 80 per cent of cases during life without extensive investigations and prohibitive costs. The criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, *when strictly applied*, make the clinical diagnosis of this disease much less difficult than is generally believed. This fact is demonstrated in a recent prospective study of elderly psychiatric patients in England designed to assess the ability and predictive value of the aforesaid rigorous clinical criteria. The study, which is the first to attempt to validate the criteria, showed their validity in 88 per cent of patients suspected to have Alzheimer's disease.

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