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APPLICATION AND PROBLEM SOLVING IN HEALTH RESEARCH FOR THE DEVELOPING COUNTRIES

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Introduction

The present decade has witnessed a numerous and diverse group of national and international committee and conferences, each seeking in some way to define new approaches to the overwhelming problems of poverty and disease in the developing countries (publications from a few of them are listed in Annex 1). Their genesis derives, of course, from the recognition that rapid progress in basic biomedical research and a broader understanding of the behavioral sciences open hitherto unimagined prospects for disease prevention and treatment. Thus far, however, efforts to harness these forces have proved disappointing; the development of effective agendas to do so have proved elusive; and, indeed the adaptation and application of known and well-tested interventions has proved to be more difficult than most expected them to be.

The most recent publication deriving from such deliberations, the product of a three-year study by a Subcommittee of WHO's Advisory Committee in Health Research, is entitled "Enhancement of Transfer of Technology to Developing Countries with Special Reference to Health." The subcommittee's charge (abridged) was a broad one: to identify modern scientific concepts which offer potential applications for major impacts on health development; to determine the technical implications of translating these concepts into practical application; and to propose means for matching the new science and technology with endogenous possibilities of the socioeconomic environment. As has been the case with many other study groups, it is apparent from the report that the scope of inquiry proved to be so great and both the potential and problems so vast and so geographically varied as to defy the definition of a comprehensive and intelligible blueprint leading to specific action. Many opportunities and possible programs are discussed in the report, but the summary eventually identified four specific recommendations which called for: (1) the designation of WHO Collaborating Centers for the design and fabrication of medical equipment and instruments; (2) the establishment of Research and Development Units in developing countries to evaluate technology and to facilitate technology transfer; (3) the continual monitoring by the ACMR of new and emerging technologies; and (4) WHO-established pilot demonstration projects in measles vaccine production and health manpower planning.

This strategy may prove to be a productive one but its emphasis and structure for problem solving and application focuses primarily on products and the institutions producing or applying them. For new products for use in curative or rehabilitative medicine, this may be the best approach given the fact that all countries have a cadre of trained clinicians and some sort of structure of hospitals and health centers where new technologies can be evaluated and appropriately adapted. Moreover, most of the conditions for which curative interventions are the approach of choice are prevalent both in industrialized and developing countries. Communication and understanding are thus facilitated.

For the development of products and strategies which are cost-effective and have the potential for large-scale community-wide interventions, the strategy leaves much to be desired. And yet it is in this sector that the most important steps for the improvement of health care can be foreseen. At present, large-scale community-based programs are still limited in scope and many, such as family planning and oral rehydration, are recent in origin. Management systems are unsophisticated, epidemiologists are few in number and the application of the behavioral sciences is still in its infancy. Moreover, most of the health problems for which prevention or treatment in community-based programs are the approach of choice have no counterpart in the industrialized world. Consequent problems in communication and understanding coupled with a lack of structure and trained manpower such as pertains for the delivery of curative services makes it difficult to identify suitable priorities and agendas deserving immediate actions.

Thus, it is my thesis that our principal efforts should not now be directed toward developing prescriptive and inevitably speculative agendas for research and development but rather, toward developing the institutions and the scientists in areas where the problems exist so as to encourage the proper questions being asked and to relate them to a collaborative network of institutions extending across both developing and industrialized countries.

The Genesis of Present Quandaries

Our present quandary, characterized by optimism, frustration and malaise, is better understood and the solutions more evident if we examine its historical antecedents.

In the industrialized countries, the dramatic improvements in health which occurred during the first half of this century are widely acknowledged to have been the product of a variety of community-wide programs to which curative medicine contributed only marginally. Economic development and education are acknowledged to have been important but health-sector programs were no less vital elements - pasteurization of milk, chlorination of water supplies, fluoridation, improved sewerage, recognition of the need to consume a variety of foods for a balanced intake of nutrients, immunization, birth spacing, fortification of foodstuffs with vitamins and iodine, prenatal care, education in food preservation and others. We need to recall that each of these, both in their identification and application, required a close working relationship between those with experience and knowledge in basic science with those whose professional milieu was the community - program managers, epidemiologists, clinicians and others fundamentally concerned with the behavioral sciences. Introduction of each of these interventions was marked by on-going experimentation, change and controversy but, by the middle of this century, most had become so institutionalized in industrialized countries that they were regarded as accepted social practices.

Although more can and needs to be achieved through community-based programs, attention shifted soon after the second World War to curative medicine. Advances in pharmacology and surgery made possible a host of new interventions for treatment and rehabilitation. A building boom ensued in the hospital industry, new medical schools were founded and older ones expanded and a major pharmaceutical and hospital supply industry emerged. Preventive medicine and public health were virtually deleted from the curriculum of medical schools and all but ignored in government policy formulation. Change is beginning to occur, driven by concern for escalating health care costs and the uneasy sense that gains in health have not been commensurate with expenditures. But the changes are recent and still rudimentary.

Health care systems in the developing countries have largely been developed over the past 30 years, during a period when donor countries and academic medical centers alike were substantially preoccupied with providing curative services. Not surprisingly, these concerns and interests were replicated in the developing world. Priority was given to the construction of hospitals, to the training of physicians in curative medicine and to the development of health care systems which supported a network of curative care facilities. So-called primary health centers were developed but their activities, when closely examined, resemble most closely those of the private medical practitioner in the industrialized world. Maintenance of what is most accurately described as a medical care system, rather than a health system, accounts for all but a minute fraction of government budgets and private expenditures for health. In brief, the development stage of community-based programs was essentially bypassed.

The ineffectual performance of present health systems may be more clearly illustrated by several examples. It is widely recognized that the single, most cost-effective medical procedure is immunization and yet, as recently as 1977 - 10 years ago - it is estimated that not more than 2% of children in the developing countries received the inexpensive and well-tested antigens - DPT, measles and poliomyelitis - all of which are diseases of profound significance in the developing world and which account for untold numbers of clinic visits and hospital admission. The record of the United States, by the way, is little more distinguished, as was illustrated by a major epidemic of measles in Miami last winter. In a city which lacks neither physicians nor clinics nor hospitals, surveys showed that 50% of two year old children were unimmunized. But the problem was worse than even these figures would suggest. Of 18 unvaccinated children who developed measles and for whom a history was obtained, 17 had been seen in a so-called health facility within the preceding 12 months. They had not been vaccinated, however. More than this, 53% of the infections had actually been acquired in a clinic or out-patient department of a hospital.

Change is not readily effected. Experience has shown, for example, that acceptance of the efficacy of oral rehydration therapy is highest among mothers and lowest in academic medical centers, many of which still employ intravenous solutions as the procedure of choice. When community-based programs have been introduced which require the participation of community groups and organizations, they have often been vigorously resisted by the traditional medical organization. In some countries, the administration of vaccines has been restricted solely to physicians.

In brief, it is important to recognize that the present infrastructures of preventive services are still vestigial at best and that there is little knowledge of the value of or support by governments of community-based services. Surveillance systems which document disease occurrence are all but unknown and there is, in fact, an all but total absence of interest in the community-wide prevalence of disease. Health structures and management systems are primarily designed to support the curative-care service network. Research, where conducted, has focused primarily on clinical conditions of greatest interest to the industrialized world; knowledgeable specialists in tropical medicine have all but vanished. Epidemiological investigations involving field studies are so few that we have begun to talk of clinical epidemiology as a specialty. Not surprisingly, preventive medicine and its principal science, epidemiology, is poorly taught, if taught at all, in most medical schools. In brief, there is today little infrastructure, tradition or trained manpower to realize the potential of application of contemporary biomedical science. Moreover, there is little private sector interest. A drug for arthritis which has to be taken several times daily is obviously far more interesting and profitable than a vaccine which need be given only once or twice or, for that matter, a drug against a disease which occurs primarily in poor tropical areas.

Directions for Future Development in Research

As we look to technology application and problem solving in developing countries, it is helpful to examine successful ventures of the past to identify principles which may be of value. Three specific illustrations which I believe, are worth citing are yellow fever control, the development of oral rehydration in the prevention of death from diarrhea and smallpox eradication. Approaches to each were different but there were common characteristics as well.

The development of a scientific understanding of yellow fever transmission and a successful approach to its control occurred more than 80 years ago, in 1901. Walter Reed, as director of a U.S. Army Yellow Fever Commission in Cuba, was charged with the responsibility of controlling this major endemic disease which was regularly exported to seaports along the Atlantic coast. At the time he arrived, the prevalent belief was that it spread directly from person-to-person or by fomites, that it was caused by a bacillus and that unsanitary conditions were somehow related to its occurrence. The provisional research agenda was, in fact, based on these premises. The agenda rapidly changed, however. Utilizing epidemiological observations, clinical and laboratory studies and eventually human volunteer studies, he very quickly showed that the disease was spread by a specific species of mosquito, that the mosquito bred in water close to domestic dwellings, that an extrinsic incubation period occurred in the mosquito and that the agent was a virus. Within a year, a control program, directed by William Gorgas, was put into operation. It provided for the removal of containers which held standing-water, the destruction of larvae in such vessels and their protection from egg-laying adult mosquitoes. Within eight months, the last case of yellow fever occurred in Havana not as a result of eliminating the mosquito but as a result of reducing sharply its numbers. This, in turn, laid the groundwork for a hemisphere-wide yellow fever program which, when implemented, rapidly eliminated urban yellow fever throughout the Americas. It was a unique example of a multidisciplinary group working together to solve a problem in the setting where the disease was prevalent.

The development of the oral rehydration regimen for prevention of death due to dehydration from cholera (as well as other diarrheal diseases) likewise arose from work by research groups endeavoring to find a better treatment for cholera patients. The three groups - in Taipei (Naval Medical Research Unit), Calcutta (Calcutta School of Tropical Medicine and Johns Hopkins University) and Dakha (now the International Center for Diarrheal Disease Research) - were comprised of a multidisciplinary staff with a specific set of goals but wide latitude in determining how best to achieve their objective. Intravenous fluids were first used and a practicable regimen devised which permitted monitoring of the patient's state of hydration and need for additional fluids and electrolytes. Although this served to reduce patient fatality rates from more than 50% to less than 1%, its applicability was limited because of the vast numbers of cases during an epidemic, the lack of adequate intravenous fluids and the limited clinical facilities. Antibiotic therapy was added to the regimen which considerably reduced the amounts of fluid required, but this was not the ultimate answer. Oral therapy was the only feasible answer. Through physiological studies conducted in these centers and collaborating institutions in other countries, it was discovered that the addition of glucose to a salt solution permitted the body to absorb water and electrolytes from the small intestine which otherwise did not occur. Determining the proper balance of electrolytes and glucose posed yet another problem and initial failures led to the temporary suspension of this line of research. The exigency of recurrent cholera epidemics, however, forced reexploration of this approach and eventually its acceptance as the preferred therapy.

Research during the smallpox eradication campaign was more widely dispersed with program field staff undertaking epidemiological, behavioral and operations research supported by a network of laboratories in Atlanta, London, Moscow, Calcutta, Utrecht (Netherlands) and Dhaka. As has been documented, this resulted in changes in program strategy, improved vaccines and methods of production, improved vaccine instruments, a broader understanding of the poxvirus family and the discovery and characterization of a new human pox virus infection.

Although the principal contributions from the laboratory came from those in the industrialized countries, the research agendas were mutually decided upon in regular meetings of field and laboratory staff and during frequent field trips of those who worked in the laboratories.

It is notable that in each of these three examples, a multidisciplinary group was involved, that ultimate goals were identified, but wide latitude was given in reaching these goals and that the principal focus of work was at the site where the problem was occurring. Research today in tropical disease problems is heavily weighted toward laboratory studies, few of which are in areas where the disease is extant; to satisfy funding agencies, the objectives usually narrowly drawn; clinical studies of patients with tropical diseases are all but unknown and epidemiological studies are few and far between. Such centers as once existed, whose interest was the diseases of the tropics and which were in the tropics, have diminished over the years both in number and quality. Few indeed represent cooperative international undertakings. The only two of which I am aware is the International Center for Diarrheal Disease Research in Bangladesh and the Institute for Nutrition in Central America and Panama which is located in Guatemala. Both now deal with problems extending, respectively, beyond diarrhea and nutrition, but each receives less support than the smallest of the international agricultural research centers. In fact, both have endured countless fiscal crises and yet each has made and continues to make extraordinarily valuable contributions in the application of science and technology to development and in training. Institution-strengthening programs have not seriously addressed the problem. Although WHO's

Tropical Disease Research Program recognized the present deficiency in capable research institutions, its institution-strengthening program usually provided less than $300,000 per year to a large number of centers and seldom for more than five years (Table 1). Little capacity has yet emerged.

Prospects for Application

The receptivity of governments to community-based programs, fortunately, has begun to change although, as yet, priority for financial support continues to be given to curative services. Family planning programs have played an important role in mobilizing government and community support and the cooperation of those in behavioral science and operations research. In many countries, however, the health systems has tended to remain uninvolved and detached from family planning initiatives. The success and minimal cost of the community-based smallpox eradication program has led to the Expanded Program of Immunization which was launched by WHO in 1974, and is now reaching 50% of the childhood population; oral rehydration therapy for diarrhea, introduced in 1975, dispensed one million packets of the salt and sugar mixture in its first 18 months but is now dispensing one million packets daily.

Most governments, however, have only recently begun to appreciate that the costly but generously funded curative measures which reach only those who happen to appear at some sort of health facility have marginal effects at best on the health of their citizens. To apply community-wide interventions effectively however, requires a knowledge of the occurrence of disease throughout a community, a knowledge of how and where it is being spread, a knowledge of behavioral factors concerned with their acceptance and field research in all of these areas. It is a significant departure from the approach to providing health services during recent decades and, there are as yet few professionals and few centers who are experienced in examining problems through field research.

Strategy

It is painfully apparent that there is, at most, a meager foundation of institutions and personnel upon which to build a coherent structure of basic and applied research and of education; that the health care policy and structure in most developing countries is oriented toward curative medicine; that social science research is little appreciated. The problem is further complicated by the fact that the potential contributions of neither epidemiology nor management are well-understood.

Some sort of structural building process is needed. What form this should take is by no means clear. To me, the greatest danger would be to assume that what should be done is known or can be known and to develop the now-typical, highly prescriptive three- to five-year program project which permits little latitude in the project and no opportunity for a learning process to occur. Better, I believe, is to create an appropriate milieu in which people and institutions can grow and mature in a fabric in which the realities of the socioeconomic, political and cultural realities must be continually tested. A process for evolution rather than prematurely anticipated end results would seem most logical.

A possible paradigm may be found in agricultural research, a sector which has made extraordinary progress in developing and introducing new plant varieties, in changing farming patterns and, as a bottom line, in producing vastly more food per acre. Much of the success is attributed to the establishment of International Agricultural Research Centers. The first of these, dealing with rice, was established in the Philippines in 1960 as a joint effort on the part of the Rockefeller and Ford Foundations and over the next decade, three others followed - in Mexico, Nigeria and Colombia. In 1971, an internationally funded and directed Consultative Group on Agricultural Research was established. Today, there are 13 centers which are part of the Consultative Group (Table 2). Note that they are comparatively recent in origin. The total budget of the centers of the Consultative Group is this year $191 million. The Group has a governing board which establishes overall policies and levels of support and individual governing boards which have oversight of individual centers. Note that most of the centers have <u>core</u> budgets in the range of $10 to $20 million <u>each</u>, that they are, in general, located in the larger countries which have the potential to contribute to their sustenance; that each of the centers receives additional funds from donors to undertake additional specific projects; and that support to these centers is not envisaged to be a three- to five-year investment but, rather, a long-term one. These 13 centers are not the only ones. Indeed, there are 9 other centers which are now also internationally funded (table 3). The international centers have also had a further stimulatory effect in fostering many additional agricultural centers supported nationally and/or by donors to form quite extensive networks which bridge industrialized and developing countries.

The charge of the Centers is four-fold:

1. to undertake research which provides technology to solve agricultural problems;

2. to provide practical and scientific training to developing country personnel;

3. to take part in a research network to facilitate exchange of scientific information and materials among all relevant laboratories; and

4. to assist individual countries in national food production programs.

If "health" were substituted for "agriculture" or "food production," it would appear to represent a reasonable agenda for a network of international health centers.

There is nothing similar to this network in health and few counterpart institutions in the industrialized countries. For example, the U.S.

Institute of Medicine has issued a report this year on U.S. capacity in tropical medicine. The report identifies only eight U.S. centers with as many as 20 faculty with academic training in tropical medicine, all but one of which has 20-30 faculty. For comparison, there are in the U.S. alone more than 25 centers for international agriculture research with more than 20 full-time faculty each.

Proposal

An international network of health centers is appealing as the first step in a necessary building process which, over time, would serve to identify opportunities in application and problem-solving in health.

For the components of such a structure, I would look to the lessons of public health and preventive medicine during earlier decades of this century, tempered by more recent experiences in agricultural research. To prosper, such centers would require meaningfully substantial and continuing support.

What might be their characteristics? I would suggest a number.

1. A population laboratory of not less than 200,000 - 500,000 persons for field studies of disease epidemiology, selective interventions as they are developed and behavioral factors associated with their use. This would not imply a fully-censused population but, rather, one whose government and leaders were assiduously and continually consulted with

regard to aims, objectives and methods and whose social and demographic characteristics were at least broadly defined.

2. A clinical tropical medicine patient care and teaching service to foster the expansion of a now almost negligible number of persons who are fully knowledgeable of the pathophysiology of diseases of the tropics and who are capable of relating basic research developments to the disease process and its epidemiology.

3. Laboratory facilities which, at a minimum, are supportive of the clinical needs but which hopefully would be appropriately staffed and equipped to deal with selected field studies and which, likewise, would serve as a nucleus for training of national staff and those in other countries.

4. A formal working relationship for education and research between each developing country center and one or more identified academic centers in the industrialized world which would foster ongoing collaborative enterprises, as well as the exchange of faculty and students.

5. Recognition by the center personnel and by the government of the need for mutual involvement in national health programs - in policy, in their planning, in their execution and in their evaluation.

As with agricultural centers, those for health would most logically be based in countries with larger populations, in countries which themselves were prepared to make a national contribution to the effort and in those which were likewise sympathetic to the need for a significant restructuring of health services and interactions.

Other approaches to addressing the broad issues in health and development can be identified. The most obvious are those related to international consultations to decide on priorities and possible approaches but these have already been a frequent occurrence. Special units could be created for the evaluation and adaptation of new technologies but without the ongoing reality testing of field experience, it seems unlikely to me that they are apt to be especially productive. The longer-term approach described above seems to me to be the most appropriate direction to take but action is needed. If we don't act, I'm afraid we will continue, as we have, with marginally effective curative interventions provided at great cost while such promising approaches as recombinant and carrier antigens, micronutrient supplementation, improved drugs applicable on a community-wide scale and others, languish in the laboratory.

DAH/lj

Annex 1

An incomplete list of publications and proceedings during the 1980s dealing with health research issues in developing countries.

1. National Research Council (1982). Priorities in Biotechnology Research for International Development, National Academy Press, Washington.

2. Rockefeller and Ford Foundations (1984). Child Survival Strategies for Research, edited by Mosley, W.H. and Chen, L.C., Supplement to Population and Development Review, volume 10, Population Council, New York.

3. Office of Technology Assessment (1985). Status of Biomedical Research and Related Technology for Tropical Diseases, Washington.

4. Institute of Medicine (1985). Vaccine Supply and Innovation, National Academy Press, Washington.

5. Institute of Medicine (1985-1986). New Vaccine Developments, Vols. 1 and 2, National Academy Press, Washington.

6. Rockefeller Foundation (1985). Good Health at Low Cost, edited by Halstead, S.B., Walsh, J.A. and Warren, K.S., Rockefeller Foundation, New York.

7. UNICEF (1985). Universal Child Immunization by 1990, in Assignment Children 69/72, edited by Mandl, P.E., UNICEF, New York.

8. Task Force for Child Survival (1986). Protecting the World's Children, Rockefeller Foundation, New York.

9. National Research Council and the Institute of Medicine (1987). U.S. Capacity to Address Tropical Infectious Disease Problems, National Academy Press, 1987.

10. World Health Organization (1987). "Enhancement of Transfers of Technology to Developing Countries with Special Reference to Health," a Report of a Subcommittee of the Advisory Committee on Health Research. Document WHO/RPD/ACHR(TT)/87, WHO, Geneva.

Table 1

INSTITUTIONS WITH COMPLETED WHO TROPICAL DISEASE RESEARCH GRANTS

COUNTRY	CITY	ACCRONYM	YEARS	ANNUAL TDR SUPPORT ($ 000's)
Cameroon	Yaounde	CUSS	1980-84	231
Kenya	Nairobi	ICIPE	1979-81	175
Senegal	Dakar		1977-81	100
Nigeria	Ibadan		1980-84	156
Kenya	Nairobi	KEMRI	1980-84	207
Mozambique	Maputo		1981-85	140
Ghana	Accra		1982-86	107
Zambia	Ndola		1976-86	955
Brazil	Rio de Janiero	FIOCRUZ	1979-84	304
Venezuela	Caracas		1979-83	193
Argentina	Buenos Aires	CEMIC	1979-83	71
Peru	Lima		1979-85	106
Cuba	Havana		1979-85	116
Mexico	Chiapas	CIES	1982-86	131
Argentina	Buenos Aires	ILAIMUS	1980-85	134
Argentina	Buenos Aires		1984-85	20
Malaysia	Kuala Lumpur		1978-84	136
Philippines	Manila		1978-83	211
Thailand	Bangkok		1979-83	488
Indonesia	Jakarta		1979-83	115
Thailand	Bangkok		1979-83	97
Malaysia	Penang		1981-85	55

Table 2

CONSULTATIVE GROUP FOR INTERNATIONAL AGRICULTURAL RESEARCH

Country	Accronym	Yr. Est.	Program (partial)	1984 Budget $ Million U.S.
Philippines	IRRI	1960	Rice	22.5
Mexico	CIMMHYT	1966	Maize, Wheat, Barley	21.0
Nigeria	IITA	1967	Tropical African Crops and Systems	21.2
Colombia	CIAT	1968	Cassava, Field Beans	23.1
Peru	CIP	1971	Potato	10.9
Liberia	WARDA	1971	African rice	2.9
India	ICRSAT	1972	Semi-arid crops	22.1
Kenya	ILRAD	1973	Trypanosomiasis, theileriosis	9.7
Ethiopia	ILCA	1974	African Livestock	12.7
Syria	ICARDA	1976	Semi-arid crops, West Asia	20.4
Italy	IBPGY	1974	Plant genetic resources	3.7
USA	IFPRI	1975	Food Policy	4.2
Netherlands	ISNAR	1980	National Agric. Research	3.5

Table 3

OTHER INTERNATIONALLY FUNDED RESEARCH CENTERS

Country	Accronym	Yr. Est.	Program (partial)	1987 Budget $ Million U.S.
Kenya	ICIPE	1970	Insect physiology and ecology	4.8
China (Taiwan)	AVRDC	1972	Tropical vegetables	3.6
Philippines	ICLARM	1973	Aquatic resources	1.7
USA (Illinois)	INTSOY	1973	Soybeans	1.0
USA (Alabama)	IFDC	1974	Fertilizer	6.7
Kenya	ICRAF	1978	Agroforestry	2.2
Sri Lanka	IIMI	1984	Irrigation Management	5.0*
Being Established				
	IBSRAM		Soil Management	4.5*
	INIBAP		Bananas and plantains	1.8*

* Planned annual recurrent expenditure.