

WHO/GENEVA

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Challenges of Field Research

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The past decade of the biomedical revolution has portrayed hitherto unimaginable vistas for disease prevention and treatment and has raised the hopes and expectations of scientists and the public alike as no other decade before. The presentations of previous speakers reflect this. What seems less to be appreciated, however, is the gulf which exists between a laboratory discovery and its successful application in the field. For example, I must remind you that reasonably satisfactory control of smallpox throughout most of tropical Africa - I don't mean eradication - was not achieved until about 1970. This was nearly 175 years after the discovery of the vaccine, some 50 years after the first heat stable vaccine had been developed and some 20 years after the

vaccine was commercially produced in the form which was subsequently employed in the smallpox eradication campaign. In part, this reflected a deficiency of resources and of management; in part, the preoccupation of these countries with curative medicine; but, also, it reflected a lack of knowledge of the epidemiology of smallpox and, in consequence, of optimal tactics for vaccine use under field conditions. Having available an effective vaccine or drug which performs well in animals or even in Phase II trials in humans does not represent the end of a quest but only the beginning of an important second chapter. Regrettably, however, our capacity for field research - both in terms of professionals and institutions - has declined steadily since the 1940s and other than for tinkering at the margins of the problem, I would submit that we are doing very little about this. I believe there is now both need and opportunity to address this problem and, indeed, unless we do, I fear that the promise of the past decade will expire at the door of the laboratory. I shall offer certain suggestions to address this need.

My credentials are neither those of a basic scientist nor, really, of a practicing epidemiologist. Rather, my career has primarily been devoted to the applications of technology to public health problems. These efforts span a gamut of activities from policy formulation to program implementation - from political advocacy for health policies to media publicist.

- + My first 10 years as an epidemiologist at CDC convinced me that the problems one encountered in the field were seldom as

conventional wisdom portrayed and that if one framed one's questions appropriately, there was usually interest, in fact, real desire on the part of those in the laboratory to assist in their solution. More often than not, it seemed to me that there was a substantially greater laboratory research capacity than there were good questions. The end products were not inconsequential, ranging from major modifications in methods for production and testing of the live attenuated polio vaccine to application of the bifurcated needle for multiple puncture vaccination.

- + My second 10 years with WHO gave me an opportunity to apply research in the context of a major operational program and to discover how significantly the logistics and prospects for success were modified by modest investments of effort in epidemiological, behavioral and virological research, all of which were stimulated by practical field experience.
- + My most recent 10 years have largely been those of a research administrator and professional committee attendee.
  - o At the JHSPH where we now have a budget of some \$75 million per annum and a full-time faculty of 300.
  - o At the Carter White House where I directed a regrettably unsuccessful effort to develop an Institute for Science and Technology in Development.

- o As a member of STAG some several years ago.
- o And, now, as a member of USAID's research policy advisory committee and as Chairman of PAHO's technical advisory group for polio eradication.

The experience has been educational - leading me to one important observation; i.e., "The more important the committee, the poorer the coffee." TDR is the exception which proves the rule. However, these recent experiences have proved to be unexpectedly illuminating, in particular as a result of the opportunity to examine research programs in other sectors and a word (later) about those in agriculture deserve mention, as I believe they may hold lessons for us.

During the past few decades, we have made enormous strides in medicine. I need not rehearse them for you. But they have not, until recently and only in some areas, been translated into significantly improved health for the vast populations which inhabit tropical and semitropical areas. Customarily, this is attributed to socioeconomic problems and/or the lack of scientists, institutions and resources in these areas to address the problems. However, it seems to me that the roots of the problem and the derivative solutions are more complex than this. It is worth spending a moment on a necessarily simplified retrospective history for if we appreciate from whence we have come, new directions are perhaps easier to identify.

A basic constraint to the improvement of health - and indeed the development of field research - has been and continues to be the fact that our health systems, both in the industrialized and developing countries, have been designed and developed primarily as curative care systems. It is to this end that we have allocated and are allocating most of our resources and it is this aspect of health which has commanded the bulk of research funds. Hospitals, so-called primary health centers and private physicians have been and continue to be primarily preoccupied with providing services to those who seek them. But, as has been amply demonstrated in numerous studies, these curative services have had, at most, marginal effects in diminishing the community-wide occurrence either of morbidity or mortality. Preventive measures have been ignored and this can be illustrated very simply. The single most cost-effective medical procedure is immunization and yet, as recently as 1977, - 10 years ago - it is estimated that less than 2% of children in the developing countries received the inexpensive and well-tested antigens - DPT, measles and poliomyelitis - all diseases of major significance. The record of my own country is no more distinguished. For the past decade, a well-publicized measles eradication program has been in progress and yet a survey in Miami last December revealed that only 50% of two year old children had received vaccine - and this in an area where there are, in fact, an excess of physicians. But the problem is even worse than these figures suggest. Of 18 unvaccinated children, 17 had been in a so-called health facility within the previous 12 months. More than this, 53% of infections had actually been acquired while waiting in a clinic or out-patient department of a hospital. I know something of European programs and

many, I believe, are equally poor or worse. This absence of interest in prevention is paralleled by a lack of interest in the community-wide prevalence of disease, in how it spreads and certainly in how it can be prevented.

During the early decades of this century, public health had emerged as an important force, originating, as it did, in the great sanitary reforms. It was associated with improved water, milk, sewerage and housing - in more general than specific disease prevention, simply because the science of the time offered little which targeted specific diseases. However, progress in reducing morbidity and mortality was dramatic, and as most would acknowledge, curative medicine played only a marginal role. By the midpoint of this century, most industrialized countries had substantially achieved what they could by these approaches and beginning in the 1950s, public health and the field research needed to advance it, lapsed into a decline throughout the industrialized world and this was echoed throughout the developing world. The star of curative medicine rose. New insights into human biology permitted the development of a whole range of diagnostic tools, drugs, types of surgery and rehabilitative methods. An army of practitioners were trained in their use while medical supply houses and pharmaceutical producers tumbled over each other to support their research and application. Unfortunately, the same could not be said for research on vaccines and prevention devices. A drug for arthritis which has to be taken several times daily is obviously far more interesting 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.

New medical schools were created to provide more physicians to provide care, more hospitals were built and more funds were made available to cover these costs. The governments' principal policy makers were drawn primarily from those who cared for patients and this only reinforced the allocation of resources for more of the same. For nearly a generation, we worshipped at the shrine of curative and palliative care. Epidemiologists withdrew from the field to the extent that we began to talk of clinical epidemiology as a specialty; the effect was especially pronounced in the tropics where indeed knowledgeable specialists in tropical medicine all but vanished.

During the past decade, however, change has begun to occur. The success and minimal cost of the community-based smallpox eradication program 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; a TDR program was established to support research on six major tropical diseases. It has only recently begun to be appreciated, however, that the costly but generously funded curative measures which reach only those who happen to appear at some sort of health facility have insignificant effects on morbidity and mortality. Substantial improvements demonstrably derive only from community-wide interventions, preferably preventive. It has also become apparent that to apply these effectively 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 major departure from that of recent decades and, not surprisingly, there are as yet few professionals and few centers who are experienced in examining problems through field research. The institution strengthening program of TDR was intended, in part, to address this problem but given the limited resources and their wide dispersal, the results have generally proved disappointing.

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 IDDRB in Bangladesh and INCAP in Guatemala. The Clinical Research Center in Nairobi offers promise of being a third although the stability of funding for its recurrent costs is by no means clear to me. These centers have endured countless fiscal crises and yet all have made and are making extraordinarily valuable contributions in the application of science and technology to development. Meanwhile, the private sector which has been so important to the development of curative measures has offered little support and little hope of support given the necessary emphasis on simple and inexpensive measures which offer little return in investment.

I would contrast this to the situation in agriculture of which I find many of my medical colleagues ignorant. In several of my many committee incarnations, I had the opportunity to review research programs in

agriculture, a sector in which, as you know, phenomenal progress has been made in 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; three others followed - in Mexico, Nigeria and Colombia - before 1971 when the internationally funded and directed Consultative Group on Agricultural Research was established. Today, there are 13 centers which are part of the Consultative Group (Table 1). Note that most 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 almost all of the centers have core budgets in the range of \$10 to \$20 million each, 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 - there are 9 other centers which are internationally funded by other mechanisms (Table 2).

Let me contrast these centers with the 22 centers which have been supported by TDR grants and whose grants, with one exception, have now been terminated (Table 3). Only time will tell whether each of these will be viable and productive institutions but one has to wonder what such a small investment over such a short period of time will accomplish.

To return to the International Agricultural Centers; their charge 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.

Since their establishment, many other centers supported nationally and/or by donors have been created to form quite extensive networks.

Their successes have been well-publicized and this, in turn, has encouraged the United States, as well as a number of other national governments, to provide support to national academic research centers to work as counterparts. This has not happened in health. The U.S. Institute of Medicine will shortly issue a report on U.S. capacity for tropical medicine which identifies three centers with as many as 20 faculty concerned with international health and only one, our own at Johns Hopkins, with as many as 50. For comparison, there are in the U.S. alone at least 25 international centers for agriculture with more than 20 full-time faculty.

There is the argument, of course, that agriculture is an investment while health is an expenditure. In crass terms, this implicitly expresses the view that one can replace a child or perhaps a wife at no real economic cost to society while the loss of a cow is quite another matter. However, this attitude may now be changing. I would note that the World Bank has begun to regard health as an investment rather than an expenditure and is now supporting some \$500 million in new projects each year; the IADB this past year supported its first health project - one for polio eradication in the Americas.

Likewise, the political climate appears to be changing from what it was only a decade ago - from one in which health was all but synonymous with curative medicine to one in which preventive medicine is viewed as a promising thrust for the future. However, if we are to realize the potential of preventive medicine, we must be able to take the products of the laboratory into the field and apply them; we need to understand

the epidemiology of each disease in order to attack it most effectively at its weakest link; we need diagnostic tools to identify cases; and last, although not least, we need to understand the clinical ramifications and pathophysiology of the disease in order to devise optimum approaches for an attack upon it.

We are not now well-equipped to do so. I for one have difficulty in identifying more than one or two centers in clinical tropical medicine whose quality would be internationally recognized. We have a number of funded laboratory research programs of high quality, predominantly in the industrialized world, and although some of the scientists are knowledgeable of the disease and its ramifications, many so engaged have never been out of their own country and would not recognize a patient with the parasite if they saw one. Some indeed would not recognize the whole parasite on which they are working. Sites for field research, with competent national personnel and a rapport with local populations, are precious few indeed. This became all too apparent to us this past year as we sought to establish replicate field studies to measure the effect of vitamin A application in large populations. We had difficulty in finding two which were even marginally satisfactory. As for epidemiologists who are competent to undertake such studies, they are equally scarce. Finally, most of those skilled in clinical tropical medicine are in their 60s and 70s. The once legendary clinician researchers who provided broad integrative insights into a problem are literally an endangered species.

Given our perhaps belated recognition that community-based programs of prevention and perhaps therapy are the only feasible ones which may be expected to have significant impact on disease, should not our priorities in research be similarly decided? If diagnostic methods are to be pursued should these not be for epidemiological definitions of problems rather than for treatment of individual patients?

Should we not now begin to provide the structure, continuity of support and process to address problems in the field? No one questions the need of a molecular biologist for a laboratory and equipment but those concerned with the problems of the field need support and laboratories as well. This has been recognized, accepted and funded for agriculture, it has not for health. Thus, taking certain lessons from the experience in agriculture, I would propose that substantial and continuing support be provided to a selected few national centers of quality to create a national-international partnership of health research institutions.

I would visualize such centers have four characteristics; at its hub, a first-class clinical tropical medicine service for investigation and student training; second, laboratory facilities suitable for clinical diagnosis, appropriate research training of students, and support to field services; third, a large population laboratory for on-going studies of disease epidemiology, new diagnostic tools, vaccines and other community-based interventions; and fourth, a program of support and assessment services for on-going government health programs to assure practical translation of new developments. As with agriculture, centers would most logically be based in countries with larger

populations and in countries which themselves were prepared to make a national contribution to the effort. Is it conceivable that Ford and Rockefeller or other foundations or governments might be persuaded to play a role as they did in agriculture, in funding the beginning of such an infrastructure?

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.

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Table 1

CONSULTATIVE GROUP FOR INTERNATIONAL AGRICULTURAL RESEARCH

| <u>Country</u> | <u>Accronym</u> | <u>Yr. Est.</u> | <u>Program (partial)</u>              | <u>1984 Budget<br/>\$ Million U.S.</u> |
|----------------|-----------------|-----------------|---------------------------------------|----------------------------------------|
| Philippines    | IRRI            | 1960            | Rice                                  | 22.5                                   |
| Mexico         | CIMMYT          | 1966            | Maize, Wheat, Barley                  | 21.0                                   |
| Nigeria        | IITA            | 1967            | Tropical African Crops<br>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          | IILRAD          | 1973            | Trypanosomiasis,<br>theileriosis      | 9.7                                    |
| Ethiopia       | ILCA            | 1974            | African Livestock                     | 12.7                                   |
| Syria          | ICARDA          | 1976            | Semi-arid crops,<br>West Asia         | 20.4                                   |
| Italy          | IBPGV           | 1974            | Plant genetic<br>resources            | 3.7                                    |
| USA            | IFPRI           | 1975            | Food Policy                           | 4.2                                    |
| Netherlands    | ISNAR           | 1980            | National Agric.<br>Research           | 3.5                                    |

Table 2

Other Internationally Funded Research Centers

| <u>Country</u>           | <u>Accronym</u> | <u>Yr. Est.</u> | <u>Program (partial)</u>         | <u>1987 Budget<br/>\$ Million U.S.</u> |
|--------------------------|-----------------|-----------------|----------------------------------|----------------------------------------|
| Kenya                    | ICIPE           | 1970            | Insect physiology<br>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*                                   |
| <u>Being Established</u> |                 |                 |                                  |                                        |
|                          | IBSRAM          |                 | Soil Management                  | 4.5*                                   |
|                          | INIBAP          |                 | Bananas and plantains            | 1.8*                                   |

\*Planned annual recurrent expenditure.

Table 3

## INSTITUTIONS WITH COMPLETED TDR GRANTS

| <u>COUNTRY</u> | <u>CITY</u>    | <u>ACCRONYM</u> | <u>YEARS</u> | <u>ANNUAL TDR SUPPORT</u><br>(\$ 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 Janeiro | 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                                      |