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The Contributions of Health Science

D.A. Henderson, M.D., M.P.H.

Dean

The formidable burden of disease and disability in the developing countries is regularly and vividly documented in many publications; indeed, even to the casual visitor in these countries, the burden is apparent and often overwhelming. But are conditions worse or better than they were a brief quarter century ago when the Agency for International Development formally came into existence? Has any progress been made and, if so, what implications might it have for the future? A brief, necessarily selective, review of the past 25 years provides an interesting and instructive perspective in identifying not only future research priorities but productive approaches in health research as well.

What comparative data do we have and what does it show?

Obtaining accurate information regarding mortality and morbidity, especially those which are disease specific, is difficult. More accurate overall mortality data, however, are gradually becoming available as a result of efforts being made by statisticians at UNICEF and the United Nations Population Division. Data have recently been published for 1960 and 1985 for the 130 largest countries comprising more than 99% of the world's population. Changes in health which have occurred are surprisingly encouraging.

Infant mortality rates provide one important, closely followed indicator of health status (table 1). Data for 1960 show 11 countries with a rate of more than 200 deaths per 1,000 live births and indeed, 47 countries had rates exceeding 150 per 1,000. As of 1965, only seven countries recorded rates of this magnitude.

Those in UNICEF suggest that a better indicator of health is the proportion of newborns who survive to the age of five (table 2). During 1960, one-third of all children in eight countries died before their fifth birthday and one in four children died in a total of 42 countries. Twenty-five years later, only eight countries fall in this latter category. Note also that in 26 countries, fewer than 2 in 100 newborns die before their fifth birthday. Admittedly, almost all of these are industrialized countries but included among them are Singapore, Hong Kong and Cuba.

As one might expect, life expectancies have risen (table 3). In only two countries in 1985 was life expectancy under 40 years, this contrasts to 24 countries only 25 years ago. Indeed, the median life expectancy among the 129 countries has risen from 49 years to 61 years - a gain of 12 years in a span of only 25 years.

Although the subsequent speaker will be discussing population issues, I would be remiss in not making at least passing reference to changes in birth rates (table 4). Crude birth rates have also fallen sharply from a median for the 130 countries of 46 per 1,000 population to 30 per

1,000 - far from sufficient to compensate for improved survival rates but certainly moving in the right direction.

Unquestionably, many factors beyond specific health interventions have contributed to these remarkable changes. But dramatic changes have occurred in the nature of health interventions and unquestionably, these have played a role. The Agency for International Health, as we shall see, has played a central or major supporting role in the development and/or application of all of these.

The early 1960s marked the beginning of my own involvement in international health and thus, these years are particularly vivid ones to me. Health in development was characterized by three characteristics which deserve mention - a somewhat different view than now regarding health and development, different program directions and different approaches to the delivery of health services. It is important to note these briefly in order to set the stage for what later ensued.

Development theory in the early 1960s held that with economic development, improved health would follow as night the day and that this, rather than specific health initiatives, should command priority. The belief that improved health itself could contribute significantly to economic development was not generally accepted and thus, the health sector was assigned comparatively few resources either for programs or research. From an admittedly biased perspective, such views - albeit mitigated - continue unfortunately to prevail in some quarters.

The principal health program at that time and the one which commanded the bulk of resources was malaria eradication. A global program had started in 1955 which relied almost wholly on the systematic application of residual DDT to the walls of houses. This was predicated on the knowledge that mosquitoes rested on walls after taking a blood meal and, having been exposed to the insecticide, died soon after. Thus, at least in theory, transmission of malaria would soon be stopped. The prevalent philosophy of the program's directors was that the task was primarily one of meticulous management and administration. The scientific basis for the program was tenuous at best but few resources were assigned to research. As wryly observed by the British malariologist, Sir Ian Macgregor - "The program failed to eradicate malaria but it eradicated the malariologists." By the early 1970s, vector resistance to insecticides, parasite resistance to drugs and insuperable administrative problems had doomed the program as conceived. But, by then, there was no suitable research infrastructure to which to turn.

The method of delivery of other health services presented yet a third problem. In the industrialized countries, evolutionary advances were beginning to be made in the diagnosis of disease, its treatment and the rehabilitation of patients. It was difficult to build hospitals fast enough or to train enough physicians in the paradigm of curative medicine. As is so often the case, that which was most appropriate to the industrialized world was likewise deemed appropriate for the developing countries. Thus, substantial national and international resources were directed toward the development of curative care networks of hospitals and health centers and to the training of personnel to man

them. Forgotten in the process was the fact that the major gains in health and well-being in the industrialized countries had resulted from preventive measures such as safe water, milk pasteurization, nutrition and immunization - measures which were little known throughout the developing world and which, if to be affordable, required research and adaptation in the application of these technologies. A number of small but significant pilot demonstration programs were undertaken which demonstrated that community-based primary-care programs could be cost-effective and have significant impact, but they were footnotes to the literature and never extended over large populations.

In the early 60s, family planning services were all but unknown and other than for the sporadic use of frequently impotent smallpox vaccine, immunization was uncommon. Where hospitals existed, whole wards were given over to those afflicted with smallpox, poliomyelitis, tetanus, measles and whooping cough. Few questioned the failure to employ the single most cost-effective and most simple medical procedure available either then or now - the application of vaccines. Research dealing with diseases known only to the tropics had diminished almost to nil, as had research in nutrition and sanitary engineering.

Perhaps the most significant action taken by the newly constituted Agency for International Development was its investment in a likewise new research enterprise, then called the Pakistan SEATO Cholera Research Laboratory located in what is now Dakha, Bangladesh. It, too, celebrates its 25th anniversary this year. In the health field, it is now the world's only disease-oriented international research center in

any way comparable to the great network of agricultural research centers.

Cholera in 1962, was a major problem of Asia and just beginning its seventh pandemic spread. Death rates of those hospitalized frequently exceeded 60%. Only four years before, however, Robert Phillips, a physiologist, then at the Naval Medical Research Unit in Taiwan, had demonstrated that mortality rates could be decreased to less than 1% through generous use of intravenous solutions - a patient sometimes requiring 50 or more liters of fluid. This was an extraordinary advance but still of limited practical use because of the tremendous quantities of fluid required, the shortage of such fluids as well as facilities to administer them and the fact that the disease customarily occurred in epidemics with thousands of cases at a time.

Soon after the Dhaka laboratory opened, Phillips, who soon became its director, discovered that oral as opposed to intravenous hydration was a feasible approach. Oral replacement of the tremendous fluid loss had not previously been possible even when the proper amounts of sodium, potassium and chloride had been added to the water. Phillips discovered, however, that if a small amount of glucose was added to the solution, the water and salt were absorbed through the small intestine. This discovery, emanating from basic physiological studies of a disease process, was hailed by the British medical journal, *Lancet*, in a 1978 editorial as "potentially the most important medical advance of this century."

Practical application, however, proved to be more difficult than might have been expected. The proper balance of sugar and salt had to be determined and failures occurred. Not until 1968 was it first successfully used under epidemic conditions. Even then, a traditional medical profession demanded more data and further demonstrations. Not until 1975 did UNICEF order its first million packets of salt and sugar for the oral rehydration solution. Even though oral rehydration proved to be useful for diarrheas of all types, the packets lasted 18 months. Finally, with a strong impetus from USAID as well as WHO and UNICEF and extensive social marketing, traditional practices began to change. Today, it is estimated that more than one million packets are used daily and in Egypt, for example, deaths due to diarrhea decreased by 50%. Research, in part supported by AID, is continuing to develop simpler, more applicable formulations. Meanwhile, in the industrialized countries, it was also discovered to be of value - resulting in fewer and shorter hospitalizations but traditional clinicians, wedded to customary practice and more sophisticated technologies, have been slow to accept it although change is beginning to occur.

Parenthetically, I would note that the Dhaka laboratory continues to make extraordinary contributions to our understanding of infectious diseases and nutrition, of vaccine efficacy and in family planning. Many who worked there, including more than 10 on our faculty, have continued productive research careers in international health. Regrettably, however, the Dhaka Center and the Nutrition Center in Guatemala (INCAP) represent the only two international health research centers in any way comparable to those in agriculture.

A second important development of the past 25 years has been the development and application of vaccines. As of 1962, the principal vaccines which were available and widely applicable were DPT, poliomyelitis, smallpox, BCG, yellow fever and rabies. However, DPT and polio vaccine were seldom given in any developing country and the other vaccines, except for the UNICEF-supplied BCG vaccine, were generally of poor quality and thermolabile. Significant developments, beginning in the early 1960s, transformed this situation and promise to do more.

In 1961, USAID supported the first field trials of the new measles vaccine in a developing country and, subsequently, a series of studies, both at NIH and CDC, which demonstrated that several vaccines could be given simultaneously with safety and efficacy. Spurred on by the U.S. Army's development of a practical jet injector, suitable for field use, USAID, in 1965, launched a smallpox-eradication-measles control program in a population of 100 million persons in western and central Africa. This incidentally provided the essential stimulus to WHO to undertake its intensified program of smallpox eradication beginning in 1967.

During the course of this program and the family planning program which began about the same time, an important impetus was given to vaccine development and application as well as changes in health policy, priorities and mechanisms for the delivery of health services. To be successful, both the immunization and family planning programs required the active marketing and delivery of health services throughout the whole of a population rather than being delivered at established health centers or hospitals to persons who presented themselves. They opened

the way for a whole new range of research initiatives to explore alternative approaches in operations, health education and behavioral modification - more recently dignified by the term, social marketing. New techniques for evaluation, surveillance and demography emerged. Persons from a far-wider range of disciplines than medicine alone were required and brought into the programs. When programs for distribution of the packets of oral rehydration therapy were added, they served to reinforce the recognition that community-based programs such as these required quite different skills, management structures and approaches than did the provision of curative services.

For many countries, it was a revelation during the smallpox eradication program to discover how much could be achieved and at how little cost through a vaccination program and this, in turn, led to the decision by the World Health Assembly (1974) to launch an expanded program of immunization involving six antigens - against poliomyelitis, measles, diphtheria, tetanus, pertussis and tuberculosis. Today, nearly 50% of the world's children are fully vaccinated, an increase from an estimated 2% only ten years ago. The goal is to reach 90% by the year 1990. Sufficient progress has already been made with regard to poliomyelitis for the Pan American Health Organization to decide (1985) on a hemisphere-wide poliomyelitis eradication campaign whose objective is to eliminate poliomyelitis by 1990. Supported by AID, WHO, UNICEF and Rotary International, the program is well underway, notably with provision being made for an ongoing program of research to improve diagnostic capabilities and an understanding of the epidemiology of the disease, especially in the tropics.

Greater priority is now being given by AID, as well as other agencies, to develop other vaccines given the potential offered by modern biotechnology. AID is now the principal resource and major driving force in the development of a malaria vaccine which, when realized, will lift from the developing countries, one of the most onerous disease burdens which they now bear. Other promising vaccines include those against hepatitis B, rotavirus (a diarrheal disease agent), respiratory syncytial virus, typhoid, shigellosis and leprosy.

Despite these successes, the application of modern biotechnology both for vaccine development and for approaches to dealing with the major problem diseases of the tropics has so far progressed less rapidly than it should. Two principal reasons account for this. Government intervention and support for research in tropical disease problems diminished sharply in the post-colonial era and evidences few prospects for improvement. A tropical disease research program is being conducted through WHO although it amounts, in all, to only \$25 million; AID is providing such support as it can from a limited health budget; and NIH, the military, foundations and other governments also provide funds. The funds, however, are modest at best to unravel the complexities of at least a dozen diseases of truly major importance. The private sector, likewise, has exhibited little interest, understandably because of the marginal profits which can be expected from new vaccines as well as drugs, vaccines or diagnostic instruments for diseases primarily extant in the poor tropical areas. In brief, opportunities far outstrip available resources.

Finally, attention has recently been drawn to the also long-neglected problem of nutritional challenges in developing countries as the result of a recent serendipitous discovery (1984) by Summer and his colleagues, in USAID supported trials. They found that vitamin A deficiency was associated with much more than vision impairment and blindness and that marginal but important deficiencies of vitamin A were far more widespread than any had suspected. In comparing two groups of Indonesian village children, one group given vitamin A and the other a placebo, it was discovered that death rates due to respiratory and diarrheal diseases among those under five years was 35% lower among those who had received a single vitamin A supplement once in six months. Further studies now show that vitamin A is important in sustaining the integrity of the epithelial lining of the respiratory and gastroenteric tract, in red blood cell production and in the functioning of the immune system. Studies in other areas are beginning to confirm those in Indonesia and have led WHO and UNICEF to advocate its community-wide use in all populations where, as an indicator, measles case-fatality rates exceed 1%.

The discovery of the importance of vitamin A to the body's natural defense systems against disease and the recognition that iodine deficiency, for example, is also a serious problem in many large areas of the developing world, raises the question of whether there might not be other micronutrient deficiencies which could readily be corrected. Here is yet another field crying to be explored.

As briefly described, the past 25 years have been associated with the most profound changes in the health status of the developing countries which has ever been witnessed and the wonders of modern biotechnology promise vastly more. With an increasing understanding of the social sciences associated with their application, the pace of change could be markedly accelerated. And, as has been only partially illustrated, health care in our own country benefitted in the process.

There are a number of critical constraints to progress, however. First is the lack of adequate resources to conduct necessary basic research into disease processes and defense mechanisms for those diseases found only in the tropics and resources to adapt and apply the technology now emerging. Second is the paucity of investigators experienced in tropical medicine. With the limited resources available and with a corresponding lack of a career structure, there are few indeed of our most capable scientists who are prepared to commit themselves to addressing health problems of the developing world. Third are the constraints imposed by traditionally trained physicians whose experience and education have been in curative practices and who have little grasp of epidemiology, of techniques of social marketing, of management and of disease surveillance. Fourth is the lack of institutions in the developing world and no less in the USA with facilities and a critical mass of trained manpower whose interests are in the major diseases of tropical countries. We must not forget that if we intend to be serious in our efforts, all of these constraints must be addressed.

Disease does not recognize national boundaries, this we learned again and again with smallpox, and as we are now learning, to our consternation, with the AIDS virus. However, not until we took a global view did we resolve the smallpox problem - to our own benefit and to the world's benefit. With increasing travel and a growing interdependency in commerce, it becomes more and more unrealistic to take an insular, national view with regard to any of the world's diseases. While the past 25 years have witnessed spectacular change - and AID has played a central role in this change - the future promises much, much more.

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Table 1

MORTALITY RATES FOR INFANTS (under 1 year) -- 130 COUNTRIES

<u>No. of Deaths/1,000 Births</u>	<u>No. of Countries</u>	
	<u>1960</u>	<u>1985*</u>
≥ 200	11	0
150-199	36	7
100-149	31	32
50-99	26	32
25-49	17	21
< 25	9	37

(Unknown: Iran)

Source: State of the World's Children, 1987

Table 2

CHILD SURVIVAL: PERCENTAGE BORN WHO REACH 5 YEARS OF AGE -
129 COUNTRIES

<u>Percentage Reaching 5 Years</u>	<u>No. of Countries</u>	
	<u>1960</u>	<u>1985</u>
< 65	8	0
65-74.9	34	8
75-84.9	33	33
85-94.9	32	38
95-97.9	21	24
98+	1	26

Table 3

LIFE EXPECTANCY AT BIRTH - 129 COUNTRIES

<u>No. of Years</u>	<u>No. of Countries</u>	
	<u>1960</u>	<u>1985</u>
< 40	24	2
40-49	43	30
50-59	18	28
60-69	29	28
70+	16	42

Source: State of the World's Children, 1987

Table 4

CRUDE BIRTH RATE

<u>Births/1,000 Population</u>	<u>No. of Countries</u>	
	<u>1960</u>	<u>1985</u>
50+	22	10
40-49	70	45
30-39	5	26
20-29	17	16
10-19	16	33