

6/5/92

**Childhood Precursors of Adult Morbidity and Mortality in Developing Countries:  
Implications for Health Programs**

by

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**A version of this paper was first presented at the  
Workshop on Policy and Planning Implications of the  
Epidemiological Transition in Developing Countries**

**sponsored by**

**The Committee on Population of the National Academy of Sciences  
Washington, D.C.  
November 20-22, 1991**

## **ACKNOWLEDGMENTS**

The authors acknowledge the assistance of Dr. Aida Abashawi and Dr. Laura F. Robin in the preparation of this paper. Partial support for the work was provided by the U.S. Agency for International Development under Child Survival Cooperative Agreement DPE-5951-A-00-5051.

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**May 1992**

**Introduction**

The developing countries of the world are in the midst of a demographic and epidemiologic transition which is profoundly transforming their health picture (Mosley and Cowley, 1991). Prior to World War II, most developing countries experienced high rates of mortality, with infectious diseases of childhood dominating the epidemiologic picture. In the postwar period, largely as a result of advancements in medical technology directed against infectious and parasitic diseases, there have been rapid declines in infant and child mortality which, coupled with the high levels of fertility, produced rapidly growing populations with a very young age structure. Beginning in the 1960s and accelerating through the 1970s and 1980s, birth rates began to decline in much of the developing world, initiating a process of slower population growth. This reduction in the growth rates, however, initially occurs among infants and children; the population of adults will continue to grow for decades into the future because of the large numbers of children already born who will survive to reach the older age groups (Chenais, 1990).

There have been dramatic changes in the age structure of the world's population between 1960 and 1990 which will continue into the first quarter of the next century

according to estimates and projections by the United Nations (1991). For example, in developing countries in particular, while the population under age 15 will have only slightly more than doubled over this 60-year time span, adults age 15 to 64 will have increased by almost four times to 4441 million in 2020, and the elderly over age 65 will have increased almost six times to 472 million in 2020. This rapid aging of the population will have a profound impact on the health system which will have to shift its priorities toward the prevention and management of chronic diseases among adults (Mosley, Bobadilla, Jamison, forthcoming 1992).

This paper will examine only one aspect of this health transition in developing countries. It will look at the emerging health problems among the adults and the aged and assess to what degree these chronic diseases and disabilities might be a consequence of infectious diseases and other adverse conditions which were experienced decades earlier in infancy and childhood. A recognition of these relationships can enhance our understanding of the cost-effectiveness and cost benefits of programs to promote child health. Child health interventions are not only cost-effective in saving lives and preventing disabilities in the short run but, more importantly, in the long run can result in major cost savings to health systems and accelerate national development by improving the health and productivity of these children when they become adults.

## **Background**

Recently Elo and Preston (1992) completed a review of the literature examining the effects of early life conditions on adult mortality. Their review begins with a discussion of the epidemiologic evidence for some of the major mechanisms whereby exposures and morbidity in childhood may have health consequences for adults. Initially they examined a number of specific infectious diseases of childhood with well documented long-term

health effects among adults (tuberculosis, hepatitis B, rheumatic heart disease) and then the authors look at the growing literature suggesting that a number of chronic cardiovascular and pulmonary diseases may be related to a range of risk factors beginning in the intrauterine environment (intrauterine growth retardation) and extending through disease exposures and behavior patterns acquired in childhood (acute respiratory infections, dietary consumption of fat and salt). Other associations they examine include a number of studies postulating that viral infections acquired in childhood may be linked to a wide variety of chronic diseases ranging from cancer to multiple sclerosis, juvenile diabetes, rheumatoid arthritis, and presenile dementia as well as the extensive literature linking short stature and adult mortality. Elo and Preston's review then turns to population-based studies among cohorts of adults which seek to link conditions around birth and early childhood to differentials and subsequent mortality. They find a wide variety of studies drawing on data from 19th and 20th century Europe were generally consistent with the hypothesis that the childhood environment plays a substantial role in adult mortality.

The analysis in this paper will extend the work of Elo and Preston (1992) in several ways. First, it will take a more epidemiological approach looking at a broader range of disease conditions in infancy and childhood where the evidence supports a direct relationship to adult morbidity and mortality. Second, our analysis will be oriented to the current situation in developing countries with the objective of trying to assess the probable magnitude of the health impact of selected childhood diseases on adult morbidity and mortality. Our assessment admittedly will be more speculative, given the data limitations in most developing countries. Our purpose will be achieved, however, if this analysis

highlights the need for more research on these issues as well as the importance of maintaining and expanding programs to promote child health in the developing world.

### **A Classification of Diseases and Conditions of Infancy and Childhood with Consequences for Adults**

There are a wide range of health conditions affecting infants and children in developing countries which have long-term consequences for adult health. Table 1 classifies these conditions into four groups. These are: 1) conditions acquired in the perinatal period; 2) infectious diseases of childhood; 3) nutritional deficiencies of infancy and childhood; and 4) environmental hazards. This classification system is by no means comprehensive but it does include many of the major diseases and conditions which have a substantial impact on adult health and survival.

The first part of this paper will briefly discuss each of these conditions, focusing particularly on the available information relating childhood diseases to adult health consequences. Where data are available, the magnitude of the problem in terms of impact on adult health will be provided. In the concluding section of this paper we will take a more integrated approach by examining some of the interactions among childhood risk factors in producing adult diseases. Also, we will examine recent trends in adult cause-of-death data from selected developing countries to assess how their mortality picture may be related to conditions acquired in childhood several decades earlier.

#### **A. Perinatal Conditions**

##### **1. Low birthweight**

Twenty million newborns per year, or 16 percent of all children born worldwide, are considered to be low birthweight as defined by a weight of less than 2,500 grams (WHO, 1990). Ninety percent of low birthweight infants are born to mothers in developing

countries. Over two-thirds of these occur in the countries of South Asia where approximately one birth in four is low birthweight. The overall risk of delivering a low birthweight infant in a developing country is three times that in an industrialized country. In South Asia the risk is four times greater.

In developing countries, around 80 percent of low birthweight infants are a result of intrauterine growth retardation (IUGR) rather than prematurity (Villar and Belizan, 1982). IUGR is primarily a consequence of inadequate energy and protein intake during pregnancy, often coupled with excessive energy expenditure during the latter stages of pregnancy because of the heavy workload of most poor women in the developing world (Kramer, 1987). Adolescent pregnancy and maternal stunting are associated with low birthweight (Herrera, 1985). Additional factors are traditional practices of dietary restrictions during pregnancy, maternal infections such as malaria, and possibly close spacing of births (Kramer, 1987). Cigarette smoking and smoke from biomass cooking fuels may also be implicated (Ferraz, *et al.*, 1990; Mavalankar, *et al.*, 1991).

Studies in Guatemala, Colombia, India, Mexico, the United States and Canada have confirmed that supplemental nutrition can increase birthweight (Pinstrup-Anderson, *et al.*, forthcoming 1992). Improvement in birthweight appears to be greatest if supplementation is provided in the third trimester of pregnancy. Noteworthy, most low birthweight newborns in societies suffering from chronic malnutrition are found to remain stunted at below the tenth percentile for height and weight at three years of age (Mata, 1978).

Elo and Preston (1992) review the evidence indicating that stunted growth is associated with higher risks of mortality among adults, particularly from cardiovascular disease and chronic obstructive pulmonary disease (COPD). The former relationship will be examined below in the discussion of protein energy malnutrition. Here we will look at

the evidence specifically relating low birthweight to respiratory infection in childhood and COPD in adults.

Low birthweight infants have a higher incidence of lower respiratory tract infections than infants with normal birthweight (McCall and Acheson, 1968). As a consequence, low birthweight has been shown to be associated with a higher prevalence of cough and poor lung function in later childhood (Chan, *et al.*, 1989). Recently Barker and colleagues (1991) completed a study relating birthweight and childhood respiratory infections to risk of death from chronic obstructive pulmonary disease and to pulmonary function among men ages 59-67 years in England. They confirmed that low birthweight and severe respiratory infections in infancy were associated with higher risks of death from COPD as well as with compromised lung function among the survivors. They note that an association between low birthweight and obstructive lung disease is biologically plausible, as fetal lung growth, particularly growth of the airways, is largely completed in-utero (Bucher and Reid, 1961). Barker *et al.* (1991) conclude from their study that "prevention of chronic obstructive airway disease may partly depend on promotion of fetal and infant lung growth and reduction in the incidence of lower respiratory tract infection in infancy" (page 674).

COPD is a leading cause of death among adults in developing countries, and the high incidence of low birthweight in these settings is undoubtedly a contributing factor. Because there are other important contributing factors in developing countries (see below), COPD will be discussed in more detail in part two of this paper.



## **2. Birth trauma, asphyxia, metabolic disorders**

In developing countries only about 50 percent of the births are attended by trained personnel (WHO, 1990). One consequence is a perinatal mortality rate 4 to 6 times higher than seen in developed countries where over 99 percent of births have a trained attendant, typically in a hospital setting. Unfortunately, data are lacking on the incidence of birth injury, asphyxia, and preventable metabolic disorders (such as hyperbilirubinemia secondary to physiologic jaundice) which can produce permanent disabilities among surviving infants in developing country settings. Brain damage leading to mental retardation, cerebral palsy, and other neurological disabilities would be among the most serious consequences with a life-long impact on health status.

Although incidence data are not available, there are some clinical studies suggesting that birth injury is a significant contributor to chronic neurological disease. Nottidge and Okogbo (1991) found that among 413 children presenting with cerebral palsy in Ibadan, Nigeria, 41 percent appeared to be related to bilirubin encephalopathy and 20 percent to birth asphyxia. The patients seen in this urban referral center are by no means representative of the population, however, the data do suggest that possibly a high proportion of brain damage seen in infants is attributable to conditions preventable in the perinatal period. While it is not clear how these observations may relate to neurological disability seen among adults, the data at least are consistent with the thesis that inadequate antenatal and childbirth care can contribute significantly to the level of chronic disability in a population. This is an important area that requires far more research.

### **3. Congenital and perinatal infections**

There are a number of maternal infections which may be transmitted to the fetus in-utero or to the newborn around the time of childbirth that have significant consequences for adult health.

#### **a. Hepatitis B**

By far the most prevalent and serious disease in this category is related to the maternal-infant transmission of hepatitis B virus (HBV) (Francis, 1986; Kane, *et al.*, forthcoming 1992). The World Health Organization estimates that more than two billion individuals have been infected with HBV of which 280 million are chronically infected carriers of the virus (WHO, 1990). Prospective population-based studies indicate that ultimately approximately one-quarter of these chronically infected individuals will die from chronic active hepatitis, cirrhosis, or primary liver cancer. Annually, HBV infection is directly related to one to two million deaths per year (WHO, 1990). The prevalence of chronic HBV infection ranges from 6 to 10 percent throughout much of East and Southeast Asia and Sub-Saharan Africa. For the rest of Asia, HBV prevalence is 3 to 5 percent, while it is 1 to 2 percent in Latin America (Francis, 1986).

Mother-infant transmission in the perinatal period is the primary reason for the high carrier rates in areas where hepatitis B is prevalent. Figure 1 from Beasley (1982) provides a schematic representation of the cycle of HBV infections and liver cancer from generation to generation. If the mother is an HBV carrier, approximately 50 percent of newborns will be infected, 95 percent of whom will become carriers. The daughters will grow up to transmit the virus to the next generation. Ultimately, about half the sons and 14 percent of the daughters will die of chronic liver disease and liver cancer later in life.

Demographically, HBV is an important cause of mortality among adults in developing countries. Primary liver cancer is a leading cause of cancer death in males in most of Sub-Saharan Africa and much of East and Southeast Asia and the Pacific Basin. Figure 2 (from Barnum and Greenberg, forthcoming 1992) compares the age-specific liver cancer mortality rates from China, where HBV is prevalent, with those from the United States, where maternal-infant HBV transmission is rare, to illustrate the relative importance of this condition in developing country settings. A two-year prospective of 22,707 Chinese men in Taiwan documented that primary hepatocellular carcinoma and liver cirrhosis associated with HBV as accounted for approximately 20 percent of all deaths (Beasley, *et al.* 1981). Consistent with this, Elo and Preston (1992) review a number of demographic studies in East Asia and suggest that the Far Eastern Pattern of Mortality, characterized by very high death rates at older ages (30+) relative to younger ages and present primarily among males, may relate to excess mortality as a consequence of a high prevalence of chronic carriers of HBV.

Hepatitis B vaccine is now available and studies have documented that it is highly effective in preventing maternal-newborn transmission of HBV when administered to newborns (Francis, 1986). With recombinant genetic techniques, the cost of production of this vaccine has dropped to approximately \$1 per dose, making this a highly cost-effective health intervention in most developing country settings.

#### **b. Syphilis**

Syphilis and gonorrhea are two other infections transmitted from mothers to infants which can have consequences for adult health. Both of these problems are most serious in Sub-Saharan Africa (Over and Piot, forthcoming 1992). The prevalence of syphilis seroreactivity among pregnant women attending antenatal clinics has been found to range

from 4 to 15 percent in a number of regions in eastern and central Africa (Schulz, *et al.*, 1987). Based on prospective studies in a variety of settings, from 50 to 80 percent of the pregnancies in these infected women will have an adverse outcome caused by syphilis. In the large majority of cases, congenital syphilis will result in spontaneous abortion or perinatal deaths, however, in 10 to 20 percent of cases, there will be a surviving infant with latent congenital syphilis who may develop active manifestations later in life (Hira, *et al.* 1990). These may include blindness, deafness, paralysis, and a variety of bone lesions. Therefore, in some African populations where about 10 percent of childbearing women are infected, approximately 1 percent of newborns may have congenital syphilis which, if untreated, will result in disabling disease and premature death in adulthood (Schulz, *et al.*, 1987).

### **c. Gonorrhea**

Maternal newborn transmission of gonorrhea can lead to gonococcal ophthalmia neonatorum (GON) which, if untreated, often leads to blindness. While prophylaxis or treatment of the eyes with antibiotics is simple and highly effective, it is not available in most poor areas of the world where the vast majority of births occur at home.

The WHO gives a minimal estimate of the annual incidence of gonorrhea at 25 million cases (WHO, 1990). Again, as with syphilis, a high proportion of these will be in Sub-Saharan Africa where diagnosis and treatment are not generally available. The prevalence of *N. gonorrhoea* in pregnant women has been reported as ranging between 3 and 22 percent in a dozen countries in Sub-Saharan Africa (Schulz, *et al.*, 1987). These reported studies were undertaken in urban settings and some researchers believe that gonorrhea is more prevalent in towns than in rural settings. Since about one-third of the infants exposed to *N. gonorrhoea* during birth will develop GON if prophylaxis is not given,

one can estimate that the incidence of GON in neonates in Africa may range from 0.5 percent to 6 percent (Schulz, *et al.*, 1987). Considering that Sub-Saharan Africa has over 20 million births annually, this represents a very large number of children who are exposed to the risk of blindness. Unfortunately, there are no data on the incidence of blindness related to GON in developing countries.

## **B. Infectious Diseases of Childhood**

### **4. Tuberculosis**

Tuberculosis represents the classical example of an infection acquired in childhood which predominantly manifests itself with disease among adults. The epidemiological features of tuberculosis were elucidated by Frost in the 1930s (Frost, 1939). Tuberculin skin test surveys in developing countries generally reveal a rather consistent increase in the proportion testing positive for infection with each year of age up to about age 20. The general picture, as represented by a cohort studied in the Netherlands is that in populations where tuberculosis is endemic, approximately 40 percent of the infections will occur before the age of 5, 67 percent before age 10, and 90 percent by age 19 (Sutherland, 1976). Clinical disease, however, is infrequent with the primary infection; rather, after a latent period of some years, approximately 6 percent to 10 percent of infected individuals will go on to develop active tuberculosis. Eighty-five percent of these cases will be among adults in this most productive age group 15-59 years. About 45 percent of these will be sputum positive, continuing the cycle of disease transmission to the next generation of children. As shown in Figure 3, the vast majority of infectious cases are concentrated in adults between the ages of 15 and 59. The economic consequences of this disease are enormous when one considers the estimates that

tuberculosis accounts for 18.5 percent of all deaths in the 15 to 59 age group or 26 percent of all avoidable adult deaths (Murray and Feachem 1990).

Tuberculosis is the single most serious infectious disease in the developing world (Murray, *et al.*, forthcoming 1992). Annual infection rates are highest in Sub-Saharan Africa and Asia, ranging from 1 to 2.5 percent; in South and Central America, North Africa and Western Asia the range is 0.5 to 1.5 percent. These authors have estimated for the developing world in 1990 an annual incidence of 7.3 million cases and 2.7 million deaths.

With the diagnostic technology and chemotherapeutic agents currently available, demonstration projects in a number of developing countries have shown that short-course chemotherapy can be applied on a national scale with cure rates approaching 90 percent (Styblo, 1989). Epidemiologically, treatment of smear-positive tuberculosis will rapidly accelerate the decline in disease incidence. Analysis of health intervention programs has shown that tuberculosis case therapy is one of the most cost effective health interventions available (Jamison, forthcoming 1992).

## **5. Rheumatic Fever**

Rheumatic fever is a systemic complication of pharyngitis due to group A streptococcal infection which can result in inflammatory manifestations principally in the joints and the heart. Infection in children is associated with low socioeconomic status and crowding and continues to be prevalent in developing countries. While significant mortality accompanies the acute disease, the chronic consequences of rheumatic heart disease resulting in disability and ultimately death among young adults in the economically productive ages represents a significant cost to society. A recent WHO report notes that "...among the majority of the world's population, rheumatic heart disease remains the

most common cardiovascular cause of death in the first four decades of life." (WHO, 1988).

Rheumatic heart disease remains a significant problem in the developing world (Michaud, *et al.*, forthcoming 1992). Prevalence rates per 1000 among school-age children from surveys in different regions and countries of the world were: North Africa, 9.9 to 15.0; Nigeria, 0.3 to 3.0; Latin America, 1.0 to 17.0; Asia, 0.4 to 21; Pacific, 4.7 to 18.6. Hospital studies in nine Sub-Saharan African countries revealed that rheumatic heart disease accounted for from 10 to 35 percent of all cardiac admissions (Hutt, 1991).

The complications of group A streptococcal pharyngitis (GASP) can be prevented with early diagnosis and treatment with antibiotics. Community-based approaches to promote early detection of pharyngitis coupled with selection of cases for antibiotic therapy based on the use of a clinical algorithm have been proposed; at present, however, these are not cost-effective because of the rarity (0.4 percent) with which GASP is followed by rheumatic fever (Michaud, *et al.* forthcoming, 1992.) With the growing evidence of a genetic risk factor for rheumatic heart disease, there is an urgent need for more research to simplify the identification of susceptible persons so that more specific preventive interventions could be developed.

## **6. Polio**

Polio is a viral illness transmissible through fecal-oral and pharyngeal-oral routes. Although highly effective oral and injectable vaccines are available and the international community is moving toward universal childhood immunization, a substantial fraction of the world's children have not yet been reached, particularly in Sub-Saharan Africa and South Asia (Jamison, *et al.*, forthcoming 1992). The majority of the unimmunized children in developing countries will be infected in the first few years of life. In the 1980s, the

annual incidence of poliomyelitis was estimated at 200,000 to 250,000 cases, approximately 25,000 of whom died (WHO, 1990). Residual paralysis with lameness is the health condition of consequence for adults.

During the late 1970s and early 1980s, lameness surveys were carried out in many regions of the world. Table 2 summarizes the results of these surveys in Asia and Africa. The median prevalence of lameness due to polio ranged from 3 to 6 per 1000 with considerable variation in each of these settings. Based on these surveys, it is estimated that between 10 and 20 million people are currently living with disability due to polio.

The international community, with national governments, has embarked upon a program of global polio eradication (Grant, 1991). Already eradication efforts are proving highly effective in Latin America. China has also reached very high levels of vaccine coverage. It is likely that by the turn of the century polio will become a rare disease, although the disabled victims will be around for decades to come.

## **7. Trachoma**

Trachoma is a chronic infectious conjunctivitis caused by *Chlamydia trachomatis*. The disease is characterized by progressive exacerbations and remissions which, over a period of many months, result in gradual scarring of the cornea with progressive corneal opacity resulting in varying degrees of permanent vision loss or blindness. The infectious agent is transmitted among children by direct contact or by sharing contaminated articles such as towels and handkerchiefs. The disease can be effectively treated with antibiotic eye ointments, although this requires application two to four times a day for four to six weeks. Advanced disease with scarring requires surgical treatment.

Trachoma is one of the major causes of blindness in the world today. It accounts for 6 to 9 million blind persons representing about 25 percent of all the blind in the world



(WHO, 1990). The disease is endemic throughout large parts of East and West Asia. It is estimated that 500 million people live in areas with endemic blinding trachoma (WHO, 1990). Given the conditions of transmission, prevention will require education of the population to reduce disease transmission through improved hygienic conditions, early recognition of infection manifestations, and ready availability of treatment through a primary health care system.

## **8. Chagas' Disease**

Chagas' disease is a chronic disease caused by the protozoan *Trypanosoma cruzi*. This disease, which is limited to South and Central America, is also called South American trypanosomiasis (Marsden, 1986). (Another form of trypanosomiasis causes sleeping sickness in Africa). The agent of Chagas' disease is transmitted by contamination of the bite wound of the "assassin" or "kissing" reduviid bugs (*triatoma* and related *reduviidae*) with the infected feces of the insect. The bug vector typically lives in cracks in the walls, floor, or ceiling of primitive brick or wood houses built by poor people, most often in rural areas. The bug can be killed by insecticides, however, a control program requires a comprehensive approach involving application of insecticide, monitoring of bug infestation, and housing improvement to eliminate cracks that harbor the bug (Marsden, 1986).

Small children are typically infected while sleeping at night when the bug will leave its habitat to obtain a blood meal. The acute phase of infection in humans typically passes unnoticed, although the child may have some fever and an enlarged spleen or liver. The disease then progresses to the so-called indeterminate phase manifest only by positive serology. After two decades or more, signs of damage to target organs begin to appear, principally the heart. The destruction of the muscle fibers produces heart

failure and cardiac arrhythmias leading to death. Heart failure appears mainly between ages twenty and fifty.

Based on epidemiological studies, the WHO estimates the number of infected people in Latin America to be on the order of 15 to 18 million (WHO, 1990). Of infected individuals, approximately 10 percent go on to develop chronic Chagas' cardiopathy. Recent evidence suggests that chronic Chagas' disease may be responsible in some endemic areas for up to 10 percent of deaths among the adult population (WHO, 1990).

As noted above, Chagas' disease is strongly associated with poverty. Control measures will require a concerted and sustained effort to upgrade the housing conditions, particularly among the rural poor.

## **9. Schistosomiasis**

Schistosomiasis is a visceral parasitic disease caused by blood flukes of the genus *Schistosoma* (Warren, 1986; Warren, *et al.* forthcoming 1992). Fresh water snails in streams polluted by feces or urine are the intermediate hosts. Human infection follows contact by bathing or wading with the free swimming cercariae of the parasite that penetrate the skin and are carried by the bloodstream to the liver where they mature. Adult worms then migrate to the venules of the bladder or intestines. Three species cause clinical disease; *S. haematobium* affects the bladder while *S. mansoni* and *S. japonicum* involve the intestine. In these sites, the worms lay their eggs which penetrate the mucosal surface to be excreted in the urine or stool, continuing the cycle of transmission if the eggs enter fresh water with an intermediate snail host.

Because these worms do not multiply in the human host, the severity of symptoms relates to the intensity of infection which is governed by the rate of acquisition of new worms and the lifespan of the worms in the body (less than five years). Infections are

acquired through the course of childhood so that the heaviest worm burdens are typically seen in adolescence and young adults. Clinical disease primarily relates to lowgrade disability among adults secondary to immune responses in the host, producing some tissue destruction and fibrosis in the liver with intestinal infection, and in the bladder and ureters with genital urinary infection. On a population basis, the primary health impact of schistosomiasis is a decreased capacity for heavy work (Warren, *et al.* forthcoming, 1992). In a number of areas, heavy infection has been clearly implicated in reduced labor productivity. Death is rare.

Schistosomiasis is endemic in 76 countries in Asia, Africa, and Latin America. The WHO estimates that about 200 million people are infected with schistosome parasites (WHO, 1990). Elimination of schistosomiasis from the population will require major changes in human behavior and in environmental improvement in many populations to reduce the contact with infected water sources. A more practical and cost-effective intermediate term measure that is currently being considered is mass chemotherapy with the drug praziquantel (Warren, *et al.* forthcoming 1992). Mass administration of this chemotherapeutic agent to school-age children at intervals of about two years, while not interrupting transmission, could dramatically reduce the intensity of infection and, thus, the load of morbidity in the population.

#### **10. Helicobacter Pylori**

*Helicobacter pylori* are bacteria that are associated with chronic atrophic gastritis, an inflammatory precursor of stomach cancer. Stomach cancer is estimated to be the world's second most common cancer (after lung cancer) (Parkin, *et al.*, 1988). In the 1930s it was the most common cancer in the United States. Over the past fifty years there has been a dramatic decline in the incidence of stomach cancer in the United States

and Western Europe which has led some to proclaim an "unplanned triumph" (Howson, *et al.*, 1986). Stomach cancer rates, however, remain very high in much of Asia and Latin America (Barnum and Greenberg, forthcoming 1992). This can be seen in Figure 4 which compares age-specific mortality rates for stomach cancer in China and the United States.

The relationship between infection with *H. pylori* and stomach cancer has only recently begun to be elucidated. Over two decades ago, pioneering studies by Haenszel *et al.* (1972) of Japanese who had migrated to Hawaii and California showed that the risk of gastric carcinoma was determined largely by environmental factors early in life. It is now known that one difference between populations at high risk and those at low risk of gastric carcinoma is that in high risk populations there is a high prevalence of *H. pylori* infection among children, apparently associated with poor environmental sanitation (Correa, 1991). Once an individual acquires *H. pylori*, infection persists for life if not treated, producing the chronic atrophic gastritis associated with gastric carcinoma.

Because *H. pylori* infection is prevalent among adults in all populations studied, a number of epidemiologic studies were required to establish a causal relationship with gastric carcinoma. Initially these were case-control studies documenting that the risk of having stomach cancer was higher among persons who were currently infected than among uninfected persons (Correa, 1991). More definitive evidence for a causal relationship came from the recent investigations by Parsonnet *et al.* (1991) and Nomura *et al.* (1991) which demonstrated a higher risk of gastric carcinoma in individuals in whom infection with *H. pylori* could be documented by serological tests on blood samples collected twenty years earlier as compared to uninfected individuals. Based on migrant studies cited above and the fact that *H. pylori* is a lifelong infection, it appears that the risk of gastric cancer is primarily due to *H. pylori* acquired early in childhood. It should be

noted that although *H. pylori* is very prevalent in the adult populations, over a twenty-year period the risk of gastric carcinoma among infected individuals is relatively low, amounting to 2.5 percent. It is likely that, in addition to *H. pylori* infection as an initiator, co-factors, possibly excessive salt intake and a diet low in fresh fruits and vegetables, are important as promoters in inducing gastric carcinoma.

The data so far suggest that up to 60 percent of stomach cancers are attributable to *H. pylori* infection. While this implies that approximately 60 percent of the gastric carcinomas in these populations could be prevented if *H. pylori* infection were eliminated (by antibiotic treatment), this is not a practical measure. The dramatic decline in stomach cancer in the developed world is an encouraging sign; it suggests that by improving environmental sanitation to reduce the risk of acquiring *H. pylori* infection early in life, and by promoting better diets we may expect to see corresponding declines in gastric cancer in the developing regions of the world. These interventions will, of course, have immediate health benefits for the children as well.

#### **11. Epstein-Barr Virus**

Epstein-Barr (EB) virus is the agent commonly associated with infectious mononucleosis in children and young adults. Once EB virus infection occurs, a persistent (lifelong) infection follows. EB virus is spread through close contact, mainly by the oral-respiratory route. In areas of poor sanitation and hygiene in developing countries, primary EB virus infections usually occur in infancy and are silent or too mild to be diagnosed. In higher socioeconomic groups, primary exposure to EB virus is often delayed until adolescence or later when infections usually lead to infectious mononucleosis.

Persistent EB virus infection acquired in childhood is relevant to the health of adults because of the epidemiological evidence that this infection is involved in the etiology of Burkitt's lymphoma and nasopharyngeal cancer (Barnum and Greenberg, forthcoming 1992). Burkitt's lymphoma is essentially confined to Sub-Saharan Africa. Nasopharyngeal carcinoma, while rare in most of the world, is the most common cause of cancer death in some southern Chinese populations. Nasopharyngeal cancer occurs with peak frequency among adults in the 35 to 65 year age category.

As with other cancers, it seems clear that other factors in addition to EB virus are necessary for the induction of malignant disease. A suggested co-factor for nasopharyngeal cancer is traditionally prepared Chinese salted fish. Immunization with an EB virus vaccine has been proposed as a preventive measure in the southern Chinese population where nasopharyngeal cancer occurs at high frequency, however, an effective vaccine for EB virus has not yet been developed. Dietary change may be helpful although this is problematical since the precise co-factors are not known. Regarding Burkitt's lymphoma, epidemiological evidence suggests that malaria might be a co-factor. So far, no preventive measures have been proposed.

### **C. Nutritional Deficiencies in Infancy and Childhood**

#### **12. Protein energy malnutrition**

Chronic protein energy malnutrition (PEM) is a serious condition that continues to affect both children and adults in developing countries. The sequelae of PEM among children include excess morbidity and mortality, with growth stunting among survivors. The World Health Organization estimates that globally 25 percent, or 1.3 billion, of the world's population are stunted (WHO, 1990). Regionally in the developing world, the

prevalence of stunting ranges from 48 percent in Asia and 38 percent in Africa to 26 percent in Latin America (Table 3).

PEM and the accompanying stunting have a variety of health consequences for adults (Pinstrup-Anderson *et al.* forthcoming 1992; Gopalan, 1989). In terms of mental development, PEM has been associated with poor school performance and possibly delayed cognitive development. In working-age adults, stunting has been associated with lower productivity. Among pregnant women, short stature is a risk factor for life-threatening pregnancy complications, particularly obstructed labor due to pelvic insufficiency. Further, as noted earlier, maternal stunting is an important determinant of low birthweight; thus there is an intergenerational consequence of undernutrition.

As summarized in the review by Elo and Preston (1992), in recent years there has been growing evidence that height is related to risks of death among adults in developed countries. Waaler (1984), in an analysis of the relation between height and mortality among Norwegians, observed that the risks of death ages 40-59 for men who were below 165 centimeters was 71 percent higher than for men who were greater than 182.5 centimeters. This relationship was especially marked for cardiovascular diseases, tuberculosis and chronic obstructive lung disease. A similar investigation by Marmot, *et al.* (1984) of British civil servants revealed a strong relationship between short stature and mortality, particularly a higher risk for coronary artery disease. Elo and Preston (1992) summarize other work in Finland and in the U.S. supporting a relationship between short stature and coronary artery disease mortality both among men and women. The difference in relative risks of death between the shortest and tallest groups in these studies was generally a factor of 3. Elo and Preston (1992) also report on a recent study of 22,000 male physicians in the United States by the American Heart Association

showing that the risk of heart attack declined by 3 percent for every inch in height, a relationship that could not be accounted for by known risk factors such as obesity, high cholesterol, and elevated blood pressure.

Based on their review, Elo and Preston (1992, page 9) conclude that since "height is probably the best single indicator of nutritional conditions and disease environment in childhood... [these relationships] represent at present the firmest statistical support for the belief that childhood conditions can make a good deal of difference for adult death rates." With the available data, it is not possible to measure the potential magnitude of the impact growth stunting may have on adult mortality in developing countries. Given the very high prevalence of stunting that is reported above, however, it is probable that the impact is substantial and that significant reductions in adult mortality may be expected with improvements in childhood nutritional status among developing country populations.

### **13. Micronutrient deficiencies**

There are three micronutrient deficiency conditions in infancy and childhood that can impact on adult morbidity, particularly as it relates to intellectual development. These relate to iodine, iron, and vitamin A. (Levine, *et al.* forthcoming, 1992).

#### **a. Iodine**

Approximately 1 billion persons globally are at risk of iodine deficiency in the developing world with the highest risks in South and East Asia (Levin, *et al.*, forthcoming 1992). The WHO estimates that approximately 20 million people suffer from measurable mental and/or motor retardation due to iodine deficiency while 5.7 million suffer from full cretinism (WHO, 1990). Iodine deficiency disorders (IDD) are prevalent in highland areas in many countries. IDD is due either to inadequate intake of iodine because the soils and



water are deficient or because local diets may contain foods high in naturally existing "goitrogens" which interfere with the utilization of iodine.

The primary manifestations of severe iodine deficiency during pregnancy for the offspring are dwarfism and severe mental retardation known as cretinism. Of more concern than these extreme forms of deficiency are the possibility that non-cretinist children may be mentally and neurologically handicapped in endemic areas. This milder impairment may go unnoticed in many poor communities although it can limit social and economic growth (Stanbury, 1987).

Cretinism is obviously irreversible. It is also likely that mild mental retardation resulting from impaired structural development of the brain during fetal life is also irreversible. Thus, correcting iodine deficiency in reproductive-age women is of highest priority. In the short run this can be accomplished by injection of iodized oil (Lipiodol); over the long term, fortification of commonly used foods (salt) is the most cost-effective strategy.

#### **b. Iron**

Iron deficiency anemia affects approximately 800 million people worldwide (WHO, 1990). The regions with the highest prevalence of anemia are Africa and South Asia where upwards of 40 percent of the population is anemic. Lower rates in the range of 10 percent to 30 percent are seen in Latin America and East Asia. Major associated causes of iron deficiency anemia besides dietary deficiency of iron are heavy parasitic infections (hookworm and schistosomiasis) and repeated pregnancies and lactation (Levin, *et al.* forthcoming, 1992).

A significant consequence of iron deficiency anemia in infancy and childhood for adults is its potential effects on mental development. A number of investigations have

clearly documented that infants with anemia score lower on tests of mental development than infants without anemia (Soewondo, *et al.*, 1989). Of interest and concern in the long term is that after a period of iron supplementation therapy which results in a good hematologic response, previously anemic infants have not consistently shown improvement on their mental test scores (Levin, *et al.* forthcoming 1992).

Recently Lozoff *et al.* (1991) reported on a four-year follow-up of children who had iron deficiency anemia in infancy that had been corrected with iron treatment. These carefully controlled studies suggested that the previously anemic children had long-lasting developmental disadvantages as assessed by a variety of tests of mental and motor development when compared to a control group without anemia in infancy. These developmental disadvantages persisted when the studies were statistically controlled for a variety of other background risk factors. The authors concluded that while they could not rule out that earlier detection and more vigorous treatment of iron deficiency anemia in infancy and childhood could be effective in preventing a developmental disadvantage later in life, the safest approach, given current knowledge, would be vigorous efforts directed to the primary prevention of iron deficiency in the population.

### **c. Vitamin A**

Vitamin A deficiency afflicts around 40 million preschool children in 37 countries, producing an estimated 250,000 to 500,000 cases of blindness annually (West and Sommer, 1987). Approximately two-thirds of these, however, die within weeks to months after becoming blind (Sommer, 1982). Cumulatively the survivors account for an estimated 2.8 million or 10 percent of the blind persons in the world today (WHO, 1990). In the short term, vitamin A deficiency can be prevented by the administration of one

vitamin A capsule every six months, and this is the strategy in many developing countries. In the long run, dietary change and food fortification programs will need to be established.

#### **D. Environmental Hazards**

##### **14. Indoor air pollution**

Contrary to the general belief that air pollution is more severe in the cities of developed countries, recent studies by the UNEP/WHO Global Environment Monitoring Systems are demonstrating that the worst ambient conditions are in the cities of developing countries (Chen, *et al.* 1990). More importantly, studies of indoor air quality reveal that the largest pollutant concentrations and exposures are found in the houses in developing countries in both rural and urban areas.

The major source of indoor air pollution in developing countries is the cook stove. On a global scale, Chen *et al.* (1990) estimate that more than half of the world's households cook daily with unprocessed solid fuels such as dried animal dung, crop residues, wood, charcoal and coal. In a high proportion of these households, cooking takes place under situations where much of the smoke is released into the living area. A second, somewhat less prevalent source of indoor pollution is space heating with biomass fuels which is common at least part of the year in high altitude areas of Africa, Asia and Latin America.

Chen *et al.* (1990) review a wide range of epidemiological studies relating household air pollution to acute respiratory infections in children and chronic obstructive pulmonary disease (COPD) among adults. Their review describes studies in China, India, Nepal, The Gambia, and other countries documenting a strong relationship between the frequency of respiratory symptoms among children and their exposure to household smoke from cooking with wood and other biomass fuels. Correspondingly, adults in

these settings had higher rates of chronic bronchitis and chronic obstructive lung disease but it is not possible to determine whether adult COPD is due to childhood exposures and/or the cumulative effects of smoke at later ages.

COPD is a very serious health problem in most developing countries where there is heavy exposure to household smoke from open fires using biomass fuels. This is clearly illustrated in Figure 5 which compares the age-specific mortality rates for COPD from China and the United States for males and for females (Bumgarner and Speizer, forthcoming 1992). In the United States, COPD is due almost entirely to cigarettes so that COPD death rates are approximately three times higher in males than in females. As the figure illustrates, in China COPD mortality rates are four to six times higher than in the United States with death rates at essentially the same level among males and females. Furthermore, in China death rates in the rural areas are more than three times higher than in the urban areas, again reflecting the very high rates of exposure to indoor household smoke.

In the context of this review on the childhood precursors of adult disease, it must be noted that chronic obstructive lung disease typically occurs after two or three decades of smoke exposure. Thus, the childhood exposure alone cannot be blamed for these adverse consequences. On the other hand, it is likely that when exposure begins in infancy and childhood resulting in recurrent acute respiratory infections, and continues for a lifetime, the onset of disabling symptoms will begin earlier among adults and lead to chronic disability and death at much younger ages.

## **15. Lead exposure**

The addition of lead to gasoline has been called "the mistake of the 20th century" (Shy, 1990). Combustion of leaded petrols since 1925 accounts for about 90 percent of total atmospheric lead. In the United States in the peak year 1972, 250,000 metric tons of lead were utilized for leaded petrol amounting to an average of 2.4 pounds of lead per person per year (USEPA, 1986). National household surveys between 1976 and 1980, when lead free fuels were being introduced, have documented a direct correlation between declining ambient lead concentrations and blood lead levels in the United States population (Shy, 1990).

It is important to recognize how exposure to lead occurs in the population. Although combustion of leaded petrol initially disperses lead into the atmosphere, actually inhalation of lead from the air contributes only 1 to 2 percent of the total lead intake of humans. More important is indirect exposure to atmospheric lead via ingestion and inhalation of lead in dust, soil, food, and water impacted by the fallout of atmospheric lead. One study in Italy confirmed that an estimated 60 percent of blood lead levels in the city of Turin was attributed to ingestion of leaded petrol emission in dust, food, and water (Facchetti and Geiss, 1982). Not surprisingly, lead exposure is highest among children in urban areas where there is a high density of air, soil, and dust lead levels.

A number of epidemiological studies have documented that the developmental effects of chronic low level lead exposure in early life include low birthweight, impaired mental development in the first two years of life, I.Q. deficits in school-age children, and disturbances in sensory pathways within the central nervous system persisting for five or more years (Shy, 1990). These effects, particularly the neurological and cognitive effects, occur at very low blood lead levels. For example, recent studies in the U.S. and Australia

in the early 1980s documented evidence of measurable declines in cognitive functions among infants at blood lead levels that were lower on the average than those detected in U.S. school children based on measurements taken in the NHANES II Survey (Bellinger, *et al.* 1987; McMichael, *et al.* 1988). The data from these and other studies leads Shy to conclude that: "With respect to lead, there should be as little human exposure as possible, and all evidence points to a greater risk of a variety of adverse effects, particularly on cognition and hematological function at what were formerly considered normal blood lead levels" (Shy, 1990, p. 174).

The adverse impact of lead on human health is well documented in developed countries. Unquestionably the cognitive and neurological deficiencies detectable in children will have consequences for their intellectual development in school and their mental abilities as adults. There are essentially no data on the risks to lead exposure in developing countries, however, the rapid urbanization and increase in the use of motor vehicles indicate that it will be a growing problem in the future. In this context it is noteworthy that in the United States leadfree petrol was introduced in the 1970s in order to protect catalytic converters rather than to prevent disease in human beings. Catalytic converters have not been mandated in most developing countries because of cost considerations; therefore, the use of leaded petrol is the norm. Consequently one can predict that there will be a growing problem with lead exposure in these settings.

### **The Synergism of Childhood Risk Factors Producing Adult Disease**

The preceding discussion has examined a series of infections and other conditions in childhood in isolation from each other, focusing on their established or possible biological links to morbidity and mortality among adults. This approach, however, oversimplifies the situation since typically there are common underlying risk factors for

many of these conditions which are associated with the impoverished living conditions in developing country settings. Chronic obstructive pulmonary disease will be taken as an example to illustrate how multiple risk factors in childhood can be operating simultaneously and even synergistically to produce disability and death among adults (Samet, *et al.*, 1983).

Figure 8 illustrates schematically some of the possible underlying childhood determinants of COPD in developing country settings. The use of low-grade, biomass fuels for cooking results in heavy indoor air pollution which has been well established as a direct contributor to a high rate of acute respiratory infections in infants in children. Indirectly, indoor air pollution may potentially contribute to low birthweight if there is poor ventilation so that women in pregnancy are exposed to significant concentrations of carbon monoxide (Mavalankar, *et al.*, Trivedi, 1992). More importantly, under impoverished conditions the mothers may already be stunted and this condition, along with poor diets and heavy exertion during pregnancy, can result in low birthweight infants. Low birthweight, as noted earlier, is associated with impaired lung development; this also increases the risk of acute respiratory infection. In the long run, all of these conditions in combination become precursors of chronic airway obstruction leading to COPD.

A similar scenario may be sketched out for infant malnutrition which can result in growth faltering in childhood producing the long-term health consequences of stunting among adults noted earlier. As with COPD, there are social and environmental determinants of growth faltering and stunting including poor hygiene and sanitation leading to a high incidence of diarrheal disease.

A key point about these theoretical examples is that curative interventions limited to the treatment of acute respiratory infections and episodes of diarrhea can be lifesaving

in the short-run but may not produce major reductions in adult morbidity and mortality in the long-run unless the underlying risk factors are addressed. In the cases cited above, improvements in stove construction, household ventilation, and water and sanitation programs might be expected to produce both short-term and long-term health gains in the population. Relevant in this context is an analysis by Preston and Van de Walle (1978) of the gains in survival in a number of French cities in the last century following the improvements in water supply. Data were available to document that over several decades after sanitary improvements were instituted, gains in survival were initially seen in infants and children and then successively in older age groups as the young cohorts aged over time.

#### **The Adult Mortality Impact of Childhood-Acquired Diseases - Country Studies**

The data presented above on individual diseases and conditions provides a general assessment of the morbidity and mortality consequences of these conditions for adult health. While the numbers of persons affected on a global scale are in the tens of millions, it is difficult to assess from such data the relative importance of these childhood conditions as compared to other diseases acquired later in life which contribute to adult morbidity and mortality. One problem with making such assessments is the fact that very few developing countries have adequate data at the national level on cause-of-death. India does have a national sample registration system for vital events which in recent years has included cause-of-death. These data have limitations, as cause-of-death is based on lay reporting. Indian data do reveal that among adults ages 15-54, tuberculosis alone accounted for 18 percent of deaths among males and 11 percent of deaths among females, indicating that this disease is not inconsequential in contributing to premature mortality (Feachem, *et al.*, 1991).



Much better data are available from China which has a national sample registration system providing cause-of-death information, most of which is medically certified, for more than 100,000,000 people. Table 4 from Feachem, *et al.*, (1991) summarizes the leading causes of death for Chinese men and women between the ages of 15 and 60 in the year 1988. Noteworthy, cancers of the liver and stomach, primarily due to infections acquired in infancy, account for 13 percent of deaths in men and 9 percent in women. COPD accounts for 11 percent in both men and women. Tuberculosis and rheumatic heart disease together account for 6 to 7 percent of deaths, while chronic liver disease, much of which is related to hepatitis B virus, accounts for another 3 to 4 percent. Overall, conditions which are largely related to childhood precursors accounted for more than 30 to 34 percent of all of the premature and largely preventable deaths in this age group.

### **Conclusion**

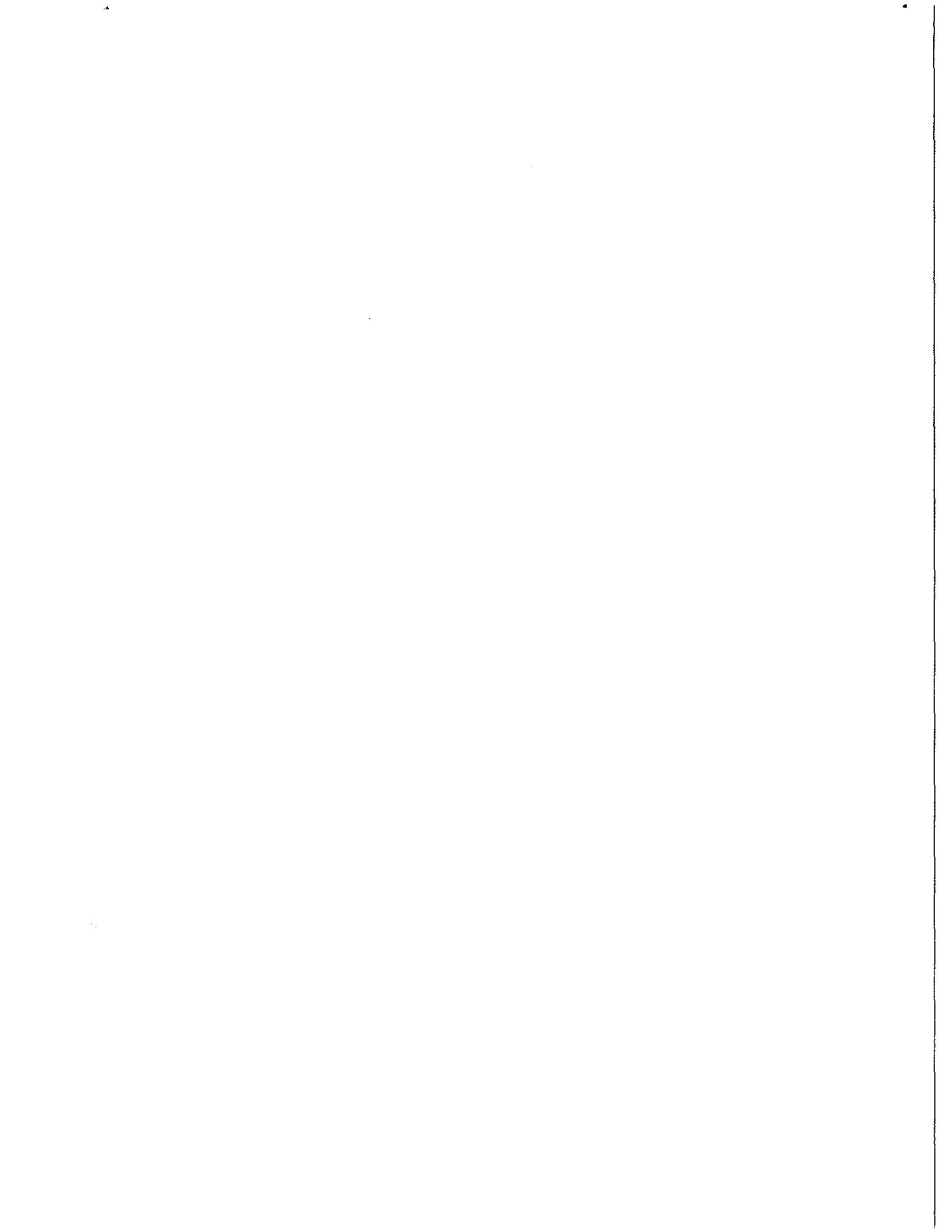
Typically when one considers the health conditions in developing countries, the focus of attention is on the high levels of infant and child mortality. This is reasonable because children under five generally account for 15 to 20 percent of the population and the vast majority of deaths in this age group are preventable. What is less appreciated is that the surviving adults in these populations also experience very high rates of preventable morbidity and premature mortality. For example, while we may expect to see 6 to 10 percent of adults dying between the ages of 15 and 60 in developed countries, in developing countries upwards of 25 to 35 percent of adults may die in this period of life. As this review suggests, as many as one-third of these premature deaths may be the consequence of infections and other conditions acquired in infancy and childhood. Although not discussed here, it should be clear that since most of these fatal conditions produce death only after a prolonged chronic illness, the burden of morbidity in the

population is far greater. Added to this must be the burden of lifetime disability from non-fatal conditions of childhood producing blindness, paralysis, mental retardation, etc.

The recent child survival revolution in the developing world promoted by UNICEF, the WHO and the international donor community, has brought to the forefront of the world's attention the cost-effectiveness of a number of selected technical interventions such as immunizations and oral rehydration therapy in saving the lives of infants and children. More recently, additional interventions such as antibiotic therapy for acute respiratory diseases have been added to the child survival strategy. For the most part, the goal of child survival programs has been to produce an immediate mortality reduction, and the accomplishments have been noteworthy in many countries (Grant, 1991). A recent exception to this short-term strategy has been the introduction of hepatitis B vaccine into childhood immunization programs in a number of countries in Africa and Asia, including China.

The premise of this review is that far more attention should be given to the long-term as well as short-term benefits of programs to promote child health. This is relevant not only for direct child health interventions like vaccines but particularly relates to interventions which will have cross-cutting effects on reducing the risks of multiple conditions simultaneously. Interventions such as reducing indoor air pollution, upgrading housing and sanitation, and improving pregnancy care and nutrient intake would fit in this category. Too often, when only narrowly defined, short-term benefits are taken into account, such broad-based intervention programs are considered too costly. However, as shown by Briscoe (1978) in the case of improving water supply, when the multi-faceted and long-term health benefits are considered, intervention programs in these areas become quite cost-effective.

A major limitation of this analysis is the paucity of empirical data from population-based studies, particularly from developing countries, which could provide a firm basis for establishing the links between childhood exposures and adult morbidity and mortality. More precise knowledge of these linkages would be important for policy and programmatic purposes as well as having scientific significance. While we can generally expect health conditions to improve in developing countries with rising incomes and better diets and living conditions, in a resource-constrained environment it would be invaluable for health policymakers to have better information about specific linkages between childhood conditions and adult morbidity and mortality so that development strategies could be formulated that would maximize the health gains to the population. In this context, as noted in this paper as well as in the review by Elo and Preston (1992), such health policies and programs may not only be directed toward reducing the current burden of disease seen in developing countries, for example, by the introduction of hepatitis B vaccine, but also limiting the emergence of the "diseases of development" such as cardiovascular disease by promoting the maintenance or adoption of healthy dietary practices in infancy and childhood as economies grow. Given the potential magnitude of the health gains in populations that could be achieved by directing more attention to risks and exposures in childhood, the importance and need for far more research in this area should be self-evident.



**TABLE 1**

**The Consequences of Selected Infant and Childhood Health Problems  
for Morbidity and Mortality in Adults**

| <b>Conditions in Children</b>                              |   | <b>Consequences in Adults</b>   |
|--|---|---|
| <b>A Perinatal conditions</b>                              |   |   |
| 1  | Low birthweight                             | Growth stunting, chronic obstructive pulmonary disease  |
| 2  | Birth trauma, asphyxia, metabolic disorders | Brain damage, cerebral palsy, mental retardation  |
| 3  | Congenital and perinatal infections         |   |
|  | a. Hepatitis B                              | Liver cancer, chronic liver diseases  |
|  | b. Syphilis                                 | Blindness, deafness, paralysis, bone disease  |
|  | c. Gonorrhea                                | Blindness   |
| <b>B Infectious Diseases of Childhood</b>                  |   |   |
| 4  | Tuberculosis                                | Tuberculosis  |
| 5  | Rheumatic fever                             | Chronic rheumatic heart disease   |
| 6  | Poliomyelitis                               | Residual paralysis  |
| 7  | Trachoma                                    | Blindness   |
| 8  | Chagas' disease                             | Heart failure   |
| 9  | Schistosomiasis                             | Liver cirrhosis, general debility   |
| 10   | Helicobacter pylori                         | Stomach cancer  |
| 11   | Epstein-Barr virus                          | Nasopharyngeal cancer, Burkitts lymphoma  |
| <b>C Nutritional Deficiencies in Infancy and Childhood</b> |   |   |
| 12   | Protein-energy malnutrition                 | Growth stunting, obstetrical complications, cardiovascular disease, chronic pulmonary diseases, Intellectual impairment |
| 13   | Micronutrient deficiency                    |   |
|  | a. Iodine                                   | Cretinism, Intellectual Impairment  |
|  | b. Iron                                     | Learning disabilities, intellectual impairment  |
|  | c. Vitamin A                                | Blindness   |
| <b>D Environmental Hazards</b>                             |   |   |
| 14   | Indoor air pollution                        | Chronic obstructive pulmonary disease, lung cancer  |
| 15   | Lead exposure                               | Intellectual impairment   |

| <b>TABLE 2</b>                                     |                          |                            |                |
|--|--------------------------|----------------------------|----------------|
| <b>Prevalence of Lameness Due to Poliomyelitis</b> |                          |                            |                |
| <b>Region</b>                                      | <b>Number of Surveys</b> | <b>Prevalence per 1000</b> |                |
|  |                          | <b>Median</b>              | <b>(Range)</b> |
| Asia   | 19                       | 3                          | 0.4 - 17       |
| Sub-Saharan Africa                                 | 16                       | 6                          | 0 - 12         |
| Near East/North Africa                             | 12                       | 4                          | 1 - 10         |

Source: Jamison, Torres, Chen and Melnick, forthcoming 1992.

**TABLE 3****Global estimates of the prevalence of stunting by region, 1985**

| <b>Region*</b>        | <b>Approximate<br/>Total Population<br/>(millions)</b> | <b>Percent<br/>Stunted</b> | <b>Total Stunted<br/>(millions)</b> |
|-----------------------|--|----------------------------|-------------------------------------|
| Africa                | 448  | 37.9                       | 125                                 |
| Americas              | 722  | 18.5                       | 134                                 |
| Southeast Asia        | 1309   | 47.8                       | 626                                 |
| Europe                | 842  | 3.8                        | 32                                  |
| Eastern Mediterranean | 369  | 26.4                       | 97                                  |
| Western Pacific       | 1562   | 18.7                       | 293                                 |

\*WHO Regions

Source: WHO 1990.

**TABLE 4**

**Percent Distribution of Deaths by Cause  
for Chinese Women and Men in the Age Group 15-59  
1988**

**Causes Marked by Asterisk (\*) are Largely Related to Childhood Conditions**

|   | <b>Causes of Death</b>                             | <b>Women (%)</b> | <b>Men (%)</b> |
|---|--|------------------|----------------|
| 1 | <b>Communicable</b>                                | <b>7.1</b>       | <b>7.8</b>     |
|   | Tuberculosis                                       | 3.5*             | 3.8*           |
| 2 | <b>Maternal</b>                                    | <b>1.8</b>       | <b>-</b>       |
| 3 | <b>Cancer</b>                                      | <b>23.6</b>      | <b>27.3</b>    |
|   | Liver  | 4.3*             | 8.3*           |
|   | Stomach  | 4.8*             | 5.0*           |
|   | Lung   | 3.8              | 3.9            |
|   | Esophagus  | 2.5              | 2.9            |
|   | Colon-rectum                                       | 1.4              | 1.4            |
|   | Nasopharynx  | 0.3*             | 0.9*           |
|   | Breast   | 1.7              | -              |
|   | Cervix   | 0.8              | -              |
| 4 | <b>Cardiovascular</b>                              | <b>23.8</b>      | <b>20.4</b>    |
|   | Cerebrovascular                                    | 11.2             | 10.8           |
|   | Ischemic   | 4.3              | 3.6            |
|   | Rheumatic  | 4.3*             | 2.2*           |
|   | Hypertensive                                       | 2.0              | 2.3            |
| 5 | <b>Respiratory</b>                                 | <b>9.9</b>       | <b>10.4</b>    |
|   | COPD <sup>a</sup>                                  | 9.5*             | 9.3*           |
| 6 | <b>Digestive</b>                                   | <b>5.6</b>       | <b>7.5</b>     |
|   | Chronic liver disease                              | 2.6*             | 4.2*           |
| 7 | <b>Endocrine</b>                                   | <b>0.8</b>       | <b>0.8</b>     |
|   | Diabetes   | 0.6              | 0.8            |
| 8 | <b>Other non-communicable</b>                      | <b>6.5</b>       | <b>5.7</b>     |
| 9 | <b>Injuries</b>                                    | <b>20.9</b>      | <b>20.1</b>    |
|   | <b>All Causes</b>                                  | <b>100.0</b>     | <b>100.0</b>   |
|   | Probability of dying (%)<br>between ages 15 and 59 | 11.87            | 14.29          |

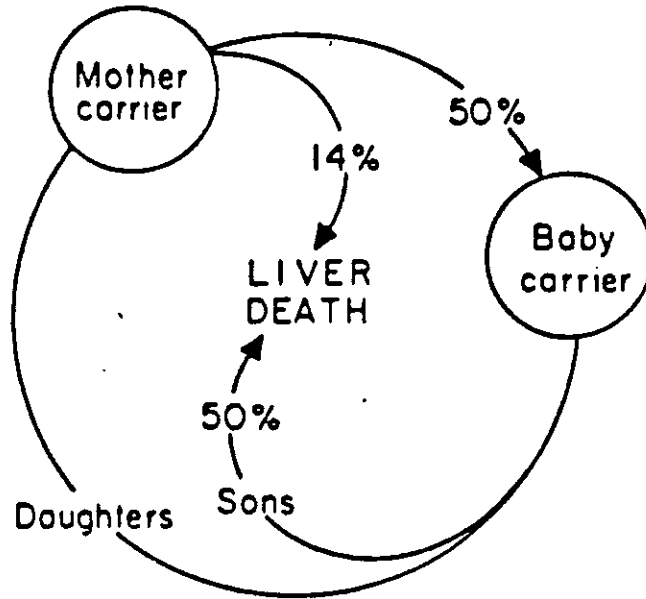
<sup>a</sup> Pulmonary heart disease is included with COPD.

Source: Derived from Table 2.14 in Feachem, et al, 1991.



FIGURE 1

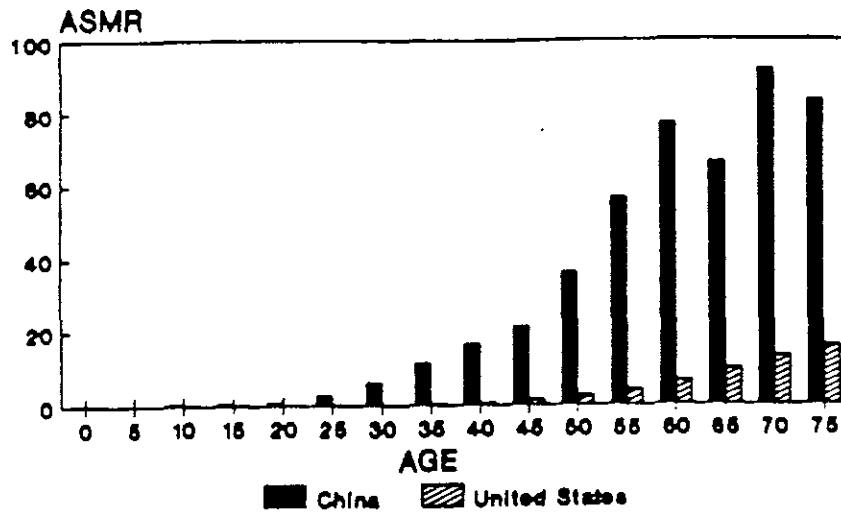
Schematic Representation of the Cycle of HBV Infections, Chronic Liver Disease, and Liver Cancer from Generation to Generation



Source: Beasley, 1982.

FIGURE 2

Liver Cancer: Age Specific Mortality Rates per 100,000

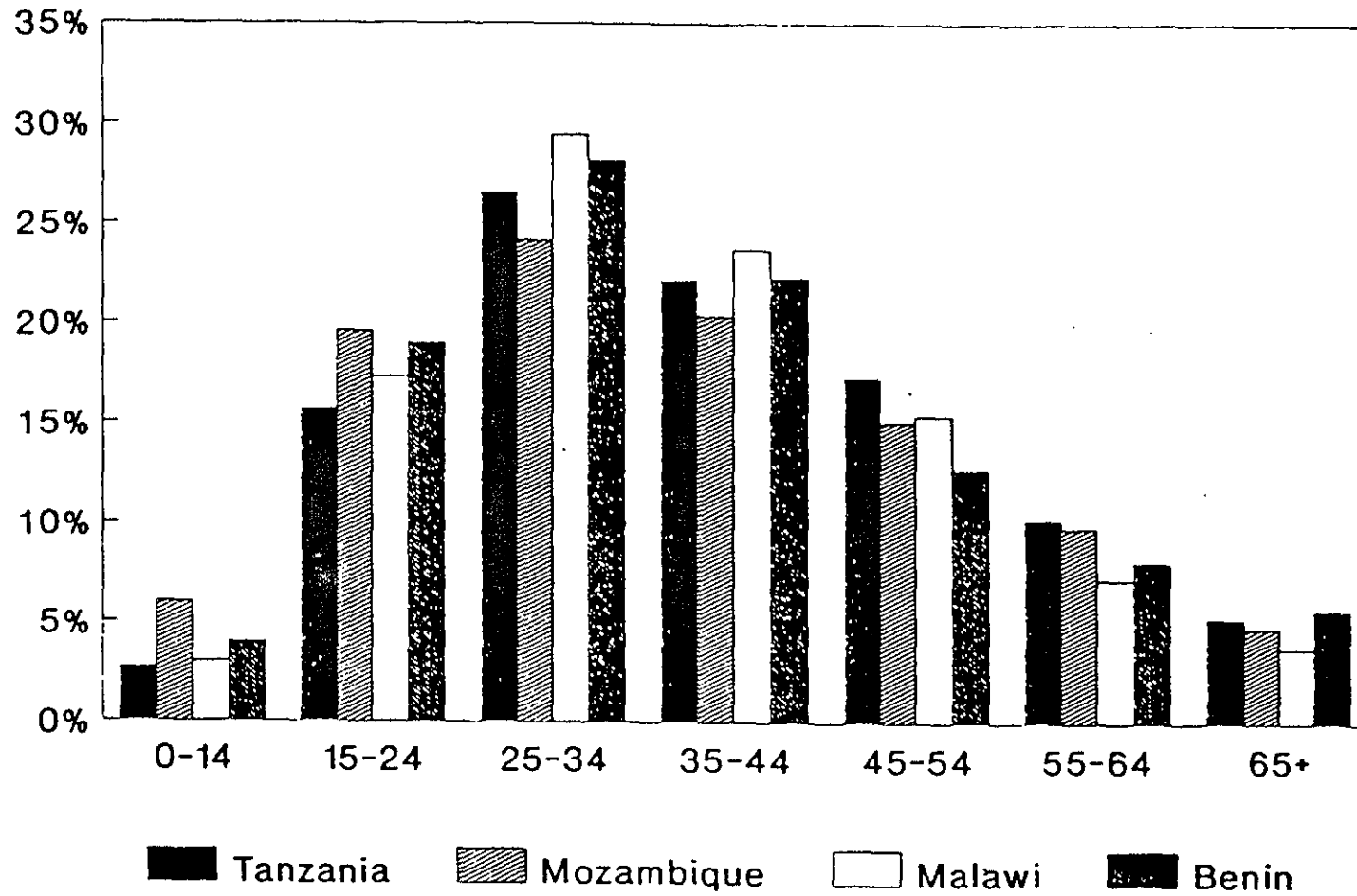


Source: China 1986 DSP and US 1987 NIH

Reference: Barnum and Greenberg, forthcoming 1992.

**FIGURE 3**

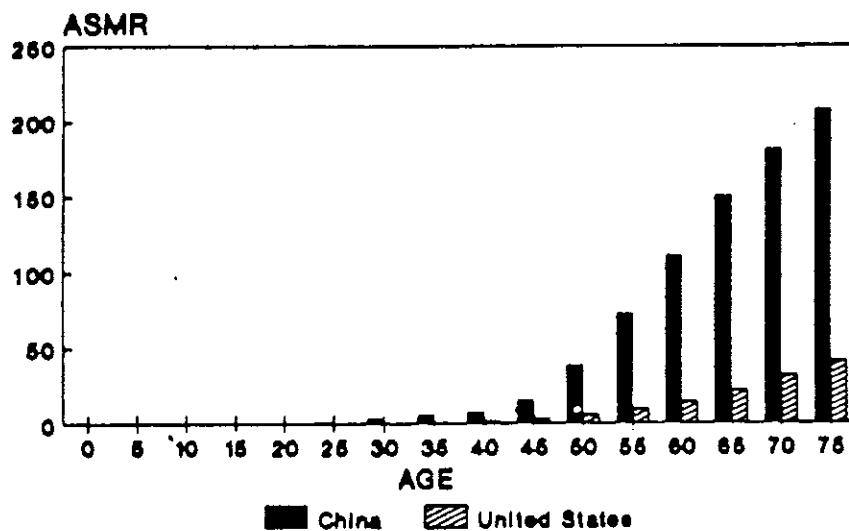
**Age-Distribution of Smear-Positive Tuberculosis  
in Four Sub-Saharan Tuberculosis Programmes**



Source: Murray, Styblo, Rouillon (Figure 2), forthcoming 1992.

FIGURE 4

Stomach Cancer: Age Specific Mortality Rates per 100,000

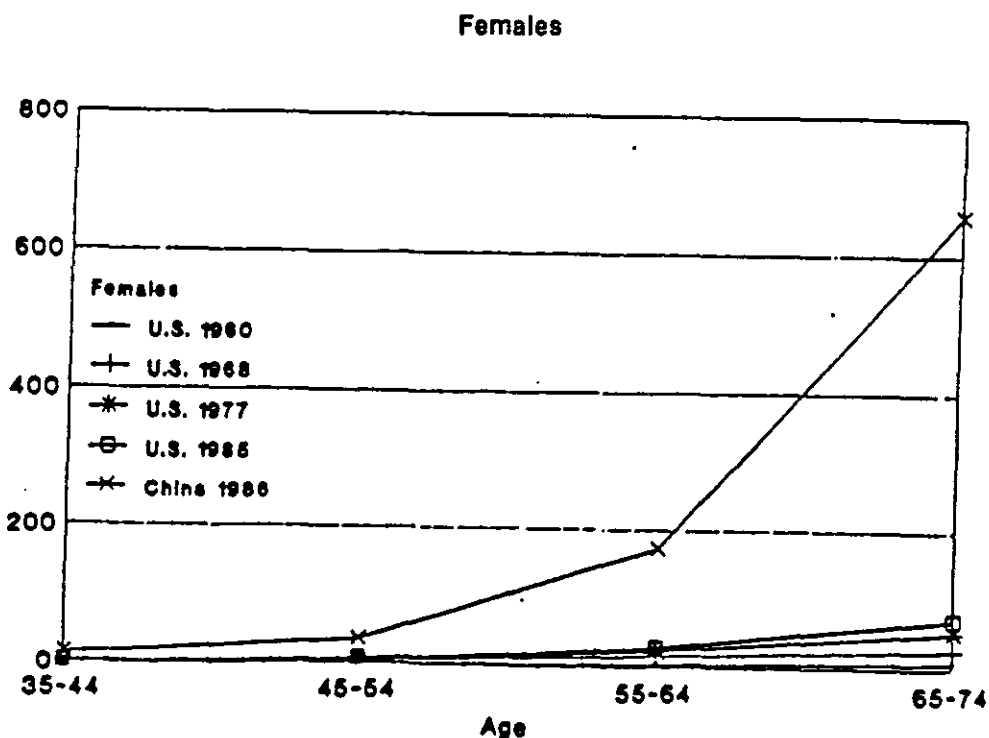
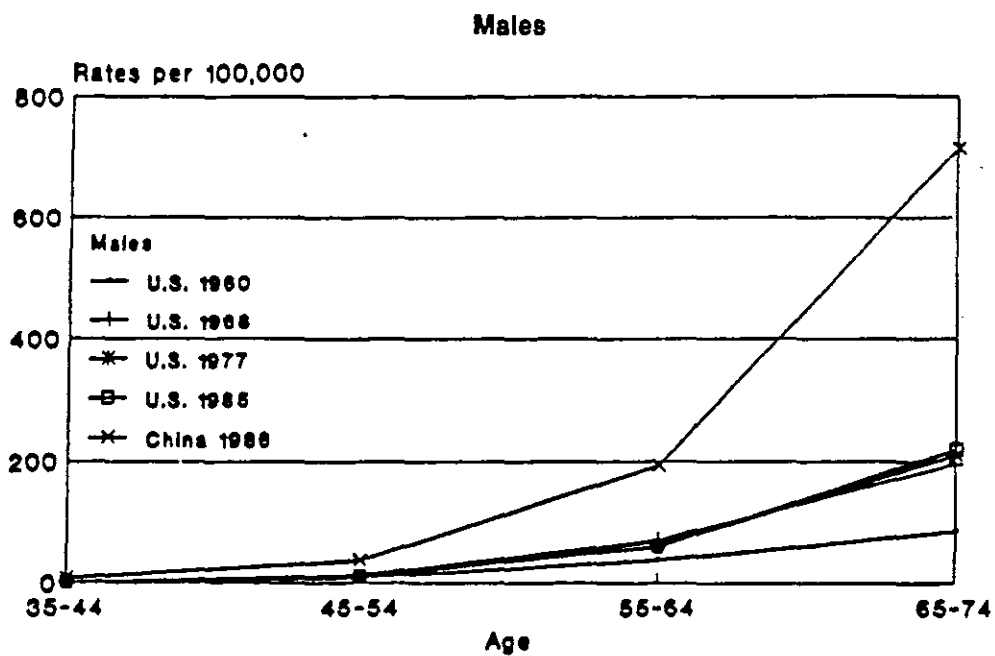


Source: China 1986 DSP and US 1987 NIH

Reference: Barnum and Greenberg, forthcoming, 1992.

FIGURE 5

Age-Specific Mortality Rates for COPD  
China and the United States

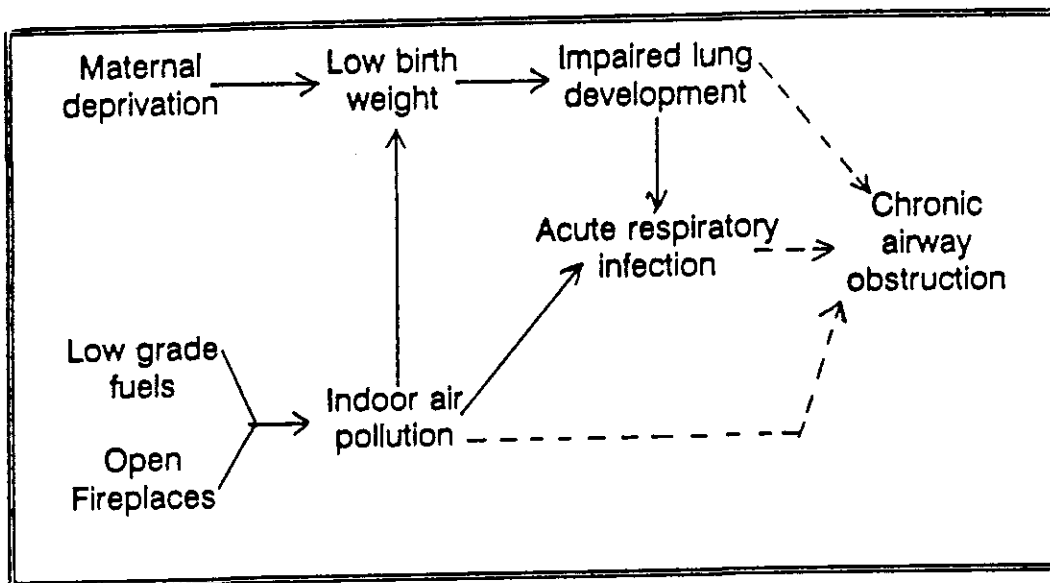


Source: NCHS for U.S.; DSP data for China

Reference: World Bank, 1990.

FIGURE 6

Underlying/Childhood Determinants  
of Chronic Obstructive Pulmonary Disease



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