

---

# *Reducing Perinatal and Neonatal Mortality*

*Child Health Research Project Special Report*



**Report of a Meeting**  
**Baltimore, Maryland**  
**May 10 -12, 1999**  
*Volume 3 Number 1*

---

## *Sponsors*

*The Child Health Research Project*

*Johns Hopkins Family Health and Child Survival*

*World Health Organization—Department of Child and Adolescent Health and Development*

*Harvard: Applied Research on Child Health*

*ICDDR,B: Centre for Health and Population Research*

*International Clinical Epidemiology Network (INCLLEN)*

*The Maternal and Neonatal Health Program*

The international public health and development community has had much success, but has many remaining challenges. Over the last thirty years maternal and infant mortality has declined, and people are generally living longer lives filled with greater opportunity. And yet there remains an unfinished agenda in child survival. Twelve million children under the age of five continue to die each year from preventable causes. Five million die within the first 28 days of life, and almost two-thirds of those die within the first week. Add to this 4.3 million annual fetal deaths, and the importance of combating neonatal and perinatal mortality becomes self evident.

Better means must be found to increase early diagnosis and treatment of perinatal and neonatal infections. Greater understanding of the causes of low birth weight and premature birth are necessary to decrease their incidence. As the world approaches the new millenium, we must renew our commitment to increase coverage of prenatal care; and guarantee the presence of trained attendants at each birth to safely deliver our children into their new world.

The public health landscape is constantly shifting, presenting us with new problems to solve. The AIDS pandemic continues its terrifying spread, undoing many public health gains. Many infectious diseases that we thought had been vanquished, such as tuberculosis and malaria, are reemerging, and immunization rates in many parts of the world are either stagnant or declining. The key to mastering these challenges is having a cadre of innovative researchers breaking new ground and testing the effectiveness and feasibility of new approaches.

The discussions at this conference and follow-up meetings will be used to guide research, develop programs for implementation and formulate national health policies. Basing our decisions on solid empirical evidence will allow the international community to build upon its successes and avoid future failures. More than nine million deaths will continue to occur before or just after birth each year, unless the international health community finds solutions for and implements programs to reduce these unnecessary deaths. As we return to our laboratories and offices, let us think of those nine million, and let them remind us why we need better answers to the problems of perinatal and neonatal mortality now.

*Duff Gillespie, Ph.D.,  
Deputy Assistant Administrator  
USAID Population, Health and Nutrition/Global Programs*

The World Health Organization estimates that more than nine million infants die before birth or in the first few weeks of life each year, and that nearly all of these deaths occur in developing countries. Most of these deaths are caused by infectious diseases; pregnancy-related complications such as *placenta previa* and *abruptio placentae*; delivery-related complications, including intrapartum asphyxia, birth trauma, and premature birth. Sadly, very few programs currently exist to specifically target perinatal and neonatal mortality. However, a cost-effective, and efficient way to introduce interventions would be to make additions to already existing programs.

Priority interventions prior to birth include: increasing the quality and scope of syphilis screening; improving the diagnosis and treatment of ascending reproductive tract infections in pregnant women; expanding maternal immunization with tetanus toxoid; including malaria prophylaxis in routine antenatal care visits, and nutritional support for pregnant women to improve birth outcomes.

Regarding delivery, programs are urgently needed for regular re-education of community health workers and the use of economic incentives to improve the identification and management of malpresentation and prolonged labor; referral of complicated cases to health center or hospital, and combating the barriers to referral compliance, including transportation of mothers and care of other children.

In the early weeks of life, the lives of many neonates could be saved by wider use of resuscitation techniques for asphyxiated infants; proper management of neonatal sepsis and other infections; skin-to-skin Kangaroo Care for preterm infants, and immediate and exclusive breastfeeding for all children.

Research is needed to determine the causes of, and risk factors for neonatal infections at the community level. Specific studies include: community-based surveillance to identify the principal bacterial and viral agents of neonatal infections and their drug resistance profiles, and assessment of the consequences of sexually transmitted diseases to fetuses and newborns. Also useful would be evaluation of neonatal care provided in the home by caretakers, traditional birth attendants, and community health workers, and following cohorts of neonates for infectious outcomes.

Integrated Management of Childhood Illness (IMCI) is being adapted for acute management of common infectious illnesses in the neonate. Priority research in the design of diagnosis and management approaches include: identification of the signs and symptoms that are most predictive of acute neonatal infection; development of an algorithm for use in identifying neonatal infection, and training and testing the abilities of community health workers to use the algorithm to identify acutely infected neonates.

Since more than 60% of infants are born at home in developing countries, more knowledge is needed at the community level regarding obstetric care and care for neonatal illness. Priority research includes the development of training curricula and continuing medical education for mid-level health workers, including traditional birth attendants. Also needed is the design of a package of simple practices for the routine post-partum care of neonates born in the community, including proper thermal control; recognition and resuscitation of asphyxiated neonates; promotion of early and exclusive breast feeding; application of prophylactic antibiotics to the eyes; optimal skin and hygienic cord care; and provision of immunizations. Evaluation of program effectiveness and impact is also necessary.

---

In 1994, 45 million pregnant women were living in malarious areas, with over 23 million in Sub-Saharan Africa alone. In settings of moderate to high malaria transmission, malaria may cause up to 30 percent of preventable low birthweight in newborns. Research priorities for malaria prevention and treatment include: efficacy studies of presumptive, intermittent treatment as part of routine antenatal care in areas of high transmission; design of methods for treatment during pregnancy using safe, effective and simple regimens in areas of high, medium, and low transmission; evaluation of the safety and efficacy of newly available antimalarial drugs (alone or in combinations) for treatment and prevention in pregnancy, and studies of means to reduce malaria exposure during pregnancy such as insecticide-permeated bed nets.

Low birth weight (LBW), or birth weight less than 2500 grams, is one of the principal contributors to neonatal morbidity and mortality worldwide, and accounts for up to 70% of neonatal deaths in some countries. Intrauterine growth retardation (IUGR) is the most common form of LBW in the developing world (accounting for more than 60%), whereas most low birth weight in infants in developed countries is due to prematurity. Risk factors for IUGR include untreated urinary tract infections (bacterial vaginosis); ascending reproductive tract infections, including syphilis, gonorrhea and chlamydia; low pre-pregnancy maternal weight and height, and low caloric intake and poor weight gain during pregnancy. Importantly, the problem of low birth weight is intergenerational: low birth weight infants remain poorly nourished during childhood and grow up to be stunted adults who in turn give birth to small infants, and thus must be combated at several points during the life cycle.

Specific research activities to reduce low birth weight due to bacterial vaginosis and sexually transmitted diseases include: surveillance studies to establish the rate and etiology of bacterial vaginosis in different countries; evaluation of simple methods for detection of bacterial vaginosis, and appropriate treatment, such as comparing a once versus three-times daily treatment with metronidazole, and development of strategies to improve knowledge and practice of methods to prevent sexually-transmitted diseases.

Studies to increase birth weight by lowering maternal malnutrition and undernutrition throughout the life cycle include: evaluation of the safety and efficacy of maternal caloric supplementation for reducing low birth weight; design of strategies to improve caloric intake before and during pregnancy with the use of locally available and acceptable food supplements; development of methods to reduce maternal anemia through the use of iron supplements, antihelminths and antimalarials; evaluation of micronutrient supplementation (vitamin A, calcium and zinc) for the reduction of LBW, and improved neonatal health; and testing of optimal delivery methods for micronutrient supplementation of children, adolescents and women.

One of the greatest challenges facing the international public health community is creating sustainable interventions in countries where the needs are greatest. Crucial to the success of programs is national ownership, and public-private partnerships to ensure long-term funding. Finally, an ongoing dialogue



must be established between governments and researchers to combat perinatal and neonatal mortality. Governments must be able to call upon researchers to help them solve health problems, and research results must be used to formulate national programs and policies.

---

*Introduction  
to the  
Meeting*

In May of 1999 USAID's Child Health Research Project and Maternal and Neonatal Health Program sponsored a meeting on Reducing Perinatal and Neonatal Mortality that was intended to help

- **understand the magnitude and determinants of perinatal and neonatal mortality**
- **identify interventions that can be implemented now**
- **determine needed research**

The meeting attempted to define risk factors for perinatal and neonatal mortality; identify immediate causes of mortality; establish the efficacy of interventions in ideal situations, and their effectiveness when implemented in programs; and determine future program and research priorities.

Perinatal mortality is usually defined as a death of the fetus after 22 weeks of gestation or of the newborn through the first week after birth. Neonatal mortality is death of a live-born infant in the first 28 days of life. Thus, the two periods for mortality assessment overlap in the first week after birth (referred to as the early neonatal period). Because the causes of perinatal and neonatal mortality are similar, interventions to prevent these deaths can appropriately be considered together. In most of the world, under-5 year and infant (under-1 year) mortality rates have declined substantially in the past three decades. In spite of this overall decline, largely due to the success of programs targeting family planning and health services for children, neonatal mortality levels have declined less quickly and now make up 40% to 70% of all infant mortality in developing countries. To further reduce child mortality, a new focus of programs will have to be on reducing neonatal deaths, particularly those in the first week of life.

Most perinatal and neonatal deaths are caused by infectious diseases, such as sepsis and pneumonia; pregnancy-related complications, such as placenta previa and abruptio placentae; and delivery-related complications, including premature birth, intrapartum asphyxia and birth trauma. Additionally, there are many indirect causes of early infant death, including poor maternal health, untreated maternal infections, including sexually-transmitted diseases, urinary tract infections, and chorioamnionitis. Failure to fully immunize adolescent girls and pregnant women also increases neonatal deaths from tetanus, as does unsanitary delivery and umbilical cord care. Premature birth, fetal malnutrition, and failure to exclusively breastfeed also contribute to the risk of early death. Other indirect causes of perinatal and neonatal death include inability to recognize severe illness in a newborn, poor care-seeking behavior, and inadequate access to good quality medical care. Underlying these direct and indirect causes is widespread poverty, illiteracy and gender discrimination faced by both mother and her female children in developing countries.

Perinatal and neonatal mortality can be addressed by interventions in pregnancy, during labor and delivery, and in the first few weeks of an infant's life. For each possible intervention, it is necessary to determine what proportion of the risk factor or cause could be addressed, the impact of the intervention in an ideal program setting and most importantly its effectiveness in actual developing country program conditions. For program efforts already underway, it is critical to learn how to make the intervention more successful. The need for action is compelling, as is the need for research that will enable informed policies, more effective and efficient programs, and greater reduction of perinatal and neonatal deaths.

*Robert E. Black, M.D., M.P.H.  
Meeting Organizer  
Johns Hopkins School of Public Health*

PERINATAL AND NEONATAL MORTALITY: LEVELS, TRENDS, CAUSES AND RISK FACTORS . . . . .	6
Levels and Trends in Perinatal and Neonatal Mortality in Developing Countries . . . . .	6
Causes of Perinatal Mortality . . . . .	7
Causes of Neonatal Mortality . . . . .	8
Child Spacing and Other Correlates of Perinatal and Neonatal Mortality . . . . .	10
Parity and Neonatal Mortality . . . . .	10
Effect of HIV on Perinatal and Neonatal Mortality . . . . .	11
Prematurity and Intrauterine Growth Retardation . . . . .	12
Multicountry Study of Infections in Early Infancy . . . . .	12
Complications of Pregnancy and Delivery . . . . .	12
 INTERVENTIONS PRIOR TO OR DURING PREGNANCY . . . . .	 15
Interventions against Toxic Exposures . . . . .	15
Nutritional Interventions . . . . .	16
Malaria Prophylaxis . . . . .	18
Prevention and Treatment of Reproductive Tract Infections . . . . .	19
Immunizations in Pregnant Women and Neonates . . . . .	20
 INTERVENTIONS DURING DELIVERY . . . . .	 21
Overview of Interventions during Delivery . . . . .	21
Prevention and Management of Delivery Complications . . . . .	22
Resuscitation of the Newborn . . . . .	23
 INTERVENTIONS AFTER DELIVERY . . . . .	 23
Overview of Interventions after Delivery . . . . .	23
Basic Care and Thermal Control in the Newborn . . . . .	24
Kangaroo Care Method . . . . .	24
Breastfeeding and Nutritional Support . . . . .	25
Prevention and Management of Infections . . . . .	26
 IMPLICATIONS FOR RESEARCH AND PROGRAMS . . . . .	 28
Community and Health System Barriers . . . . .	28
Program Experience with Integrated Interventions . . . . .	28
The Woman-Friendly Health Services Approach . . . . .	29
Adapting Integrated Management of Childhood Illness (IMCI) to the Neonatal Period . . . . .	30
Experience with Integrated Community Interventions in Indonesia . . . . .	32
Community-Based Neonatal Care in India . . . . .	32
 WORKING GROUP REPORTS . . . . .	 33
PROGRAM PRIORITIES . . . . .	33
RESEARCH PRIORITIES . . . . .	35
CONCLUSIONS . . . . .	38
REFERENCES . . . . .	39
ACKNOWLEDGMENTS . . . . .	44
LIST OF PARTICIPANTS . . . . .	45

*Table of Contents*

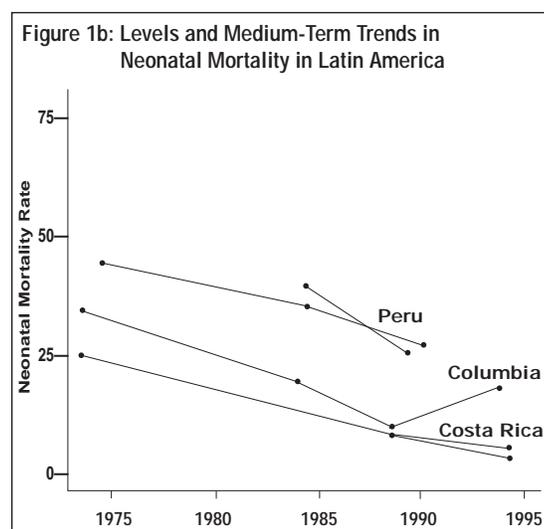
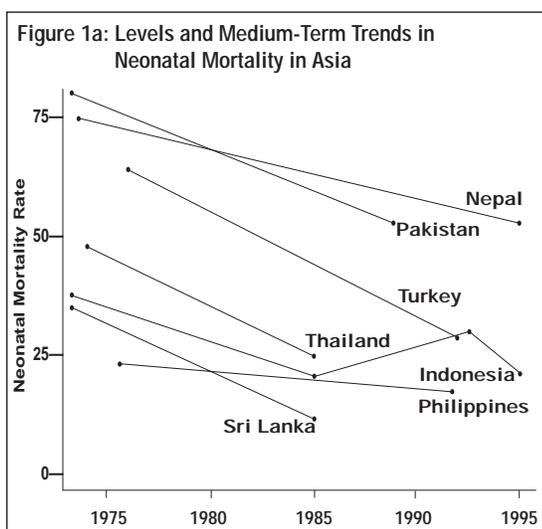
## Levels and Trends in Perinatal and Neonatal Mortality in Developing Countries

Ken Hill began the meeting by discussing long-term trends in neonatal mortality in the United Kingdom and the United States. Early in the 20th century, neonatal mortality was 40–45 per 1,000 live births in both countries, and by 1997 it had been reduced to 4–5 per 1,000. By comparison, the decline in neonatal mortality in the developing world has varied widely among regions. In the 1970s, neonatal mortality in Asia was, on average, 52 per 1,000, and in the 1990s it was 32 per 1,000 (Figure 1a). In Latin America the average neonatal mortality rate in the 1970s was 34 per 1,000, while in the 1990s it had fallen to 22 per 1,000 (Figure 1b). Less of a decline was noted in the Middle East and North Africa, where the neonatal mortality average for the region fell from 46 per 1,000 in the 1970s to 32 per 1,000 in the 1990s (Figure 1c). Sub-Saharan Africa displayed slower progress in reducing neonatal mortality, and in some countries clear downward trends were difficult to ascertain (Figure 1d). In the 1970s, the average neonatal mortality rate was 44 per 1,000, and by the 1990s it had only been reduced to 39 per 1,000.

The reliability of any mortality estimate depends on the completeness with which births and deaths are reported. Vital statistics registration—the conventional source of information about births, stillbirths, and early child deaths—does not exist in many developing countries. Birth histories, such as those that have been done in the *World Fertility Surveys*<sup>(1)</sup> and the *Demographic and Health Surveys*,<sup>(2)</sup> on the other hand, can provide reasonable estimates of early neonatal and neonatal mortality. The use of reproductive calendars to record information about each of a woman's pregnancies in some of the surveys also makes them the best source for data on perinatal deaths, although some stillbirths, especially those early in pregnancy, are not reported.

Dr. Hill went on to describe the relationship of neonatal deaths to all infant deaths. In the United Kingdom and the United States, the proportion of deaths that are neonatal increased steadily as the infant mortality rate fell to approximately 25 deaths per 1,000. After this point, the proportion of neonatal deaths decreased sharply—largely due to technological improvements in birthing practice and advances in care for premature infants. Currently, almost 65% of all infant deaths in the United States occur during the neonatal period. There is a large amount of variation in the data from Asia, but the proportion of deaths that are neonatal is between 45% and 65%. In Latin America the proportion of deaths that are neonatal varies between 50% and 70%, and in the Middle East and North Africa, between 40% and 70%. Sub-Saharan Africa has very few sub-regional variations, and in most countries, 50% of all infant deaths occur in the neonatal period.

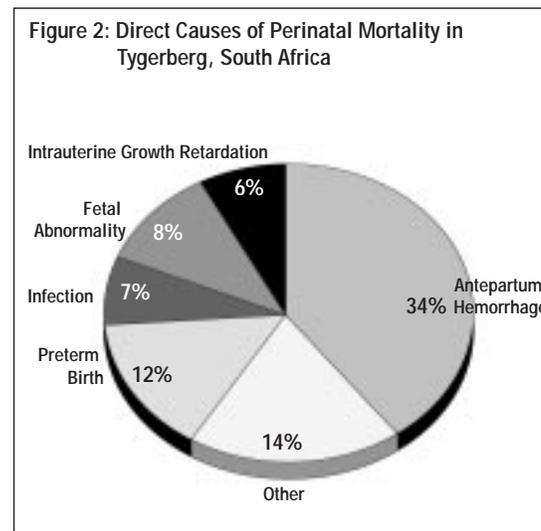
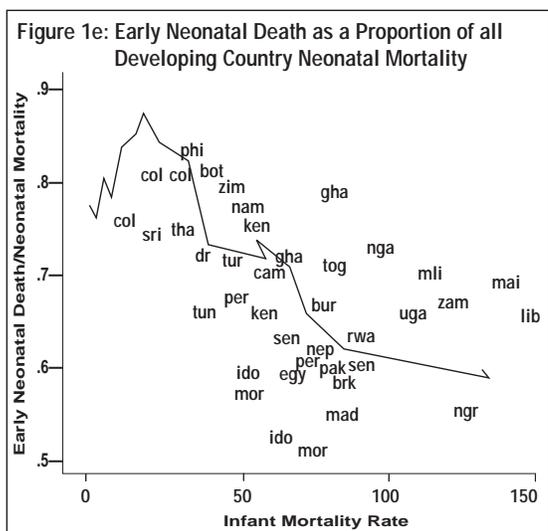
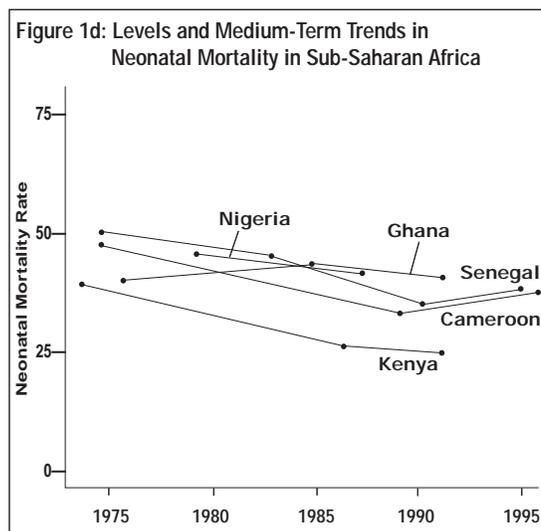
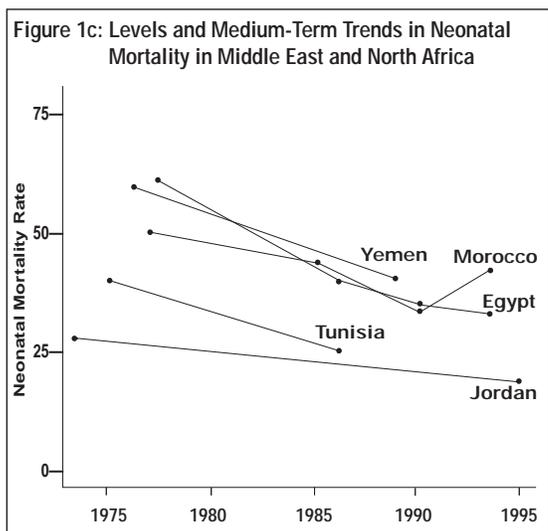
In the developed world (US and UK) early neonatal mortality, or death within the first week of life, has increased steeply as a proportion of total neonatal mortality since these rates have declined.



Early neonatal deaths now represent a large proportion of all neonatal deaths. This is largely due to the difficulty in preventing these early deaths. Developing countries show similar trends (Figure 1e). Those countries that have high neonatal mortality tend to have a lower proportion of early neonatal death, and countries with a relatively low neonatal death rate tend to have high levels of early neonatal death.

### Causes of Perinatal Mortality

It is clear that perinatal mortality rates are extremely high in the developing world, explained Staffan Bergstrom, who said that almost half of the women interviewed for his current study in Luanda, Angola, reported at least one previous stillbirth. He stated that, in the developing world, most perinatal deaths are caused by congenital malformations; pregnancy-related complications, such as *placenta previa* or *abruptio placentae*; delivery-related complications, including intrapartum asphyxia and birth trauma; and infectious diseases (Figure 2).<sup>(3)</sup> In most developing countries, a large residual proportion of perinatal deaths escapes diagnosis. This is because of lack of diagnostic facilities, inadequate or absent post-mortem examination, and poor histopathological and microbiological capabilities, and because many of these deaths occur at home with the mothers receiving little or no medical attention.



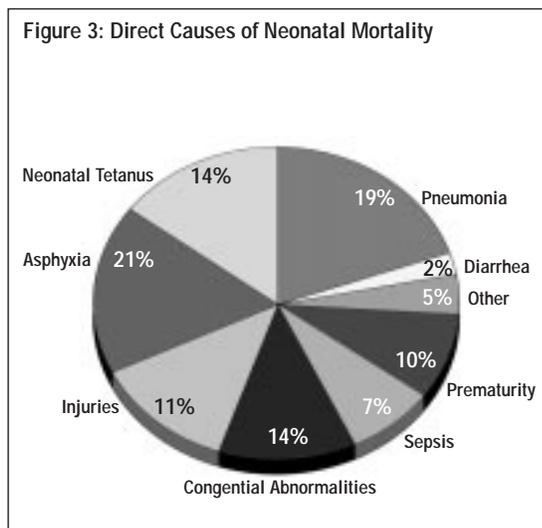
Transplacental transmission of infection is a major cause of perinatal mortality. Syphilis is the most common maternal systemic infection and threatens the survival of the fetus from the very beginning of pregnancy. In his studies in Maputo, Mozambique, where the syphilis infection seroprevalence is 15%, Dr. Bergstrom found 50% syphilis seropositivity among parturient women with fetal death.<sup>(4,5)</sup> Dr. Bergstrom also called for more studies examining the role of listeria in perinatal sepsis and death, due to its symptomatic association with chorioamnionitis, which was found in 95% of women who suffered late fetal death in his studies in Mozambique.<sup>(6)</sup> The global impact of non-bacterial intrauterine infections is unclear.<sup>(7)</sup>

Since the publications by Naeye and collaborators<sup>(8-10)</sup> intrauterine infections due to ascending bacteria from the lower genital tract of pregnant women have been considered increasingly important. In the developing world, *Escherichia coli* is the most commonly found ascending infection that is fatal to the fetus. In his studies in Mozambican and Zimbabwean stillbirths, Dr. Bergstrom found the bacterium in 24% and 13% of cultured fetal cardiac blood and in 15% and 11% of fetal lung cultures respectively.<sup>(7,11)</sup> Repeating this study design in Kaunas, Lithuania, he also found *E. coli* in postmortem heart blood culture in 20% of all stillborn infants. In sharp contrast to the developed world, he noted that his research team encountered very little group-B streptococcus (GBS) infection in their studies in low-income countries.

In conclusion, Dr. Bergstrom recommended more intervention programs and research to counter syphilis in pregnant women, including better screening, treatment, and contact tracing, and development of a seromarker for severe chorioamnionitis for use in prenatal diagnosis.

### Causes of Neonatal Mortality

The World Health Organization estimates 5 million children under 1 month of age die each year, and that nearly all (98%) of these deaths occur in developing countries.<sup>(12)</sup> A large proportion of these neonatal deaths (3.4 million) take place in the first week of life.<sup>(13)</sup> However, according to Barbara Stoll, causes of neonatal death are often difficult to ascertain, because most of the births occur at home unattended by medical personnel, or because the neonates present with non-specific diagnostic signs.



The major causes of neonatal death are infectious diseases, birth injury, asphyxia and prematurity (Figure 3). Accurate data on causes of death are useful for many reasons. It is important for providers of primary care, for investigators as they design interventions for prevention and treatment, for local and national health administrators, and for decision makers who implement and evaluate health care programs.

Infection	Number of Cases	Case Fatality Rate (%)	Number of Deaths
Acute Respiratory Infections	2,500,000	30	750,000
Neonatal Tetanus	438,000	85	372,000
Sepsis	750,000	40	300,000
Diarrhea	25,000,000	.6	150,000
Meningitis	126,000	40	50,400

*Stoll, BJ. The global impact of infection, Clin Perinatol 1997; 24:1-21.<sup>(14)</sup>*

**Table 1.**  
**Estimated Global**  
**Burden of Disease:**  
**Major Neonatal**  
**Infections**

Infectious diseases are associated with 30–40% of all neonatal deaths, or 1.5 to 2 million deaths per year, said Dr. Stoll, who reported that the infections responsible for most of the early mortality were acute respiratory infections (ARI), neonatal tetanus and sepsis, diarrhea and meningitis (Table 1). She reviewed 49 hospital-based studies to determine the incidence of neonatal sepsis and meningitis in different regions of the world. The incidence of sepsis is highest in Sub-Saharan Africa (6–21 cases/1,000 live births), followed by select countries in South and East Asia and the Pacific (2.4–16/1,000); Middle East and North Africa reported the next highest rates (1.8–12/1,000), and the Americas and Caribbean had the lowest incidence (2–9/1,000). Case fatality rates for sepsis were highest in Asia, followed by Sub-Saharan Africa, the Middle East and the Americas. Incidence rates for meningitis followed a similar pattern, with Sub-Saharan Africa reporting the highest rates (.7–1.9/1,000), followed by the Middle East and North Africa (.3–1.5/1,000), and the Americas having the lowest incidence at .4–2.8/1,000. No country-wide data on the incidence of meningitis were available from India. Case fatality rates for meningitis were variable but roughly held to the same pattern with Sub-Saharan Africa having the highest rates (18–59%), followed by Asia (45%), and the Middle East (16–32%), and the Americas (13–35%).

Dr. Stoll then presented data from 58 studies to establish the spectrum of bacterial pathogens that cause these illnesses. Overwhelmingly, gram-negative organisms, such as *E. coli* and klebsiella, were found to cause sepsis and meningitis in the developing world, while group-B streptococcus infection rates were found to be much lower than in the developed world. Given the high maternal colonization rates of GBS (as high as 18%), higher rates of neonatal disease would be expected in the developing world. Low rates could be explained by the possibility of less virulent strains; genetic differences in susceptibility, or the underestimation of the true rates of GBS in hospital-based studies, because most infants with early-onset sepsis get sick and die at home. She also emphasized that the organisms responsible for sepsis and meningitis change over time, vary according to geographic region, and that prospective microbiological surveillance was crucial to the prevention and treatment of these diseases.

Of the 750,000 neonates who die each year from acute respiratory infections, most die due to pneumonia, bronchiolitis, or laryngotracheitis. Dr. Stoll cautioned that respiratory distress may be a clinical presentation of neonatal sepsis or meningitis as well as pneumonia, so global estimates of these diseases may overlap. She also said that studies suggest that organisms causing pneumonia in newborns are similar to those that cause sepsis and meningitis, and that additional neonatal studies are needed to determine actual rates of pneumonia, the organism spectrum causing disease and the case fatality rate.

Between 400,000 and 500,000 cases of neonatal tetanus cause approximately 372,000 deaths each year, and 78% of these deaths occur in only 12 countries. Neonatal tetanus is a completely preventable illness. It can be prevented by immunizing mothers before or during pregnancy, or by ensuring a clean delivery, clean cutting of the umbilical cord, and proper care of the cord in the days following the birth. Between 1990 and 1997, five countries with large populations, high birth rates and very high rates of neonatal tetanus (China, Indonesia, Bangladesh, India, and Pakistan) have made significant progress in reducing the disease.<sup>(14)</sup>

## Child Spacing and Other Correlates of Perinatal and Neonatal Mortality

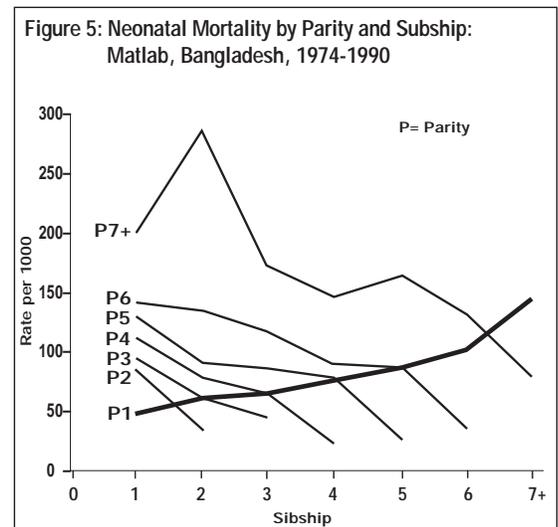
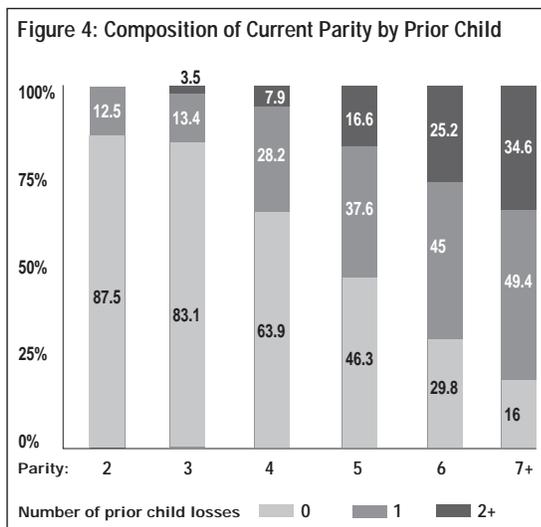
Shea Rutstein, in analysis of the *Demographic Health Surveys* from 18 countries, reported that the risk of perinatal mortality was highest in women with very short and very long intervals between pregnancies. Women with less than 15 months between pregnancies, or more than 39 months, had a 43% greater chance of experiencing a perinatal death than women who spaced their pregnancies between 16 and 38 months. Women who waited 15–26 months between pregnancies had only an 11% risk of losing their child. Further, the risk of a perinatal death was highest in women with no previous children, and in women in the extremes of their reproductive years (<18 and >35–years of age). Education also affected perinatal mortality rates—women with secondary or higher education had fewer fetal deaths than women with no formal education or one limited only to primary school.

The risk of neonatal mortality was significantly higher in women with less than a 24 month birth interval, and women with no previous children. Again, the risk of neonatal mortality was highest in women at the extremes of their reproductive years. Boys had a 26% higher risk of dying than girls, and either sex of child was 22% more likely to die in the first month of life if his or her mother received no prenatal care. Importantly, antenatal tetanus vaccinations reduced the chance of neonatal death by almost 50%.

### Parity and Neonatal Mortality

The Matlab, Bangladesh study area provides an excellent opportunity to consider the relationship of parity to neonatal mortality in a developing country context. The Matlab study area is a large population under demographic surveillance by researchers associated with the ICDDR,B: Centre for Health and Population Research in Dhaka since the mid–1960's. Michael Koenig presented an analysis of all live births from 1974 to 1990 in both the Matlab health intervention and comparison areas, in which there were 57,435 births in 24,032 sibling relationships (sibships); parity (number of children born) ranged from 1 to 11 children.

The relationship between high parity and infant mortality is one of the most enduring associations that has been studied. Yet to begin his presentation, Dr. Koenig suggested that the relationship is not causal, as had long been assumed, but rather that women who experienced high levels of infant death self-select to higher parities. As can be seen in Figure 4, the death of one infant was experienced by only 12.5 percent of mothers with two births, and no mothers in that birthing category experienced the death of both of their children. By comparison, almost half of women with seven or more births had experienced the death of an infant, and 34% of them had two or more infant deaths.



Looking within sibships, he found that the risk for neonatal mortality actually decreases with the increasing number of sibling relationships within a single family (Figure 5). The Matlab analysis also confirmed that a higher risk for neonatal mortality is associated with prior child loss. Dr. Koenig also called for more research on unwanted births, saying that the Matlab data suggest an indirect link between unwanted births and higher neonatal and infant mortality.

### Effect of HIV on Perinatal and Neonatal Mortality

Andrea Ruff assessed the impact of HIV on perinatal and neonatal mortality, and concluded that estimates have been limited by a number of factors including lack of routine antenatal HIV counseling and testing, particularly in areas with the highest prevalence of HIV, and difficulty in determining HIV infection status among young infants. Available data suggest that the effect of HIV on pregnancy outcome and neonatal mortality may be greater in developing country settings. Some studies in developing countries observed decreased fertility or an increase in stillbirths and spontaneous abortions (Table 2).<sup>(15-29)</sup> While lower birthweights were detected among infants born to HIV seropositive women in several developing countries,<sup>(30-33)</sup> significant differences were not noted among children ultimately shown to be HIV-infected.<sup>(34-35)</sup> However in most early studies, determination of HIV status depended on a child's surviving to at least 12 months of age, precluding any assessment of the effect of HIV infection earlier in life. The effects of HIV on pregnancy outcome seen in many developing country studies have not for the most part been found in industrialized country settings.<sup>(36)</sup>

Early loss to follow-up and potential confounders have limited the use of many of the prospective cohort studies of maternal-infant HIV transmission to evaluate the effect of HIV on perinatal and neonatal mortality. In their meta-analysis of 31 prospective cohort studies, Brocklehurst and French<sup>(37)</sup> found an increased risk of perinatal mortality among infants born to HIV seropositive women (OR=1.79, 95%CI = 1.14-2.81). Although they also observed a somewhat higher rate of neonatal mortality among infants born to HIV-infected women (OR=1.10, 95%CI = 0.63-1.93), data were available from only three studies.

In summary, Dr. Ruff said that available data suggest that in developing country settings in particular, HIV adversely affects pregnancy outcome and perinatal mortality. As HIV prevalence rates among pregnant women continue to increase in many parts of the world, the risk of perinatal and neonatal mortality and morbidity due to HIV may also increase. Identification and implementation of effective strategies to prevent maternal HIV infection, as well as perinatal transmission, are essential.

	Abortion	Stillbirth	Preterm Births	Low Birth Weight (LBW)	Small for Gestational Age (SGA)	Neonatal Mortality	Table 2. Effects of Maternal HIV Infection
Zambia <sup>(16)</sup>	–	–	–	OR 3.8	NA	NA	
Congo <sup>(17)</sup>	NA	–	–	OR 7.9	NA	↑	
Zaire <sup>(18-19)</sup>	NA	↑	↑	↑	NA	OR 5.0	
Kenya <sup>(21)</sup>	NA	–	NA	OR 3.0	NA	NA	
Malawi <sup>(22)</sup>	–	–	–	–	–	NA	
Kenya <sup>(20,22)</sup>	OR 3	OR 2.1–2.9	OR 2.1	↑	OR 2.3	NA	
Rwanda <sup>(23)</sup>	NA	NA	–	↑	NA	–	
Zimbabwe <sup>(24)</sup>	NA	RR 1.6	NA	NA	NA	RR 2.7	

*Adapted from Nicoll et al, 1994<sup>(15)</sup>*

## **Prematurity and Intrauterine Growth Retardation**

Almost 16% of all developing world children are born with low birth weight (LBW), or weighing less than 2,500 grams, with the highest regional rates found in South Asia—ranging from 14 to 22% in Nepal, to 28% in India, and 47% in Bangladesh. Two-thirds of all low birth weight is due to intrauterine growth retardation (IUGR), and the remaining 33% is due to preterm birth—some of whom also have IUGR.<sup>(38)</sup> The term “small for gestational age” (SGA) is generally used as a measure for IUGR, and is defined as birth weight under the 10th percentile for that gestational age and gender.

Shams El Arifeen explained the relationship of birth weight to the relative risk for mortality in selected developing countries. As can be seen in Table 3a, there is a remarkable consistency of birth-weight-specific relative risks across populations and a large range of years. Considering the relative risks and attributable risks of LBW, SGA and preterm birth (birth prior to 37 completed weeks of gestation), Dr. Arifeen showed (Table 3b) that in the urban slums of Dhaka, Bangladesh, SGA/LBW is associated with many more neonatal deaths (18%) than are preterm births. By contrast, in a more developed area—Pelotas, Brazil—43% of neonatal deaths were due to prematurity. Dr. Arifeen concluded that a significant proportion of infant deaths due to pneumonia and diarrhea may also be attributed to low birth weight.

## **Multicountry Study of Infections in Early Infancy**

Pneumonia, sepsis, and meningitis are estimated to cause over 1 million infant deaths per year, and yet, very little data exist on the relative importance of the organisms that cause these diseases. Kim Mulholland reported on the results of a WHO-supported multicenter study designed to identify the bacterial and viral agents responsible for serious infections in infants under 90 days of age in developing countries, and to identify the simple clinical signs that best predict serious infection in infants under 90 days of age.

Over 4,500 sick infants under 90 days of age were studied in Papua New Guinea, The Gambia, Philippines, and Ethiopia. Ten percent of the 2,400 neonates died, and death was associated with a blood or cerebrospinal fluid culture that tested positive for one of several bacterial agents. The most common gram-positive organisms noted in the sick neonates were *Streptococcus pneumoniae* (33 cases), *Staphylococcus aureus* (34 cases), and group-A streptococcus (29 cases). *E. coli* and *Salmonella spp* were the most common gram-negative organisms causing illness. The most common viruses noted were respiratory syncytial virus (RSV), influenza A, parainfluenza, and influenza B.

The researchers then devised a system by which to rank clinical symptoms. Rapid breathing, followed by elevated temperature, low weight-for-age Z-score, and the inability to nurse were all significant predictors of morbidity and mortality. Other important clinical presentations were crepitations, cyanosis, history of convulsions, lower chest wall indrawing, no arousal with minimal stimulus, and history of change in activity. Dr. Mulholland concluded by noting that efforts to improve early infant mortality should focus on preventing bacterial infections, as well as on early detection and prompt referral of suspected cases. Further, this study has shown that clinical signs can reliably identify those neonates who are most ill.

## **Complications of Pregnancy and Delivery**

Carine Ronsmans discussed the role of childbirth complications in perinatal death. Citing data from Matlab, Bangladesh, from 1987 to 1993, she recounted perinatal mortality rates by obstetric complication, and found that the perinatal mortality rates were the highest for fetal malpresentation with a mortality rate of 422/1,000, followed by eclampsia causing 323 deaths per 1,000 births and twinning causing almost 275 per 1,000.<sup>(43)</sup> Intrapartum bleeding resulted in 112 deaths per 1,000 births; pre-eclampsia resulted in 156 per 1,000, and prolonged labor resulted in 202/1,000.

**Table 3a.**  
Relative risks of neonatal mortality by birth weight: Selected developing countries (smaller studies)

Birth Weight (g)	India (Delhi) 1969-72	India (N Arcot) 1969-75	Guatemala (Santa Maria Cauque) 1964-72	Bangladesh (Dhaka) 1993-6
1000-1499	94.6	16.7	--	} 3.4
1500-1999	30.9	4.4	27.3	
2000-2499	4.5	1.4	3.4	2.6
2500-2999	1.0	1.0	1.0	1.0
3000-3499		0.8	0	} 1.8
3500-3999	} 1.1	0.6	--	
4000-4499		} 1.4	--	
4500+			--	
<b>NMR/1,000</b>	<b>21.2</b>	<b>34.8</b>	<b>39.0</b>	<b>35.9</b>
<b>LBW %</b>	<b>23.2</b>	<b>31.9</b>	<b>41.7</b>	<b>46.6</b>
<b># of Births</b>	<b>4,590</b>	<b>4,220</b>	<b>416</b>	<b>1,677</b>

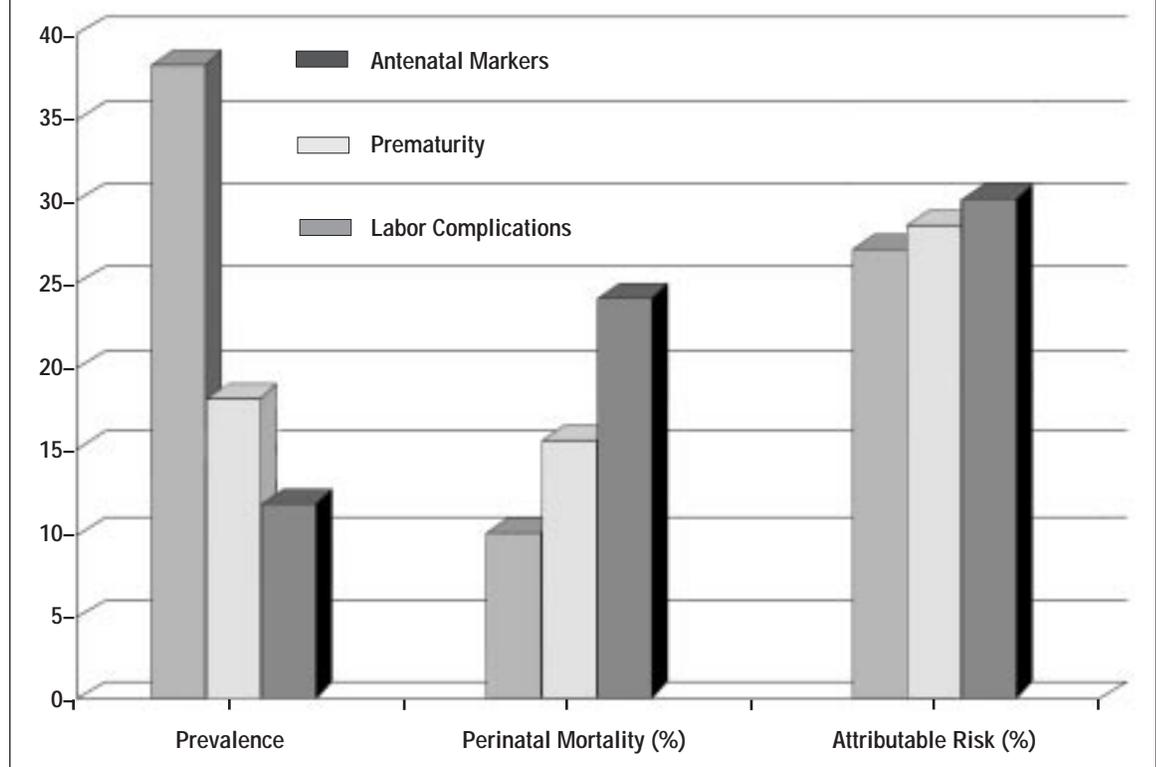
Arifeen, 1997 <sup>(38)</sup>, Ann Ashworth, 1998 <sup>(39)</sup>

**Table 3b.**  
Risk ratios and attributable risks of neonatal mortality by birth weight, SGA and prematurity

Risk Factor		Brazil <sup>(40)</sup> (Pelotas) 1982-4 n=5,914	Indonesia <sup>(41)</sup> (Madura) 1982-4 n=687	Sudan <sup>(42)</sup> (Medani/Sennar) 1989-90 n=1,475	Bangladesh <sup>(38)</sup> (Dhaka) 1993-6 n=1,677
LBW	RR	23.9	8.0	4.0	2.3
	Prevalence	8.8	9.5	18.0	46.6
	AR	67%	40%	35%	38%
SGA	RR	5.1	--	2.7	2.0
	Prevalence	9.0	--	13.2	40.2
	AR	27%	--	18%	29%
		(SGA-PT/FT)		(FT/LBW)	(SGA/LBW)
PT	RR	13.1	--	7.6	4.5
	Prevalence	6.3	--	4.7	6.4
	AR	43%	--	24%	18%
		(PT/AGA)		(PT/LBW)	(PT/LBW)

Barros, 1992 <sup>(40)</sup>; Kusin, J, 1989 <sup>(41)</sup>; Taha, 1993 <sup>(42)</sup>; Arifeen, 1997 (Adjusted) <sup>(38)</sup>

Figure 6: Prevalence, Perinatal Mortality and Attributable Risks Matlab, Bangladesh 1987-1993



Examining the rates for stillbirths, and early and late neonatal deaths separately, she showed that in Matlab, malpresentation caused the highest stillbirth rate (359/1,000), with prolonged labor (156/1,000), and eclampsia (128/1,000) also being important causes. On the other hand, the early neonatal death rate was the highest for eclampsia (205/1,000), and intrapartum bleeding (28/1,000) was associated with the highest mortality in the late neonatal period.

Looking at prevalence of risk factors for perinatal mortality, and attributable risks within the same population, she showed that complications during delivery accounted for the largest attributable risk. Prematurity caused a similar proportion (28%) of perinatal deaths (Figure 6). In conclusion, Dr. Ronsmans said that the current program emphasis of safe motherhood programs on management of conditions that arise during labor and delivery will help to further reduce perinatal mortality. However, prematurity remains one of the single most important contributors to perinatal deaths, and understanding its causes and possible solutions remains one of the priorities in research on perinatal mortality.

---

## Interventions against Toxic Exposures

## *Interventions Prior to or During Pregnancy*

Iain Aitken explored the effects of toxic exposures (tobacco, social drugs, lead, and pesticides) on perinatal and neonatal mortality. He began by stating that the issue of toxic exposures is a complicated one because of the number of substances that people are exposed to and because exposures may occur simultaneously.

The main impact of tobacco smoking on pregnancy is low birth weight, usually via intrauterine growth retardation. An estimate of the relative risk for LBW is approximately 2.4.<sup>(44)</sup> The effect of tobacco substances is usually to reduce the birth weight by about 200 grams. It is estimated that 20% of women in the industrialized world are smokers, which leads to an attributable risk of about 22% for LBW. In developing countries about 7% of women smoke, giving an attributable risk of 9%, but there is wide variation among regions. In Latin America, as in North America and Europe, about 23% of women smoke. However, in Mexico over 40% of women smoke, while in Brazil it is estimated that 50% of women smoke.

Another issue is the effect of environmental tobacco smoke. In studies that have not done formal measurement of exposures, there is a reported relative risk for low birthweight of about one-half of that involved in direct smoking, yielding a relative risk of passive smoking of 1.2. These studies suggest that passive smoking reduces birth weight by 100 grams. If we assume that the husband is a smoker and the wife is not, and that about 40% of husbands smoke, the attributable risk of passive smoking for low birth weight is about 7%. Studies which have investigated timing of exposure during pregnancy have made it quite clear that the main effect is during the third trimester.

With social drugs, WHO estimates that worldwide about 15 million people risk their own health due to use of psychoactive substances. There is currently a rapid increase in use of opiates, cocaine and psychotropic drugs in many developing countries. There is also widespread use of marijuana, particularly among poorer groups. Marijuana is used by about 3% of pregnant women in the United States. It is suggested that its use is associated with smaller babies, but this evidence comes from studies that have not controlled for other confounders such as poor antenatal care and weight loss or failure to gain weight during pregnancy.

The most well-known birth defects come from alcohol. Fetal alcohol syndrome (FAS) is associated with heavy, chronic drinking, and evidence is mounting that binge drinking is also a risk factor. Incidence of FAS in the United States is estimated to be between 1/300 and 1/2000. FAS is associated with underdevelopment of the face, lower growth during pregnancy, lower growth rates after birth, and in extreme cases, a variety of CNS abnormalities. If the prevalence of this drinking pattern is 2–3% of women, the attributable risk of alcohol-related birth defects is approximately 2%. There is also growing evidence that women who drink 2–3 drinks a day may be at risk for having an infant with low birth weight, with an odds ratio of 1.8.

Cocaine and heroin are associated with about 1–5% of pregnancies in the United States, but this obviously varies enormously depending on the part of country. Both cocaine and heroin are associated with smaller babies, neurodevelopment problems, and behavioral problems, and both have acute withdrawal syndromes in the newborn in some situations. Also, there is the suggestion that heroin may be related to congenital abnormalities. An additional limitation to these studies is that there are difficulties in discerning the differences among drugs because most of the women using these types of drugs are using more than one type, or the women may be using tobacco at the same time.

Air pollution is becoming a major problem around the world. Again, there are a wide variety of substances in the air, but the effects of lead are the best studied. Fetal lead exposure results in low birth weight from IUGR, and it is associated with reduced head circumference and neuropsychological deficiencies. Lead exposure is not, however, associated with an increase in stillbirths. A study in Norway investigated all of the births in the country between 1970–1993. They looked at the registered

occupations of the mothers and were able to get an estimate of the ones with a high or medium exposure to lead and from that, work out the effect of the exposure. The relative risk of LBW for the high exposure women was 3.5; the relative risk for low exposure was 1.25. Other studies have investigated paternal lead exposure. One study, done in Baltimore, has shown that the risk of LBW is as much as 5 times greater in babies with paternal exposure to lead. In addition, there were a variety of heart defects associated with lead exposure. Measures to reduce lead emissions from vehicles include fuel-efficiency reforms, pollution charges, and increasing fuel taxes.

There are several million acute pesticide poisonings each year. Both acute poisoning and long-term exposure have been associated with spontaneous abortion, perinatal deaths, birth defects, and reduced male fertility. In the Sudan, one study found an odds ratio for perinatal mortality of >2 for women who were exposed in domestic situations, and an odds ratio of 3.6 for women who were exposed in farming—where exposure to pesticides was greater. They calculated an attributable risk for perinatal mortality of 20% among the women with domestic exposure and 35% for women working on farms.

Although there is an international code of conduct on the distribution and use of pesticides, a 1993 survey found that 20% of governments had no registration and control scheme; 40% had problems of inadequate labeling; 50% had no poison centers to provide guidance or information to health care workers; 35% had no official distribution outlets; 39% reported no attempt by industry to devise safer formulations; 48% admitted to having unsafe storage and disposal; 66% had improper control of factory waste; and 45% lacked safety controls in factories.

### **Nutritional Interventions**

Laura Caulfield stated that maternal malnutrition before or during pregnancy can lead to spontaneous abortion, stillbirth, small for gestational age babies, preterm delivery, or increased risk of perinatal and neonatal death. Also, certain forms of maternal malnutrition limit neurologic development in the fetus. Furthermore, maternal malnutrition may increase the risk of maternal infection, and impair development of the fetal immune system.

An example of the effects of protein/calorie malnutrition on the fetus can be found by examining statistics from the World War II Dutch famine.<sup>(45)</sup> At this time, there was a dramatic drop in energy intake from about 1700 kcal to about 700 kcal/day. When this timing of severe energy restriction occurred in the periconceptual period, there was reduced fertility and an increase in neural tube defects. When severe caloric restriction occurred during the first trimester, there was a twofold increase in stillbirth rate, increase in preterm delivery rates, and an increase in early neonatal death. The babies that did survive were born at an average birth weight of 3200 g. When the energy restriction occurred during the third trimester, babies were born at significantly lower weights. Also, data from Baltimore illustrated the effects of maternal body-mass index (BMI) entering pregnancy and weight gains during pregnancy on the probability of delivering a small baby or a relatively large baby.<sup>(46)</sup> Very thin women (BMI <20) had an increased risk of having a small-for-gestational-age infant (when compared to normal BMI women) unless they gained a recommended amount of weight (10 kg) during pregnancy.

There is evidence to suggest that we can improve infant outcomes by increasing maternal nutritional status.<sup>(47)</sup> In 1997, Prentice and colleagues supplemented Gambian women with an extra 900 calories per day, with most of the calories coming from fat in a ground nut-based biscuit. The supplement also provided calcium and iron. The researchers noted that there was an increase in birth weight of about 136 grams. Head circumference was increased by about 3 mm. LBW was reduced by 35%, and stillbirths by 55%. Overall there was a 49% reduction in perinatal deaths and 40% reduction in early neonatal deaths but no effect on post-neonatal deaths. These women also received prenatal care, including iron and folate supplements, tetanus toxoid if needed, and chloroquine in malaria season (Table 4).

Three recent studies also examined the effect of maternal anemia management on perinatal and neonatal death. The first one found a 50% reduction in LBW (birth weights <1500 g) and a 45% reduction in perinatal deaths after anti-helminthic treatment along with iron-folate supplementation (60mg. elemental iron).<sup>(48)</sup> The second trial, which treated severe anemia resulting from a high malaria parasite load with Fansidar alone, noted a 32–50% reduction in severe anemia across the various villages, coupled with a 22% reduction in perinatal deaths and a 38% reduction in neonatal deaths.<sup>(49)</sup> And in the third randomized placebo-controlled trial, women received iron (100 mg elemental). There was a substantial reduction in iron deficiency, and an 86% decrease in fetal and neonatal deaths.<sup>(50, 51)</sup>

Severe maternal iodine deficiency may lead to cretinism and is preventable with simple supplementation or fortification of food or salt. A paper, published in 1998 provided an interesting community-based intervention. After a major water supply in China was iodized, they were able to document an approximately 50% reduction in neonatal mortality.<sup>(52)</sup>

Evidence is also mounting that zinc supplementation during pregnancy improves infant outcomes. In a Peruvian trial, 15mg of zinc was added to the folate and iron supplements provided to pregnant women beginning at 16 weeks gestation and continuing daily throughout pregnancy. It did not affect duration of pregnancy, birth weight, or head circumference. However, in a substudy which used electronic fetal monitoring to look at neurobehavioral development, Dr. Caulfield and colleagues observed evidence of greater fetal movement, greater reactivity, more accelerations of the heart, fewer decelerations, and greater heart rate variability and range, indicating more advanced neurologic development. They were also able to document increased transfer of immunoglobulins to the fetus, especially IgG, and were able to show a reduced level (about 30%) of ARI and diarrheal morbidity in the first year of life.<sup>(53)</sup>

Pre-eclampsia and hypertension are important pregnancy complications, and result in extremely high rates of perinatal death if untreated. Many studies have documented an approximately 70% reduction in the likelihood of pre-eclampsia and hypertension with calcium (1–2 grams/day) supplementation.

In closing, Dr. Caulfield pointed out that although efficacy studies seem to show an improvement of neonatal and perinatal outcomes with improved maternal nutrition, there are no programs in operation to implement these results. Clearly, studies have shown that the potential is there for a mortality reduction impact for the baby and perhaps even the mother. Finally, she said that the scientific community needs to stop focusing on women having bigger babies but rather on them having healthier babies.

Wafaie Fawzi then spoke about the role of vitamins in perinatal and neonatal health. He began by reviewing the findings of a large trial from Nepal by West et al,<sup>(54)</sup> where over 44,000 women of reproductive age were randomized to receive a weekly dose of 23,300 IU (equivalent to 7 times the RDA each week) as preformed vitamin A or as  $\beta$ -carotene, or a placebo. A strong protective effect of the supplements on maternal mortality was found among more than 20,000 pregnancies that occurred during the period of the trial. Compared to placebo, vitamin A resulted in a 40% reduction in maternal mortality, while  $\beta$ -carotene resulted in a 49% reduction in mortality. However, there were no effects of either supplement on birth weight or prematurity.

Outcome	Change
Birth weight	↑ 136 g
Head circumference	↑ 3 mm
LBW	↓ 35%
Stillbirths	↓ 55%
Deaths after birth:	
Day 1	↓ 37%
Days 2-7	↓ 72%
Days 8-28	0%
Perinatal deaths	↓ 49%
Neonatal deaths	↓ 40%
Postneonatal deaths	0%

**Table 4.**  
Effect of increased dietary intakes from 20 weeks gestation throughout pregnancy in The Gambia

He then presented the design and results of a randomized, double-blind, placebo-controlled trial that examined the effects of vitamin supplements on birth outcomes among pregnant women infected with HIV-1 in Dar es Salaam, Tanzania.<sup>(55)</sup> The study used a 2x2 factorial design to examine the effects of supplements of vitamin A and/or multivitamins (including B1, B2, B6, B12, niacin, B12, folate, C, and E but excluding vitamin A). All women, irrespective of the assigned experimental regimen, were given daily doses of ferrous sulfate, and folate, and weekly doses of prophylactic chloroquine phosphate as per standard prenatal care in Tanzania. Multivitamins resulted in a statistically significant reduction of 39% in risk of fetal loss. Multivitamin supplementation also resulted in about 40% reductions in low birth weight, severe preterm birth, and small-for-gestational-age birth. Vitamin A supplementation did not affect any of these outcomes. The protective effects of multivitamins may have been mediated through an improvement in immune function of these HIV-infected women, hence generalizability of the findings to HIV-negative women is difficult.

He noted that there were limited additional data on the potential efficacy of individual vitamins, other than folate and vitamin A, in pregnancy. These studies were reviewed briefly. Among low income women in Camden, NJ, use of nutritional supplements was associated with a 34% reduction in the risk of preterm birth and a 41% reduction of low birth weight.<sup>(56)</sup> The protective association was confined to very low birth weight (<1500 g) and severe preterm birth (<33 weeks). There was no significant relationship between supplement use and the risk of small-for-gestational-age births. The study was non-randomized, and hence it is not possible to exclude the possibility of residual confounding by other variables, including socioeconomic status, education, and access and use of prenatal care. Moreover, the supplements used usually contained folate, and iron (in addition to zinc, calcium, and other vitamins), and hence it is possible that protective associations were, at least in part, due to the effect of folate and iron supplements.

### **Malaria Prophylaxis**

In 1994, 45 million pregnant women were living in malarious areas, with over 23 million in Sub-Saharan Africa alone. Although the effect of malaria on perinatal and neonatal mortality depends on the rate of transmission, malaria may cause up to 30% of the preventable low birth weight, and 3–5% of neonatal mortality in highly endemic regions. Malaria is also associated with an increased risk of spontaneous abortions and stillbirths. Although WHO recommends antimalarials for prevention of malaria in pregnant women in endemic areas, many African countries lack control programs because of low efficacy and availability of drug regimens, and competing program priorities, said Rick Steketee.

Simple strategies for malaria prevention in pregnancy include targeting populations at risk during their antenatal medical visits. Some 40% of Kenyan women visit an antenatal clinic by their 24<sup>th</sup> week of pregnancy—an useful time to screen for disease. Case management may be effective in low transmission areas, but in endemic areas where women are more likely to be asymptomatic while having a high parasite load, intermittent, presumptive treatment is preferred. This treatment regime was just studied in Kenya. Between January 1996 and April 1997, 1,264 primigravid women were recruited when they attended clinic for antenatal care and randomly assigned sulphadoxine-pyrimethamine (640) or placebo (624). Women received one, two, or three doses of study medication depending on the duration of gestation at enrolment. Thirty (5.3%) of 567 women in the sulphadoxine-pyrimethamine (Fansidar) group and 199 (35.3%) of 564 in the placebo group had peripheral parasitaemia (protective efficacy 85%). Eighty-two (14.5%) and 134 (23.7%) had severe anaemia (protective efficacy 39%). Even women who were enrolled late and received only one dose of sulphadoxine-pyrimethamine benefited significantly from the intervention.<sup>(49)</sup>

According to Dr. Steketee, chloroquine is safe and the drug of choice to combat *Plasmodium falciparum* in the few areas where it is still effective, while quinine may be effective for complicated malaria. Mefloquine or a combination of mefloquine and artemisinin can be used in multidrug resistant areas, although there is some evidence that it may increase the rate of stillbirths—an issue

that requires further study. Pyrimethamine is a folic acid antagonist but is not associated with congenital abnormalities in humans, even in the first trimester. Proguanil is safe, and clindamycin is also safe, but there is a possibility of build up in the fetal liver. The medications that should be most avoided when treating pregnant women are tetracyclines, which cause abnormalities in skeletal and muscular growth, tooth development, and in the lens and cornea. Primaquine can also cause hemolysis in G6PD-deficient infants. The Mangochi trial in Malawi found that two doses of Fansidar in the second and third trimesters is effective in clearing parasites and increasing birthweight,<sup>(57)</sup> and Malawi has since instituted a policy of monthly Fansidar to all women attending antenatal clinics; however, issues of mounting cotrimoxazole resistance with the use of Fansidar should be considered.

## **Prevention and Treatment of Reproductive Tract Infections**

The World Health Organization estimates that there are 333 million cases of sexually transmitted diseases worldwide each year. These include viral and bacterial infections and can cause either localized or systemic disease. According to Ronald Gray, infections during pregnancy may result in a wide spectrum of adverse outcomes, such as spontaneous abortion, premature rupture of fetal membranes prior to labor, preterm birth, and congenital infection.

Premature rupture of the fetal membranes (PROM) may result from a weakening of the fetal membranes due to collagenolytic enzymes secreted by a variety of bacteria and parasites. After the membranes are breached, chorioamnionitis and infection of the fetal cord may occur. In the developed world, 16% of all PROM cases proceed to preterm delivery. Premature birth is probably associated with a cytokine cascade resulting from an inflammatory response to infection. Cytokine production is associated with an inflammatory response, which may begin with the corticotrophin releasing hormone process, and then leads to cortisol production, and subsequently uterine contractions.

Dr. Gray stated that the prevalences of gonorrhea and chlamydia drastically vary in different studies. Gonorrhea prevalence is reported to be from 0–22%, and chlamydia prevalence is reported from 5–37%. For both of these infections, there may be infection through ascending organisms or during the intrapartum period, with transmission rates higher for chlamydia (70%) than for gonorrhea (40%). A major cause of infant morbidity related to chlamydia and gonorrhea is neonatal ophthalmia. With chlamydia infection, the ophthalmia is non-blinding, but gonorrhea causes 12–28% of all infant blindness. Another possible consequence of perinatal chlamydia exposure is pneumonia.

Active syphilis is associated with a 20% spontaneous abortion rate, especially if it occurs in the second or third trimester of pregnancy. There is also a high rate of perinatal death and congenital infection associated with syphilis, and it has been estimated that 75% of babies born to infected mothers will be adversely affected in some way. In developing countries, disease incidence and transmission is high because of lack of resources, inadequate screening procedures, and little or no treatment for seropositive women.

Dr. Gray then summarized a pair of treatment trials. First, he spoke of the trial in Nairobi, Kenya, where cefetamet-pivoxil was presumptively used to treat gonorrhea and syphilis and compared to a placebo. After the intervention, this community exhibited an increase in mean birth weight and decreases in neonatal ophthalmia and postpartum endometritis and decreases in HIV transmission. Although small, this study demonstrated the utility of presumptive treatment in areas where treatable disease prevalence was high.<sup>(58)</sup> The second study was his placebo-controlled trial in Rakai District, Uganda. The intervention arm consisted of treatment with azithromycin, ciprofloxacin, and metronidazole; in addition, if the woman tested seropositive for syphilis, she would be treated with penicillin. The control arm consisted of vitamins and anthelmintic drugs. The results revealed a decrease in trichomonas and bacterial vaginosis, decreases in maternal gonorrhea and chlamydia; reductions in neonatal ophthalmia, but no decrease in maternal HIV incidence and vertical transmission.<sup>(59)</sup>

## Immunizations in Pregnant Women and Neonates



Mark Steinhoff discussed the potential of maternal immunization to prevent tetanus, pertussis, group-B streptococcus, haemophilus, pneumococcus, meningococcus, influenza, rotavirus, and respiratory syncytial virus in neonates and infants. With maternal immunization, maternal antibodies are transferred to the unborn infant via active transport thus preventing many of the infections that occur in very early life. Antibody levels in an infant born to an immunized mother may exceed levels in the mother, and last from three to six months (and sometimes nine months) in the baby. Vaccination of pregnant women or women likely to become pregnant also increases breast milk antibody levels and protects the mother herself.

A study in Bangladesh showed a reduction in infant mortality when pregnant women were given tetanus toxoid vaccinations. With two doses of tetanus toxoid, there was a reduction in deaths from day 4 to day 14 of life (the age at which most neonatal tetanus deaths occur) from 30/1,000 to less than 10/1,000. Also, there was a substantial reduction in deaths for the three years after vaccination.<sup>(60)</sup>

There have also been studies of pneumococcal vaccine in Bangladesh. These results showed that babies had half of the antibody level of their mother, but it was still twice as high as unimmunized adults or children, and that these levels persisted until about five months of age.<sup>(61)</sup> If all women of childbearing age were administered a single dose of the existing pneumococcal vaccine, it could prevent 60–84% of all pneumococcal deaths before 6 months of age. This represents a substantial proportion of all the pneumococcal deaths before 5 years of age, 34% of all deaths before 5 years and also 6–8% of pneumonia deaths before five years. However, timing of maternal immunization is very important. The more time that there is for the mother to create an antibody response and transfer the antibody, the more antibody the baby receives.

Dr. Steinhoff then discussed the results of the Collaborative Perinatal Project of the U.S. National Institutes of Health which, in 1973, provided information on the safety of maternal immunization.<sup>(62,63)</sup> Several thousand of the 50,000 pregnant women enrolled in the study were given polio, influenza, and other recommended vaccines. After a seven-year follow-up, none of the infants born to immunized mothers had adverse immunization-related sequelae. On the other hand, one possible drawback to maternal immunization is inhibition of the infant's own immune response to vaccines after birth. This has been shown with maternal pertussis vaccination. Infants with higher levels of maternal antibody had less of their own antibody production; however, it is not clear if this had any detrimental effects on the health of the infant. It is also possible that high levels of maternal antibody may alter the repertoire of the infant immune response. That is, immunologic feedback systems monitor if there is already antibody present, and if there is, the response may be shifted. More studies are urgently needed to clarify this issue.

The World Health Organization currently recommends maternal immunization for neonatal tetanus in the second and third trimesters, but estimates that only 47% of women receive it during routine antenatal care visits. Public policy in the United States recommends that pregnant women receive tetanus and diphtheria toxoid vaccine if the woman never had primary immunization, or if a booster is needed. Influenza vaccination is also recommended for pregnant women after the first trimester but is received by very few women. If maternal immunization programs are to expand, further research is needed to remove the barriers to progress, which include concerns about safety and liability. Neonatal vaccine priorities include early delivery of rotavirus, influenza, and meningococcal, and pneumococcal, vaccines; a number of these vaccines are in development and testing.

---

## Overview of Interventions during Delivery

## *Interventions during Delivery*

Although it is commonly believed that perinatal mortality should decrease with improved maternal and child health programs, Frederik Broekhuizen began by presenting evidence from a study in the United Arab Emirates (UAE) which found that the increases in maternal and child health services in the UAE over the past 20 years have resulted in decreases in infant mortality rates and not perinatal mortality rates.<sup>(64)</sup> One possible explanation for this finding is that women who receive care are the ones who have fewer risk factors for perinatal death (i.e., higher socioeconomic status, and better health-seeking behaviors). Therefore, the care may not be reaching the women with the highest risk of perinatal death.

On the other hand, perinatal audits have been successful in reducing perinatal mortality in both clinic and community settings. A perinatal audit reviews the cases of perinatal death within that population; and offers suggestions regarding future intrapartum interventions, such as improved labor management. The major drawbacks to perinatal audits are the expense and time commitment needed to complete them.<sup>(65)</sup>

There are many complications of labor that may lead to perinatal death. Some involve the health delivery system, including lack of transportation and essential obstetric skills, while others are more specific to the woman herself. These complications include delayed admission to the delivery area, dystocia, fetal distress, multiple gestation, intrauterine growth retardation (IUGR), and preterm delivery.

Preterm birth may be responsible for 10-15% of all perinatal deaths in the developing world. Therefore, it is definitely an issue that needs to be addressed. To prevent mortality from preterm birth, many issues need to be examined. Factors affecting the risks and management of preterm birth are prevention of lower genital tract infection; location of birth (health system transport to hospital that is prepared for preterm deliveries), better ability to diagnose premature rupture of membranes (PROM) and premature labor, increased use of tocolysis and corticosteroids to delay labor and improve birth outcomes, expanded training in essential obstetric care, improved neonatal resuscitation techniques, and better management after rupture of membranes and during labor and delivery.

Antibiotic treatment after rupture of membranes may prolong gestation and thus lessen neonatal morbidity and mortality. Antibiotic intervention should be considered for use in developing countries in the management of preterm PROM. In addition to the benefit of prolonging the pregnancy, antibiotic treatment may reduce maternal infectious mortality, neonatal sepsis, intraventricular hemorrhage, perinatal morbidity, chorioamnionitis, and endometritis.

Identification and treatment of maternal hypertension and identification antenatally of IUGR can reduce asphyxiating intrapartum problems. Antenatal care is necessary to make these diagnoses and to benefit the mother and child. Intrapartum asphyxia associated with IUGR and hypertension can lead to perinatal mortality and morbidity. Interventions that may reduce morbidity of intrapartum and postnatal asphyxia include meconium management (including amnioinfusion), active labor management, attendance by trained obstetric staff, neonatal resuscitation techniques, and resources for operative delivery.

An estimated 4-8% of perinatal mortality is due to neonatal sepsis or amnionitis. To prevent these conditions, the following should be available: active labor management, prevention of prolonged labor, oxytocics, antibiotic treatment of both mother and neonate, increased training of obstetric staff with experience in operative interventions, and improved neonatal resuscitation by skilled providers.

## Prevention and Management of Delivery Complications

Marge Koblinsky began by discussing an intervention in Shunyi, China, that examined a risk-specific approach to perinatal health.<sup>(66)</sup> From 1983–1986, 96% of the pregnant women in seven townships participated in the study, and there were 1,928 live births and 50 perinatal deaths. In 1983, the causes of perinatal death in this population were mainly asphyxia (20%), congenital anomalies (30%), and unidentified/stillbirths (32%). As can be seen in Table 5, a survey of risk-specific perinatal mortality placed eclampsia as the condition most likely to result in fetal death. Prolapsed cord, prolonged second stage labor, and breech delivery were also important risk factors. Basically they found that “untrained” caretakers or community members had poor ability to detect complications and little or no facility to prevent or treat the problems if they occurred. At the next care level, midwives had greater ability to detect and manage risk factors, and specialists in institutions with full emergency obstetric care (EOC) units had the greatest success.

Correct implementation of Model 1 in Shunyi caused a 34% decline in perinatal mortality from 25.9/1,000 to 17.1, and a decrease in early neonatal mortality from 11.9 to 9.0%. One of the reasons for the intervention’s success was that the provincial health officials were determined to use a full system approach. They first defined the three levels of obstetric care: village doctors, township services, and county full services. For example with asphyxia, village doctors were able to monitor fetal heart rate and mother’s blood pressure and then refer. The township doctors were able to diagnose, treat with IV, and oxygen, and refer when stable. The county doctors were able to do fetal monitoring and perform a Cesarean section if necessary.

During the study period, improvements were also made in referral practices by using buses, tractors, and cars between sites. Communications were improved by using television and video to explain the program. Other changes included support of maternity waiting homes and improved village doctor salaries.

Direct communication with women and their husbands regarding pregnancy was made at the time of marriage registration, and pamphlets on the signs and symptoms of pregnancy and necessity for prenatal care were distributed. During pregnancy, the couples were brought together with the providers to teach about how to maintain health through proper nutrition and adequate rest, education on fetal growth, movement, possible complications, how to monitor fetal heart rate with wooden stethoscope, how to measure fetal growth with tape measure, mother-in-laws’ workshop was also offered to prevent potential problems within the family and promote the use of care.

**Table 5: Risk Factor Specific Mortality in Shunyi County, China 1983-1984**

Risk Factor	Pregnancy Frequency (%)	Perinatal Mortality Rate (per 1000)	Delivery Frequency (%)	Perinatal Mortality Rate (per 1000)
Eclampsia	0.1	100%	.2	750
Prolapsed Cord			0.3	250
Prolonged 2nd Stage Labor			1.1	136
<i>Abruptio placentae</i>				118
Breech Presentation	12.2	45	4.0	117
Pre-eclampsia	1.3	71	1.9	108
Hypertensive Disease of Pregnancy	15.1	53	7.8	27
Abnormal fetal heart rate	1.1	571		

*From Yan et al, 1989 (56)*

An analysis of the birth procedures and outcomes in Shunyi allowed these researchers to create four models of safe motherhood: Model 1: Home deliveries by a briefly trained community member who has the ability to refer and transport a woman to clinic or hospital (as in China, Brazil, Guatemala); Model 2: Home deliveries by a professional; transport and referral support must be available to a full emergency obstetric care facility if complications occur (Malaysia and the Netherlands); Model 3: Professional provision of basic emergency obstetric care; transport and referral support must be provided. (Sri Lanka and Malaysia), and Model 4: Professional provision of basic and comprehensive EOC (UK, US).

### **Resuscitation of the Newborn**

Small infant size, congenital malformation or prolonged labor predisposes a newborn to asphyxia and can lead to stillbirth, early neonatal death or brain damage if immediate resuscitation is not implemented after birth. In developing countries, there are approximately 4-9 million cases of birth asphyxia each year, but only 1-2 million newborns are resuscitated correctly.<sup>(67)</sup> Almost 1 million annual neonatal deaths are due to birth asphyxia. Jelka Zupan said that the most crucial barrier to delivering proper care in developing countries is that 60% of births occur in the home and skilled attendants are not always available.<sup>(68)</sup> Institutions also frequently lack equipment and skills for this life-saving procedure. Generally, if a baby is not breathing at birth, resuscitation should be initiated immediately.

Standard resuscitation guides recommend a range of interventions for newborn resuscitation, including ventilation by bag and mask, intubation, support of the circulation with chest compressions, drugs, and intensive care. However, a study from Sweden found that almost 80% of newborns who required resuscitation only needed the bag and mask intervention,<sup>(69)</sup> and more complex interventions such as intubation, chest compression, or drugs were rarely needed. Another recent study showed that most newborns could be successfully resuscitated with room air and that pure oxygen was unnecessary.<sup>(70)</sup>

Lack of resuscitation in the developing world is largely due to shortage of resources and lack of or poor quality and maintenance of necessary equipment. Occasionally, it is also due to barriers such as absence of authority to resuscitate—in some countries only a physician is allowed to deliver resuscitation techniques. Dr. Zupan concluded by calling for safe motherhood programs to increase women's access to skilled birth attendants through, for example, midwifery programs, and to give midwives and others good resuscitation skills with continuing education to sustain them.

---

### **Overview of Interventions after Delivery**

**F**irst days after birth are particularly important for the health of the newborn. Jelka Zupan discussed basic interventions that, when performed after delivery, could reduce early neonatal mortality. Interventions included resuscitation, cleanliness or hygiene, warmth, early and exclusive breastfeeding, eye prophylaxis (to prevent ophthalmia), early identification and timely treatment of neonatal problems, timely initiation of immunization, and prevention of HIV infection from positive mothers to their infants. Birth attendants must properly care for the umbilical cord during and after cutting, in an effort to prevent neonatal tetanus and infections from the environment. Measures should be taken against body temperature loss after delivery for all babies. In particular small babies would benefit most from skin-to-skin contact with their mothers beyond the first few hours after birth to maintain a healthy temperature. Early and exclusive breastfeeding is the best way of feeding infants, but HIV-positive mothers must choose between this and supplementary feeding methods. Birth attendants should have skills to detect early infant problems, but families should also be alert and aware of danger signs and have the means to get timely care.

Dr. Zupan concluded by saying that for newborn health, access to health services is essential. Women should have access to a skilled birth attendant, and quality services within easy reach are also needed in the postnatal period. Referral facilities within reasonable distance, affordable services, and

### *Interventions After Delivery*

advanced care for women and newborns with complications are all part of the continuum of care—which is so important for maternal and perinatal/neonatal survival.

### **Basic Care and Thermal Control in the Newborn**



Warmth and food are the two basic needs of a newborn according to Kyllike Christensson. Infant wrapping after delivery may seem like a standard procedure, but a study in Africa concluded that most infants were not wiped and wrapped in a sufficient way, even if the attendant at their birth was trained to do so. Most often only the face was wiped, and this resulted in loss of heat through evaporation of fluids that remained on the skin.<sup>(71)</sup> Incomplete warming can cause hypothermia. In the same African study, 50% of the babies had hypothermia at time of discharge. Dr. Christensson said that these results also pointed to the growing concern of separation of newborn and mother. In a randomized trial, the differences in body temperatures were analyzed among babies kept skin to skin with their mother and those that were assigned to the nursery within

minutes of delivery, and it was found that there was a substantially reduced risk of hypothermia with neonates kept with their mothers. In addition, blood glucose levels at 90 minutes were higher than in the nursery neonates. In another trial that investigated rewarming of infants, 90% of babies who were kept skin to skin with their mothers reached normal temperatures, while only 60% of the babies in incubators were able to reach the same state. Thermal protection of neonates is not only important in the period immediately after birth, but there are a small number of infants who will need it longer. For example, in desert areas, with large daily variations in temperature, it should be stressed that infants need to be protected against heat loss during the cold nights as well. Skin-to-skin contact with the mother also stimulates the newborn, even very small preterm infants, to find the nipple and start to feed within one hour.

### **Kangaroo Care Method**

Rose Kambarami spoke on the impact of the Kangaroo Care method (skin-to-skin contact between the mother and newborn immediately after delivery) on reducing perinatal and neonatal mortality. Neonatal units are overcrowded, and often mothers and infants are required to share beds and incubators. Neonatal nursing skills are minimal, most attendants are overworked, and morale is very low. In an overview of 1998 data from Harare Central Hospital, Dr. Kambarami found that they deliver 19,000 babies per year. There were 18,544 live births with 1,062 early neonatal deaths. Perinatal mortality rates were high at 109/1,000. The mean age of neonatal death was two days after birth, but the majority of infants died on their first day of life.

Current management of preterm babies in Sub-Saharan Africa is mainly incubator based. The problems with incubators are that most are imported, so they are expensive and in short supply, and therefore must be shared. Sharing of incubators increases the risk of infection. The incubators are rarely cleaned, electricity supplies are sometimes sporadic, and parts are often not available for repair.

In the Kangaroo Care method, a well preterm infant, wearing only a diaper is placed between the mother's breasts in skin-to-skin contact, instead of being placed in an incubator. This method has been shown to have many benefits. The safety, effectiveness, and improved survival of preterm babies cared for in this manner has been demonstrated in Zimbabwe by Bergman<sup>(72)</sup> and Kambarami,<sup>(73)</sup> and also shown to have better survival rates in Mozambique. The improvement in survival has been documented between 20-60%. The bigger the baby, the better the survival. Potentially fatal apnea was also reduced.

In a study examining the benefits of Kangaroo Care for very low birth weight infants (<1500 grams), Dr. Kambarami found that the infants allocated to Kangaroo Care had better health outcomes than infants placed in a standard incubator setting.<sup>(73)</sup> The Kangaroo Care babies grew faster. Their median weight and hospital discharge weight was higher, frequency of illness and median duration of hospital stay was less, there was a more rapid increase in weight, and survival rates were better. There was a statistically significant difference in growth rates, with the intervention group growing faster, and the frequency of illness was less but not statistically significant. In conclusion, Dr. Kambarami urged the immediate implementation of Kangaroo Care in developing countries to protect preterm infants.

## Breastfeeding and Nutritional Support

Sandra Huffman defined the importance of the timing and type of breastfeeding on neonatal mortality, the evidence for this effect, and implications for breastfeeding promotion programs.<sup>(74)</sup> She said that late neonatal deaths (from 8 to 28 days) are more likely to be prevented by breastfeeding than are earlier deaths, which are principally related to the infant's status at birth and delivery. However, there is some evidence that in the first week of life, breastfeeding can help prevent hypothermia and hypoglycemia in newborns, which are contributory causes of death. Suckling increases body temperature, and the nearness to the mother that breastfeeding provides is beneficial in reducing hypothermia. Since fasting is associated with a fall in blood glucose, practices that restrict the early initiation of breastfeeding are likely to increase the incidence of hypoglycemia. Therefore, WHO recommends that infants should be put to breast within one hour after birth and should not go without breastfeeding for more than three hours between feeds.<sup>(75)</sup> However, over 80% of women report delaying breastfeeding beyond one hour after delivery in Bangladesh, El Salvador, Indonesia, Mali, Nepal, Pakistan, and Senegal, and over half of women in Bangladesh, El Salvador, Haiti, and Pakistan delay breastfeeding beyond 24 hours postpartum.

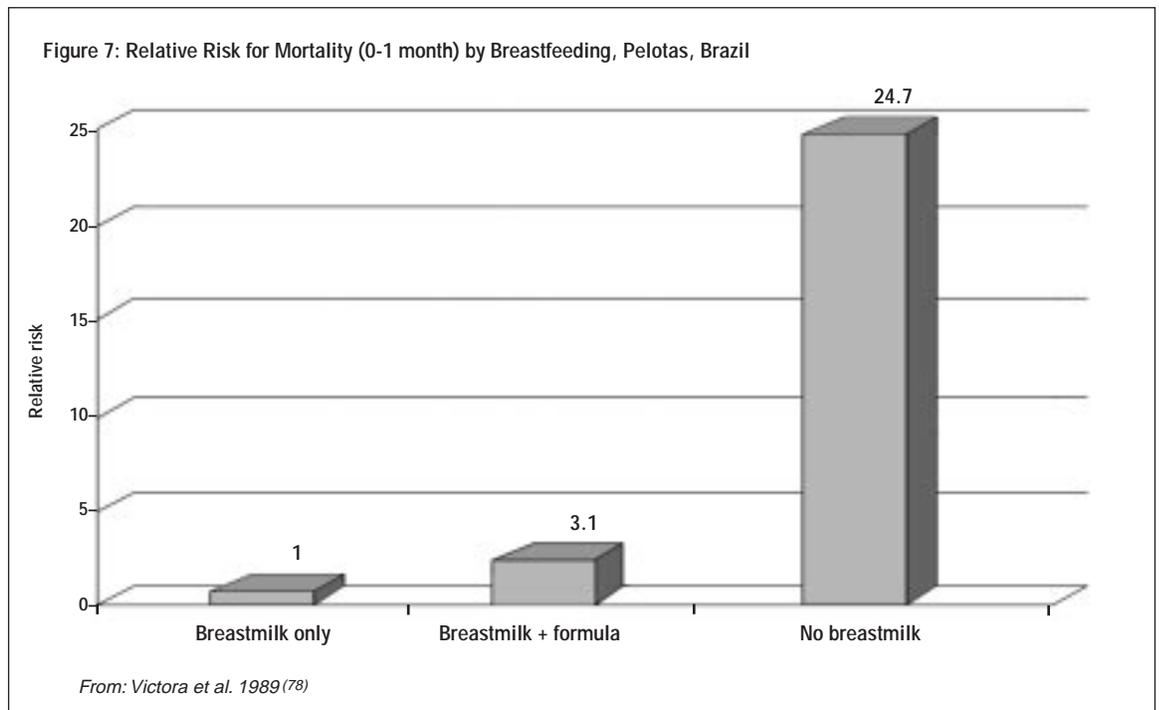


In addition, early initiation of breastfeeding is important because colostrum has higher levels (compared to mature mother's milk), of immunoglobulins, lactoferrin, betacarotene, zinc, and vitamin E, which may help protect infants from infection. In a study in India, the infection rate in the first week of life among low-birth-weight newborns was lowest in the children exclusively fed raw human milk (10.5%) when compared to children given pasteurized human milk and formula (33%), pasteurized human milk alone (14.3%) and raw human milk mixed with formula (16%).<sup>(76)</sup>

Breastfeeding especially protects against late neonatal deaths that are primarily due to infections such as sepsis, pneumonia, meningitis, umbilical infection (omphalitis), and diarrhea. In studies in Brazil and the Philippines, there were major protective effects of breastfeeding for infants 0-1 months of age.<sup>(77-79)</sup> The relative risks for mortality were much higher in infants who were not breastfed (Figure 7). While the major difference in relative risk is due to a lack of breastfeeding, the addition of supplements to breastfeeding in the first month of life is damaging. As shown in Brazil, there were substantial benefits of exclusive breastfeeding over partial breastfeeding. The relative risk of death found to be 24.7 for infants not breastfed, and 3.1 for infants partially breastfed, compared to 1 for those exclusively breastfed.

Clear evidence shows that both rates of early initiation and exclusive breastfeeding can be increased, said Dr. Huffman. Lutter and colleagues<sup>(80)</sup> showed that early initiation and exclusive breastfeeding were increased by the counseling of mothers in both Brazilian and Honduran hospitals, and Morrow et al<sup>(81)</sup> showed that home visits were successful in increasing exclusive breastfeeding rates in Mexico.

Policies and training of staff of maternity centers can affect breastfeeding rates, especially early initiation of breastfeeding. A significant proportion of births can be reached through hospital deliveries and with trained attendants present at delivery. In Latin America, 66% of deliveries occur in hospital, while 76% are completed by a trained attendant. Though less, in Africa, 34% of deliveries are in hospitals, and 42% take place with trained attendants, and in Asia, 33% of all infants are born in hospitals and 56% with a trained attendant present.



In health centers where the Integrated Management of Childhood Illness (IMCI) is in place, when children are brought for health care, mothers are counseled about exclusive breastfeeding and if breastfeeding difficulties are observed, support is provided by the health attendants. Yet information regarding whether these practices have been successful in promoting exclusive breastfeeding have not yet been published. Community-based interventions are especially needed to maintain rates of exclusive breastfeeding for the WHO recommended 4–6 months of age and to promote early initiation of breastfeeding for home deliveries. Dr. Huffman concluded with a plea for programs to work harder at increasing early initiation and exclusive breastfeeding rates with interventions at the community level.

### Prevention and Management of Infections

Most of the reductions in infectious morbidity and mortality will come from indirect, cost-effective, and quite simple antenatal, perinatal, and neonatal health services, predicted Gary Darmstadt, who cited the WHO projection that 40–60% of all neonatal deaths could potentially be averted by the institution of their Mother-Baby Package Interventions.<sup>(13, 82)</sup> A key aspect in strengthening community-based health facilities is educating health providers in early recognition and appropriate management of ill neonates, including referral, and, if possible, delivery of those with serious illness for more advanced care. There are also a number of very simple things to do with hospitalized infants to prevent them from contracting nosocomial infections, including hand washing, rooming in and early contact with the mother, promotion of exclusive breastfeeding, early discharge from hospital for well infants, and caring for infected infants in a group or cohort.

Proper identification of signs of illness in neonates, such as refusing to nurse and temperature abnormalities, cannot be underestimated as a valuable infection detection method. In order to identify problems in infants early, we need to have case definitions since nearly one-half of all early-infant deaths occurred in the first two days after admission to hospital.<sup>(83)</sup>

Also needed are effective preventive and intervention strategies, which require regional determination of community pathogen prevalence and antimicrobial susceptibility patterns. The importance of many pathogens in the community is almost entirely unknown. We need this informa-

tion, however, so we can devise optimal empiric treatment strategies. Another principle to keep in mind is that parenteral therapy, initially with penicillin or ampicillin plus an aminoglycoside such as gentamicin, is recommended by WHO for all seriously ill neonates.

To get an idea of what antibiotics may be useful to combat neonatal infections, we can consider those antibiotics that have been useful in treating infections *in utero*, he continued. A recent study conducted in Panama showed that when mothers who had PROM were given a single dose of intramuscular or intravenous cephtriaxone, lower colonization rates of gram-negative bacilli and group-B streptococcus and significantly decreased sepsis-like illnesses in the first five days of life were noted in their infants.<sup>(84)</sup> In India, oral cotrimoxazole was shown to reduce neonatal deaths from pneumonia by 40% when combined with gentamicin and administered twice daily.<sup>(85)</sup> In devising alternate empiric antimicrobial regimens other than those recommended by WHO (i.e., penicillin/ampicillin plus an aminoglycoside), however, the potential impact on promoting the emergence of antibiotic resistant strains must be considered carefully.

Historically, the introduction of penicillin into the Yale nursery in 1945 caused sepsis mortality to decrease from almost 100% to 66%.<sup>(86)</sup> With the addition of gentamicin in 1963, the mortality of sepsis came down to between 25 and 50%, and parenteral ampicillin plus gentamicin has remained the gold standard therapy since then. With the introduction of neonatal intensive care units (NICUs), the rates have further decreased to 10–15% under the best of conditions. However, since sepsis is very difficult to manage, and antimicrobial resistance is increasingly problematic worldwide, there is still the need for prevention.

Attempting to increase epithelial barrier functions in these newborn babies may be an important preventative intervention. Epithelial barriers provide our first-line defense against infection. These barriers are developmentally immature, and easily injured, and are often functionally compromised among neonates especially when they are born prematurely or when they are born to a malnourished mother. We know that deficiencies of zinc, fatty acids, or amino acids in particular can lead to compromised barrier function. We believe that agents of sepsis are likely to enter through epithelial tissues of the gastrointestinal tract, respiratory tract, skin, or conjunctiva. Transepidermal water loss is the best single measure of epidermal (i.e., skin) barrier function in the newborn baby. Epithelial barrier function increases with greater gestational age at birth and with increasing postnatal age. There is a drastic change by 33 weeks of age; below that, it is immature, above it, it is quite mature. Evidence may link nutritional intervention *in utero* with increased level of protection. Vernix may provide a naturally protective barrier on the skin of the newborn. Washing it off can cause hypothermia and also skin irritation, and its impact on preserving fluids and heat and preventing infections has never been addressed.

In a pilot study of newborn infants less than 33 weeks gestational age at Stanford University, treatment with the topical emollient Aquaphor was associated with a decreased incidence of positive blood and cerebrospinal fluid cultures (3.3%) compared to control infants (26.7%).<sup>(87)</sup> Additional benefits of topical ointment therapy with Aquaphor included a reduced number of episodes of perceived clinical deterioration consistent with sepsis (nine episodes compared to 37 episodes in control infants); significantly decreased transepidermal water loss during the first 6 hours after initial application; and superior skin condition scores on days 7 and 14.<sup>(87)</sup> Aquaphor is a preservative-free ointment containing petrolatum, mineral oil, mineral wax, and lanolin alcohol. Application of Aquaphor to a 2 kg baby for one month costs approximately \$6.50. Aquaphor presumably is protective through enhancement of epidermal barrier function. It does not appear to act by changing the cutaneous flora, as topical emolliation had little effect on the density of colonization of the skin with potentially pathogenic bacteria or fungi.<sup>(87, 88)</sup> Its efficacy, however, as a barrier-enhancing therapy that is capable of decreasing infections in preterm infants must be confirmed before its wide-scale use can be recommended. Alternatively, other emollients, such as locally available vegetable oils, may be useful and less expensive, but their safety and clinical efficacy have not been evaluated.



## *Implication for Research and Programs*

### **Community and Health System Barriers**

Jeanne McDermott presented the preliminary results of a community-based study of care-seeking behaviors among women with perinatal deaths in Guatemala. A social autopsy, using a structured questionnaire, was conducted with mothers of the identified perinatal deaths and, if possible, a second informant who had attended the birth. The interview collected information on problems the women reported in pregnancy and labor and delivery, and problems the newborn had following delivery of live births. In addition, information on general care the women received in pregnancy, place and attendant at birth, signs to determine if the birth was a stillbirth or live birth, and general newborn care practices was obtained.

One hundred thirty-seven perinatal deaths were recorded during the study period, and each of their mothers were interviewed. This was twice as many as had been estimated during the study design. Only half of the mothers of the 101 stillbirths actually saw their babies after delivery, and only 15 (15%) of the still births were confirmed by the mothers, indicating that mothers are not the best information sources for defining signs to determine vitality at birth.

Eighty-seven (64%) of the mothers who lost an infant reported a problem during labor and delivery. Care was sought from outside for 83%; outside alone for 43 mothers and from both inside and outside the home for another 29 mothers. The source of care sought, however, remained a problem. Only 16 mothers who sought outside care received it from formal health services. The overwhelming majority received care from informal health services, including traditional birth attendants (TBAs). Surprisingly, most of the 19 women referred went for their referrals.

Over half of the 36 neonatal deaths in this study occurred in the first 12 hours after birth. Hypothermia was noted in 32 (89%) of the neonatal deaths, the cord was cut with scissors for 31 (86%), and nothing was applied to cord for 19 (53%). Thirteen (37%) of the mothers reported that their newborn would not breastfeed. Dr. McDermott concluded by calling for more qualitative studies among mothers and care providers to better understand care-seeking and care-giving behavior.

### **Program Experience with Integrated Interventions**

Harshad Sanghvi reported on the results of two hospital-based studies: the Nairobi Birth Study and the Ugandan Maternal Health Care Preservice Training. In the Kenyan study, prior to the implementation of an essential package of interventions, 51% of all perinatal deaths were due to labor and delivery-related difficulties (35% asphyxia and 16% cerebral birth trauma), 15% to preterm birth, and 8% to infections. Preterm rupture of membranes was a significant risk factor.

The perinatal death rate was 35 per 1,000. Approximately 7.5% of births were in the low birth weight range (less than 2500 grams), and about half of those children died. Two percent of women had significant malaria parasite loads. Identified problems included significant overcrowding of hospitals and staff shortages, especially in the evenings and on weekends—when the majority of deaths occurred.

The team of researchers then introduced a variety of interventions intended to reduce the perinatal death rate. To reduce overcrowding, they increased early discharge and transfers to health centers of uncomplicated cases. If both mother and child were normal, they could be discharged six hours after birth, and patients with more complications, or women who were Cesarean delivered, left the hospital after three or four days. Conversely, admission rates for women with hypertensive disorder were increased. Twenty-four-hour staff (including students) coverage was instituted, in an effort to reduce deaths resulting from unattended births. Standardized treatment protocols were adopted, and better in-service training was provided. Presumptive antibiotic treatment was instituted for PROM, and malaria prophylaxis and syphilis screening were introduced. Perinatal audits were also implemented to regularly review the causes of perinatal death. As a result of the interventions, perinatal mortality dropped from 80 to 55/1,000 over a six-year period in the main hospitals. Recently, there has been a marked increase in low-birth-weight deliveries, hospital crowding, and shortages of supplies, in large part due to the climbing HIV infection rate.

In the Ugandan study, some of the identified problems with management of pregnancy and delivery included lack of preparedness for the seriously sick (including pain and discomfort of the patient), insufficient use of adequate equipment, and lack of motivation, and poor training of attendants. Many inadequacies were also noted in the training of clinical staff, such as students who graduated with limited skills and were immediately posted to health facilities, clinical instructors without practical skills, and a curriculum in great need of modernization. Interventions implemented to date include simple and clear job descriptions to direct staff activities, and importantly, many interventions in the training of staff. There was development of an essential obstetric care technical update—a week-long workshop for medical and midwifery faculty—followed by updated guidelines and protocols.

In conclusion, Dr. Sanghvi stressed the need for joint planning with institutional and in-country health officials, and the introduction of an essential package of interventions to reduce perinatal mortality in a hospital setting. He also endorsed the continued need for supervision, monitoring, and mortality audits.

### **Women-Friendly Health Services**

The UNICEF baby-friendly hospital initiative was highly successful in promoting breastfeeding around the world. Now, UNICEF is launching a new program of women-friendly health services based on a synthesis of 25 country experiences. According to Koen Vanormelingen, achievement of women-friendly health services requires improvements in access to services, including adjustments to price and distance, and upgrading of staff skills by the introduction of training, protocols, and audits. Certification can also be given to women-friendly services or facilities, as has been done in Peru and Bangladesh, to acknowledge their accomplishments.

In addition to women-friendly health services, UNICEF is calling for the creation of women- and child-friendly societies. These societies would consider maternal mortality as a social injustice, promote women- and child-friendly health services, develop women and child friendly communities, and improve home-based care. Enactment and enforcement of human rights law, advocacy for women-friendly policies in the home and workplace, and sustained social investment are also important parts to this new vision of society.

Implementation of these strategies will require adaptation to local settings and joint planning including institutional and country health officials. Support and recognition of the health staff will

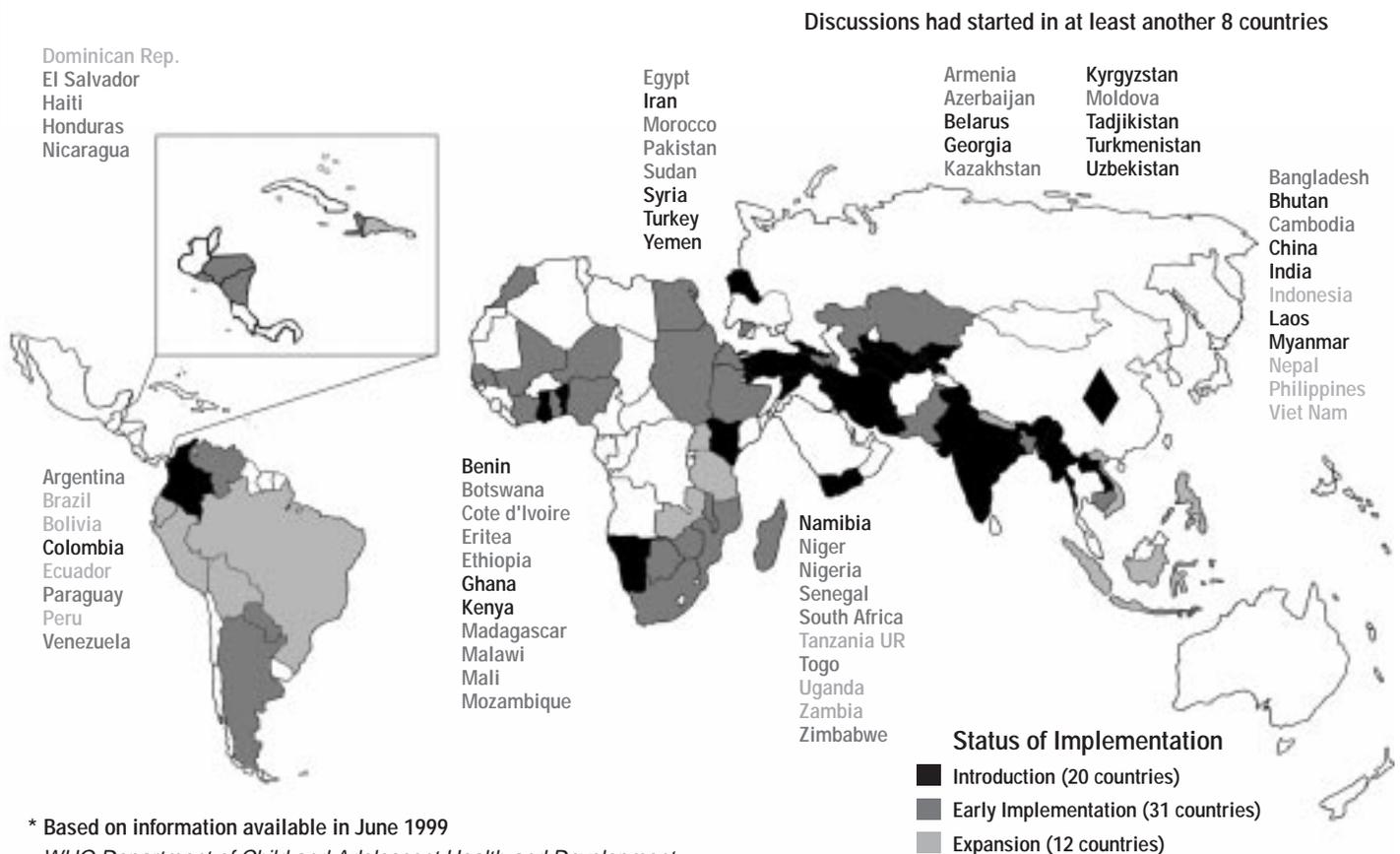
be key to enhancing the quality of the services. National task forces can carry out development of these services, but they will need to be supported by a global advocacy initiative. In closing, Dr. Vanormelingen said that interventions to reduce perinatal mortality and maternal mortality are complimentary and require a holistic, rights-based approach to assure long-term success.

### Adapting the Integrated Management of Childhood Illness (IMCI) to the Neonatal Period

The WHO/UNICEF Integrated Management of Childhood Illness (IMCI) guidelines yield accurate identification of illnesses in outpatient settings, ensure more appropriate and combined treatment of all major illnesses, and provide speedy referral of severely ill children.<sup>(89)</sup> In addition, the strategy also improves the counseling of caregivers and the provision of preventive services, and aims to improve the quality of care of sick children at the referral level. In the home setting, it promotes improved nutrition and preventive care, appropriate care-seeking behaviors, and the correct implementation of prescribed care.

Olivier Fontaine explained that the IMCI guidelines are a simplified system of diagnosis and treatment designed for use by health workers with limited training and little or no laboratory support. According to the guidelines, the health worker first assesses the child's health status, asking questions and examining the child and checking immunization status. Then, he or she classifies the child's illness and identifies the treatment: urgent referral, specific medical treatment and advice, or simple advice on home management, based on a color-coded triage system. If the child is being

Figure 8: Implementation Of IMCI (June 1999)\*



referred urgently, health workers give only initial treatment before departure. As of 1999, IMCI was implemented in 20 countries in the introduction phase; 31 countries in early implementation; and 12 countries in expansion phase (Figure 8). When interviewed, mothers reported satisfaction with IMCI services. In 1997 in Peru, mothers reported better care than before IMCI (79%), more information on child's disease (89%), information on when to come back (48%), information on home treatment (88%), and improved health service (90%).

Jelka Zupan then spoke about current efforts to adapt the IMCI guidelines to problems of the early neonatal period. She said that including the problems of the first week of life in IMCI was important because most mothers (60%) give birth at home with no skilled attendant present, and the only health provider in the first week of life might be the IMCI-trained health worker.

However, if real neonatal mortality reduction is the goal, services must be accessible all day and every day, and provided by health workers with midwifery skills. Dr. Zupan said that work is in progress to organize an effective package of services during pregnancy, delivery, postpartum and the neonatal period (Table 6). It will provide guidance on preventive care as well as for early detection and treatment of most frequent and severe neonatal problems. If the mother decides to deliver at home, the health worker with the skills from that package will be able to advise her on precautions for home delivery and care for her newborn. Special emphasis is being placed on the care of moderate preterm and low-birth-weight infants, with particular regard to feeding, thermal protection, and preventive interventions. Immunizations will also be administered as soon as possible. In a separate component, health workers will be trained to counsel pregnant women and mothers on the reduction of HIV transmission to their infants.

#### **During pregnancy**

- \* Preparedness and counselling on safe childbirth
- \* Treatment of maternal complications
- \* Infection control in endemic area (malaria, syphilis and hookworm)
- \* Control of nutritional deficiencies
- \* Immunizing the mother with tetanus toxoid
- \* Avoiding harmful substances and practices

#### **During childbirth**

- \* Safe and clean delivery
- \* Effectively managed pregnancy complications and referral for essential obstetric care
- \* Support and care
- \* Controlling nosocomial infections

#### **For the newborn**

- \* Routine care and vigilance for all newborns, especially during adaptation/stabilisation and transition period (6-12 hours after birth)
- \* Special care for preterm and/or low birth weight infants, including kangaroo care
- \* Identification and treatment of infections
- \* Support for mothers on providing newborn care, on recognizing danger signs and taking appropriate action
- \* Immunization
- \* Prevention of mother-to-child HIV/AIDS transmission

**Table 6: Neonatal Health Interventions to be Included in the Revised IMCI Guidelines**

## **Experience with Integrated Community Interventions in Indonesia**

Reporting on the results of the community-based village midwife program, Mohammed Hakimi stated that in 1993, the government started a midwifery training program. The objective was to train 60,000 midwives throughout the country, and in 1997, 55,000 were trained in birthing, family planning, supervision of other birth attendants, and referral of complicated cases to the health center or hospital. Training consisted of three years in school followed by one and a half years of hands-on clinical training.

In a 10% sample of the entire district, there was no reduction in neonatal mortality between the years of 1995 (21.8/1,000) and 1997 (23.9/1,000). The level of mortality was even high at the district hospitals. Causes of death included asphyxia (38.5%) and low birth weight (42%). High mortality rate may be due to the low quality of care and lack of coverage on weekends. The greatest risk for perinatal mortality in the intervention communities was prolonged labor. In the program, midwives were trained to recognize the second stage of labor; they performed better on skills evaluations, but in six months, their skills and knowledge were gone. Reasons for program failure may include insufficient training of midwives, and leaving the program during or soon after training for a better position. Thus, further research is needed to establish the effectiveness of village midwife program, including information, education, communication, and emergency obstetric care insurance.

## **Community-Based Neonatal Care in India**

With most of the world's women giving birth at home, Abhay Bang questioned the relevance of hospital-based studies as he discussed the success of his intervention which provided home-based neonatal care in rural India.<sup>(90)</sup> The most significant of traditional problems, beliefs and practices that he noted at the onset of the study were that women starved themselves in the last trimester, believing that smaller babies are safer and easier to deliver; lack of breastfeeding in the first three days of life; lack of thermal control in the crucial early days of life; families not recognizing prematurity and birth asphyxia as high-risk problems, and, even if sick, a newborn couldn't be moved out of the home.

The study took place in an area of 39 villages and control area of 47 villages with about 40,000 population in each group. A baseline period lasted from 1993 to 1995, and an intervention phase of three years followed in 1995–98. The intervention was incrementally introduced. In year one, only home visits were made for observation with very little intervention. Of 1,000 births in this area, 75% were covered by home visits. In year two, home visit proportion reached 85%, and in addition, management of sick newborns was added. In year three, the home visit coverage increased to 93%, with managed care of sick infants, and health education of mothers through group meetings was about 70%. Hospital care was not part of this intervention package, though there was a government hospital in each area and the parents were free to seek hospitalization.

After completion of the baseline phase, 39 female villagers, usually 20–40 years old with 5 to 10 years of schooling, were selected to be trained as health workers to visit the home and provide neonatal care. They were trained to keep lists of pregnant women, keep a mother's health record, attend and observe the process of labor, (deliveries were conducted by TBAs) examine the baby for asphyxia for one to five minutes, and record respiratory rate and weight. The health workers also conducted follow-up visits at regular intervals and on days of sickness, at which time they examined and took histories. A physician visited each village every 15 days to supervise the health workers, and found that there was 92% agreement between the doctor's and the workers' findings. Economic rewards and punishments were also given to the workers for not attending deliveries or for poor quality of data.

Of 280 parents who were asked if they would seek care provided by somebody trained in the village, 97.5% said yes, 1.5% said no, and 0.7% said they didn't know. So in the second year of the study, the health workers began delivering care, which included educating the mother, preventing

infections, educating women on breastfeeding and temperature maintenance, giving an injection of 1mg of vitamin K, identifying sick or high-risk newborns, managing illness, and keeping records. The sicknesses they managed were birth asphyxia, hypothermia, breastfeeding, prematurity, sepsis, and superficial infections. They also learned resuscitation using tube and mask. Knowledge and skills were reinforced by monthly training classes.

The major cause of death was neonatal sepsis, and it was unclear that a simple, effective method of management was needed. After determining basic patterns of antimicrobial resistance in the intervention area, the health workers were instructed to treat sepsis with injections of gentamycin and oral cotrimoxazole for seven days in preterm infants and for 10 days for all other children. After implementation, case fatality fell from 18.5% to 2.8%. During the same period some parents missed or refused treatment (33 infants), and the case fatality was 21%. There was 14% case fatality for infants treated in hospital. In closing, Dr. Bang reported that in the three years of their intervention, there was a 71% reduction in perinatal mortality and a 62% reduction in neonatal mortality. At the same time, the infant mortality rate decreased 46% and the under-5 death rate by 42%.

At the conclusion of the presentations, participants split into working groups for focused discussion. It was widely agreed that the quantity and quality of data on perinatal and neonatal mortality, morbidity, and risk factors were grossly inadequate. Suggestions to improve data collection included the strengthening of vital registration, improvement of community-based (as opposed to hospital-based) statistics through the use of verbal autopsy and prospective surveillance, and the use of data for international advocacy to draw attention to the enormous problem of perinatal and neonatal deaths.

Once research has established the efficacy of an intervention, it was thought to be crucial to introduce the intervention into a population, and assess the effectiveness in a realistic program setting. Initially, the implementation of an essential neonatal health service package was thought to be the key to successful intervention. Also important was involvement of all parties in the implementation process; incorporation of monitoring, evaluation, and dissemination into programs and interventions; and the use of scientific information to guide policy and program development. Optimally, reproductive health and safe motherhood programs could implement family planning interventions to widen intervals between pregnancies; improve the diagnosis and treatment of sexually transmitted diseases and HIV; improve malaria prophylaxis; and boost nutrition during pregnancy through education and supplementation. Currently operating child health programs could also increase breastfeeding and child nutrition through counseling and feeding initiatives, and improve the training of health workers and birth attendants to use neonatal resuscitation techniques and to properly identify and manage sepsis.

Most of the nine million perinatal and neonatal deaths that occur each year are caused by infectious diseases; pregnancy-related complications such as placenta previa and abruptio placentae; delivery-related complications, including intrapartum asphyxia, birth trauma, and premature birth. Sadly, very few programs currently exist to specifically target perinatal and neonatal mortality. However, a cost-effective, and efficient way to introduce interventions would be to make additions to already existing programs.

In most developing countries, a large number of early deaths escape diagnosis. This is because of lack of diagnostic facilities, inadequate or absent post-mortem examination, and poor histopathological and microbiological capabilities, and because many of these deaths occur at home with the mothers receiving little or no medical attention. However, it is known that transplacental transmis-

---

### *Working Group Reports*

---

### *Program Priorities*

sion of infection is a major cause of early mortality. Some key interventions that can be implemented prior to birth to decrease perinatal and neonatal mortality include:

- Increasing the quality and scope of syphilis screening;
- Improving the diagnosis and treatment of ascending reproductive tract infections in pregnant women;
- Expanding maternal immunization with tetanus toxoid;
- Presumptive malaria treatment or prophylaxis during routine antenatal care visits, and
- Nutritional support for pregnant women to improve birth outcomes.

There are many complications of labor that may lead to perinatal and neonatal death. Some involve the health delivery system, including lack of transportation and essential obstetric skills, while others are more specific to the woman herself. These complications include: delayed admission to the delivery area, dystocia, fetal distress, multiple gestation, intrauterine growth retardation (IUGR), and preterm delivery. The following programs are urgently needed to reduce mortality due to obstetric complication:

- Regular re-education of health workers and birth attendants and the use of economic incentives to improve the identification and management of malpresentation and prolonged labor;
- Referral of complicated cases to health center or hospital;
- Combating the barriers to referral compliance, including transportation of mothers and care of other children, and
- Institution of perinatal and neonatal audits at hospitals and health centers

The first days after birth are particularly important for the health of the newborn. Birth attendants, health workers and families must guard against body heat loss after delivery, and promote early and exclusive breast-feeding. Measures feasible now to prevent further neonatal death include:

- Wider use of resuscitation techniques for asphyxiated infants;
- Proper management of neonatal sepsis and other infections;
- Skin-to-skin Kangaroo Care for preterm infants, and
- Immediate and exclusive breastfeeding for all children.



One of the greatest challenges facing the international public health community is creating sustainable interventions in countries where the needs are greatest. Crucial to the success of programs is national ownership, and public-private partnerships to ensure long-term funding. Finally, an ongoing dialogue must be established between governments and researchers to combat perinatal and neonatal mortality. Governments must be able to call upon researchers to help them solve health problems, and research results must be used to formulate national programs and policies.

Although research needs vary according to regional conditions, a small number of priorities were identified at the meeting which will greatly contribute to our knowledge of the causes of perinatal and neonatal mortality, and provide strategies for combating these millions of preventable deaths.

Almost all knowledge of infectious disease etiologies in developing country neonates has been based on studies of hospitalized patients, or on retrospective, verbal autopsy-based surveys, neither of which accurately reflect the true burden of disease in the community. In order for the most effective prevention and treatment strategies to be designed, precise identification, relative importance, and antimicrobial susceptibility patterns of the agents infecting neonates in the community must be determined on a regional basis. Priority research to better understand causes of, and risk factors for neonatal infections at the community level include:

- Community-based surveillance to identify the principal bacterial and viral agents of neonatal infections, with special emphasis on Asia and Africa;
- Assessment of the burden of disease due to herpes simplex virus, cytomegalovirus, toxoplasmosis, syphilis, chlamydia and ureaplasma;
- Determination of the antimicrobial resistance profiles of the common bacterial agents of serious infections in neonates on a regional basis, in both community and hospital settings;
- Evaluation of neonatal care provided in the home by caretakers, traditional birth attendants, and community health workers, and follow cohorts of neonates for infectious outcome, and
- Case-control studies to identify the principal risk factors for morbidity and mortality from neonatal infections, including organism-specific risk factors. Risk factors to be evaluated include low birth weight; unhygienic delivery, skin and umbilical cord care; birth asphyxia; hypothermia; smoke inhalation; and feeding practices.

Clinical differentiation of sepsis, meningitis and pneumonia in neonates is difficult because the signs and symptoms are variable, often vague, nonspecific, and overlapping among these diseases. Identification of the historical information and clinical signs and symptoms most predictive of the presence of acute, neonatal infection (principally pneumonia, sepsis and meningitis) is needed to devise accurate case definitions and effective case management protocols for use in health care facilities and at home by trained health care workers.

Integrated Management of Childhood Illness (IMCI) is being adapted for acute management of common infectious illnesses in the neonate, and may make major contributions to reducing infectious morbidity and mortality. It has been predicted that implementation of IMCI protocols will reduce the total global disease burden by 14%, and ARI case management may prevent 50% of pneumonia deaths in children. Determination of the most useful predictors of infected neonates and development of protocols for use in the field is an ongoing effort at WHO, but the efficacy of this approach in neonates has not been tested. Priority research in design of diagnosis and management approaches include:

- Identification of historical information and clinical signs and symptoms that are most predictive of the presence of acute neonatal infection;
- Development of an approach for identifying neonatal infection, and
- Training and testing the abilities of community health workers to use the approach to identify acutely infected neonates

An estimated 63% of infants are born at home in developing countries. In some countries such as Bangladesh, over 80% of births occur at home, emphasizing the need to expand the capacities of community health workers in routine care of the pregnant woman and neonate. A number of simple practices, when instituted by properly trained traditional birth attendants and community health

workers, can have profound effects. These practices include detection of pregnancy-related and obstetric complications; hygienic delivery and umbilical cord care; resuscitation of the asphyxiated newborn, thermal control, early and exclusive breastfeeding, and nutritional supplementation when indicated, antibiotic prophylaxis of *ophthalmia neonatorum*, avoidance of smoke inhalation in the house, and provision of immunizations. Priority research on community care of the pregnant woman and neonate includes:

- Community-based studies to determine existing obstetric practices and neonatal care;
- Studies to evaluate health-seeking behavior for neonatal illnesses;
- Evaluation of knowledge, attitudes and beliefs regarding neonatal health among family members, trained birth attendants and village health workers;
- Development and evaluation of training curricula and continuing medical education for mid-level health workers, including traditional birth attendants, in obstetric care;
- Design of strategies to improve access to emergency obstetric care;
- Testing of quality assurance mechanisms for obstetric care in developing countries, at the levels of community, health center and referral hospital;
- Studies of methods to increase referral rates to health center or hospital for complicated pregnancies;
- Design and evaluation of a package of simple practices for the routine post-partum care of neonates born in the community, including proper thermal control; recognition and resuscitation of asphyxiated neonates; promotion of early and exclusive breastfeeding; application of prophylactic antibiotics to the eyes; optimal skin and hygienic cord care; and provision of immunizations;
- Training of traditional birth attendants and community health workers to implement the package of basic neonatal care practices, and
- Evaluation of program effectiveness and impact.

In 1994, 45 million pregnant women were living in malarious areas, with over 23 million in Sub-Saharan Africa alone. In settings of moderate to high malaria transmission, malaria may cause up to 30 percent of preventable low birth weight in newborns, and accounts for 3 to 5% of neonatal mortality in highly endemic regions. In settings of low malaria transmission, malaria also is associated with an increased risk of spontaneous abortion and stillbirth. Although WHO recommends antimalarial drugs for prevention of malaria in pregnant women in endemic areas, many pregnant women at risk do not receive appropriate prevention or treatment as part of prenatal care. Research priorities for malaria prevention and treatment include:

- Efficacy studies of presumptive, intermittent treatment to prevent malaria as part of routine antenatal care in areas of high malaria transmission;
- Design of methods for treatment of malaria during pregnancy using safe, effective and simple regimens in areas of high, medium, and low malaria transmission;
- Evaluation of the safety and efficacy of newly available antimalarial drugs (alone or in combinations) for malaria treatment and prevention in pregnancy, and
- Studies of means to reduce malaria exposure during pregnancy, such as insecticide permeated bed nets. Research Priorities Add Ons place at end

Low birth weight (LBW), or birth weight less than 2500 grams, is one of the principal contributors to neonatal morbidity and mortality worldwide, and accounts for up to 70% of neonatal deaths in some countries. Intrauterine growth retardation (IUGR) is the most common form of LBW in the developing world (accounting for more than 60% of the LBW), whereas most low birth weight in infants in developed countries is due to prematurity. Risk factors for IUGR include untreated urinary tract infections (bacterial vaginosis); ascending reproductive tract infections, including syphilis, gonorrhea and chlamydia; low pre-pregnancy maternal weight and height, and low caloric intake and poor weight gain during pregnancy. Importantly, the problem of low birth weight is intergenerational: low birth weight infants remain poorly nourished during childhood and grow up to be stunted adults who in turn give birth to small infants, and thus must be combated at several points during the life cycle. Specific research activities to reduce low birth weight include:

- Surveillance studies to establish the rate and etiology of bacterial vaginosis in different countries;
- Evaluation of simple methods for detection of bacterial vaginosis, and appropriate treatment, such as comparing a once versus three-times daily treatment with metronidazole;
- Development of strategies to improve knowledge and practice of methods to prevent sexually-transmitted diseases;
- Evaluation of the safety and efficacy of maternal caloric supplementation for reducing low birth weight;
- Design of strategies to improve caloric intake before and during pregnancy with the use of locally available and acceptable food supplements;
- Development of methods to reduce maternal anemia through the use of iron supplements, antihelminths and antimalarials;
- Evaluation of micronutrient supplementation (vitamin A, calcium and zinc) for the reduction of LBW, and improved neonatal health; and
- Testing of optimal delivery methods for micronutrient supplementation of children, adolescents and women.

---

## *Conclusions*

The summary of the meeting was given by Anthony Costello, who said that one of the most important messages that the symposium provided for policy-makers was that neonatal mortality accounts for 60% to 70% of infant mortality in many developing countries—and there are very few programs that specifically target it. He also said that one of the most efficient ways to reduce neonatal mortality would be to expand already existing programs to address illness in the neonatal period.

Priority interventions before delivery include better syphilis screening and treatment—especially in Sub-Saharan Africa; improved treatment of ascending infections in pregnant women, including bacterial vaginosis, chorioamnionitis, and preterm rupture of the uterine membranes; maternal immunization with tetanus toxoid and pneumococcus (when it becomes widely available); and malaria prophylaxis during routine antenatal care visits. Multivitamin and micronutrient supplementation also improves pregnancy outcomes and may help battle infection in the post-neonatal period.

Better management of obstetric complications is also necessary to reduce neonatal mortality. Identification and management of malpresentation and prolonged labor is important, as is the need to increase the referral rates to a health center or hospital for problem pregnancies. Important for improving the referral process is combating the barriers to compliance, which include transportation and care of other children. Training of village health workers to supervise and manage the birthing process could help—but it is important to offer regular re-education and economic incentives to ensure the continued quality of services.

Interventions after delivery are also important, such as resuscitation of asphyxiated infants; the proper management of neonatal sepsis and other infections; skin-to-skin Kangaroo Care for preterm infants, and immediate and exclusive breastfeeding for all children. Twenty-four-hour staffing and introduction of perinatal and neonatal audits are useful in improving hospital and health center-based outcomes.

Dr. Costello called for the application of research results in programs and policies. A large number of effective interventions with clear impact data were presented at the symposium. The challenge currently facing the public health community is making them sustainable in the countries where the needs are greatest. He felt that the answers lie in partnerships between public and private donors and national governments and institutions—national ownership of programs is crucial to their long-term success. He also said that the most important research needs were to develop further potentially important interventions, adapt them to local situations, and evaluate their effectiveness and cost in program settings.

1. *The World Fertility Surveys*, a collection of high-quality, internationally comparable surveys of human fertility conducted in 41 developing countries in the late 70s and early 80s. Available on the Internet at: <http://opr.princeton.edu/archive/wfs>
2. *Demographic and Health Surveys*, the successor to World Fertility Survey, which has completed three additional runs of surveys in the 80s and 90s. Available on the Internet at: <http://opr.princeton.edu/archive/dhs1>
3. Pattinson RC, De Jong G, Theron GD. Primary causes of total perinatally related wastage at Tygerberg Hospital. *South African Medical Journal* 1989; 75: 50-53
4. Bique-Osman N, Folgosa E, Gonzales C, Bergstrom S. Genital infections in the aetiology of late fetal death: an incident case-referent study. *J Trop Ped* 1995;41:258-266.
5. Folgosa E, Bique-Osman N, Gonzalez C, Hagerstrand I, Bergstrom S, Ljungh A. Syphilis seroprevalence among pregnant women and its role as risk factor for stillbirth in Maputo, Mozambique. *Genitourin Med* 1996;72:339-342.
6. Folgosa E, Gonzalez C, Bique-Osman N, Hagerstrand I, Bergstrom S, Ljungh A. A case-control study of chorioamniotic infection and histological chorioamnionitis in stillbirth. *APMIS* 1997;105:329-336.
7. Nelson CT, Demmler GJ. Cytomegalovirus infection in the pregnant mother, fetus, and newborn infant. *Clin Perinatol* 1997;24:151-160.
8. Naeye RL. Causes and consequences of chorioamnionitis. *N Engl J Med* 1975;293:40-41.
9. Naeye RL, Tafari N, Judge D, Gilmour D, Marboe C. Amniotic fluid infections in an African city. *J Pediatr* 1977;90:965-972.
10. Ross SM, Naeye RL. Causes of fetal and neonatal mortality in a South African black community. *S Afr Med J* 1982;61:905-909.
11. Moyo SR, Tswana SA, Nystrom L, Bergstrom S, Blomberg J, Ljungh A. Intrauterine death and infections during pregnancy in Harare, Zimbabwe. *Int J Gynecol Obstet* 1995;51:211-218.
12. World Health Organization: *Perinatal mortality: A listing of available information*. Geneva Switzerland, World Health Organization, 1996. FRH/MSM 96.7
13. World Health Organization. *Mother-baby package: implementing safe motherhood in countries*. Maternal Health and Safe Motherhood Programme. Geneva, Switzerland, WHO, 1994, FHE/MSM/94.11.
14. Stoll, BJ. The global impact of infection. *Clin Perinatol* 1997; 24:1-21.
15. Nicoll A, Timaues I, Kigadye RM, Walraven G, Killewo J. The impact of HIV-1 infection on mortality in children under 5 years of age in sub-Saharan Africa: a demographic and epidemiologic analysis. *AIDS* 1994 Jul;8(7):995-1005.
16. Hira SK, Kamanga J, Bhat GJ, Mwale C, Tembo G, Luo N, Perine PL. Perinatal transmission of HIV-I in Zambia. *BMJ* 1989 Nov 18;299(6710):1250-2.
17. Lallemand M, Lallemand Le Coeur S, Cheymier D, Nzingoula S, Jourdain G, Sinet M, Dazza MC, Blanche S, Griscelli C, Larouze B. Mother-child transmission of HIV-1 and infant survival in Brazzaville, Congo. *AIDS* 1989 Oct;3(10):643-6
18. St Louis ME, Kamenga M, Brown C, Nelson AM, Manzila T, Batter V, Behets F, Kabagabo U, Ryder RW, Oxtoby M, et al. Risk for perinatal HIV-1 transmission according to maternal immunologic, virologic, and placental factors. *JAMA* 1993 Jun 9;269(22):2853-9.
19. Ryder RW, Nsuami M, Nsa W, Kamenga M, Badi N, Utshudi M, Heyward WL. Mortality in HIV-1-seropositive women, their spouses and their newly born children during 36 months of follow-up in Kinshasa, Zaire. *AIDS* 1994 May;8(5):667-72
20. Braddick MR, Kreiss JK, Embree JB, Datta P, Ndinya-Achola JO, Pamba H, Maitha G, Roberts PL, Quinn TC, Holmes KK. Impact of maternal HIV infection on obstetrical and early neonatal outcome. *AIDS* 1990 Oct;4(10):1001-5.
21. Miotti PG, Dallabetta G, Ndovi E, Liomba G, Saah AJ, Chipangwi J. HIV-1 and pregnant women: associated factors, prevalence, estimate of incidence and role in fetal wastage in central Africa. *AIDS* 1990 Aug;4(8):733-6.
22. Miotti PG, Dallabetta GA, Chipangwi JD, Liomba G, Saah AJ. A retrospective study of childhood mortality and spontaneous abortion in HIV-1 infected women in urban Malawi. *Int J Epidemiol* 1992 Aug;21(4):792-9.

23. Temmerman M, Plummer FA, Mirza NB, Ndinya-Achola JO, Wamola IA, Nagelkerke N, Brunham RC, Piot P. Infection with HIV as a risk factor for adverse obstetrical outcome. *AIDS* 1990 Nov;4(11):1087-93.
24. Temmerman M, Lopita MI, Sanghvi HC, Sinei SK, Plummer FA, Piot P. The role of maternal syphilis, gonorrhoea and HIV-1 infections in spontaneous abortion. *Int J STD AIDS* 1992 Nov-Dec;3(6):418-22.
25. Lepage P, Dabis F, Hitimana DG, Msellati P, Van Goethem C, Stevens AM, Nsengumuremyi F, Bazubagira A, Seruflira A, De Clercq A, et al. Perinatal transmission of HIV-1: lack of impact of maternal HIV infection on characteristics of livebirths and on neonatal mortality in Kigali, Rwanda. *AIDS* 1991 Mar;5(3):295-300
26. Lepage P, Msellati P, Van de Perre P, Hitimana DG, Dabis F. Characteristics of newborns and HIV-1 infection in Rwanda. *AIDS* 1992 Aug;6(8):882-3.
27. Lepage P, Van de Perre P, Msellati P, Hitimana DG, Simonon A, Van Goethem C, Mukamabano B, Karita E, Stevens AM, Mathieu G, et al. Mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) and its determinants: a cohort study in Kigali, Rwanda. *Am J Epidemiol* 1993 Mar 15;137(6):589-99
28. Aiken CG. HIV-1 infection and perinatal mortality in Zimbabwe. *Zimbabwe 1992 Arch Dis Child* 1992 May;67(5):595-9.
29. Gray RH, Wawer MJ, Serwadda D, Sewankambo N, Li C, Wabwire-Mangen F, Paxton L, Kiwanuka N, Kigozi G, Konde-Lule J, Quinn TC, Gaydos CA, McNairn D. Population-based study of fertility in women with HIV-1 infection in Uganda. *Lancet* 1998; 351:98-103.
30. Halsey NA, Boulos R, Holt E, Ruff A, Brutus J-R, Kissinger P, Quinn TC, Coberly JS, Adrien M, Boulos C. Transmission of HIV-1 infections from mothers to infants in Haiti. Impact on childhood mortality and morbidity. *JAMA* 1990;264:2088-2092.
31. Mmiro F, Ndugwa C, Guay L, et al. Effect of human immunodeficiency virus-1 infection on the outcome of pregnancy in Ugandan women. *Pediatr AIDS HIV Infect* 1993;4:67-73.
32. Bulterys M, Chao A, Munyemana S, Kurawige J-B, Nawrocki P, Habimana P, Kageruka M, Mukantabana S, Mbarutso E, Dushimimana A, Saah A. Maternal human immunodeficiency virus 1 infection and intrauterine growth: a prospective cohort study in Butare, Rwanda. *Pediatr Infect Dis J* 1994;13:94-100.
33. Temmerman M, Chomba EN, Ndinya-Achola J, Plummer FA, Coppens M, Piot P. Maternal human immunodeficiency virus-1 infection and pregnancy outcome. *Obstet Gynecol* 1994 Apr;83(4):495-501.
34. Taha TE, Dallabetta GA, Canner JK, Chipangwi JD, Liomba G, Hoover DR, Miotti PG. The effect of human immunodeficiency virus infection on birthweight, and infant and child mortality in urban Malawi. *Int J Epidemiol* 1995 Oct;24(5):1022-9.
35. Bobat R, Coovadia H, Coutsooudis A, Moodley D, Grow E. Neonatal characteristics and outcome in a cohort of infants born to HIV-1-infected African women from Durban, South Africa. *J Acq Immune Defic Syndr* 1999;20:408-409.
36. Brocklehurst P. Antenatal serum screening for genital herpes: a study of knowledge and attitudes of women at a central London hospital. *Br J Obstet Gynaecol* 1998 Jan;105(1):125-6.
37. Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *Br J Obstet Gynaecol* 1998 Aug;105(8):836-48.
38. Arifeen SE. Birth weight, intrauterine growth retardation and prematurity: a prospective study of infant growth and survival in the slums of Dhaka, Bangladesh. Doctor of Public Health dissertation. Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland, USA. 1997.
39. Ashworth A. Effects of intrauterine growth retardation on mortality and morbidity in infants and young children. *Eur J Clin Nutr* 1998 Jan;52 Suppl 1:S34-41.
40. Barros FC, Huttly SR, Victora CG, Kirkwood BR, Vaughan JP. Comparison of the causes and consequences of prematurity and intrauterine growth retardation: a longitudinal study in southern Brazil. *Pediatrics* 1992 Aug;90 (2 Pt 1):238-44.

41. Kusin JA, Kardjati S, de With C. Infant mortality in Madura, Indonesia. Implications for action. *J Trop Pediatr* 1989 Jun;35(3):129-32.
42. Taha TE, Gray RH, Abdelwahab MM. Determinants of neonatal mortality in central Sudan. *Ann Trop Paediatr* 1993;13(4):359-64.
43. Vanneste AM, Ronsmans C, Chakraborty J, de Francisco A. Prenatal screening in rural Bangladesh: from prediction to care. *Health Policy and Planning*, (In press)
44. Kramer MS. Intrauterine growth and gestational duration determinants. *Pediatrics* 1987 Oct;80(4):502-11.
45. Susser M, Stein Z. Timing in prenatal nutrition: a reprise of the Dutch Famine Study. *Nutr Rev* 1994 Mar;52(3):84-94.
46. Caulfield LE, Stoltzfus RJ, Witter FR Implications of the Institute of Medicine weight gain recommendations for preventing adverse pregnancy outcomes in black and white women. *Am J Public Health* 1998 Aug;88(8):1168-74.
47. Ceesay SM, Prentice AM, Cole TJ, Foord F, Weaver LT, Poskitt EM, Whitehead RG. Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomised controlled trial. *BMJ* 1997 Sep 27;315(7111):786-90.
48. Atukorala TM, de Silva LD, Dechering WH, Dassenaeike TS, Perera RS. Evaluation of effectiveness of iron-folate supplementation and anthelmintic therapy against anemia in pregnancy—a study in the plantation sector of Sri Lanka. *Am J Clin Nutr* 1994 Aug;60(2):286-92.
49. Shulman CE, Dorman EK, Cutts F, Kawuondo K, Bulmer JN, Peshu N, Marsh K. Intermittent sulphadoxine-pyrimethamine to prevent severe anaemia secondary to malaria in pregnancy: a randomised placebo-controlled trial. *Lancet* 1999 Feb 20;353(9153):632-6
50. Preziosi P, Prual A, Galan P, Daouda H, Boureima H, Hercberg S. Effect of iron supplementation on the iron status of pregnant women: consequences for newborns. *Am J Clin Nutr* 1997 Nov;66(5):1178-82
51. Christian P. Antenatal iron supplementation as a child survival strategy. *Am J Clin Nutr* 1998 Aug;68(2):404-5.
52. DeLong GR, Leslie PW, Wang SH, Jiang XM, Zhang ML, Rakeman M, Jiang JY, Ma T, Cao XY. Effect on infant mortality of iodination of irrigation water in a severely iodine-deficient area of China. *Lancet* 1997 Sep 13;350(9080):771-3.
53. Merialdi M, Caulfield LE, Zavaleta N, Figueroa A, DiPietro JA. Adding zinc to prenatal iron and folate tablets improves fetal neurobehavioral development. *Am J Obstet Gynecol* 1999 Feb;180(2 Pt 1):483-90.
54. West KP Jr, Katz J, Khatri SK, LeClerq SC, Pradhan EK, Shrestha SR, Connor PB, Dali SM, Christian P, Pokhrel RP, Sommer A. Double blind, cluster randomised trial of low dose supplementation with vitamin A or beta carotene on mortality related to pregnancy in Nepal. The NNIPS-2 Study Group. *BMJ* 1999 Feb 27;318(7183):570-5.
55. Fawzi WW, Msamanga GI, Spiegelman D, Urassa EJ, McGrath N, Mwakagile D, Antelman G, Mbise R, Herrera G, Kapiga S, Willett W, Hunter DJ. Randomised trial of effects of vitamin supplements on pregnancy outcomes and T cell counts in HIV-1-infected women in Tanzania. *Lancet* 1998 May 16;351(9114):1477-82.
56. Scholl TO, Hediger ML, Bendich A, Schall JI, Smith WK, Krueger PM. Use of multivitamin/ mineral prenatal supplements: influence on the outcome of pregnancy. *American Journal of Epidemiology* 1997;146:134-41.
57. Steketee RW, Wirima JJ, Slutsker WL, Khoromana CO, Breman JG, Heymann DL. Objectives and methodology in a study of malaria treatment and prevention in pregnancy in rural Malawi: The Mangochi Malaria Research Project. *Am J Trop Med Hyg* 1996;55(1 Suppl):8-16
58. Gichangi PB, Ndinya-Achola JO, Ombete J, Nagelkerke NJ, Temmerman M. Antimicrobial prophylaxis in pregnancy: a randomized, placebo-controlled trial with cefotametil-pivoxil in pregnant women with a poor obstetric history. *Am J Obstet Gynecol* 1997 Sep;177(3):680-4.
59. Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N, Wabwire-Mangen F, Li C, Lutalo T, Nalugoda F, Gaydos CA, Moulton LH, Meehan MO, Ahmed S, Gray RH. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Rakai Project Study Group. *Lancet* 1999 Feb 13;353(9152):525-35.

60. Black RE, Huber DH, Curlin GT. Reduction of neonatal tetanus by mass immunization of non-pregnant women—duration of protection from one or two doses of aluminum-adsorbed tetanus toxoid. *Bull WHO* 58:927-930, 1980.
61. Shahid NS, Steinhoff MC, Hoque SS, Begum T, Thompson C, Siber GR. Serum, breast milk, and infant antibody after maternal immunisation with pneumococcal vaccine. *Lancet* 1995;346(8985):1252-7.
62. Nelson KB, Ellenberg JH. Predisposing and causative factors in childhood epilepsy. *Epilepsia*. 1987;28 Suppl 1:S16-24.
63. Hirtz DG, Nelson KB, Ellenberg JH. Seizures following childhood immunizations. *J Pediatr*. 1983 Jan;102(1):14-8.
64. Sedaghatian MR, Noor AM. Maternal-child health system and perinatal mortality in the United Arab Emirates. *J Perinatol* 1997 Mar-Apr;17(2):161-3.
65. Lucas GN, Ediriweera RC. Perinatal deaths at the Castle Street Hospital for Women in 1993. *Ceylon Med J* 1996 Mar;41(1):10-2
66. Yan et al, 1989 (Yan RY). How Chinese clinicians contribute to the improvement of maternity care. *Int J Gynaecol Obstet* 1989 Sep;30(1):23-6).
67. World Health Report, 1998: Life in the 21st Century-A Vision for All. WHO Geneva, Switzerland.
68. Coverage of maternity care. A listing of available information. WHO/RHT/MSM/96.28
69. Palme-Kilander. Methods of resuscitation in low-Apgar score newborn infants—a national survey. *Acta Paediatrica*, 1992, 81:739-44.
70. Saugstad OS, Rootwell T, Aalen O. Resuscitation of asphyxiated newborn infants with room air or oxygen: an international controlled trial: The Resair 2 Study. *Pediatrics*, 1998;102:1.
71. Christensson K, Siles L, Moreno L, Balaustei A, De La Fuente P, Lagercrantz H, Puyoi P, Winberg J. Temperature, metabolic adaptation and crying in health full term newborns cared for skin to skin or in a cot. *Acta Paediatr* 1992; 81: 488-93.
72. Bergman NJ, Jurisoo LA. The 'kangaroo-method' for treating low birth weight babies in a developing country. *Trop Doct* 1994 pr;24(2): 57-60.
73. Kambarami RA, Chidede O, Kowo DT. Kangaroo care versus incubator care in the management of well preterm infants—a pilot study. *Ann Trop Paediatr* 1998 Jun;18(2):81-6.
74. Huffman, SL, Zehner, ER, Victora, C, Breastfeeding and neonatal mortality. LINKAGES, Academy for Educational Development. Washington, D.C. 1999.
75. World Health Organization. *Hypoglycaemia of the newborn. A review of the literature*. World Health Organization. Geneva. 1997. WHO/CHD/97.1
76. Narayanan I, Prakash K, Murthy NS, Gujral VV. Randomised controlled trial of effect of raw and holder pasteurized human milk and of formula supplements on incidence of neonatal infection. *Lancet* 1984 Nov 17;2(8412):1111-3.
77. World Health Organization. Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. How much does breastfeeding protect against infant and child mortality? A pooled analysis of seven studies from less developed countries. *Lancet*, in press. 1999.
78. Victora CG, Smith PG, Vaughan JP, Nobre LC, Lombardi C, Teixeira AM, Fuchs SC, Moreira LB, Gigante LP, Barros FC. Evidence for protection by breastfeeding against infant deaths from infectious diseases in Brazil. *Lancet* 1987;Aug;8, 319-321.
79. Cesar J, Victora C, Barros F, Santos I, Flores J. Impact of breastfeeding on admission for pneumonia during postneonatal period in Brazil: nested case-control study. *British Medical Journal* 1999;May 15, 318: 1316-1320.
80. Lutter CK, Perez-Escamilla R, Segall A, Sanghvi T, Teruya K, Wickham C. The effectiveness of a hospital-based program to promote exclusive breastfeeding among low-income women in Brazil. *Am J Public Health* 1997 Apr;87(4):659-63.
81. Morrow AL, Guerrero ML, Shults J, Calva JJ, Lutter C, Bravo J, Ruiz-Palacios G, Morrow RC, Butterfoss FD. Efficacy of home-based peer counselling to promote exclusive breastfeeding: a randomised controlled trial. *Lancet* 1999 Apr 10;353(9160):1226-31.

82. Maine D, Rosenfield A. The Safe Motherhood Initiative: why has it stalled? *Am J Public Health* 1999 Apr;89(4):480-2.
83. Mulholland K. Serious infections in young infants in developing countries. *Vaccine* 1998;16:1360-2.
84. Moreno MT, Vargas S, Poveda R, Sáez-Llorens X. Neonatal sepsis and meningitis in a developing Latin American country. *Pediatr Infect Dis J* 1994;13:516-20.
85. Bang AT, Bang RA, Morankar VP, Sontakke PG, Solanki JM. Pneumonia in neonates: can it be managed in the community? *Arch Dis Child* 1993 May;68(5 Spec No):550-6.
86. Gladstone IM, Ehrenkranz RA, Edberg SC, Baltimore RS. A ten-year review of neonatal sepsis and comparison with the previous fifty-year experience. *Pediatr Infect Dis J* 1990 Nov;9(11):819-25.
87. Nopper AJ, Horii KA, Sookdeo-Drost S, Wang TH, Mancini AJ, Lane AT. Topical ointment therapy benefits premature infants. *J Pediatr* 1996;128:660-9.
88. Lane AT, Drost SS. Effects of repeated application of emollient cream to premature neonates' skin. *Pediatrics* 1993;92:415-9.
89. Bulletin of the World Health Organization, 1997; 75 (Supplement).
90. Bang AT, Bang RA, Baitule SB, Reddy MH, Deshmukh MD. Home-based neonatal care and management of sepsis to reduce neonatal mortality: A field trial in rural India. *The Lancet* (in press).

---

*Acknowledgments*

We greatly appreciate the support of the United States Agency for International Development, Office of Health and Nutrition and Global Programs for support during this meeting and in the development of this publication.

Thanks also to Ruth Frischer for her support and foresight in initiating this meeting.

Thanks to Barbara Ewing, the conference coordinator, who was extraordinarily resourceful and dedicated and provided logistical support to all of the participants, and also to Donna Cotton, who provided excellent administrative support before, during and after the meeting.

Special thanks to Laura Kelley, who wrote and edited a concise summary of the proceedings that was faithful to the views of the participants, and who coordinated the review and publication of the report.

And hats off to Royce Faddis for assistance in designing this publication, and to doctoral students Ruby Nguyen for editorial assistance, and Mohammed Khalequzzaman for logistical assistance during the conference.

## *List of Participants*

Iain Aitken, MBBChir, M.P.H.  
Harvard School of Public Health  
677 Huntington Ave.  
Boston, MA 02115  
iaitken@hsph.harvard.edu

Adrienne Allison, M.A., M.P.H.  
JHPIEGO Corporation  
115 Thames St., Suite 100  
Baltimore, MD  
aallison@jhpiego.org

Jean Baker  
LINKAGES  
1825 Connecticut Ave., NW  
Washington, DC 20009-5721  
202-884-8000

Judith R. Bale, Ph.D.  
Institute of Medicine  
FO-3048  
Washington, DC 20418  
jbale@nas.edu

Abdullah Baqui, MBBS, MPH, DrPH  
Public Health Sciences Division  
ICDDR,B Dhaka 1000  
Bangladesh  
ahbaqui@icddrb.org

Dr. Abhay Bang, M.D., M.P.H.  
Society for Education, Action and  
Research in Community Health  
Gadchiroli (Maharashtra), India  
orbitbom@bom3.vsnl.net.in

Victor K. Barbiero, Ph.D.  
USAID/G/PHN/HN/CS  
Ronald Reagan Building  
3rd floor  
Washington, DC 20523-3700  
vbarbiero@usaid.gov

Al Bartlett, M.D.  
USAID/G/PHN/HN/CS  
Ronald Reagan Building  
3rd floor  
Washington, DC 20523-3700  
abartlett@usaid.gov

Staffan Bergstrom, M.D., Ph.D.  
Karolinska Institute  
Department of Public Health Sciences  
SE0171 76 Stockholm, Sweden  
staffan.bergstrom@phs.ki.se

Robert E. Black, M.D., M.P.H.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
rblack@jhspsh.edu

Annette Bongiovanni  
USAID LAC/RSD-PHN  
Ronald Reagan Building  
5th floor  
Washington, DC 20523  
abongiovanni@usaid.gov

Kent Bream, M.D.  
3400 Spruce Street  
Philadelphia, PA 19104  
bream@mail.med.upenn.edu

Dr. Ken Bridbord  
Division of International  
Training and Research  
Fogarty International Center  
bridbord@ficod.fic.nih.gov

Fredrik F. Broekhuizen, M.D.  
Department of Obstetrics and  
Gynecology, University of  
Wisconsin Medical School  
fandjbroek@aol.com

Laura Caulfield, Ph.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
lcaulfie@jhspsh.edu

Dr. Kyllike Christensson  
Division of International Health  
Care Research Karolinska Institute  
Stockholm, Sweden

Anthony Costello  
Institute of Child Health  
30 Guilford St.  
London WC1N1EH  
England  
a.costello@ich.ucl.ac.uk

Gary Darmstadt, M.D.  
Department of Pediatrics  
Children's Hospital and Regional  
Medical Center  
Seattle, WA 98105  
gdarms@chmc.org

Marc Debay, M.D., M.P.H.  
Dept of Population and Family  
Health Sciences  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
mdebay@jhu.edu

Duane L. Dowell, M.D.  
929 Logan Wood Ave.  
Richardson, TX 75080  
dowellduane@worldnet.att.net

Dr. Scott Dowell  
Centers for Disease Control and  
Prevention Respiratory Diseases  
Branch, Mailstop C-23  
Atlanta, GA 30333  
SFD2@cdc.gov

Shams El Arifeen, MBBS, DrPH  
ICDDR,B Dhaka 1000  
Bangladesh  
shams@icddrb.org

Wafaie Fawzi, M.D., Dr.PH.  
Harvard School of Public Health  
677 Huntington Ave.  
Boston, MA 02115  
mina@hsph.harvard.edu

Dr. Rolando Figueroa  
LINKAGES  
1825 Connecticut Ave., NW  
Washington, DC 20009-5721

Dr. Olivier Fontaine  
World Health Organization  
1211 Geneva 27, Switzerland  
fontaineo@who.ch

Dr. Nadra Franklin  
LINKAGES  
1825 Connecticut Ave., NW  
Washington, DC 20009-5721  
(202) 884-8000

David Fraser, M.D.  
INCLIN, Inc.  
3600 Market St., Suite 380  
Philadelphia, PA 19104-2644  
fraser@inclin.org

Ruth Frischer, Ph.D.  
USAID G/PHN/HN/CS  
Ronald Reagan Building  
3rd floor  
Washington, DC 20523-3700  
rfrischer@usaid.gov

Molly Gingerich  
USAID/G/PHN/HN/NMH  
Ronald Reagan Building  
3rd floor  
Washington, DC 20523-3700

Dr. Charletta Guillory  
Division of Neonatology  
Baylor College of Medicine  
Houston, TX 77030

Ronald Gray, M.B.B.S., M.Sc.  
Dept of Population and Family  
Health Sciences  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
rgray@jhsph.edu

Duff G. Gillespie, Ph.D.  
USAID/ G/PHN/DAA  
1300 Pennsylvania Ave., NW  
Washington, D.C. 20523-3700  
dgillespie@usaid.gov

Mohammad Hakimi, M.D., Ph.D.  
Gadjah Mada University  
Community Health and Nutrition  
Research Laboratory  
Yogyakarta Indonesia 55281  
cebu@yogya.wasantara.net.id

Kenneth Hill, Ph.D.  
Dept of Population and Family  
Health Sciences  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
khill@jhsph.edu

Ruthe Hope  
NGO Networks for Health  
1620 I Street NW, Suite 900  
Washington DC. 20006  
rhope@savechildren.org

Dr. Christopher Howson  
March of Dimes  
Birth Defects Foundation  
1275 Mamaroneck Ave.  
White Plains, NY 10605  
chowson@modimes.org

Sandra Huffman, Sc.D.  
Academy for Educational  
Development  
1825 Connecticut Ave., NW  
Washington, DC 20009  
slhuffman@aol.com

Robert Johnson, M.D.  
JHPIEGO Corporation  
1615 Thames St., Suite 200  
Baltimore, MD 21231  
rjohnson@jhpiego.org

Katherine M. Jones, MSPH  
USAID/BHR/PVC  
Ronald Reagan Building  
7th floor  
Washington, DC 20523-7600  
kjones@usaid.gov

Rosa Kambarami, M.D.  
University of Zimbabwe  
School of Medicine  
Harare, Zimbabwe  
rkambarami@healthnet.zw

Ruth Karron, M.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
rkarron@jhsph.edu

Mohammad Khalequzzaman, MD, MPH  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
mkhalequ@jhsph.edu

Barbara Kinzie  
Maternal and Neonatal  
Health Program  
JHPIEGO Corporation  
Baltimore, MD  
bkinzie@jhpiego.org

Marjorie Koblinsky  
MotherCare John Snow, Inc.  
1616 N. Fort Myer Drive  
11th Floor  
Arlington, VA 22209  
marge\_koblinsky@jsi.com

Michael Koenig, Ph.D.  
Dept of Population and Family  
Health Services  
Johns Hopkins School  
of Public Health  
Baltimore, MD  
mkoenig@jhsph.edu

Ronnie Lovich  
Save the Children  
54 Wilton Road  
Westport, CT 06881  
rlovich@savechildren.org

Dr. Chewe Luo  
University of Zambia  
Medical School  
PO Box 3120  
Lusaka, Zambia  
cheweluo@zamnet.zm

Ron Mataya  
ADRA  
12501 Old Columbia Pike  
Silver Spring, MD 11220  
1.2641@compuserve.com

Jeanne McDermott, CNM, Ph.D.  
MotherCare  
John Snow, Inc.  
1616 N. Fort Myer Drive  
11th Floor  
Arlington, VA 22209

Pamela McInnes, DDS, MSc (Dent)  
DMID/NIAID/NIH Solar 3B04  
Bethesda, MD 20892  
pm23v@nih.gov

Judith Moore  
The BASICS Project  
1600 Wilson Blvd., Suite 300  
Arlington, VA 22209  
jmoore@basics.org

Dr. Kim Mulholland  
World Health Organization  
1211 Geneva 27 Switzerland  
mulhollande@who.ch

John Murray, M.D., M.P.H.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
jmurray@jhsph.edu

Nancy Myers, RN, M.Ed.  
Kaiser Permanente  
1260 Independence Ave.  
Akron, OH 44310  
nmyers@neo.rr.com

Maureen Norton, Ph.D  
USAID/POP Ronald Reagan  
Building Washington, DC  
mnorton@usaid.gov

Joy Riggs-Perla, MPH  
USAID/G/PHN/HN/CS  
1300 Pennsylvania Ave., NW  
Washington, DC 20523-3700  
jriggs-perla@usaid.gov

Carine Ronsmans, M.D., Dr.P.H.  
Maternal and Child Epidemiology  
Unit, London School of Hygiene  
and Tropical Medicine  
London WC1E 7HT  
England  
carine.ronsmans@lshtm.ac.uk

Susan Rae Ross, BSN, MPH  
CARE  
151 Ellis St.  
Atlanta, Ga 30303  
ross@care.org

Andrea Ruff, M.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
aruff@jhsph.edu

Dr. Shea Rutstein  
Macro International, Inc.  
11785 Beltsville Drive, Suite 300  
Calverton, MD 20705-3119  
rutstein@macroint.com

David Sack, M.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
dsack@jhsph.edu

René Salgado  
BASICS  
1600 Wilson Blvd., Suite 300  
Arlington, VA 22209  
rsalgado@basics.org

Harshad Sanghvi, M.D.  
Maternal and Neonatal Health  
Program  
JHPIEGO Corporation  
Baltimore, MD  
hsanghvi@jhpiego.org

Mathuram Santosham, M.D., M.P.H.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
msantosh@jhsph.edu

Bettina Schwethelm, Ph.D., M.P.H.  
Maternal and Child Health Programs  
Project HOPE  
Millwood, VA 22646  
bschweth@projhope.org

Theresa Shaver  
NGO Networks for Health  
1620 I Street NW, Suite 900  
Washington DC. 20006  
tshaver@savechildren.org

Eric Simoes, M.D.  
The Children's Hospital  
1056 East 19<sup>th</sup> Ave., B070  
Denver, CO 80218-1088  
eric.simoes@uchsc.edu

Alfred Sommer, M.D., M.P.H.  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205

Mary Ellen Stanton, CNM, MSN  
USAID G/PHN/HN/NMH  
Ronald Reagan Building  
3<sup>rd</sup> floor  
Washington, D.C. 20523-3700  
mstanton@usaid.gov

Mark Steinhoff, M.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
msteinho@jhsph.edu

Patricia Stephenson, Sc.D.  
USAID/G/PHN/HN  
Ronald Reagan Building  
3<sup>rd</sup> floor  
Washington, D.C. 20523-3700  
pstephenson@usaid.gov

Richard Steketee, M.D., M.P.H. MS  
E46 NCHSTP, CDC  
Atlanta, GA 30333 rsl@cdc.gov

Barbara Stoll, M.D.  
Grady Memorial Hospital  
Division of Neonatology  
Atlanta, GA 30335-3801  
stoll@oz.ped.emory.edu

Donald Thea, M.D.  
ARCH Project  
14 Story St.  
Cambridge, MA 02138  
dthea@hiid.harvard.edu

James Tielsch, Ph.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
jtielsch@jhsph.edu

Jorge Tolosa, M.D., M.S.  
Thomas Jefferson University  
Department of Obstetrics  
and Gynecology  
Philadelphia, PA 19107  
jorge.tolosa@mail.tju.edu

Koen Vanormelingen  
Health Division  
UNICEF -TA-24A  
New York, NY  
kvanormelingen@unicef.org

Rema Venu  
Health Division  
UNICEF -TA-24A  
New York, NY  
rvenu@unicef.org

Keith West, Ph.D.  
Department of International Health  
Johns Hopkins School  
of Public Health  
Baltimore, MD 21205  
kwest@jhsph.edu

Dr. Cyndy Whitney  
Centers for Disease Control and  
Prevention Respiratory Diseases  
Branch, Mailstop C-23  
Atlanta, GA 30333  
CGW3@cdc.gov

Dr. Jelka Zupan  
Maternal/Neonatal Health and  
Safe Motherhood Programme  
World Health Organization  
zupanj@who.ch

*Photo Credits: Front Cover (clockwise): Laura Kelley; Robert and Maureen Black; Johns Hopkins Center for Communications Programs (JHU/CCP); Page 3: Ricardo Wray, JHU/CCP; Page 20: E. McDaniel; Page 24 Inter-American Development Bank; Page 25 Robert and Maureen Black; Page 28 JHU/CCP; Page 34 Marilyn Pfaltz.*

*Designed and Produced through the Johns Hopkins University Office of Design and Publications*