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March
of Dimes

EXECUTIVE SUMMARY

MARCH OF DIMES

GLOBAL REPORT ON BIRTH DEFECTS

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EXECUTIVE SUMMARY

MARCH OF DIMES

GLOBAL REPORT ON BIRTH DEFECTS

THE HIDDEN TOLL OF DYING AND DISABLED CHILDREN

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March of Dimes Birth Defects Foundation
White Plains, New York
2006



PREFACE

PREFACE

President Franklin Roosevelt established the March of Dimes Foundation in 1938 to defeat polio. He created a partnership of volunteers and researchers that led to the development of the polio vaccines. Today the March of Dimes mission is improving infant health by preventing birth defects, premature birth and infant mortality. A birth defect is defined as any abnormality affecting body structure or function that is present from birth. The March of Dimes mission is carried out through research, community services, education and advocacy.

In 1998, the March of Dimes broadened its mission beyond the United States and established its office of Global Programs. Global Programs conducts its work through mission alliances—close working partnerships with private and public organizations in countries—to improve perinatal health and prevent birth defects. In the past six years, March of Dimes has helped implement effective, affordable and feasible programs on four continents

In 2000, Global Programs initiated a process to document the global toll of birth defects and provide policy makers, funding organizations and health care providers with feasible, cost-effective recommendations for reducing this toll. In 2004, it commissioned the current report from Professors Arnold Christianson of the National Health Laboratory Service and University of the Witwatersrand, Johannesburg, South Africa, and Bernadette Modell of the Royal Free and University College Medical School, London, England

Professor Modell compiled the data presented in Appendix B. The methods she used are detailed in Appendix A. The data in this report represent the culmination of work that Professor Modell began in the early 1980s for the World Health Organiza-

tion on hemoglobin disorders, which ultimately expanded to encompass all serious birth defects of genetic or partially genetic origin. This work draws on data from a range of existing databases and the authors would like to express their appreciation of those experts whose meticulous work and scientific dedication have contributed so much to the development of this global overview. Professor Christianson provided a first draft of the report based on his expertise as a clinical geneticist, experience in implementing medical services for the care and prevention of birth defects in South Africa and years of consulting on this topic with experts from other middle- and low-income countries. Dr. Christopher Howson of the March of Dimes drafted additional sections of the report and contributed his analytic and programmatic perspective as an epidemiologist and project manager with many years of experience in conducting joint programs with international partners to improve newborn health in middle- and low-income countries.

How The Data in This Report Were Derived

There is a paucity of data on the birth prevalence of birth defects in middle- and low-income countries. Constrained diagnostic capability, poor health-related statistics, lack of birth defect surveillance and registries and reliance on hospital-based rather than population-based studies have contributed to this situation and led to a systematic underestimation of the toll of birth defects in these regions (Christianson and Modell. 2004; Penchaszadeh, 2000; WHO, 1985, 1999).

This report is the first to provide global estimates of birth prevalence for serious birth defects of genetic or partially genetic origin. The estimates in this report, presented by country in Appendix B of

the full report¹ were derived from extrapolation of pooled data from a variety of sources. These include (1) birth prevalence rates of selected birth defects in populations of northern European origin from two birth defects registries, one located in western Canada (Baird et al., 1988) and the other in Hungary (Czeizel and Sankaranarayanan, 1984); (2) global data on carrier rates for common recessive conditions (WHO, 1989, 1994); (3) data on national prevalence rates of pregnant women of advanced maternal age (United Nations, 2003); (4) national rates of consanguineous marriage—i.e. marriage between close relatives, usually cousin-cousin but including uncle–niece (Bittles, 1990; Murdock, 1967) and; (5) national demographic profiles (UNICEF, 2003).

Additional description of how the country-specific estimates in Appendix B were derived is provided in Appendix A.

Report Structure

The report has three major parts. The first is the main body, with a stand-alone Executive Summary, which summarizes the report's main points, including its conclusions and recommendations. Subsequent sections deal with the definition, early knowledge and causes of birth defects; the global impact and epidemiology of major birth defects; the importance of medical genetic services for care and prevention; the nature of recommended services; the promotion of equity through overcoming barriers to medical genetic services; and the reference list.

Appendices A and B comprise the second major part and contain the data that underlie the report. Appendix A explains how the data were derived and Appendix B provides the raw data by country in accordion format. These include selected demographic indices, annual birth prevalence rates for categories of birth defects (e.g., total dominant, total recessive, total X-linked) and annual prevalence rates for specific birth defects. The third part of the

report is a stand-alone wall chart that summarizes key data and depicts the global distribution of birth defects graphically.

Readers interested in an overview of the report's findings, conclusions and recommendations may choose to focus on the Executive Summary and wall chart. Those wishing to learn more about the content of the report are encouraged to read the main narrative. Readers interested in country-specific rates of birth defects will find these in Appendix B.

Acknowledgments

The authors are indebted to many colleagues who contributed to this report. In particular, they thank Dr. Michael Katz (March of Dimes) for his expert opinion on all aspects of the report and Ms. Shelley Grim (Division of Human Genetics, University of the Witwatersrand) for her substantive research and editing assistance and her contribution to formatting the database and wall chart. The authors also thank Mrs. Mary Hager for her expert help in editing the report, Ms. Jo-Anne Richards for her initial edit of the manuscript, and Ms. Wendy Scott-Williams for her assistance in finding and checking references. In addition, the authors acknowledge with gratitude the creative contribution of Mr. Michael Kristof to the design of the report, its database, and wall chart, and they thank Mr. Marshall Hoffman and his staff at Hoffman & Hoffman Worldwide for their substantive input into the presentation of the report. In particular, the authors thank Ms. Rachel Diamond for her vigilant oversight and many contributions throughout all the stages of report preparation.

The authors are indebted to the substantive contribution of the following reviewers: Dr. Ala'din Alwan, World Health Organization; Dr. Patricia Baird, University of British Columbia; Dr. R.J. Berry, Centers for Disease Control and Prevention; Ms. Janis Biermann, March of Dimes; Dr. Eduardo E. Castilla, Eclamc/Genetica/Fiocruz; Dr. José F.

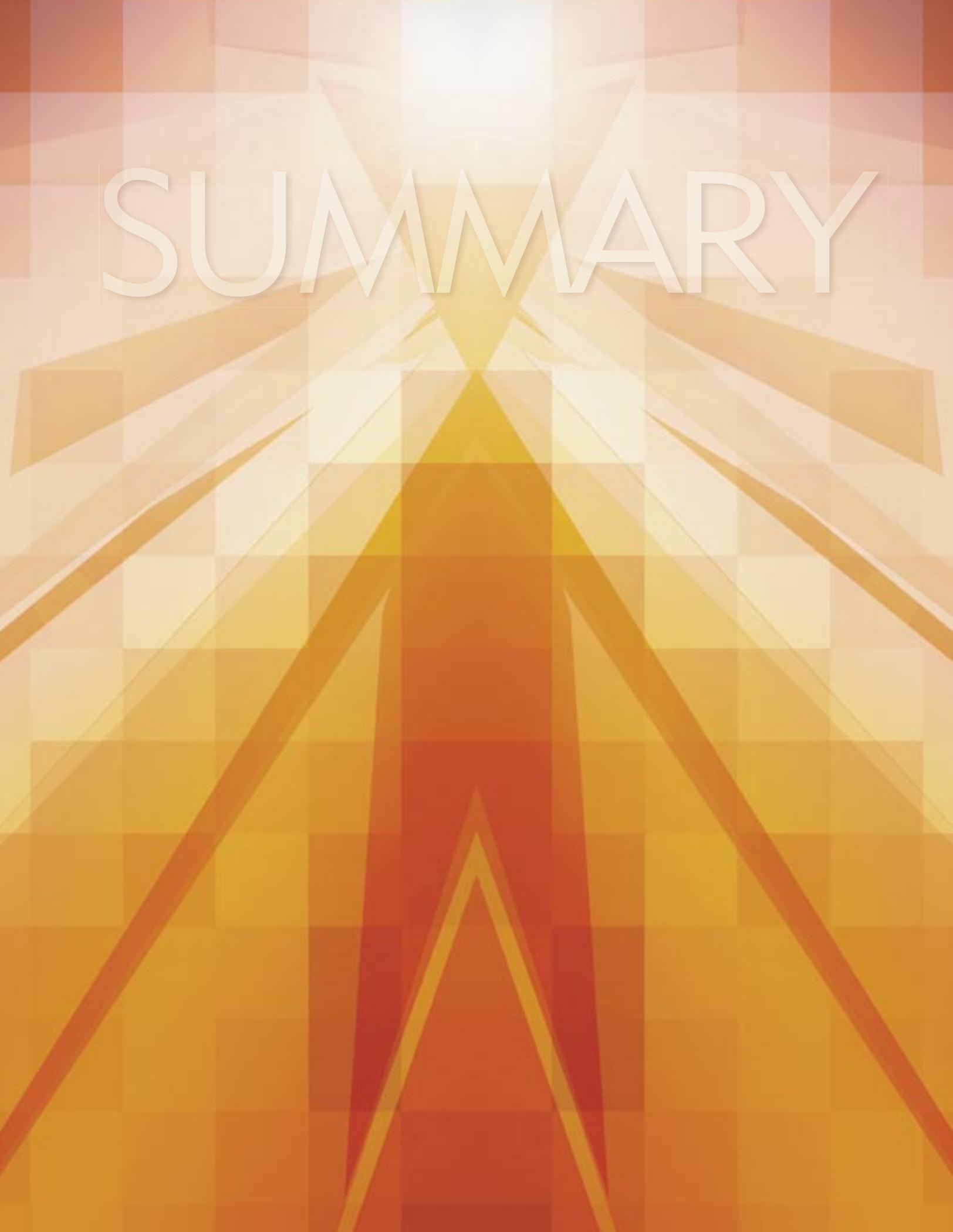
¹ The full report, *March of Dimes Global Report on Birth Defects: The Hidden Toll of Dying and Disabled Children*, which includes Appendices A and B, is available from the March of Dimes at <http://www.marchofdimes.com/globalreport1>

Cordero, Centers for Disease Control and Prevention; Dr. David Erickson, Centers for Disease Control and Prevention; Dr. Nancy Green, March of Dimes; Mr. Alastair Kent, Genetic Interest Group; Mr. Richard Leavitt, March of Dimes; Dr. Osvaldo Mutchinick, Instituto Nacional de la Nutrición Salvador Zubirán; Dr. Irmgard Nippert, University of Muenster; Mr. Ysbrand S. Poortman, Vereniging Samenwerkende Ouder-en Patientenorganisaties (VSOP); Dr. Mary-Elizabeth Reeve, March of Dimes; Dr Giovanni Romeo, European School of Genetic Medicine; Dr. Jai Rup Singh, Centre for Genetic Disorders, Guru Nanak Dev University; Ms. Sharon F. Terry, Genetic Alliance; and Professor William Winship, Nelson Mandela School of Medicine. The report is as strong as it is because of their time and commitment to review.

Finally, the authors thank Dr. Jennifer Howse, President of the March of Dimes, whose vision and support of the March of Dimes Global Programs made this report possible.



SUMMARY

The background features a grid of squares in various shades of orange and yellow. Overlaid on this grid are several large, stylized, radiating shapes that resemble a sunburst or a starburst, with lines extending from the top center towards the bottom corners. The overall color palette is warm and vibrant.

EXECUTIVE SUMMARY

Every year an estimated 7.9 million children—6 percent of total births worldwide—are born with a serious birth defect of genetic or partially genetic origin². Additional hundreds of thousands more are born with serious birth defects of post-conception origin, including maternal exposure to environmental agents (teratogens) such as alcohol, rubella, syphilis and iodine deficiency that can harm a developing fetus.

Serious birth defects can be lethal. For those who survive, these disorders can cause lifelong mental, physical, auditory or visual disability. Data presented in this report show that at least 3.3 million children under five years of age die from birth defects each year and an estimated 3.2 million of those who survive may be disabled for life.

Birth defects are a global problem, but their impact is particularly severe in middle- and low-income countries where more than 94 percent of the births with serious birth defects and 95 percent of the deaths of these children occur³. The proportion of births with birth defects as well as the absolute number of births are much higher in middle- and low-income countries than in high-income countries because of sharp differences in maternal health and other significant risk factors, including poverty, a high percentage of older mothers, a greater frequency of consanguineous marriages and the survival advantage against malaria for carriers of sickle cell, thalassemia, and glucose-6-phosphate dehydrogenase (G6PD) deficiency genes.

This report identifies for the first time the severe, and previously hidden, toll of birth defects, highlighting the extent of this serious and vastly unappreciated public health problem. The accompanying database in Appendix B provides the first systematic, country-by-country summary of annual births of infants with specific serious birth defects of genetic or partially genetic origin.

The modeled estimates in Appendix B are based on the best statistics available, but they do not allow for the most precise comparisons of birth prevalence among countries. Such an analysis must await the collection of additional empirical data on birth prevalence. The data, however, do permit broad comparison of specific birth defects across countries. These analyses show that the birth prevalence of all genetic birth defects combined ranges from a high of 82 to a low of 39.7 per 1,000 live births worldwide. As the bar chart on pages 3-4 indicates, many of the highest birth prevalence rates are found among the world's poorest countries, while many of the lowest rates are found among the world's wealthier countries, with the exception of countries where common recessive disorders and marriages between first cousins and other close relatives are common.

According to the data in this report, five common serious birth defects of genetic or partially genetic origin in 2001 were: (1) congenital heart defects (1,040,835 births); (2) neural tube defects (323,904 births); (3) the hemoglobin disorders, thalassemia, and sickle cell disease (307,897 births);

² Birth defects as defined in this report are abnormalities of structure or function, including metabolism, which are present from birth. Serious birth defects are life threatening or have the potential to result in disability (physical, intellectual, visual or hearing impairment or epilepsy). More than seven thousand different birth defects have been identified to date. Some birth defects are clinically obvious at birth; others may only be diagnosed later in life. Spina bifida is one example of a structural defect that is obvious at birth. The bleeding disorder hemophilia is a functional defect usually not clinically obvious until infancy or childhood. The authors accept that the term 'birth defect' is not considered appropriate by some, but it has been used extensively in medical literature over time and is widely understood by the broad audience of this report.

³ This report refers to three categories of countries based on 2004 gross national income (GNI) per capita. These are high-income (industrialized) countries which have a GNI of >\$10,065 and middle- and low-income countries (sometimes referred to as developing countries), which have GNIs of \$826-10,065 and <\$826, respectively (World Bank, 2005).

(4) Down syndrome (trisomy 21) (217,293 births); and (5) glucose-6-phosphate dehydrogenase (G6PD) deficiency (177,032 births). Combined, these five conditions account for about 25 percent of all of birth defects of genetic or partially genetic origin. To date, more than 7,000 different birth defects of genetic or partially genetic origin have been identified.

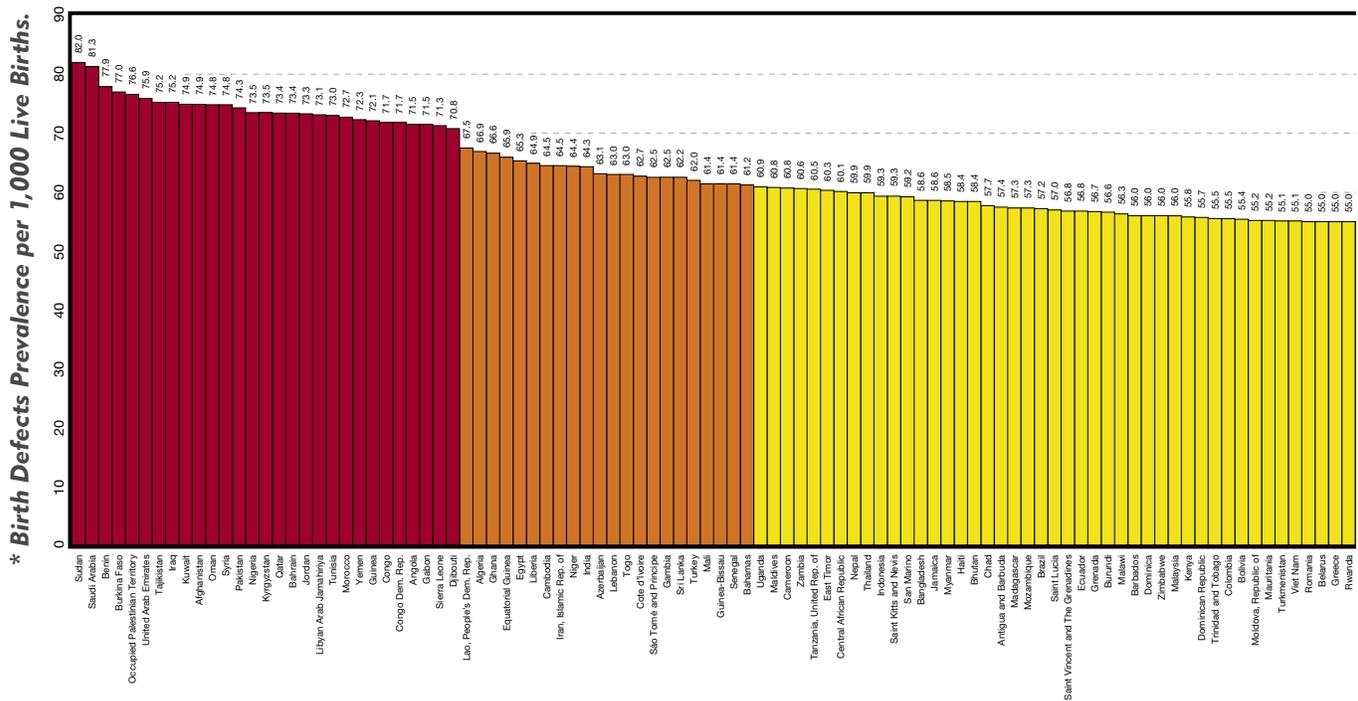
Comparable data could not be derived for birth defects due to post-conception damage caused by maternal exposure to teratogens, such as alcohol, drugs, some infections and a number of toxic environmental agents. What limited data do exist suggest the highest toll results from the following four post-conception birth defects: fetal alcohol spectrum disorder, iodine deficiency disorder, congenital rubella syndrome and congenital syphilis. Together, these disorders account for hundreds of thousands of affected births. As with birth defects of genetic or partially genetic origin, post-conception birth defects are more common in low- and middle-income countries, where the potential for exposure to teratogenic agents is greater and fewer preventive measures are in place than in high-income regions.

Experience from high-income countries shows

that up to 70 percent of birth defects can either be prevented, or that affected children can be offered care that could be life saving or would reduce the severity of disability. These interventions include appropriate treatment, particularly surgery, and prevention, especially before conception or in very early pregnancy. For example, the United States reported a remarkable 46 percent decline in infant mortality rates from birth defects over the period 1980 to 2001, and much of this reduction can be attributed to improvements in diagnosis, care and prevention. Other high-income countries have reported similar declines.

On the other hand, limited data from low- and middle-income countries suggest that there has been little to no improvement in infant mortality rates from birth defects over the same general time period. The recommendations in this report are designed to address this disparity and reduce the unacceptably high rates of infant deaths from birth defects in low- and middle-income countries.

Most middle- and low-income countries currently lack the comprehensive health services needed to reduce their toll of birth defects. The report focuses

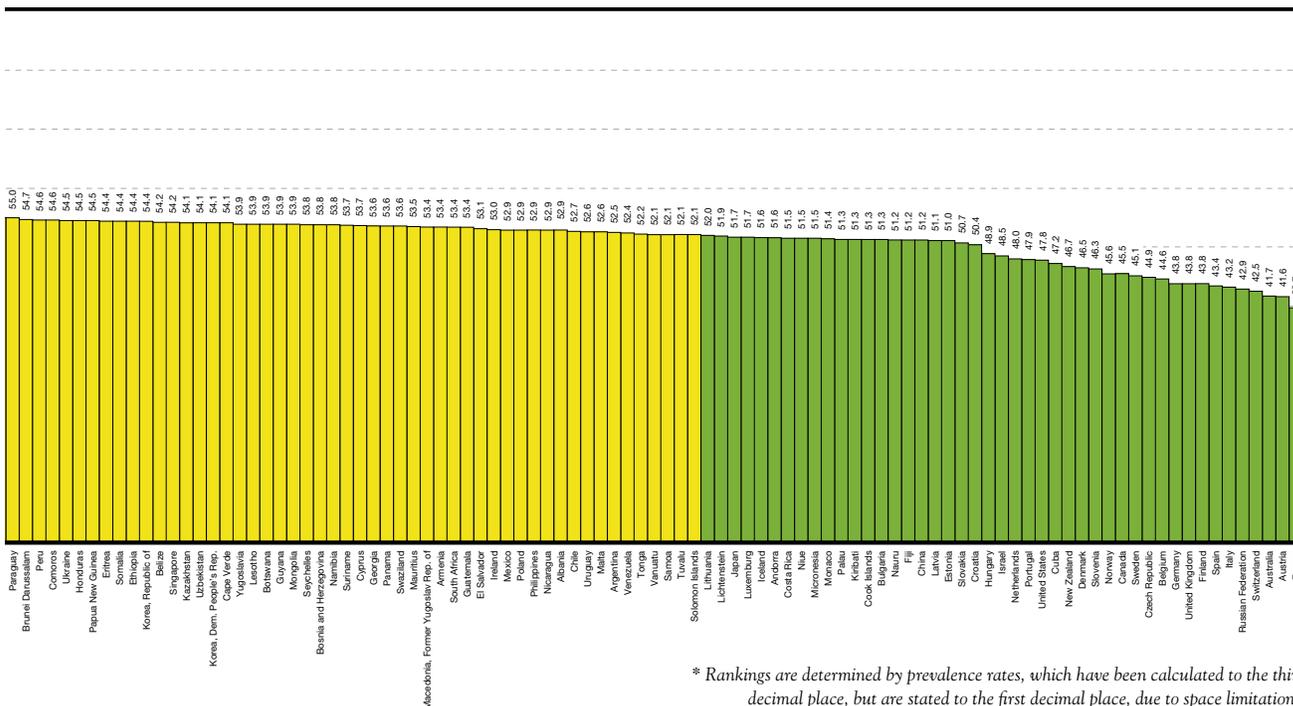


on both the prevention of birth defects as well as the care of those with birth defects and outlines simple and cost-efficient steps that must be taken to equip primary health care programs in less developed countries to focus on this problem.

The report gives numerous examples of successful strategies for care and prevention. For example, structural birth defects including congenital heart defects, congenital cataracts, cleft lip and palate and clubfoot, can be corrected with pediatric surgery. Children with functional problems, including thalassemia, sickle cell disorders and congenital hypothyroidism, also can survive with appropriate treatment. On the side of prevention, ongoing global efforts to fortify salt with iodine have led to a significant reduction in morbidity from iodine deficiency disorder, though an estimated 60,000 babies were born with severe congenital hypothyroidism in 1998 and about 28 million pregnancies still are at risk from maternal iodine deficiency. In the United States alone, fortification of the grain food supply with folic acid has produced a one-third decline in neural tube defects each year, with an overall cost savings calculated at \$400 million annually.

Data compiled for this report constitute an important addition to the ongoing and extensive worldwide effort to reduce infant and child mortality. The United Nations Millennium Development Goals (MDGs) for 2015, set in 2000, included reducing child mortality by two-thirds from 1990 levels. By the beginning of 2004, efforts to achieve this goal fell well below United Nations projections.

The newborn was a focus of efforts to improve child health and survival in both the World Health Report 2005, *Make Every Mother and Child Count*, and the first *Lancet Neonatal Survival Series*. Despite this long overdue focus on newborn health, both reports failed to include birth defects as a major cause of childhood death and disability and, consequently, did not highlight care and prevention of birth defects as an essential and integral part of women's, maternal, newborn, and child health programs in all countries. Both concluded that the UN's MDG for reducing child mortality would not be met unless the international community did more to reduce neonatal deaths. The data presented in this report make a strong argument for recognizing and addressing the significant global contribution of birth defects to infant and childhood mortality if



* Rankings are determined by prevalence rates, which have been calculated to the third decimal place, but are stated to the first decimal place, due to space limitations.

they are to succeed.

This report urges that efforts to promote healthy birth outcomes should target all women of child-bearing age, in addition to mothers, newborns and children. The growing understanding of the importance of pre-conception health underscores the fact that good health practices, including regular access to health care, must be established before conception if the pregnancy and newborn are to be as healthy as possible.

Strategies for improving the health of women, mothers, newborns and children are essential for effective prevention and care of those with birth defects. Investing in the care and prevention of birth defects reduces child mortality and disability and, therefore, should be an integral component of any comprehensive women's maternal, newborn and child health program. This includes development of basic medical genetic services for both the prevention of birth defects and the care of affected children in middle- and low-income countries. This investment will ensure that all countries benefit from current knowledge and technology in medical genetics and genomics and that they also will benefit from future advances as they become available.

Several misperceptions identified in the report help to explain why care and prevention of birth defects have received little attention from international donors and health agencies. These misperceptions have been impediments to the development of appropriate programs, and need to be corrected.

The first is that health policy makers have not been aware of the immense global toll of birth defects, including the true extent of death and disabilities, a deficiency that should be corrected by the data presented in this report. In a few documented instances, where the burden of disease has been quantified, funding and corrective measures have

usually followed. The implementation of rubella immunization in South America and the Caribbean following publication of the data on the high toll of congenital rubella syndrome in that region provides one such example.

A second misunderstanding is the belief that effective care and prevention of birth defects require costly high-technology interventions that are beyond the health budgets of low- and middle-income countries. In fact, most such efforts should be carried out in primary and secondary care settings. Effective interventions—including family planning, optimizing women's diets, managing maternal health problems and avoiding maternal infections—are both feasible and affordable, even for financially-constrained health systems, and have proven cost effective where implemented.

A third misperception is the belief that attention to birth defects will draw funding away from other high-priority maternal and child health efforts. Again, the reverse is true. Many risk factors for birth defects—including advanced maternal age, maternal medical complications, infection, poor nutrition, smoking, alcohol and drug use—are common to other maternal and child health problems. In fact, increasing efforts to reduce birth defects will also contribute to the overall health of women, mothers, newborns and children.

Recommendations

Experience shows that the care and prevention of birth defects are feasible and can be cost-effective. Such care and prevention requires comprehensive women's, maternal, newborn and child health programs and provision of basic medical genetic services to ensure that people with birth defects or at reproductive risk of having children with birth defects can live and reproduce as normally as possible.

The following steps should be taken to prevent

birth defects and improve the care of affected children in middle- and low-income countries. These steps can be implemented in two phases, according to the health needs and economic capacities of a given country.

Recommendations: Phase 1

- ❖ Educate the community, health professionals and workers, policy makers, the media, and other stakeholders about birth defects and the opportunities for effective care and prevention. To achieve this end, each ministry of health should designate an expert or an individual with responsibility for coordinating strategies for care and prevention. These strategies need to be woven into existing public health strategies. Ministries do not need to create a new position, but they should ensure that a knowledgeable, trained and effective person holds this responsibility.
- ❖ Promote family planning, allowing couples to space pregnancies, plan family size, define the ages at which they wish to complete their family and reduce the proportion of unintended pregnancies.
- ❖ Ensure a healthy, balanced diet during a woman's reproductive years through an adequate intake of macronutrients (protein, carbohydrates and fats) and a broad range of micronutrients. Special attention should be given to adding 400 micrograms of synthetic folic acid daily to the diet through fortification and/or supplementation, while also promoting a diet rich in food folates; correcting iodine and iron deficiencies; and removing teratogenic substances, the most important of which is alcohol, from the diet.
- ❖ Control infections in all women of reproductive age.

- ❖ Optimize maternal health through control of chronic illnesses associated with an increased risk of birth defects. These include insulin-dependent diabetes mellitus, epilepsy and its control with anti-epileptic drugs; and heart disorders for which sodium warfarin is prescribed.
- ❖ Train physicians, nurses, allied health professionals and workers in the fundamentals of the recognition of causes and care of children with birth defects.
- ❖ Conduct physical examinations of all newborns by a physician, nurse or allied health professional trained to recognize birth defects before hospital or clinic discharge.
- ❖ Establish appropriate child health services to care for infants with birth defects.
- ❖ Establish national capacity for surveillance and monitoring of common birth defects to inform policy and to allow for more robust evaluation of national interventions, such as fortification of the food supply with folic acid.
- ❖ Promote lay support organizations, including patient/parent support groups, to improve patient care and birth defect prevention by facilitating community and professional education and advocating for increased funding for research on the causes of birth defects.

Recommendations: Phase 2

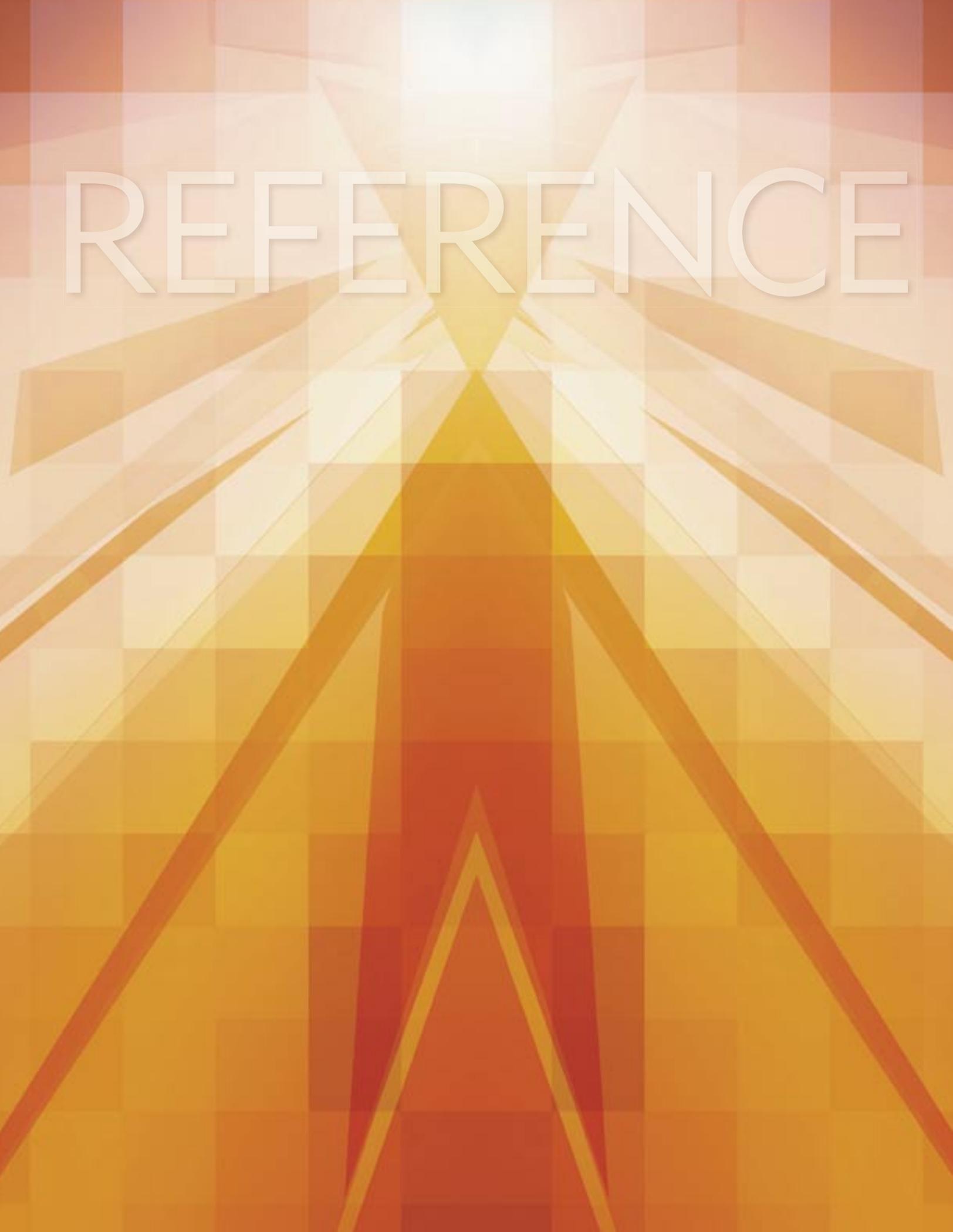
- ❖ Train physicians, nurses and allied health professionals in the essentials of medical genetics. This training should include the recognition of birth defects; means of treatment where possible in the primary health care setting; knowing when to refer a patient for more specialized treatment; basic genetic counseling, including best practices in communicating unfavorable health information

to parents; and support for families who have a child or are at risk of having a child with a birth defect.

- ❖ Establish peri-conception medical services to assist women and their partners to attain optimal physical and mental health and well-being at the beginning of pregnancy to facilitate a normal pregnancy and delivery of a healthy infant. These include screening for the risk of genetic, partially genetic and teratogenic birth defects.
 - ❖ Implement pre-conception or prenatal medical genetic screening to identify couples at risk of having a baby with hemoglobin disorders, Down syndrome, blood type incompatibility, congenital syphilis and congenital malformations, particularly neural tube defects.
 - ❖ Establish newborn screening to identify congenital hypothyroidism, phenylketonuria, galactosemia, sickle cell disease, G6PD deficiency and other metabolic disorders.
 - ❖ Educate the public about birth defects and the steps mothers and fathers can take with their health care provider to maximize the chances of a healthy pregnancy.
- 



REFERENCE

The background features a grid of squares in various shades of orange and yellow. Overlaid on this grid are several large, stylized, radiating shapes that resemble a sunburst or a starburst pattern. These shapes are composed of overlapping triangles and lines, creating a sense of depth and movement. The overall color palette is warm and vibrant, ranging from light yellow to deep orange and red tones.

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