



**BIRTH DEFECTS—CHALLENGES IN PREVENTION**

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I am pleased to be able to be here to pinch-hit for Phil Lee. From my own experiences working on smallpox and polio eradication and childhood immunization, I know well the value -- necessity -- of international collaboration and cooperation. Your own efforts to create a new consortium are to be commended, especially in an area as important as birth defects.

I was asked to speak to you about certain of our own Public Health Service activities in the prevention of birth defects and to offer personal reflections on the challenge posed. Obviously, we are all both pleased and excited by the recent breakthrough in understanding which permit substantial prevention of one of the most serious and common birth defects, the neural tube defects. Neural tube defects (NTDs), including spina bifida and anencephaly are, as you know, often fatal or severely disabling. Results of the two randomized, controlled trials and several observational studies have now clearly shown that consumption of folic acid immediately before and during the early months of pregnancy can markedly reduce their occurrence.

The Public Health Service has issued recommendations that all women capable of becoming pregnant consume 0.4 milligrams of folic acid daily. This, it is believed, could reduce the incidence of neural tube defects by as much as 50% to 70%. If applied worldwide, this could translate into the prevention of 200,000 to 300,000 children with neural tube defects -- a number of some significance.

Proving that folic acid could be effective in preventing NTDs was truly an international effort. We salute our colleagues in Britain who conducted the first randomized, controlled trial and colleagues in Hungary who confirmed it. Other studies in England, Ireland, Australia, and the United States have provided valuable additional information. And, so I am told, a number of those who played key roles are with you at this meeting.

When the importance of folic acid became apparent, the Centers for Disease Control and Prevention (CDC) began immediately to inform women of the recommendation to consume supplemental folic acid daily, to assist state health departments in designing programs, and to work with other PHS agencies to find the best method to implement folic acid supplementation measures. FDA has now published proposed rules that allow vitamin product labels to state that folic acid will prevent NTDs and FDA has proposed a rule which will require that all enriched grain products be fortified with folic acid. PHS will continue the effort to educate the American public and health professionals on the need for folic acid.

All too few appreciate that birth defects are now the leading cause of infant mortality in the United States, accounting for more than 20% of infant deaths each year. In developing countries, infectious diseases and prematurity are still the leading causes of infant mortality but, as these causes are brought under control, we inevitably will see birth defects emerging as the leading cause. The U.S. infant mortality rate is now 9 deaths per

1,000 births. Thus, of 4 million infants born each year, about 36,000 will die before their first birthday --about 8,000 of those deaths, nearly 25%, caused by birth defects. Families from all racial and ethnic groups share a comparable risk of having a child with a serious birth defect, a risk of about 3 per 100 live births -- or about 120,000 babies so afflicted each year -- many with permanent disabilities. They are responsible for about 30% of all pediatric admissions to hospitals.

Prevention is the critical strategy and, as you know, when definitive methods for prevention can be identified, the results may be dramatic as was seen with rubella vaccine. In the U.S. the rubella epidemic of 1964-65 resulted in 20,000 babies born with congenital rubella syndrome and some 2,000 deaths. Today we count, at most, a handful each year and with a strengthened immunization program, launched this year as a special initiative of the President, there should be none. Because of progress in biomedical research, we can look forward with confidence to other vaccines such as one for cytomegalovirus. Rh hemolytic disease in newborns in the early 1970s was one of our leading complications in newborns -- affecting about 3,800 children per year -- but this is now prevented by immune globulin.

We have only begun our efforts to identify preventable birth defects. There are far too many of unknown etiology. However, current developments in biomedical research provide me confidence to believe that the time is ripe for making far more rapid progress in birth defects prevention.

An international effort is both important and necessary at this time and an international consortium for purposes of strategic planning and cooperative implementation is an obvious answer.

The March of Dimes Birth Defects Foundation has been an important catalyst in the efforts to prevent NTDs as well as other birth defects. The Foundation and the National Institute for Child Health and Human Development provided start-up grants to help the Public Health Service begin a national surveillance program utilizing hospital discharge records of newborns from hospitals around the nation -- the International Clearinghouse for Birth Defects Monitoring Systems, a voluntary, nongovernmental association. Many of you are associated with this excellent organization. Until 1982, the March of Dimes was the sole financial support of this Clearinghouse. Gradually, the Foundation reduced its support until, in 1986, the Clearinghouse became a self sufficient organization.

In 24 countries now, the International Clearinghouses provides for the exchange of information, collaboration in research, and consultation and assistance in preventing birth defects. Such Clearinghouses were responsible for the early recognition that the anti-convulsant drug, valproic acid, was a cause of spina bifida and for the rapid, worldwide communication of this information. First recognition of such a relationship came from Dr. Elizabeth Robert, in France. Within 3 months, the association was confirmed and the information distributed to physicians around the world. This rapid resolution and spread of information would not have been possible without the registries being available and the

willingness of members and staff, notably Professor Bengt Kallen of Sweden, to work to resolve the issue swiftly. By comparison, we should note that it took more than 3 years for thalidomide to be recognized as a human teratogen.

There are several special areas where we could substantially expand our efforts. I will mention but a few which to me seem important.

First, we need to greatly strengthen our science base to better understand developmental biology. Identification both of essential growth factors as well as potential toxicants and their mechanisms of action will greatly assist the search for preventative interventions. In this regard, it is highly salient to recall the history of the March of Dimes which, from soon after its founding, began to provide substantial support for basic research in virology. It could equally as well have invested these funds in added patient care, improved respirators better designed wheelchairs and the like -- the application of half-way technologies, in Lew Thomas' parlance. It did not. With great prescience, it invested in the creation of a solid foundation of basic virological research which eventually culminated in a vaccine -- and a total victory over the disease. If we are to achieve comparable successes in birth defect prevention, we must sustain and expand a relevant science base.

Second, surveillance programs and case-control studies could usefully be strengthened and expanded to determine what other drugs, nutritional factors, exposures to

environmental hazards, maternal illnesses and genetic factors cause, or are risk factors for, birth defects. This is a complementary approach but demonstrably an important one, as we have discovered with folic acid deficiency.

CDC has begun a new continuous birth defect case-control study in three locations. This study has been designed so that data can be continuously available for analysis for possible new causes, hopefully obviating the need for more time consuming case-control studies or, at the very least, permitting them to be more sharply targeted. This approach deserves careful evaluation and perhaps expansion.

Special circumstances will point the way toward other possible causes. Recently, citizens and local health professionals in Brownsville, Texas, identified a cluster of babies born with anencephaly and suggested the possibility of environmental pollutants. State officials, with CDC help, found that the incidence of spina bifida and anencephaly was high, not only in Brownsville, but in the entire county and in adjacent counties. The rate was much higher in Hispanic populations, in both the United States and other countries. International efforts are now needed to determine exact causes, whether dietary, genetic or environmental. I am confident that through watchful surveillance, other unusual clusters of birth defects will serve to identify yet other causes subject to preventative measures.

Continuing surveillance for birth defects has other uses. It provides health agencies with incidence rates for specific defects and permits these rates to be followed closely to

determine whether they are increasing, decreasing, or remaining stable. Sudden changes in these rates serve as a warning that something new has been added to or deleted from the diet or the environment and may be an important clue to the cause of the birth defect.

Such programs also permit the effectiveness of prevention strategies to be monitored.

Knowing that discrete areas have a high incidence of a specific disability or that a racial or ethnic group is at high risk for a specific condition is also valuable information for planning prevention strategies.

The development of prevention programs is not always an easy task as illustrated by the problems of preventing fetal alcohol syndrome. Even though the cause has been known since the early 1970s, control has proven difficult. It is estimated that FAS accounts for some 4,000 to 8,000 children born with preventable birth defects each year in the United States. Further research is needed to understand the pathophysiology of this problem so as to improve surveillance methods and to implement effective prevention efforts.

I would also draw your attention to iodine deficiency -- still a problem in many parts of the world but scarcely being addressed as yet despite the availability of simple, inexpensive and well-known means for intervention.

## Summary

There is now a special opportunity for international cooperation to prevent birth defects. The successes with folic acid and rubella vaccine are but a harbinger of possibilities to come. With advances in biomedical science and strengthened and expanded surveillance systems, I am confident that much, much more will be possible. We can do so much more working together than we can working independently and the folic acid story is adequate testimony to that.

Once the methods are in hand, they will need to be applied in all countries -- a challenge as formidable as the discovery process itself. Even today, and with inexpensive interventions, we are doing poorly vis-a-vis iodine deficiency; rubella vaccine use is essentially confined to industrialized countries; and we are, as yet, without so much as a strategic concept as to how to make folic acid supplementation universally available. Prevention services, however cost-effective, have yet to be accorded priority in my own country.

To date, health services throughout the world continued to have focus primarily on the provision of curative services. But the agenda is beginning to change and I would specifically call to your attention the World Bank's World Development Report of last year. It provides our own analysis of costs and benefits of health care programs broadly and on strategies for the development of health services. It unequivocally concludes that far more

resources should be shifted toward disease prevention -- at the expense of curative services.

Having attending several seminars with Ministers from other countries, it is apparent that the advise is being taken seriously -- including in the U.S.

A consortium such as you propose could greatly abet and guide this process.

Hopefully this international meeting will serve as an important catalyst to successful future efforts.