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ABSTRACT

Proceedings from the International Summit on Prevention of Mental Retardation from Biomedical Causes are provided. After a list of participants and summary of the highlights of the conference, the keynote address by H. Moser is presented. The following 13 papers are provided along with workshop recommendations and a list of main points elicited from the discussions (which are included for most papers): "Preventing Mental Retardation--More Can Be Done" (J. Dion); "A National Program to Prevent Neural Tube Disorders" (A. Milunsky); "Regionalization and Expansion of a Metabolic Screening Program for New Borns" (R. Guthrie); "Prevention of Rh Hemolytic Disease" (R. MacCready); "Strategies for Prevention of Mental Retardation at the Federal Level" (H. Boggs); "Nutrition, Brain Growth, and Prevention of Mental Retardation" (P. Rosso); "Prenatal Supplements and Breast Feeding" (R. Acosta); "Regionalization of Perinatal Care" (L. Gluck); "A Model Program for Lead Screening" (S. Pionelli); "Immunizations and What Can Be Done to Improve Their Use" (J. Browder) with comments and concerns expressed by T. Tjossem; "Maternal Alcoholism and Fetal Abnormalities" (K. Jones); and "Down's Syndrome and Its Potential Prevention" (M. Giannini). A list of commitments made by participants is followed by a concluding statement by R. Koch. (PHR)

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INTERNATIONAL SUMMIT ON PREVENTION OF MENTAL
RETARDATION FROM BIOMEDICAL CAUSES

sponsored by

President's Committee on Mental Retardation (PCMR)
American Association on Mental Deficiency (AAMD)
Canadian Association for the Mentally Retarded (CAMR)
National Association for Retarded Citizens (NARC)

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INTRODUCTION

Two out of every 100 people in the United States and Canada are born mentally retarded, or become mentally retarded after birth. This condition is not a disease in itself, but can be a symptom of any number of disorders, many of which at the present time, are preventable or treatable. Despite the fact that medical science now has the knowledge and techniques to prevent many forms of mental retardation--indeed to cut the incidence of mental retardation by half in the United States--the general public, and even many members of the medical profession are unaware of these advances.

The International Summit on Prevention of Mental Retardation From Biomedical Causes was held at Wingspread, December 15-16, 1978, to explore the many avenues open at the present time to scientists and physicians in working toward the laudable and achievable goal of significantly reducing the incidence of mental retardation. The stated purpose of the conference was "... to provide a forum which facilitates the abilities of representatives of Canadian and United States organizations and agencies, to think, plan, collaborate, and develop short and long range strategies." Experts from many medical and research facilities were brought together under the auspices of the President's Committee on Mental Retardation; the American Association on Mental Deficiency; the Canadian Association for the Mentally Retarded; and the National Association for Retarded Citizens, in cooperation with the Johnson Foundation.

The physical facilities at Wingspread and the philosophy of the Johnson Foundation provided a most welcome atmosphere for the thinking that took place, the ideas that were generated, and the personal commitments that were made in the effort to reduce significantly the incidence of mental retardation from biomedical causes.

Frank Lloyd Wright designed the building and called it Wingspread. It is situated on a rolling prairie site north of Racine, Wisconsin, and was built in 1938 as a residence for the Johnson family. In 1960, through the gift of Mr. and Mrs. H. F. Johnson, it became the headquarters of The Johnson Foundation and began its career as an educational conference center.

In the years since, it has been the setting for many conferences dealing with subjects of regional, national, and international interest. It is the hope and belief of the Foundation's trustees that Wingspread will take its place increasingly as a national institution devoted to the free exchange of ideas among people.

The rolling expanse of the Midwestern prairies was considered a natural setting for Wingspread. In the limitless earth, the architect envisioned a freedom and movement. The name Wingspread was an expression of the

nature of the building, reflecting aspiration through spread wings--a symbol of soaring inspiration and, in more recent years, the free expression of ideas..

In his 1971 Johnson Foundation Report, Mr. Leslie Paffrath, president of the Johnson Foundation, described the atmosphere which contributed immeasurably to the success of the Summit:

"Individuals travel thousands of miles to attend Wingspread conferences in the belief that constructive work will be done. We act to meet this expectation with a climate favorable to personal exchange of ideas. The goal of the Foundation is to encourage such exchange, for modern communication does not insure this, despite its capacity to inform on a global basis. Man can transmit words from earth to moon and moon to earth, but the essence of all he has learned over the ages about relating to other men comes into play humanly only when his eye is at the level of another man. We believe in the good effect of quiet and reasonable exchanges of ideas expressed in mutual respect. Meaningful dialogue prospers where the several senses come into play; when men are free to use intuition and spiritual experience, as well as intellect. We encourage people to discover and act out their individual humanness, in opposition to the forces which dehumanize."

In this atmosphere, the International Summit on Prevention of Mental Retardation From Biomedical Causes took place. Mrs. Laverdia T. Roach, Program Specialist from the President's Committee on Mental Retardation, planned and coordinated the conference. The following manuscript is a record of the problems it considered, the suggestions and recommendations it produced, and the commitments that were made by the participants.

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Highlights of the Conference

The Summit theme was "Prevention of Mental Retardation From Biomedical Causes: A Realistic and Achievable Goal." It was opened by Dr. Margaret Giannini, president of the American Association on Mental Deficiency, after which the participants were welcomed to Wingspread by Mr. Leslie Paffrath, president of The Johnson Foundation. Then Mr. Fred J. Krause, executive director of the President's Committee on Mental Retardation, gave a statement of the purpose and objectives of the Summit; and the keynote address was given by Dr. Hugo Moser, director of the Kennedy Center for Mental Retardation, Johns Hopkins Medical Center.

In his address, Dr. Moser reminded the group that it has been six years since the President of the United States established as a national goal, that by the year 2000 the incidence of mental retardation be reduced by half. Since about one-fifth of that time has now passed, Dr. Moser emphasized the importance of the Summit in determining whether our present courses of action will permit us to reach this target. He noted that we have the capacity to completely prevent retardation due to phenylketonuria (PKU), hypothyroidism, galactosemia, and certain rarer disorders. The elimination of retardation from these causes is based on mass screening (testing) of newborns to identify these disorders, which are diagnosable and treatable. Dr. Moser discussed the use of amniocentesis and abortion in the prevention of the birth of Down's syndrome individuals and emphasized the troublesome problem in this field due to the religious and ethical controversies about abortion.

In this regard, Dr. Richard Koch of the Children's Hospital of Los Angeles stated in his summation of the conference, that we must meet the challenge of the "Right to Life" movement head-on, as it could pose a threat to the science of genetics, amniocentesis programs, sex education in public schools, and to our efforts to help with the problem of teenage pregnancy. He emphasized the importance of the protection of equal rights; the right of the child to be well born and the right of the mother to have healthy children. He said both forces should join hands to spur progress so that abortion would become an unnecessary solution.

The problem of the continuing incidence of common childhood diseases was discussed. Even though there are now vaccines for measles, rubella (German measles), whooping cough, and mumps, these diseases are still occurring among children and young adults. Dr. J. Albert Browder of the University of Oregon Health Science Center reported that, while most States have immunization regulations requiring immunizations for rubella, diphtheria, pertussis, and tetanus for school attendance, these rules

have generally not been enforced. Dr. Browder said that before live vaccines became available in 1963, four million people contracted measles annually in the United States, resulting in 4,000 cases of encephalitis, 1,300 cases of mental retardation, and 400 deaths.

Between 1964 and 1974, 707,000 cases of measles were averted, 2,400 lives were saved, and 7,000 cases of mental retardation prevented due to immunizations. Dr. Browder also noted that, not only the present generation, but the next one is affected by childhood diseases, if they are contracted by women during pregnancy. Measles, although it is usually a mild disease in the mother, can cause deafness, blindness, mental retardation, and other handicaps in the fetus. Dr. Browder said that a major concern is apathy and ignorance by the public, and even some physicians, about the need for immunizations.

Dr. Aubrey Milunsky of the Eunice Kennedy Shriver Center for Mental Retardation made a presentation on the establishment of a National Program To Prevent Neural Tube Disorders. These disorders are usually serious birth defects such as spina bifida, hydrocephaly, and anencephaly (no brain). Dr. Milunsky reported that nine out of ten of these defects can now be detected by amniocentesis, blood tests, and ultrasound methods, and that with proper national planning, 90 percent of them could be detected in the early stages of pregnancy.

Mr. Joseph P. Dion of the United States General Accounting Office said that each dollar invested in screening with a battery of seven tests to diagnose treatable diseases which cause mental retardation in newborn infants saves more than \$20.00 spent for programs to care for retarded individuals. Mr. Dion reported that the Department of Health, Education, and Welfare (HEW) has designated the incoming Assistant Secretary of HEW to be a focal point to implement a national prevention strategy, monitor and coordinate the efforts of various HEW agencies and offices, and develop a method of determining the progress being made in reaching the goal of reducing the incidence of mental retardation by half by the end of this century.

Until 1968, Rh hemolytic disease often caused cerebral palsy, deafness, seizures, and mental retardation in Rh positive infants born to Rh negative mothers. This occurred after the mother's body was sensitized to Rh positive blood. At the present time, there is no reason why any child should suffer from Rh hemolytic disease, and yet infants are still being damaged by this disorder.

Dr. Robert A. MacCready, retired director of the Massachusetts Department of Public Health Laboratories, reported that Rh immune globulin (RhIG), which was developed in 1968, can completely prevent Rh hemolytic disease; yet it is estimated that only 80 percent of the Rh negative

women who should receive it, actually get it. Dr. MacCready said it has been estimated that in 1974, 7,000 infants were born in the United States with Rh hemolytic disease. He explained that the RhIG, if administered to a woman within 72 hours of the time she has received Rh positive blood cells from any cause, such as delivery, abortion, or blood transfusion, will destroy those positive cells before her body has had time to produce the antibodies which could damage a subsequent infant. Dr. MacCready emphasized that RhIG is effective only for Rh negative women not already sensitized, and that the RhIG must be administered after each delivery or abortion.

In Connecticut, where a well organized program to reduce the incidence of Rh hemolytic disease was instituted, the numbers declined from 102 in 1970 to 19 in 1976. Dr. MacCready said the relatively modest cost of the administration is far less expensive than treating the children afflicted with the disease. He said the utilization of RhIG is now standard medical care and its appropriate administration to maternity patients should be paid for by H&W for Medicaid patients, and that Blue Cross/Blue Shield and other medical insurance plans should also provide it.

Malnutrition during pregnancy leads to increased incidence of prematurity, still births, low birth weight babies, and babies that are functionally immature. Dr. Phyllis B. Acosta of the School of Medicine at Emory University reported that it has been known for nearly 30 years that nutritional supplements during pregnancy increase the length of gestation and the birth weight of the infant. Since there is a higher rate of mental retardation among premature infants and infants of low birth weight than among full term infants and those weighing over 2500 grams at birth, nutritional supplements during pregnancy are an important factor in preventing mental retardation. Dr. Acosta noted that there is evidence that breast milk contains E-coli antibodies, thyroid hormone and taurine, and that breast fed babies have fewer respiratory illnesses, allergies, and less diarrhea than bottle fed babies; thus, it is important to encourage mothers to breast feed their infants.

Dr. Pedro Rosso of the Institute of Human Nutrition at the College of Physicians and Surgeons, Columbia University of New York, explained in his presentation on Nutrition, Brain Growth, and Mental Retardation why children who are undernourished prenatally and during infancy tend to have a much higher incidence of mental retardation than others. He said that experiments on animals have shown that undernutrition during pregnancy causes a slowing of cell division and a reduction in the ultimate number of cells in each organ, including the brain. This condition becomes permanent once the normal time for cell division has passed. Dr. Rosso pointed out that children suffering the effects of malnutrition usually also suffer from environmental deprivation and the combination of conditions has a devastating effect on their physical and intellectual growth.

It has become apparent that, to be successful in eliminating certain causes of mental retardation and to better serve the public, some special services need to be regionalized so that they can be made available to every area. These services involve complicated techniques that would entail excessive expense and inefficiency if they were carried out at every individual hospital or clinic.

Dr. Robert Guthrie of State University of New York at Buffalo gave a presentation on Regionalization and Expansion of a Metabolic Screening Program for Newborns. Dr. Guthrie said that, with the use of automated equipment, mass screening can be done for galactosemia, homocystinuria, maple syrup urine disease, and histidinemia, in addition to PKU. He also discussed recently developed screening techniques to detect hypothyroidism in newborns. He emphasized the importance of liaison between screening programs and medical centers to assure good follow up and treatment after a disorder is detected.

Dr. Louis Gluck of the School of Medicine at the University of California at San Diego noted that since 1970, the United States has rated 11th - 15th in the world in infant mortality. He pointed out that perinatal medicine is of utmost importance because over 90 percent of all non-hereditary developmental problems (brain damage, cerebral palsy, mental retardation, behavior disorders, learning problems, etc.) are produced during the perinatal period, and many of these could be prevented with proper care. He said, not only do intensive care perinatal units need to be regionalized so that these services can be available to the entire population, but doctors need better training in obstetrical methods and pediatric care for infants. The rapid growth of knowledge in this field and the expansion of regionalization of these services should bring about a reduction in infant mortality and a corresponding reduction in mental retardation from perinatal causes.

Lead poisoning has long been recognized as a cause of mental retardation. It was once thought that it was caused almost exclusively by the eating of lead-containing paint by children. Dr. Sergio Piomelli of the New York University School of Medicine reported that this is no longer completely true. He reported that lead in the atmosphere and in our bodies has been increasing since 1923 when lead was first used as an additive for gasoline. He said there is no such thing as a "normal blood lead level," and that in 1975, 150,000 tons of lead were emitted into the air in the United States and that 100 milligrams is enough lead to kill a child.

In 1971, 2,000 children in New York were found to have unsafe levels of lead in their blood; however, the blood lead level of New York children is now going down because the city has passed an ordinance limiting the amount of lead in gasoline. Dr. Piomelli added that children are especially prone to ingest lead from dust because they suck their thumbs

and put their fingers in their mouths. According to Dr. Picinelli, there is also lead in some tin cans which leaches out into food. There seemed to be consensus of opinion among the conference participants that we need legislation to remove all lead from gasoline.

Down's syndrome and Its Potential Prevention was discussed by Dr. Margaret J. Giannini, president of the American Association on Mental Deficiency and director of the Mental Retardation Institute, New York Medical College, who said that Down's syndrome can now be detected prenatally by amniocentesis and the mother may opt to have the pregnancy terminated. Genetic counseling is important in the prevention of this form of mental retardation. She also stressed that the ultimate solution to the problem of Down's syndrome lay in further research to find the cause of non-disjunction.

Maternal alcoholism has only recently been identified as a cause of mental retardation and other abnormalities in the infant. Dr. Kenneth Lyons Jones of the University of California at San Diego said that more publicity is needed in this area to make the public aware of the dangers associated with excessive drinking by pregnant women. In the same vein, Dr. Koch noted that it has been proven that excessive cigarette smoking during pregnancy often causes prematurity and babies of low birth weight.

Dr. Elizabeth Boggs of the Governmental Affairs Committee of the National Association for Retarded Citizens made a presentation on Strategies for Prevention of Mental Retardation at the Federal Level. Dr. Boggs said that the Federal role is changing and multiplying. She noted that the prevention of mental retardation requires that many targets be attacked concurrently, using different strategies. She pointed out eight different activities Federal agencies should be carrying out through the Public Health Service to prevent biomedical disorders. She said, for each of the targets to be attacked in the prevention of mental retardation, clear objectives should be established, specific coalitions mobilized, progress charted, and successes proclaimed.

Dr. Cecil B. Jacobson, chairman of the Task Force on Biomedical Prevention of the President's Committee on Mental Retardation gave a report on Regionalization for Genetic Services and Amniocentesis in which he said that the technique of amniocentesis to diagnose chromosomal and biochemical defects prenatally was first reported by independent laboratories in 1967. Since the technique was first developed, these laboratories have performed over 27,000 amniotic fluid studies. Dr. Jacobson pointed out that at the present time, over 60 inborn errors of metabolism, plus all known chromosomal anomalies can be detected by this method, and that a study done by the National Institute of Child Health and Human Development has determined that the procedure does not significantly increase the risk of maternal or fetal loss or injury.

Workshops were held on all the subjects presented, in which the problems were discussed and recommendations were made to the conference participants. After these recommendations were ratified by the group, the conference closed with a Celebration of Commitment in which each individual explored specific strategies on which he or she would work to assist in the implementation of the Summit objectives and priorities.

Keynote Address

PREVENTION OF MENTAL RETARDATION

FROM BIOMEDICAL CAUSES

by

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PREVENTION OF MENTAL RETARDATION

FROM BIOMEDICAL CAUSES

It is now six years since the President of the United States established as a national goal, that by the year 2000 the incidence of mental retardation be reduced by one-half. About one-fifth of the allotted time has passed. It is indeed important that we meet so that we can decide if our present courses of action will permit us to reach this target.

In this statement, I would like to focus on four points:

1. Truly remarkable progress has been achieved in some areas.

In order to give a general overview of the problem, I have prepared a table which lists the major causes of severe mental retardation (I.Q. <50) and gives an estimate of the degree to which each of these might be prevented by the effective application of current knowledge. The incidence figures are based upon surveys of severely retarded residents in two institutions (Central Colony in Madison, Wisconsin and Walter E. Fernald State School in Waltham, Massachusetts), and on published incidence figures in large population groups. The numbers I have listed here are approximations only, and designed only to indicate order of magnitude.

In regard to the prevention of mental retardation due to metabolic disease, I have taken as a given reason our capacity to prevent completely, retardation due to phenylketonuria, hypothyroidism, galactosemia, and certain rarer disorders. To arrive at the figure for the prevention of Down's syndrome, I have assumed that amniocentesis will be performed on all pregnant women over 35 years old, and that all Down's syndrome fetuses are aborted. As I discuss below, this approach is controversial.

I have assumed entirely arbitrarily, that it will be possible to reduce by one-half, brain damage due to perinatal injuries. However it is quite possible that with a regional network of perinatal centers, we can achieve even better results. Prompt therapy of bacterial brain and meningeal infections, and effective immunizations against measles and rubella should allow major reduction in mental retardation due to these causes, but allowance must be made for the fact that we cannot as yet deal with cytomegalic or herpes simplex virus, or disorders such as toxoplasmosis. I have assumed that amniocentesis of relatives of patients with neural tube defects might allow prenatal detection of roughly half of the cases.

On the basis of these very rough figures, which I am sure will be altered and refined during the discussions of the next two days, I have made the estimate that approximately 30 percent of severe mental retardation might be prevented by the widespread application of presently known techniques.

2. The causes and types of mental retardation are, and will continue to be, in a state of flux. While we have, for practical purposes, eliminated phenylketonuria as a cause of severe mental retardation, we must now prepare to counsel the treated phenylketonuric women. To prevent retarded offspring, it is likely that they either must not have children or must resume dietary therapy during pregnancy. In spite of their effectiveness (and in part because of it), our neonatal units will result in the survival of some handicapped children who in the past would have died. Finally, new drugs and new environmental hazards may cause previously unrecognized fetal malformations. In regard to the thousands of possible teratogens, there is the need and, I believe, the possibility of developing screening assays analogous to the Ames assay for carcinogens. The changing nature of mental retardation means that we cannot rely on a fixed set of prevention strategies. We must be prepared to re-evaluate and to adjust.

3. There is, and there will probably always be, genuine and legitimate conflict between the urge to apply existing knowledge and the search for new knowledge. I suspect that everyone agrees that both should go forward simultaneously. However, with limited resources, priorities have to be set. I would submit that these must be decided individually for each specific problem. Let me clarify this with some examples: In respect to many aspects of metabolic screening or to the prevention of Rh disease, the challenge now is the fail-safe implementation of existing knowledge. We know that we can prevent serious disease, and at low cost. However, in respect to Down's syndrome, the situation is very different. If amniocentesis is performed for all pregnant women over age 40, and if all Down's fetuses detected in this way were to be aborted, this would reduce the total incidence by approximately 15 percent. If the age figure is set at 35 years, then we could detect prenatally and prevent 30 percent. With the present state of knowledge, the complete elimination of Down's syndrome would require amniocentesis and karyotype studies of all pregnancies. This would entail unacceptable cost and might be associated with low-incidence complications of amniocentesis which so far have not been recognized.

In addition, we are all aware of the religious and ethical controversies about abortion. In respect to Down's syndrome, these controversies are, if this be possible, still more troublesome since children with Down's syndrome, in fact, have such considerable capacity for growth and development. I would submit, admittedly as my personal bias, that in respect to Down's syndrome, our priority should be the search for additional knowledge. The most desirable new knowledge would be to understand the cause of non-dysjunction in the ovum so that the very occurrence of trisomy could be prevented. We do not know the cause for mental handicap in Down's syndrome. Perhaps it is not inextricably related to the existence of the chromosomal abnormality, and thus, it may become possible to improve the mental handicap. If neither of the

above are successful, we ought, at the very least, to search for markers of couples at risk in addition to maternal age, so that we can identify with greater precision those parents who are at risk of having a child with Down's syndrome and thus reduce the number of pregnancies that need to be monitored.

The main point I wish to make is that while the effective implementation of existing knowledge will allow us to reduce the incidence of some forms of mental retardation, I suspect that this might not permit us to reach the target of 50 percent reduction. I believe that to reach this goal, we must also continue to search out what is not known. To be able to make the best judgement on how to distribute resources between implementation of the known and search for the new requires facts, wisdom, and good faith.

In conclusion, it is truly exciting to see so many biomedical causes of mental retardation crumble simultaneously under the attack of new knowledge. I believe that we can indeed achieve the goal of 50 percent reduction by the year 2000, provided that we exercise to the maximum our intelligence, judgment, and good faith and provided that we are able to engage and maintain the commitment and support of the general public.

SEVERE MENTAL RETARDATION
(I.Q. 50)

Major causes and estimate of
percentage that might be prevented
by effective application of
existing knowledge

	percent of severe MR	percent of severe MR that could be prevented
. Inborn errors of metabolism and hypothyroidism	5	2.5
. Chromosome disorders (mainly Down's)	30	9
. Neural tube defects	3	1.5
. Other genetic	6	---
. Perinatal injuries prematurity	20	10
. Infectious disease (viral, bacterial)	7	5
. Rh disease	20.5	0.5
. Lead poisoning	1	1
. Postnatal trauma	2	1
. Unknown	25	---
TOTAL	<u>100</u>	<u>29</u>

PREVENTING MENTAL RETARDATION:

MORE CAN BE DONE.

by

Joseph P. Dion
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Los Angeles, California

One of the questions I have often been asked is how a congressional investigative agency got involved in mental retardation? The General Accounting Office (GAO) evaluates program effectiveness wherever Federal funds are spent. Our work is initiated in one of three ways:

1. Periodic audits required by law;
2. Review generated internally by GAO; or
3. Investigations requested by individual legislators or congressional committees.

Our work in mental retardation falls into the second category.

About 4 years ago, the GAO established a Mental Health Activities Task Force to assess the impact that Federal programs have had on this country's mental health problems. The Task Force was designed to cut across previously existing functional and organizational lines to focus its evaluations on the problems and issues themselves, rather than on the programs set up to deal with the problems or the agencies delivering the services.

The Task Force initiated a two-pronged effort in evaluating mental retardation programs. First, we examined Federal and State efforts to deinstitutionalize retarded persons and second, we evaluated Federal efforts to prevent retardation. As an agency concerned with improved effectiveness, we directed our recommendations to other Federal agencies. This was the case in this report. That is not to minimize or ignore the roles of the private sector.

As you all know, mental retardation is one of the nation's greatest long-term public health, social, and economic problems. It is estimated that over 100,000 new cases of retardation occur each year--as many as four million of the 80 million children expected to be born (at present birth rates) by the year 2000 will be born mentally retarded, or will become mentally retarded.

In 1974, the Department of Health, Education, and Welfare (HEW) estimated that national cost of mental retardation at between \$8.5 and \$9 billion annually, including care, treatment, and the economic losses attributable to the decreased productivity of retarded persons. HEW estimated that it alone spent over \$1.7 billion in fiscal year 1976 for mentally retarded persons.

In 1976, the President's Committee on Mental Retardation (PCMR) called for reducing the incidence of mental retardation:

1. from biomedical causes by at least 50 percent by the year 2000,
- and

2. associated with social disadvantage to the lowest level possible by the end of the century.

We made our review to determine what has been done to prevent retardation and what can and should be done to reduce it.

We found that despite the President's goal of reducing mental retardation by half by the end of the century, (1) no HEW agency has been made responsible for monitoring the implementation of the goal; (2) the goal has not been designated an objective by those HEW agencies with prevention responsibilities; and (3) systems have not been established or methods developed to assess progress in achieving the goal.

Although some HEW organizations have major responsibilities for coordinating or operating mental retardation activities or programs, none has overall responsibility for developing a prevention strategy, determining and implementing efforts needed to accomplish the President's goal, or defining the responsibilities of agencies and programs that do or could have an impact on the goal. In addition, agencies that have major responsibilities for improving child health, and preventing childhood disabilities, primarily the Bureau of Community Health Services, Health Services Administration, have neither developed a strategy for, nor established methods of measuring progress in reducing its incidence.

If the incidence of mental retardation is to be reduced to the maximum extent possible, a specific group within HEW must be made responsible for implementing and monitoring a national prevention strategy, clarifying agency roles, and determining which HEW programs can best assist in the effort, and how they can accomplish this task. The responsibilities of this organization should include coordinating the mental retardation prevention efforts of the various HEW programs and developing a method to measure the progress being made.

We recommended that the Secretary of HEW:

- 2. Designate a focal point within HEW to implement a national prevention strategy, monitor and coordinate the efforts of the various HEW agencies and offices, and develop a method of determining the progress being made in reaching the goal.
- o Designate prevention of mental retardation an objective in HEW's operational planning system.

HEW agreed with our recommendation to designate a focal point in HEW for the mental retardation prevention effort. The Office of the Assistant Secretary for Health will be the focal point. Specific responsibility will be designated by the incoming Assistant Secretary for Health.

The remaining chapters of our report focus on selected causes of mental retardation for which it appears that more intensive implementation of certain techniques would result in reduced incidence. Neither the selection of specific causes nor the arrangement of chapters in this report are intended to stress the importance of any one cause or minimize the significance of other causes.

While we have concentrated in this report on actions that can be taken to prevent mental retardation with existing knowledge and technology, we recognize that research is needed and is ongoing into the causes and possible methods of preventing mental retardation.

METABOLIC DISORDERS

Although almost all States have newborn screening programs for PKU, at the time of our review, screening for other metabolic disorders was done routinely by only eight States. Also, improvements are needed in many State PKU programs to more effectively reach all infants.

In 1975, Dr. Robert MacCready sent a questionnaire to health officials in each State. Only 15 States had statistics showing that their screening programs were reaching 90 percent, two were reaching 70 to 80 percent, and four were reaching only 60 to 70 percent.

Dr. Robert Guthrie reports that a primary reason why testing has not been expanded in more States to include other metabolic disorders is that screening programs have primarily been restricted to within the State boundaries and many State populations are too small to justify testing for the rarer disorders. He has reported that to get full value from automated screening, it must be done on a large scale--a minimum of 25,000 births a year. Therefore, he argues that consolidation of screening is needed (1) within large States where screening is fragmented into many programs, each too small to make multiple testing practical, and (2) between or among States where populations are too small to warrant multiple screening within each State. Bureau of Community Health Services officials agree that consolidation or regionalization of screening programs is needed.

We estimated that PKU screening, under a well-organized automated system, and lifetime treatment of afflicted individuals would cost about \$3.3 million a year. However, such screening could prevent about 270 cases of mental retardation and avoid \$189 million a year in costs of providing care and services for individuals who, without screening and treatment, would be retarded.

We also estimated that adding screening and treatment of six other disorders would raise costs to about \$18.5 million a year, but could prevent as many as 305 cases of mental retardation each year and increase the savings of lifetime care costs to about \$437 million.

Although the concept of relating benefits to costs is simple, its actual application is complex and difficult. The major benefit usually cited in preventing retardation is the avoided costs of caring for the retarded individual. Another factor that should be considered, however, is the benefit to society of having an individual who is not retarded, but who would have been without the program. These benefits accrue continuously over his or her lifetime, taking different forms and affecting different sectors of society such as: reduced unemployment, reduced welfare payments, increased job productivity and increased tax revenue. We did not analyze the latter benefits because of the inherent difficulties in measuring their monetary value. For the same reason, we did not consider the savings in human suffering associated with avoiding retardation. We recognize, therefore, that the benefits of screening are understated in our analysis.

We recommend that HEW help improve newborn screening by:

- Evaluating State screening programs to identify those which are not effective and provide them with necessary assistance;
- Supporting expansion of newborn screening to include treatable metabolic disorders in addition to PKU; and
- Assisting States to cooperate to establish cost-effective regionalized metabolic screening programs.

LOW BIRTHWEIGHT INFANTS

National Center for Health Statistics data obtained from 42 States and the District of Columbia showed that, in 1973, about 202,000 of the 2.7 million babies born alive weighed 2,500 grams or less.

According to the National Center for Health Statistics, about 37,600 women who gave birth in 1973 received no prenatal care, and another 60,700 did not get prenatal care until their eighth or ninth month of pregnancy. Of those who received no prenatal care, 21.1 percent gave birth to low birth weight babies.

The guidelines for maternal and child health services programs of projects published by HEW recognize that many women in low-income families receive little or no prenatal care. The guidelines provide that a State plan for maternal and child health services should indicate the overall nature and extent of the need for such services throughout the State. In the States we reviewed, this need has not been adequately analyzed.

In addition, headquarters and regional officials of HEW's Bureau of Community Health Services told us that they had not evaluated the effect

of maternity and infant care projects on preventing mental retardation. According to the mental retardation specialist in the Bureau's Office of Special Concerns, it is difficult to document the extent of prevention of mental retardation because it would take several years of followup to prove, and maternal and child health projects do not have the resources to perform such followup.

To be able to establish priorities for allocating prenatal care funds most effectively and to the areas of greatest need, we recommend that the Secretary of HEW direct the Bureau of Community Health Services to evaluate the State procedures used to determine needs for prenatal care services and ensure that State plans outline a clear strategy for reaching the population in greatest need.

CHROMOSOME ABNORMALITIES

Chromosome abnormalities are estimated to account for about 16 percent of the clinically caused cases of mental retardation. A 1974 study reported that over 10 percent of the residents of public residential facilities for mentally retarded persons reporting such information were diagnosed as having a chromosome abnormality.

Since treatment of chromosome abnormalities is limited, the main role of medical genetics is prevention through genetic counseling and testing. Persons with chromosome defects, or at high risk of having children with defects, can be identified and counseled. Additionally, chromosome abnormalities can be diagnosed in an unborn child, thus allowing the parents to make an informed decision about continuing the pregnancy.

However, it appears that only a small portion of those who could benefit from genetic services receive them. Neither HEW nor the States we reviewed have made efforts to assure that persons needing the service or at risk are screened or served. In addition, the geneticists we interviewed generally believed that only a small percentage of those who obtain services are from lower socio-economic groups.

Federally funded family planning programs, and possibly other Federal programs, might be a good means of providing the needed outreach and identification, and for serving lower income families. However, the family planning programs in the States we reviewed generally did not attempt to identify families in need of genetic services.

We recommended that the Secretary of HEW:

- ° Direct Federally supported family planning programs to routinely include screening for individuals who are "high risk" for genetic disorders and refer such individuals to diagnostic and counseling services.

- Monitor the demand on existing genetic resources created by outreach, and develop strategies for increasing resources as needed.
- Explore how other Federal programs could better be used to provide genetic screening and services.

INFECTIOUS DISEASES FOCUSING ON MEASLES AND RUBELLA

The Center for Disease Control (CDC) estimates that about one of every 1,000 reported cases of measles results in brain inflammation, and that about 25 to 35 percent of those cases result in mental retardation. CDC has also estimated that the 1964-65 rubella epidemic caused about 1,800 cases of mental retardation, about 2,200 deaths, about 6,300 miscarriages, left about 12,000 children deaf or deaf-blind, and caused 5,000 women to seek therapeutic abortions.

In the 1960's, vaccines against both these diseases became available, and since then the incidence of each disease has dropped dramatically. However, CDC reports that cases are still occurring and that immunity levels are unnecessarily low, particularly among preschool children, giving rise to the possibility of a major epidemic in the future.

From a national perspective, two elements are necessary to effectively combat these diseases: comprehensive data on immunity levels to pinpoint problem areas and aggressive immunization programs targeted at areas with low immunity levels. However, in the past, immunity level data has not been adequate to pinpoint problem areas, nor have vaccination programs raised immunity to acceptable levels.

Federal programs can improve national surveillance data and help prevent mental retardation by helping to raise immunity levels for rubella and measles. The Medicaid Early and Periodic Screening Diagnostic and Treatment Program could collect and provide immunization surveillance data to the Center for Disease Control and increase immunization levels among the children served; Head Start programs could collect and provide CDC with immunity level data on the children they serve; and Federally funded family planning programs could screen their women clients and provide immunizations to those in need.

Federal funding for immunization projects has been substantially reduced since 1970, on the premise that Federal programs such as Early Periodic Screening, Diagnosis and Treatment (EPSDT), and the States themselves would be assuming increasing responsibilities for immunizing children. However, CDC is concerned that as Federal funds continue to be reduced, immunization efforts will falter because EPSDT and States are not effectively taking up the slack. This corresponds to experience we had in the 1960's when we saw the withdrawal of Federal funds for the State

supported immunization programs. The incidence of both measles and rubella skyrocketed overnight. With the reinstatement of Federal funds, the rate plummeted again almost immediately.

We recommended that the Secretary of HEW:

- ° Examine the alternatives of expanding CDC support of State vaccination programs or making arrangements between CDC and the Medical Services Administration that will enable EPSDT to more effectively support national and State immunization activities.
- ° Expand EPSDT requirements to specifically require screening for immunization status and reporting of the number screened and immunized.
- ° Require Head Start projects to develop data on the results of their immunization screening.
- ° Require Federally funded family planning and other appropriate programs to include rubella susceptibility testing and immunizations, where appropriate, among their routine services.

LEAD POISONING

Lead poisoning has generally been associated with children eating lead-based paint chips. Steps have been undertaken to reduce lead poisoning hazards, including urban renewal and laws restricting lead-based paint. However, other sources of lead, such as airborne emissions from automobiles or smelters may be causing excessive lead absorption in other segments of the population.

More widespread screening is needed to determine the full extent of the lead poisoning problem. Except in certain known high-risk areas, lead poisoning is not a recognized problem, and screening is not routine. Even Medicaid's EPSDT program, which strongly encourages lead screening, apparently does not perform such screening on a large scale; reporting requirements are inadequate to determine the extent of screening and the results in locales where screening is being done.

Part of the justification for the \$5.5 million decrease (from \$9 million to \$3.5 million) in CDC's fiscal year 1976 budget for lead poisoning prevention was that EPSDT and other health service delivery programs were to fill the gap. However, systematic wide-scale screening for lead poisoning is not being done. HEW does not even require that the number of children screened for lead poisoning under EPSDT be reported; it only requires reporting of those cases referred for diagnosis and/or treatment.

We recommended that the Secretary of HEW:

- Guide the States on how best to use their EPSDT programs to identify areas needing expanded lead poisoning prevention efforts; encourage the States to embark upon aggressive lead screening efforts; and support expansion of public and physician education on the problem of lead poisoning.
- Require reporting under EPSDT of the number of individuals screened for lead poisoning as well as the number referred for treatment.
- Require HEW agencies that are screening for lead poisoning to report on the results of screening to aid in identifying problem areas.
- Consider having CDC develop a surveillance system to analyze the problem at the national level.

Rh DISEASE

In 1972, a Public Health Service report estimated that every year about 20,000 infants are born with Rh disease, and another 5,000 pregnancies end in stillbirth. It further estimated that 5 to 15 percent of those born with the disease develop severe central nervous system complications if untreated. The most recent information available shows that there were 7,000 infants born in 1974 with Rh disease.

In many areas, women having an easily diagnosed need for immunoglobulin are not receiving it. Most States (1) have not established mechanisms to monitor Rh hemolytic disease, (2) do not require premarital or prenatal blood typing, and (3) do not compile comprehensive surveillance data on immunoglobulin use, Rh disease incidence, or the effectiveness of prevention efforts.

Without a continuous effort to identify Rh negative women and to provide immunoglobulin to those women who need it, this disease will not be eradicated. Federally supported family planning programs could help by typing their clients' blood for Rh factor. In addition, other Federal programs that pay for or provide delivery services could provide blood typing and vaccinate women found to be at risk.

We recommended that the Secretary of HEW:

- Instruct CDC to determine if the incidence of Rh disease is lower in States having mechanisms for monitoring Rh disease and immunoglobulin use. If such surveillance mechanisms are

effective, encourage States to develop comprehensive systems to test all pregnant women for Rh incompatibility, and report incidence of Rh hemolytic disease and use of Rh immunoglobulin to CDC, thereby establishing a national program for monitoring the incidence of the disease.

- ° Require Federally supported family planning programs to include Rh blood typing as a routine part of family planning services.
- ° Encourage Rh testing in all deliveries, miscarriages or abortions paid for with HEW funds and provide immunoglobulin to women who need it.

The final chapter of our report addresses psycho-social causes of retardation which I will not discuss at this time. If any of you are interested in obtaining copies of this report, they are available free of charge to faculty members, students, government officials, and non-profit organizations. They can be obtained by the general public at a cost of \$1.00 per copy. To request a copy, write to:

U.S. General Accounting Office
Distribution Section, Room 4522
441 G Street, N.W.
Washington, D.C. 20548

Workshop Recommendations

MORE CAN BE DONE

Group Leader: Joseph Dion

Recorder : Robert G. Jordan, M.D.

We recommend that the Secretary of HEW:

- Designate a focal point within HEW to implement a national prevention strategy, monitor and coordinate the efforts of the various HEW agencies and offices, and develop a method of determining the progress being made in reaching the goal.
- Designate prevention of mental retardation an objective in HEW's operational planning system.

SCREENING FOR INBORN ERRORS OF METABOLISM

We recommend that the Secretary of HEW help improve newborn screening by:

- Evaluating State screening programs to identify those which are not effective, and provide them with necessary assistance.
- Encourage and assist States to cooperate in the establishment of cost-effective regionalized metabolic screening programs.

PRENATAL CARE

We recommend that the Secretary of HEW:

- Direct the Bureau of Community Health Services to evaluate the State procedures used to determine needs for prenatal care services, and insure that State plans outline a clear strategy of how to reach the population in greatest need.

GENETIC SCREENING AND COUNSELING

We recommend that the Secretary of HEW:

- Direct Federally supported family planning programs to routinely include screening for individuals who are "high risk" for genetic

disorders and refer such individuals to diagnostic and counseling services.

- Monitor the demand on existing genetic resources created by outreach and develop strategies for increasing resources as needed.
- Explore how other Federal programs could better be used to provide genetic screening and services.

IMMUNIZING AGAINST RUBELLA AND MEASLES

We recommend that the Secretary of HEW:

- Examine the alternatives of expanding CDC support of State vaccination programs or making arrangements between CDC and the Medical Services Administration that will enable EPSDT to move to effectively support national and State immunization activities.
- Expand EPSDT requirements to specifically require screening for immunization status and reporting of the number screened and immunized.
- Require Head Start projects to develop data on the results of their immunization screening.
- Require Federally funded family planning and other appropriate programs to include rubella susceptibility testing and immunizations, where appropriate among their routine services.

SCREENING FOR LEAD POISONING

We recommend that the Secretary of HEW:

- Guide the States on how best to use their EPSDT programs to identify areas needing expanded lead poisoning prevention efforts; encourage the States to embark upon aggressive lead screening efforts; and support expansion of public and physician education on the problem of lead poisoning.
- Require reporting under EPSDT of the number of individuals screened for lead poisoning, as well as the number referred for treatment.
- Require HEW agencies that are screening for lead poisoning to report on the results of screening to aid in identifying problem areas.

- Consider having CDC develop a surveillance system to analyze the problem at the national level.

Rh DISEASE

We recommend that the Secretary of HEW:

- Instruct CDC to determine if the incidence of Rh disease is lower in States having mechanisms for monitoring Rh disease and utilizing immunoglobulin. If such surveillance mechanisms are effective, encourage States to develop comprehensive systems to test all pregnant women for Rh incompatibility, and report incidence of Rh hemolytic disease and the use of Rh immunoglobulin to CDC, thereby establishing a national program for monitoring the incidence of the disease.
- Require Federally supported family planning programs to include Rh blood typing as a routine part of family planning services.
- Encourage Rh testing in all deliveries, miscarriages, or abortions paid for with HEW funds, and provide immunoglobulin to women who need it.

Discussion

MORE CAN BE DONE

Following the formal presentation of the group's recommendations, Dr. Jordan mentioned several areas on which the group spent most of its time.

1. Teenage pregnancy. One of the discussants felt, and most others agreed, that this is the number one problem we have in the prevention of mental retardation. Included in the discussion were health problems, such as growth retardation in the affected adolescent that ensue as a result of teenage pregnancy, repeat pregnancies, and the need for better educational programs which can point out to teenagers the specific negatives of pregnancy at that age.

2. Contraceptive measures were discussed; specifically, the fact that there has not been enough emphasis on the use of contraceptives by the male. More publicity should be given to this concept.

3. Abortion was discussed, with some feeling that it should be available in certain instances; for example, in the age group in which it is medically too risky to allow pregnancy to continue. The social and religious problem of abortion was also considered.

4. The resources allocation issue (what we do with the money we have) was discussed. There could be cost-benefits to picking specific targets that we could go after and publicizing what can be done. Dr. Dion pointed out that the GAO has no legal authority over State operations of programs. It has input only on the form of the grant process at the Federal agency level. Reporting requirements regarding incidence and prevalence and outcome should be tightened in Federal formula grant programs.

5. Priorities should be given both to prevention of low-incidence hard issues such as hypothyroidism, neural tube defects, etc., and high-incidence soft issues such as teenage pregnancy for which we do not have such specific data as we do on the hard issues. We need more documentation of soft causes of mental retardation. The arguments about allocation of resources should take these data into account.

6. In reading over the goals of the GAO report, it was felt that there is a need to establish a Federal intermediate technology development and transfer center.

7. Radiation exposure was discussed. The FDA has initiated a pilot program to reduce radiation exposure by the use of a radiation record.

The conference should endorse the attempt to reduce genetic defects in the future due to radiation effects.

8. The assumption that biological factors produce only severe mental retardation is inaccurate and should not be implied indirectly. In general, it is quite possible that biological factors cause a larger incidence of mild than severe mental retardation.

9. Pertussis vaccine is important in prevention, and should be included in any discussion of vaccination programs.

10. In addition to a high need for programs to prevent teenage pregnancy, there are needs for prenatal care, postnatal and early infancy care, prevention of infections of various types, and the use of newly available vaccines and other methods to carry this out. Another need is to develop regionalized resources for amniocentesis and metabolic screening. There are unmet needs of the child population as a whole, not just those served by the Federal health delivery services.

11. Great support is needed for research in developmental neurology in NINCDS.

12. Where a given program will affect additional conditions other than mental retardation, corresponding constituencies should be asked for their support.

13. The right to be well born and the rights of the fetus should be articulated in terms of responsibility of biological parents and health professionals before and during pregnancy.

General Discussion

MORE CAN BE DONE

A general discussion by the conference participants followed the presentation by Dr. Jordan.

DR. KOCH: Teenage pregnancy is a very serious problem. Were there some recommendations on how this could be approached?

DR. LOWE: There is substantial interest in a fairly major effort to fund what has been called "comprehensive adolescent pregnancy programs" involving rather extensive social, psychological, medical, vocational, and educational efforts to work with the teenager who becomes pregnant. Under such a program would also be active efforts for more effective primary prevention through approved contraceptive methods. In general, the latter has been the major emphasis of a number of efforts, and those have been only partially successful because of the resistance of the teenager trying to defy the establishment and feeling the need to have an infant as a way of demonstrating maturity and receiving some emancipation from the family. It is a very complex issue, and most of the people working in this field seem to feel as though you have a better chance of preventing the 2nd or 3rd pregnancy more easily than the first; since there is an opportunity to develop close relationships with the teenage parents, rather than simply handing out contraceptives the way much of the present family planning effort is handled in low income populations.

There are some demonstration programs in existence. The Maternal and Infant Care Program in Minneapolis is supposedly a very effective program, and in Baltimore, there is a fairly model program funded in part by private foundation money and public money. What has been demonstrated is a considerable reduction in prematurity and a marked improvement in terms of school performance. School drop-out rates had been running almost 80 percent in the school. They are running 20 percent in groups that are adequately served.

MR. DION: There is also a movement to try to develop a strong curriculum on sex education for use in the schools that want it. There is now a curriculum in health education developed by the CDC, to be used as an add-on which will concentrate on sexuality, reproductive processes, etc. There is one issue which has not been resolved; whether it is profitable to address teenage pregnancy as an isolated issue or whether the real maximum need is to address adolescent health, with teenage pregnancy as an intercurrent problem.

DR. COOKE: I feel very strongly that if we only address the pregnancy, we have only about 3 months of contact with the young woman. If we take adolescent health, we have a decade; and it's possible that we can do a lot more. Our offices argue very strongly that the initiative should be adolescent health and underneath that, teenage pregnancy.

COMMENT: Not speaking from the Secretary's prospective, but my own, I think politically, to have a comprehensive adolescent health program would be prohibitively expensive at this time, and doesn't have a chance in the world of approval. As a consequence, I don't think anything will happen if that is the way it goes. It seems to me that there is enough interest in the high risk pregnancy to indicate that the first step should be in the area of adolescent pregnancy, and the adolescent health program would tend to follow.

MR. PAFFRATH: (Mr. Paffrath spoke of the search of the Johnson Foundation for guidance in this area.) We have several commitments in various stages of crystalization. One is a commitment to work with the private sector and also with the United Nations, itself on the Year of the Child, which is 1979. The Johnson Foundation has made a grant to that non-governmental effort. As you may know, unlike many UN years, there will not be a great conference as there was on the environment at Stockholm, but they are asking that meetings be conducted regionally within the United States and other countries. In these regional meetings in the United States, there will be nothing massive such as the Women's Rights conference at Houston. At the same time, we have held a planning meeting working toward a Greater Midwest Conference on the subject of the Family In Change, or as it has sometimes been called, The Disintegration of the American Family. We hope to convene a group this size, or somewhat larger, of people who are dealing with family problems and try to establish priorities that should be passed along to those who are planning the White House conference on the family. In this way, everything will not originate with the Administration and there will actually be a flow from the heartland of the country as to what the priorities are.

One final comment is our deep concern with teenage pregnancy. We have done meetings on adolescent sexuality, which is a kind of euphemism for teenage pregnancy and the venereal disease epidemic. We are presently considering the possibility of reaching the teenage maternity patient through the use of clinical chaplains. We are contacting the American Hospital Chaplain's Association, and are looking for the equivalent in the Jewish hospitals. This is all quite preliminary but it seems to me that during the maternity period, you have a captive whom you might reach through an education program in child care, or a referral system to prevent a second pregnancy, etc. I would welcome guidance from this group.

DR. MacCREADY: In Massachusetts, we are just beginning to explore the possibility of helping to improve the health education in junior high schools. It seems to us that there are a lot of people who feel that the health education in the schools can be greatly improved, and we have had one or two meetings with some of the educators who seem interested. I agree very much with the concept of improving the whole gamut of adolescent health education rather than just addressing teenage pregnancy. Actually, in New Hampshire, the March of Dimes has been quite active already. They have one young lady who has visited a number of schools and handed out material. They have also had one or two conferences which the students are encouraged to attend. Perhaps this group could explore more of that sort of approach.

DR. GUTHRIE: In 1960-62, I got National Science Foundation grants for some high school students in science, and we ran programs in the summer on the university campus. At that time, the Biological Study Curriculum Committee textbooks had very good material, and it was impressive to me to see the great interest of these very bright young people (about one-third of them from New York City and others scattered from all over the country) in both mental retardation and genetics. Young people aged 16-18 were fascinated by genetics and the idea of preventing mental retardation. That has been reinforced by my contacts with Youth NARC.

Dr. Charles Skriver gave a talk at the Albany meetings on genetics about work with the Montreal school board on genetics. This came about as a result of work with Tay-Sachs screening. He made the same points Dr. MacCready just made. Dr. Skriver showed slides indicating that at that age level, teenagers have much more positive interest in, and retention of the genetic counseling ideas than do adults. I would like to reinforce the concepts that Dr. Skriver mentioned that there should be thought eventually, if not immediately, of convening a group such as ours, on how to plug in the facts about human reproduction at that age, and in the long run it would pay off.

COMMENT: As a followup to that, for the NARC people present, in terms of the youth, ARC groups have been very active in the prevention area. Those of you from the Wisconsin area are well aware that the Wisconsin Youth ARC has a DD grant to explore this very area of prevention and health education among junior and senior high school youth. Building some of that energy and concern into some of our recommendations is important.

MARY ETTA LANE: The Youth ARC is very involved. Their officers were instrumental in getting the volunteer lead poisoning screening program started.

COMMENT: In speaking to junior and senior high school people on PKU, I have found their questions just as good as those of adults.

QUESTION: Do we actually have figures on the amount of mental retardation caused by teenage pregnancy?

COMMENT: Dr. Dan Thompson and his wife, Marie, at Emory University have done some extensive work on this. Probably the main cause of mental retardation in teenage pregnancies is the high incidence of low birth weight and prematurity associated with it. Marie Thompson has given her work to a personal friend of Rosalynn Carter and Mrs. Carter has expressed interest in it.

WORKSHOP MEMBER: We covered some things in our group session that bothered some people. We recognize some weaknesses built into the report just from the massive substance of the topic.

QUESTION: What is going on in Congress, itself?

COMMENT: There have been no committee hearings on the GAO report.

FRED KRAUSE: Senator Humphrey has entered comments on the GAO report into the Federal Registry, but no committee or subcommittee of Congress has initiated any hearings.

In the report, five States were singled out as trying to do a more intensive study. Only California has followed it up with a State-wide conference on prevention in which the report will be used as one of the principle documents to high light either what is not progressive in prevention or what is needed to be considered for advancing prevention in that State, such as in genetic counseling, for which the Governor has increased the overall allocation.

Recently, I had the opportunity to spend about an hour with the Governor of a State and he started talking about community services. Because his health director was there and had earlier briefed me on the fact that the immunizations program was very successful, I commented on that, and the Governor immediately wanted to know what else they could do in his State on prevention. He was not aware, outside of immunizations, what could be done. I had a call a few days ago from one of the Governor's staff members saying he would like more detailed information on a program on prevention for that State. Perhaps within the States, we have an opportunity, whether it is through AAMD or NARC or teenage groups, etc. who could possibly reach Governors, health directors, or key legislative groups, to see what can be initiated. The action really is at the State and local level. The Federal level can only initiate some funding and guidance and programming, but if it is not picked up and implemented on the State and local level, it is not going to succeed.

DR. GUTHRIE: A number of us are going to stay here Friday evening and Saturday morning as a followup to this meeting, and talk about how to

initiate a State model plan for prevention in a given region of States, using the framework of the AAMD regional setup or that of NARC. I am hoping that those of us who will be working on this will be able to plan a rather specific way to develop a State model plan, working with States through this regional setup.

DR. BOGGS: Most of the strategies targeted on specific low-incidence severe conditions, as well as those dealing with less well defined etiologies responsive to good prenatal care can be defined in a way capable of demonstrating a favorable ratio--present cost to future benefits. This should be done and arguments about allocation of resources should take these data into account and should not be on an either/or basis.

The right to be well born and the rights of the fetus should be articulated in terms of responsibility of biological parents and health professionals before and during pregnancy.

DR. LOWE:

1. Need for better pertussis vaccine.
2. High need program areas:
 - a. Teenage pregnancy
 - b. Prenatal care
 - c. Postnatal (early infancy) care
 - d. Prevention of meningitis (H influenza and e-coli and pneumococcus) by newly available vaccines and other methods.
3. Need to develop regionalized resources for amniocentesis and metabolic screening.
4. Need to stress the unmet needs of the childhood population as a whole, not just those served by Federal health delivery services. This GAO report stresses the latter but not the former.

DR. BOGGS: We should seek an early agreement on some indicators and a baseline for biomedically based mental retardation.

Greater support is needed for research in developmental neurology in NINCDS.

Reportive requirements regarding incidences and prevalence and outcomes should be tightened in Federal formula grant programs, including Title XIX. The objective should be cumulative data.

Where a given program will impact additional conditions other than that justified, it should so indicate and corresponding constituency support be recruited.

DR. COOKE: The FDA has initiated a pilot program to reduce radiation exposure by the use of a radiation record. The conference should endorse this attempt to reduce genetic defects in the future.

In general, it is quite possible that mild mental retardation may be caused in larger numbers than severe retardation from biological factors. The assumption that biological factors produce only severe mental retardation is inaccurate and should not be implied indirectly.

DR. MOSER: Priority should be given both to prevention of low-incidence hard issues (hypothyroidism, neural tube defects, etc.) and on high-incidence soft issues such as teenage pregnancy. The latter ought to be approached with common sense strategies that are not yet proven. Concurrently, we must fund pilot research studies to document which aspects of prenatal care are decisive and what strategies can be shown to be valid.

A NATIONAL PROGRAM TO PREVENT NEURAL TUBE DISORDERS

by

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CONSIDERATION FOR IMPLEMENTATION OF A
NATIONAL MATERNAL SERUM ALPHA-FETOPROTEIN SCREENING PROGRAM */

I am pleased to share with you some of the more exciting aspects of the prenatal detection of neural tube defects viewed in the context of a nationwide plan. Possibly Francis Bret Harte may have summarized your proceedings in a better way than I, and more succinctly, for sure.

"If of all words of tongue and pen,
The saddest are, it might have been,
More sad are these we daily see,
It is, but hadn't ought to be."

I have had a long interest in the prevention of genetic disease and mental retardation, and have long been interested in the initiation of principles which underlie the delivery of such programs which are essentially based on voluntarism and equal access. With this focus in mind, we can look at where we are with the neural tube defects prevention program and more specifically, at details in operation. Thereafter, we can look at the possibilities of a nationwide plan with reference to your understanding of how it really now works in practice.

The spectrum of the neural tube defects is well known, varying from acephaly, to anencephaly, through-rachischisis, myelomeningocele defects to closed spina bifida lesions. Sometimes other defects such as paraplegia and hydrocephalus are associated or complicate management. Anencephaly may occur together with spina bifida lesions or occur separately in subsequent or sequential pregnancies. These disorders are collectively considered among the polygenetic disorders, whose rate of recurrence at least in the United Kingdom is 3 to 5 percent.

Data from our studies in the United States and supported by studies from Philadelphia and elsewhere, suggest a rate of recurrence closer to 2 percent. The essential point here is not exact frequencies, but the family history which is of consequence in drawing attention to the needs for future studies in subsequent pregnancies.

Neural tube defects are not always straight-forward polygenic disorders and there is therefore a need to be sure that infants born with these defects actually have a polygenic disorder. For example, it is important to differentiate Meckel syndrome (cardinal features include encephalocele, polycystic kidneys, polydactyly) with the 25 percent recurrence risk of autosomal disease, from the polygenetic neural tube

*/ Prepared from recorded presentation.

defects. Without careful differentiation, the parents may be falsely reassured that the risk of recurrence is only 3 to 5 percent.

Dr. David Shurtleff in Seattle has extensive experience with the care of children with neural tube defects. Both his data and extensive data from the United Kingdom point to the facts that some 20 percent of individual survivors have moderate to severe mental retardation combined with moderate to severe physical handicap.

AMNIOTIC FLUID ALPHA-FETOPROTEIN

In 1972, Brock in Edinburgh noted that alpha-fetoprotein (AFP), a fetus-specific protein, was present in the amniotic fluid at higher levels than normal in association with leaking neural tube defects, such as anencephaly and spina bifida. AFP has a half life of 3 to 5 days in the newborn period, and strangely enough, after birth, the infant tends to turn off the formation of this particular protein except in situations such as hepatitis, liver tumors, or other kinds of tumors or conditions. About 29 days along in gestation, the AFP is detectable in fetal blood. It reaches a peak at about 12 weeks along in pregnancy, and tails off to be almost non-detectable at term. The concentration of AFP in amniotic fluid peaks at about 12 to 14 weeks, the very time you should be offering or talking about offering amniocentesis for neural tube defects (14 to 16 weeks).

AFP is synthesized by the fetal liver, yolk sac, and the gastrointestinal tract and secreted into the fetal blood. From there it enters the fetal urine, and is urinated into the amniotic fluid and thence into the maternal circulation. In the presence of an open leaking defect, another source of egress is provided for this protein into the amniotic fluid. Hence, quantitatively there is simply more AFP present. There is no defect in catabolism or synthesis of AFP. Any defect that leaks will also lead to an increase in the concentration of AFP in the amniotic fluid on a simple quantitative basis. Hence, this is a non-specific test on amniotic fluid. It doesn't make a diagnosis in the true sense. It signals an elevation of a protein most often associated with an open leaking lesion, most often a neural tube defect.

We have completed amniotic fluid AFP studies on over 10,000 pregnancies (Table 1). From Table 1, it can be seen that the recurrence rate when there has been a previous child with a neural tube defect is less than 3 percent. We have not yet missed an open leaking neural tube defect. At the moment, we have diagnosed over 90 such cases. We are talking about open and closed defects. It is important to recognize that when I say "closed," I mean that it is skin covered and doesn't allow egress of that particular protein. Nine out of 10 neural tube defects are open.

Only one out of 10 is closed. So by that very token then, using techniques for AFP analysis, you theoretically, at least, have an approach to about 90 percent of the cases.

A previous child with hydrocephalus is hardly an indication for assessment of AFP in the amniotic fluid, nor an indication, in my view, for amniocentesis. However you see (Table 1) that probably on the basis of either concern or anxiety, 88 couples decided to have amniocentesis and, indeed, one of them was found to be carrying in the second pregnancy, a fetus with anencephaly, after having had one child with hydrocephalus. You notice that this will give some kind of recurrence figure, but in fact, this could be fortuitous. The point is that causes of hydrocephalus are heterogeneous and I am sure that some of them may relate to the spectrum of the neural tube defects.

Furthermore, once an amniotic fluid is drawn for other reasons, for example, maternal age (which is the reason over 90 percent of amniocenteses are done), then it seems to me to be judicious to submit that sample, essentially drawn for chromosome studies and tissue culture, to also simultaneously assay it for alpha-fetoprotein. We have done this in some 7,000 cases (Table 1) and the frequency is about one in 417 cases in families with no provided history of a neural tube defect and where an open, leaking neural tube defect is detected. A one in 400 detection rate contrasts strikingly with the frequency of PKU where you have to screen a million and a quarter individuals to find, perhaps 89 cases--one in 14,000 or one in 25,000 frequency. This does, of course, bring to our attention the fact that neural tube defects together with Down's syndrome, constitute the two most common major birth defects that occur in this country. The incidence of neural tube defects is about one in 500 births. The \pm one in 400 figure (Table 1) may also reflect the additional association between advanced maternal age and neural tube defects. There is evidence dating back at least 20 years on this point.

One or two additional points should be made about these experiences represented here (Table). The first is that even when a high level of this particular protein is found, it doesn't remain static in the amniotic fluid. The level tends to decrease quite briskly. In one case, by the time pregnancy termination was elected (some 5 weeks after diagnosis of anencephaly), the level had dropped from about 18 mg percent down to about 4 mg percent.

This is of consequence because if you delay the amniocentesis and prenatal studies to about the 19th or 20th week, when there is already a natural decrement of AFP, it is possible to miss the diagnosis. There is considerable questioning about what is normal. We have pursued the question of the standard deviation technique and I have been carefully warned by the Harvard biostatisticians that the standard deviation technique is essentially not, at least theoretically, valid because there is not an

equal distribution of AFP for each pregnancy week. However, I went back to them some 8,000 cases later to discuss this question of percentiles, standard deviations and medians. We went over what we had found and they then quietly confided the bottom line. That was that standard deviations are acceptable if they really work in practice. We had used the third standard deviation above the mean as the arbitrary cut-off, but had actually been operating at five standard deviations above the mean so that with anything above three, we would send out signals. "What's happening?" "We want a repeat sample." "We want to look at it again." "We have other ancillary techniques." We have not yet had an open neural tube defect below five standard deviations above the mean.

The diagnosis of anencephaly in amniotic fluid before 24 weeks of gestation is close to 100 percent accurate. In the literature one case was missed and would't you know it, that one case was a urine sample that had been provided by mistake instead of amniotic fluid. Published data suggest detection of spina bifida in about 90 percent of cases. More realistically, I think, figures for spina bifida defects probably will range between 60 and 80 percent, and not as high as this. There are a variety of other considerations besides the more technical matters which will be omitted from this discussion.

The presence of fetal blood in the amniotic fluid sample is a serious problem. It serves to confuse and confound because the concentration of alpha-fetoprotein in the fetal blood is about 150 to 200 times higher than it is in amniotic fluid. So in view of that steep gradient, the presence of a few drops of fetal blood in the amniotic fluid may make interpretation extremely difficult, if not impossible. We still find that about one of every 400 or 500 amniotic fluid samples sent to us from all around the Nation is actually a urine sample drawn inadvertently, to the great chagrin of the doctor and the dismay of the patient.

One difficult aspect is the estimation of the stage of pregnancy. Women are often off in their dates and physical examination is frequently not much more accurate. This is of consequence because there is a continuing decrease in the concentration of amniotic fluid AFP after the 12th to 14th week of pregnancy. If you think the pregnancy is 14 weeks, the level would be higher than it would be when the pregnancy is, say 18 weeks. If you are wrong by 4 or 5 weeks in the assessment of gestational age, the interpretation of the result can be extremely misleading. False positives in the best hands in Scandinavia and England range around the 0.1 percent mark, or less. This is our false positive rate as well. In about one in 1,000 cases, there will be an elevated AFP without an explanation--no defect and no fetal blood contamination. False negatives refer to cases where there is a closed defect not amenable to prenatal diagnosis using the AFP analysis. We have had two false negatives that we already know of in this group of 10,000. There are still about 2,000 where we haven't had deliveries yet. I regard the repeating of the

amniocentesis for confirmation as a mandatory exercise. As in all medicine, it is unwise to make major decisions on a single test at any one time. I regard any elevated value as an indication to repeat the amniocentesis. This takes care of those human frailties which, I am afraid exist among us. For example, one day we received a batch of 50 samples that had been sent simultaneously from one laboratory in another State. We assayed them all and found one elevated AFP value. We reported that and the parents, despite my advocacy about repeating the test, moved to terminate the pregnancy. It turned out to be an entirely normal fetus. What had happened was that the technician in that laboratory has mislabeled the tubes. Need I tell you that in that State, some 5 months later, a baby with anencephaly was delivered, the tube of amniotic fluid having been mixed up with the adjacent tube. We repeated the assay with the correct numbering and they recognized where they had made the mistake. That's just one simple reason why one should do this assay twice, besides the fundamental philosophy of not relying on a single reading for making critical decisions.

There are other ancillary techniques one needs to offer, amniography being one and ultrasound the other.

In summary, the AFP analysis of amniotic fluid is a valuable though non-specific technique which also signals other diseases which might leak AFP.

MATERNAL SERUM ALPHA-FETOPROTEIN

I think we can now come to the main point most relevant to the purpose of this meeting. If you are concerned about the prevention of neural tube defects, it is possible to tackle nine out of 10 such defects with the AFP approach. The use of amniocentesis techniques alone will allow possible prevention of only about 10 percent of the cases, because nine out of 10 cases occur in families where there has not been a previous affected child. In other words, families who have already had a child with a neural tube defect should routinely be offered prenatal genetic studies via amniocentesis. What about the other 90 percent? That is why the maternal serum AFP technique has arisen.

AFP enters the maternal circulation and is easily measurable by radio-immunoassay best done between 16 and 18 weeks of pregnancy. The United Kingdom Collaborative Study reported in June 1977, about 19,000 cases from nine centers. By screening the maternal serum between the 16th and 18th weeks of pregnancy, they were able to detect about 90 percent of anencephaly, and 79 percent of spina bifida lesions. That is a tremendous advance when we remember that nine out of 10 of the neural tube defects occur in a family without prior warning. This is therefore the fundamental rationale for initiating a nationwide plan for screening.

The serum AFP may seem to be elevated if gestational age is incorrectly estimated (the most common pitfall). Maternal serum concentrations of AFP are rising exponentially to reach a peak at about 28 to 32 weeks along in pregnancy. So there is a very steep and continuing rise in the maternal serum AFP concentration from 14 to 24 weeks. The need to know the exact gestational age is hence self-evident. The first step following the determination of elevated maternal serum AFP is to immediately obtain an ultrasound to accurately assess gestational age. That means that the person who does the ultrasound must have established expertise and be able to provide the most reliable determination. Once having determined that the dates are accurate and that the AFP elevation is real, other considerations are necessary. For instance, multiple pregnancy, threatened abortion, fetal death, ectopic pregnancy, and some rarer conditions may lead to a true elevation of AFP in maternal serum. The latter are situations occurring in relationship to a pregnancy as opposed to various concurrent diseases or disorders where there is an associated raised serum AFP. They may, of course, also occur concurrently in pregnancy. Hepatitis or cancer of the liver might be the two that would draw your attention to such decidedly unusual situations.

There are a variety of limitations and reservations in the application of the maternal serum AFP screening program. To begin with, there is the gestational assessment mentioned earlier. Secondly, in major urban centers a significant percentage of women come in to see their doctor for the first visit at about 16 to 20 weeks. There is just no way major programs of prevention can be successfully launched unless one educates society at large that the time to address preventive measures is when pregnancy is to be planned, and not when pregnancy is half or three quarters through. Education therefore would be the first major recommendation. To indeed be effective, it would ensure that women understand that their discussions with an obstetrician should be when they are planning to have a pregnancy. There are differences in serum AFP according to race and hence, different normal values for blacks as opposed to whites. We have also used medians as have the English--two and one-half times the median representing the arbitrary upper limit of normal.

In a very closely studied population, we have screened about 3,000 maternal sera, and so far have missed no neural tube defects and have found five. These were in pregnancies where the defect was not suspected. The implication is that the radioimmunoassay for AFP is highly reproducible and accurate. Thus, the problems that require particular consideration when you get to the question of a nationwide screening plan will not really be the technical ones because these are fairly well mastered (as long as we can get the Food and Drug Administration to license the necessary reagents).

There are still major gaps in understanding by both the patient and the physician about what these tests can do. Even in the face of careful and elaborate informed consent arrangements for our 3,000 cases that we have already done, we have had women to, when they deliver a child with

a birth defect, can't understand it, since they thought this test would exclude all birth defects. In reality, the test is just a maternal serum screening for AFP. Both the physician and the patient need to understand the clear limitations of a screening as opposed to a diagnostic test.

The economic constraints are very real. Who pays for screening for every pregnancy? There are about 3.2 million pregnancies a year in the United States. There is also the question of race, because the frequency of the disorder will vary according to race. These neural tube defects are extremely unusual among blacks. The question is not only who pays for the screening, which might be an easily quantified amount, but what about the costs of ancillary tests? No sooner do you determine an elevated level of AFP than a whole cost sequence is initiated--possible repeat serum assay, ultrasound, genetic counseling, amniocentesis, amniotic fluid AFP assay and possible elective abortion. In fact, we have had experiences in Boston where we have signaled the elevation of maternal serum alpha-fetoprotein, to be met with the response, "She doesn't have the money for an ultrasound." It sounds horrendous, but there it is.

Unnecessary amniocentesis may pose a real problem if the question of surveillance and control is not carefully watched. This would mean that if you found an elevated serum alpha-fetoprotein, you would check the dates. If the dates seemed consonant with what you would expect, you would do an amniocentesis. If you found a normal value, essentially, then, the amniocentesis was unnecessary. The United Kingdom studies show a 3.3 percent rate of false positive maternal serum AFP. So far, and with considerably less experience, we are finding a lower false positive rate. An elevated maternal serum AFP may cause the patient to take another risk, namely an amniocentesis. Or they will decide to terminate the pregnancy without further ado because they are too anxious or for other reasons. This has happened three times in our 10,000 amniotic fluid cases. In fact, two of them were doctors, whose families, as it happens, were falling apart and they were seeking some reason to terminate pregnancy anyhow.

As soon as we signaled the elevation, they took part in no more discussions. They simply wanted the pregnancy terminated, even though there was clear and definitive advice, both written and otherwise, that we were seeking another fluid to enable accurate interpretation.

"Administrative" inefficiency is extremely common. Calls to obstetricians about an abnormal result or a result that needs further action may be followed by 10 days or 2 weeks of inaction while the doctor "waits for the patient to come in so that they could talk about it."

The ancillary techniques include ultrasound (which will allow the delineation of the fetal head, gestational aging, placental localization

and other features) and amniography. These techniques are critical and work hand in glove with the AFP technique. The neural tube defect prevention program is inextricably dependent upon superior ultrasound services. On occasion there are opportunities for amniography, which is the injection of a radio-opaque contrast into the amniotic fluid which enables delineation of the fetal silhouette, including myelomeningocele.

Certain prerequisites are necessary prior to the institution of a national plan. Pilot studies in progress now, require completion. It would be a mistake to rush at a nationwide plan until the problems and pitfalls are well delineated. Education is critical for both the patient and physician and includes the question of the need for informed consent as it relates at least, to the pilot studies. I don't think anyone here will argue that informed consent actually does exist in screening programs. It really is not possible. The same would apply to maternal serum AFP screening. It will not be possible to get informed consent from 3.2 million individuals seen each year in private offices and clinics for every pregnancy. So the pilot studies must delineate whether the procedures are safe or not safe; accurate or not accurate, etc.

Definition of the population at risk would be important. As mentioned earlier, neural tube defects are rare among blacks. This raises a useful and important point. Testing whites would be fine, but testing blacks for neural tube defects on a national plan would probably not be cost-effective. However, AFP analysis of maternal serum potentially has other benefits. When the values are high--say two and one-half times above the median--it appears from studies in Scandinavia that you can select out pregnancies complicated by twins, fetal death, prematurity, or postmaturity. These findings have now been duplicated by others. It will probably become clear that there are other benefits as well which will have application to your goal in the lines of preventing mental retardation occurring as a consequence of prematurity or postmaturity. If that is the case, it will pay to screen all people in a program based on equal access and voluntarism. The assay should be accurate and reproducible, automated, and the word that invalidates all the foregoing, inexpensive.

We have talked about genetic counseling and the services that are necessary because they will not be covered by third parties. Nor will the costs be insignificant. There is no question, of course, about the cost benefit equation. There is an enormous economic benefit to this prevention technique and this does not even go into the questions that we all know so well; the questions of family pain and suffering. So in the development of a national plan, we would have to be considering all the points mentioned. I am sure there are many we could add. Assay requirements will include the need for surveillance, standardization, and circulation of blind samples between laboratories. In my view, there will be the question of Federal funding for what is

essentially a public health service activity. Finally, it is the President's Committee on Mental Retardation and other groups which will be able to facilitate or initiate enabling legislation where necessary. I like the Oregon law which was passed in June 1977, facilitating and supporting amniocentesis. I thought that was an enormously forward-looking kind of legislation. It doesn't mandate amniocentesis in the sense that everyone should have it, but it makes it possible for those who wish to have it, to do so. Ultimately, even with the application of all the techniques we have talked about, in the foreseeable future, I could not anticipate a reduction of greater than 75 percent in the occurrence of neural tube defects, and I think even this figure is probably a reflection of my general optimism. It takes into account the fact that only about 90 percent of these defects can be reached prenatally, and that there are a considerable number of people who will not want to go this way anyhow. What that percentage is, I leave to your judgment.

In essence, then, I think there is going to be a place for a nationwide plan to screen for neural tube defects in maternal serum. Before that time, I would hope that those concerned with the development of these tests are sure that the problems and pitfalls are first fully recognized.

Workshop Recommendations
PREVENTING NEURAL TUBE DISORDERS

Group Leader: Aubrey Milunsky, M.D.

Recorder : Fred Krause

The technique of testing serum for alpha-fetoprotein content has tremendous potential for preventing mental retardation. This test is done at 16 weeks of pregnancy and is followed by a second test if a positive high protein is found. An amniocentesis is recommended if the second test is also high. An ultrasound test should be performed if an amniocentesis is to be done. We formulated eight recommendations we felt were essential to any plan for screening for neural tube disorders.

1. There must be definition of the population for testing.
2. Education is important, not only for the general public, but for some members of the medical profession. Included in education is counseling of parents, once an elevated alpha-fetoprotein is reported.
3. Education of our legislators is important as we develop a national plan.
4. Ancillary procedures, such as ultrasound testing and genetic counseling must be available to make a screening program successful.
5. Cost-benefit statistics must be determined.
6. Application, equal accessibility and voluntarism are important factors.
7. We must develop legislation to facilitate screening.
8. We must document the ultimate potential of screening.

Screening is more than just screening, per se. It is a diagnostic tool. We need a national regional effort to implement such a program.

Discussion

PREVENTING NEURAL TUBE DISORDERS

DR. COOKE: Obviously, in screening, there are false positives that require ultrasonography and you have other expenses such as transportation and equipment. Do you have any data from pilot studies on exactly what screening costs when you put in all the false positives?

DR. MILUNSKY: In this country, nobody has done cost-accounting of this procedure in the way you are describing it.

DR. COOKE: I think that is a very important point. I don't believe society and particularly government is going to support programs unless there is an economic analysis. You really should have a medical economist working along with you so you can establish what all this will cost. That way, you can make an argument for it in terms of getting a specific result from a specific expenditure.

DR. MILUNSKY: There seemed to be unanimity in the group that the way to approach a national strategy was not to offer nationwide screening, but to move toward centers of excellence where there would be all the components such as the assay technologies, the genetic counseling, the ultrasound; all the things you would need in one center. These centers would be regional, and would grow as the subject developed. No center in this country has sufficient data at this time to do a reasonable cost-analysis, but in these center, data would be generated. Then one could look at the subject in a hard way and come up with public policy statements founded on sound economics. It is not possible to do that now because no one even knows the rate of false positives in this country. The English say 3.3 percent of amniocentesis are unnecessary. We find appreciably less than that here. Of course, that is a critical figure because it creates a wave effect. As soon as you signal "noise" in the system, the wave goes all the way down the line and you run into costs of ultrasound, second amniocentesis, anxiety, counseling, etc. We know we need to be collecting data and analyzing them.

DR. COOKE: I think it is important, in terms of the educational process. There is one type of education for the general public and for the medical profession, but for the legislator, I stress the important fact that one of the first questions he will ask is, "What is the cost?"

DR. KOCH: At the Children's Hospital in Los Angeles, it costs \$125.00 for an amniocentesis, and they never take a loss on anything. Their usual margin of profit is about 50 percent.

DR. COOKE: Institutions bear no relationship to each other. They set the price at wherever somebody wants the price to be, but it is rare that anyone does a real cost-analysis. I know that is the charge, but I don't know whether that is way above or below what it should be.

DR. KOCH: I agree, but that seems to be a running average so it must have some validity.

DR. COOKE: I have a feeling someone picked it out of the air.

QUESTION: What does the group mean by the term, screening? I have some concern about this. It has been pointed out that it is very difficult to get informed consent with respect to screening. It is almost impossible. Yet you have a procedure here which has a rather different outcome from every type of screening we have discussed in the past. It is a type of outcome that is not particularly acceptable to some segments of our society. Therefore, I wonder whether you would want to use the term, screening, or whether what you are basically talking about is making a service available to as large a segment of the population as possible who will make use of it. Do you really mean screening in the sense of universal screening?

DR. MILUNSKY: We are talking about voluntary screening within as large a circle as will ultimately be available. The key is voluntarism. It will not be mandatory.

COMMENT: So this is different from some other screening programs, in which the procedure has been mandated.

DR. GUTHRIE: But isn't it true that there has not been enough emphasis on the fact that obstetricians and others are rapidly becoming aware of all the other benefits besides diagnosis of neural tube defects, which are very important to obstetrics, in general?

DR. KOCH: Ultrasound is being used for many other obstetrical conditions.

DR. GUTHRIE: I mean the screening. The initial alpha-fetoprotein screening has other benefits other than diagnosis of neural tube defects, which will help offset the costs.

COMMENT: I think there is a new area that we have to be aware of. The assumption you make is correct at the present time--the alternative is either birth or abortion. I would remind the group that about 100 years ago, if we were having this discussion about pyloric stenosis, the decision would be either the death of the baby or some medical means that wasn't very satisfactory so that the baby eventually died. I believe you will see develop, as you improve your diagnostic tools, intra-uterine surgery as a possible alternative for those families that do not

wish abortion. I think this whole new field of medicine will be opening up in the next 25 to 50 years. There is no reason why one cannot accomplish certain procedures in utero just as you can accomplish them post-natally if you develop the technology. It is possible to do this in animals at the present time. I don't mean the closure of a neural tube defect, but the carrying out of fairly successful intrauterine surgery. It seems to me we are just on the threshold of a whole new approach. The screening tool is obviously a necessary accompaniment to that.

DR. OAKLEY: The procedure involved in screening for alpha-fetoprotein in maternal serum is a complex one, hence it seems that the project should be started in a limited number of centers of excellence with highly trained personnel who could perform, not only the initial screening, but the ancillary procedures as well. These centers might then educate the public, physicians, and legislators about the procedure and allow for further spread towards fuller screening and utilization of this very promising area.

REGIONALIZATION AND EXPANSION OF
A METABOLIC SCREENING PROGRAM FOR NEWBORNS

by

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Phenylketonuria (PKU) was discovered by Fohling in Norway in 1935, as an abnormally high concentration of urine phenylpyruvic acid, or phenylketone, passed on from both parents by Mendelian inheritance, with a chance of occurrence in each offspring. Soon afterward, Jervis showed that the abnormality was lack of a single enzyme that converted the essential amino acid, phenylalanine, by a simple hydroxylation step, into the amino acid, tyrosine. In 1939, Block described a simple method for removing phenylalanine from a protein digest and suggested this as a basis for a low phenylalanine diet treatment. In 1953, Bickel demonstrated that such a diet produced a dramatic normalization of behavior in a hyperactive young child with PKU. During the next 15 years, this dietary method was applied to many young PKU children to prevent further damage to brain development. Successful effects, however, were only obtained in very young infants discovered by a blood phenylalanine test, performed because an older sibling, already severely retarded, had previously been diagnosed as having PKU.

In the mid 1950's, Dr. Willard Centerwall urged the screening of the urine of infants by testing their wet diapers with the FeCl_3^* test for PKU. Large programs were organized in various countries, but results were very disappointing, although some infants were discovered and treatment begun within the first year of life.

Obviously, what was needed was a reliable, but, economical test for blood phenylalanine. In 1961, we were fortunate enough to develop such a test, using dried blood spots on filter paper. By coincidence, that year the National Association for Retarded Children (now called the National Association for Retarded Citizens, or NARC) used as its "poster child," two children--sisters with PKU--showing prevention of retardation in the younger sister due to diet treatment to emphasize that retardation could sometimes be prevented, and also showing the need for more research into causes and prevention. I was a NARC research grantee, at that time, and willingly cooperated with that organization's use of my work and the PKU test in their publicity. The NARC, through its many State chapters, were successful in getting State laws passed requiring PKU testing, so that by 1967, nearly 40 States had such laws. With the notable exception of Massachusetts, these laws were passed in spite of lack of support, and often active opposition by the States' medical societies. As a result, by 1970, the United States Maternal and Child Health Service found that 90 percent of infants in the United States were being tested for PKU. In a few States without these laws, only approximately 50 percent of the infants were screened, and this rate continues at present.

* FeCl_3 Ferric Chloride

With the dried blood spot specimen and the principle of the bacterial inhibition assay, we developed four more tests by 1967. These were immediately put to trial by four collaborating laboratories, as an organized effort supported initially by the U.S. Children's Bureau and the Maternal and Child Health Service within the HEW. These laboratories covered Massachusetts, Oregon, portions of Los Angeles, and western New York.* Their use of this battery of tests was facilitated by a "punch-index" machine which automated processing of the dried blood spots. However, in the United States, the PKU specimen was not used for other tests, with the exception of these four laboratories. In other countries with national health care systems, results were much more encouraging. The PKU test was adopted rather quickly in most of these countries, with no need for laws. In many countries, our other tests were added to the PKU test during the late 1960's, with active assistance from us in training laboratory personnel and supplying some starting materials.

In 1968-69, during my sabbatical year in New Zealand, a Pacific Multiple Test Program was established (by Professor A.M.O. Veale) for 10 Pacific Island groups who sent their infant dried blood specimen by air mail to the New Zealand laboratory.

In 1971, we began a series of three small annual conferences in Buffalo to interest other States and Canadian provinces in the addition of other tests to their PKU programs. At these conferences, the directors of our collaborating laboratories testified that use of the punch-index machine had allowed them to add tests for galactosemia, homocystinuria, maple syrup urine disease, tyrosinemia and histidinemia, with only marginal increases in costs, since no additional laboratory staff was required. As a result, Maryland and Ohio added other tests, and New York applied the western New York program to that of the rest of the State. However, for most States, the legacy of the controversy of the 1960's concerning PKU testing continued in the 1970's in the form of three problems:

1. Lack of liaison between the medical centers and the screening programs: even well organized regional screening programs located in State health departments often had little or no contact with medical centers, with resulting problems in medical followup. This is in complete contrast to all other countries where the screening laboratory, often for an entire country (as in Austria or the Republic of Ireland) is usually located in the pediatric department of a university medical school.

*The directors of these laboratories were Dr. R. A. MacCready, Mr. G. Brandon, Dr. R. Straus, and Dr. J. Puleo.

2. Many States with laws requiring PKU testing, simply do not have sufficient population to make multiple testing of newborn infants practical.

3. Many States with large populations allow private laboratories to each perform a small number of PKU tests for a profit, thus causing the same problem that exists in the small States.

In 1972, we published a paper on this subject, calling on the existing State PKU program to reorganize into cost-effective regions, suggesting that States with small populations could cooperate with each other. We discussed this possibility with the Maternal and Child Health Service, without collaborating laboratories and with appropriate persons in a number of other States, where we showed a film prepared for this purpose. Meanwhile, a very significant development was occurring in the Quebec province that proved to be of great assistance to this effort.

The Quebec genetic network has the features of the European countries in that the screening center is located in a university medical center, with the program directed by the four universities and funding supplied by the Ministry of Health. A unique feature is that the government supplies an extra 50 percent of funding for research and development of new genetic services. This made possible, during 1971-75, a successful field trial of Dr. Jean Dussault's new radioimmunoassay for hypothyroidism on the dried blood specimens collected for PKU testing. Since every physician knows of the treatment of hypothyroidism by thyroxine to prevent cretinism and mental retardation, the success of the Quebec program aroused intense interest elsewhere.

In 1975, Dr. William Murphey first introduced the thyroxine test into the United States in the Oregon health department, using a minor modification of the punch-index machine to integrate this test into the Oregon State program. As a result, the States of Montana, Alaska, Idaho, and Nevada made arrangements to send their specimens to Oregon. In 1976, the New England region was established after Drs. Levy and Mitchell added the thyroxine test to the Massachusetts program, with Maine, Rhode Island, Connecticut, and New Hampshire sending their specimens to the Boston Laboratory.

Maryland, Ohio, and New York States have also added thyroxine testing, but for most other States, the fragmented nature of PKU screening has made it too costly to add the thyroxine test.

Results of screening so far have demonstrated that the frequency of hypothyroidism is approximately 1/5,000, or more than double that of PKU, and that none of these infants would have been detected during the first 3 months of life without the screening test, even when born in the most sophisticated academic medical center. Thyroxine treatment is much

simpler than treatment for PKU, and screening for hypothyroidism is even more cost-effective. The General Accounting Office (GAO) report states that each dollar invested in screening with a battery of seven tests saves more than \$20.00 spent for care programs. We agree with the GAO.

We also agree with the GAO's recommendation that the Department of HEW assist the States in organizing cost-effective screening regions. Thirty-two regional laboratories in the United States could be equipped for \$75,000 each, for a total of \$2.4 million. Each laboratory could screen 100,000 infants, for a total of 3.2 million infants annually. The cost would be \$2.50 per infant for a total of \$8 million.

The Center for Disease Control (CDC) could give valuable assistance in providing training programs and quality control, as it has done so effectively in the past for other laboratory health programs.

In Canada, the provinces outside of Quebec also need to act. For example, the four western provinces could logically form a single screening region. The Canadian Association for Mental Retardation (CAMR), joining forces with the five medical schools involved, could aid materially in persuading the separate provincial health departments to work together.

Four important aspects, other than screening, must be emphasized.

1. Clinical followup treatment has to be planned simultaneously with the screening program. This requires involvement of the pediatric centers from the beginning.
2. The community to be screened must be fully informed and the professional community educated.
3. An advisory committee for the regional program should be created to represent the public and professional community.
4. As in Quebec, Massachusetts, Oregon, and elsewhere, the screening program should be used as a resource for development of new screening services through research and trial of new methods. This purpose will also require close relations with academic medical centers.

Finally, in urging organization of national newborn screening programs for the United States and Canada, let me refer to the present situation in Japan; a country of 110 million people, half the size of the United States. Here, the Japanese government, 3 years ago, agreed to support a national program as a result of a campaign carried out by a coalition of Japanese pediatricians and parents' associations for mentally retarded individuals. The Kitasato Institute in Tokyo provided a training program for 80 technicians from all over Japan, in which I participated

1 year ago. The institute also assists with quality control. As in certain other endeavors, Japan started years later than the United States, but appears to already be ahead of us. May I close with the plea that, in newborn screening (if not in cameras and television sets) we can catch up with Japan!

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Workshop Recommendations

REGIONALIZATION OF METABOLIC SCREENING FOR NEWBORNS

Group Leader: Robert Guthrie, M.D., Ph.D.

Recorder : Max R. Addision

Widespread screening for the early detection and prevention of various metabolic disorders should be implemented immediately, utilizing a network of regional screening laboratories which could adequately serve all newborns in all sectors of the country. It is recommended that this method of preventing metabolic causes of mental retardation be implemented as follows:

1. That Federal funds be made available for planning activities related to establishing regional screening centers and programs. Specifically, it is recommended that 32 regional screening laboratories be established, each of which should screen approximately 100,000 specimens from infants each year.
2. That Federal funds be made available for adequately equipping the regional screening laboratories. Specifically, approximately \$2.4 million is required, or \$75,000 per laboratory for equipment.
3. That Federal support be available to offset operating costs during the initial period (first 3 years of operation). Operational costs should be covered by Federal and State monies and laboratory fees. Approximately \$8 million annually would be required for operating the regional screening programs, based on a cost of \$2.50 per infant.
4. That States should actively encourage the involvement of a greater number of universities in regional screening efforts, since this procedure could yield the most cost-effective approach to prevention in the area of metabolic disorders.
5. That during the initial efforts to plan and establish regional screening programs, precautions should be taken to ensure that the efforts of the laboratory and the referring physician are maximally integrated in order to ensure the effective implementation of followup and treatment programs.

ADDENDUM

DR. ADDISON: Dr. Guthrie and I would like to suggest that we add three recommendations. These are as follows:

1. The Federal Government should assist in establishing 32 newborn regional screening laboratories, each testing specimens for approximately 100,000 infants per year.

2. Initial equipment cost should not exceed \$75,000 for each laboratory for a total cost of \$2.4 million. The use of Federal funds for this initial cost would be of great assistance in establishing screening regions.

3. The annual budget for each laboratory should not exceed \$250,000 or \$2.50 per infant. Since costs for newborn screening of PKU only have been paid for in a variety of ways in different States, including the use of Federal funds, State funds, the use of private laboratories charging fees, or a combination of these methods, a fair and reasonable formula for Federal support for the actual screening program presents some problems. However, some Federal support during the initial period of 1 to 3 years appears reasonable.

DR. ADDISON: I am sure Dr. Guthrie feels this is already implied in the overall terminology of screening, but the laboratory end of it is really only part of it, possibly not the most important part. One of the major concerns is to ensure the completeness of the coverage--the response to the positive signal and the followup. Many of the screening programs fall down there, not so much in the laboratory operation. If you don't have the response to the positive signal and an adequate followup and a method of assuring a totality of the screening, treatment and followup, the screening really makes no sense at all.

MR. HORMUTH: In the reference to 32 newborn regional screening laboratories, does that mean screening laboratories, or would they be combinations of screening laboratories plus followup?

DR. GUTHRIE: It refers to the combination. The figures are, of course, only for screening. If you included treatment and followup, with which I agree, it nearly doubles the cost and brings it pretty much in line with the figure given in the GAO report, which includes a battery of tests and treatment.

Discussion

REGIONALIZATION OF METABOLIC SCREENING FOR NEWBORNS

QUESTION: Are you not pushing your authorization ceiling, as far as appropriations are concerned?

RESPONSE: Yes

COMMENT: It seems to me that if this group is going to back any kind of legislation, such as appropriations for laboratory work or prenatal work, we ought to support an increase in the authorization for Maternal and Child Health programs because they are right up to that authorization ceiling now.

MR. HORMUTH: In our group, we talked about the possibility of increasing the authorization and the appropriation, and of perhaps even earmarking a portion of the increase for a specific purpose. It is generally much easier to raise the ceiling and to increase the appropriation than to try to come up with new legislation.

COMMENT: I think it is essential that this group gets behind the increased authorization or very little is going to happen.

Specific Comments

MANDATORY SCREENING

DR. BOGGS: I would like to find some method by which this group, or some other one could resolve the dilemma about mandatory screening. A certain amount of opposition has appeared in some segments of the professional community after some of the State legislatures passed legislation requiring screening tests for certain conditions. Of course, there are good laws and bad laws, in terms of the way they are phrased and what types of screening are covered, and under what circumstances it is carried out; but supposing we are talking about good laws. As a result of that opposition, the National Research Council mobilized a fairly prestigious commission on genetic screening, involving not only physicians, but lawyers and others having competence in the issues being discussed. The net result, which has now been very well publicized, is the recommendation which suggests that mandatory screening programs are unduly invasive of people's privacy. In addition to our area of involvement, the issue was precipitated, in part, by the unintended adverse consequences of some screening for sickle cell trait, which resulted in some people with the trait being denied their health insurance. At any rate, we have a report from a prestigious committee composed of people whom I respect, and the net result is that it makes it quite difficult to get screening programs established in States that do not have them. What is the opinion of this group on this?

DR. GUTHRIE: In that report, they carefully separated the two kinds of conditions: (1) the screening for conditions for which there is no treatment available at the moment, such as sickle cell trait, and (2) conditions such as PKU. These were considered as two separate kinds of problems. It is very important to separate them. The right to be well born seem to be in conflict with the right of the privacy of the parents to do what they please.

DR. KOCH: In California, we tried to get a screening law through the legislature in 1964, and we failed; but in 1965, the law was passed. During a 15 year period, starting in 1956 when we first became interested in PKU, we had only two babies with that disorder referred to Children's Hospital of Los Angeles from a reservoir of two million people with over 100,000 births per year. The year mandatory screening started, we had 11 new PKU babies referred. So I feel, from my experience in that State, that mandatory screening had a very beneficial result. We tried again with screening for hypothyroidism, but with a different approach. In 1973, a bill was passed and signed by the governor, which encouraged the health department to screen for hypothyroidism. This is 1977, and we still don't have hypothyroid screening. I think we made a mistake when we submitted that bill. We should have had a mandatory bill because the evidence in favor of hypothyroid screening today is overwhelming.

DR. BOGGS: Regarding the possible mandatory reporting of treatable genetic conditions, it seems to me that many times by-product results can be obtained at little or no additional cost. For instance, if a condition that may not be treatable at the moment, can be identified and reported in the process of identifying one that is treatable, and at little or no extra cost, we should encourage that reporting for epidemiological purposes. An example, not related to genetic screening occurred in New Jersey where, for many years, we have had a law that requires doctors to report congenital anomalies that are visible at birth. The theory was that these would be reported and the Crippled Children's Services would be offered. That should have included all visible anomalies, including Down's syndrome, but we found that there was very little reporting of Down's syndrome and the health department was not encouraging doctors to report it because it was felt they had no treatment to offer. That destroyed the opportunity for us to get indications of fluctuations in the incidence and other data that might have had some sort of useful results. Similarly, with some of the inborn errors, for which we do not yet have treatment, I feel they should be reported if there is not a substantial additional cost associated with it.

MR. HORMUTH: In order to use a sample to get results on other than just the one or two disorders for which it is intended, you would have to get the informed consent for every kind of procedure you would intend to carry out. This has been part of the problem in some States. They are reluctant to utilize such screening because they have not fully thought through all of the implications of informed consent and some of the things they might want to record. There are implications regarding keeping some sort of register on conditions. This gets back to some of the problems that were encountered regarding the sickle cell trait screening.

DR. BOGGS: It seems to me that the public has accepted a number of other mandatory things such as immunizations for school attendance and pre-marital testing for venereal disease. People with religious scruples must have the opportunity to withdraw, but most people accept these things. We might also talk about the possibility of suing some physicians who fail to actively promote this preventive measure.

COMMENT: There is no objection to screening per se, but many times it is the issue of confidentiality that worries many physicians in practice. If you can build in some way of preserving confidentiality, there would be no problem.

MR. HORMUTH: Yes, you would have to maintain confidentiality if you kept registers of other conditions. Care would have to be exercised as to what the registers were used for and who had access to them. However, even if you destroyed the personalized record after you turned it back to the individual or his physician, and only maintained the statistical record, you would much better off than if you didn't have it.

DR. GIANNINI: I hope there will be some way, in the presentation for screening, to avoid the word confidentiality. Whenever we get to that word, we are in a frozen position. We lose many months and years of progress. If we talk about a central registry, the whole thing dies. I hope that we will be able to make a presentation that avoid trigger words. We must know certain things. I don't think it is the intent of anyone who has such information, to make it public. If you have good professionals involved, who have integrity, everything will be preserved.

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REGIONALIZATION FOR
GENETIC SERVICES AND AMNIOCENTESIS*

by

Cecil Jacobson, M.D.

Chairman Task Force on Biomedical Prevention
President's Committee on Mental Retardation

*Based on Amniocentesis: Update 1976 by Kathleen M. Majerus

INTRODUCTION

The use of amniocentesis to diagnose chromosomal and biochemical defects in the fetus was first reported by independent laboratories in 1967/1/ and 1968./2/ Since that time, tests have been developed to enable diagnosis in utero of over 60 inborn errors of metabolism and all known chromosomal anomalies./3/ A study done by the National Institute of Child Health and Human Development has determined that the procedure does not significantly increase the risk of maternal or fetal loss of injury. /4/

PURPOSE OF THE STUDY

This survey was designed to determine the number of amniocentesis performed each year, the location of the primary laboratories* that analyze amniotic fluids, and the geographic region that each laboratory serves. Questions also sought information about the use of sonograms, tissue culture facilities, tests for alpha-fetoprotein, financing of laboratory fees and the number of laboratories opening each year.

- /1/ Jacobson, C.B., Barter, R.H., Intrauterine Diagnosis and Management of Genetic Defects, American Journal of Obstetrics and Gynecology, 99:796, 1967.
- /2/ Nadler, H.L., Antenatal Detection of Hereditary Disorders, Pediatrics, 42:912, 1968.
- /3/ Littlefield, J.W., Milunsky, A., and Lenz, W., An Overview of Prenatal Genetic Diagnosis. In Motulsky, A., and Lenz, W., (eds.), Birth Defects, New York, American Elsevier Publishing Company, 1974, p.221.
- /4/ NICHD National Registry for Amniocentesis Study Group, Midtrimester Amniocentesis for Prenatal Diagnosis: Safety and Accuracy, Journal of the American Medical Association, 236:1471-76, 1976.

*The term primary laboratory is used to indicate one that usually performs amniocentesis, analysis and karyotyping of tissue culture, and offers diagnosis and genetic counseling. The primary laboratory sometimes sends individual fluid samples elsewhere for more sophisticated tests.

ABSTRACT

This report is the result of an extensive survey conducted to determine the activities of United States laboratories which provide prenatal diagnosis of fetal genetic and biochemical defects. The study indicates that, as of June 1, 1976, 141 laboratories in the United States offer major cytogenetic and/or biochemical analyses on amniotic fluid samples obtained through amniocentesis. These laboratories have performed over 27,000 amniotic fluid studies since 1964.

METHODS

THE QUESTIONNAIRE

Questionnaires were sent to 607 medical professionals in all 50 States and the District of Columbia. A total of 342 responded. The survey consisted of 11 short questions printed on an 8-1/2 x 3-1/2 inch pre-paid postcard. Questions could be answered by filling in blanks or checking boxes.

SELECTION OF THE MAILING LIST

The mailing list was compiled from 5 major sources:

All persons in the United States, listed in the National Foundation/March of Dimes' International Directory of Genetic Services (Fourth Edition, March 1974).

All departments of Obstetrics and Gynecology with a residency program that was approved by the Residency Review Committee on the Council on Medical Education, the American Board of Obstetrics and Gynecology, and the American College of Obstetricians and Gynecologists.

Researchers publishing in the United States on amniocentesis.

All centers or professionals who were recipients of National Foundation/March of Dimes Research Grants or Medical Service Program Grants for 1975-76.

State Mental Retardation Directors, State Developmental Disabilities Directors, Regional Maternal and Child Health Directors, and Directors of University Affiliated Facilities. In States where further information was required, medical professionals were asked to help identify all such facilities in the State.

RESULTS

THE RESPONSE

A total of 342 cards were returned, showing 141 primary laboratories that analyze amniotic fluids for prenatal diagnosis in this country. The relevant laboratories are listed in Appendix II.

CHARACTERISTICS OF THE SAMPLE

Only two commercial laboratories of those responding are included; the rest are non-commercial facilities. There were 117 laboratories (83 percent of those surveyed) which reported that outreach clinics, hospitals

or private physicians referred patients to their laboratory for amniocentesis. Only 25 laboratories (17.7 percent) relied on facilities other than their own for all or part of their tissue culture results.

Sonograms are accepted as a routine, pre-amniocentesis procedure in order to: 1) determine the presence of more than one fetus, 2) locate the placenta, 3) establish accurate fetal gestational age, and 4) determine the best location for placing the needle. Routine sonograms were performed prior to amniocentesis by 108 laboratories (76.6 percent of the sample). The majority of those laboratories polled did not screen all patients for alpha-fetoprotein, a test which can diagnose a variety of neural tube defects. Only 53 laboratories (37.6 percent) performed this test routinely.

LABORATORY COSTS

About half of the responding laboratories (73) received Federal or State funds for partial support of expenses. Sixty six laboratories did not receive such funds. Fifty four of the laboratories reported that the patient or her insurance paid for more than half of the costs. Sixty three laboratories reported that the patient paid for less than half of the costs (TABLE 1).

Between 1964 and 1969, according to the study, 35 independent laboratories began analyzing amniotic fluid samples for diagnosis of fetal defects. The number of labs in service has continued to grow at the rate of about 18 per year through 1973. Since that time, only 32 new facilities have opened, with just 7 of these in 1976. While fewer laboratories have entered the field in the past 3 years, there has been a tremendous increase in the number of procedures performed during that time. (FIGURE 2).

EXPERIENCE

A total of 27,430 procedures had been performed as of June 1, 1976. The number has more than doubled in the past 2 years. (FIGURE 2). More than 5,500 laboratory studies on amniotic fluid had been completed up to June 1, for the year 1976.

The number of cases handled by each laboratory varies from 1 - 2 analyses per year, to up to 300-400 per year. TABLE 2 shows the number of studies completed per laboratory in 1975.

The 134 laboratories in operation in the United States during 1975 analyzed 7,585 amniotic fluids samples for prenatal diagnosis. More than half of these samples, over 4,000, were handled by just 20 of the existing laboratories. Most of these 20 facilities are located in medical schools or university hospitals.

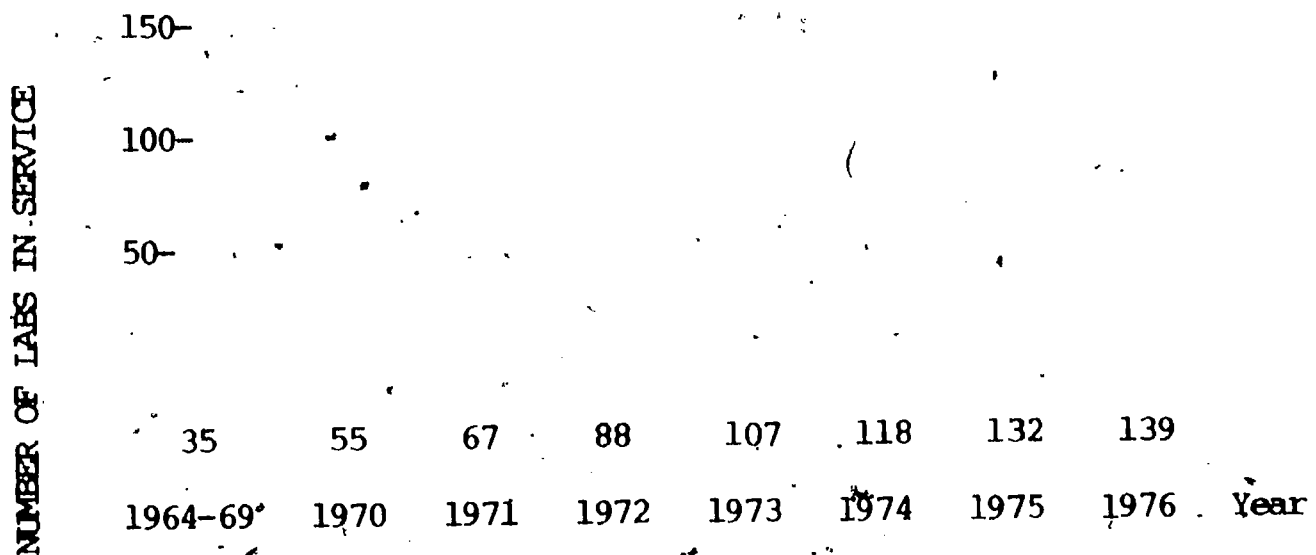
TABLE 1

Percentage of Costs Supported by Patient Fees and Insurance

<u>Percent Reported</u>	<u>Number of Laboratories Responding in that Percentile</u>
0 %	10
1 - 25%	26
26 - 50%	27
51 - 75%	16
76 - 99%	16
100%	22
No. Response	24

The Growth of Facilities

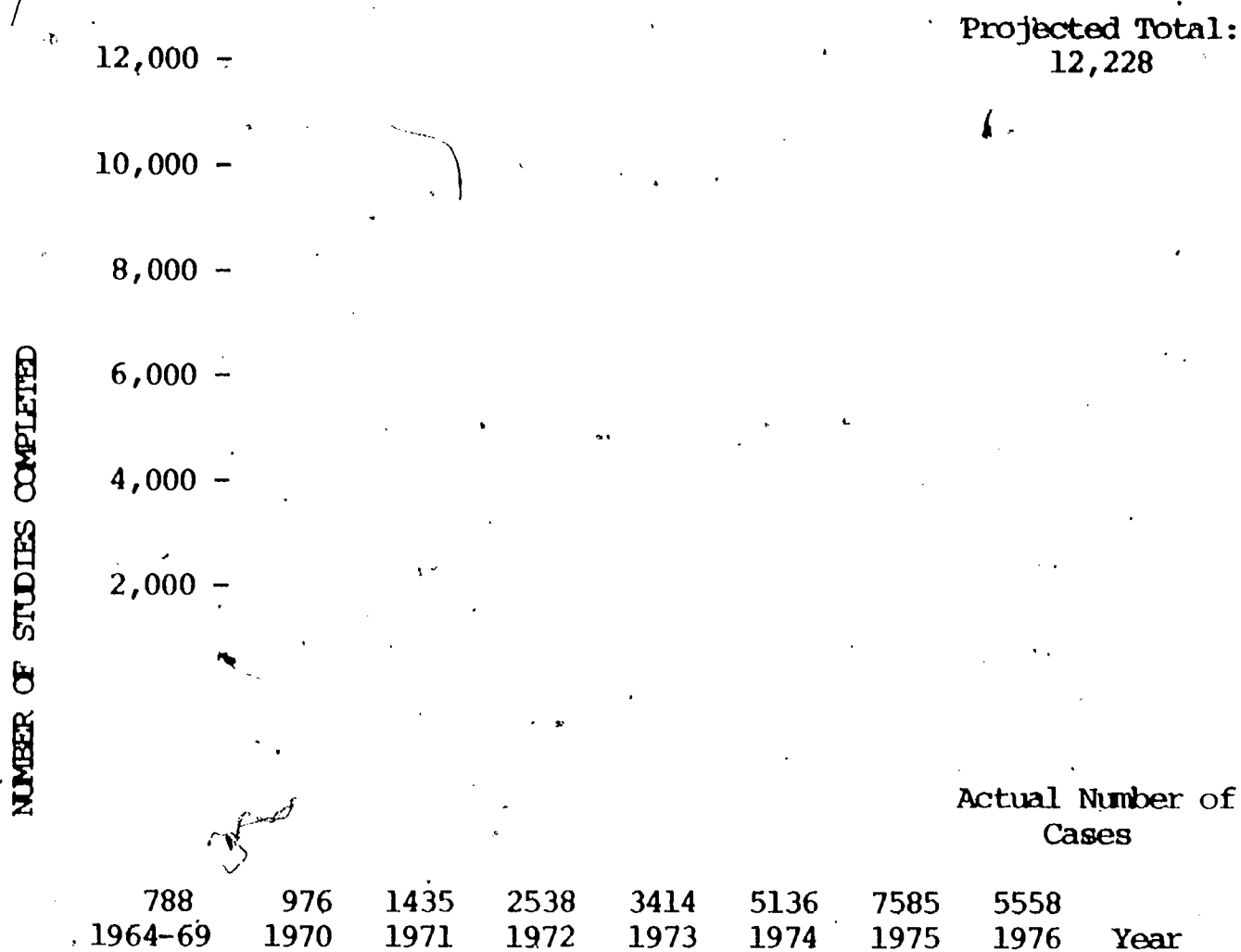
FIGURE 1: The Number of Laboratories in Service Per Year*



*No Response - Labs

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FIGURE 2: Number of Amniotic Fluid Studies Per Year*



*No response from 1 Lab.

TABLE 2

NUMBER OF STUDIES COMPLETED BY LABORATORIES IN SERVICE IN 1975

Number of Studies	Number of Laboratories in Each Range
Less than 25 studies	58
25 - 100	52
101 - 200	16
201 - 300	4
More than 300	3
No Response	1

GEOGRAPHIC DISTRIBUTION

The locations of the 141 primary laboratories included in our survey are shown in FIGURE 3. The centers capable of testing amniotic fluid are located in 43 States and the District of Columbia. The remaining 7 States do not have resident laboratory facilities for analyzing such samples. The individual centers in each State are listed in Appendix II.

OUTREACH PROGRAMS FOR GENETIC SERVICES

Several States have organized regional genetic service programs which extend into some of the States lacking a primary facility. (TABLE 3, and FIGURE 4).

Neither North Dakota nor South Dakota has a resident primary facility to process amniotic fluid samples, nor are they included in any organized regional program. Patients seeking amniocentesis in North Dakota are referred to the University of Minnesota- Minneapolis. Those in South Dakota are referred to the Northwestern University Children's Hospital, in Chicago.

SUMMARY

As of June 1, 1976, there were 141 primary laboratories which had analyzed a total of 27,430 amniotic fluid samples for the purpose of antenatal diagnosis.

The number of procedures has increased by more than 50 percent in the past year alone.

The number of laboratories entering the field seems to be low, compared to the great increase in demand for services.

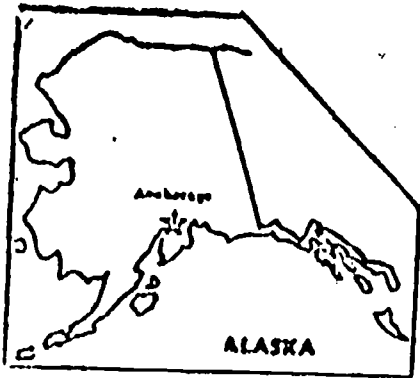
More than half of all cases are handled by less than 15 percent of the laboratories.

Sonograms are accepted as a routine pre-amniocentesis procedure.

Routine tests for alpha-fetoprotein levels are not performed by a majority of laboratories.

The proportion of laboratory costs supported by government funds or patient fees varies greatly.

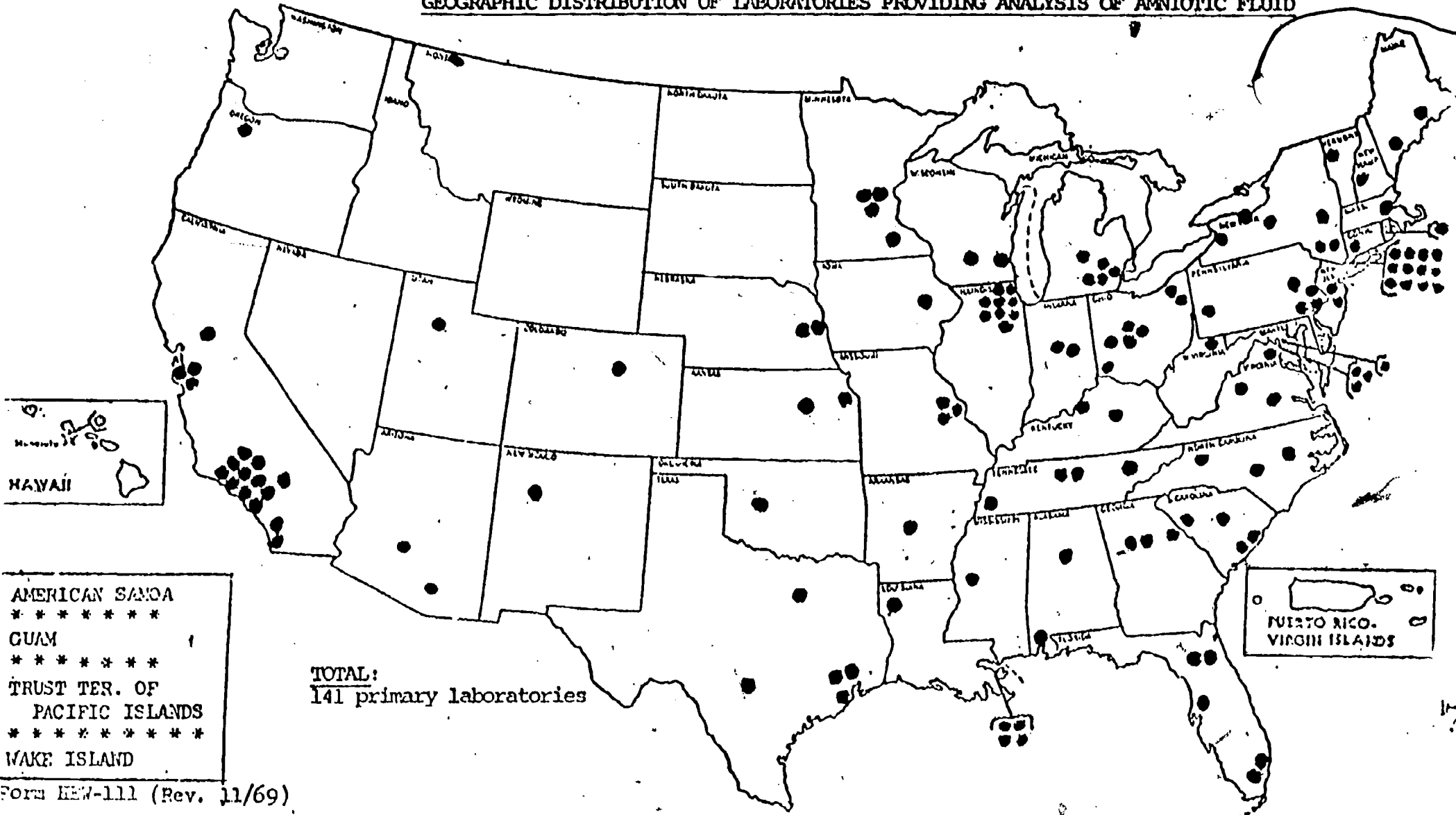
Only two States, North and South Dakota, do not have resident, primary laboratory facilities, and are not covered by any regional program.



THE UNITED STATES OF AMERICA
AND ITS TERRITORIES AND POSSESSIONS
(Outline Map)

FIGURE 3

GEOGRAPHIC DISTRIBUTION OF LABORATORIES PROVIDING ANALYSIS OF AMNIOTIC FLUID



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APPENDIX II

LOCATION OF PRIMARY LABORATORIES PROVIDING ANALYSIS OF SAMPLES
FROM AMNIOCENTESIS

STATE	CITY	CENTER
Alabama	Birmingham	University of Ala. Medical Center
	Mobile	University of So. Ala Medical Sch.
Arizona	Phoenix	St. Joseph's Hospital
	Tucson	Univ. of Arizona Medical School
Arkansas	Little Rock	Univ. of Arkansas Medical School
California	Davis	Univ. of California Medical Sch.
	Duarte	City of Hope Medical Center
	Glendale	Glendale Adventist Hospital
	Harbor City	So. Cal. Permanente Medical Group
	Irvine	University of California <u>1/</u>
	La Jolla	University of Cal. Medical Center
	Loma Linda	Loma Linda Univ. Medical Center
	Los Angeles	Calif. Hospital Medical Center Children's Hospital Univ. of Calif. at Los Angeles Univ. of Southern California
	Panorama City	Kaiser-Permanente Medical Center
	San Diego	San Diego County Univ. Hospital
	San Francisco	University of California
Santa Clara	Kaiser Hospital	
Stanford	Stanford University Medical Sch.	
Torrance	Harbor General Hospital	
Van Nuys	Bio-Science Laboratories	
Colorado	Denver	Univ. of Colorado Medical School
Connecticut	Farmington	University of Connecticut <u>4/</u>
	New Haven	Yale University Medical School
Delaware	Wilmington	Wilmington Medical Center
Dist. of Columbia	Washington	Armed Forces Inst. of Pathology Georgetown Univ. Medical Ctr. <u>1/</u> George Washington U. Med. Ctr. Howard Univ. Medical School

1/ A primary laboratory, but did not respond to survey.

4/ A primary laboratory will open here in the immediate future.

APPENDIX II- (a)

STATE	CITY	CENTER
Florida	Gainesville	University of Florida <u>3/</u>
	Miami	Palmetto Park Genetic Associates Univ. of Miami Medical School
	Tampa	Univ. of South Florida
Georgia	Atlanta	Center for Disease Control Emory University Medical School
	Augusta	Medical College of Georgia
Hawaii	Honolulu	Kauikeolani Children's Hospital
Illinois	Chicago	Cook County Hospital Mercy Hospital and Medical Center Mt. Sinai Hospital Medical Ctr. Northwestern Univ. Children's Memorial Hospital Northwestern University/Prentice Women's Hosp. & Maternity Ctr. Parkridge Luthern General Hospital Rush Presbyterian/St. Luke's Medical Center Univ. of Chicago Med. Sch. <u>3/</u> So. Ill Univ. Med. Sch.
		Springfield
Indiana	Indianapolis	Indiana Univ. Medical Ctr.
	Methodist Hospital	
Iowa	Iowa City	Univ. of Iowa Hospitals
Kansas	Kansas City	Univ. of Kansas Medical Center
	Topeka	Genetic Counseling Center
	Wichita	Wesley Med. Research Foundation <u>1/</u>
Kentucky	Lexington	Univ. of Kentucky Med. Ctr. <u>2/</u>
	Louisville	Univ. of Louisville Med. Ctr.
Louisiana	New Orleans	Louisiana State Univ. Med. Sch. <u>3/</u> Ochsner Clinic Tulane Univ. Medical School
		Shreveport

1/ A primary laboratory, but did not respond to survey.

2/ Figures on the number of procedures performed per year at this primary laboratory were not made available to this study.

3/ There is more than one independent, primary laboratory facility at this location.

APPENDIX II - (b)

STATE	CITY	CENTER
Maine	Ellsworth Portland	Maine Genetic Counseling Center Maine Medical Center
Maryland	Baltimore Bethesda	Johns Hopkins Univ. Med. Ctr. National Institutes of Health <u>6/</u>
Massachusetts	Boston	Massachusetts General Hospital
Michigan	Ann Arbor Detroit East Lansing Royal Oak	Univ. of Michigan Medical Ctr. Henry Ford Hospital Wayne State Univ./C.S. Mott Center Michigan State Univ. Med. Ctr. William Beaumont Hospital
Minnesota	Minneapolis Rochester	Univ. of Minnesota School of Medicine and Dentistry <u>3/</u> The Mayo Clinic
Mississippi	Jackson	Univ. of Mississippi Med. Ctr.
Missouri	St. Louis	Cardinal Glennon Hospital <u>5/</u> St. John's Mercy Hospital Washington Univ. Medical Sch.
Nebraska	Omaha	Children's Memorial Hospital Univ. of Nebraska Med. Center
New Hampshire	Hanover	Dartmouth Medical Center
New Jersey	Hackensack Newark	Metpath Laboratories New Jersey College of Medicine
New Mexico	Albuquerque	Univ. of New Mexico Medical Sch.

3/ There is more than one independent, primary laboratory facility at this location.

5/ This laboratory provided testing on amniotic fluid at one time, but has since closed.

6/ Individual laboratories at the National Institutes of Health provide a variety of specific diagnostic tests utilizing amniotic fluid cell cultures. The NINCDS have performed more than 400 tests for Gaucher's disease, Nieman Pick's disease, Fabry's disease and Tay Sach's disease.

APPENDIX II - (c)

STATE	CITY	CENTER	
New York	Albany	Albany Medical College	
	Buffalo	State Univ. of New York/Children's Hospital	
	East Meadows	Nassau County Medical Center	
	New York City		Albert Einstein College of Medicine
			Beth Israel Medical Center
			Brookdale Hosp. Medical Center
			Columbia University 1/
			Cornell Univ. Medical Center
			Jewish Hospital Medical Center
			Kingsbrook-Jewish Medical Center
			Long Island College Hospital
			Long Island Jewish-Hillside Med.Ctr.
			Mt. Sinai Medical School
	New York Medical College		
	New York Univ. Medical School		
	North Shore Univ. Hospital		
	State Univ. of New York/Downstate Medical Center		
	Univ. of Rochester Medical School		
	State University of New York/Upstate Medical Center		
	Letchworth Village Cytogenetics Laboratory		
North Carolina	Chapel Hill	Univ. of North Carolina Med. Sch.	
	Durham	Duke Medical Center	
	Winston-Salem	Bowman Grey/Wake Forest Med. Sch.	
Ohio	Cincinnati	Univ. of Cincinnati Children's Hosp.	
	Cleveland	Case Western Reserve Med. Sch.	
		Cleveland Metro General Hosp.	
	Columbus	Children's Hospital	
		Ohio State University Hospital	
	Dayton	Medical Genetics Laboratory	
Mt. Vernon	Mt. Vernon State Institute		
Oklahoma	Oklahoma City	Univ. of Oklahoma Children's Hosp.	
Oregon	Portland	Univ. of Oregon Health Sciences Ctr.	

1/ A primary laboratory, but did not respond to survey.

APPENDIX II - (d)

STATE	CITY	CENTER
Pennsylvania	Hershey	Hershey Medical Center
	Philadelphia	Temple Univ. Medical Center Thomas Jefferson Medical School Univ. of Pennsylvania Med. Ctr.
	Pittsburg	University of Pittsburg/Magee Women's Hospital
Rhode Island	Providence	Rhode Island Hospital
South Carolina	Charleston	Medical Univ. of South Carolina <u>3/</u>
	Columbia	Univ. of South Carolina School of Medicine
	Greenwood	Greenwood Genetics Center
Tennessee	Knoxville	Univ. of Tennessee Med. Center
	Memphis	Univ. of Tennessee Medical Ctr.
	Nashville	Meharry Medical Center Vanderbilt Medical Center
Texas	Dallas	Children's Medical Center
	Galveston	Univ. of Texas Medical Branch
	San Antonio	Univ. of Texas Medical Branch
	Houston	Baylor Medical College Univ. of Texas Medical Center
Utah	Salt Lake City	University of Utah Medical Center
Vermont	Burlington	Medical Center Hosp. of Vermont
Virginia	Alexandria	Alexandria Hospital
	Charlottesville	Univ. of Virginia Medical School
	Fairfax	Reproductive Genetics Center <u>4/</u>
	Norfolk	Eastern Virginia Medical Center <u>4/</u>
	Richmond	Medical College of Virginia
Washington	Seattle	Univ. of Washington Med. School
Wisconsin	Madison	Univ. of Wisconsin Med. Ctr.
	Milwaukee	Milwaukee Children's Hospital

3/ There is more than one independent, primary laboratory facility at this location.

4/ A primary laboratory will open here in the immediate future.

APPENDIX II - (e)

STATE	CITY	CENTER
West Virginia	Morgantown	West Virginia Univ. Medical Ctr.
Federal	Bethesda, MD	National Institutes of Health <u>6/</u>

6/ Individual laboratories at the National Institutes of Health provide a variety of specific diagnostic tests utilizing amniotic fluid cell cultures. The National Institute of Neurological and Communicative Disorders and Stroke have performed more than 400 tests for Gaucher's disease, Nieman Pick's disease, Fabry's disease and Tay Sach's disease.

TABLE 3

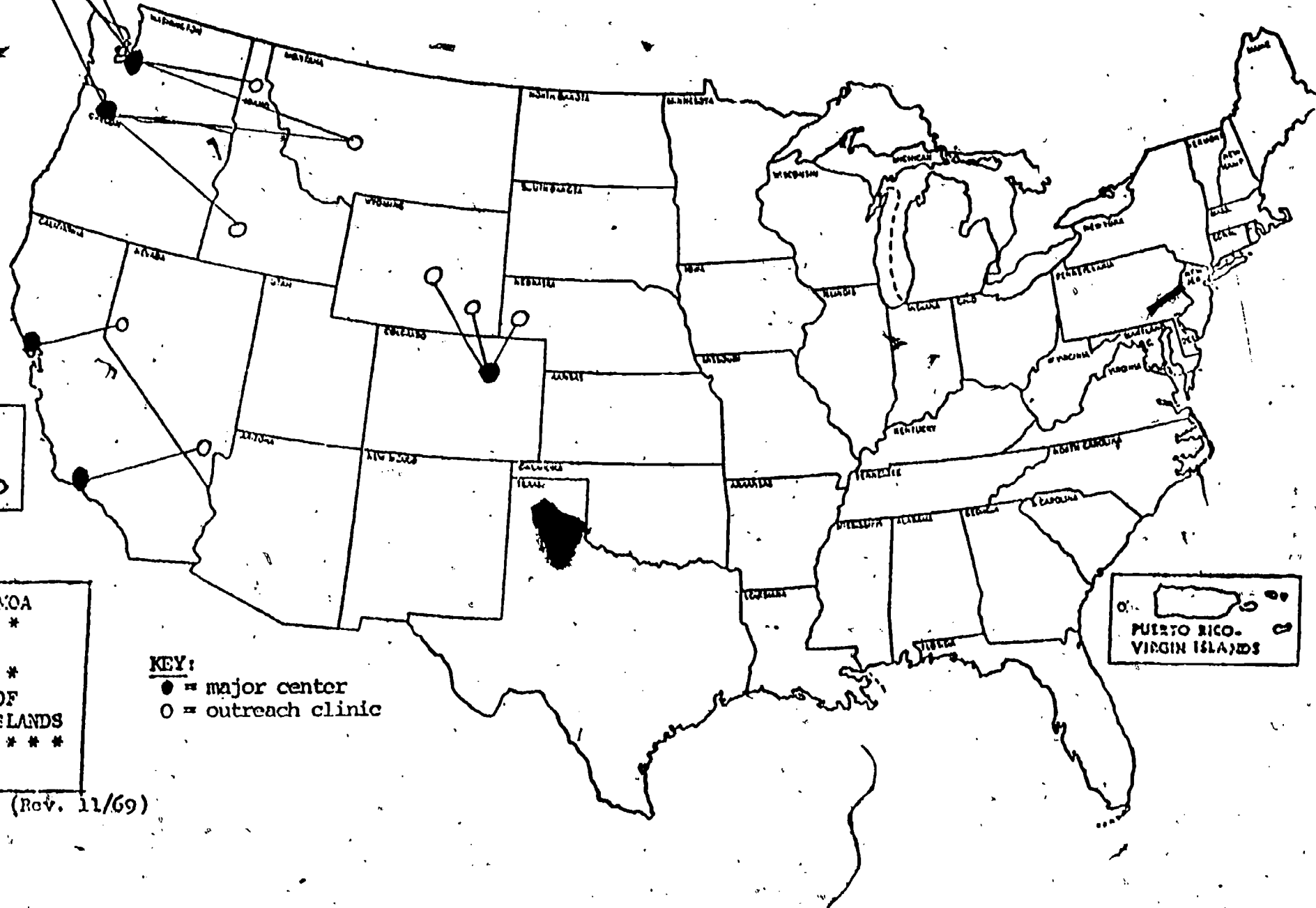
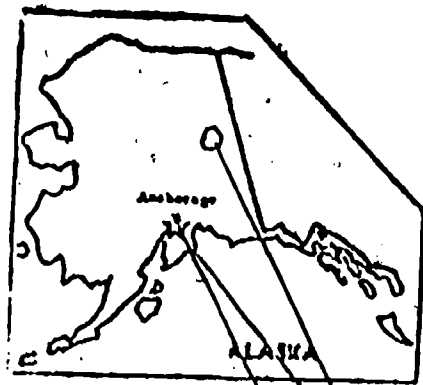
REGIONAL GENETIC SERVICE PROGRAMS PROVIDING AMNIOCENTESIS

<u>Primary Facility</u>	<u>Outreach Clinic</u>	<u>Comments</u>
California -		
California State U. Loma Linda	County Health Dept. Las Vegas, Nevada	Serves Southern Nevada
U. of California San Francisco	Washoe County Health Dept., Reno, Nevada	Serves Northern and Central Nevada
Colorado -		
U. of Colorado Denver	Scottsbluff, Nebraska	Serves Panhandle
	Casper, Cheyenne, Wyoming	Clinics held monthly
	Rock Springs, Riverton Wyoming	Clinics held every three months
Oregon -		
U. of Oregon Health Science Center, Portland	Boise, Statehouse, Idaho	Serves Southern Idaho
	Billings, Montana	Serves Western Montana
	Anchorage, Alaska	Individual referrals
Washington -		
U. of Washington Medical School, Seattle	Anchorage, Alaska (Juneau, Fairbanks)	Bi-monthly clinics (as needed)
	Montana	Serves 8 Western Counties
	Idaho	Serves 10 Northern Counties

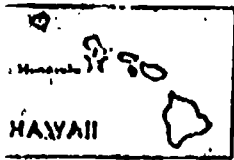
THE UNITED STATES OF AMERICA
AND ITS TERRITORIES AND POSSESSIONS
(Outline Map).

FIGURE 4

REGIONAL OUTREACH PROGRAMS PROVIDING AMNIOCENTESIS



70



AMERICAN SAMOA

GUAM

TRUST TER. OF
PACIFIC ISLANDS

WAKE ISLAND

KEY:
● = major center
○ = outreach clinic

87

88

Form HEW-111 (Rev. 11/69)

APPENDIX I

AMNIOCENTESIS QUESTIONNAIRE

This is a facsimile of the questionnaire postcard.
A code number was given to each individual on the mailing list.

con code # _____

THE FOLLOWING QUESTIONS SEEK INFORMATION FROM YOUR LABORATORY CONCERNING THE PERFORMANCE OF AMNIOCENTESIS FOR THE ANTENATAL DIAGNOSIS OF FETAL GENETIC DEFECTS:

<u>YES</u>	<u>NO</u>	ARE ANTENATAL DIAGNOSTIC STUDIES BEING PERFORMED IN YOUR LABORATORY?	THE YEAR OF YOUR FIRST AMNIOTIC FLUID STUDY: _____
<input type="checkbox"/>	<input type="checkbox"/>	DO OUTREACH CLINICS REFER PATIENTS TO YOUR LABORATORY FOR AMNIOCENTESIS?	THE NUMBER OF AMNIOTIC FLUID STUDIES COMPLETED IN YOUR LABORATORY PER YEAR:
<input type="checkbox"/>	<input type="checkbox"/>	DOES YOUR LABORATORY UTILIZE PERIPHERAL OR SATELLITE TISSUE CULTURE FACILITIES?	1964-69 _____ 1973 _____
<input type="checkbox"/>	<input type="checkbox"/>	ARE SONOGRAMS ROUTINELY PERFORMED PRIOR TO AMNIOCENTESIS?	1970 _____ 1974 _____
<input type="checkbox"/>	<input type="checkbox"/>	ARE ALL AMNIOCENTESIS PATIENTS SCREENED FOR ALPHA-FETOPROTEIN?	1971 _____ 1975 _____
<input type="checkbox"/>	<input type="checkbox"/>	ARE LABORATORY COSTS PARTIALLY SUPPORTED BY FEDERAL/STATE FUNDS?	1972 _____ 1976 _____
<input type="checkbox"/>	<input type="checkbox"/>	ESTIMATED PERCENTAGE OF YOUR LABORATORY COSTS SUPPORTED BY PATIENT FEES OR INSURANCE?	<u>YES</u> <input type="checkbox"/> <u>NO</u> <input type="checkbox"/> WOULD YOU CONSIDER PARTICIPATING IN A MORE DETAILED QUESTIONNAIRE?
			<input type="checkbox"/> <input type="checkbox"/> ARE YOU INTERESTED IN RECEIVING THE RESULTS OF THIS STUDY?

In conclusion, this survey has accomplished two major objectives:
1) The identification and location of primary laboratories which analyze amniotic fluid samples from early second trimester amniocentesis for the purpose of fetal diagnosis, and 2) the recording of the number of cases performed each year by these laboratories. In addition, this study has indicated the need for more coordinated efforts toward planning for services and funding for amniocentesis as a demonstrated program in the prevention of mental retardation.

Workshop Recommendations

REGIONALIZATION FOR GENETIC SERVICES AND AMNIOCENTESIS

LEADER: Cecil B. Jacobson, M.D.

RECORDER: Laverdia T. Roach

The State of the Art: In series which now exceed 40,000 patients in the United States and 10,000 in Europe, the following statement holds true: Transabdominal amniocentesis during the middle trimester (by a competent obstetrician) is an acceptable, safe procedure. Efficiency and safety are well established. Tissue culture of fetal cells is predictable in centers with experience. There is a success rate of over 95 percent. The diagnostic accuracy of chromosomal analysis is better than 99 percent. Biochemical studies for inherited metabolic defects are also reliable from both fetal cultures and/or supernatants. Open neural tube fusion defects can be reliably detected by elevated alpha-fetoprotein in amniotic fluid. Regarding application within the human population, established clinical risk groups are well defined. They are characterized by increased maternal age (35 years and over), maternal carriers of X-linked disease; previous trisomic offspring, previous neural tube defects in offspring, carriers of established translocation and parental carriers of biochemical disease.

General Recommendations:

1. That ultrasonic testing be made available prior to amniocentesis.
2. That the laboratory in which the amniocentesis procedure is performed must be an experienced one. Samples must be split with another laboratory, observing quality control standards as set by the Center for Disease Control (CDC).
3. That a minimum number (approximately 100) of amniocentesis procedures must be performed in a laboratory or center before it is eligible for certification; that all such centers be University-affiliated; and that there must be a 95 percent successful culture rate and accuracy on 25 consecutive samples.
4. That the laboratory in which the amniocentesis procedure is performed must submit a certified report to the CDC.
5. That there must be appropriate counseling, monitoring, and follow-up to assure adequate evaluation.

6. That informed consent to amniocentesis does not commit the woman to a future abortion; and that this informed consent be a part of the patient's official record.

Specific Recommendations Regarding Funding and How it Should be Implemented:

1. That the number of genetic diagnostic units be extended from the current 150, to 250, to 500, to 1000 within the next 5 years.

2. That funding should be sought through increasing the availability of maternal and child health funding categorically sought for genetic services.

3. That the existing Genetic Disease Act be allocated toward quality control activities by CDC, model programs with the States, outreach programs and affiliated medical centers.

Discussion

REGIONALIZATION FOR GENETIC SERVICES AND AMNIOCENTESIS

DR. KOCH: Is it a foregone conclusion that you are in favor of regionalization?

DR. JACOBSON: Yes. The States work with regional medical centers.

DR. LOWE: On genetics legislation, it would be important for the Report to emphasize the need for adequate appropriations.

DR. JACOBSON: \$4 million has been appropriated this year. The Genetic Services Act has been funded. But it must be renewed annually. If you spend all the money by October, there is no more money. We did not feel that we should put our funding on the Genetic Services Act, but that the money should be under Title V. If this group feels that we could be stronger in seeking funding from other sources, that part of our recommendations is open to amending.

DR. MILUNSKY: Perhaps some of the group is not familiar with the public hearings in which some of us participated last week in Washington concerning the National Genetic Disease Act and its implementation. Part of that is the already appropriated \$4 million, which may be followed by the \$30 million already in the Act in sequential years. The trouble is that the Act runs out as of next September. Renewal or re-writing is going to be necessary. The plan of implementation is through HSA. For the first \$4 million, that is likely to set a pattern for subsequent expenditures. If that is the fact of the case and they do appropriate multi-millions in each sequential year, it will go through HSA to States with medical genetic advisory committees which will disburse funds on the basis of a State bank of genetic services.

COMMENTS: One of the major problems is that the bill must be passed again when it comes up, with the hope of getting at least the \$30 million that was originally appropriated.

MR. HORMUTH: There was some discussion that, rather than have it a 3-year authorization, there would be authorization without a time period.

COMMENT: The way to do that is to get authorization without dollars for a kind of activity, and then insist that the program be adequately funded.

DR. JACOBSON: The recommendation that would be a real stimulus of your medical center and your State organizations is to see that each State does comply with a State genetics plan. They have to do this to

qualify for any type of acceptance. Many States do have such plans, but others are not in the process of developing them. What money is available to States, will not be available to those that don't have a State plan.

DR. ACOSTA: One of the primary problems is the follow-up care even for the present programs, such as PKU, for example. Many States have the Act, but there is no money for diagnosis and follow-up treatment. Does the Genetic Disease Act address this problem in terms of money for follow-up of these patients that are found or is it just for screening services?

DR. HORMUTH: It would provide money for follow-up care. The States would have to specify what the needs are, such as how they were proposing to meet those needs, which genetic centers and which laboratories they would utilize in meeting those needs and how they would propose to evaluate the total program. Then there would be further review, but I think the recommendation that came out of our group related primarily to the support of these regional genetic centers; for which, at the moment, there seems to be no way of supporting through the money authorized by the Genetic Disease Act. In terms of our plans, the capacity building within the centers would be implemented further through the utilization of Title V funds. But the State genetic disease programs would include many of the outreach programs such as the Tay-Sachs Screening Program and the Sickle Cell Clinic Program, which would be covered as part of the State-side plan and service delivery.

PREVENTION OF RH HEMOLYTIC DISEASE

by

Robert A. MacCready, M.D.

Retired Director
Massachusetts Department of Public Health
Diagnostic Laboratories

I. PURPOSE

Rh hemolytic disease is quite preventable, and has been since the introduction of Rh immune globulin (RhIG)*/ in 1968. Unfortunately, of the Rh negative mothers in the United States who should receive the RhIG after each delivery of an Rh positive baby and each abortion, only an estimated 80 percent do receive it. It is imperative to increase the use of RhIG when indicated to virtually 100 percent, and thereby avoid cerebral palsy, deafness, seizures and mental retardation in large numbers (estimated at 7,000 in 1974 in the United States). Our purpose, accordingly, is to consider specific measures to achieve this goal, using the tools already available and found effective.

II. SYNOPSIS OF FORMAL PAPER

A brief review of the mechanism which results in Rh hemolytic disease is first given to clarify how the use of RhIG can prevent the disease. At the time of an Rh negative mother's delivery of an Rh positive baby, a variable amount of the baby's Rh positive blood courses through the placenta into the body of the mother, thus invading her Rh negative blood. As a result, she may become sensitized to produce antibodies that destroy the Rh positive cells coming from the baby, since they are foreign to her body.

At a later pregnancy of this Rh negative mother, when again she may be carrying an Rh positive baby, her already-made anti-bodies can pass from the sensitized mother through the placenta into the blood of the Rh positive baby she is carrying. The anti-bodies will then destroy the red blood cells of this Rh positive baby. The result is Rh hemolytic disease in the fetus even before it is born.

Rh immune globulin is a biologic product developed to prevent such a result. It is made through the injection of Rh positive blood cells into the blood streams of Rh negative donors, who, as a result, develop anti-bodies that will destroy Rh positive cells. If the proper dosage of RhIG is administered to the Rh negative mother within 72 hours after the birth of an Rh positive child, then these anti-bodies in the product will destroy the baby's Rh positive cells which had entered her body at the time of delivery, before the Rh positive cells can sensitize the mother to make anti-bodies of her own. Thus, the next Rh positive baby is protected from the danger of Rh hemolytic disease, since the mother has not been sensitized to produce the anti-bodies that could damage such a baby's Rh positive blood cells.

It is important to understand that the RhIG is effective only for Rh negative mothers not already sensitized. This can have occurred through the previous delivery of an Rh positive baby or abortion, or through the previous administration of an incorrect type of blood. The RhIG must be administered to the eligible Rh negative mother after the delivery of each Rh positive baby and after each abortion.

*/ RhIG is frequently referred to also as "RhoGAM" the trade name of the first manufacturer licensed to produce and distribute it.

How complete is the usage of Rh immune globulin in the prevention of Rh hemolytic disease in this country? Actually this information is not directly available, for very few States maintain adequate records. The Center for Disease Control (CDC) in Atlanta, however, has divided the number of doses that should have been administered to the eligible Rh negative women after their deliveries. The quotient was judged at least a reasonably accurate estimate of the completeness of utilization of Rh immune globulin, and expressed in percentage, is approximately 80 percent for the United States.

The use of RhIG has given excellent results in reducing the incidence of Rh hemolytic disease. Consequently, it is of the utmost importance that the 80 percent utilization of this effective tool rapidly be increased to a goal as close to 100 percent as possible. What concrete action can be taken? We can well look at the handful of States that do have good programs, in particular Connecticut, whose program is outstanding.

In Connecticut, a well organized monitoring program under the Maternal and Child Health Section of the State Department of Health is coordinated by a capable research analyst. She routinely visits and helps all the hospitals with maternity services in the State in the shared goal of reducing the incidence of Rh hemolytic disease by complete utilization of Rh immune globulin in the case of every eligible Rh negative mother, who delivers an Rh positive baby or has an abortion. In 7 years, the program has achieved an RhIG utilization rate slightly over 99 percent. This has been accompanied by a gratifying reduction in babies afflicted with Rh hemolytic disease (from a morbidity total of 102 in 1970 to 19 in 1976). Combined fetal and neonatal deaths have likewise markedly decreased (from 32 deaths in 1970 to 6 deaths in 1976 of babies of sensitized mothers).

The modus operandi of a preventive monitoring program for any State needs to be tailored to the particular State involved. The State health department responsible for the program should have official sanction, as well as specific funds that are adequate. The monitoring, however, should not be unduly expensive. Certainly the program is cost-effective, for it is far less expensive than treating children afflicted with Rh hemolytic disease, both as infants and in later life. Finally, it should be generally agreed and understood in all the States, that the cost of RhIG and its indicated administration to maternity patients is to be paid by HEW for its Medicaid patients, and likewise by Blue Cross, Blue Shield and other medical insurance providers for the maternity patients under their umbrella coverages.

III. SUMMARIZATION STATEMENT (AS APPROVED BY SUMMIT WORKSHOP GROUP AFTER PRESENTATION OF PAPER).

Rh hemolytic disease, which can cause cerebral palsy, deafness, seizures and mental retardation afflicts thousands of infants yearly in

the United States (an estimated 7,000 in 1974). It is quite preventable through the use of Rh immune globulin (RhIG). However, based on proper administration of RhIG to eligible Rh negative mothers, following the delivery of each Rh positive baby, and after each abortion or miscarriage, the utilization rate in the United States is estimated at only 80 percent for term deliveries and 50 percent for abortions.

Consequently there is need to stimulate aggressive State and Federal action in the United States to eliminate Rh hemolytic disease. Carefully organized State monitoring programs, adequately funded, are recommended to assure that indicated utilization of RhIG approaches as close to a goal of 100 percent as possible, both at times of deliveries, and of abortions or miscarriages. The relatively modest cost involved is far less expensive than treating the numbers of children afflicted with the disease. The utilization of RhIG as indicated is now standard medical care and its appropriate administration to maternity patients should be paid by HEW for its Medicaid patients, and likewise by Blue Cross, Blue Shield and other medical insurance providers, for the maternity patients under their umbrella coverages.

IV. SUGGESTED RESOURCES FOR ADDITIONAL INFORMATION

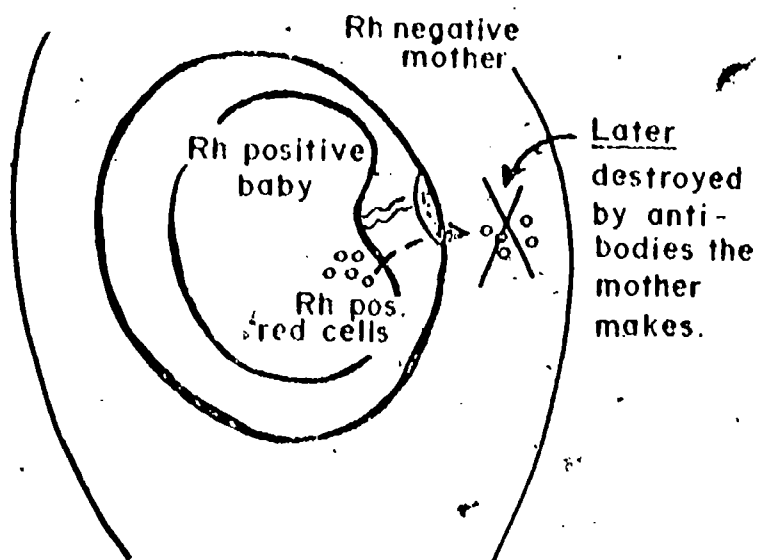
1. Center for Disease Control: Rh Hemolytic Disease Surveillance 1974, Issued August 1976, Atlanta, Georgia.
2. Rh Prophylaxis Program Development Guide 1975, Connecticut State Department of Health, Maternal and Child Health Section, 79 Elm Street, Hartford, Connecticut 06115.
3. Hemolytic Disease of the Fetus and Newborn Due to Rh Isoimmunization, prepared by Jane S. Lin-Fu, M.D., F.A.A.P., Pediatric Consultant, Division of Health Services, Children's Bureau. September, 1968.
4. Gorman, John G., M.B., B.S., (Director Blood Bank, Presbyterian Hospital, New York City): The Role of the Laboratory in Hemolytic Disease of the Newborn, Lea & Febiger, 1975. Philadelphia.

Rh HEMOLYTIC DISEASE

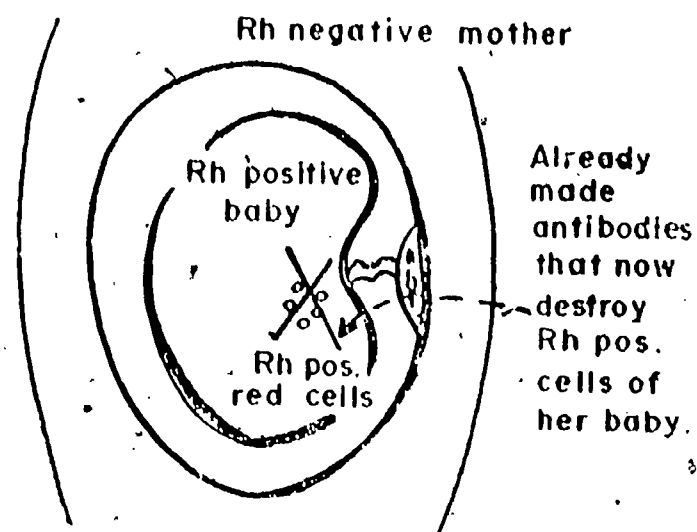
(Diagrams are schematic only)

Likely course without the usage of Rh immune globulin (RhIG) : 1) and 2) *

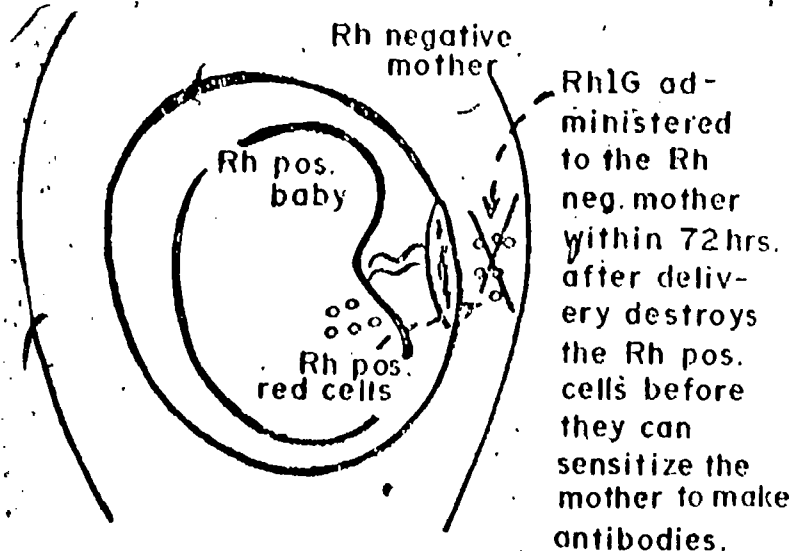
1) First pregnancy - Rh positive baby of an Rh negative mother



2) At a later pregnancy of an Rh positive baby



3) BUT with the usage of RhIG: 3) and 4)



4) The RhIG is administered within 72 hours after delivery. It is important to understand that it is effective only for mothers not previously sensitized. This can have occurred through an earlier delivery of an Rh positive baby or abortion, or through a transfusion of the wrong type of blood.

The RhIG must be administered to the eligible Rh negative mother after each Rh positive baby and after each abortion.

* RhIG is frequently referred to also as "RhoGAM" the trade name of the first manufacturer licensed to produce and distribute it.

Workshop Recommendations

PREVENTING RH HEMOLYTIC DISEASE

LEADER: Robert MacCready, M.D.

RECORDER: Benjamin Saltzman, M.D.

Rh hemolytic disease, which can cause cerebral palsy, deafness, seizures and mental retardation afflicts thousands of infants yearly in the United States (an estimated 7,000 in 1974). It is quite preventable through the use of Rh immune globulin (RhIG). However, based on proper administration of RhIG to eligible Rh negative women following the delivery of each Rh positive baby, the utilization rate is only 80 percent. Also important, based on the administration of RhIG to Rh negative women following an abortion or miscarriage, the estimated utilization rate is no more than 50 percent.

Consequently there is need to stimulate aggressive State and Federal action generally in the United States, to eliminate Rh hemolytic disease. Carefully organized State monitoring programs, adequately funded, are recommended to assure that indicated utilization of RhIG approaches as close to a goal of 100 percent as possible at times of delivery, miscarriage and abortion with nation-wide reporting to CDC. The relatively modest cost involved is far less expensive than treating the potentially large number of children afflicted with the disease. Further, it should be generally agreed and understood in all the States, that the cost of RhIG and its indicated administration to maternity patients be paid by HEW for its Medicaid patients, and likewise by Blue Cross/Blue Shield and other medical insurance providers for the maternity patients under their umbrella coverages.

Discussion

PREVENTING RH HEMOLYTIC DISEASE

COMMENT: I thought we had struck the sentence about Blue Cross/Blue Shield.

DR. SALTZMAN: We didn't get around to striking it.

COMMENT: I don't think we can tell people what to do or that we can tell the government what to make available. Perhaps we should just make a statement that this should be available to people.

DR. COOKE: This is an important point - this whole matter of when you recommend what was a research procedure that has been shown to be highly effective, and when that procedure should become standard practice approved under Medicaid or Blue Cross/Blue Shield. At the present time, this whole activity is extremely capricious. In one State, it is paid for and in another, it isn't. In one State, Blue Cross pays and in another, it doesn't, and the decisions are made by people who do not look at the data in any depth. It seems to me it is necessary for a group such as this to suggest that there be a regularized process for looking at and approving a conversion from what has been research, to innovative practice, and then on to standard practice. I would like to suggest that the mechanism for doing this is a commission that approaches the question from the standpoint of the public, as well as professionals, as well as medical economists, etc. Until there is a regularized process, none of these advances that are obviously of benefit, will be picked up on a regular basis nationally. It is going to be hit or miss, and it may be 10 years before Blue Cross/Blue Shield will pay for that sort of thing in some parts of the country. You can't force them, but when you create such a national trend and the Federal government pays for it in their program, it will be strong encouragement for private payers to go that way, just as they have done in other areas.

DR. ROOS: You have proposed a rather specific strategy or recommendation. I assume this transcends the particular group. It is a general recommendation for the conversion of innovative practices into accepted standard practice for which reimbursement would be made. This seems to be a substantive proposal which warrants further discussion.

DR. MOSER: There wasn't complete agreement in our group about this. I have been told by at least two Blue Cross/Blue Shield representatives that, indeed, they did provide RhIG. When I asked about Medicaid patients, I couldn't get any clear idea, so in New Hampshire, I called up the State office in Concord. The people there all seemed to think it was a good

idea for it to be included, but there seemed to be uncertainty about it, so it made me feel that, perhaps it is not generally done. There seems to be so much variation among the various States. The practice should, at least, be uniform. It is not fair for some hospitals to provide the RhIG because they think they are going to be repaid, while others do not. Maybe we should just state that we feel this is standard medical care, or make a statement that this is a by-product of research that is now standard medical care.

DR. GUTHRIE: Three or four years ago, in the prevention committee of NARC, we decided that there were four topics that deserved priority, as they were non-controversial, all the knowledge was available on causes and methods of prevention and no religious controversy was involved. These were the expansion of lead poisoning testing, the expansion of newborn screening, the expansion of preschool immunizations, and the control of Rh disease. In every one of them, there was enough knowledge that it was just a matter of pushing and expanding. We used the criteria of simplicity, ease of understanding, and lack of controversy to pick those four topics.

DR. COOKE: I suggest that a national commission be established to review in depth, innovative practices prior to their acceptance into standard practices. The benefit to cost ratios as well as value in relation to existing practices would be determined with studies, public hearings, etc. When a practice is judged meritorious, that practice would be considered acceptable for Federal funding under Medicaid and would be urged for funding by private health insurance carriers.

COMMENT: I would think it would be extremely practical and highly effective to do a study on the cost-effectiveness and the value of the RhIG immunization and send it to Medicaid and the various Blue Cross/Blue Shield plans and others, emphasizing that it ought to be specifically reimbursed. In both jobs that I have had, I have seen many people deprived of services because the various plans did not pay. I would make it a strong plea to make this a specific recommendation.

COMMENT: We could do that. It would be easier to determine what the cost would be, which would not be very great, comparatively speaking, but it would be a little difficult to know exactly how much we would save in the cases prevented. In other words, the amount might vary, but I think we could come up with a figure that would be average.

THE FEDERAL ROLES IN PREVENTION OF MENTAL RETARDATION

by

Elizabeth M. Boggs, Ph.D.

Past President of the
National Association for Retarded Citizens

Governmental Affairs Committee
National Association for Retarded Citizens

THE BROAD ROLE

There is and has been for many decades, in fact, for nearly two centuries, a Federal role in the prevention of disease and disability, but the role is changing and multiplying. What are the appropriate roles today, how do they apply to mental retardation, and what can be done to assure that they are implemented? It appears that we need clear consensus on what Congress and the Executive Branch should be doing, and what others, including the voluntary organizations, should be doing.

In broad terms, it would appear that the Federal role in prevention of biomedical disorders generally should subsume the following major activities:

1. Support of basic research in the life sciences, primarily through the National Institutes of Health but also through the National Science Foundation, Veterans' Administration and Department of Defense.
2. Support of applied research, including research in service delivery, together with prompt dissemination of validated research findings from all fields relevant to prevention strategies.
3. Direct intervention, where the "commerce clause" can be invoked, in matters pertaining to public and personal health, and to control of contaminants, toxic substances and communicable diseases.
4. Guidance, technical assistance, and financial aid to States and municipalities in the development of prevention policies and strategies, including drafting of legislation and ordinances.
5. Support for pre-service and continuing education of professionals relative to prevention.
6. Education of the public, particularly target populations such as teenagers, relative to personal practices which increase or decrease the risk of disease and disability in themselves or their children.
7. Designing health care funding and other fiscal mechanisms in such a way as to provide incentives rather than disincentives for practices--professional, industrial and personal--which contribute to prevention.
8. Collection and analysis of consistent data, relevant to policy and planning.

The nature of these eight activities requires a complex organizational structure; the Public Health Service is such a structure. Within the Public Health Service-National Institutes of Health (PHS-NIH) complex, communication, coordination and cooperation are constantly at risk; moreover, despite our self-imposed limitation to "biomedical causes," we here cannot confine our attentions to biomedicine. Even when, as here,

hematologists talk with biochemists and neonatologists, even when sanitarians get the message from the primary investigator, it is not enough. A system is a set of components so linked that when something happens at one point, the effect is felt at other, often distant points; for purposes of prevention of disease of biomedical origin generally, and mental retardation in particular, the "health system" is not a discrete system; it is inevitably strongly linked to other systems, the ecosystem, the social system, the economic system, and with the current value system, including especially our emphasis on individual self-determination, the "right to choose" and the "right to refuse."

THE DIVERSIFIED TARGETS

Everything mentioned above applies to almost any major prevention target, even one which is reasonably well-defined, such as lung cancer. Prevention of mental retardation from biomedical causes, as we all know, is itself a still more complex goal, encompassing a large number of discrete causes only remotely related to one another. Faced with such confusion, it is easy to yield to frustration, easy to talk about "fragmentation" and the need to centralize, easy to rally around the banner of a "mental retardation institute," to advocate reorganization, to say, as President Carter rather foolishly did at the recent White House Conference, that the 100 or so programs for the handicapped should be consolidated in one agency. 1/ It is one thing to have a clearing house and advocacy focal point, such as the President's Committee on Mental Retardation (PCMR), but another to imagine that the prevention of mental retardation, with its multiplicity of causes is an appropriate mission for a single agency.

As Richard Masland said 20 years ago, "Progress in the program for the prevention of mental retardation will take place by small advances along a broad front"; 2/ The specific individual identification of specific causes, the recognition of their different roles in mental retardation, and the development of strategies specific to them is essential; the planners of this conference all recognized this need and reflected it in the agenda. One of our tasks is to identify timely salients. That is what the Government Accounting Office sought to do in part, in its timely report, Preventing Mental Retardation--More Can Be Done. 3/ The

- 1/ Carter, J. (President): Remarks, in White House Conference on Handicapped Individuals, Volume II: Final Report, Part A, pp. 99-102, Washington, D.C., U. S. Government Printing Office, 1977.
- 2/ Masland, R. L., Sarason, S.B., and Gladwin, T.: Mental Subnormality - Biological, Psychological, and Cultural Factors. New York, Basic Books, 1958. p. 28
- 3/ Comptroller General of the United States: Report to the Congress - Preventing Mental Retardation--More Can Be Done. (HRD -7-37). Washington, D.C., Government Accounting Office, 1977.

prevention manuals of the National Association for Retarded Citizens (NARC) and the California Association for the Retarded (CAR) also respond to this model. 4/5/.

Having recognized this structural complexity, we who identify ourselves as the external mental retardation constituency, must, along with PCMR, recognize that, as there are many causes, so there are many focal points towards which our efforts must be orchestrated. Unlike many of our sister voluntary agencies; NARC cannot limit its attention to a single disease oriented institute in NIH. Not only the National Institute of Child Health and Human Development (NICHD) but the institutes concerned respectively with neurology, infectious diseases, and general medical sciences (with its thrusts in genetics) contain loci of high potential for us on the frontiers of new knowledge.

As Dr. Cooke has pointed out on numerous occasions, however, "our" institutes are not the ones dealing in the "dread diseases," the diseases that kill, that visibly invade the halls of Congress. The National Institute of Neurological and Communication Disorders and Stroke (NINCDS), NICHD and the National Institute of Arthritis and Infectious Disease (NIAID) and all running well below the National Institutes of Health (NIH) averages for percent of approved applications actually funded, by numbers and by dollars. Their appropriations have not accelerated in recent years; indeed they have hardly kept pace with inflation, and their percentage of the NIH budget has dropped. They need our consolidated support, concurrently, not as competitors.

Similarly, the findings of the investigators supported by the institutes must be applied in many and sometimes unlikely places. We need lead-free gasolines, as well as hospitals that can detect lead poisoning. We want children immunized against rubella; we want a wider understanding that pregnancy in the young teenager is not merely an embarrassment to her family and perhaps a welcome diversion from school for her, but entails a high risk of long-term disaster for herself, her child and society. We need fungicides that don't put mercury in the food cycle, X-rays that don't add mutations to the gene pool, pregnancies without toxemias, metabolic screening which maximizes efficiency, minimizes false positives and results in effective follow-up. The pressure points for these desiderata are widely dispersed.

But there is also an affirmative side to this diversity, something we have going for us, if we use it. Just as many diverse causes contribute to the functional end product we call mental retardation, so do many of these single causes have multiple outcomes. That which prevents rubella, prevents deafness. That which minimizes Rh factor disease lowers the incidence of cerebral palsy: reduction in the fetal alcohol syndrome is a reduction in birth defects. As we reduce early head trauma or lead

4/ National Association for Retarded Citizens: Prevention Handbook: Arlington, Texas, NARC. No date.

5/ California Association for the Retarded: Prevention: An Agenda for Action. Sacramento, California. CAR, 1977.

poisoning, we will reduce epilepsy. Myelomeningocele is a crippling condition, as well as one that is frequently associated with mental retardation. Out of these specific concurrences, we can develop task oriented alliances - consortia of constituencies, each with a clear common goal and a set of strategies agreed to in common.

I am proud to say that NARC, United Cerebral Palsy (UCP), the National Society for Autistic Children (NSAC), and the Epilepsy Foundation of America (EFA) have formed one such alliance around their common interests in neurological impairments and related research at both NICHD and NINCDS. Recently a 2-day meeting of volunteer and professional leaders of these organizations developed a common agenda, including an objective of increasing appropriations for the two institutes to permit each to fund 80 percent of its approved applications, as compared to 30 percent and 26 percent respectively in 1976. The four organizations will present unified testimony to Congress and each organization has undertaken to prepare a component issue paper. Central to the success of this effort is the recognition by all participants, of substantive commonalities of interest that are not semantically linked to their respective banners.

In the Public Health Services' Forward Plan for Health FY 1978-82 ^{6/} there is a major chapter on prevention. Mental retardation is not mentioned by name (although Down's syndrome is mentioned once in connection with amniocentesis), yet the chapter is replete with priorities confluent with ours, and phrases which anticipate this conference. In the child health area, for example, priorities include decreasing the incidence of disabling conditions, decreasing the rate and adverse consequences of teenage pregnancies, achieving higher immunization levels, and conducting special studies of hyperkinesia. Reduction and control of toxic substances in the environment and reduction of adverse drug reactions also come in for attention. Specific reference is made to the adverse effects of alcohol abuse during pregnancy. Certainly we can also find virtue in Secretary Califano's zeal to discourage smoking, particularly among young mothers.

SPECIFIC STRATEGIES

Among our available strategies, piggy-backing on the agenda of others, with an occasional twitch on the reins, is certainly an acceptable and cost effective one, along with the formation of ad hoc coalitions. I would like to suggest some others:

^{6/} U. S. Public Health Service: Forward Plan for Health - F.Y. 1978-82. DHEW Publication # (OS) 76-50046. Washington, D. C., Department of Health, Education and Welfare, 1976.

1. Enunciate Measurable and Achievable Specific Objectives.

Reduction of mental retardation by 50 percent by the Year 2000 is not such an objective. Aside from Dr. Moser's sobering figures on feasibility (this volume), the fact is, we have no base line for any such broad objective, nor any satisfactory measuring tool or indicator. Moreover, the Year 2000 is too far off. All of us, and that includes Congressmen, like to be reinforced by successes, and most of us can't wait 22 years. Some Federal agencies are suspected of setting as goals a new status which is really the "base case" - that is the state of affairs that would have been achieved naturally without further intervention. I am not suggesting any such strategem, but I am suggesting such things as a 5-year target for reduction of the number of non-immunized school children to a tolerable minimum.

2. Establish Practical and Acceptable Indicators.

An "indicator" is a defined measure capable of being given a numerical value relatively easily, which is used and accepted as a surrogate for some other variable which is harder to measure, but with which it is presumed to be correlated. We are all familiar with economic indicators such as the Dow Jones Industrial Average, or the official poverty level, or cost-of-living index. An example in our field is the infant mortality rate. Reduction in this rate can be regarded as an adequate indicator of our relative success in reducing those forms of mental retardation known to be associated with perinatal hazards and inadequate prenatal care. When he was Director of Maternal and Child Health, Arthur Lesser was successful in using this indicator to persuade both the Budget Office and the Congress to continue support for the maternity and infant care projects. These had been inaugurated to implement the recommendations of President Kennedy's Panel on Mental Retardation (1962) relative to prevention through improved pre- and post-natal care for high risk mothers. The projects were localized and Dr. Lesser could show a significant difference in infant mortality and in spacing of births in the targeted census tracts, as compared to control tracts without projects.

While infant mortality is an adequate indicator for the specific objective of reducing mental retardation among infants of mothers at risk of inadequate care, other indicators will be needed for other component objectives. For example, our knowledge that I.Q. may be an unreliable clinical measure of the potential of an individual should not deter us from using I.Q. data as an indicator which is statistically valid and significant when certain group trends are to be evaluated. Clinicians and epidemiologists alike must recognize that indicators are management tools, not scientific or clinical verities. Laymen and professionals alike should agree on a format for stating the measurable objectives, and persist in unison until each objective is approaching achievement.

3. Establish Good Base Line Data.

This really precedes the indicators. We do not know the incidence of mental retardation: for our purposes it is probably not needed. The incidence of Down's syndrome will vary with the overall distribution of maternal age at birth. In order to monitor causative factors, age specific data should be used and updated. ^{7/} But there is a lot missing. NINCDS recently tried to estimate the extent of the population impacted by disorders in which NINCDS has an interest. The result was an embarrassingly crude aggregate of apples and potatoes. Until we get data such that a proposed objective involves a change of a higher order than the level of uncertainty in the baseline, let's confine ourselves to statements of objectives which do meet this test. This may be a good place to mention mining the collaborative perinatal study data, both for possible baselines and for their heuristic values. ^{8/}

4. Keep Working on "Less Drastic Alternatives."

Fifteen years ago it would have been easy to remain satisfied with exchange transfusion of the newborn as the treatment of choice for Rh disease. But it was heroic, invasive and somewhat risky, justified only by comparison with the risks of no treatment. Today, we have a simpler and safer method which can be made available on any maternity service. As of 1977, the same dilemma applies to Down's syndrome. The route of amniocentesis and abortion is theoretically a "prevention," but in practice, it is, for the patient at least, heroic, invasive and emotionally risky, as well as controversial. A major breakthrough that gets at prevention of Down's syndrome at an earlier stage in the reproductive cycle is a very supportable priority, an understandable objective, and one which, it seems to me, is not unrealistic 20 years after that 47th chromosome was first counted. NICHD has espoused this focus, and should be commended for it.

5. Make Sure that the Low-income Childless Pregnant Woman is Eligible for Prenatal Screening and Care Under Medicaid.

While we are pursuing the Will-o-the-Wisp of National Health Insurance (NHI), we should not delay making some rational changes in Medicaid. In many States, eligibility is still limited to welfare-eligible persons. A single woman, or a couple, without a child, is not eligible even if the income test is met. States may include as welfare eligible, a woman who is pregnant and who, on delivery of a live born baby, would become eligible as an Aid to Families with Dependent Children mother. They may also include as Medicaid-eligible children, those

^{7/} Stein, Z.A. & Susser, M.: Recent Trends in Down's Syndrome, in Mittler, P.: Research to Practice in Mental Retardation, Volume III Biomedical Aspects. Baltimore, Univ. Park Press, 1977.

^{8/} Brohan, S. H., Nichols, P.L., & Kennedy, W.A.: Preschool I.Q. - Prenatal and Early Developmental Correlates. Hillsdale, N.J., Erlbaum, 1975.

children who would be eligible on financial grounds but who are in two parent families. Somewhere in between these options, the low-income primipara falls between the cracks of Medicaid. Unless she is picked up by a maternal and child health project, she may well skimp on prenatal care. I recommend that States be mandated under Title XIX to provide prenatal care and delivery for every income-eligible woman (regardless of marital status) whose infant will become categorically eligible at birth. The virtues of Medicaid coverage are: a) it is open-ended, i.e., if the patient qualifies, the funds are available; b) it is patient-triggered; and c) it will set minimum parameters for NHI.

COMING TO GRIPS WITH A CHANGING VALUE SYSTEM

The strategies, or tactics, just suggested are intended to be practical, even political, and of immediate applicability. However, there are arising new barriers of a more fundamental nature to some of our objectives. We live in an era when patients have newly enunciated rights, and professional motives are suspect. These issues go far beyond the protection of human subjects in research or the future consequences of new technologies. They reach to the heart of issues that are on the front burner today, and which affect our strategies for prevention.

Karen Davis, a well-known health economist, who is currently Deputy Assistant Secretary for Planning and Evaluation - Health, in HEW, said recently that three factors - genetics, environment and personal life style, have more to do with the Nation's health than all the dollars spent on the delivery of health care to the ailing. ^{9/} These three factors are certainly prominent in our deliberations at this conference. They are also all factors around which value-based controversies are swirling. Who chooses what life style? What are society's rights and responsibilities versus those of the individual? Does a family have a right not to know about a genetic trait? Does a physician really have a right to withhold information? Who is responsible for mercury in the river or for PBB in the milk? What about a treatment, such as radiation, believed therapeutic at the time but later found teratogenic?

We are increasingly finding paradoxes and conflicts stemming from our ideas of individual liberty on the one hand and our sense that there is no freedom to negligently impose a handicap on an individual or to aggravate the burden of handicap on society, on the other. Along with a right to treatment, there arises the right to refuse treatment. If one refuses treatment, what obligation remains with society to assist the individual to meet the consequences? Should national health insurance cover an individual for the costs of treating a condition which he could have prevented? Above all, these questions become fraught with emotion and

^{9/} Davis, K.: in a symposium on "Health and Welfare: The Evolution of National Health Policy", at Round Table Conference, American Public Welfare Association, December 6, 1977.

paradox when we are dealing with persons such as infants, or with fetuses, who are not in a position to exercise their own choice and to give any kind of consent. If surrogates are liable, will not many decisions go by default, including decisions with implications for prevention?

We should all be grateful to Dr. Cooke and the Kennedy Foundation and the Hastings Center for fostering interdisciplinary debate on some of these issues. We also welcome the recent publication of a compendium of seminal documents on this topic by Reiser, Dyck and Curran, 10/ as well as Dr. Milunsky's book on genetics and the law. 11/ But as yet these treatises are read, and the debates are conducted primarily in academic circles.

The Executive Branch of the Federal government is clearly "in the middle" on these matters - in the middle of a debate which is anything but academic. It is clearly not its role to tell the American people what ethical, moral or legal standards to follow. Its regulation writing is pursuant to directives of Congress and the Courts. Right now, it is desperately seeking guidance as to likely real life consequences of alternative ways of approaching the "hot potatoes". Congress is handing out, and which exemplify some of those "academic" issues. We are all painfully aware of the Medicaid abortion issue (recently debated so publicly in Congress) with its direct implications for several of the specific targets of prevention which are being discussed at this conference. In December, 1977, HEW issued proposed regulations which would continue the moratorium on HEW funding for sterilizations as a form of contraception for all persons under 21 years and for mentally incompetent persons, thus denying mentally retarded adults an option open to others. This is but one application and interpretation of the complex "consent issue", about which the American Association on Mental Deficiency has recently issued a unique monograph. 12/

Abuses of persons unable to speak up for themselves, children, the institutionalized, the "mentally infirm", have caused a backlash which is threatening the right of retarded persons to receive novel treatments available to those who can give informed and voluntary consent. Even if theoretically available, surrogate decisions are now being hedged about with such elaborate procedures as to make them practically unavailable. Similarly, it is seriously proposed that each person who is screened in what is designed as a mass genetic or metabolic screening program must give (or withhold) individual informed consent, with such consent explicitly dealing with the issue of what portion of the findings will be later imparted to the screenee. 13/

10/ Reiser, S.J., Dyck, A., and Curran, W.J. (eds.): Ethics in Medicine Historical Perspectives and Contemporary Concerns. Cambridge, Mass. MIT Press, 1977.

11/ Milunsky, A. and Annas, G.J. (eds.): Genetics and the Law. New York, Plenum Press, 1975.

12/ Turnbull, H.R., (ed.): Consent Handbook. Washington, D.C., American Association on Mental Deficiency, 1977.

13/ Committee for the Study of Inborn Errors of Metabolism: Genetic Screening: Programs, Principles and Research. Washington, D.C., National Academy of Science. 1975

If these issues are not to paralyze public agencies with their paradoxes, and if decisions made in view of the "big picture" are to be compatible with the true rights and interests of the small inarticulate minorities of the atypical, it is essential that the various constituencies interested in the mentally retarded work for greater participation in the timely generation of consensual positions. The need is urgent for the development of policies against which pragmatic decisions can be tested. The Legal Advocacy and Research Committee of NARC underwent an intensive year-long examination of the issues around the participation of mentally retarded subjects in research and the Legislative and Social Issues Committee of AAMD spent several years hammering out a series of policy statements, including one on sterilization, as a way of explicating the UN Declaration on General and Special Rights of the Mentally Retarded in terms of highly topical issues in the United States. The writing of the Consent Handbook took a year and changed in some measure, the views of everyone who participated, whether attorney, physician, social worker, psychologist or parent. But, to paraphrase GAO, more can be done! "Feds" can play a supportive role, but initiative must also come from without.

One way to accelerate the consolidation of opinion is to involve people in particular projects, to invite them to participate in a heterogeneous group decision-making process. For this reason, I would like to suggest several examples of specific activities which, I believe, would break down some of the road blocks which threaten efforts to prevent one or another type of mental retardation.

1. Enlist Young People in Activities and Issues which Pertain to Youth Behavior.

There is some evidence that, in situations where young people are oblivious to, or even challenged by risks to themselves, they may be more prudent if they perceive that they are placing someone else at risk. This is the message behind a Youth-NARC flyer captioned, "Your head is your own thing, but... Don't blow your KID's mind. 14/ If the risks inherent in very youthful pregnancies were better understood within the peer group, perhaps some danger could be put upon the rising number of pregnancies among girls under seventeen. 15/ More social research should be supported in this area, since there are observers who feel that some of these girls are alienated beyond reach, that having a baby is something they see as attention-getting or even emancipating, more than as an inadvertent risk of a sexual encounter. Be that as it may, the public at large, and teenagers in particular, are not fully aware of the growth retardation in the mothers and the great risk to the infants. We can do more to involve youth in formulating its own values in this area. 16/

14/ Youth ARC: Your Head Is Your Own Thing, But... Don't Blow Your Kid's Mind. Arlington, Texas, undated pamphlet.

15/ Venturá, S.J.: Teenage Childbearing: United States, 1966-75. Monthly Vital Statistics Report 26: #5, (9.8.77)

16/ McCoy, K.: Adolescent Sexuality: A National Concern - Report on the Wingspread Conference on Adolescent Sexuality and Health Care. J. Clinical Child Psychology. III #3, 1974

2. Make EPDST, Alias Child Health Assessment Program (CHAP) Really Work for the Potentially Retarded Child.

It is now more than 10 years since Congress required the respective States to offer to all Medicaid eligible children, early and periodic screening and diagnosis "to ascertain their physical and mental defects," together with treatment to ameliorate the conditions found. Although the State must offer the service, acceptance is optional with the client. In 1977, the Carter Administration proposed a modification of the law designed to bring greater involvement of the practicing pediatrician and to make assessments more "comprehensive." This is known as the "Child Health Assessment Program" or CHAP. The proposed law originally had a provision which would mandate followup treatment for disabling conditions other than mental and developmental disabilities, a discrimination against the retarded and others, which was vigorously protested. This, however, is not the most invidious discrimination in the program. The problem with which those interested in prevention should be most concerned arose in implementing the original law, still in effect at this writing. It is that the guidelines provided to the States are not really designed to identify evidence of incipient mental retardation or its precursors. States have had for several years, good guidelines for dental problems and iron deficiency anemias and checks on the booster shots, but not for delayed speech, abnormal reflexes or signs of poor sensori-motor integration.

The Medicaid agency commissioned the American Academy of Pediatrics to develop a guide to screening, ^{17/} but, under the supposition that "developmental screening" was a mental health problem, it also commissioned a professional organization in that field to produce the "developmental" guide. The society, in turn, operated on two apparent assumptions:

a) Their task was to develop an interview schedule for use with the parent, which would sensitively probe the mother-child interaction; b) any child identified as a "positive" in the screen was at great risk of being indelibly labeled with a pejorative brand. There was even some intimation that the whole thing was a plot against the poor. (California dealt with that by making their EPSDT programs applicable to all children under six, with third party payments being collected to cover the costs for the non-Medicaid eligible.)

The people who opposed this sabotage of EPSDT were not the pediatricians or the mental retardation professionals but the voluntary groups - the National Society for Autistic Children (NSAC), NARC and United Cerebral Palsy Association (UCPA). Finally, in April 1977, a small

^{17/} Frankenburg, W.K., & North, F.A.: A Guide to Screening for the Early and Periodic Screening Diagnosis and Treatment Program (EPSDT) Under Medicaid. Washington, D.C., Department of Health, Education and Welfare, 1974.

monograph appeared produced under different auspices, reflecting an approach which can be more productive in prevention of mental retardation and other disorders characterized by developmental delay in infancy. The result was a more balanced approach, albeit one still lacking in sufficient specificity to get the job done:

"A mass, government financed screening program should be limited to:

1) Those measures of organic functioning and basic, adaptive coping skills which enjoy a high degree of consensus within the health professions and affected communities; and 2) those behavioral factors especially associated with learning, language and speech development, motor skills and perceptual abilities. Specific assessment of emotional and behavioral adjustment and parent/child interactions should be left to parental initiative and sensitive clinical observations." 18/

Our Canadian friends, being ahead of us in National Health Insurance, also have a more comprehensive recommendation: this one is in language of a recent conference in Toronto:

"Universal development assessment: In order to ensure that each child reaches maturity functioning at a maximum level of development, there should be a national policy of universal, periodic, comprehensive, developmental review from birth to 18 years. This should identify strengths and competencies as well as weaknesses and defects. Parental involvement is mandatory, and there must be provision for follow-through of recommended procedures with some accountability." 19/

3. Work to Remove the Stigma from "Hereditary" or Genetic Disorders.

The self help groups which have grown up around Tay-Sachs disease, Huntington's disease, Cooley's anemia, Sickle Cell anemia and the like suggest that many affected persons, once they understand the mechanisms, are able to surmount any sense of stigma. However, there have been a number of incidents in which lawyers and others have used the "right to privacy" and related doctrines to impede genetic screening activities on the grounds that persons who are identified as either phenotypes or

18/ American Association of Psychiatric Services for Children, Inc.: Developmental Review in the Early and Periodic Screening, Diagnosis and Treatment Program - Final Report - April, 1977. p. 33. DHEW Publication #HCFA 77-24587. Washington, D.C. DHEW 1977.

19/ Trainor, D.: New Needs Seen For Child MR For Future: Psychiatric News, January 6, 1978. p. 43.

carriers are damaged by stigmatization. This is also a variant of the "labeling" issue. Although this is a broad and less specific strategy, it is, at the same time, one in which there are many allies, actual and potential. Dr. Milunsky's new book should help. 20/

4. Promote Development of a Rational Policy on Confidentiality of Patient Records.

The barriers now being put up to inhibit linkages of records not only interfere with longitudinal research important to prevention strategies and the development of good baseline data, they also can work against the interests of the individuals they are designed to protect, particularly the mentally impaired. More reality-oriented debate among "consumers", parents, professionals and attorneys is needed.

SUMMARY

The prevention of mental retardation requires that many targets be attacked concurrently, using different strategies. 21/ For each, clear objectives should be established, specific coalitions mobilized, progress charted and successes proclaimed. On a longer time line, attention should be directed toward resolving, at least in practice, the bioethical and medico-ethical dilemmas which presently stall, or threaten to stall actions relevant to prevention, using presently known or future techniques. In both these thrusts, there are many Federal roles; each of these roles requires nationally mobilized coherent and sustained reinforcement from without.

20/ Milunsky, A.: Know Your Genes. Boston, Houghton Mifflin, 1977.

21/ Clarke, A.D.B. and Clarke, A.M.: Prospects for Prevention and Amelioration of Mental Retardation: A Guest Editorial. American Journal of Mental Deficiency. 81:523-533, 1977.

NUTRITION, BRAIN GROWTH AND PREVENTION
OF MENTAL RETARDATION

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INTRODUCTION

Undernutrition is a major associated cause of infant morbidity and mortality in developing countries. In these nations, poor living conditions, low income, inadequate parental education and a limited supply of food are the obvious determinants of this condition. The vast majority of the U. S. population is not afflicted with these problems. Yet, in the pockets of poverty of the inner cities and some rural communities, there are still children and adults affected by malnutrition. In contrast to the developing countries, the problem of poverty in the U. S. is not entirely an economic one. Cultural and sociological factors are likely to play an important role. In both cases, however, regardless of their different causes, the ultimate results in the children are similar: stunted growth, higher morbidity and environmental deprivation.

In recent years, researchers have become aware that the combination of inadequate food intake and deprived family environment has a devastating effect, not only on the physical growth of a child, but also on his intellectual development.

The establishment of a truly causal relationship between undernutrition and deficient mental function, however, is a very difficult task, and it is only in the last five years that some of the mechanisms involved have begun to be understood.

UNDERNUTRITION AND BRAIN GROWTH

Experiments done in rats have demonstrated that when undernutrition is imposed during the proliferative phase of growth, the rate of cell division is slowed and the ultimate number of cells of every organ, including the brain, is reduced. ^{1/} This change is permanent and can not be reversed once the normal time for cell division has passed. In contrast, undernutrition imposed during the period of hypertrophic growth will curtail the cellular enlargement, but on subsequent rehabilitation, the cells will regain their normal size. These experiments have shown that total brain cell number can be permanently reduced by 15-20 percent when the rat is undernourished throughout the entire period of lactation. No matter what feeding regimen is attempted thereafter, this reduction in cell number persists. Also in the rat, it is possible to retard fetal growth by restricting food intake or the percentage of protein in the maternal diet. In this species, fetal growth retardation first becomes apparent at 15 days of gestation (length of gestation is 21 days). ^{2/ 3/}

- ^{1/} Winick, M. and Noble, A.: Cellular response in rats during malnutrition at various ages. *J. Nutr.* 89:300, 1966.
- ^{2/} Winick, M.: Cellular growth of the placenta as an indicator of abnormal fetal growth. In Adamson K. (ed.): *Diagnosis and treatment of fetal disorders.* New York, Springer-Verlag, 1969 p. 83.
- ^{3/} Zamenhoff, S., vanMarthens, E. and Margolis, F.L. DNA (cell number) and protein in neonatal brain alteration by maternal dietary protein restriction. *Science* 160:322, 1968.

After that, there is a progressive decrease in cell number in all organs. The reduction in brain cell number is proportional to the reduction in the number of cells in the other organs. By term, brain cell number is only 85 percent of normal. These findings demonstrate that the magnitude of the effect of undernutrition depends largely on the rate of cell division. Moreover, they demonstrate that the maternal placental barrier in the rat is not effective in protecting the fetal brain from discrete cellular effects caused by maternal food restriction.

The effects on the brain of the exposure to postnatal undernutrition of pups undernourished in utero are extreme. As previously mentioned, rats subjected to prenatal undernutrition alone showed a 15 percent reduction in total brain cell number at birth. Rats subjected to postnatal undernutrition alone showed a reduction of 15 to 20 percent of their brain cells by weaning. However, when the pups were restricted both prenatally and postnatally, cell number showed a 60 percent reduction. These data demonstrate that undernutrition applied constantly throughout the entire period of brain cell proliferation will result in a profound reduction in brain cell number, greater than the sum of effects produced during various parts of the proliferative phase. It appears that the duration of undernutrition as well as the severity during this early critical period is extremely important in determining the ultimate cellular make-up of the brain.

Deficiencies in specific nutrients such as Vitamins A, B6, Folic Acid, Zinc and Magnesium may also affect fetal development. Experiments in rats have demonstrated that when these deficiencies are imposed during early pregnancy, almost all fetuses are malformed and the malformations involve, among other tissues, those of the nervous system. 4/

In the human brain, there is a type of response to undernutrition similar to that which has been described in lower animals. During proliferative growth, cell division is curtailed; during hypertrophic growth, the normal enlargement of cells is prevented. 5/ In the brains of infants who died of undernutrition during the first year of life, wet weight, dry weight, total protein, total RNA, total cholesterol, total phospholipid, and total DNA content were proportionally reduced. 6/ Thus, the rate of DNA

4/ Giroud, A.: Nutrition of the Embryo. Fed. Proc. 27:163, 1968.

5/ Winick, M., Rosso, P. and Waterlow, J.: Cellular Growth of Cerebrum, Cerebellum and Brain Stem in Normal and Marasmic Children. Exptl. Neurol. 26:393, 1970.

6/ Rosso, P., Hormazabal, J. and Winick, M.: Changes in brain weight, Cholesterol, Phospholipid and DNA content in marasmic children. Am J. Clin Nutr. 23:1275, 1970.

synthesis slowed and cell division was curtailed, reducing the number of cells. Since the reduction in the other elements was proportional to the reduction in DNA content, the ratios were unchanged and the size of cells, as well as the lipid or RNA content of the individual cell was not altered. If the undernutrition persists beyond about 8 months of age, not only the number of cells, but also their size is reduced. In addition, the lipid per cell is also reduced. ^{6/} Total cholesterol or phospholipid content is reduced; hence the number and/or length of myelin sheaths is reduced. But because both phospholipid and cholesterol concentration are unaffected, the thickness of those myelin sheaths that are present is unaffected. One could then argue that the major effect of undernutrition is to interfere with cellular growth. During the first 8 months of life, this interference would reduce the number of glia (specifically oligodendroglia) and myelination would be proportionally reduced. Continued undernutrition would reduce cell size. In neurons, this would probably be associated with a reduction in the number of length of processes, and myelination would be proportionally curtailed. However, the deposition of myelin around those processes which are present and which do not grow, proceeds normally.

Recently, it has been shown that galactoside concentration is reduced in the brains of human infants who died of severe undernutrition. ^{7/} This would indicate that early undernutrition will selectively reduce the concentration of certain gangliosides. If ganglioside concentration reflects the number of dendrite arborizations, then the process of dendritic branching may be retarded by early undernutrition.

It now seems clear that early undernutrition will affect both cell division and myelination in the developing human brain. It would appear that the vulnerable periods coincide with the maximum rate of synthesis of DNA and of myelin. All brain regions seem to be vulnerable, but their vulnerability will vary, depending on the timing at which the maximum rate of synthesis of DNA in the particular region takes place. All neural cell types so far studied are affected by undernutrition if they are dividing at the time that the insult occurs. Finally, there would be a selective reduction in the number of dendritic arborizations subjected to early undernutrition.

The effects of prenatal stimuli on the cellular growth of the fetus are more difficult to assess. Indirect evidence suggests that cell division in the human fetus may be inhibited by maternal undernutrition, so that fetal growth is retarded and birth weight reduced. From available information on infants who died after exposure to severe postnatal undernutrition, three patterns emerge. Breast-fed infants malnourished

^{6/} Ibid. p.

^{7/} Dickerson, J.: Personal Communication.

during the second year of life have a reduced protein/DNA ratio but a normal brain DNA content. Full-term infants who died of severe food deprivation during the first year of life have a 15 to 20 percent reduction in total brain cell number. Infants weighing 2000 gm or less at birth who died of severe undernutrition during the first year of life have a 60 percent reduction in total brain cell number.^{8/} It is possible that the children in this last category were deprived in utero and represent a clinical counterpart of the "doubly deprived" animal. It is also possible that these were true premature infants and that the premature is much more susceptible to postnatal undernutrition than the full-term infant.

UNDERNUTRITION AND MENTAL DEVELOPMENT

Investigators in several countries have tried to examine the effects of undernutrition early in life on subsequent mental capacity and behavior. Most of these studies have focused on measuring intelligence because testing procedures are readily available and because the demonstration of persistent intellectual deficits would have immediate social impact.

The problem, however, remains unsolved because a number of theoretical and methodological issues make the clarification of the relationships between malnutrition and mental functioning extremely difficult. These are: 1) Lack of precision in the definition of nutrition. In studies of malnutrition and mental functioning, there is a tendency to overlook the fact that the term, undernutrition may cover deficits in one or more nutrients. In addition, the age at which the subject is deprived of food intake, the severity, the repetition of the food deprivation and the concomitance of the episode with other deprivations of a non-nutrition character, all distort the picture of psychological functioning. 2) Occurrence of undernutrition within the context of massive deprivation. In most instances, the specific effects of undernutrition on brain development in humans are inseparable from the environmental. Adequate nutrition generally is part of a good environment and undernutrition occurs primarily within poor environments in which many other forces may also limit the individual development. 3) Lack of precision in the measurement of psychological deficits. This lack of precision is derived from two main sources. On the one hand, it is probable that undernutrition affects differentially several areas of psychological function. Furthermore, whichever the areas affected, and whichever the areas that are taken into consideration, the actual measurement of psychological function is extremely difficult.

In spite of the methodological problems discussed above, the several studies done throughout the world suggest that early undernutrition in a deprived environment interferes with subsequent learning ability. Among

^{8/} Winick, M. and Rosso, P. The Effect of Severe Early Malnutrition on Cellular Growth of the Human Brain. *Pediat. Res.* 3:181, 1969.

poor children, the better nourished, taller ones generally score higher in I.Q. tests than the previously undernourished, shorter children. The lowest I.Q.'s are usually associated with the poorest prior nutritional status. 9/ It is not clear, however, to what extent the reduced I.Q. is a result of the episode of nutrition and to what extent it is due to other factors. The problem of finding an adequate control population is not easily solved by matching socio-economic backgrounds. In a study done in Jamaica, siblings without a history of hospitalization for undernutrition were used as a control group for those who had such a history, and it was found that the undernourished group reached the same height, weight and I.Q. score as the control group. 10/ In this study, the control children probably also were undernourished, subclinically, if not clinically. Both groups of children had poor growth and development compared to generally accepted Jamaican norms. In populations of uniform socio-economic backgrounds in Mexico and Guatemala, performance on psychological tests was found to be related to dietary practice and not to differences in personal hygiene, housing, cash income, crop income, proportion of income spent on food, parental education, or other social or economic indicators. 10/ 11/ Moreover, performance of both preschool and school children on the Terman-Merrill, Gesell and Goodenough Draw-A-Man tests was positively correlated with body weights and heights. Since the shorter children did not come from families significantly lower in socio-economic status, housing and parental education than those of the taller children, it was concluded that the most important variable reflected by the short stature was poor nutrition during early life, and that this also led to the lag in development of sensory integrative competence. The exact time span when undernutrition has the most serious effect on the brain is not yet known. In the Jamaican study mentioned above, for example, all of the children undernourished at any time during the first two years of life had significant behavioral abnormalities at school age.

The possible harmful effect of prenatal malnutrition on brain growth and subsequent mental capacity has been the focus of numerous studies. This is an extremely difficult task because of the influence of postnatal factors. Women that are malnourished during pregnancy are generally poor and, in many cases, likely to offer their children an environment that is also emotionally and intellectually deprived. A deprived environment is known to have a negative effect on mental development.

- 9/ Winick, M. and Rosso, P. The Effect of Severe Early Malnutrition on Cellular Growth of the Human Brain. *Pediat. Res.* 3:181, 1969.
- 10/ Hertzog, M.E., Birch, H.G., Richardson, S.A. and Tyzard, J.: Intellectual Levels of School Children Severely Malnourished during the first two years of life. *Pediatrics* 49:814, 1972.
- 11/ Cravioto, J., Espinoza, C.G. and Birch, H.G.: Early Malnutrition and Auditory-Visual Integration in School Age Children. *J. Special Ed.* 2:75, 1967.

Some of the postnatal environment variables that can negatively affect development were not present in the majority of the Dutch population exposed to famine in 1944-45. This fact made the Dutch famine a unique source of information. Using data collected in the 18 year old male population at the time of military induction, it was possible to establish that the subjects presumably exposed to famine were similar to those not exposed, in terms of physical growth and mental capacity. Except for the higher neonatal mortality in this group, there were no indications that other factors may have created a selective process by which only the less affected individuals reached military induction. ^{12/} Unfortunately, there are no behavioral data on these individuals. Although the background data do not suggest the possibility of any serious behavioral problems, they do not rule out the possibility that famine may have induced changes in this area. As will be discussed later, the most striking differences between prenatally malnourished and control rats are behavioral, rather than performance ones.

Again, it must be emphasized that the implications of prenatal under-nutrition in a baby born in the low socio-economic group of a developing country probably differs from that of the Dutch situation. In Holland, a previously well-nourished population was acutely undernourished for a brief period of time and then allowed to eat again ad libitum and to re-establish for the surviving babies, the stimulating environment of a highly educated and technological society. In the low income groups of the less industrialized nations, a baby born with a similar deficit in brain growth is likely to suffer a superimposed deficit caused by postnatal undernutrition and the negative influences of a deprived environment.

The only nutrition intervention study presently available, in which the effect of nutrient supplementation on maternal nutritional status and the central nervous system were determined, was carried out in a group of low-income, black women in Philadelphia. ^{13/} The subjects were randomly assigned to two groups, one of which was provided with a protein-mineral supplement from the time of enrollment, before the 28th week of gestation, until term. The babies were assessed on the third day of life, using Brazelton Neonatal Behavioral Assessment measures. Two significant relationships were found with the nutrition intervention, and none with the variables considered most important developmentally. As discussed before, however, it is unlikely that these women suffered from undernutrition during pregnancy since both controls and supplemented groups had a similar rate of weight gain. Further, since tests were performed during the newborn period, it may be premature to consider the results as final ones.

^{12/} Stein, Z., Susser, M., Saenger, G. and Maroila, F.: Famine and Human Development, Oxford University Press, New York, 1975.

^{13/} Osofsky, H. J.: Relationships Between Nutrition During Pregnancy and Subsequent Infant and Child Development. Obstet Gynec Survey 30:227, 1975

In contrast with the previous study, an observational prospective study, part of the "Collaborative Perinatal Study" of the National Institute of Neurological Diseases and Stroke, found an inverse correlation between the percentage of infants with abnormal physical and mental development at one year of age and maternal weight gain during pregnancy. ^{14/} The population included in this study was largely urban and from a low socio-economic strata. Although the differences between groups are highly significant, they cannot be accepted as proof that nutritional inadequacies during pregnancy are recognizable by the retarded physical and mental development observed. It is conceivable that women that failed to gain adequate weight were also less likely to provide after birth, the environment conducive to optimal development of the infants. Thus, the lower performances may reflect postnatal rather than prenatal events.

Women that fail to gain an appropriate quantity of weight during pregnancy are not the only group at risk. There is evidence that ketonemia during prolonged periods of gestation, for example, obese women losing weight, may affect psychomotor development in their offspring. ^{15/} Although these studies have been interpreted as an indication that ketone bodies per se may have a harmful effect, it is conceivable that other associated factors may also play a role. For example, besides ketonemia, a fasting woman is likely to have marked changes in the plasma concentration of amino acids and lower levels of glycemia.

As previously mentioned, maternal undernutrition is associated with a higher incidence of low birth weight infants. Many studies have shown that low birth weight is antecedent of reduced mental competence, and that the lower the birth weight, the greater the subsequent deficit in mental capacity. ^{16/17/18/} In babies with birth weight under 1,500 grams, it is conceivable that perinatal complications resulting in brain damage, such as hypoxia or hypoglycemia play a role in their later lower performances. This possibility is supported by the fact that this group also has the highest incidence of cerebral palsy and other neurological sequelae. In babies with more moderate reductions in birth weight, the situation is less clear. Two groups of babies can be found in these categories, namely prematures and infants small-for-gestational age. The premature group is more susceptible to perinatal complications associated with subsequent neurological abnormalities, and therefore their subsequent lower mental capacity may reflect perinatal injuries. In contrast, the small-for-gestational age babies are less afflicted by perinatal complications, thus, their subsequent lower mental capacity may preferentially reflect prenatal events. A recent prospective study has shown that cerebral palsy is

^{16/} Benton, A.L.: Mental Development of Prematurely Born Children: A Critical Review of the Literature. Amer J Orthopsychiatry, 10:719, 1940

^{17/} Drillien, C.M.: The Small-for-Date Infant: Etiology and Prognosis. Pediat Clin North Am. 17:9, 1970

^{18/} Wiener, G.: The Relationship of Birthweight and Length of Gestation to Intellectual Development at Ages 8 to 10 Years. J of Pediat. 76:694, 1970.

uncommon in this group but there is a high incidence of minimal brain dysfunction characterized by hyperactivity, a short attention span, poor fine coordination and hyper-reflexia. 19/ The average I.Q. is lower than that of the general population, and their school performance is poor.

REHABILITATION FROM UNDERNUTRITION

Studies on non-deprived populations strongly suggest that early under-nutrition may retard development temporarily, but that recovery is possible, given the proper subsequent environment. Studies have been done, in which an attempt is made to enrich the environment of children who have been undernourished as infants. Generally children from a low socio-economic class have been randomly assigned to either a treatment or a control group. The treatment group receives a variety of special care and instruction, through home visits and day care center experience. The results, in general, have shown that the "stimulated children" develop better and show a higher I.Q. at the end of the experiences.

In order to examine the effects of "environmental enrichment" on the development of undernourished children, three groups of Korean children, some of whom had been severely undernourished during the first year of life, and who had then been adopted by families in the United States, has been studied. 20/ All of the infants were adopted before their second birthday, with all the adoptions being entirely by random on a first come, first served basis. The foster parents had no idea of a child's previous nutritional history. All of the families were carefully screened to ensure an adequate home environment for the adopted child. Questionnaires were sent to all of the families and records were obtained from the schools the children were attending. Their ages at the time of follow-up ranged from 7 to 16 years. Intelligence tests were administered by the schools. Achievement, based on a number of other test scores which were available, was evaluated by two psychologists who had no prior knowledge of the children's history.

At the time these children reached seven years of age, there were no differences in average weight among the three groups. All had reached normal by Korean standards. Changes in height were similar to those in weight, except that the undernourished children remained slightly, but significantly smaller.

The mean I.Q. of the previously undernourished groups was 102.05. The marginally nourished children achieved a mean I.Q. of 105.95. This is not a statistically significant difference. By contrast, the previously

19/ Fitzhardinge, P.M. and Stevens, E.M.: The Small-for-Date Infant. II Neurological and Intellectual Sequelae. Pediatrics 50:50, 1972.

20/ Winick, M., Meyer, K.K. and Harris, R.: Malnutrition and Environmental Enrichment by Early Adoption. Science 190:1173, 1975.

well-nourished children reached a mean I.Q. of 111.68, which does represent a significant difference from the undernourished children. When achievement in these three groups was compared, the results were similar. Both the severely undernourished and the marginally undernourished children were achieving exactly at expected norms for American children of the same age and grade. The previously well-nourished children were achieving slightly, but significantly better.

These findings show that severely undernourished children, when reared in a middle-class environment before their second birthday, can catch up in height and weight and reach an I.Q. and school achievement level which is perfectly normal for well-nourished children raised in an industrialized nation. They demonstrate in this unique population, exactly what has been shown in animal studies, that environmental stimulation will reverse many, if not all of the behavioral deficits elicited by early undernutrition. The data also suggest that when well-nourished children are placed in this more stimulating environment, they do even better. Their I.Q. scores and achievement scores are not only higher than those of the undernourished children, but also are higher than the norms for American children in general. From a practical standpoint, the importance of this study lies in its pointing out the reversibility of effects of early undernutrition. In all previous studies, when the child was returned to his or her previous environment, the I.Q. was 70 or below at school age.

In the previous studies when children were reared in a poor socio-economic environment, even those who were adequately nourished and used as controls reached a maximum I.Q. of 82. The undernourished children averaged about 10 points lower. Thus the difference between the undernourished and the well-nourished children is similar in this study to the previous studies. All of the children simply do better.

In a prospective study in Colombia, severely undernourished children after recovery have been placed in an "enriched" environment at about two years of age. ^{21/} The children are exposed to all types of stimulating experiences in terms of both play and learning. Their nutrition has been kept adequate. These children are being compared with randomly picked similarly undernourished children who were not placed in this program and with and with previously well-nourished children of higher socio-economic class both in and out of the program. The results suggest that stimulation will improve the learning of these children. The test levels of the stimulated undernourished children were higher than those of the non-stimulated undernourished children and approached those of the children from the

^{21/} McKay, H., McKay, A. and Sinisterra, L.: Intellectual Development of Preschool Children in Programs of Stimulation and Nutritional Supplementation, in Symposia of the Swedish Nutrition Foundation XIII, Early Malnutrition and Mental Development, Cravioto, J., Hambræns, L. and Vahlquist, B. (eds), Uppsala, Almqvist and Wiksell, 1974, p. 226.

higher socio-economic group who were not stimulated. The well-nourished, stimulated children had the highest learning capacity but as the study progresses their lead is shortening.

A final group of studies of human populations, has focused on improvement in the nutrition of pregnant women and young infants. The basic design of these studies involves comparing a population undergoing severe under-nutrition with a similar population that is given nutritional supplements. ^{22/} After a given period of time the results are evaluated in terms of whatever outcome measures the investigators choose. Not only are such studies technically difficult to carry out, but they also involve ethical problems, especially with regard to the non-intervention groups. For these reasons only a few have been performed and these under conditions and in populations that have been carefully selected. One study is being done in three rural Guatemalan villages. One village receives a food supplement in the form of a high protein supplement drink that is consumed by the young children and the pregnant mothers. A second village is supplied with a supplement of some caloric value but no protein content. Both villages are given medical care. The third village receives medical care only. Preliminary results show that growth rates are increased in the children receiving the high-protein supplement. Moreover, the women who get a protein supplement during pregnancy have babies whose birth weight is significantly higher than those of babies born in the non-supplemented village. Finally it would appear that the development of the children is better in the protein supplemented village than in the other villages.

In another study in Formosa, supplementation of mothers' diets after they have had a baby and throughout their next pregnancy has significantly increased the birth weight of the second infant. In a small study in rural Mexico, food supplements have been given to children of families carefully selected to represent the norms of their community. When the growth rate of the supplemented children was compared with that of their previously studied, unsupplemented siblings, a marked increase was observed. The supplemented children also demonstrated marked superiority in physical strength, independence, attentiveness and ability to perform certain behavior tests. They tended to explore their environment more thoroughly, play with toys more frequently and interact with adults better than the non-supplemented children. It must be emphasized that the children in this study who did not receive the supplement were picked because they were undernourished.

^{22/} Halicht, J. P., Yarbrough, C., Lechtig, A. and Klein, R.E.: Relation of Maternal Supplementary Feeding during Pregnancy to Birthweight and other Sociobiological Factors. In Winick, M. (ed) Nutrition and Fetal Development, John Wiley & Sons, New York, 1974, p. 127.

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The sparse information that is available from intervention studies, then, would suggest that improvement in the diet during either pregnancy or early life will significantly alter birth weight, subsequent growth rate, and subsequent mental capacity.

Prevention of the problem should be directed, therefore, to comprehensive prenatal care and programs that tend to provide adequate nutrition together with an environment conducive to the adequate development of the genetic potential of the individual.

More specifically the following recommendations should be considered:

A. Prenatal Undernutrition

Our task under these conditions would be to identify those women at risk and to verify criteria for including women in a food supplementation and nutrition education program, as part of their overall prenatal care. We must then set up a program of food supplementation and education similar to the present Women's and Infant Care (WIC) program, but targeted at these high risk women. Our present WIC program functions without this comprehensive care.

We would continue to define "risk" by income level, since there are data supporting the fact that low-income people comprise the highest risk segment of our population. We would also strengthen the WIC program, increasing its educational component and regularly evaluating the results of the program with an ongoing monitoring system.

B. Postnatal Undernutrition

The rationale for these recommendations is based on the fact that the bulk of evidence today would strongly suggest that nutritional influences on behavioral development cannot be considered apart from concurrent social and environmental influences known to have a substantial impact on children's psychological development. Thus all of the options recommended are with a view to improving early nutrition as part of an overall plan to improve the general environment. From data already available, we find there are certain existing programs which should be strengthened, and new programs which should be introduced.

1) Programs which support effective mothering and parenting should incorporate a strong nutrition education provision. Conversely, programs which are primarily aimed at maintaining good childhood nutrition should incorporate components intended to support effective parenting or child rearing.

2) Programs for high risk infants (those of low birth weight, those whose families are under severe economic or social stress, handicapped infants in foster or institutional care) should be developed

which emphasize environmental and nutritional enrichment.

3) Programs should be developed to meet nutritional needs of young people during puberty and adolescence (especially pregnant teenagers if they intend to carry the pregnancy to term) as part of an overall "education for parenthood" effort.

4) Incorporate a stronger nutritional component into all child development and early child care programs.

PRENATAL SUPPLEMENTS AND BREAST FEEDING IN PREVENTION

by

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INTRODUCTION

At the Fourth Congress of the International Association for the Scientific Study of Mental Deficiency, Begab stated that "Among unresolved problems in biomedical causes of mental retardation, those deserving highest priority relate to prematurity (small-for-date babies), low birth weight (under 2500g) and malnutrition". 1/ Data from Lubchenko 2/ demonstrate the damaging effect of low birth weight on subsequent mental development; he found that 85 percent of children weighing 950g or less were seriously damaged, while among those weighing 1350-1500 g, the incidence was 35 percent.

Weiner and coworkers 3/ compared intelligence quotients (IQ) of 428 low birth weight children with that of 405 full term children between the ages of 8 and 10 years. They found that low birth weight children were impaired on a wide variety of psychological factors. The degree of impairment was greatest for children with small birth weight. These data support previous reports that implicate low birth weight as a cause for mental deficit. 4/5/6/ 7/ 8/ 9/ 10/

The purpose of this report is to focus attention on the effects of prenatal nutrition on birth weight and subsequent development of offspring.

- 1/ Begab, M.J.: Some priorities for Research in Mental Retardation. In Research to Practice in Mental Retardation. Vol. I. Care and Intervention. Ed. by P. Mittler. Baltimore: Univ. Park Press, 1977.
- 2/ Lubchenko, L.O.: M. Delivaria-Papadopolous, D. Seals. Long-term Follow up of Premature Infants, II. J. Pediat. 80:509, 1972.
- 3/ Wiener, G., R.V. Rider, W.C. Oppel, P.A. Harper. Correlates of Low Birth Weight. Psychological status at Eight to Ten Years of Age. Pediat. Res. 2:110, 1968.
- 4/ Churchill, J.A. The Relationship Between Birth Weight and Intelligence in Twins. Neurol. 15:341, 1965.
- 5/ Dann, M. S.Z. Levine, E.V. New. The Development of Prematurely born Children with Birth Weights or Minimal Postnatal Weights of 100 grams or Less. Pediat. 22:1037, 1958
- 6/ Dann, M. S. Z. Levine, E.V. New. A Long-term Follow-up of Small Premature Infants. Pediat. 33:945, 1964.
- 7/ Douglas, J.W.B. Mental Ability and School Achievement of Premature Children at Eight years of Age. Br. Med. J. 1:1210, 1956
- 8/ Rabinovitch, M.S., R. Bibace, H. Caplan. Sequelae of Prematurity: Psychological Test Findings. Can. Med. Assoc. J. 84-822, 1961.
- 9/ Robinson, N.M., H.B. Robinson. A Follow-up Study of Children of Low Birth Weight and Control Children at School Age. Pediat. 35:425, 1965.
- 10/ Weiner, G.: Psychological Correlates of Premature Birth: A Review, J. Nerv. Ment. Dis. 134:129, 1962.

EFFECTS OF MALNUTRITION ON PREGNANCY OUTCOME

Burke and coworkers 11/ concluded the report of a study on maternal nutrition 34 years ago with the following statement:

If the diet of the mother during pregnancy is poor to very poor, she will undoubtedly have an infant whose physical condition will be poor. In the 216 cases considered in this study, all still-born infants, all infants who died within a few days of birth except one, and all functionally immature infants were born to mothers whose diets during pregnancy were very inadequate.

Smith from Harvard Medical School stated that proof was needed that the infants' condition was the result of the mother's diet. 12/ He collected data on all infants born to women in Rotterdam and the Hague before, during, and after a hunger period which began in September of 1944, and ended with the liberation of the Northwestern Netherlands in May of 1945. Energy intake by pregnant women during the hunger period was one-fourth to one-third recommended; protein intake was one-third to one-half that recommended. All nutrients except Ascorbic Acid and Thiamine were reduced in a parallel manner. Births declined to about one-third their usual figure. Birth weights declined by about 240 g; birth lengths were slightly decreased. A baby was considered premature if it weighed less than 2250 g; with this definition of prematurity, there was a 1.3 percent increase in premature births during the hunger period.

Antonov 13/ reported effects of malnutrition on children born during the siege of Leningrad in 1942. Energy allowances from bread rations ranged from 420 to 1400 kcal daily. Live births decreased from 3056 in 1941 to 468 in 1942. The still birth rate doubled, prematurity rates increased to 41.2 percent (six times normal), with average weights of infants born at term 500 to 600 g less than normal. Mortality rates were usually high, 9 percent for those born at term, 30.8 percent for those born prematurely.

McGanity and coworkers 14/ and Thomson 15/ state that malnutrition is not the cause of prematurity (i.e., low birth weight); rather, that the disorder leading to malnutrition is the cause for low birth weight.

- 11/ Burke, B.S., V.A. Beal, S.B. Kirkwood, H.C. Stuart. The Influence of Nutrition during Pregnancy Upon the Condition of the Infant at Birth. J. Nutr. 26:569, 1943.
- 12/ Smith, C.A. Effects of Maternal Under-nutrition Upon the Newborn Infant in Holland (1944-1945). J. Pediat. 30:229, 1947.
- 13/ Antonov, A.N. Children Born during the Siege of Leningrad in 1942. J. Pediat. 30:250, 1947.
- 14/ McGanity, W.J., R.O. Cannon; E.B. Bridgforth; M.P. Martin; P.M. Densen; J.A. Newbill; G.S. McClellan; A. Christie; J. C. Peterson; W. J. Darby. The Vanderbilt Cooperative Study of Maternal and Infant Nutrition. VI. Relationship of Obstetric Performance to Nutrition. Am. J. Obst. & Gynec. 67:501, 1954.
- 15/ Thomson, A.M. Diet in Pregnancy. 3. Diet in Relation to Course and Outcome of Pregnancy. Brit. J. Nutr. 13:509, 1959.

EFFECTS OF NUTRITION SUPPLEMENTS ON BIRTH WEIGHT

Studies published by Balfour in England, Ebbs in Canada and the People's League of Health in England, more than 30 years ago, showed that by supplementation of the maternal diet, it was possible to decrease the number of premature births, neonatal deaths and miscarriages. 16/ 17/ 18/

A recent ongoing study at the Montreal Diet Dispensary (MDD) has demonstrated the efficacy of Diet Services in significantly increasing birth weight. This study, initiated in 1962, provides diet counseling and food supplements to meet nutrient needs imposed by deficiencies, stress, underweight, and pregnancy. A correction is made for undernutrition by providing an amount of protein equal to the daily deficit. Ten calories are allowed for each gram of protein added to normal pregnancy requirements. Twenty grams of protein and 500 calories per day are added to the diet of the underweight female to permit a gain of one pound per week. If nutrition stress (defined as pernicious vomiting, pregnancies spaced less than one year apart, previous poor obstetrical history, failure to gain 10 pounds by 20th week, serious emotional problems) is found, 20 g protein and 200-calories per day are added to normal pregnancy requirements for each stress condition. This program provided services to 2004 women from 1963 to 1975. Seventy-four percent of the women were below poverty level. The Diet Dispensary services increased mean daily intake by 529 kcal and protein by 32 g. Mean birth weight of infants was 3265 g. Perinatal mortality (13.0/1000 live births) and prematurity (7.2 percent) were similar to those of the private patients and lower than for the other public clinic patients. 19/

Dr. Rush and his colleagues at Columbia University analyzed the MDD data using a matched pairs design for analysis. 20/ For 1,182 pairs, they found lower perinatal mortality among those receiving dietary services (16.9/1000 vs. 24.5/1000). Infants of MDD mothers had significantly higher birth weights than controls (87 g for first trimester registrants).

- 16/ Balfour, M.I. Supplementary Feeding in Pregnancy. Lancet 1:208, 1944.
- 17/ Ebbs, J.H., W.A. Scott; F.F. Tisdall; W. J. Moyle; M. Bell. Nutrition in Pregnancy. Can. M. Assn. J. 46:1, 1942
- 18/ People's League of Health. Nutrition of Expectant and Nursing Mothers. Lancet 2:10, 1942
- 19/ Higgins, A. C. (Executive Director, Montreal Diet Dispensary). Personal Communication.
- 20/ Rush, D./ A. C. Higgins; M.D. Sadow; S. Margolis. Dietary Service During Pregnancy and Birthweight: A Retrospective Matched Pair Analysis. Pediat. Research. 10:349, 1976 (Abstr.).

Children born to mothers who received services from MDD during pregnancy are now being sought for evaluation of intellectual performance.

The Special Supplemental Food Program for Women, Infants and Children, now labeled WIC, was authorized by a September 26, 1972 Amendment to the Child Nutrition Act of 1966. The Amendment provided cash grants to State Health Departments for the purpose of providing nutritious food to low income pregnant and lactating women, infants and children up to 4 years of age who are nutrition risks. The program is administered by the Food and Nutrition Service of the United States Department of Agriculture.

Under the program, women were provided coupons to exchange for milk fortified with Vitamins A and D, eggs, Iron fortified cereals and fruit juices. The foods were selected for WIC to correct nutrient deficiencies of Iron and Vitamins A and C.

Nineteen projects located in 14 States participated in a medical evaluation of WIC. This evaluation was conducted by Edozien at the Department of Nutrition, School of Public Health, University of North Carolina, Chapel Hill, 21/ between November 28, 1973 and June 1, 1976.

The Edozien report has been seriously criticized for many reasons. Some of these criticisms are related to lack of an adequate control group, small sample size and methods of statistical analyses.

Ethnic distribution of women participating in the evaluation was 24.5 percent white, 38.6 percent black, 33.8 percent Spanish American and 2.5 percent others.

Initial diets of pregnant women provided them with less energy, Calcium, Iron, Vitamin A, Thiamine, Riboflavin and Niacin than is recommended for pregnant women. Participation in WIC increased daily mean consumption of protein by 5 g, Calcium by 123 mg, Iron by 1 mg, Vitamin A by 377 I.U., Ascorbic Acid by 17 mg and Folic acid by 24 ug. Mean energy intake did not increase due to WIC supplements.

Supplemented women gained an average of 1.3 kg (2.86 lb.) more than non-supplemental women throughout pregnancy. Length of gestation was increased by about 5 days in the supplemented women.

The WIC program was associated with an increase in mean birth weight of babies. The 139 babies born to mothers who participated in the program for more than 6 months weighed over 100 g more than the 41 control babies born to mothers who did not participate in WIC. The impact of the program was greater on black and Spanish American babies than on white babies. Supplementation for less than 3 months had no effect on birth weight.

21/ Select Committee on Nutrition and Human Needs. United States Senate. Medical Evaluation of the Special Supplemental Food Program for Women, Infants and Children. Washington, D.C.: U. S. Government Printing Office, 1976.

Susser, Stein and Rush ^{22/} reported that a daily protein-calorie supplement to pregnant women in a United States urban population improved birth weight of babies born to high risk women by 125 g. I will describe this study shortly.

EFFECTS OF NUTRITION SUPPLEMENTS DURING PREGNANCY AND LACTATION ON MENTAL DEVELOPMENT OF OFFSPRING

Only one well-controlled study on humans providing data on mental development of offspring of energy supplemented mothers during pregnancy is available. ^{23/ 24/} Experimental treatment consisted of food supplementation in four closely matched Guatemala villages. In two of the villages, a high protein-calorie supplement was made available daily in a central dispensary. In the other two villages, a non-protein, low calorie drink was provided daily.

Data in Table 3 describe nutrient content per 180 ml supplement. Major differences are in content of energy, protein, calcium and phosphorus. Information collected in this study includes mothers' attendance at feeding dispensary, amount of supplement ingested; infants' physical growth, mental development, mortality, birth interval, information on delivery, clinical examination, dietary and morbidity survey (Table 4). Data on Table 5 indicates numbers of children measured at birth and at 6 months of age.

In this ongoing study, it was found that energy was the limiting variable in the diets of pregnant women. Energy supplementation was defined as low, intermediate or high by criteria outlined in Table 6.

There was a higher rate of infant mortality in infants born to mothers who had "low" supplementation versus intermediate or high supplementation (91/1000 vs. 47/1000) (Table 7). Infants born to mothers who were in the "high" supplement group weighed significantly more at birth than infants born to women in the "low" supplement group. Infants with low birth weights were two times more frequent in the "low" supplement group than in the "high" supplement group (Table 8). At 6 months of age, infants born to mothers in the "high" supplement group weighed significantly more than infants born to mothers in the "low" supplement group. Height followed the same trend, but differences were not significant. (Table 9).

^{22/} Susser, M., Z.A. Stein; D. Rush. Prenatal Nutrition and Subsequent Development. Proc. 4th Congr. IASSMD, Vol. 3, In Press.

^{23/} Lasky, R.E., A. Lechtig, H. Delgado; R. E. Klein; P. Engle; C. Yarbrough; R. Martorell. Birth Weight and Psychomotor Performance in Rural Guatemala. Am. J. Dis. Child. 129:566, 1975

^{24/} Delgado, H.; A. Lechtig; C. Yarbrough; R. Martorell; R.E. Klein; M. Irwin. Maternal Nutrition - Its Effect on Infant Growth and Development and Birth Spacing. In Nutrition Impacts on Women. Edited by K. S. Moghissi and T. N. Evans. New York: Medical Department, Harper and Row, Published, 1977.

Four hundred seventy two infants were tested at 6 months of age by a Composite Infant Scale of 91 items drawn from Bayley, Catell, Merrill-Palmer, and Gesell scales. It was found that infants born of mothers who had had a high level of caloric supplementation during pregnancy and lactation obtained significantly higher scores ($p < 0.05$) on the Mental Scale and somewhat higher scores on the Motor Scale than children born of mothers who had had low caloric supplementation during pregnancy. (Table 10).

The Prenatal Project 22/, instituted in New York City in 1970 has as its objective, the study of the effects of prenatal nutrition supplements on birth weight and subsequent development of children born to poor black Americans. It aims to answer the following questions:

1. Can prenatal nutrition supplements raise the mean birth weight of infants born of women at risk for having children of low birth weight?
2. Can nutrition supplementation during pregnancy in such a population influence other measures of development at birth, and after, such as head circumference, body length, skinfold thickness, neurologic integrity, and psychodevelopmental measures?

Study design is outlined in Figure 1. Composition of substances to be provided during pregnancy is described in Table 11. The group receiving the supplement is given a beverage providing 40 g protein and 470 kcal daily. In addition, Vitamin and Mineral needs of pregnancy are nearly all met by the supplement. The complement is significantly lower in protein and somewhat lower in energy, Vitamins and Minerals. The non-intervention group receive a Vitamin-Mineral tablet. (Table 11).

A great deal of data will be collected during pregnancy and on the infant during the first 44 weeks of life. Appropos to this report are evaluations of motor and mental development to be obtained at 44 weeks of age. (Table 12). The mean increase of 125 g in birth weight was expected. We all look forward to information on infant development at 44 weeks of age.

INTERACTION OF GENETICS AND NUTRITION IN PRODUCING MENTAL RETARDATION

Bessman has proposed that genetic differences in ability to synthesize non-essential amino acids might be an important cause of mental retardation. 25/ 26/ A homozygote for such inability would suffer marked deprivation in utero for he would be in an heterozygous mother who could supply below

22/ Ibid. p.

25/ Bessman, S.P.: Genetic Mental Retardation, A Fetal Deficiency Syndrome. Discussion. Am. J. Dis. Child. 113:27, 1967

26/ Bessman, S. P.: Genetic Failure of Fetal Amino Acid "Justification". A Common Basis for Many Forms of Metabolic, Nutritional, and "Non-specific" Mental Retardation. J. Pediat. 81:834, 1972.

normal amounts of the non-essential amino acid he is unable to make himself. The deprivation of any one amino acid from the substrate required for protein synthesis could retard the rate of protein synthesis and result in a failure of brain development during a period of rapid growth.

A typical example of a deficiency of a non-essential amino acid occurs in phenylketonuria (PKU). Phenylalanine cannot be hydroxylated to tyrosine. Other genetic lesions could occur in the enzymes required to construct all the non-essential amino acids.

The incidence of the gene for PKU is about one in forty individuals, based on the incidence of the homozygote. ^{27/} According to Bessman ^{28/}, since half of these heterozygotes could be born to a heterozygous mother, approximately 1.25 percent of all children are at risk for damage from this type of genetic-nutrition interaction. All other genetic diseases of amino acid metabolism constitute a gene pool about equal in size to the PKU gene pool. If the genetic-nutrition interaction also occurs in these diseases, about 2.5 percent of all children are at risk for deficiency for one or another essential amino acid.

Fuller ^{29/}, Ford and Berman ^{30/}, and Bessman, et al., ^{28/} provided data that suggest that the heterozygote for PKU has a lower I.Q. than his normal siblings. Bessman's data show that heterozygotes for PKU have an I.Q. 14 points lower, on the average, than their normal siblings. Further, supportive data for this hypothesis have been reported by Moghissi ^{31/}

^{27/} Anderson, J.H.; K. F. Swaiman (Editors). Phenylketonuria and Allied Metabolic Diseases. Washington, D.C.: U. S. Department of Health, Education, and Welfare, 1967.

^{28/} Bessman, S. P.; M. L. Williamson; R. Koch. Diet, genetics, and Mental Retardation. Interaction Between Phenylketonuric Heterozygous Mother and Fetus to Produce Non-specific Diminution of I.Q.—Evidence in Support of the Justification Hypothesis. Proc. Nat'l Acad. Science (Accepted for Publication).

^{29/} Fuller, R.; J. Shuman.: Genetic Divergence in Relatives of PKU's Low I.Q. Correlation among Normal Sibs. Develop. Psychobiol., 7:323, 1974.

^{30/} Ford, B.C.; J. L. Berman. Phenylalanine Metabolism and Intellectual Functioning Among Carriers of Phenylketonuria and Hyperphenylalaninemia. Lancet 1:767, 1977.

^{31/} Moghissi, K.S.; J. A. Churchill; D. Kurrie.: Relationship of Maternal Amino Acids and Proteins to Fetal Growth and Mental Development. Am. J. Obstet. & Gynecol. 123:398, 1975.

who found a relationship between mother's blood amino acid levels and birth weight, length, cranial volume and mental development. In Division of Medical Genetics, Emory University, we are exploring the families of PKU children for data that would support or negate Bessman's hypothesis. Should this hypothesis be proven true, protein or tyrosine supplements provided to the pregnant women should significantly decrease intellectual deficits from this cause.

SUMMARY

It has been known for more than 30 years that malnutrition in women during pregnancy leads to an increased incidence of prematurity, still births, low birth weight babies and babies that are functionally immature. It has been known for almost as long and recently reconfirmed that nutrition supplements during pregnancy increase length of gestation and birth weight.

Knowledge of effects of low birth weight and prematurity on development has been obtained in the past 20 years. Data indicate that the lower the birth weight, the greater is the intellectual deficit at ages 8 to 10 years.

Studies in the last seven years provide data suggesting that nutrition supplements during pregnancy and lactation significantly increase mental development measured at six months of age.

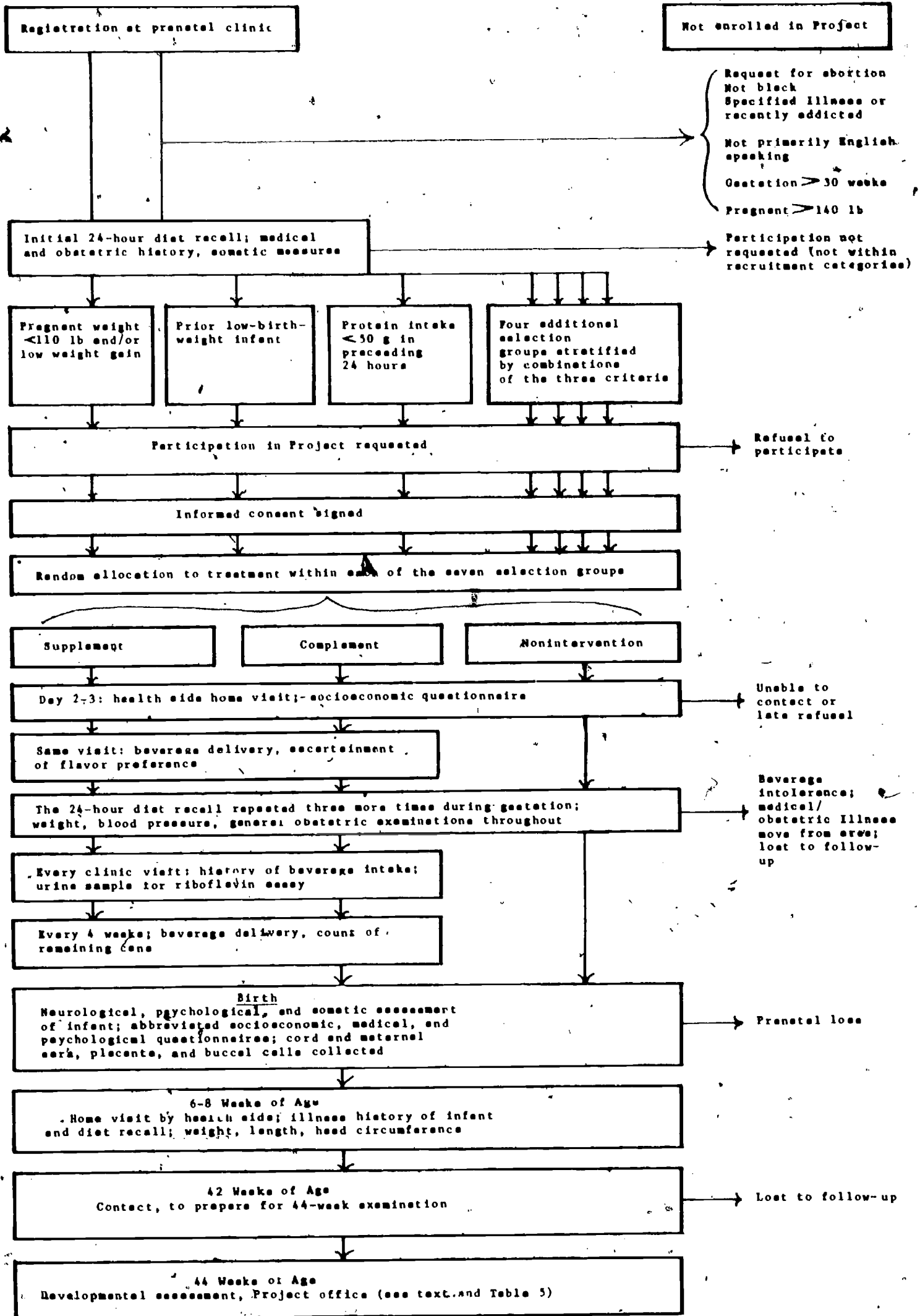


Fig. 1. Sequence of procedures for women registering for prenatal care.

Table 1
Montreal Diet Dispensary^(a)

Prescribe diet based on:
Extent of undernutrition
Extent of underweight
Nutrition stress
Normal requirements for pregnancy, age, activity
Nutrition counseling
Food supplement: milk, eggs, oranges

(a) Agnes C. Higgins, P.Dt., Executive Director

Table 2

Montreal Diet Dispensary
1963-1975

Study Group	
Number	2004
Below poverty line (%)	74
Illegitimacy (%)	32
Birth Weight	
Birth weight (g)	3265
Birth weight less than 2501 g (%)	7.2
Perinatal Mortality Rate/1000	
28 or more weeks gestation	13.0
Dietary Intake	Daily Increase by DD
Protein (g)	32
Energy (kcal)	529

Table 3

Nutrient Content Per 180 ml of Supplement

VARIABLE	ATOLE	FRESCO
Energy (Kcal)	163	59
Protein (g)	11	—
Fat (g)	0.7	—
Carbohydrate (g)	27	15.3
Ascorbic acid (mg)	4.0	4.0
Calcium (g)	0.4	—
Phosphorus (g)	0.3	—
Thiamine (mg)	1.1	1.1
Riboflavin (mg)	1.5	1.5
Niacin (mg)	18.5	18.5
Vitamin A (mg)	1.2	1.2
Iron (mg)	5.4	5.0
Fluoride (mg)	0.2	0.2

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and Irwin at INCAP.

Table 4

Data Collected in INCAP
- Longitudinal Study

Maternal & Child Information

Independent variable:

Subjects attendance to feeding
Amount of supplement ingested

Dependent variables:

Physical growth
Mental development
Infant mortality
Birth interval

Addition variables:

Obstetric history
Information on delivery
Clinical examination
Dietary survey
Morbidity survey
Socioeconomic survey of family

Data from Delgado, Lechtig, Yarbrough,
Martorell, Klein, and Irwin of INCAP.

Table 5

Sample Size for Variables
Examined: INCAP Study

Variable	Number
Children available	671
Physical growth	
At birth	405
At 6 months	447
Mental development	
At birth	157
At 6 months	472

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein,
and Irwin at INCAP.

Table 6

Definition of Low, Intermediate
and High Calorie Supplement-
ation Status Since
Conception

Time Interval (Months)	Subject	Supplemented Calories in Thousands		
		Low	Intermediate	High
Pregnancy	Mother	< 10	10-19.9	≥ 20
0-3 Postpartum	Mother	< 5	5-9.9	≥ 10
3-6 Postpartum	Mother	< 5	5-9.9	≥ 10

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and Irwin of INCAP

Table 7

Infant Mortality by 3 Categories
of Cumulative Maternal Energy
Supplementation during
Pregnancy and Lactation

	Level of Maternal Energy Supplement		
	Low	Intermediate	High
Number of infants	274	258	121
Infant deaths	25	12	7
Death rate/1000	91	47	58

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and Irwin at INCAP.

Table 8

Birth Weight by 3 Categories
of Maternal Energy Supple-
mentation during Pregnancy

	Level of Maternal Energy Supplementation			t- Test ^(a)
	Low	Intermediate	High	
Mean birth weight (g)	2986	3036	3120	2.62 ^(b)
Percent low birth weight (≤ 2.5 kg)	18.3	15.8	9.4	2.33 ^(c)
Number of infants	153	82	170	

(a) High vs. Low

(b) $p < 0.01$

(c) $p < 0.05$

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and
Irwin at INCAP.

Table 9

Attained Weight and Height at
6 Months of Age by Categories
of Caloric Supplementation
since Conception

	Level of Maternal Energy Supplement			T- Test (a)
	Low	Intermediate	High	
Weight (kg)	6.58	6.61	6.81	1.99 ^(b)
N	133	217	97	
Height (cm)	62.1	62.1	62.7	1.92
N	134	217	96	

(a) High vs. Low

(b) $p < 0.05$

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and
Irwin at INCAP.

Table 10

Psychologic Test Performance
 by 3 Categories of Cumulative
 Maternal Energy Supplementation During
 Pregnancy and Lactation

	Level of Maternal Energy Supplement			F- Test
	Low	Intermediate	High	
Composite Infant Scale at 6 Months				
Mental				
Mean	73.8	76.3	77.8	2.87 ^(a)
N	150	221	101	
Motor				
Mean	70.0	70.6	72.7	1.13
N	150	221	101	

(a) $p < 0.05$

Data from Delgado, Lechtig, Yarbrough, Martorell, Klein, and Irwin at INCAP.

Table 11

The Prenatal Project

Composition of Daily

Diet Supplements

COMPONENT	SUPPLEMENT	COMPLEMENT	NONINTERVENTION
Protein (g)	40.0	6.0	--
Energy (kcal)	470	322	--
Calcium (mg)	1000	250	250
Magnesium (mg)	100	12	0.15
Iron (mg)	60	40	117
Zinc (mg)	4	0.084	0.085
Copper (mg)	2	0.15	0.15
Iodine (mg)	150	100	100
Vitamin A (IU)	6000	4000	4000
Vitamin D (IU)	400	400	400
Vitamin E (IU)	30	--	--
Vitamin C (mg)	60	60	60
Thiamine (mg)	3	3	3
Riboflavin (mg)	15	15	2
Niacin (mg)	15	10	10
Pyridoxine (mg)	2.5	3	3
Pantothenic acid (mg)	1	1	1
Biotin (ug)	200	NA	--
Folic acid (ug)	350	350	350
Vitamin B ₁₂ (ug)	8	3	3
Volume	16 oz.	16 oz.	1 Tab

Table 12

The Prenatal Project

Evaluation of Infant at 44 Weeks of Age:

1. Mental and motor development by series of observations, including Bayley Scale of infant development.
2. Assessment of concept development.
3. Evaluation of habituation to repeated visual stimuli.
4. Anthropometric measures: height, weight, arm circumference, triceps and subscapular skinfolds, head circumference.
5. Neurological examination.
6. Parent interview; medical dietary and the social history of family and child since birth; 24-hour diet recall.

Table 13.

F-Ratios and Probabilities
 for Differences among Mean I.Q.
 Scores for Three Groups of
 Non-PKU Offspring of Obligate
 Heterozygous Mothers (a)

IQ Test and Group	N	Mean Age	Mean IQ	SD	Adj Mean IQ(b)	F- Ratio
Stanford-Binet WAIS/WISC Full Scale						
Offspring						
1. Low P ² /T ratio	15	9.8	117	13	116	
2. Middle P ² /T ratio	16	13.2	109	10	109	4.02(c)
3. High P ² /T ratio	16	15.2	103	12	104	
Heterozygous Mothers	22		112	15		

(a) Data of Bessman, Williamson, and Koch

(b) Adjusted on mean age.

(c) p < 0.01

Workshop Recommendations

NUTRITION, BRAIN GROWTH AND PREVENTION OF MENTAL RETARDATION
and
PRENATAL SUPPLEMENTS AND BREAST FEEDING IN PREVENTION

LEADER: Pedro Rosso, M.D. and Phyllis Acosta, Ph.D.

RECORDER: David Touch

1. Attention to nutrition should be addressed in all prenatal and perinatal programs.
2. Nutrition education should begin in elementary school and continue through college. It should be incorporated as part of parenting and sex education classes and other social studies programs.
3. Research projects addressing the effects of prenatal nutrition relating to brain growth and development should be implemented.
4. To achieve better health of infants and better bonding between mothers and their babies, breast feeding should be encouraged.
5. More attention should be directed to WIC (Women, Infants and Children) and other food supplement programs, especially the educational components.

Discussion

NUTRITION, BRAIN GROWTH AND PREVENTION OF MENTAL RETARDATION and PRENATAL SUPPLEMENTS AND BREAST FEEDING IN PREVENTION

DR. BOGGS: I am under the impression that the WIC program is up for renewal within the next year and that some specific recommendations have been made with respect to certain possible reforms in this matter. Since we are trying, in this conference, to bring out a few specific recommendations, I would like to know whether your group would consider that that last recommendation could be interpreted to cover legislation extension of the WIC program and whether you have any suggestions for reform.

DR. ACOSTA: We felt, as a short term strategy, that WIC was a very important program. The most basic reform that is needed is an educational component, which presently is not there. There is really no educational component to help assure that mothers use what is allocated for mothers, and that fathers or some other members of the family do not use the food. We felt this to be a very important aspect that is not now addressed by WIC. We all felt, however, that, as a short term strategy, it was very important for it to continue.

LAVERDIA ROACH: You may be interested to know that PCMR is sponsoring in March of next year, a Congressional People's Conference on Maternal and Infant Malnutrition in America. This exact issue has come up repeatedly in the steering group meetings. We want to know if the WIC program should be continued as it is now or if it should be revised or expanded, or if there should be something totally different. It is expected that this conference will be attended by governors, representatives from Congress, etc. I suspect that those of you who have a specific interest in nutrition may be called on to become involved in that.

DR. BOGGS: I just wanted to get an endorsement or a counter-endorsement from the group that is expert in this area with respect to that way of implementing the general idea that good nutrition is important because it interacts with the Federal strategy. It seems to me, the fact that PCMR is going to do a Conference doesn't negate the necessity for reinforcing it in this report. One of the complaints we often have is that five different conferences may recommend five different sets of things to do. Reenforcement, I believe, is part of what we need.

Report to the President's Committee
on Mental Retardation

REGIONALIZATION OF PERINATAL CARE

by

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University of California, San Diego
La Jolla, California 92093

In recent years, especially during the past 7-10 years, the survival of high risk and ill infants, including very small premature infants has improved dramatically. To a significant extent, this is owing to the principles and concepts behind regionalization of perinatal care. However, these have not been carried out uniformly, nor, it seems, will the goal every be achieved in regionalization of perinatal care for high risk pregnant women.

In 1971, the American Medical Association House of Delegates formulated a policy on regionalized perinatal and intensive care which in part said: "...application of recent advances in scientific knowledge and skills in the intensive care management of high risk pregnant women and high risk newborn infants will result in reduction of maternal and infant mortality ...a major contribution to such a program is the development of centralized community (or regional) hospital based newborn intensive care units...The program goals should include...programs to identify the high risk pregnancy and sufficient time to allow for delivery at those hospitals which are staffed, equipped and organized for optimal perinatal care."

These statements were supported by similar statements from the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics and the American Academy of Family Practice. There has been a clear and dramatic lowering of perinatal mortality in those hospitals which have installed newborn intensive care units, whether or not high risk obstetrical programs were developed. The rapid expansion of neonatal intensive care units truly has revolutionized newborn care of the high risk infant. Whole new armies of trained specialists are now available, as are a wide variety of sophisticated laboratory and monitoring techniques and equipment that, prior to 1970, barely existed. Even special social workers have been developed for Neonatal Intensive Care Unit (NICU) care.

Of great disappointment has been the failure to develop obstetrical regional intensive care. There are many reasons for this, in part economic and in part the problems of "rugged individualism" of physicians with respect to relinquishing patients to medical centers.

The dramatic gains both in newborn care and in obstetrical perinatal medicine are perhaps best highlighted against the backdrop of the history of the field. Rules and regulations about management of pregnancy and childbirth go back in recorded time to even before Hippocrates when midwives, who were members of, given tribal groups, had developed a good hierarchy of care which was delivered to women in childbirth for many centuries before Christianity. During the time of and Golden Age of Greece and into Roman times, the women was much respected and childbirth and pregnancy were managed in highly civilized fashion. In fact, the whole course of civilization can be evaluated according to the kind of care given to women in childbirth. During the Dark Ages, following the beginnings of Christianity, childbearing became brutal. Superstition replaced science and not until the late 1500's and with the invention of the obstetrical forceps did the modern science of obstetrics begin.

The modern era of perinatal obstetrics began in the 1950's with the early development of fetal heart rate monitoring, and has advanced to a high degree of sophistication. Today, without ever viewing the fetus directly, we can visualize it with ultra-sound, measure the size, check many of the vital functions, measure blood gases, measure metabolism, record biophysical measurements, and assess when the lungs are mature so that delivery will be safe. We can develop a clear picture, including even the sex and any diagnosable genetic, metabolic and chromosomal diseases the fetus may have. These are truly astounding advances!

The story of interest of the premature and the development of newborn intensive care is fascinating in a bizarre way. The beginnings occurred in France in the middle and late 1850's, during the time when the premature was considered at very high risk of dying. If they lived, fine; if they died, that was God's will. The French found that if they just kept babies warm, the survival of prematures rose significantly. This led to their invention of the incubator. At the turn of the century, Paris was not the center of learning that Berlin was. In 1892, six French incubators were sent to the Berlin world's fair, and with permission of hospital authorities in Berlin, six prematures at a time were shown in a special exhibition utilizing babies from the Free Hospital in Berlin. The physician who was sent along from Paris to supervise this and provide care for the infants was a man named Martin Couney. This became the most popular exhibit and began an event where, for every year until 1938, first in Europe and then in the United States, premature babies were exhibited at the annual world's fairs that were held during those years. Sophisticated pavilions were built to exhibit these babies.

Through it all, Martin Couney became the hero. In managing the prematures in these centers, he amassed an amazing survival record, one respectable even by today's standards. More importantly, he stimulated Dr. Julius Hess in Chicago to found the first premature center at the Michael Reese Hospital there. Somewhat traumatically, Hess regressed from the beautiful incubators devised by the French and exhibited by Couney, to a Copper tank in which the baby could be seen only with difficulty. Nevertheless, he did stimulate the hospitals in Chicago, New York and eventually throughout the United States to seriously consider the care of premature infants. From 1894 (and beyond), clear incubators were re-developed which allowed better visualization of the baby. The specialized care of low birth weight infants began to burgeon with the development of many premature units in the United States.

There were, however, no intensive care units because doctors feared mixing together babies of different ages and weights with varieties of problems, due to concerns about infection. In 1960, at Yale, we had the pleasure of founding the first intensive care unit, mixing in-born, out-born, medical, surgical, premature, full term, babies of all sorts. In subsequent years, together with Dr. Edward Hon, the father of fetal heart rate monitoring, we founded the first perinatal center. Subsequently, we altered the architecture of the NICU, especially toward the large room concept. By 1967, after several centers had the opportunity to evaluate intensive care, this became widely accepted,

The sophistication and subsequent development has been stupendous. Any physiological and modality can be monitored, and monitoring becomes more and more sophisticated because we are learning that more and more functions are important in the optimal management of very ill infants. We have, for example, pumps for infusion of fluids, wide varieties of mechanical ventilators, and equipment allowing infants to be transported anywhere by any means, from automobiles to helicopters, while getting high level care. One can even monitor oxygen continuously by measurements from the skin.

The human aspects of care have become evermore important. Reaffirmation of the necessity for mother-child bonding is an important part of the care given in the many nurseries through the years, including our own. Mothers are considered part of the therapy, and they are encouraged to touch and handle their babies. Nurses are highly trained, having advanced from where one could learn newborn intensive care in 2-3 weeks, to where it now takes a minimum of six months to develop a reasonable competence.

Thus, regionalizing this kind of care at different levels among units from the most advanced (the tertiary unit), to the primary one that stabilized the baby, has resulted in significant lowering of perinatal mortality. But there are significant criticisms of the plan, and particularly of the document, Toward Treating the Outcome of Pregnancy, upon which the recommendations are based. The initial motivation for the recommendations was a sense of shame because, since around 1970, the United States has ranked between 11th and 15th in the world in infant mortality. Infant mortality has been considered an important indicator of the health status of a population. Thus, one of the valid purposes of these recommendations was to reduce mortality by the early detection of abnormalities of any sort, to give higher quality of care, and provide better access to the scarce resources that existed in this field, with earlier dissemination of advanced technology.

However, nothing in these recommendations talks about any human aspects or human values. The criticism of this document must begin with the recognition that it was totally conceived and produced by a task force of consultants, who were either practicing or academic obstetricians, pediatricians, family practitioners or members of specially selected societies. The recommendations were oriented very heavily toward the treatment of disease, high risk care, crisis intervention and treating the already present problems at the end of pregnancy in the perinatal period. In no place does it really talk about prevention, although it avows prevention. Nothing in the guidelines spells out any kind of a program for prevention or toward intervention in early pregnancy. There is rather heavy reliance on statistically identified risk factors, maternal age, and the need for newborn care, but not about education for childbirth, counseling, instructing parents in their roles, or anything else that might decrease the numbers of high risk deliveries. Thus, the recommendations did not constitute a preventive document, despite the strong avowal of prevention.

equipped service. But, in fact, it has not worked out this way. Only in rare and exceptional instances have these goals of closing down delivery services which are inadequate and whose personnel are inexperienced, been accomplished. Economic and ego problems of physicians have prevented this from being done, despite the fact that maternity units traditionally lose money, that there is a falling birth rate and that the many highly trained obstetricians are not being utilized properly in tiny units. Obstetricians are in competition with family practitioners and even, in some areas, with midwives for delivery of normal babies.

Perhaps the major reason why obstetrical regionalization has not been successful is illustrated by the case of a very good, competent obstetrician in a small community, who has a woman with a particularly severe problem and who feels that a university hospital would be a better place for her care. This physician, who has spent many years in training and practice and knows the family is very concerned. He calls the hospital to refer her, but the first person to meet this woman at the hospital is an intern, who frequently takes charge of the care and may exercise judgments that could be detrimental. This has happened in enough cases that practicing obstetricians, anxious to have the best of care for their patients and rankled by the apparent disregard of their recommendations, have become very wary of referrals, to the point of rejecting regionalization altogether. Our academic institutions, charged with the responsibility to train physicians in specialties, sometimes fail to train these physicians to recognize that certain priority patients require more competence than an intern possesses.

Although it is important to acknowledge the positive aspects of regionalization of perinatal care and to recognize clearly that there has been a marked lowering in mortality and morbidity, nevertheless, perhaps the most constructive aspect of this discussion would be to point out the excesses, the problems, and the areas that still require changing, and in which education to physicians and consumers alike remains important.

The report from the President's Committee on Mental Retardation says "The possible causes of mental retardation from disorders of the brain are many, but divide principally into two groups: those with genetic origins and those involving insult to the fetus." The report then does not go on to define what these insults to the fetus are. Specifically, it does not talk about doctor-insults to fetus. Insults do not occur magically or at random. For example, drugs are given to women in labor or during pregnancy, despite knowledge that, virtually everything given the mother crosses into the fetus and that there is an incredible sensitivity of fetal tissues to almost any drug.

We recently have begun to appreciate that drugs may inhibit, to some extent, the process of synaptogenesis, wherein the complexity of the brain is developed, involving growth of axons and dendrites with some 700 billion inter-connections. Diethylstilbestrol is still being given during pregnancy, despite the fact that it is a carcinogenic whose effects are latent

and do not become visible for perhaps 20 years. Thalidomide, which produces malformations was given to pregnant women in the past. Corticosteroids are now being given to hasten acceleration of the babies' lungs. Here is a situation where an obstetrician may feel that it is perfectly all right to deliver a baby who is premature if the dangers of hyaline membrane disease to not exist, not understanding that being premature is the single greatest factor leading to perinatal morbidity. Oxygen continues to be used, frequently unfettered, and retrolental fibroplasia thrives in many centers throughout the country. When we decide arbitrarily that premature infants are not growing fast enough, all manner of intravenous compounds are fed them, such as fat emulsions and amino acid mixtures whose effects we simply do not know. We do know that amino acid mixtures may produce blood levels of tyrosine and phenylalanine that may be higher than is seen in the pathologic conditions associated with mental retardation, tyrosinosis and phenylketonuria.

In the 1940's, it was decided withat cow's milk by virtue of the higher content of protein, was better than breast milk for prematures. Subsequently, this was followed by "breast milk simulators" and modified cow's milk and human milk was totally different. This involved differences in amino acids and produced prolonged, high levels of amino acids now thought to be toxic to the developing brain. We still see interventions in pregnancies where a physician, for his or the mother's convenience, decides to bring a baby into the world. The marked increase in Caesarean section has led, and will continue to lead to the birth of more prematures. This, again, is a matter in which, while we see significant gains on the one hand, we also see enormous problems being developed on the other hand, at an almost equal pace.

Perhaps the most important problem is the evaluation of therapies. Fifty new therapies may come down the pike in a given decade, but under our current priorities, where we do not have adequate follow-up studies, not a single one will be evaluated properly, and by the next decade, 50 new therapies will emerge. The major part of this problem is the lack of responsibility by public agencies which should insist that good follow-up studies on new therapies be done. Today, good follow-up studies are very few and very far between. Studies are published that follow 100 babies and even fewer, and these become the basis in the literature for pronouncements or prognoses. They may even have been followed from a previous decade or two, and will have little or no meaning relative to therapies being given today. None of these studies that have been published previously are adequate enough to guide us in any profound way. In order for us to understand the significance of what our therapies are doing, we desperately need ongoing studies and continuing intake to involve 3,000 to 4,000 babies over a period of ten to fifteen years.

Exceedingly distressing to me has been our lack of candor in this field, where, although one may talk at length about chromosomal and hereditary genetic defects as causative factors in mental retardation, these causes

are miniscule when compared to the rest of perinatal medicine which accounts for over 90 per cent of non-hereditary mental retardation, brain damage, cerebral palsy, behavioral disorders, hyperkinesia, epilepsy, and communications disorders. As the old, often quoted Sutton's Law goes, when Willy Sutton was asked why he robbed banks, he responded by saying, "Because that's where the money is." So it is with the field of mental retardation. The perinatal field is where the money is. When conduct and management of patients in the perinatal area are optimized, then we can anticipate a drop in mental retardation, behavior disorders, brain damage, cerebral palsy, epilepsy, communications disorders - greater than with any other preventive measure.

The crux of perinatal problems is on two major charges. One of them is the identification and prevention of prematurity and the other is the identification and prevention of asphyxia. Were these two conditions to disappear, perinatal morbidity would be negligible. We already have discussed the fact that the incidence of prematurity, instead of being lowered, is going up. This is, in some measure, due to the increased incidence of Caesarean sections, although Caesarean section to prevent the development of asphyxia or other trauma to a baby is an important advance.

There are several major points in dealing with asphyxia. On the one hand, an increase in Caesarean sections because of possible asphyxia has resulted from the many new fetal monitors being bought and used by community hospitals where persons frequently make interpretations although they do not really understand what these traces mean. Virtually every drop in fetal heart rate (late decelerations) may stimulate a Caesarean section whether truly warranted or not. If a section is warranted, owing to fetal distress, there will be a late deceleration heart rate pattern with loss of beat-to-beat variability and a low pH sample from the fetal scalp. Today, sections are done for heart rate drop alone, despite a return to normal when the contractions ceases.

The current management of distressed labor deserves a re-examination. Currently, hospitals take great comfort and pride in the fact that a "crash" Caesarean section can be done in 20-30 minutes. In fact, this is more likely to be 40-60 minutes or more. All during this time, the fetus continues to suffer the hypoxic stress. Although the American College of Obstetricians and Gynecologists optimistically talks about its goal of 8 minute sections, the mechanics of doing the sections effectively preclude this. The problem of a baby continuing to have intermittent asphyxia, hypoxia and even anoxia for an hour while awaiting the Caesarean section to get underway or to be finished poses one of the most important ones that continues to feed the pool of babies who are brain damaged. What we need urgently and specifically is the means of inhibiting labor immediately so that the fetus can be oxygenated, whereupon the Caesarean section on the mother can be done comfortable. There is little or no evidence at this time in the United States that this goal of oxygenating the fetus exists or that the technique is even being considered. Where some anesthetic agent (e.g., Malathane) should be used or some betamimetic agent, as used

worldwide (except in the United States) to inhibit labor, this must become a significant national goal if we are to eliminate a major cause of brain damage and mental retardation.

I do not want to end this pessimistically, for actually I do not feel pessimistic. I have chosen to be vigorously blunt and out-spoken in a seeming denunciation of current practices because I feel this tone is necessary to bring to the attention of authorities that a massive amount of work still needs to be done in the entire perinatal medicine area. I must, however, end this on an optimistic note in saying that, at least the care of the newborn infant is getting better and will continue to get better. Our pressing needs, as mentioned, include good follow-up studies. There must be encouragement of more neurophysiological evaluations of babies, especially premature infants, while in nurseries.

Most importantly, perhaps, it is time to begin to worry about premature infant "husbandry." By this, we mean the elimination of undersirable stimuli to infants in the nurseries, to be replaced by the provision of meaningful stimuli. In other words, we must recognize that the growing brain of the premature infant needs proper stimulation to develop normally. Our task is to study the premature and establish what these needs are. Our current practice of taking the baby out of the warm, snug environment prematurely where the fetus gets constant vestibular, somesthetic and auditory stimuli in darkness and replacing these with 24-hour daylight, putting the baby on a hard mattress with essentially no meaningful stimulation, and exposing it to 24 hours a day of very high levels of white noise, does not seem compatible with the needs of the developing brain. The amount of over-stimulation may be injurious, but we do not have urgently needed follow-up figures to make this judgment with any degree of confidence.

It is my hope that this report, as part of the recommendation of the PCMR may help the public focus on this source of mental retardation and brain damage which outstrips, by far, all the other causes combined. My hope is that, once attention is directed properly to these problems, allocation of public health funds and the provision of priorities to this area, ultimately could result in billions of dollars in savings to the American public through a decreased necessity for special schooling, institutionalization and drug management, as well as to avert the uncountable billions in human tragedy.

Workshop Recommendations

REGIONALIZATION OF PERINATAL CARE

Group Leader: Louis Gluck, M.D.

Recorder : Rudolph Hormuth

We spend much time trying to extend the three-tiered regionalized system into a local area. Half of the prematurity problems come from poverty areas, where there is a lack of prenatal care. If somehow, the system can be expanded and extended into these areas, we could more readily detect high risk pregnancies, as well as provide access for those women into the system which ultimately will have impact on the reduction of prematurity and morbidity in those areas. *g*

We considered what had happened to the maternal and infant care projects which were established years ago by HEW and which had been taken over by the states at the conclusion of the grant funding. However, as far as we could tell, at the moment, where they still existed, these were not related particularly to the system that we were discussing.

We were also concerned with the fact that the three-tiered system ultimately is related to the very sophisticated university setting at the tertiary level, and that this setting permeates down to the affiliated secondary and primary level hospitals. What really is needed are outreach programs to the target poverty areas that largely produce the primary problem - prematurity. We need to think of ways to utilize midwives as outreach workers who could provide access to the target population, particularly in the poverty areas and to provide access for them to the system so that we can be in a better position to affect a reduction in prematurity. We could then channel the problem infants up through the system to tertiary care where needed. Primarily we were in the process of exploring problems we saw in the system and gaps in the system rather than being able, in the short time available to us, to come up with specific recommendations. One of the purposes of the outreach work was to try to affect some change in lifestyle.

Centers providing perinatal care are classified in one of three categories:

1. Primary care hospital: A hospital having 1000 or fewer deliveries per year. This hospital might do Caesarean sections. The primary care center would stabilize the infant and discharge him or refer him to another center.

2. Secondary care hospital: A hospital having between 1000 and 2500 deliveries per year. The physician in charge could be any practitioner with interest and experience in taking care of newborns. Preferably, he

should be a qualified/certified neonatologist, but this is not required.

3. Tertiary care hospital: A very sophisticated center which has the equipment and personnel with the expertise to care for critically ill infants and tiny prematures. One or more certified neonatologists are on the staff.

Summary of Paper Presented At
International Summit on Prevention of Mental
Retardation from Biomedical Causes
Racine, Wisconsin

December 15 - 16, 1977

A MODEL PROGRAM FOR LEAD SCREENING

by

Sergio Piomelli, M.D.
Director, Division of Pediatric Hematology
New York University School of Medicine

Undue absorption of lead from the environment may cause neurological alterations, mental retardation, and, in extreme cases, death in children.

Due to the insidious nature of lead intoxication in children, it is necessary to detect an excessive body burden of lead before clinical signs and symptoms become apparent, at which time irreparable damage may have already occurred.

In 1969, the city of New York tested about 2,700 children for lead poisoning, and in 1970, a group of concerned citizens put enough pressure on the city that the Bureau of Lead Poisoning Control was established. As a result of this, 85,000 children were screened. This was the beginning of massive screening for lead poisoning in New York City. The results in 1971 showed about 2,000 children who had blood lead levels greater than 60, which at that time, was considered to be an unsafe level. We now know that this is the level at which the incidence of severe neurological complications and even death start to occur. The main problem with the program was the method of screening, which was done by testing the lead content of the children's blood. This test was expensive, and often inaccurate, due to day-by-day variability and the ease of contamination of the blood samples from ubiquitous environmental lead during collection. Recently, it has been possible to demonstrate that it may be more medically significant and cost-effective to detect children at risk by testing for the earliest biochemical evidence of undue effects of lead (elevation of free erythrocyte protoporphyrin). Measurements of free erythrocyte protoporphyrin can presently be done rapidly, economically and accurately, using only a drop of blood, collected by finger puncture. The blood may be spotted on a piece of filter paper for mailing to a central laboratory; alternatively, the result may be obtained instantly with a portable instrument, so that confirmatory diagnosis and medical attention can be obtained without delay.

Large-scale surveys of urban children have demonstrated that the level of free erythrocyte protoporphyrin is a much more effective indicator of adverse effects than the lead content of the blood. An additional advantage of using this test for large-scale screening of children is that it also detects iron-deficiency anemia, a common problem in early childhood. This method of screening has been employed by the Bureau of Lead Poisoning Control of the city of New York to test more than one half million children in the past few years, and it was adopted by the Center for Disease Control in 1975 as the best choice for nation-wide screening for undue lead absorption. This technical advance makes it possible to screen every child at risk in this country with a much greater degree of cost-effectiveness, sensitivity and accuracy. It is of interest that the level of blood lead considered acceptable by the Surgeon General as recently as 1970, is no longer considered safe. We now classify as "children at risk" those children who have a blood lead level as low as 30 micrograms per hundred ml of blood when they have some evidence of metabolic interference in heme synthesis as measured by erythrocyte protoporphyrin.

Screening for lead poisoning is not the only way by which prevention of undue lead absorption in young children can be achieved. A much more effective control will be achieved if lead, the source of the intoxication is eliminated from the environment. A significant number of severe cases of lead poisoning in children may be directly attributed to ingestion of lead-containing paint present in older homes. However, it has recently become more evident that this is not the only mechanism by which children absorb excessive amounts of lead, and that the ingestion of lead-containing paint is additive to the extremely high background of lead in the environment. Children get a certain amount of lead because they breathe, as we all do, but they breathe faster than we do and at a lower level. Another thing people tend to forget is that children have a normal hand-to-mouth activity. They suck their thumbs and the dust which is all around, gets into their mouths. If that dust contains lead, the children get lead. Mounting evidence indicates that a significant source of lead in children is from lead-containing dust inside, as well as outside the home. The importance of the ingestion of lead-containing dust in children has been directly shown by studies of children of lead factory workers, for whom the only source of lead was the dust brought into the home on the parents' clothing. Similar studies have also shown the importance of lead contained in the dust of homes of children living in urban areas. The source of lead in dust for urban children is not just lead-containing paint. A significant amount of lead derives from environmental contamination, primarily from the huge amount of lead emitted by automobile exhausts. In a study of the snow in the glaciers in Greenland, lead concentrations were measured from the year 800 BC by drilling to different depths within the glaciers and measuring the lead. The study showed the level of lead started increasing as the world started industrializing. At one point, it jumped dramatically. The year in which this large increase in environmental lead took place was 1923 - the year lead was introduced as an additive to gasoline. In 1975, 150 thousand tons of lead went into our air from gasoline, and you must remember that it takes 100 milligrams of lead to kill a child. The only reason we are still alive is that we do not absorb a good deal of this lead, but our children do.

Additional sources of lead can be identified in the environmental lead ingested with the diet. In addition, cans contain a lot of lead, which can leach out into food, despite the fact that it is technically feasible to make cans which do not contain lead.

Lead is an element which has no function in the human body. It has recently been shown that the content of lead in the blood of populations living in "primitive" conditions is negligible. This was demonstrated in 1975 by a group of geneticists from Ann Arbor, Michigan, who were doing studies among members of a tribe at the sources of the Orinoco River in Venezuela far away from anything that we would call civilization, and they made the very surprising observation that these individuals had blood lead levels which were almost undetectable. We have recently had similar observations made in the mountains of Nepal. In contrast, among populations living in Western civilization, there is a progressive increase in the blood lead content from

rural to suburban to urban dwellers, with the latter having the highest blood lead content. This evidence indicates that any lead in the human body results from man-made environmental pollution.

It has been shown that evidence of biochemical damage caused by lead occurs at hitherto unsuspected low levels of exposure. An increase of free erythrocyte protoporphyrin reflects lead interference with mitochondrial function, and is an expression of general damage to all cells of the body. Elevations of free erythrocyte protoporphyrin can be demonstrated, in fact, in children when the blood lead exceeds 15 ug/dl, a level until now, considered to be quite safe and well below the national average blood lead level. These data indicate that excessive intake of lead by urban children is much more widespread and biologically significant than previously suspected.

In 1970, the same group of people in New York City who has asked that children be screened for lead poisoning, exerted enough political pressure that the city passed an ordinance which limited the amount of lead present in gasoline. Between 1970 and 1976 in New York City, approximately 600,000 children were studied and it was found that the blood lead level of these children decreased progressively, and there was a decrease ~~by several fold in the~~ number of children with clinical lead intoxication.

Thus, the recent knowledge indicates that it may be possible to minimize and even completely eradicate lead poisoning in children by a combination of:

- a. legislative efforts to reduce or completely eliminate lead from the air, the food and the home, and
- b. by an appropriate program of screening and detection aimed at identifying those children who are primarily ~~at~~ greatest risk.

Workshop Recommendations

A MODEL PROGRAM FOR LEAD SCREENING

Group Leader: Sergio Piomelli, M.D.

Recorder : Mary Etta Lane

1. This Summit conference should issue a statement reflecting that lead poisoning is presently a completely preventable cause of mental retardation, not unique to the urban ghetto, but rather in existence in all areas.
2. Funding for lead poisoning prevention should be increased to, at least, the present level of congressional authorization.
3. Recognition should be given to evidence of multiple sources of lead such as gasoline, paint, canned foods, etc.
4. The EPA standards should be enforced, as presently stated, relating to all forms of lead.
5. Legislation should be developed to monitor the control of lead utilization in cans containing food for both infants and adults.
6. Efforts should also be made to lower the lead content in both interior and exterior paint.
7. Periodic screening (at least annually and more frequently in high risk communities) should be available and accessible for all children between the ages of 1 and 6 years.
8. Pilot regional laboratory facilities should be developed and equipped to handle large volumes of filter paper blood samples of porphyrin. These facilities should demonstrate the economic benefits for primary screening and be available and accessible to all communities in both rural and urban settings. The data of these facilities should be utilized to exemplify the broadness of the problem and evidence of lead poisoning across geographic and socio-economic lines.
9. Aggressive action should be taken to effectively eradicate lead poisoning in institutions for the mentally retarded. Also, special responsibility should be assumed for the appropriate following action by the Summit's sponsoring agencies and organizations.
10. In order to generate the necessary support toward adequately addressing and correcting the problem of lead poisoning, a massive public education campaign should be developed to heighten the awareness of the general public that lead poisoning is a universal problem.

11. Lead poisoning screening programs must have a mechanism for appropriate follow-up in terms of medical treatment and environmental correction.

12. The Lead-Based Paint Act should be retitled to read, Lead Poisoning Prevention Act.

Discussion

LEAD SCREENING

There was a question from the group as to whether there is lead in the tubes for tooth paste. Dr. Picomelli said he thought not. He explained that lead is contained in the solder of cans, such as fruit juice cans and that the lead of the solder can leach out into the fruit juice. He emphasized that the industry can make cans that are not soldered, but so far, has not done it.

Marry Etta Lane was asked to report on the 5-year program on lead poisoning in Illinois. She reported that one of the significant things they found when they started lead screening in cooperation with the Illinois Health Department and the ARC, was that there was a surprisingly large amount of lead in rural communities. They had not dealt exclusively with urban ghettos, but had started in rural communities, where they found a significant amount of lead.

Mention was made of the observations of a person at Yale explaining the special vulnerability of children to airborne lead. In her model, she showed that there is an inverse gradient from the ground up, and the increase in lead close to the ground is a geometric function, not a linear function. The volume of air used by the infant, the child and the older child, is also a geometric function of height. With the combination of these two, the extreme vulnerability of the toddler in comparison with the adult is understandable.

Dr. Picomelli felt that to be important, but in his opinion, even more important is the ingestion of dust. He brought out the fact that there are clear-cut data on children who are living in far-away, remote communities where the main industry is a smelting plant and the children had lead poisoning caused by the dust that the parents brought home on their clothing.

It was noted by another participant that a high percentage of children of workers in battery factories have high blood lead levels, although the parents claim that they change their clothes and take showers before leaving the plant. It has still not been determined how the children are exposed. The paint in the homes has been checked and it is lead-free.

Dr. Guthrie said that the Canadian Association for Mental Retardation, the NARC and the AAMD must all publicize and work on the problem of lead poisoning among persons in institutions. This is still happening all over the United States and Canada.

PROGRESS AND PROBLEMS

"IMMUNIZATIONS: WHAT CAN BE DONE TO IMPROVE THEIR USE"

Presented at the International Summit
on Prevention of Mental Retardation
from Biomedical Causes

by

Dr. James Albert Browder

BACKGROUND

Medical science in the 20th century has developed potent, safe vaccines to prevent the common contagious childhood diseases that frequently cause serious neurologic damage, mental retardation, and even death. Paralytic polio and smallpox are familiar examples of catastrophic diseases virtually eliminated by these modern vaccines. Equally effective vaccines are available for measles, mumps, pertussis (whooping cough), rubella and tetanus, but utilization varies widely. As a result of failure to adequately immunize, serious outbreaks of these preventable diseases continue.

Measles, or rubeola, is a vivid example. Before live vaccines became available in 1963, this common childhood disease occurred at an annual rate of four million cases in the United States. This led to 4,000 cases of encephalitis, 1,300 cases of mental retardation, and 400 deaths.¹ Prior to measles immunization in Oregon, the average annual rate was 8,700 cases of measles per year, causing 29 retarded children. From 1964 to 1974, 87,000 cases would have been expected in Oregon, a small state of two million people. Only 10,295 cases occurred, presumably due to increasing use of the vaccine licensed in 1963. By 1974, the number of cases reported had declined to only 23.² Table I summarizes this experience in terms of reduced morbidity and mortality along with projected savings.

Table II presents similar figures on a ten-year national scale for rubeola. Here 23,707,000 cases were averted, 2,400 lives saved, and 7,900 cases of mental retardation averted with the projected net benefits for the period estimated as 1.3 billion dollars.¹

German measles, or rubella, is a common childhood illness. Although characterized as mild with a brief nondescript rash, rubella can cause mental retardation, deafness, blindness, and other serious handicaps when it infects the unborn baby, as in the congenital rubella syndrome. Congenital rubella occurs in many babies whose mothers had the disease during the first half of their pregnancy. Rubella varies in frequency and usually occurs in epidemics every six to ten years. In the worst epidemic in the United States in 1963-64, 20,000 to 30,000 children were born with congenital rubella.³ Figure 1 shows the declining incidence since an effective live vaccine was introduced in 1968. The vaccine probably prevented an epidemic which was expected in the early seventies. Oregon was projected to have had more than 12,000 cases of rubella with about 150 babies born with congenital rubella.⁴ In contrast, there was actually an average of 280 reported cases for 1970 to 1974 as compared to an average of about 1,000 cases per year from 1966 to 1970. These 280 cases resulted in only one or two cases of congenital rubella. Table III summarizes these cost benefits.

THE PROBLEMS

Preventable common childhood contagious diseases, especially measles, rubella and whooping cough, are still occurring and causing major neurologic disease,

mental retardation, and even death. Yet a vaccine for each of these had been available for nine years or more. Obviously, the major concern is apathy and ignorance on the public, including physicians, about the need for immunizations.⁵ After several years of no large-scale outbreaks of any of the preventable diseases, the population has followed the familiar "out-of-sight, out-of-mind" pattern of behavior. If we are to eliminate these illnesses and their severe complications, we must rekindle public concern and, where appropriate, legislate to assure our children the protection so vitally needed. Most states have immunization laws and regulations, but these have generally not been enforced.

Oregon prides itself in being a more progressive state, a leader, but in 1974, Oregon immunizations paralleled other areas of the United States. Some counties reported 30-34% of children inadequately immunized.⁶ These figures are similar to other areas of the United States, especially among preschoolers. They reflect, not only core-city and rural restricted health services, but also the patients of private pediatricians.⁷ With support of the Oregon Association for Retarded Citizens (OARC), an Oregon law was passed in 1974 requiring immunization for entry into school. Yet in June of 1976, 20-28% of first graders in several counties still were unimmunized for rubella and 20-25% for DPT.⁸ As a result, Oregon had 366 cases of measles the first 11 months in 1977, a dramatic increase from 23 cases four years ago. Other western states had similar outbreaks. Our neighboring state of California, which has a population of 20 million, had almost 10,000 cases in 1977 with the expected deaths and handicaps.⁹

New problems are arising with rubella. Prior to the use of the vaccine, most adults (90-95%) had had the disease and were immune. As a result of the present vaccination programs, we have created a population of young adults who were not exposed to the disease, but were also not vaccinated. The group were adolescents at that time when we were not immunizing teenagers. This has resulted in significant populations of young women of childbearing age who are susceptible to the disease. Outbreaks in closed populations, such as campuses, are occurring and can cause congenital rubella. In 1974, 300 students had rubella on the Oregon State University campus.⁴ In Wisconsin in October and November, 1977, 45 cases of rubella were diagnosed at Marquette University. Data from the Marquette population report 20-25% of students are susceptible.¹⁰ Other campuses have had similar outbreaks.

The Oregon Association for Retarded Citizens (OARC) has responded to these continued problems with new efforts at legislation. First, in 1977, they modified the school immunization law so that it is now enforceable and more acceptable to school administrators. OARC next introduced legislation to try to protect pregnant women in the future by requiring them to have pre-marital blood tests for rubella susceptibility as well as Rh typing and a blood test for syphilis. Final action was not taken on this legislation and it will be reintroduced at the next session. OARC also strongly supports prenatal screening for susceptibility in order to allow for immunization of susceptible women in the immediate post-partum period. Additional public education to ensure acceptance and follow-up immunizations will be needed if this is to be effective.

SUMMARY AND RECOMMENDED ACTION

Our goal is to reduce the incidence of mental retardation and related developmental disabilities by eradicating all preventable childhood infectious diseases through effective immunization programs for DPT, measles, rubella and polio. To reach this goal, we propose the following objectives:

1. Increase public awareness and concern for immunizations for women of childbearing age through the news media.
2. Increase private and public health professionals' concerns for immunizations.
3. Increase immunization of school age children to the 95% level by enforcing immunization requirements for school attendance.
4. Require immunizations for children attending day care, nurseries, and preschools.
5. Assure adequate funding for immunization programs to be provided by primary health care facilities, public and private, including EPSDT and headstart programs.
6. Require adequate surveillance of immunization levels as a part of federally funded state immunization programs.
7. Immunization teams to carry out mass immunization clinics in areas with low levels of immunity and in cases of disease outbreaks.
8. Adult women of childbearing age should be protected from rubella by:
 - a. Family planning clinics to conduct blood tests and provide immunizations when women are not immune.
 - b. Premarital blood tests and immunizations when not immune (with appropriate precautions to avoid pregnancy for two to three months after vaccination).
 - c. Prenatal blood tests and immunization after delivery for women not immune.
 - d. College entrance blood tests and immunization of susceptible women (with appropriate precautions to avoid pregnancy for two to three months after vaccination).
9. Federal programs should provide "no fault" financial liability protection for adverse reactions to vaccines.
10. Immunize all unvaccinated girls at junior high school level.

TABLE I

PROJECTED COSTS, BENEFITS AND SAVINGS

MEASLES VACCINATION PROGRAM

OREGON 1965-1974

<u>MORBIDITY AND MORTALITY</u>	<u>EXPECTED OCCURRENCE WITHOUT VACCINATION PROGRAM</u>	<u>OBSERVED OCCURRENCE WITH VACCINATION PROGRAM</u>	<u>PROBABLE NUMBER OF CASES PREVENTED</u>
Number of Cases	87,323	10,295	77,028
Number of Deaths	8	2	6
Patients Hospitalized with Encephalitis	87	10	77
Mentally Retarded	29	11	
Other Patients Hospitalized	432	51	381
<u>PROJECTED COSTS AND SAVINGS</u>	<u>WITHOUT PROBLEM</u>	<u>WITH VACCINATION</u>	<u>BENEFITS</u>
Physician Services	\$ 430,615	\$ 51,475	\$ 385,140
Hospital Services:			
Encephalitis Cases	114,318	13,140	100,178
Other Cases	238,680	28,178	210,502
Lifetime Care for Mentally Retarded	5,075,000	1,925,000	3,150,000
	<u>\$5,864,613</u>	<u>\$2,017,793</u>	<u>\$3,845,820</u>
TOTAL SAVINGS			\$3,845,820
COST OF VACCINE			<u>474,702</u>
NET SAVINGS			<u>\$3,371,118</u>

TABLE II

ESTIMATED BENEFITS OF 10 YEARS OF MEASLES IMMUNIZATIONS
IN THE UNITED STATES

<u>TYPE OF SAVINGS</u>	<u>NUMBER</u>
Cases Averted	23,707,000
Lives Saved	2,400
Cases of Retardation Averted	7,900
Additional Years of Normal and Productive Life by Preventing Premature Death and Retardation	709,000
School Days Saved	78,000,000
Physician Visits Saved	12,182,000
Hospital Days Saved	1,352,000

PROJECTED NET BENEFITS \$1,300,000,000

TABLE III

PROJECTED COSTS, BENEFITS AND SAVINGS RUBELLA VACCINE PROGRAM

(Based on Expected 1970-1973 Epidemic Producing 150 Children with Congenital Rubella)

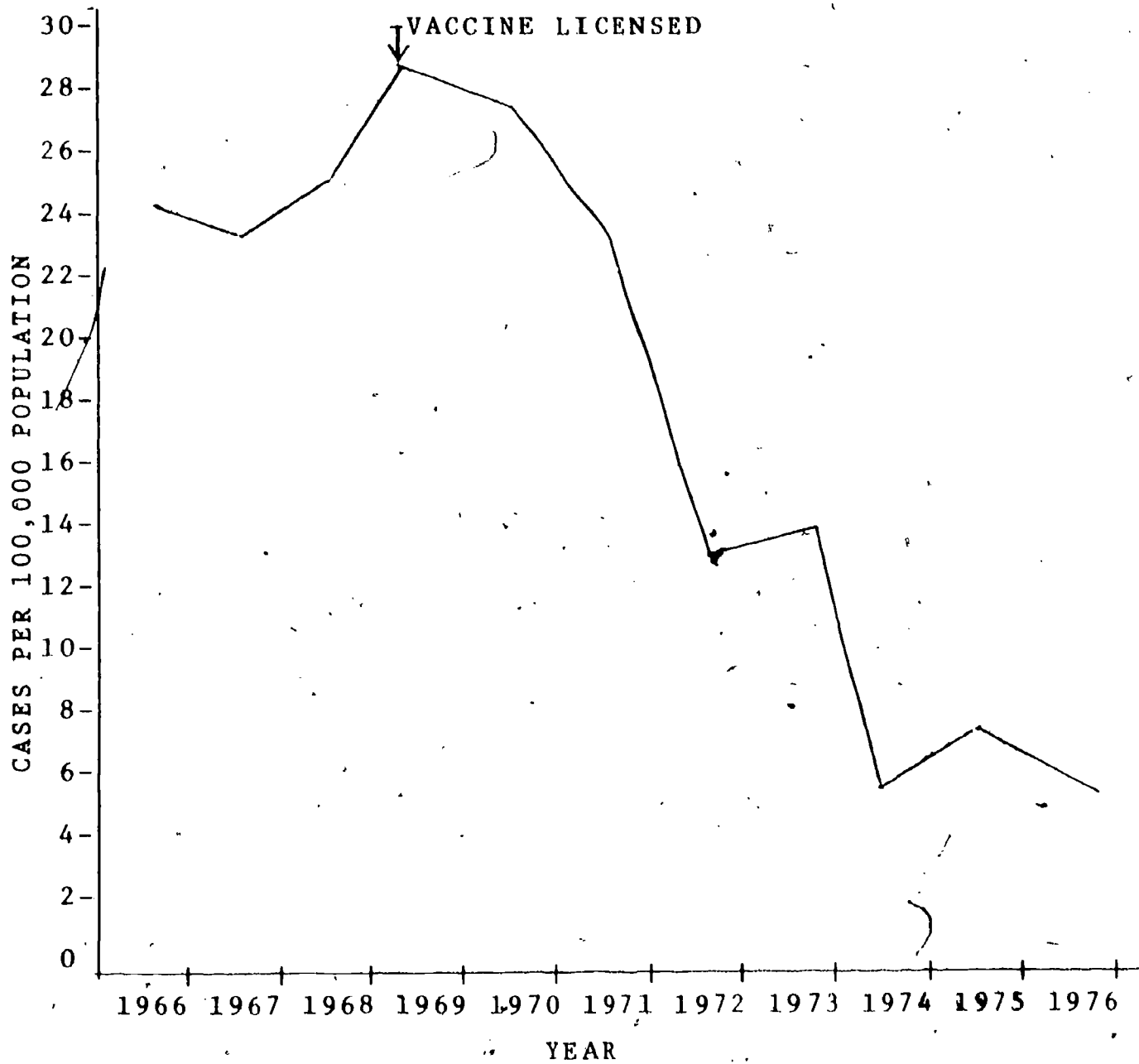
O R E G O N

1970-1974

1.	Surgical costs if 30% of the 150 congenital rubella birth have cardiac defects (\$2,400/case)	\$ 103,000
2.	Medical and educational services to age 20 if 50% would have hearing defects (\$6,000/case)	\$ 4,500,000
3.	Surgical costs and special training to age 20 if 20% require eye surgery for cataracts and/or special training (\$7,000/case)	\$ 2,100,000
4.	If 20% require lifetime care (estimated at \$175,000/case)	\$ 5,250,000
	TOTAL COST	\$11,953,000
	RUBELLA VACCINE COST	\$ 350,000
	ESTIMATED NET SAVINGS	\$11,603,000

FIGURE I

RUBELLA - (Reported Cases per 100,000 Population by Year, United States) 1966-76, Annual Summary for 1976, Center for Disease Control, M.M.W.R.



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Workshop Recommendations

IMMUNIZATIONS WHAT CAN BE DONE TO IMPROVE THEIR USE

Group Leader: J. Albert Browder, M.D.

Recorder : Theodore D. Tjossem

Goal: To reduce the incidence of mental retardation by eradicating all preventable childhood infectious diseases through effective immunization programs for DPT, measles (including rubella) and polio.

Objectives

1. Increase public awareness and concern for immunization for women of child bearing age.
2. Increase private and public health professionals' concerns for immunizations.
3. Increase immunization of school age children to the 95% level by enforcing immunization requirements for school attendance.
4. Require immunizations for children attending day care centers, nurseries and preschools.
5. Assure adequate funding for immunization programs to be provided by primary health care facilities, public and private, including EPSDT and Headstart programs.
6. Require adequate surveillance of immunization levels as part of federally funded state immunization programs.
7. Immunization teams to carry out mass immunization clinics in areas with low levels of immunity and in cases of disease outbreaks.
8. Adult women of child bearing age should be protected from rubella by:
 - a. Family planning clinics conducting blood tests, with immunizations for women not immune.
 - b. Premarital blood tests and immunizations when not immune (with appropriate precautions to avoid pregnancy).
 - c. Prenatal blood tests and immunization after delivery if not immune.

d/ College entrance blood tests and immunizations of susceptible women (with appropriate precaution to avoid pregnancy).

9. Federal programs should provide "no fault" financial liability protection for adverse reactions to vaccines.

10. Rubella immunizations for all unprotected 7th grade students.

Discussion

IMMUNIZATIONS WHAT CAN BE DONE TO IMPROVE THEIR USE

COMMENT: I would like to suggest that if immunizations are given at pre-schools, day care centers and nurseries, as stated in your recommendations, that these immunization programs be expanded so that parents of children not actually in the school program could be encouraged to participate in the immunization program, where perhaps the immunizations could be provided at cost. These could be public clinics for people who just don't have the money to go to pediatricians.

DR. BROWDER: We attempted to cover that in item number 5, which said, "Assure adequate funding for immunization programs to be provided by primary health care facilities, public and private, including EPSDT and Headstart programs."

Workshop Recommendations

IMMUNIZATIONS WHAT CAN BE DONE TO IMPROVE THEIR USE

Comments by Theodore Tjossem, Ph.D.

During the discussion of these recommendations, we became involved with the requirements for enforcement of immunizations, and this touched off a concern of mine. I have been asked to speak in greater depth about it.

I want to call your attention to the fact that, in a great part of our concern, as expressed at this conference, we have been dealing with, what is essentially, lifestyle problems. It seems to me that the medical orientation of this meeting has suggested that primary prevention is only possible through biomedical and medical endeavors. But I would suggest to you that a great part of what we are concerned about has to do with the primary prevention that begins at the behavioral level.

There is the matter of low birthweight infants and our need for regional intensive care units. The second one is teenage pregnancy - very closely related to the first. I would submit that the problem of low birthweight and prematurity in the United States is one which is a consequence of lifestyle in a certain minority population. If the minority contribution to the morbidity and mortality statistics were removed, our morbidity and mortality figures would compare favorably with those of any other country in the world. But we have paid very little attention to the factors within our society that contribute to the lifestyles that make for teenage pregnancy and to those societal factors that make the minority populations far more vulnerable. To my mind, this is an area where primary prevention really can begin by changing those conditions.

In the field of nutrition, it is the minority population that is vulnerable. This applies to immunizations and to the problem of the fetal alcohol syndrome, as well.

You have, in your remarks, placed heavy reliance upon health education as a means for accomplishing many of your goals. I submit that you should really carefully study the effectiveness of health education in the United States before placing so much reliance in this area. My review over the past year has suggested that health education is not a singularly effective device. It is effective only in conditions of total saturation and where anxiety is a motivating force for compliance. The totality of our effort should not go without making reference out of this conference, to the importance of interceding where lifestyle and environmental factors are major contributors.

When you take a look at the broken windows of schools - schools with graffiti written all over them, where the children are fearful, and where oftentimes teachers are assaulted and abused, you are asking an awful lot of health.

education in such institutions, particularly when 20% of our adult population today is functionally illiterate. How then, are you going to accomplish your health education goals? The reason I am saying these things is because the matter of making the schools the enforcer of immunizations points the finger at the school as the shaping force, sometimes against the cultural background of experience of minority pupils.

I would like to suggest that, in our future planning, we give some attention to the developments in Brookline and in Cambridge where health and education have merged to provide services to families during the first five years of life. Increasingly I have become more aware of the potential that exists in these programs. Would it not be something that we could be offering today where you could have primary health care of the public health variety concerned with issues such as immunizations, etc., provide observation of child development, and provide outreach guidance for families, such as are being provided by Cambridge and Brookline, so that families begin to look at schools as a supportive network of services? Thus the school would be a place where we could quickly pick up problems that could be referred to private practitioners, hopefully until they were corrected. If our schools, which are the most readily accessible of any of our societal services, had adequate, well trained staff to provide these firstline services, I would think they could be a tremendous complement to our efforts to prevent mental retardation. If, out of this kind of endeavor, we were able to keep girls in school and keep them happy so that they had alternatives in life other than pregnancy, we would go a long distance toward eradicating teenage pregnancy.

To meet one of the major problems that has been identified with mental retardation - that of low maternal education, why could not the school be providing education to the mother with her firstborn so that that child would be helped by educational experiences, to reach school age developmentally sound and in good health? And out of that educational experience, a mother's successive children could benefit by that kind of endeavor. It seems to be that imaginative planning should go into our thinking even though it may be down the road and some distance in the future, but there are these opportunities that now exists. I would think that some models like Brookline and Cambridge might be expanded at the office of Program Development and Innovation that is now established, and the Office of Education might be given some help and stimulation to develop some of these kinds of programs and to have some of our federal and state planners begin to consider how we can start to modify our social environments and lifestyles of our people so that one day, Canada and the United States will both be giving our populations alternatives to that kind of endeavor.

DR. GUTHRIE: May I support what Dr. Tjossem has said by mentioning what two Canadian cities have done. The school board in Vancouver, just two months ago, organized and sponsored a symposium on perinatal care, and in Montreal, the school board has taken real interest in incorporating ideas in genetics and reproduction in the high school program as an outgrowth of the basis.

LAVARDIA ROACH: I would like to thank Dr. Tjossem for his very substantive comments, and to indicate to those of you who have had similar concerns, that the sponsors of this Summit recognize that there are many overlaps when you look at causes of mental retardation. It is not always clear, when you look at etiology, how to separate the environmental from the biomedical causes. We believe, however, that the most effective strategies for prevention relative to biomedical causes differ in so many instances from appropriate techniques for preventing environmental causes. So, while recognizing the overlaps, we wanted to keep this primarily biomedical in nature. Two months ago, we met in Norfolk, Virginia, concentrating primarily on environmental strategies for preventing mental retardation. Several persons in that audience articulated almost exactly Dr. Tjossem's concerns. "This is not limited to environmental," they said. "Understand that there are some biomedical contributors that overlap." We do understand this.

MATERNAL ALCOHOLISM AND FETAL ABNORMALITIES

by

Kenneth Lyons Jones, M.D.
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A pattern of altered growth and morphogenesis, referred to as the "Fetal Alcohol Syndrome,"¹ has now been reported in over 200 children, all of whom were born to severe chronic alcoholic women who continued to drink heavily throughout their pregnancy.

Since the initial discrimination of this disorder, historical evidence has been brought to light indicating that an association between maternal alcoholism and serious problems in the offspring is not a new observation. Evidence is even available from classical Greek and Roman mythology suggesting that maternal alcoholism at the time of conception can lead to serious problems in fetal development. This led to an ancient Carthaginian ritual forbidding the drinking of wine by the bridal couple on their wedding night in order that defective children might not be conceived.²

In 1834, a select committee of the British House of Commons was established to investigate drunkenness, prior to the establishment in that same year of an Alcoholic Licensure Act. Evidence presented to that committee indicated that infants born to alcoholic mothers sometimes had a "starved, shriveled, and imperfect look."³

In 1900, Sullivan investigated female alcoholics at the Liverpool Prison.⁴ He was able to document an increased frequency of early fetal death and early infant mortality in their offspring. Other investigators have found increased frequency of prematurity, and decreased weight of surviving children born to chronic alcoholic mothers.

Animal experiments relative to the effects of ethanol on early morphogenesis have led to variable results. However, recent experiments by Chernoff have demonstrated ethanol-induced dysmorphogenesis in mice which exhibited both a dose-response effect and strain differences in susceptibility, indicating that chronic maternal alcoholism is embryolethal and teratogenic in mice.⁵

The principle features of the fetal alcohol syndrome are summarized in Table 1.

The prenatal growth deficiency has been more severe with regards to birth length than birth weight. This is in direct contrasts to most studies of generalized maternal undernutrition, in which the newborn infants are underweight for their length.

The immutable nature of the prenatal effect on growth rate is demonstrated by the consistency and severity of the postnatal growth deficiency. In the patients who could be followed after one year of age, linear growth rate was 65 percent of normal, while the average rate of weight gain was only 38 percent of normal, despite excellent foster care placement and adequate caloric intake.

Intelligence quotients ranged from below 50 to 83, with an average I.Q. of 63.

With regard to the microcephaly, in the majority of cases head circumference was below the third percentile not only for chronologic age, but for height age as well.

The joint anomalies were variable, and consisted of congenital hip dislocation; inability to completely extend the elbows; camptodactyly of the fingers; clinodactyly of the toes; and inability to completely flex the metacarpal-phalangeal joints.

Altered palmar crease patterns were variable, and consisted of the following: rudimentary palmar creases, aberrant alignment of palmar creases, or a single upper palmar crease.

Cardiac anomalies consisted of ventricular septal defects, atrial septal defects and patent ductus arteriosus.

Anomalies of the external genitalia consisted of hypoplastic labia majora and in one patient a septated vagina.

Fine motor dysfunction was manifest by a weak grasp in some patients, poor eye-hand coordination in others, and by tremulousness in the newborn period.

Two children with the Fetal Alcohol Syndrome, have had serious problems with neonatal respiratory adaptation. One had difficulty with the initiation of respirations, and was noted in the delivery room to have, "alcohol on his breath." The other had multiple apneic episodes, culminating in death at five days of age. The findings in the brain noted at the autopsy of that child are of special pertinence. There were extensive developmental anomalies which resulted primarily from aberrations of neuronal migration, and thereby in multiple heterotopias throughout the leptomeninges and cerebral mantle, as well as the subependymal regions.

Some of the functional and structural abnormalities in this syndrome, such as microcephaly, development delay and fine motor dysfunction may all be secondarily related to the type of malorientation of the brain observed in this patient. Even the joint anomalies could well be related to neurologic impairment of the fetus, including diminished movement in utero, resulting from this type of malorientation of brain structure.

An association between chronic maternal alcoholism and serious problems in fetal development is now clear. However, a number of practical issues now face us, i.e., the incidence of the Fetal Alcohol Syndrome in the offspring of chronic alcoholic women who continue to drink heavily throughout pregnancy and the incidence of fetal problems arising from moderate or low levels of maternal alcohol consumption. With respect to the former a study was undertaken in 1974, the purpose of which was to set forth the incidence and nature of problems of morphogenesis and function in the offspring of a group of women who were ascertained purely by the history of chronic alcoholism.⁶ The total sample of 23 was drawn from the Collaborative Perinatal Project of

the National Institute of Neurologic Disease and Stroke. This has been a prospective study of 55,000 pregnant women and their offspring, followed up to seven years postnatally in 12 medical centers. Two non-alcoholic control women were matched for socio-economic group, maternal education, race, maternal age, parity, marital status, and institution where the mother and child were followed. The results of that study suggest the overwhelming magnitude of the handicapping problems that maternal alcoholism can impose on the developing fetus. Four of the 23 offspring of women who drank heavily prior to and during pregnancy died prior to one week of age, a perinatal mortality of 17 percent, as opposed to 2 percent for the control group.

The most frequent problem noted in the surviving children of women who drank prior to and during pregnancy was deficient intellectual performance at 7 years of age, manifest by an I.Q. of 79 or below, occurring in 44 percent of the children, as opposed to 9 percent of their matched controls. With respect to prenatal growth deficiency, a greater percent of infants born to alcoholic mothers were below the third percentile for head circumference, length, and weight than their matched controls. In addition, structural anomalies such as short palpebral fissures, ptosis and strabismus, as well as joint anomalies and cardiac murmurs all occurred more frequently in infants born to alcoholic mothers than controls.

Relative to the incidence of the Fetal Alcohol Syndrome, 6 of the 19 surviving children born to chronically alcoholic women (32 percent) had enough abnormal features to suggest the possibility of the Fetal Alcohol Syndrome from the physical findings alone, whereas not one of the matched controls was so affected.

In order to study the question of fetal hazards arising from moderate or low levels of maternal alcohol consumption, a study has recently been published on the offspring of non-alcoholic women who drank moderately during their pregnancy.⁷ The results of that study indicate that if average maternal alcohol consumption is less than one ounce of absolute alcohol per day, the apparent risk for abnormalities is low. In the range of 1 to 2 ounces of absolute alcohol per day, the risk may approach 10%. Among the women who drank an average of 2 or more ounces of ethanol daily, 19% had infants who were considered abnormal.

Further studies are now clearly indicated, relative to the effects on the offspring of "binge drinking" during early pregnancy. In addition, more basic studies must be performed relative to the specific cause and possible prevention of this tragic disorder.

Table 1: ABNORMALITIES FOUND IN 50% OR MORE OF CHILDREN WITH THE FETAL ALCOHOL SYNDROME

PERFORMANCE

Prenatal Onset Growth Deficiency

Postnatal Growth Deficiency

Mental Retardation

Fine Motor Dysfunction

CRANIOFACIES

Microcephaly

Short Palpebral Fissures

Maxillary Hypoplasia

LIMBS

Joint Anomalies

Altered Palmar Crease Pattern

OTHER

Cardiac Anomalies

ABNORMALITIES OCCURRING IN 10 TO 50% OF CASES

CRANIOFACIES

Epicanthal Folds

Strabismus

Ptosis of Eyelids

OTHER

Pectus Excavatum

External Genital Anomalies

Hemangiomas

Ear Anomalies

ABORNMALITIES FOUND IN LESS THAN 10% OF CASES

CRANIOFACIES

Microphthalmos

Cleft Palate

OTHER

Small Nails

Hirsutism

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Workshop Recommendations

MATERNAL ALCOHOLISM AND FETAL ABNORMALITIES

Group Leader: Kenneth Lyons Jones, M.D.

Recorder : Laverdia T. Roach

Maternal alcoholism is one of the many biomedical contributants to mental retardation which can clearly be prevented through the application of appropriate strategies. We recommend that:

1. Relevant agencies, organizations and institutions authorized to provide programs and services to teenage and adult females be used as vehicles through which information regarding the serious consequences of maternal alcoholism is passed on to the target population, i.e.

- Alcoholics Anonymous
- Family Planning Groups
- High Schools (for inclusion in health education packages)
- YWCA's
- Drug Outreach Programs

2. Public awareness campaigns be initiated and closely monitored to educate the general public regarding the consequences of maternal alcoholism. Appropriate vehicles for heightening public awareness may include:

- Youth ARC's
- Printed handouts
- The National Foundation

3. Physicians (obstetricians and gynecologists) be educated regarding the most effective ways to inquire of a pregnant women specifics about her drinking habits.

4. Representatives of organizations and agencies participating in this Summit encourage such agencies to support, verbally and in writing, the Food and Drug Administration proposal to include on containers of alcoholic beverages, a warning citing the potential consequences.

5. Motivational studies based on operant conditioning be supported to determine which motivational factor(s) most effectively discourage maternal alcoholism.

Example: Innovative project for post-graduate fellow, using financial reward.

6. Persons affected or potentially affected by maternal alcoholism are educated or presented with information about this condition by persons having the same national origin.

Example: Indians increase the awareness levels of Indians; Blacks educate Blacks, etc.

DOWN'S SYNDROME AND ITS POTENTIAL PREVENTION

by

Margaret Giannini, M.D.

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Down's syndrome is now the single most common form of severe mental retardation. New approaches regarding the prevention of this syndrome are raising fundamental issues for public health discussion today.

In a study in 1960 in Middlesex, England, one-third of the total number of severely retarded individuals were classified as Down's syndrome (Goodman and Tizard, 1962). This has occurred in spite of the fact that the incidence of the birth of Down's syndrome infants has been declining over the past half century because of the shift in maternal age to younger women in many societies (Collman and Stoller, 1969). For example, in New York City in 1953, the estimated incidence rate of Down's syndrome births was 1.25 per thousand live births, while the estimate declined about 10% to 1.13 per thousand in 1967 (Stein and Susser, 1971). Recent estimates by the Epidemiology Division of the Public Health Service in Atlanta have suggested that the incidence is going down even further.

However, in spite of this shift, prevalence has increased markedly over the past fifty years. Using the Middlesex, England study as an example, the prevalence of Down's syndrome in 1925 at ages ten to fourteen was about 0.3 per thousand children but in 1960, it had risen to 1.0 per thousand children. The rates are not fully comparable, but this is one of the best comparison studies we have over a period of time (Lewis, EO, 1929). Apparently the reason for this increase in prevalence is related to the treatment of the patients. There is now a greater expectation for life in infants with Down's syndrome; whereas in 1929 life expectancy was nine years. It was twelve years in 1947 and is certainly higher today. Down's syndrome children are very susceptible to infectious diseases but since the use of immunizations, antibiotics, etc. these diseases are no longer fatal. Cardiac disease is also often now corrected by surgery. Thus, there is, in effect a larger number of these patients in spite of the fact that fewer are born.

As is well known, the risk of bearing a Down's syndrome child rises dramatically with increased maternal age. At maternal age of 15 to 19 years, the incidence rate is estimated to be 0.43 per thousand live births. By 35 to 39 years of age, it has risen to 3.5 per thousand. At 40 to 44 years of age, it has risen to 9.93 per thousand, and at 45 years and over, the rate has soared up to 22 per thousand. This means that one out of every 50 births to women past 45 years of age will result in a Down's syndrome individual. It is interesting to note that the number of pregnancies among women over 35 has decreased in the past decade. The widespread use of contraception is probably the most significant reason for this reduction. It should be pointed out, however, that it has been estimated that 80 percent of the conceptions with trisomy 21 terminate in spontaneous abortion and only 20 percent are live born (Lilienfeld, 1969).

The translocation form of Down's syndrome, which is inherited, conceivably could be detected and prevented by mass screening of parents; however only half of the parents who have a translocation Down's syndrome child evidence the double chromosome.

Since the advent of amniocentesis, the prevention of Down's syndrome has entered a new historical phase. Just for review, amniocentesis is a relatively minor, out-patient procedure in which the obstetrician withdraws 10-20 ml. of amniotic fluid using local anesthetic during the 14th week of gestation. The fluid specimen is then sent to a specialized laboratory for culture fixation and microscopic examination so that the fetal karyotype can be determined. The technique is currently at a level of safety and efficiency that would allow its use on a mass scale. It is clear that many parents, especially those in the high risk categories, for instance mothers forty years of age and older, might choose to have an abortion if they were carrying a fetus with trisomy 21 rather than let the pregnancy come to term. Though it is possible to detect medically the presence of a Down's syndrome fetus, the final decision on interrupting pregnancy is an individual matter in which personal religious, moral and ethical factors are involved.

At present, amniocentesis is a rather random procedure depending on the obstetrician and the pregnant woman who requests the possibility of selective abortion. To have a total or major impact on the problem of the number of patients with Down's syndrome would require a mass prenatal diagnostic program directed toward all high-risk pregnant women.

A cost-benefit analysis was made of the economic benefit resulting from terminating pregnancies effected with Down's syndrome. This analysis indicated that the potential economic benefit would be greater than the cost of the program for women forty years of age and older. It probably would be about equal to costs for those between the ages of 35 and 40. However, it was estimated that for women below 35 years of age, the cost of the program would be greater than the savings (Haggard and Carter, 1976).

The use of amniocentesis, followed by selective abortion for women carrying trisomy 21 fetuses may, of course, be a traumatic procedure. Thus, ideally, prevention of Down's syndrome would be determined by its etiology and measures taken to prevent the conception of such a child in the first place.

Although there are many intensive studies in the etiology of Down's syndrome currently under way in the world, many of them stimulated by the recent discovery that almost a third of patients with trisomy 21 are of paternal rather than maternal origin, to date the cause has not been identified. Under investigation are all forms of radiation, including cosmic radiation, viral etiologies (in particular the hepatitis virus), familial factors

such as the presence of autoimmune disease in families and studies of the relationship of these errors in mitosis and meiosis to similar errors that cause cancer. However, until the etiology of trisomy 21 is adequately determined, corrective measures cannot be instituted. Until then the prevention of Down's syndrome lies in the combination of genetic counseling and amniocentesis, but cannot be expected to be totally effective because of the large number of Down's syndrome infants who are born to women at the age of least risk.

In conclusion, the most important preventive measures to reduce the incidence of Down's syndrome are the following:

1. Preconceptional study and counseling, i.e.
 - a. Patients beyond age 35 to 40 and those others known to be at high risk to be advised on high incidence of Down's syndrome.
 - b. Use of contraceptive measures to prevent pregnancy.
2. Birth Control - In selected couples, based on age and/or history of genetic problems, use of contraceptives to prevent pregnancy.
 - a. IUD's
 - b. Diaphragm/condom methods
 - c. Sterilization
3. Termination of pregnancy (abortion) based on amniotic fluid studies. This is the least desirable and acceptable alternative in the prevention of Down's syndrome.

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Workshop Recommendations

DOWN'S SYNDROME AND ITS POTENTIAL PREVENTION

Group Leader: Robert Jordan, M.D.

Recorder: Jean Koch

The most practical way of preventing Down's syndrome at present is through prenatal diagnosis, however this is a particularly sensitive subject, therefore we recommend:

1. A greater awareness among obstetricians of their role in informing their patients regarding the prevention of Down's syndrome and other forms of mental retardation early in pregnancy.
2. For greater awareness of the general public, publicizing the fact that risks are greater during pregnancy for women over the age of 35, and urging them to go to their obstetrician immediately in case of pregnancy.
3. Since some low-income women do not go to an obstetrician or seek prenatal care, counseling of these women should be done regarding early medical care in subsequent pregnancies at the time they are hospitalized for the birth of a baby.

Discussion

DOWN'S SYNDROME AND ITS POTENTIAL PREVENTION

MR. PAFFRATH: This is outside the medical province, but has anything systematic been developed to help alleviate the trauma that the birth of such a child brings to parents, as well as the special care these children need? I know that in some cases, parents have formed a sort of informal fraternity or group to help each other during the traumatic period. Do you feel that is part of the consideration, even though it is not medical?

DR. GIANNINI: I think all of us feel that that is part of the problem. Parents have anxieties in the management of such a child, and they have guilt until they find through counseling that they have nothing to be guilty about. We must be very sensitive to many of those kinds of issues. The parents must be handled in a very sensitive way. However, I find Down's children very loveable and pleasant to be with and many families find this to be true. A family may go in one of two directions in caring for a Down's syndrome child. Often, when the whole family feels that the Down's syndrome child is a special member, to be helped because of his condition, he may become the pet of the family and not develop to his potential. On the other hand, in some families, the Down's syndrome child may be hidden away, as he is thought to be an embarrassment. Other children in the family may become very anxious and many problems are created. A great deal of good counseling is important. Nothing is ever static. Old problems may, or may not disappear and new problems may arise. You really need an interdisciplinary, comprehensive approach to the problem so that the family and the Down's syndrome member can be brought into the entire picture at each level of development.

DR. BOUIWELL: In Atlanta, we tried, with Emory University and the obstetrics societies, to heighten the awareness of prenatal diagnosis, primarily for older women. The steps were to provide adequate laboratory service and then to educate physicians through individual hospital obstetrics-gynecology rounds. What has occurred there has been quite encouraging. Now 25% of women 40 years old and older in Atlanta are having amniocentesis in case of pregnancy. In the 35-39 age group, it is up to about 15%. It is unfortunate that some women in these age groups, even after they are informed that they are in a high risk category, still refuse the test. Also, we have the fact that some 20% of women still do not go to a doctor in time to be offered the test. But I think raising this as an issue and going after it where you can work hand-in-glove with the university and with the obstetrics society, you can make a substantial change.

Discussion

DOWN'S SYNDROME AND ITS POTENTIAL PREVENTION (cont.)

Comment: The approach of abortion to prevent Down's syndrome is not something to which I would feel terribly committed. We ought to make a clear distinction between those solutions that are proven and deserve our commitment to the utmost, and at the same time, not make a stand of commitment for solutions that we are not convinced of or where the proof is not in or where the solution that suggests itself is a drastic one. or those things where we are not satisfied with present solutions, we should make a very strong plea to search for acceptable solutions and not lose the thrust or the need for research for unknown solutions along with our commitment to deal with those things with which we do know how to deal.

DR. TJOSSER: It seems to me that there was an omission in the recommendations on Down's syndrome. I thought Dr. Giannini referred to a need for a search into the causes of non-disjunction, pointing out that the ultimate resolution of this problem lay in this kind of research. I think we are on the threshold of making advances in that area right now.

DR. JORDAN: It helps me to think about prevention in two categories. One is the use of the knowledge we already have. The other category is research; what is most promising and could be the most productive and what priorities should be established there. I believe that we, in our workshop on Down's syndrome, emphasized the first category, thinking that was the main thrust of this meeting. We were thinking more about what can be done with what is already known. Perhaps we should have also listed some priorities, as to what would be most productive on the research side of the ledger, and not confuse the two.

DR. KOCH: Another thing the report should include in the prevention of Down's syndrome is the fact that prenatal exposure to radiation is probably a cause of this disorder. Our recommendations should include a recommendation for precautions against the exposure of pregnant women to X-rays or radiation in any form.

Also, while the report stressed the need for women to seek medical care early in pregnancy, and for genetic counseling, it did not emphasize the importance of women having their babies during the prime child-bearing years of 21 to 35. A concentrated campaign, publicizing the fact that older mothers are much more at risk of producing Down's syndrome children than younger ones, could be an effective method of reducing the incidence of Down's syndrome.

Discussion

DOWN'S SYNDROME AND ITS POTENTIAL PREVENTION
(cont.)

We have had some discussion of the use of amniocentesis and abortion to prevent Down's syndrome. According to a prominent national survey, 70% of the people in the United States favor free choice in the matter of abortion. We should not allow a vocal minority to deny the rights of the majority to elect to have healthy children. While recommending continuing research into the causes of Down's syndrome, this Summit should not seek to deny women the option of exercising a technique that effectively prevents the birth of children with this disorder.

CELEBRATION OF COMMITMENT

LAVERDIA ROACH: Let's concentrate on what each of us is going to do in the next 18 months, as an individual or as a member of an organization, to implement the recommendations made at this Summit. I know you cannot say definitely what your organization is going to do, but you can say you will take to the board, the suggestions and recommendations made by this group. This is the kind of commitment we need, and unless we become personally involved and committed, nothing will happen. You are the experts. You were called to this Summit because you have the expertise in this field.

MR. HORMUTH: I think Laverdia's suggestion implies that, in order to get something done, we must target some specific areas. For example, for the regional AAMD group in Denver, there might be one specific area to be worked on during the next 18 months. Perhaps in New England, there will be a different priority. There may be second and third steps or priorities in these different geographical areas. But unless we set priorities, we will overwhelm everybody with the tremendous needs.

Comment: This is my concern. We must select and choose among priorities, and perhaps consciously postpone some priorities that are important so that we can get some others done. We must be very careful about the choice of priorities we set.

The national organizations of which most of us here are representatives, should have a responsibility, in the sense of defining the problems, or defining what might be done; and send out a series of working guidelines as to how these problems might be approached. I don't think the national groups should actually assign what priority should be worked on by a given local group. Each region or local group obviously has priorities of its own. Thus, different regions could work on different projects. The national organizations might rank the priorities in terms of importance, but what may be perceived as being important in New England may not be important in the southwest. If you have a wide enough portfolio, you could insure the widest participation by citizen groups across the country, recognizing at the same time, that you have to give them a fair amount of initial guidance.

Comment: The GAO report talks about 6 basic things that we can prevent right now, such as inborn errors, lead poisoning, Rh disease, measles, etc. There is this whole spectrum. We must differentiate those things where we can do something right now and we must commit ourselves to getting those things done. At the same time, knowing those areas where there must be basic research, we must support research, so that those disorders which are not presently preventable, will join the list of disorders that are preventable.

Comment: We have discussed all these different areas - Rh disease, neural tube defects, lead poisoning, etc. Can anyone venture a guess as to which should be the first one to approach?

DR. GUTHRIE: We must raise criteria which will help to establish the priorities. In other words, the easiest things should come first. That would probably mean Rh disease and preschool immunizations.

MARY ETTA LANE: It is obvious that there are two ways to go. There are long-range goals that we might say must be accomplished in the next 3-5 years. There may be two or three priority areas, and in my opinion, they should be the most visible kinds of programs that would have an impact on the greatest number of people in the general population so that we are recognized as addressing the needs of society. Then we could follow up with something that has a success-factor linked to it. For instance, we selected the lead poisoning project in Illinois because we could show results immediately. It gave people satisfaction and they were willing to get involved. Thus, we, as organizations, will be recognized as addressing the needs of society and as serving those needs directly. We would be, like the cancer society, recognized as being primarily interested in prevention.

Comment: Just a word of caution about these priorities. I hesitate a little bit about putting them in a specific numerical sequence because I would not want to have anyone pick out the first one or two and leave out some other important ones. I think we should aim to get a reasonable amount of help on about four or five of the most important ones because the importance of the program may vary in different parts of the country. For instance, Connecticut doesn't need any help on Rh disease, but some other state needs a great deal of help. But that state may not need so much help on immunization or on screening.

Comment: As to the four or five priorities, I think, before we leave tomorrow, we will have commitments and we could do a better job if we try to say now what we will work on intensively.

DR. GUTHRIE: It is important to get professionals and parents to work together. Once you get professional people who earn their living working on, and are dedicated full time to the problems of mental retardation working together with parents who have an emotional commitment to it, then you can approach the resources in a community and you can achieve your goal. I suggest that that is one of the important reasons why the AAMD, as an organization should have its leadership in prevention line up people represented here from PCMR and NARC. I think the way in which you reach the goal of prevention depends a lot on how you can get the service-oriented voluntary parent organizations and the professionals in the AAMD (who are really probably just as service-oriented as the parents) to work on the problem. I have been aware of the fact that in some parts of the United States, the professionals and the parents do work together more effectively than in others. And I have been impressed that in Canada, the professional and parent involvement is so

complete and works so well, that you hardly know who is the doctor and who is the parent. This is part of the reason why the Canadian Association for the Mentally Retarded is so far along the road toward getting a commitment from its membership toward prevention. Dr. Roeher has told us that he thinks in the 1980's, the main activity of the CAMR will be on prevention. They will have most of their service components accepted and supported. That is incredibly important to me.

DR. ROEHER: The position we are coming to in our Canadian Association is that we see ourselves as a citizen movement. The technical knowledge is available to achieve a great deal if it can be implemented. What is needed to implement this in a really effective way is a public climate that really supports this. Once you have the public climate, things fall into place. So we see our role very much like that of the cancer society. When the technical knowledge was there, the cancer organization was a very effective public educator. When they got after breast cancer examination, they put on a drive that upset the doctors and everybody. They really began to reach out and this was effective. Our prevention committee has advised us to go this way, as well. They have gone through all the discussion about what are the four or five most important areas, and have decided that we must do one area well. If you do one thing at a time and do it well, that doesn't mean that you aren't doing anything about the others, but that you are really focussing and concentrating on one, to the point where you make progress. Their recommendation to our organization is that that one thing that a citizen movement can do well at this point in time, is the immunization issue. This is one of the things we are doing and to which we are committed. I have talked to Fred Krause and Philip Roos about the possibility of doing this on a two-nation basis with massive input by the advertising councils for two or three years, just as the cancer organization has done. Thus, we would pool our resources and do that job very well.

LAVERDIA ROACH: I had hoped that, when we meet again in 18 or 24 months, we would be able to show how, as individuals, we had accomplished certain commitments. We have been talking about recommendations. Out of each prevention conference and meeting for years, have come recommendations. This is supposed to be a Summit. That implies that this is supposed to be different from the other meetings at which recommendations are made. At this Summit, we have the experts. What are you going to commit yourselves to do? You are the leaders. You have the greatest amount of expertise. You should be the greatest catalysts. What are you going to do, either individually or as representatives of the national organizations.

DR. ROEHER: I can commit myself to what our organization has set as its policy, and that is that one of the thrusts is going to be massive/public education on immunizations. The other thing I will try to do personally, is to get more members of organizations to work together on this project.

Comment: I shall report on the recommendations of this Summit at the prevention committee at The Canadian Association for the Mentally Retarded, and will express my own suggestions as to priorities which might be useful. We

have two prevention committees. One is from the Saskatchewan Association for the Mentally Retarded and the other is the Saskatchewan Government Committee on Prevention. I will make definite suggestions for each particular item where recommendations would be most applicable to our province. I shall also pass this information on to those planning our institute on prevention of mental retardation in the province, which will have educational content to change the provincial attitude and lifestyle. Lay, as well as professional education in such basic issues as compliance with immunization laws will be offered. We have all the free facilities for immunizations, and have the laws, but we have no compliance. I can immediately identify weaknesses in our provincial structures, as far as screening is concerned. There should be more extensive screening for inborn errors. We have PKU and hypothyroid screening, but no other neonatal screening. We are also lacking in lead screening. No surveys have been done in Saskatchewan. I think I should be able to organize a screening project there for lead level detection. People there are somewhat aware of the fetal alcohol syndrome and the recommendations from this group will be very helpful to my plans for teaching within the province about the dangers of maternal drinking during pregnancy.

DR. McCONVILLE: I would like to say that, in my job as Health Planning Consultant to the Canadian Federal Government, I will pass back to the Health Planning group there both the priorities of the CAMR and the identified areas of interest expressed in this meeting. And I will act as a continuing contact person with CAMR, particularly with the prevention committee. We have identified particular areas in which the federal government may be specifically helpful to the CAMR. This has to do with certain grants for certain outreach programs. We can envisage a very active interface.

MR. HORMUTH: Aside from what I, personally will do because some of this is already implied in some of your recommendations, I know areas where the Health Service Agency (HSA) has a responsibility. I will be required, in the next few months, to document costs and step-by-step development in some of these areas. I was interested in Dr. Roehrer's comments about immunizations being one of the primary focusses of his association. As all of you know, there is an immunization initiative within the Department of HEW, since it is recognized as a primary need. I wonder whether one of the immediate tasks which we can coordinate some of these activities on immunization, which are being planned and carried out by various agencies within the department, and in which some of the various groups represented here can be of great help. I would think this is the kind of thing in which PCMR could take the lead in coordinating. They could meet with the components within HEW that are struggling with this immunization issue and with people like Dr. Roehrer and others who are involved and who can make a contribution, and come up with some kind of meaningful coordinated program.

FRED KRAUSE: I will commit myself to do more coordination within the federal departments of the government on an inter and intra basis. I will try to activate that. That means that the National Institute of Child Health and Development (NICHD) and Maternal and Child Health (MCH), etc. will meet and we will attempt to examine where our resources and commitments lie. There has been, in the past, a very fine public information effort toward Down's

syndrome done by NICHD. We will re-examine some of those avenues and see what the possibilities are. That is one example and I think we can do that. Communication is an area where we also have a commitment. Perhaps as frequently as monthly, we should send out a newsletter on the new happenings and activities in the prevention field. In that regard, possibly those professionals here who are representing special interests such as nutrition, lead testing or screening, can channel to us what reports or activities are occurring that we can highlight and abstract. I think we can join the Canadians in this effort to keep a flow of information, not only within our states and provinces, but between our borders. I think, in the area of communication, here with this conference itself, we hope to do possibly four or five different steps. One is a monograph on all the papers that were given here. Second, a more popular edition of the report, in terms of recommendations. Third, Wingspread has been very helpful and cooperative in suggesting that they would like to do an abstract on all the papers and take the responsibility of providing this as a mass mailing to the medical profession. Fourth, we will continue some of the radio broadcasts and efforts in that communicational medium. So there are several different areas. I don't mean to imply that these should be solely the responsibility of PCMR, but in cooperation with NARC and the actions that they put out and the AAMD journals, etc. And we can try to push to the forefront, the newsbreaking areas of prevention. I think we can greatly aid and assist. Then, there is follow-through. We are willing, if we can have the cooperation of the co-sponsoring groups, to again try to hold follow-up meetings. I have talked with Dr. Giannini and I am sure others would feel that this one shot does not do the job. We need to follow through in 30 to 60 days, and maybe track some of the specific areas that we will again set forth as some of the principle areas where we can bring some real influence to bear, such as immunization programs. How can we approach what steps need to be taken? If it is financial, the money can be collected. We are willing to be somewhat the catalyst to bring that about, from our location in Washington, working with the federal government, as well as the liaison for which we are responsible in our executive order, to work with all public and private voluntary organizations. I think these are just a few commitments for which we are willing to be responsible. We can put these in more detail in writing and circulate them to the organizations, as well as to those members that are present here. We can refine this and organize it in a way so that we can look at the 12 month period of 1978, and at our commitment and responsibility in the area of prevention. Upon that, I assume that, not only individuals, but organizations will designate areas where they are either going to be supportive or where they will take the lead. From that, we might be able to have a more appropriate agenda this coming year.

Comment: As most of you know, in the NARC, we have been committed to the area of prevention for a long time. Some years ago, we set up a prevention committee and we have a number of people here today who are members of that committee, who are doing an outstanding job. Currently, a very significant portion of our 5 year plan is devoted to the whole area of prevention. Several important objectives have been achieved in the last year. We put together a slide show on prevention entitled, "Tomorrow's Child." We are

currently planning a national conference in 1978 which is going to focus on known causes of mental retardation from which effective prevention techniques are now available. This effort is going to be funded by the United Commercial Travelers of America and the conference goal of preventing mental retardation will be facilitated by widely distributing the conference proceedings through our Associations for Retarded Citizens to local and state levels across the country. Let me just touch on some of our major objectives in the future. First, we are going to conduct that prevention conference. Secondly, we plan to encourage increased federal financing for adequate and on-going newborn screening and treatment programs. Third, we are going to stress the need for state and local Associations for Retarded Citizens to strengthen and expand their prevention efforts through programs of implementation and public education. Of course, an equally important objective next year is going to be to work cooperatively with the co-sponsors of this Summit meeting, in terms of follow-through and implementation. The continuing goal of our association, let me assure you, is prevention. We must achieve the prevention goal that President Nixon set forth to reduce the incidence of mental retardation by 50 percent by the end of the century. We have the knowledge and the technology to do this and I think if we put our heads together, we are going to do it. More specifically, the chairman of our prevention committee is going to meet with several members of this group and put together a game plan - a set of recommendations that our prevention committee can then convey back to the senior officers of our association who are meeting in Chicago in mid January. Subsequently, our executive committee is meeting at the end of January. At that point, these recommendations will come to the executive committee for whatever appropriate action is necessary.

DR. GUTHRIE: I will commit myself to educate the membership of the AAMD, as chairman of the prevention committee. For some time, we have been discussing the idea of several of us carrying the kind of dialog that went on here, into the regional level - using the regional framework of the AAMD and of the NARC and hopefully getting some aid and encouragement from the personnel in the HEW regional offices, and aiming at state model programs on prevention. Hopefully, we can involve state Developmental Disabilities Councils. In California, Maine, Massachusetts and some other states, they are already spending some of their money on prevention. It won't happen overnight, but at least, during 1978 and 1979, through these kinds of workshops, we can educate the membership, and hopefully draw together the people who are already interested. I have already found that there are more people interested than I had thought. In Montana, there was a workshop where they expected 40 people and 80 people showed up. That is one step. I will do everything I can, as an individual, to see to what extent the AAMD, as an organization can become involved in prevention. My role, as chairman of their prevention committee will be to speak more freely.

I have one last thought for the Johnson Foundation. It wasn't discussed here, but I know you are interested in it because of the little booklets you have handed out. It is not a subject that these organizations are ready to tackle right now, but Denmark has been doing this for 30 years. It was written up in 1962 in a book, "The Sexual Education of the Mature Mentally Retarded Adult." It suggests that the retarded individual have the opportunity

for voluntary sterilization, with informed consent. According to studies done in Denmark and also in Minnesota, if 50 percent of the mentally retarded in the community reproduce, approximately 30 percent of their offsprings will be mentally retarded. Right now, many of these individuals are being moved out of institutions in the normalization wave that is going on. They are moving out into the community, and as they do this, this is going to be an on-going problem. Denmark and a few other countries are doing more than we can in this area. This is something the Johnson Foundation could think about as a challenge - the sexual education of the mentally retarded adult.

MR. PAFRATH: That is truly a challenge. I would like to say that, for us to have had this group has been a pleasure. Probably more ideas have been generated out of these formal talks and private conversations than we will know for quite a while. For example, there will be the matter of reproducing the proceedings to a Wingspread Brief - something a physician can fold and put in his pocket and read on a plane. And they are doing a post-conference press release now. We are grateful that you have taken the trouble to come and refresh us in what we ought to be doing.

Comment: On behalf of the people here, we want to thank you and your staff for your kindness. You have been superb.

CONCLUDING STATEMENT

by

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I. INTRODUCTION

First, may I express a word of gratitude and appreciation to the President's Committee on Mental Retardation, the American Association on Mental Deficiency, the Canadian Association for the Mentally Retarded, the National Association for Retarded Citizens and the Johnson Foundation for making this conference possible. Also to Laveria Roach goes our applause for a job well done in organizing and staffing the conference. So much has been said here in the last two days that summarization is a task that is difficult. I trust that I have included the significant recommendations in this summary.

II. Prevention of Mental Retardation Is Part of the Need for Improvement in the Overall Health Delivery System:

The improvement of the health delivery system is dependent in large measure, upon the state of the economy, rate of unemployment and general education of the public. But that does not excuse inaction on our part. Improvement of immunization levels and nutritional status, decrease in childhood infections, lead exposure, etc. are all such critical problems that we cannot ignore them. We must use the technology we now have available to us. Along with child health is the special problem of adolescent health. The problem of teen-age pregnancy demands priority by the very magnitude of its dimension. Dr. Lowe provided statistics showing that this is now the biggest pediatric problem faced by society today. In 1976, there were 1,500,000 pregnancies in women less than 19 years of age. Of these 1,500,000 pregnancies, 600,000 went to term, 600,000 spontaneously aborted and 300,000 were therapeutically aborted. Statistics further show that second pregnancies in teen-agers stunt growth of the affected adolescent and are accompanied by a 25 percent rate of prematurity. Third pregnancies are accompanied by a 50 percent rate of prematurity. Surely this problem is of catastrophic importance. We urge the Secretary's office in HEW to do more in this area. I recommend that the President's Committee on Mental Retardation arrange a meeting with the Secretary of Health to talk about the results of this conference and include this topic as one of our top priorities.

The occurrence of mental retardation related to lack of immunization is one of the causes which can be entirely eliminated by adequate immunization programs and education of the public regarding the importance of protecting children from childhood diseases. At the present time, vaccines are not always readily available to low income families, but ignorance, lack of motivation and the way in which child health services are delivered appear to be bigger obstacles. The shabby record of this country in providing a system to ensure adequate immunization programs is difficult to understand. Immunization for diphtheria, whooping cough, tetanus, polio, measles, German measles and mumps should be routine for all children. School health personnel should place major emphasis on immunizations, and must be given more responsibility and support to more adequately carry out thorough programs. Public education is desperately needed to encourage parents to be more aggressive in obtaining immunizations for their children. A federal law should be passed requiring immunization prior to school attendance.

III. The Relationship of Prevention of Mental Retardation to the Need for Improvement in Maternal and Child Health Programs:

Some of the most effective measures for prevention are simply a part of overall maternal and child health programs. It is a well established thesis that good maternal health and prenatal care results in healthier babies and that among premature infants, the incidence of mental retardation is much higher than in full term infants. The prematurity rate of middle class women is significantly lower than that of women from lower socio-economic classes. Prematurity is largely a socio-economic problem related to poverty, ignorance, teen-age pregnancy and pre-existing disease. Provision of sufficient prenatal care reduces the prematurity rate.

Maternal and child health programs are not doing an adequate job with regard to Rh problems. The Connecticut State Plan should be utilized in other states. State laws are needed requiring Rh identification on all premarital and prenatal blood specimens. Insurance benefits should include RhIG immunization in appropriate situations, including following abortions.

Regionalization of genetic services as an overall part of maternal and child health programs needs greater support. The provision of regional newborn metabolic screening programs, amniocentesis and alpha-fetoprotein determinations promise significant potential for prevention. The most urgent need is the initiation of newborn screening for hypothyroidism. It is time for laws mandating screening for this disorder for which we have adequate treatment and follow-up care at the present time. It is tragic that public health officials have not moved more quickly with implementation, in view of the incidence of 1/5000 births. Hypothyroidism is easily treated and accounts for 1 percent of the mentally retarded in institutions. It is obvious that, with regionalization and automated equipment, newborn screening for phenylketonuria, hypothyroidism, galactosemia, maple syrup urine disease and homocystinuria will soon become a routine procedure. Strong federal leadership is needed for this. The Genetic Disease Act needs renewal so that a significant federal framework for progress is manifest.

The recent demonstration of the severe effects upon the fetus by maternal chronic alcoholism is a significant contribution to our knowledge of prevention. Undoubtedly, the use of cigarettes and anticonvulsant drugs such as dilantin in addition to alcohol are only a few of the environmental hazards of which we are just becoming aware. Greater effort must be made to alert the public to the importance of the pregnancy period and the avoidance of all drugs during that time whenever possible. Along the same line, if women were aware of the importance of having children during the peak reproductive years of 20-35, it would also make a significant contribution to prevention. It has been estimated that 70% of Down's syndrome births occur after the maternal age of 35 years.

In summary, maternal and child health programs have not been aggressively implemented to achieve prevention. Comprehensive high risk maternity centers, improve prenatal care and greater emphasis on prevention of teen-age pregnancy

by enhanced family planning efforts are all needed. The conference participants deplored the recent withdrawal of federal funding for abortions.

IV. Improvement in Nutritional Status of Mothers and Children

Perhaps one of the most important societal changes which would reduce the incidence of mental retardation is our attitude toward nutrition. During pregnancy, we are especially delinquent. In socialized medical systems such as in the British Isles, nutritional supplements during pregnancy have been part and parcel of prenatal care for years. Yet, here in the United States, very little emphasis has been placed upon improving prenatal care in this way. We have plentiful food stores, yet do not insure adequate maternal nutrition. There is no question that the Medicaid program should develop a food supplement as part of the prenatal care which is paid for by the federal and state governments.

Breast feeding of infants would improve neonatal survival, and mothers should be encouraged to nurse their babies. The advantages of breast feeding are being documented more clearly than ever before. The discovery of E-coli antibodies, thyroid hormone and taurine in breast milk are significant new findings. In addition, respiratory illness, diarrhea and allergies are less common in breast fed babies than in those fed by a formula. The evidence supporting the need to breast feed newborns is now overwhelming.

V. Screening Procedures During the Prenatal Period

New knowledge has added to our ability to improve maternity care by utilizing screening techniques. At present, most states require prenatal screening for syphilis. We need to do more. It is now possible to screen for maternal phenylketonuria, maternal histidinemia, alpha-fetoprotein, Rh factor and rubella. In this regard, these tests can all be done on one sample blood spot on a filter paper obtained during the first prenatal visit and sent to a central laboratory where they can be done cheaply by automated procedures. Maternal phenylketonuria invariably causes mental retardation in the offspring. It is thought that a low-phenylalanine diet might prevent damage. Maternal histidinemia is also probably associated with prenatal injury to the fetus, but more evidence is needed to be certain that dietary therapy would be effective. There are large studies in progress validating the need for alpha-fetoprotein screening to identify spina bifida and anencephaly prior to delivery. A national program to determine the efficacy of this testing is needed, as it appears to have a significant potential for prevention. The presence of Rh negative status alerts the physician to the possibility of Rh incompatibility and the need for RhIG (Rh immune globulin) administration after delivery. The absence of rubella antibodies in a prenatal specimen will alert the physician to the need for future rubella immunization after the pregnancy is over. These are all relatively simple procedures which should be done routinely for good prenatal care during the first pregnancy.

After delivery, newborn metabolic screening would aid in further reduction of neonatal morbidity. As previously mentioned, regionalization for newborn screening, as recommended by Dr. Robert Guthrie is a vital link in our efforts to reduce mental retardation. Screening for PKU, hypothyroidism and galactosemia should be done on blood collected at the time of discharge from the newborn nursery. A follow-up blood test for PKU, homocystinuria, maple syrup urine disease and histidinemia should be performed on every baby between 3-6 weeks of age. In my opinion, these three procedures (prenatal, newborn and 3-6 weeks postnatal tests) would reduce the incidence of mental retardation by about 5 percent.

VI. The GAO Report on Prevention 1978

This is a valuable document, but unless we can stir up action, its value may be lost. We must demand congressional hearings. I will contact my representative on the congressional subcommittee on Health to see what can be done. I will also contact my senator. Each of you must do the same. I would hope that each of our sponsoring agencies would approach key senators and congressmen urging similar action. GAO has agreed to monitor HEW response to the report. I have asked Robert Cooke and Robert Guthrie to assist me in providing Mr. Dion with professional assistance in this endeavor.

VII. Dissemination of the Facts Regarding Prevention to the General Public and the Various Professions Involved

My recommendations on disseminating the information brought out in this conference are two-fold: the proceedings should be in two publications, one for the general public and the other for the scientific community. The proceedings should be developed in several ways. The scientific presentations should be gathered and edited by a professional to be published as a book similar to those published by the National Institute on Child Health and Human Development so that we have a permanent record of this meeting available for health professionals. We should have a publication by the President's Committee on Mental Retardation in pamphlet form, as well as individual articles on each of the topics covered by this meeting. This material should be sent to public health officials of the individual states, to appropriate national organizations and their state affiliates as well as local chapters. Lastly, we should ask all of the sponsoring organizations to urge other national organizations to explore ways they can assist us to mount a national campaign on prevention to reach its zenith during the year of the child in 1979. Organizations such as United Cerebral Palsy Society, the Council for Exceptional Children, etc. should develop prevention committees. Developmental disability councils nation-wide should participate actively to develop individual state plans for action similar to what California has done.

VIII. Potential Danger of the Right to Life Movement

The recent coalescence of the Right To Life movement into a national force of significant proportions, I believe, has been a surprise to all of us. To some, this has been an unwelcome development. If we do not meet this force head-on, it could become a threat to the science of genetics, to amniocentesis programs, to sex education in public schools, and to our efforts to help with the problem of teen-age pregnancy, and it could seriously diminish our effort to prevent mental retardation. I am suggesting that we confront this force by linking up with other organizations such as the National Organization for Women, AMA, Planned Parenthood, Community Medicine, and abortion rights organizations and public health officials working for the rights of all women to opt for or against abortion of their own free will. We must emphasize the importance of the protection of equal rights - the right of the child to be well born and the right of the mother to have healthy children. At the same time, we must respect the fact that in a country as diverse as ours, there is room for difference of opinion, and for the greatest good, both forces should join hands to spur progress so that abortion will become an unnecessary solution. For that to occur, much tact and effort will be needed.

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