

THE CARE OF INFANTS AND CHILDREN*

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The growth and development of pediatrics took place principally in the twentieth century. One result has been the reduction in deaths in the first year of life 165/1000 live births to 10/1000 live births in 1987. The birth rate was reduced by one-half during the same period. The challenges of the future are to consider the needs of American children in the context of the world's children, since isolation from global problems associated with logarithmic population growth in the developing countries and maldistribution of food is no longer possible. The time has come to consider the limits to application of our ever more sophisticated technology to support life at both ends of the spectrum of human life, the most immature and the most debilitated elderly. Human behavior continues to be unnecessarily destructive for children. Congenital AIDS and drug-abusing parents are catastrophic for the infant. Accidents remain the leading cause of death of children in America. Deaths from diarrheal diseases and malnutrition are the main causes of death of children in developing countries. Nearly all of these problems are preventable with the application of current knowledge. How could we have let the best interests of children slip so far down on our national list of priorities in health care?

Thank you for the honor of participating in this celebration and sharing my views (prejudices) about the seminal events in doctoring infants and children that took place through the past century, and to reflect on circumstances that will influence what we need to do in the next century.

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Past century

Pediatrics emerged as a distinct branch of medicine in the United States during the second half of the nineteenth century. The scientific underpinnings of knowledge about infants and children began under Holt in New York at Babies Hospital and was given an enormous boost when John Howland and McKim Marriott moved to Johns Hopkins and established a department of pediatrics by full-time clinicians and investigators /1/. Let me illustrate with a few of the contributions of pediatricians in the 20th century. For example, in 1916 the demonstration by Howland and Marriott that the acidosis that accompanied diarrhea resulted from bicarbonate loss in the stools, led to the insight into the Chemical Anatomy of Extracellular Fluid by Gamble in 1939, which opened the way to safe and effective intravenous therapy /2,3/. The extension of that knowledge, largely by Darrow and Harrison, has made possible the more recent nearly universal application of oral rehydration therapy, which promises to do for the developing countries what was achieved many years ago in this country, is to decrease dramatically deaths from the dehydration that accompanies diarrhea.

The evolution of subspecialties within pediatrics has been an important advance necessitated by the ever-increasing knowledge made possible by pediatric research. One of the first of the subspecialties was pediatric cardiology, which made possible cardiac surgery. The many contributions of the surgeons were in turn helped by development of extracorporeal oxygenators, intravenous alimentation, ever-better antibiotics, and the availability of better imaging, and interpretation made possible by pediatric radiologists /4/.

To mention just a few examples of pediatric research the increased understanding of nutritional needs of infants and children, including the role of vitamins and the subsequent elimination of rickets, was largely achieved by pediatricians, including Drs. Martha Eliot and Edwards Park.

Of course, all of mankind has profited from the increased awareness of the role of infectious diseases and the control of

some of them, at least, by appropriate antibiotics and immunization. Children have been the major beneficiaries of effective vaccines against polio, measles, diphtheria, tetanus, rubella, mumps and in some instances, meningococemia and pneumococcal disease.

The most dramatic application of existing knowledge was accomplished under the leadership of Dean Henderson and the Health Organization in the eradiction of smallpox from planet earth. Never again will humans have to be vaccinated since the virus does not exist in the wild state. The lack of an animal reservoir of infection, the ability to make correct diagnosis, and the availability of effective immunization, is also possible for polio and measles. WHO/UNICEF have embarked on a program for universal immunization, with the expectation of eliminating these diseases which remain leading cripplers and killers in developing countries.

The discovery of major blood groups by Landsteiner made possible Hart's first successful exchange transfusion in an infant affected by severe jaundice in 1925. Understanding of the pathogenesis of neonatal icterus gravis awaited the discovery of the Rh antigens by Landsteiner and Weiner in 1940. It was not until 1946 however when Diamond and colleagues introduced the technique of umbilical vein catheterization that the procedure gained wide usage /1/.

Perhaps the most important discovery of the century took place in 1953, when Watson and Crick discovered the structure of DNA and introduced modern medicine to the whole new world of molecular biology. Another major step forward was achieved within the past few years in the use of reverse genetics to identify the gene product which are responsible for Duchenne muscular dystrophy /5/ and cystic fibrosis /6/. (Formerly, knowledge of the gene product was needed to point the way to localization of the gene). Insights into hereditary disease are most important for the professions of obstetrics and pediatrics since identification of carriers and prenatal molecular diagnosis is now possible for a number of conditions that can be prevented by abortion; on the horizon is gene replacement therapy for at least some diseases.

The list of major advances in pediatrics must include the introduction of aminopterin by Farber and Diamond in 1948, which was the first time chemotherapy was effective for cancer. Advances in the treatment of leukemia in particular have been dramatic and cancer chemotherapy for all ages is now undergoing extensive evaluation with ever-increasing efficacy.

In neonatology, there has been an increasingly aggressive approach to diagnosis and therapy of specific conditions made possible by new knowledge of adaptations to extrauterine life pioneered by the English physiologist, Sir Joseph Barcroft. New technologies including micromethods for measurement of blood constituents and equipment designed to meet the needs of ever-smaller infants have made monitoring of changing conditions possible. Better incubators, ventilators, and new drugs have been life saving. Understanding of nutritional needs and meeting them with intravenous alimentation has made it possible for ever-smaller infants to survive and expect a normal lifespan.

Other examples include the reduction in deaths from hyaline membrane disease, with approximately 10 000 per year during the years 1969-73 in the United States reduced to 5 000 per year 1979-83 and an estimated approximately half that number when pulmonary surfactant replacement therapy becomes widely available within the next few years (Table I).

The reduction in mortality in low birthweight infants has been achieved not only by new technologies, but also by regionalization of intensive care, with the establishment of centers staffed by trained personnel and stage-of-the-art equipment to which babies born in outlying hospitals can be transferred safely. The package of services provided by neonatal intensive care has made possible the major reduction in mortality and morbidity among low-birth weight infants (Table II). It is unfortunate that so little effort has been expended on the most desirable goal of reducing rates of low-birth weight.

We must acknowledge that accidents account for about half the deaths of children in North America. Although poisonings

TABLE I
Annual RDS/HMD specific mortality
(U.S. vital statistics)

	1969-73	1974-78	1979-83
White	7880	5945	3837
Black	1989	1897	1345
Total	9993	7962	5271
Rates/1000 live births	2.89	2.47	1.46
% change in rates within 5-year period	+2.7	-9.4	-8.8

TABLE II
Survival by weight group
July 1, 1987 to June 30, 1988

No.	Weight groups	% Home from hospital
3	501-600	13
6	601-700	62
12	701-800	66
13	801-900	74
18	901-1000	91
25	1001-1100	> 90

Total births 9808

% Births under 2.5 kg 10 %
under 1.5 kg 4 %
under 1 kg 1 %

Data from Brigham and Women's
Hospital, Boston Courtesy of Drs. M.
Epstein and E. Lieberman

have been reduced through systematic health education and poison control centers, maternal substance abuse, one of the worst forms of poisoning is now reaching epidemic proportions particularly in our inner cities and especially with cocaine /7/. Approximately 15-20 % of infants delivered at Boston City Hospital have metabolites of cocaine identifiable in their urine. The infants are often born prematurely; they are usually somewhat small for gestational age, often irritable, occasionally have a high-pitched piercing cry, and they may have central nervous system problems that occur while still in utero /8,9/. Coupled with the wide use of intravenous drugs, especially, heroin, is the increase in promiscuity and the excess risk of HIV infection imposed on that same group of mothers and infants /10/. To be born addicted to cocaine and have AIDS as well, with predictable mortality within the first years of life, remains a totally preventable catastrophe.

Future century

It is clear that the world's population is growing logarithmically especially among those with the least opportunity for access to good medical care or education.

The world's population was approximately 3 billion in 1960, and exceeded 5 billion in 1985. Most of this increase was in the developing world. It is estimated that enormous numbers of children in the developing world are inadequately fed, and deaths from malnutrition continue to occur in the wake of man-made disasters such as war, but also in the presence of drought and a failed food distribution system. In developing countries in the 1980s, one death in every 3 was a child under age 5 years.

There is ample evidence of complacency or lack of awareness of the magnitude of these problems, particularly as they affect children. For example, one important solution is the urgent need to have widely available safe birth control. Fortunately, the "pill of choice" RU 486 is available, an estimated 25 000 women have taken it in France, where it is found to be 96 % effective /11,12/. It is specific for inducing termination of pregnancy by completely blocking a receptor for progesterone

and can be most effective within the first 9 weeks of pregnancy. The research for the development of this compound was supported by the Ford Foundation and the French government, as well as the pharmaceutical industry, but it is not available in the United States except by the black market through China. There are no U.S. funds to support the WHO special program on human reproduction and minimal U.S. funds available for study of RU 486 in this country. All of this is in the context of an estimated 200 000 maternal deaths per year worldwide, half of which are estimated to be from unsafe abortions /13/.

It is worth considering what is being done to improve child health, and thus in due course reduce the numbers born. I already mentioned that UNICEF is active in eradicating polio and measles. Perhaps as important as their program for immunization is their ongoing advocacy of oral rehydration therapy in countries where deaths from dehydration remain prominent. The teaching of maternal and child health with respect to the use of growth charts and the benefits of breast feeding and family spacing are making headway around the world. Fortunately, decrease in fertility rates usually follows the reduction in infant mortality, where as an example, Japan in 1940 had 90 deaths per 1000 live births and parents had on the average of 4 children; whereas in 1988 the comparable figures are 5.5 per 1000, and the average number of children are 1.8 per couple /14/ the same has been the case in the U.S. (Table III).

TABLE III

Year	Birth rate (Per 1000)	Births/woman (Fertility rate)
1790	55	8
1900	30	-
1940	20	2.3
1950	22	3.2
1957	22	3.7
1970	19	2.5
1985	15.5	1.8

While we acknowledge the enormously important needs of children around the world, we in the developed world at the same time are focusing considerable attention on the provision of intensive care for ever more immature infants. One of the advances only recently made available in the United States, (but used for several years in Japan) pulmonary surfactant replacement therapy, promises to produce ever more survivors of 25- and 26- week gestational age. This poses a problem with respect to definition of the lower gestational age or weight limit for which intensive care should be mobilized. Complex, ethical dilemmas surface with regularity in nurseries. For example, is the preterm infant of 25 weeks of a couple with a history of infertility, long awaited, a better candidate for surfactant replacement than a similar preterm infant born after an unwanted pregnancy in a 16-year old? Who will care for either infant? What are the chances of a normal outcome, or does that matter? Should every infant born alive at 24 weeks be given surfactants, regardless of other problems that may be present? Making the lung function precociously does not ensure normal brain development for example. In a society where we are not prepared to provide optimal supports for the child after discharge from the hospital, let alone assurance that the child will achieve education sufficient to become some kind of a competitor in society, does it make sense to provide intensive care to infants under 26 weeks or 25 weeks or 24 weeks gestational age?

What do we do? Many neonatologists try to come to some kind of consensus by taking into consideration the specific facts surrounding the given child in consultation with parents and their advisors. But we remain concerned about the paradox of extraordinary effort for the borderline viable infant in a world that allows so many infants to die of neglect.

In conclusion, what will "doctoring" become in the next 100 years? As Leon Eisenberg has noted "at the root of it is the need to recognize that doctoring is but one element in the envelope of care that should surround every child? The health of infants and children will be dependent on massive societal efforts to eliminate war and other forms of violence, to reduce

poverty, to promote birth control, and to foster education. I believe it also mandates a continued quest for more knowledge so that babies will not only be well-born, but well-cared for and supported thereafter. We are experiencing, in neonatal intensive care at least, "a half-way technology", to quote Lewis Thomas, and the only way ahead, I believe is for more new knowledge and a hope that society will use that knowledge wisely. On issues of the sort I just addressed, I tend to recall Mr. James Rouse's comment on one occasion. When I asked how he managed to convince the residents and land owners of the need for inner city rejuvenation, for which he has been so responsible, his answer was, "there is no such thing as an opponent; only an ill-advised citizen".

Walt Whitman had some wise words on these issues:

Now understand me well - it is provided in the essence of things that from any fruition of success, no matter what, shall come forth something to make a greater struggle necessary.
(from Song of the Open Road)

REFERENCES

1. Cone TE: History of American Pediatrics (Boston: Little, Brown and Company, 1979).
2. Howland J and Marriott W.McK: Acidosis occurring with diarrhea. Am J Dis Child 11: 309, 1916
3. Gamble JL: Early history of fluid replacement. Pediatrics 11: 554, 1953
4. Hendren WH, Lillehei CW: Pediatric surgery. N Eng J Med 319: 86, 1988
5. Hoffman EP, Fishbeck KH, Brown RH et al: Characterization of dystrophin in muscle-biopsy specimens from patients with Duchenne's or Becker's muscular dystrophy. N Eng J Med 318: 1363, 1988
6. Karem B, Rommens JM, Buchanan JA et al: Identification of the cystic fibrosis gene: genetic analysis. Science 245: 1074, 1989

7. Amaro H, Zuckermen B, Gabral H: Drug use among adolescent mothers: profile of risk. *Pediatrics* 84: 144, 1989
8. Bingol N, Fuchs M, Diaz V et al: Teratogenicity of cocaine in humans. *J Pediatr* 110: 93, 1987
9. Hadedd AJ, and Siegel SR: Maternal cocaine use during pregnancy: effect on the newborn infant. *Pediatrics* 84: 205, 1989
10. Blanche S, Rouzioux C, Moscato MG et al: A prospective study of infants born to women seropositive for human immunodeficiency virus type 1. *N Eng J Med* 320: 1643, 1989
11. Baulieu EE: Contraception and other clinical applications of RU 486, an antiprogesterone at the receptor. *Science* 245, 1351, 1989
12. Chefras J, Baulieu EE: In the eye of the storm. *Science* 245: 1323, 1989
13. Palca J: The pill of choice? *Science* 245: 1319, 1989
14. Wegman ME: Annual summary of vital statistics 1988. *Pediatrics* 84: 943, 1989

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