

INTRAUTERINE GROWTH RETARDATION

Mercedes de Onis

Intrauterine growth retardation (IUGR) refers to fetal growth that has been constrained in utero. It results in newborns that have not attained their full growth potential and are already malnourished at birth. Fetuses that suffer from growth retardation have higher perinatal morbidity and mortality and are more likely to experience poor cognitive development and neurologic impairment during childhood. Research shows that as adults IUGR babies have increased risk of cardiovascular disease, high blood pressure, diabetes, and related diseases. Moreover, IUGR contributes to the cycle of malnutrition between generations. The implications of this cycle for both human and socioeconomic development of the affected populations are enormous.

SITUATION IN THE DEVELOPING WORLD

Human growth is defined as an increase in size over time, not only in the fetus, but throughout childhood until the time of skeletal fusion. Size at the time of birth, therefore, is a function of two factors: the rate of fetal growth and the duration of gestation. But because valid assessment of the duration of pregnancy is difficult to obtain in developing countries, the prevalence of low birth weight has been often used as a proxy to determine the magnitude of IUGR. The availability and quality of birth-weight data is also problematic. Despite these constraints, recent estimates suggest that currently about 11 percent of newborns, or 12.6 million infants, suffer from low birth weight at term (the IUGR proxy). The magnitude of the problem varies widely across countries and geographical regions (see [table](#)).

Low birth weight at term is especially common in South Central Asia, where 21 percent of newborns are affected, accounting for about 64 percent of all affected newborns worldwide. Low birth weight at term is also common in Middle and Western Africa, but much less so in Latin America and the Caribbean. It is important to note that in the poorest developing countries, a large proportion of newborns, and not just those below an arbitrary cutoff point, are likely to suffer some degree of prenatal growth retardation.

DETERMINANTS OF IUGR

In developing countries, the major determinants of IUGR are related to the mother's nutritional status: inadequate nutritional status before conception, short stature (primarily due to undernutrition and infection during childhood), and poor nutrition during pregnancy (low gestational weight gain due primarily to inadequate diet). Micronutrient deficiencies play a part but their specific role in IUGR remains an important research question. Gastroenteritis, intestinal parasitosis, and respiratory infections are prevalent in developing countries and may also have an important effect. Malaria is a major determinant in countries where that disease is endemic. Cigarette smoking is becoming an increasingly important factor in some parts of the developing world.

The immediate causes of IUGR often operate simultaneously with deeply rooted underlying causes related to the status of women in society, access to quality health services, sanitation, household food security, education, and poverty.

CONSEQUENCES OF IUGR

The health and social consequences of being born malnourished are severe and long-lasting. For infants weighing 2,000-2,499 grams at birth, the risk of neonatal death is 4 times higher than for infants weighing 2,500-2,999 grams and 10 times higher than for infants weighing 3,000-3,499 grams. The increased risk of mortality extends into the postneonatal period and includes sudden infant death syndrome. Where diarrheal diseases and acute respiratory infections are the major causes of mortality, IUGR infants have shown an increased risk of morbidity. This is because most of these infants' immune functions are impaired.

Interventions that reduce the incidence of IUGR, therefore, can be expected to reduce neonatal as well as postneonatal mortality. In developing countries with high rates of IUGR, this reduction in mortality could be substantial.

The effects of growth retardation on cognition vary with age at the time of assessment. Deficits tend to be larger in more severely growth-retarded children and are aggravated by high levels of infection, inadequate nutrition and stimulation, low levels of parental education, and other environmental conditions. Poor school performance has been reported in more than half of the studies in which it was examined. Very little is known about the short- and long-term effects of IUGR on body composition and on physical performance and maturation. The impact of IUGR on physical work capacity, work productivity, reproductive performance, and obstetric risks also must be assessed.

FETAL ORIGINS OF ADULT DISEASE

The "fetal origins of adult disease" hypothesis originated in the 1980s, when a link between low birth weight and the incidence of cardiovascular disease was noted among middle-aged U.K. men and women by a group of researchers from the University of Southampton. A number of studies have also indicated that low birth-weight-term infants have a higher incidence of hypertension and non-insulin-dependent diabetes (NIDDM) in later life than do those with normal birth weight. The so-called "Barker hypothesis," which remains controversial, is founded on the concept that maternal dietary imbalances at critical periods of fetal development affect fetal structure and metabolism in ways that predispose the individual to later cardiovascular and endocrine diseases.

Some of the uncertainties that surround this hypothesis will be resolved when research progresses beyond epidemiological associations to greater understanding of the cellular and molecular processes that underlie them. The Barker hypothesis potentially has major implications for public health, especially in developing countries. This is because in the developing world a high proportion of births occurs in the birth-weight range with the highest risk of developing adult disease. In addition, the prevalence of factors, such as obesity, that might lead to high blood pressure, cardiovascular disease, and NIDDM is increasing rapidly in some developing countries. The fetal origins of disease provide even greater justification for prioritizing interventions that improve nutritional status, especially of girls and women, and they call for a life-cycle approach to improving nutrition.

POLICY IMPLICATIONS AND CONCLUSIONS

As we enter the new century, the quality of life of infants and young children, as opposed to mere survival, is becoming increasingly important. As more children survive, paying closer attention to the strong relationship between nutritional status and children's ability to achieve their optimal physical growth and psychological development becomes critical. The period of intrauterine growth and development constitutes one of the most vulnerable in the life cycle, with lasting, profound consequences that can compromise the ability to contribute to society. Investment in interventions to improve fetal growth and development not only will decrease the prevalence of IUGR, but will also prevent its negative consequences throughout the life cycle.

But the complex interaction among the multiple causes of IUGR explains the modest benefits achieved so far by nutritional interventions to prevent fetal malnutrition. In poor societies, where multiple pathologies coexist, it is unrealistic to expect that the intergenerational and intragenerational effect of longstanding social and nutritional deprivation on maternal and fetal health can be overcome by a single nutritional intervention during a few months in the course of pregnancy. Simple solutions will not resolve the complex problem of fetal malnutrition.

On the basis of current scientific evidence, strategies to reduce maternal smoking--using a range of approaches, from behavioral remedies to taxation--should be encouraged; efforts to improve women's nutrition should be made a priority, especially in developing countries, although the expected effect of maternal nutrition supplementation on birth weight may be modest; and antimalarial chemoprophylaxis should be considered for women who are pregnant for the first time, although more research is needed to determine the ideal timing and combination of agents.

Priority research areas include a number of promising interventions that merit further investigation following rigorous research methods. Zinc, folate, and magnesium supplementation should be evaluated. And appropriate combinations of interventions (for example, antianemic and

antimicrobial/antiparasite agents) that can be tested in population-based trials should also be made a priority.

The greatest need for research is in the developing countries, where IUGR is much more widespread and its multifactorial nature more diverse and less well understood. There is also a need to focus the attention of policymakers on prenatal and early childhood nutritional status as one of the key indicators of development, and as a precondition for the socioeconomic advancement of societies in any significant long-term sense.

For further reading see "Causes and Consequences of Intrauterine Growth Retardation: Proceedings of an IDECG Workshop," *European Journal of Clinical Nutrition* 52 (Supplement 1, 1998).

TABLE
Intrauterine Growth Retardation in Developing Countries, 2000

		Intrauterine Growth-Low Birth Weight (<-2,500 grams and =>37 weeks)	
<i>Region</i>		<i>Percent</i>	<i>Total Number</i>
Africa			
		8.9	2,590
	Eastern Africa	NA	NA
	Middle Africa	15.1	628
	Northern Africa	NA	NA
	Southern Africa	NA	NA
	Western Africa	11.1	974
Asia			
		12.2	9,248
	Eastern Asia	1.9	395
	South Central Asia	21.0	8,057
	Southeastern Asia	5.3	600
	Western Asia	3.8	196
Latin America and the Caribbean			
		6.6	767
	Caribbean	6.9	53
	Central America	7.3	250

	South America	6.3	464
	Oceania	8.8	20
	Melanesia	9.9	19
	Micronesia	NA	NA
	Polynesia	0.2	0.03
	Developing countries	10.8	12,625
<p>Source: World Health Organization, Department of Nutrition for Health and Development. Note: NA stands for not available.</p>			

Mercedes de Onis (deonism@who.ch) is medical officer at the World Health Organization in Geneva, Switzerland.