

## **DEVELOPMENT OF A STRATEGY TOWARDS PROMOTING OPTIMAL FETAL GROWTH**

### **Rationale**

The prevalence of low birth weight is estimated to be 15% world wide with a range of 3.3-38% and occurs mostly in developing countries. It is a multifaceted public health problem. Low birth weight is a major determinant of mortality, morbidity and disability in neonates, infancy and childhood and has long term impact on health outcomes in adult life. Low birth weight results in substantial costs to the health sector and imposes a significant burden on the society as a whole. Maternal size and lifestyle also determine the size of the baby at birth. At present it is unclear if the problem is LBW per se or other indicators of fetal growth, and the "optimal size" for a baby is still being discussed.

Although maternal nutrition and low birth weight are recognised as crucially important WHO does not have a comprehensive strategy to address this issue. We therefore propose to develop a WHO strategy that will address those two problems with the following objectives:

1. To review current knowledge in order to determine major risk factors and to develop approaches on how to prevent LBW
2. Identify cost- effective interventions for short-term benefits on pregnancy outcomes and actions for longer-term benefits for the next generation.
3. Propose WHO strategy for improving birth weight and maternal nutrition.

Three major steps proposed towards development of the strategy and activities to be planned accordingly are:

1. Knowledge gathering and analysis of the significance of size at birth for survival, growth, development and health in adult life and effective interventions
2. Formation of draft strategy, development and testing with Regional and country collaboration
3. Strategy approval and implementation

### **Process**

An expert consultation will be organized in 2003 help WHO identify priorities and directions towards the development of the WHO strategy based on the analysis of the available knowledge. The consultation will review the recommendations and the evidence on which they are based and advise WHO on the strategy.

Based on the recommendations of the expert consultation WHO secretariat will draft a strategy, discuss it with the Regional and country offices, and partners through a range of activities (2004)

The strategy will be submitted to World Health Assembly for adoption in 2005.

In 2003 the activities will focus on preparing background papers for the expert consultation and organizing the consultation.

## **Knowledge gathering and analysis framework**

### **Introduction**

The aim of this phase is to gather evidence which will answer questions needed to inform the development of a strategy i.e. to action. The first question to be addressed is the aim of the strategy. Should this be to prevent low birthweight as currently defined, to prevent reduced growth using some other definition, or to define and try to promote an optimal level of fetal growth? (Much of the available literature will focus on low birthweight (LBW) <2500 grams.) The framework below uses the terms “optimal fetal growth” and “low birthweight or LBW” to include all these options. The influence of duration of gestation should be considered in relation to each question.

The role of maternal nutrition for this critical time of her life for her own health is currently not a subject of this part of the project.

### **Background**

Definition of problem, including consideration of what we mean by the terms size (and weight) and growth, and the part gestation plays in these.

Size of problem, including issues of data quality and availability

Variation by country/region, population, setting

### **Questions to be asked**

#### **What are we trying to achieve for fetal growth?**

What growth is too little (and also too much)? Is there evidence for thresholds or particular shapes of the fetal growth distribution?

What are we trying to achieve from optimal fetal growth/prevention of LBW:

- ie what outcomes are we trying to influence?
  - mortality/longevity/burden of disease
  - health related quality of life
  - non-health related quality of life
  - developmental status
  - significant health related behaviours

and when do those outcomes occur?

- immediately and in infancy
- in childhood
- in adolescence
- in adulthood

How is fetal growth best measured - by attained size at birth, by body proportions or composition, by the trajectory of fetal growth?

Is optimal growth/LBW the same for all populations, or does it differ by genetic background, gender, setting or culture?

What is the contribution of gestation to optimal fetal growth/LBW?

### **Interventions**

What interventions are known to promote optimal fetal growth/prevent LBW?

- Nutritional
- Health care
- Health related behaviour
- Infection control

(Do we need to include postnatal interventions?)

How much difference will they make (in relative and absolute terms)?

What is the cost-effectiveness of each intervention?  
Are interventions accepted and valued by mothers/parents?

### **Cross cutting themes**

Several issues cut across the questions above. They include;

- The influence of the settings in which people live, the population group from which they come, and other characteristics that they have.
- The different time scales and points in the life-course when fetal growth may be influenced, interventions applied, and over which a strategy might operate.
- The nature of the evidence, its methodology and availability, and the importance of the gaps in the evidence in presenting a barrier to a strategic approach.
- What is the size of these associations (in relative and absolute terms)? Is there information, which will allow their contribution to be calculated? What heterogeneity is there?
- Does the evidence suggest causality?

Further details are given under each heading below

### **Settings/populations**

Is optimal growth/ a meaningful definition of LBW the same in all settings and for all populations? Are these different, for example, for boys rather than girls, by race or by setting e.g. in developing countries versus those in transition? From this, are universal fetal growth curves useful/appropriate?

What is the balance of relative and attributable risk for the determinants in different populations/settings?

What is the merit and value of different interventions in different settings?

What views do mothers/parents/ advocates have on these interventions and the values of different outcomes, and how do these vary by setting and population?

### **Time-scales**

What action could be taken now, during this generation (20 years), in the long-term (50 years i.e. 2-3 generations)?

What are the secular trends in fetal growth, its determinants, and the outcomes we are trying to influence?

When do we want to act in the life-course, before conception, during pregnancy, during infancy and childhood, during adolescence, during adult life (excluding peri-conceptually)?

When do mothers/babies want to reap the benefits: immediately, during childhood, in adult life?

### **What is the nature of the evidence and how can we use it?**

What are the different types of evidence and what can they tell us?

What are the methodological issues?

How can we best consider all consequences of action, including the possibility of doing harm?

What are the gaps in the evidence and how can they be filled?

### **Conclusions**

Can we answer these questions?

Where are the gaps in knowledge?

Should these gaps be filled before interventions can take place? If so, how?

What interventions can be recommended, with what certainty, in what settings and to whom?

How can these interventions be implemented?

A group of experts assisted WHO preparing for the consultation. At the preparatory meeting in 2002 the group summarized current knowledge, identified gaps and formulated technical

recommendation for the secretariat on the next steps. (Ref. The report of the meeting). Systematic analysis of available information in the above areas is needed in order to develop the strategy. Experts will be asked to prepare background papers in the priority areas and to quantify if possible the effects of interventions. Cost analysis will be based on the findings of the reviews.

## **Review titles**

### **1. Nutrition**

*An extensive review and summary of the effects of dietary behaviour, macro- and micronutrient deficiencies before and during pregnancy is required. This review should answer the following questions:*

- *How and to what extent do these deficiencies affect fetal growth (weight, length, head circumference and other, if known)? Do they produce prematurity or IUGR?*
- *How does maternal body composition pre-conception affect fetal growth?*
- *Are these mechanisms setting-dependent?*
- *How can these deficiencies be remedied in order to improve fetal growth in the short term? (Are there studies that have tried to achieve this?)*
- *Are these effects clearly quantifiable?*
- *What are the results of large-scale public health nutritional interventions?*
- *Has a negative impact of such strategies been described?*
- *Are the strategies for improvement viable?*

### **2. Fetal programming**

*A review of fetal programming of childhood and adult diseases is required. This review should include assessment of the evidence on the relationship between maternal body size and fetal growth and answer the following questions:*

- *How certain is the effect of programming on later disease or risk factors for disease? Which outcomes is it most certain for?*
- *What is the order of magnitude of these effects?*
- *How would a reduction of the programming effect impact on risk of later disease/risk factor (a quantified risk assessment)? What are the risks and benefits of shifting the birth weight distribution in different settings?*
- *What would be the time scale for expecting an improvement (results of the shift)?*
- *Are any of these above issues setting-specific?*

### **3. Fetal and infant growth curves**

*This review is to summarise the following issues:*

- *What is “normal” or “optimal” fetal growth and size during pregnancy and at birth for the important outcomes (mortality, morbidity, disability, adulthood diseases)? Is there a “universal” size that “fits all” irrespective of setting?*
- *Are there different growth curves for public health and individual perspectives?*
- *What are the gestational age distribution of low birthweight and the incidence of preterm birth by setting? Of particular interest would be the distribution among populations living in favourable environmental circumstances in developing countries;*

- *Examination of temporal trends (including intergenerational) in fetal growth and gestational duration in countries that have undergone major economic growth in the recent past (e.g. Japan, Singapore, Thailand). Whose growth needs to be improved first – the mother’s or the baby’s? To which extent are gains in outcomes achievable and over which time scale can they occur? Conversely, adverse effects of short-term economic decline should also be studied.*

#### **4. Factors affecting fetal growth**

*This review should focus on all potential factors (environmental, behavioural, diseases etc) in the mother, which may affect fetal growth. This should include population-level factors, such as societal factors that impact on individual women. Such “upstream” factors should include poverty, maternal education, and early adolescent pregnancy. The review should answer the following questions:*

- *Which factors are relevant and modifiable?*
- *To which extent do they operate (quantification)?*
- *What is the evidence that a modification of these factors results in improved fetal growth?*
- *What are potential viable interventions? Recommendations should be action orientated, report on costs, explore feasibility and time scales.*

#### General issues

- a) Reviews should concentrate on summarising and appraising what is *currently known* in this area and how this information could be used to shape recommendations for action *now*. Recommendations on further research and data collection to improve currently available data are only a second-level priority.
- b) Based on the evidence examined, reviewers should assess the time scale of implementation of recommendations.
- c) Reviewers should summarise any issues that may prevent the development of a strategy at the present time and are asked to propose a brief research agenda to remedy this.

**Table 1. What determines optimal fetal growth/LBW?**

Focusing on modifiable factors (and how modifiable).

Genetics	Nutritional	Maternal size and characteristics	Diseases	Pregnancy complications	Maternal lifestyle	Environment
Genetics factors and gene environment interactions Paternal size Sex	Timing of the effect: During pregnancy In adolescence (and before pregnancy) Childhood - protein and energy - micronutrients - famine Inter-generational issues Setting: severe, moderate or no malnutrition on population basis	Uterine capacity Multiple births Parity Birth spacing	Infections of public health importance: - malaria - anaemia - syphilis - rubella - other?	Eclampsia Pregnancy infection Preterm birth	Smoking Alcohol intake	High altitude Pollution Socio-economic factors