

Mini-Symposium: Maternal Diseases effecting the newborn

Maternal obesity mediated predisposition to respiratory complications at birth and in later life: understanding the implications of the obesogenic intrauterine environment



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EDUCATIONAL AIMS

- To detail the direct and indirect effects of maternal obesity on fetal development and risk of complications at birth.
- To discuss the impact of maternal obesity on the intrauterine conditions experienced by the fetus and subsequent downstream risk of respiratory complications at birth and in later life.
- To describe the effects of the altered nutritional environment on the regulation of fetal lung development and the association with clinical outcomes in overweight/obese obstetric subpopulations.
- To highlight the influence of maternal obesity on programming of offspring respiratory disease at birth and in later life and identify targets to minimise the detrimental effects and improve outcomes in this group.

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SUMMARY

More women than not are entering pregnancy either overweight or obese. This presents a significant health care burden with respect to maternal morbidities and offspring complications at birth and in later life. In recent years it has also become clear that maternal obesity is an even greater global health problem than anticipated, because the effects are not limited to the mother but are also programmed in the fetus, known as the 'intergenerational cycle of obesity'. Despite a large body of epidemiological evidence reporting outcomes of obese pregnancies, including offspring respiratory complications, much less is known about the molecular effects of maternal obesity on fetal lung development. This review focuses on the influence of altered substrate supply associated with the obesogenic intrauterine environment on fetal lung development. Understanding the molecular mechanisms contributing to altered fetal lung development will lead to improved respiratory outcomes for offspring at birth and in later life.

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INTRODUCTION

The world-wide incidence of obesity has reached epidemic proportions and is projected to grow to 70% by 2025 [1].

Consequently, the number of women of reproductive age classified as overweight/obese has increased [2]; as many as 1 in 5 women are obese in pregnancy. This increases the risk of maternal morbidity and mortality during pregnancy and delivery [3]. In addition, downstream effects on offspring organ development can influence the cardiorespiratory transition at birth and have lifelong consequences, including altered metabolic and cardiorespiratory function and premature death [4–7]. Of particular concern is that the effects of maternal obesity do not simply target one generation; the increased nutrient

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abundance experienced by the fetus of an overnourished mother is the basis of the intergenerational cycle of obesity [6,7]. This perpetuation of the life-long consequences of maternal obesity to the next generation is a significant public health concern, with significant implications for health care expenditure.

Infants born to obese mothers demonstrate a spectrum of outcomes, suggesting that there is a complex interplay of factors that defines the precise altered metabolic environment to which the fetus is exposed and that determines the risk of complications [5,8]. We need to improve understanding of the specific molecular factors that contribute either individually or synergistically to detrimental fetal outcomes. Moreover, we need to identify the essential maternal markers that need to be tightly regulated during pregnancy to improve outcomes. Herein, we discuss the influence of maternal obesity and factors associated with the obesogenic intrauterine environment on fetal lung development and respiratory outcomes in offspring at birth and in later life. Importantly, we identify a series of molecular changes encountered during pregnancy that may program the observed respiratory outcomes in clinical practice.

CLINICAL IMPLICATIONS OF MATERNAL OBESITY ON OFFSPRING RESPIRATORY FUNCTION AT BIRTH AND IN LATER LIFE

Respiratory consequences for the offspring of obese mothers

It is important to acknowledge both the consequences of maternal obesity and obesity related-comorbidities on offspring respiratory function in the newborn period as well as in childhood and adulthood. Fetal lung development and the subsequent risk of adverse respiratory outcomes at birth and in later life are under multifactorial control in the intrauterine environment of an overnourished mother (Figure 1). These can be direct in nature, e.g. through maternal morbidities that affect maternal physiology and hence directly influence fetal lung development, or they may be indirect by increasing the risk of secondary complications associated with an overweight/obese pregnancy (Figure 1). In some cases, complications of maternal obesity have pre-pregnancy origins with anovulatory infertility. This is thought to be a consequence of a disturbed hormonal environment in overweight/obese women [9], and increases the likelihood of women seeking

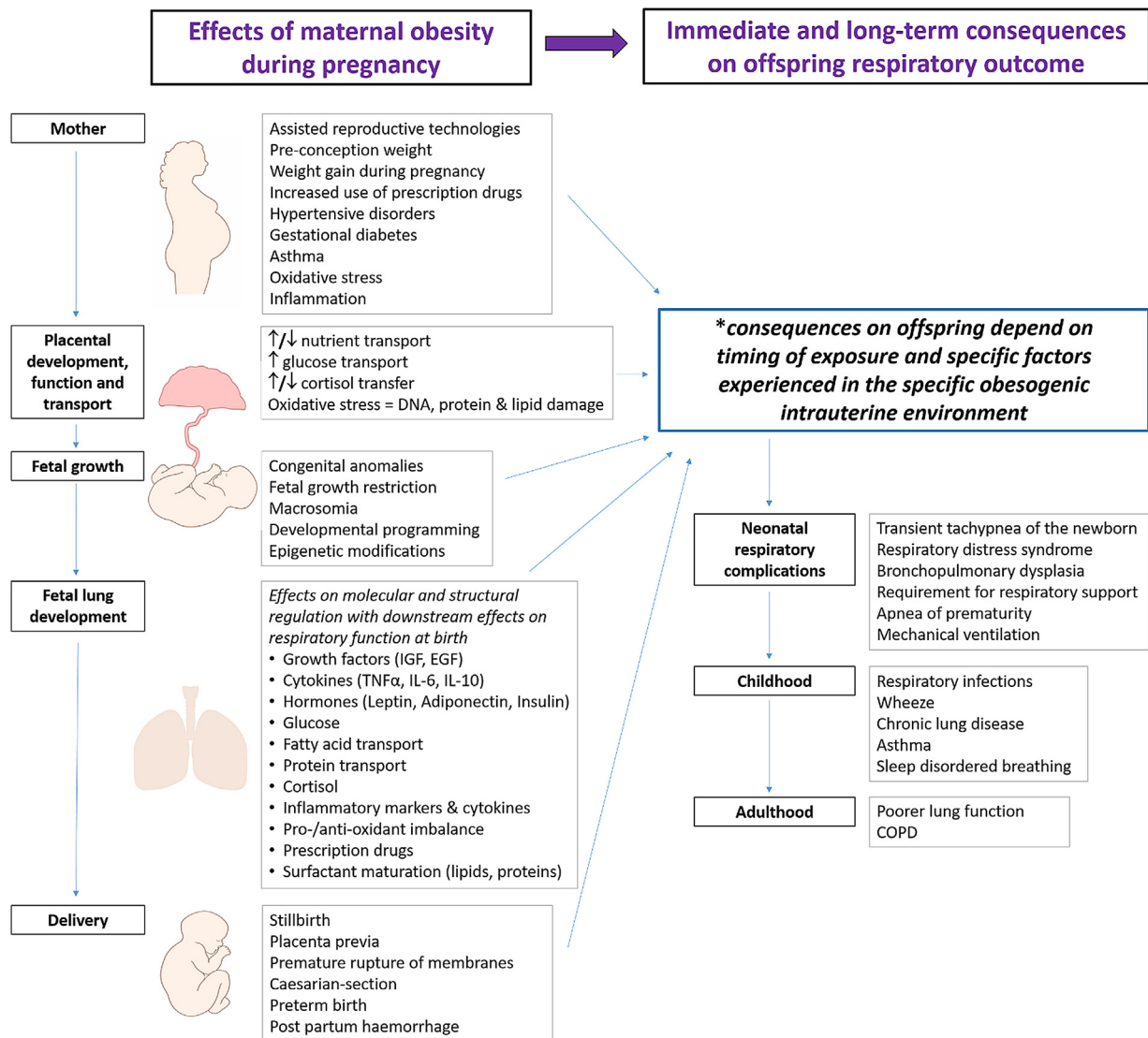


Figure 1. Summary of the effect of maternal obesity and the obesogenic intrauterine environment encountered by the fetus on pregnancy complications in addition to both immediate and long-term consequences for respiratory function. This schematic summarises the complications encountered and specific factors contributing to altered fetal lung development discussed in this review. Adapted from [81] with permission from Elsevier.

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