You are what your mother ate

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Food, glorious food – we can eat ourselves to life and, unfortunately, also to death. Everyone appears to have a stake in what we eat, telling us what we should and shouldn’t be eating. Given the rising rates of obesity and the morbid picture painted for the future of human health, it is not surprising that regulatory bodies aim to produce suitable healthy lifestyle guidelines. However, these can often be confusing and conflicting. The World Health Organisation recently recommended that we halve our daily intake of sugar to 5% of our total energy intake. On the other hand, we have headlines reporting that foods thought to be harmful to our health, such as butter, are not so bad after all. To complicate the picture further, scientific research over the last few decades presents strong evidence to suggest that your risk of obesity is determined as early as in the womb. Yes that’s right - if your mum was obese during pregnancy, you are likely to have a higher risk of obesity and type 2 diabetes. This raises a few important questions and runs the risk of opening an ethical can of worms. Can we blame our parents for our weight problems? What causes this? What does it mean for you, me and our families?

Written in the womb

Original studies in this field showed that maternal undernutrition during pregnancy increased the risk of diabetes and cardiovascular disease in the children. This led to the development of the ‘thrifty phenotype hypothesis’. The idea is that while the baby is growing in the womb, the nutritional state of the mother can signal and affect the way it develops. If the mother is malnourished, the baby develops adapted to cope in a nutritionally deprived environment; so that slice of stuffed-crust pizza with extra cheese on top (mmm...) will go the extra mile and the energy from it will be better stored as fat for backup in hard, food-less times. However, if this baby actually grows up in an environment where there’s pizza on demand (and they love pizza!), they are more prone to developing metabolic disorders such as obesity and type 2 diabetes.

More recently researchers have looked at the opposite end of the spectrum – what happens if the mother is over-nourished? It is now well recognised that maternal obesity also has negative effects on offspring health, predisposing them to obesity and cardiovascular disease. They can be programmed to be less responsive to hormones
such as insulin and leptin that are needed to maintain our energy and blood sugar levels. They can even have their appetite programmed to prefer fatty food to healthy food. Importantly, it's not all the mother's 'fault', so to speak – the health status of the father at conception can also influence offspring health, although this area is currently less well studied.

So what's causing this effect? Obesity itself is complicated with multifactorial causes, so throwing another factor into the mix doesn't help narrow down the suspects. As such, no single factor has yet been isolated for increasing offspring obesity risk. One of the mechanisms scientists are increasingly interested in is epigenetics: the study of gene regulation independent of DNA sequence. To illustrate, imagine you had an identical twin – you share the same DNA, but the way your genes are switched on and off may differ. For example, your twin's fat-burning genes are more activated meaning a pizza-devouring lifestyle has little effect on them, while you're left (literally) feeling the weight of your choices (yes, I would be jealous too). The most common epigenetic mechanism studied is gene methylation. These are little carbon-based groups tagged onto DNA sequences, making the gene more or less active.

Intriguingly, when studying children of mothers with high BMI before and after weight-loss surgery, researchers found that children born after surgery had reduced rate of obesity compared to their older siblings. Among other things, they found differences in the methylation patterns of genes involved in diabetes. These correlated with actual gene activity as well as insulin levels in the offspring, and could explain why their obesity risk is reduced\(^5\). Findings such as these are promising as they suggest that the risk is modifiable, given appropriate interventions. Recent intervention studies, such as maternal exercise or diet reversal in animal models are showing promising results in reducing offspring metabolic risk.

"Meh, I was born to be this way"
So if you're slightly heavy on the scales, and your mum was during pregnancy, it might be easy to pass the blame and reside with the fact that you were 'programmed' to be overweight. But does this mean that there is nothing you can do to change it?

Although it'll take a bit of extra effort, leading a healthy lifestyle with increased physical activity may reverse the effects of maternal obesity exposure. Intervention studies in animal models have shown that voluntary exercise in offspring of obese, high-fat fed...
mothers can reduce the extent of body weight gain and improve sensitivity to leptin and insulin compared to their sedentary siblings\textsuperscript{6}.

**What does this mean for future generations?**

The more we understand about the causes of obesity, the better we will be able to develop suitable and effective strategies to combat it. Knowing that disease risk can be determined even before we are born means parents can take steps to make sure they’re healthy before conception. Just as smoking and alcohol are now strongly advised against during pregnancy, perhaps similar guidelines will extend to dietary choices. Conversely, if you and I know we are at greater risk we, too, can take extra care to counter it. Without pushing ourselves too far in the opposite direction, perhaps we will think twice before going for that extra slice of pizza...

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\textsuperscript{1} http://www.who.int/mediacentre/news/notes/2014/consultation-sugar-guideline/en/
\textsuperscript{2} http://www.telegraph.co.uk/journalists/sarah-knapton/10703970/No-link-found-between-saturated-fat-and-heart-disease.html
\textsuperscript{3} Hales C.N. and Barker D.J. (2001). Br. Med. Bull. **60**:5-20