

# A DIET FOR GENERATIONS

**P**rof. Monika Kaczmarek from the PAS Institute of Animal Reproduction and Food Research discusses the impact of nutrition and environment on human and animal development.

**ACADEMIA: Obesity or malnutrition? Which, in your opinion, is a bigger problem in the world right now?**

MONIKA KACZMAREK: I think that a lot depends on the region of the world. Looking at statistics from recent years, one can easily conclude that countries which just six years ago were struggling with the problem of malnutrition or nutritional deficiencies are now beginning to have problems with increased obesity. These include Asian countries where home-made meals are becoming increasingly less popular and are being replaced by ready-made meals available in supermarkets, as is the case in the USA, for example. We always thought of the United States as a leader in terms of obesity, but now this is beginning to change. In Europe, we are starting to face a serious problem with obesity because processed food has become popular and we are not monitoring what we eat on a daily basis. I only hope that in a few years we will move on to the stage where the Americans are now and we will start to pay more attention to planning our meals.

On the other hand, in African countries struggling with a big food distribution problem, we are observing malnutrition.

**Is malnutrition caused by not consuming enough calories?**

Not only. It is also caused by not consuming the right types of nutrients, which can lead to irreversible health issues for the person or their offspring. Paradoxically, malnutrition does not only affect poor countries. The current trend of having a perfect and beautiful body drives some women to a diet even during pregnancy. What's worse, they undergo a Cesarean section in their eighth month of pregnancy in order to retain a perfect body.

**So malnutrition is caused by eating the wrong types of food. The same applies to obesity. What's the difference?**

In malnutrition, there is a lack of specific nutrients that are needed to maintain homeostasis. When it comes to obesity related to overeating, there is an excess of some nutrients. This also disrupts homeostasis and ultimately leads to an excess of certain elements that are responsible for the function of adipose tissue and a scarcity of others.

**Your research on malnutrition has a specific focus.**

I focus on the effects of reducing calories by 50% during a crucial period in newborn development – during lactation. The key aspect of this research is the induction of malnutrition in both mother and offspring simultaneously. The window of developmental vulnerability during the postnatal period allows us to program further development, such as reproductive functions, because we observe for example differences in achieving puberty. I conduct research on mice, but it applies to what we have observed in humans as well. For the past several years we have noticed that girls mature faster because they have a higher BMI index and more adipose tissue, which is one of the sites releasing factors responsible for accelerating or delaying puberty.

**How does this work?**

One example is the leptin-kisspeptin interplay, which is involved in the hypothalamic-pituitary-gonadal axis regulation. In mice and humans this axis develops during pregnancy, especially at the end of the third trimester and during first weeks of lactation, which



MB35/WWW.PIKABAY.COM (3)



is why proper nutrition during pregnancy and the breastfeeding period is crucial. It is also very important to ensure that baby formulas contain all the necessary nutrients.

**Do such formulas exist?**

There is no formula that is a perfect substitute for mother's milk, which is why it is recommended to breastfeed at least for some time.



PROF. MONIKA KACZMAREK



**Prof.  
Monika Kaczmarek,  
PhD, DSc**

has since 2011 led the Laboratory of Molecular Biology at the PAS Institute of Animal Reproduction and Food Research. Her research focuses on understanding the molecular aspects of endocrinology in animal reproduction. She studies the role of maternal, paternal, and embryonic factors in embryo-mother interactions in early pregnancy. She also continues the research she began during her Fulbright scholarship at the laboratory of Prof. Leslie P. Kozak, using the mice model to explain the mechanism of reproductive disorders and the functioning of the hypothalamic-pituitary-gonadal axis in offspring resulting from deficient dietary habits of nursing mothers.

[m.kaczmarek@pan.olsztyn.pl](mailto:m.kaczmarek@pan.olsztyn.pl)

**At some point children start eating other types of food. What should we pay attention to then?**

Immediately after birth children enter the stage defined by WHO as the nutritional programming peri-

od, lasting up to the age of five. This is the time when food behaviors and eating habits are formed. If the child is fed fish, he or she will choose to eat fish later in life as well, if not, he or she may never have a chance

to like fish dishes. The idea is to teach children from the earliest age about what they should and shouldn't be eating. If in the early stages of development a child's diet is in some ways deficient or monotonous, it can have a negative impact on his or her overall attitude to food in the future. I do not even want to talk about consuming processed and fast food, which provide easy stimulation of the reward system in the brain and have even been shown to be addictive.

In 2010 I was working in Louisiana as part of my Fulbright scholarship. Back then it was, and still is, one of the most "obese" states of in the United States. Conversations with locals revealed that there is a large community there where healthy eating and exercise are not priorities. For many residents, the basic form of nutrition consists of ready-to-go, unhealthy meals from the supermarket or fast foods. The bad situation is deepened by the fact that habits learned at an early age concern not only poor nutrition, but also a lack of physical activity, and are deeply rooted in this community.

Infertility problems can be caused by the bad eating habits of our mothers and grandmothers, as well as our own diets and environmental pollutants.

**Your research shows that a mother's diet has an impact on the reproductive health of not only her offspring but subsequent generations as well. How does this work?**

I would love to know the answer to that question. I've been looking for it for several years now and at this point I can only say that there may be several factors, mechanisms involved.

First of all, in animals, programming of adipose tissue can occur during lactation. The tissue is programmed to some extent either to secrete or release certain factors, such as leptin or some other fat tissue component. And since in animals and humans fat from adipose tissue is a component of milk, the milk also contains leptin and other substances that can help in the development of specific hormonal regulations between the central nervous system, gonads or other organs, such as adrenal glands. Thus, I decided to study how the composition of milk in mice changes from generation to generation in individuals who were subjected to malnutrition during nursing period just after birth.

Secondly, what happens in the central nervous system and how it affects reproduction largely depends

on our access to nutrients. Certain principle mechanisms develop, such as which receptors occur on neurons, how many neurons are developed, and how sensitive they are to signals coming from other cells. During the vulnerable period, if the body is subjected to malnutrition, these signals may not occur and this may lead to some functional or structural deficiency, such as lack or insufficient number of certain neurons in the brain, which can transmit signals for puberty to begin at the right time. We know that human and animal females, even a fruit fly, must be prepared enough for reproduction to be possible at all. And this applies not only to hormonal levels, as well as normal estrous and menstrual cycles, but also whether the woman will be able to carry pregnancy beyond 37 weeks. In anorexic women, for example, the menstrual cycle often stops and the woman does not ovulate. Her body does not receive enough nutrients to ensure giving birth to a healthy offspring.

Finally, it is also possible that the genes involved in regulating the hypothalamic-pituitary-gonadal axis, or those that encode hormones released into milk, may be influenced by epigenetic regulations, which determine the expression of genes over generations. This research is still in progress.

**Is it not because nature knows what it's doing? It says: you should not reproduce because there is something wrong. Can that be fixed?**

Many problems can be easily fixed, for example by changing the diet. Other cases require assisted-reproduction techniques.

**But we have a second generation already programmed to have bad habits. What then?**

Fortunately, it is not so black and white, there are many gray areas. There are natural ways to activate other signaling pathways in the cell and fix a defective cog. Maybe it won't work 100 percent, but perhaps 95 percent, and this will still make reproduction possible. Of course then we usually observe lower reproductive performance, but it is still possible to give birth to healthy offspring. This is also why research on reproduction is very difficult – it is based on finding these subtleties or gray areas. We must remember, however, that infertility problems are not only caused by the bad eating habits of our mothers and grandmothers, but also our own diets and constantly exposing our bodies to environmental pollutants.

**This may go beyond your scope of research and perhaps it's more of an ethical problem but, is it worth fixing?**

It seems that, to a large extent, our cells are equipped with repair mechanisms, which are responsible for the fact that humans are still around; of course with the additional help of modern medicine. However, there



PROF. MONIKA KACZMAREK

are more critical situations, such as a serious mutation that can lead to disability or death, so ideally it would make sense to fix this damaged gene. There are mutations that affect entire families, and when it turns out that the child may also carry the mutation, we could help him or her if the right tools are available... Gene editing is currently a very popular and controversial topic. In her book *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution*, Jennifer Doudna, one of the inventors of CRISPR-Cas technology, discusses a number of positive aspects of gene editing. But in this altruistic approach of giving people the chance to have healthy children, we are not far from eugenics. This is why it will be crucial to introduce appropriate regulations. I don't know how successful this will be as we can already see that it is not an easy task.

### **Is it possible to determine the line between safety and eugenics, or playing God?**

I think when it comes to eliminating genetic diseases we should give people right to use genome editing technology. On the other hand, some may argue that there are too many people on Earth and that we should allow people to die. There are many dangers of using genome editing technology, but there are as many benefits.

I am rather in favor of harnessing the latest scientific discoveries. Science seeks to discover new roads, lets us to see and learn new things. If we had no desire to learn new things, science and humans would simply disappear from the Earth. On the other hand, researchers and subsequent users of the technological advances should be aware of the consequences of unethical behavior and strive to limit them. Then again maybe the fear of genome editing is unfounded? After all, humans reason and think beyond the capabilities of the rest of the animal kingdom, and it is up to us to find rational solutions that do not threaten life on the Earth.

In terms of fixing things, I believe that prevention should play a huge role in our lives. The changes we have made as to how fast we are living, what we eat, whether we have time for our children and family, are, in my opinion, at least partially reversible. This is often just a matter of putting in the hard work and that is what we should focus on. Of course in some cases we are faced with a serious, irreversible problem, such as infertility, which affects many people at the reproductive age. I know several couples whose children were conceived using assisted-reproduction techniques and they are now very happy parents. They would not have had this opportunity without scientific achievements.

### **When we read about nutritional problems during pregnancy we think about the mother. But are the father's nutritional habits important as well?**

Of course they are important. A sperm cell does not just have a Y or X chromosome. It carries complete

information, which in combination with the oocyte creates a new life. Each of us is different because this is how it happens, whether naturally or in a test tube. Studies on mice have shown that the father's diet also has an impact on the epigenetic modifications of genes carried by the sperm. And this in turn affects the likelihood of the offspring developing diabetes, mainly due to molecular abnormalities in the Langerhans islets, regions of the pancreas containing endocrine cells. The fact that such information is stored in the sperm is particularly important to hasten trans-generational research, where we may observe the transmission and establishment of a new trait over many generations, without exposition to the factor that caused the change.

Imagine a pregnant female carrying a female fetus whose oocytes are subject to programming while still in the womb. This is an example of programming of many generations at the same time. So if our diets are poor while we are pregnant or breastfeeding, we may not only program our child but also the next generation that will be created from the oocytes. It is different when it comes to males. Semen is produced on a continuous, on demand basis, so it is easy to conduct trans-generational observations on the traits transmitted over generations.

So to summarize, both parents are responsible for the health of their child.

### **What should a couple who wants to have a child do and when should they start?**

I think we can agree that in general we are living in difficult conditions, exposed to harmful environmental factors. When I was a child, milk was stored in glass bottles, now everything is packed in plastic, and we have known for a while that plastic nanoparticles are found even in water. We also know that some packaging components that pass into the food can behave like sex hormones and affect our reproductive system. We surround ourselves with plastic and processed food. In addition, we have a growing problem with environmental pollution and a constant lack of time. I believe that returning to the former way of life is important. A good example here are the long-living populations of the Okinawa Island in Japan and Sicily in Italy, where a slower life, healthy eating and social interactions are the most important. This is the case on Okinawa, where seniors meet to support each other, exercise together – it makes them feel needed. They eat well without overeating, which is very important right now when food is always within hand's reach.

### **So moderation and common sense are the key.**

Always.

INTERVIEW BY KATARZYNA CZARNECKA

PHOTOGRAPHY BY JAKUB OSTAŁOWSKI

