



MEDIA BRIEFING: The Power of Programming 7 pages
International Congress – 6-8 May 2010 Munich

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Nutrition in the womb and in early infancy shown to affect life-long health

Scientists start to unravel the mechanisms of powerful programming factors in pregnancy and early life on life-long health

Nutrition and other environmental influences during early life can have an effect on long term outcomes such as obesity, cardiovascular disease, chronic lung disease, behavioural and cognitive problems. The EC funded EARNEST Early Nutrition Programming Project (www.metabolic-programming.org) co-ordinated by Prof Berthold Koletzko of Ludwig Maximilians-Universität (LMU) Munich, is organising the forthcoming International Conference on “The Power of Programming” (Munich 6-8 May, www.metabolic-programming.org/munich2010).

This landmark conference brings together scientists from many countries who are attempting to identify the factors that contribute to the phenomenon of ‘early nutrition programming’. They are seeking ways to capitalise on its 'good' effects and look for ways to reverse any 'bad' effects.

During the conference, speakers will present the results of the long-term follow-up of a number of trials initiated in the 1990s and early 2000s which have been followed up as part of the EARNEST Project. **(See Note 1)**

In the EU Childhood Obesity Project (CHOP), also co-ordinated by Professor Koletzko, over 1000 infants were followed over a 2 year period. The first results show that, after 2 years, the infants fed a formula with a lower protein content – closer to the composition of breast milk, weighed significantly less than those on higher protein formula, and their weights were more similar to breast fed infants. Differences emerged by 6 months of age and persisted, even after the intervention ceased and the children went onto similar diets. ***The researchers predict that these differences in early growth will reduce obesity at 14-16 years of age by 13 %.***

A new, high-technology technique applied at the Dr von Hauner Children's Hospital at University of Munich allows the measurement of a profile of more than 200 metabolites from one drop of the child's blood. This technique allows researchers to understand how infant feeding with different protein levels can affect the metabolic pathways that modulate the growth and health of children.

What are 'programmers'?

Positive Programmers

At the upcoming conference, speakers will present evidence about the different constituents of the mother and child's diet that can be regarded as 'positive programmers'. For example, breast milk (which could be described as the 'top' programming candidate) not only affects future health via its nutrients but possibly through its non nutrient components too (***See Note 2***). The research serves to highlight once again the protective effects of breastfeeding on later obesity risk.

Another 'positive programmer', the Mediterranean or 'Healthy' Diet, can protect mothers from premature delivery and pre-eclampsia and from postnatal depression, as well as improving the immune function of their babies, and the IQ of their children at the age of five. Exciting new research allows us to dissect out the top foods in these diets – which include fish and vegetables. So what are the active nutrients? Within fish, it appears to be the long chain omega 3 fatty acids which are providing the benefits, however so far researchers have not been able to pin down any specific effect of, say, folates within vegetables. (***See Note 3***)

Nutrients on their own don't always 'programme' health by direct actions on cells. We now recognise that the millions of gut bacteria in mother and child can play a major role in the programming of health but the good news is that these can be modified beneficially by diet (***See Note 4***).

Negative Programmers

But 'programming' has another side. Speakers will argue that environmental factors such as maternal smoking, air pollution and endocrine disrupting chemicals (**See Note 5**) can act as 'negative programmers' and can adversely affect the health of mother and child.

Programming might influence the 'battle of the sexes' (See Note 6)

Until now it has been assumed that any nutritional programming would have the same effects on all offspring, boys and girls alike. One session in the programme is devoted to exploring 'gender effects in programming', whilst EARNEST project information to be presented will show the effects of early nutrition on later cognitive achievements were found to differ between girls and boys born prematurely, with much larger effect sizes in boys. Other EARNEST work will suggest that infant boys and girls might have different metabolic responses to lower or higher protein diets.

Which part of your health state can be programmed?

Virtually every part! Because programming is so powerful it can have wide ranging effects, with speakers demonstrating effects on specific body 'parts'; such as bone, heart, gut and brain as well as on 'conditions' such as obesity, diabetes and impaired immune function.

It is a complex picture however and much detailed and specific research has been done, and still requires to be done, to unravel the specific effects of the different environmental exposures which could impact on the development of the fetus in the womb and the young infant.

Associations seen in observational studies are not always borne out in trials however and careful analysis is required to pinpoint the active constituent. Teasing out the specific effects of all these different potential influences requires new ways of doing research. One new approach combines traditional epidemiological and statistical principles with the use of novel or sophisticated analytic methods.

Professor Berthold Koletzko, the Co-ordinator of the EARNEST project said:

"This research has enormous potential for improving the health and well-being of future generations, reducing costs for health care and social services, and for enhancing the productivity and wealth of societies.

"However, to achieve such benefits, solid science-based knowledge is required to assess the size of the effect in contemporary European populations, to characterize underlying 3/7

mechanisms and to understand potential differences in different subgroups of the populations e.g. by genetic predisposition or gender.

“One important goal of the EARNEST Early Nutrition Programming Project is to translate solid research findings into practice. For example, the project partners have collaborated in developing evidence based recommendations on practical recommendations for dietary fat intake in pregnancy, during breastfeeding, and in infancy. Another part of this European research collaboration has explored what drives parental decisions on nutrition and lifestyle, and which messages are provided to them in information materials issued for example by governmental offices, scientific bodies and non-governmental organisations.

“Overall, we have made some significant progress in mapping out the long term consequences of early programming, but like a mountaineer, we feel like we have reached a summit, only for another to appear behind it. Much more research is required to fully understand how environmental factors adversely affect long-term outcomes and the extent to which the mother is able to protect her child against them.”

During ‘The Power of Programming’ Conference, researchers from across Europe and the United States of America are getting together to start further collaborative research aimed at building even stronger scientific foundations for long-term health prevention.

ENDS/

Notes to Editors:

Results from the EC-funded Early Nutrition Programming Project (EARNEST) will be presented at The Power of Programming International Conference 6/8 May 2010 in Munich, Germany.

For more information log on to <http://www.metabolic-programming.org/munich2010>

Journalists’ questions will be answered at the Press Conference (6 May 11am – 12noon)

Interviews can be arranged prior to, as well as during, the Conference.

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Detailed Research & Symposium Notes follow – pages 5 to 7

Detailed Research & Symposium Notes

Note 1: Research from LMU in Munich: Grote, Schiess and Peissner- early growth

Munich based researchers are investigating the effect of early diet on early growth, looking at aspects such as the effects of weaning on growth. At the Conference, **Dr Veit Grote** from LMU will describe that the time of first introducing complementary foods into the diet of some 1000 infants from 5 European countries did not predict infant growth and later obesity risk.

Another member of the team, **Dr Sonia Schiess** from Dr von Hauner Children's Hospital, has been researching the introduction of energy providing liquids such as sugared teas and juices across the five countries in the EU. She found that consumption of energy providing liquids by babies replaces breast milk or infant formula. These energy providing liquids do not contain the same nutrients as formula or breast milk and therefore lower the quality of nutrient supply in the diet. As the use of energy providing liquids is becoming more common it is important to understand how their adverse effects are likely to impact on future infant health.

The Munich team is also looking at the metabolic consequences of the different diets using the new technique of Targeted Metabolomics. **Dr Wolfgang Peissner** and his colleagues from LMU has analysed the metabolic profile of three groups of infants (breastfed and low and high protein formulas) looking at the simultaneous measurements different of more than 200 metabolites from just a drop of blood. This new, high-technology technique allows researchers to understand how infant feeding affects the metabolic pathways that modulate the growth and health of children are affected by different diets.

Note 2: Fewtrell and Tobias- breastfeeding and bone

At the session on the programming of bone health, **Dr Mary Fewtrell** will show that giving pre-term babies breast milk significantly increases their whole body bone size and mineral content 20 years later, although this was not related to the mineral content of their early diet. It is possible therefore that there are other non-nutritive components of breast milk which promote bone strength. At the same session, **Dr Tobias** will describe how increased sun exposure during the last trimester of pregnancy is associated with better bone mass at 9 years old.

Note 3: Noakes, Strom, Campoy, Meltzer, Chatzi, Granstrom – impact of maternal diet

Two sessions will examine the effects of eating more oily fish or taking fish oil supplements in pregnancy on *immune function and neurodevelopment*. Early results from the Salmon in Pregnancy Study will be presented by **Dr Paul Noakes**. Half the women in this study were given two portions of salmon a week during the second half of their pregnancy which improved the pattern and magnitude of neonatal immune responses. **Dr Strom** will present data from Lifestyle

During Pregnancy Study, which consists of 1783 mother-child pairs from the Danish National Birth Cohort to show a moderate beneficial association between dietary intake of the long-chain polyunsaturated fatty acid (PUFA) docosahexaenoic acid (DHA) during pregnancy and **intellectual ability (IQ)** of the children of five years. A similar association was seen with fish intake but this disappeared after other differences, including mothers' IQ, was taken into account.

Dr Meltzer will present results from the Norwegian Mother and Child Cohort Study (MoBa) which suggests that **vitamin D supplementation (10-15 mcg/day) may reduce the risk of pre-eclampsia in first time mothers by 27%**. Further results also suggest that a dietary pattern characterized by high intake of vegetables, plant foods and vegetable oil was associated with 28% decreased risk of preeclampsia. Mothers who ate fish twice a week during their pregnancy were less likely to have a pre-term delivery.

Dr Chatzi will conclude from the prospective mother-child cohort study ('Rhea study') in Crete that a 'Health conscious' dietary pattern based on vegetables, fruits, pulses, nuts, dairy products, fish, and olive oil, was associated with **reduced risk for postnatal depression**. **Interestingly, olive oil intake (>40-gr/day) was significantly associated with low levels of depressive symptoms.**

Dr Granstrom will use data from the Danish National Birth Cohort to show that the associations observed between **maternal dietary folate and early psychomotor development** in their 18 month old children are unlikely to reflect an effect of folate itself but may instead be attributed to some food constituent(s), which coexist with folate in specific vegetables and fruit. Higher maternal dietary folate intake was associated with higher child development, whereas higher folic acid from supplements was not. Dietary folate from onion, tomatoes, and green leafy vegetables was associated with higher child development scores, whereas folate deriving from grain, dairy, and egg was not.

Note 4 : Sanz, Koch- gut bacteria

A workshop on the role of gut microflora will explore how variations in the different bacterial species in the intestines of pregnant women could affect the health of their babies. **Dr Yolanda Sanz** will describe how they found positive correlations between the maternal intestinal *E. coli* numbers and infant's birth weight and opposite correlations for *Lacotobacillus* numbers which could be related to infant's body weight regulation. **Dr Tatiana Koch** will show how adding prebiotics to infant formula significantly affects the intestinal flora composition of the babies which can reduce the occurrence of infections and atopic dermatitis in the first couple of years.

Note 5: Newbold- smoking, pollution and chemicals

Research will be presented that is examining the possible effects of environmental toxicants such as smoking, air pollution and endocrine disrupting chemicals (such as polychlorinated biphenyls, organochlorine pesticides, brominated flame retardants, phthalates and perfluorinated compounds) on later health outcomes such as reproductive capacity and obesity.

Professor Newbold will describe how an animal model of perinatal exposure to diethylstilbestrol (DES) has been useful in studying mechanisms involved in abnormal programming of various differentiating estrogen- target tissues including adipocytes. Other examples of environmental estrogens, including the phytoestrogen genistein and the environmental contaminant Bisphenol A, have also been linked to obesity later in life. Epidemiology studies support similar findings in humans. Together, these data suggest new targets (i.e., adipocyte differentiation and molecular mechanisms involved in weight homeostasis) for abnormal programming by estrogenic chemicals, and provide evidence that for negative ‘programmers’ in “the developmental origins of adult disease”.

Note 6: Dakin, Closa and Constancia – ‘Battle of the Sexes’

During the session exploring ‘gender effects in programming’, **Rachel Dakin** will show how maternal obesity is associated with programming effects in young adult mice. Crucially, these effects are sex-specific: female offspring have raised blood insulin levels, whilst males have more profound alterations in the expression of liver genes important in lipid and glucocorticoid metabolism in the absence of altered glucose-insulin homeostasis.

In the session devoted to ‘epigenetics’. **Miguel Constancia** will talk about a small set of genes called ‘imprinted’ genes which have major functions. The imprinted genes derived from the father are greedy while those from the mother are conservative in their needs to ensure future reproductive success. The influence of programming on the battle of the sexes may yet be at the root of gender related disease effects in later life.

Other work presented by **Professor Ricardo Closa Monasterolo** from the University of Tarragona, will suggest that infant boys and girls might have different metabolic responses to lower or higher protein diets.

Refer to programme for full details of Symposia & Speakers (available by email).

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