THE EARLY NUTRITION PROGRAMMING PROJECT

Project Number: FOOD-CT-2005-007036
Acronym: EARNEST
(EARly Nutrition programming - long term follow up of Efficacy and Safety Trials and integrated epidemiological, genetic, animal, consumer and economic research.)

NEWSLETTER 5 - SPRING 2008

Report of the Prague Progress Meeting, October 2007

The sixth General Assembly meeting took place in Prague and was organised by Jan Kopecky and Martin Rossmeisl. They welcomed us all warmly to their city and laid on some glorious autumn sunshine which showed off the reds and golds of the trees and buildings to their best. The dinner in the Brevnov Monastery was an opportunity to experience some of Prague's long history at first hand. The monastery is the oldest in Bohemia, and though used as the headquarters of the secret police during the Communist era, is still one of the finest examples of Baroque architecture in Prague.

The meeting marked the half-way stage of the project and now that results are being published, Professor Koletzko reminded everybody of the need to enter their publications in the dissemination database. Professor Hadders-Algra from Theme 1 discussed some recent findings from the Groningen LCPUFA study relating to prenatal fatty acid status, measured in the umbilical wall, and neurological outcome at 18 months. They showed that mildly abnormal neurological condition was related to lower DHA and essential fatty acid status at birth and that prenatal fatty acid status might be more important than postnatal fatty acid status.

Dr Michelle Mendez described some work by members of Theme 2 to assess the extent to which dietary recommendations in pregnancy are being followed by pregnant women in their cohorts. Their preliminary findings suggested that obese women and those who smoked were less likely to follow the recommendations relating to red meat, fish and poultry intake and fruit intake. Nevertheless, poor compliance with food based dietary guidelines was widespread across all groups. Dr Sylvain Sebert explained his work on determining the critical window for effects on fat mass, energy balance and appetite control in sheep, comparing nutrient restriction and over nutrition prenatally and ewe and formula feeding postnatally. He showed that prenatal nutrient restriction but not overnutrition influenced birth weight; that prenatal nutrient restriction influenced postnatal growth rates, independently of the method of feeding and that there was an effect of postnatal feeding and exercise on growth, insulin sensitivity, and fat mass development.

Dr Monique Raats reported on progress with Theme 4. They have recruited nearly 2000 mothers for the second project in Theme 4 which is to examine mothers' understanding of early nutrition programming and to look at the drivers for milk feeding intention and behaviour. Dr Hildegard Przyrembel, the chair of the Dissemination and Exploitation Committee (DECP) gave an overview of the role of the European Food Standards Agency in the scientific substantiation of health claims. She said that the regulation was well meant but that last minute additions had detracted from its clarity and left much room for interpretation. It would keep EFSA busy for many years.

The afternoon was given over to Theme meetings and a meeting of the DECP. The following day, interactive workshops on hypertension, obesity, developmental delay and insulin resistance were held to encourage interaction between members of the different themes. They were outcome based so that those looking at the same outcomes from different disciplines would be able to identify new approaches, new opportunities and new possibilities for collaboration.

The Brevnov Monastery, Prague

Report of the Dissemination and Exploitation Consensus Platform, Prague, 2007

Dr Margaret Ashwell gave an overview of dissemination activities from April 2006 to October 2007. Highlights were the successful publicity for the Earnest project which ensued after the Satellite congress in Budapest in April 2007 and the ongoing activities of the COMMNET network of Framework 6 science communicators.The DECP then discussed future dissemination opportunities and identified routes to health professionals as being key. Possible routes discussed were: the education of young professionals and getting onto the curriculum of different disciplines; the potential role offered by the Early Nutrition Academy, both in training young scientists and as an unbiased translator of science for different target audiences in the production of material aimed at different health professionals and getting Continuing Professional Development accreditation for seminars and meetings organised. Prof Berthold Koletzko then gave a presentation on the recent findings from the Childhood Obesity Project (CHOP). The CHOP results were used by the Panel as a case study to discuss exploitable opportunities for other results within the Earnest project.

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Interview with Rita Patel on the PROBIT study

The Promotion of Breastfeeding Intervention Trial (PROBIT) is a multicenter, cluster-randomised controlled trial in the Republic of Belarus of a breastfeeding promotion intervention, modelled on the (WHO/UNICEF) Baby-friendly Hospital initiative. A total of 31 maternity hospitals and their affiliated polyclinics were randomised either to receive the breastfeeding promotion intervention or to continue current practices. Overall 17,046 healthy mothers and infants were recruited from 31 sites between June 1996 and December 1997. The current study (PROBIT III) is part of Earnest and examines outcomes in the children now aged 11.5 years.

Rita Patel with some of the Belarus team.

What differences in breastfeeding rates did you see between the two groups?
Infants from the sites receiving breastfeeding promotion were nearly twice as likely to be predominantly breastfed at 3 months compared to the control arm (51.9 vs. 28.3%) and 7 times more likely at 6 months (10.6% vs. 1.6%). And infants from the promotion arm were also 7 times more likely to be exclusively breastfed at 3 months compared to the control arm (43.3% vs. 6.4%), and 13 times more likely at 6 months (7.9% vs. 0.6%).

The PROBIT training workshop in September, 2007.

Why did you carry out the trial in the Republic of Belarus? How do the findings translate to countries in the European Union?
Belarus was chosen rather than North America or Western Europe, because maternity hospital practices in Belarus are similar to those in North America and Western Europe 20 to 30 years ago, thus providing a greater potential contrast between intervention and control study sites. However, Belarus resembles the Western developed countries in one important respect: basic health services and sanitary conditions are very similar. There is an uncontaminated water supply and hospital clinics are abundant and readily accessible, even in rural areas.

You have recently published the results of the 6.5-year follow-up, where you looked at the effect of breastfeeding on measures of adiposity and blood pressure and found no significant differences. You concluded that previously reported beneficial effects of breastfeeding on obesity and blood pressure might be the result of uncontrolled confounding and selection bias. Might your results not also have been due to smaller-than-hoped-for differences in breastfeeding rates between the groups and similar rates of breastfeeding in the two groups in the first month or so?
For the first point, although the rates of breastfeeding (both exclusive and predominant) were less than we predicted, the rates were still large in both absolute and relative terms. We were not trying to compare never breastfed infants with ever breastfed (as most of the previous literature has) but we wanted to examine high levels of truly exclusive and prolonged breastfeeding with those exposed to considerably lower levels of breastfeeding. Regarding your second point we enrolled mothers who intended to breastfeed and so it was inevitable that rates of breastfeeding at enrolment would be similar between the two groups (100%). By 1 month however there was a clear difference between the two groups. The period in between could be important but we are unable to examine the specific effect of this period with health outcomes at 6.5 years.

What outcome measures will you be looking at 11 years as part of Earnest?
We will measure anthropometry and blood pressure again, along with bioelectrical impedance. Most excitingly we will be taking blood spot samples from the children onto specially designed filter paper cards to examine levels of coronary heart disease risk factors. We are also measuring fasting blood glucose by glucometry.

What new techniques and measurements have you had to train people in?
Our 3-day training workshop in September 2007 was very successful indeed. Training was carried out by 6 of us, coming from the United States, Canada and the United Kingdom. We trained 39 paediatricians and 6 monitors. The new techniques we taught were glucometry and blood spot collection onto filter paper. Also we taught our paediatricians to use a bioelectrical impedance scale and a new automated blood pressure monitor. We used a lecture format, with a DVD of the procedures, followed by a practical session, all in Russian using our five excellent translators.

Kramer MS, Matush L, Vanilovich I, Platt RW, Bogdanovich N, Sevkovskaya Z, Dzikovich I, Shishko G, Collet JP, Martin RM, Davey Smith G, Gillman MW, Chalmers B, Hodnett E, Shapiro S; PROBIT Study Group. Effects of prolonged and exclusive breastfeeding on child height, weight, adiposity, and blood pressure at age 6.5y: evidence from a large randomized trial. Am J Clin Nutr. 2007 Dec;86(6):1717-21.

SIXTH FRAMEWORK PROGRAMME
LMU

Healthy, wealthy and wise - the importance of early nutrition

In 1758, Benjamin Franklin wrote that “Early to bed, early to rise, makes a man healthy, wealthy and wise”. Now it seems that early nutrition is more important. Direct evidence that early nutrition has a material effect on long term quality of life has been limited. However, two important papers published recently in the Lancet have reviewed the evidence linking maternal and child undernutrition with long term adult health, human capital and economic productivity. A systematic review of studies in low and middle income countries by Victora et al found that undernutrition was strongly associated with shorter adult height, less schooling, reduced economic productivity, and, for women, lower off-spring birthweight. Lower birthweight and undernutrition in childhood were risk factors for high glucose concentrations, blood pressure, and harmful lipid profiles once adult BMI and height were adjusted for, suggesting that rapid postnatal weight gainespecially after infancy is linked to these conditions. Hoddinott et al reported on the long term follow-up of a nutrition intervention study in Guatemala, carried out originally between 1969 and 1977. Men who received the nutrition intervention, primarily a protein supplement, between the ages of 0-2 years had, 25 years later, average wages which were nearly 50% higher than those who did not receive the supplement. The authors suggested that the primary pathway was probably through cognitive skills rather than through physical strength as they also showed increases in length of schooling and in reading scores.

These two studies emphasise the vital importance of adequate early nutrition in allowing for the optimal development of the brain and metabolic functions. Both studies conclude that improving nutrition in early childhood is a long term driver of economic growth and that the prevention of undernutrition should have a high priority for low and middle income countries. The World Bank's 2006 report, Repositioning Nutrition as Central to Development: a Strategy for Large Scale Action argued that the prevention of child malnutrition by targeting pregnancy and the first 2 years of life would drive long-term economic growth by leading to healthier and more productive adults. These two papers provide strong evidence to support the view that nutrition interventions should be given higher priority than they are at present.

Nevertheless, there are still some open questions, particularly regarding the timing of any adverse postnatal weight gain. Victora et al concluded that there was no evidence that rapid weight or length gain in the first 2 years of life increased the risk of chronic disease, even in children with poor fetal growth but that rapid weight gain after 2 years did increase the risk. This issue is especially important in many middle income countries in transition where children are increasingly likely to experience rapid weight gain in childhood. Further research is needed to determine the exact age when rapid weight gain does more harm than good the authors say. Whether the undernourished child has to make a trade-off between optimal cognitive development and future chronic disease also needs to be examined. However, the studies in this review found weaker associations with adult disease than studies in developed countries have done, suggesting that other factors, such as different causes of low birth weight and different rates of catch-up growth, might be important as well. Evidence-based policies need to be based on appropriate evidence and what is true for developed countries is not necessarily the same for developing countries or indeed countries in transition.

Victora CG, Adair L, Fall C, Hallal P, et al, for the Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: consequences for adult health and human capital. Lancet 2008: 371: 340-57 published online Jan 17. Hoddinott J, Maluccio J, Behrman JR, et al. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. Lancet 2008;371:411-16 World Bank. Repositioning nutrition as central to development: a strategy for large-scale action. Washington DC: The International Bank for Reconstruction and Development/The World Bank, 2006.

Can obesity and its problems be handed on through the generations?

The worrying possibility of an intergenerational cycle of obesity has stimulated new research in this area. The Avon Longitudinal Study of Parents and Children (ALSPAC) study team, who are part of the EARNEST consortium, have recently been awarded a grant by NIH to study the effects of maternal obesity, weight gain and diet during pregnancy on fat mass, fat distribution, and vascular and metabolic function in the children. The investigators, led by Prof Debbie Lawlor at the University of Bristol, hope to find out:

- the relationships between maternal BMI, weight gain and diet during pregnancy and offspring adiposity, vascular and metabolic function.
- whether any associations between maternal factors and offspring outcomes represent a specific intrauterine effect by comparing these to the corresponding paternal-offspring associations
- whether these associations are causal intrauterine effects by studying genetic variants, such as the FTO gene, as instrumental variables for maternal adiposity, glucose and lipid levels during pregnancy.
- the comparative roles of intrauterine growth, offspring nutrition and physical activity in explaining these associations.

New data on the 15 year old ALSPAC offspring and relevant data from the mother's obstetric medical records are now being collected. The first set of analyses looking at associations with offspring fat mass at age 9-11 years (Lawlor et al, 2008) showed a slightly stronger association with maternal BMI than with paternal BMI, but no difference when the FTO gene was used as an unconfounded marker of maternal adiposity. Whether a stronger effect will be seen with older offspring remains to be seen.

Lawlor DA, Timpson N, Harbord R, Leary S, Ness A, McCarthy MI, Frayling TM, Hattersley AT, Davey Smith G. Exploring the developmental overnutrition hypothesis using parental-offspring associations and the *FTO* gene as an instrumental variable for maternal adiposity: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC). *PLoS Medicine* 2008;5:e33.

Nutrimenthe - a new EU project to study the effect of early nutrition on the mental development of children.

Building on the research agenda and expertise established by EARNEST, Nutrimenthe has now secured EC FP7 funding to see if the diet of mothers, infants and children could influence long-term mental performance. This has major implications for public health practice and policy development, as well as for food product development and the economy. Nutrimenthe will look at the key issues in mental health in European children where diet could play a role. Disorders of perception, memory, intelligence, anxiety, hyperactivity, depression etc currently have a significant cost impact on European society through increased childcare costs and treatment. Professor Cristina Campoy, from the University of Granada, Spain, will co-ordinate researchers from 19 other organisations from Europe and the USA. The Nutrimenthe project will run for five years from March 2008. and will be launched on the 22nd April during Granada's Scientific Week on Healthy Lifestyle and Nutrition in Europe: From Conception to Adolescence.

www.nutrimenthe.eu

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SIXTH FRAMEWORK PROGRAMME

SOME RECENT PUBLICATIONS BY EARNEST MEMBERS

Armitage JA, Poston L, Taylor PD. Developmental origins of obesity and the metabolic syndrome: the role of maternal obesity. Front Horm Res. 2008;36:73-84.

Koletzko B, Lien E, Agostoni C, Böhles H, Campoy C, Cetin I, Decsi T, Dudenhausen JW, Dupont C, Forsyth S, Hoesli I, Holzgreve W, Lapillonne A, Putet G, Secher NJ, Symonds M, Szajewska H, Willatts P, Uauy R. The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. J Perinat Med. 2008;36(1):5-14.

Kramer MS, Matush L, Vanilovich I, Platt RW, Bogdanovich N, Sevkovskaya Z, Dzikovich I, Shishko G, Collet JP, Martin RM, Davey Smith G, Gillman MW, Chalmers B, Hodnett E, Shapiro S; PROBIT Study Group. Effects of prolonged and exclusive breastfeeding on child height, weight, adiposity, and blood pressure at age 6.5 y: evidence from a large randomized trial. Am J Clin Nutr. 2007 Dec;86(6):1717-21.

Shadid R, Haarman M, Knol J, Theis W, Beermann C, Rjosk-Dendorfer D, Schendel DJ, Koletzko BV, Krauss-Etschmann S. Effects of galactooligosaccharide and long-chain fructooligosaccharide supplementation during pregnancy on maternal and neonatal microbiota and immunity--a randomized, double-blind, placebo-controlled study. Am J Clin Nutr. 2007 Nov;86(5):1426-37.

Olsen SF, Halldorsson TI, Willett WC, Knudsen VK, Gillman MW, Mikkelsen TB, Olsen J; NUTRIX Consortium. Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study. Am J Clin Nutr. 2007 Oct;86(4):1104-10.

Cottrell EC, Ozanne SE. Early life programming of obesity and metabolic disease. Physiol Behav. 2007 Nov 22;

Krauss-Etschmann S, Hartl D, Rzehak P, Heinrich J, Shadid R, Ramírez-Tortosa MD, Campoy C, Pardillo S, Schendel DJ, Decsi T, Demmelmair H, Koletzko BV; Nutraceuticals for Healthier Life Study Group. Decreased cord blood IL-4, IL-13, and CCR4 and increased TGF-beta levels after fish oil supplementation of pregnant women. J Allergy Clin Immunol. 2007 Oct 31;

Olsen SF, Østerdal ML, Salvig JD, Weber T, Tabor A, Secher NJ. Duration of pregnancy in relation to fish oil supplementation and habitual fish intake: a randomised clinical trial with fish oil. Eur J Clin Nutr. 2007 Aug;61(8):976-85. Epub 2007 Feb 7

THE POWER OF PROGRAMMING

International Conference on Developmental Origins of Health and Disease

Organised by the Early Nutrition Academy and DOHaD Society

Munich, Germany

6th - 8th May, 2010

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For more details about the project and to read previous newsletters, please go to

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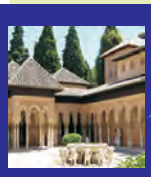

INTERNATIONAL ENA SYMPOSIUM 2008

Demonstrating Early Nutrition Programming in humans and animal models

Granada, 23 April, 2008

RELEVANT MEETINGS

International ENA Symposium: Demonstrating early programming in humans and animal models. Granada, Spain. 23rd April, 2008 www.enasymposium2008.org

16th European Congress on Obesity
Geneva, Switzerland. 14-17th May 2008 www.iaso.org

RSM: Developmental Origins of Health and Disease
London, UK. 15th May 2008 www.rsm.ac.uk

DOHaD Society Workshop: Nutritional Models of Developmental Origins of Health and Disease. Nottingham, UK. 4th July, 2008 www.metabolic-programming.org

3rd World Congress on Pediatric Gastroenterology, Hepatology and Nutrition
Iguassu Falls, Brazil. 16-20th August 2008 www.wcpghan2008.com

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