UEG Week 2015, Barcelona
Media Briefing

The Impact of Food on GI Diseases

Monday October 26th 2015
Introduction:
Professor Michael Manns
UEG Vice President and Chair Dept. of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Germany

Our Speakers:
Professor Berthold Koletzko
Professor of Peadiatrics and head of the Division of Metabolic and Nutritional Medicine at Hauner Children’s Hospital, University of Munich Medical Center, Germany

Professor John Mathers
Professor of Human Nutrition
Institute of Cellular Medicine, Newcastle University
Nutrition during the first 1000 days of life modulates later obesity risk

Professor Dr. Dr. Berthold Koletzko
Professor of Paediatrics, Ludwig-Maximilians-Universität
Head, Division of Metabolic and Nutritional Medicine
Dr. von Hauner Children’s Hospital
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Developmental programming of adult health during the first 1000 days of life

270 days of pregnancy, 2 x 365 days of first two postnatal years

Developmental plasticity: lasting effects of early nutrition and growth on physiology, function, health and disease risks
Extremely rapid growth and development during the first ≈1,000 days after conception.
Size at birth predicts later disease

Developmental programming of adult health and disease

Born small $\Rightarrow$ high later mortality from coronary heart disease
Global research collaboration on Early Nutrition Programming of Obesity

Long term effects of early nutrition on later health (2012-2017) FP7-289346-EarlyNutrition

www.project-earlynutrition.eu

Budget >11 Mio€
co-funded by NHMRC & partners

Co-ordination:
Dr. von Hauner Children’s Hospital, Univ. of Munich

36 research institutions, 16 countries, 3 continents
Early Nutrition Programming: Mechanisms

Metabolic modulators

Sensitive time windows of pre- & postnatal development
- Cyto-genesis
- Organo-genesis
- Metabolism
- Endocrine
- Gene expression

Early metabolic programming of lifelong health

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Early Nutrition Programming: Key Hypotheses

Fetal Overnutrition
- e.g. maternal obesity, high pregnancy weight gain, diet in pregnancy, gestational diabetes

Fuel mediated in utero hypothesis

Mismatch hypothesis

Fetal undernutrition & postnatal overnutrition
- e.g. maternal malnutrition, placental dysfunction

Environment
- Lifestyle
- Genes

Later offspring
- adiposity, obesity, NCDs
- insulin resistance, metabolic syndrome, diabetes, hypertension, coronary heart disease, stroke, asthma

Postnatal nutrition/growth
- e.g. overfeeding, short breastfeeding, excessive protein supply

Accelerated postnatal growth hypothesis

Long-term effects of early nutrition on later health


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Maternal Obesity

- Maternal obesity/diabetes
  - ↑ Glucose, fatty acids, insulin, leptin, inflammation
  - Developmental plasticity
  - Fetal growth, neon. adiposity
  - Offspring obesity, diabetes, other NCD
Maternal Obesity: earlier death of the child

37,709 Scottish people with birth records from 1950, follow-up of 1,323,275 person years

K-M Curve for Maternal BMI categories (WHO)

Maternal obesity: 1.35 fold increased mortality

Systematic review & meta-analysis
Reynolds et al, BMJ 2013

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Lifestyle modification in pregnancy lowers risk

RCT, 2212 pregnant overweight women, standard care or 3 x counseling in pregnancy, reinforced by 3 phone calls (less sugar & saturated fats, more physical activity)

Birthweight >4000 g
Adj. relative risk

Primary outcome LGA,
RR 0.90, n.s.

- 19%, p=0.03

Dodd JM et al. BMJ. 2014;10;348:g1285. doi: 10.1136/bmj.g1285.

EarlyNutrition
Long-term effects of early nutrition on later health

project-earlynutrition.eu

Standard Care
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Counseling
Hauner Children's Hospital, Univ. Munich

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Focussing on GWG? Behavioural intervention in obese pregnant women - UPBEAT RCT

- RCT in 1555 obese pregnant women (BMI 36.3±4.8 kg/m² 15-18 wks +6 d), randomly assigned to standard care or intensive behavioural intervention, 8 weekly health trainer-led sessions
- GWG reduced (7.19±4.6 vs 7.76±4.6 kg, P=0.041)

**Gestational diabetes**

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**Large for gest. age infants**

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*Poston L et al., Lancet Diab Endo 2015;3:767-77.*

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Rapid weight gain after birth

High weight gain in the 1st. & 2nd. year of life: increased obesity risk to adulthood
Breast feeding protects against later obesity at school age (>9 000 children, Bavaria, Germany)

Adjusted OR

Never breastfed

Ever breastfed

Overweight

0.79

(0.68-0.93)

Obesity

0.75

(0.57-0.98)


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How does breast feeding protect?
The Early Protein Hypothesis

Excessive protein intake in infancy promotes high early weight gain and later obesity.
Randomized clinical trial enrolling 1678 infants: infant feeding modulates body size at school age

BMI ≈ 0.51 kg/m² higher (P=0.009) at 6 years, early high vs low protein


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Randomized clinical trial enrolling 1678 infants: infant feeding modulates obesity at school age

Obesity (%) at 6 years

- **Conventional**: 10%
- **Lower Protein**: 4%
- **Breastfed**: 2%

**Relative Risk**
- **Unadjusted**: 0.41 (95% CI: 0.19-0.89, P=0.024)
- **Adjusted**: 0.35 (95% CI: 0.15, 0.82, P=0.016)

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Infant feeding and later obesity

- Infant feeding has large effects on later obesity
- Breastfeeding protects:
  - **Promote, protect & support breastfeeding**
- Avoid high protein supply:
  - Infants not (fully) breast fed: *infant formula with reduced protein*, but high protein quality
  - All infants: *no cows‘ milk/animal milks as a drink in infancy* if feasible and affordable
Questions?
Food and gastrointestinal cancer

Professor John Mathers
Professor of Human Nutrition

Institute of Cellular Medicine, Newcastle University
Diet, gut microbiota and bowel cancer

Marchesi JR et al. (2015) Gut. PMID: 26338727
Age-related \(\uparrow\) in bowel cancer risk in \(♀\)

High risk =
- Smoker
- High body weight
- Low physical activity
- High red/processed meat intake
- Low folate intake

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Chan AT & Giovannucci EL (2010) *Gastroenterology* 138, 2029-2043
Obesity and CRC risk

- Systematic review and meta-analysis
- 56 studies
- 7,213,335 individuals
- 93,812 cases of CRC

Ning Y et al. (2012) *Obesity Reviews* 11, 19-30
Overall 18% ↑ in Relative Risk (RR) of CRC per 5 unit ↑ in BMI

Ning Y et al. (2012) Obesity Reviews 11, 19-30
↑ waist circumference in middle age, ↑ bowel cancer risk

Song M et al. (2015) Int. J. Epidemiol. PMID: 26403814
Potential mechanisms linking diet and other factors with bowel cancer

Inflammation and intestinal cancer

- Sialidenitis: salivary gland carcinoma
- Gingivitis: oral squamous cell carcinoma
- Reflux oesophagitis: oesophageal carcinoma
- *H. pylori* infection: gastric cancer
- Inflammatory bowel disease: colo-rectal cancer

Better models make better science
Genetic susceptibility to bowel cancer

Kevin Clarke (1989) Self portrait in Ixuatio
CAPP2 Study: Lynch Syndrome as a model for bowel cancer

The CAPP 2 Study: Overview

- RCT of effects of aspirin (600mg/d) and Resistant Starch (RS) (30g/d) on neoplasia in Lynch Syndrome
- Lynch Syndrome patients have germ-line defects in DNA mismatch repair genes
- Develop tumours early

Burn J et al. (2008) NEJM359, 2567-2578
Cancer ↓ by ≈ 50% in those randomised to aspirin

Burn J et al. (2011) Lancet 378, 2081-2087
Does obesity influence bowel cancer risk in people with Lynch Syndrome?
Obesity ↑ CRC risk in Lynch Syndrome

Obesity ↑ CRC risk in Lynch Syndrome

Hazard ratio for CRC

- Normal
- Overweight
- Obese

P = 0.02

Obesity has twice as big effect on bowel cancer risk in LS patients

Does genetics matter?

MLH1 mutations are common in Lynch Syndrome

MLH1 mutations enhance effect of obesity on bowel cancer risk in LS

Aspirin ↓ effect of obesity on bowel cancer risk in LS

Additional anti-inflammatory agents

Summary

- Bowel cancer risk is strongly associated with age, obesity and diet – and is driven by inflammation.

- Rare syndromes e.g. Lynch Syndrome (LS) may be useful models for intervention studies.

- Moderate dose aspirin ↓ bowel cancer risk (and risk of other LS cancers) by > 50%.

- Obesity ↑ bowel cancer risk in patients with LS.

- Effect is greatest in those with MLH1 mutations.
Questions?