FOOD COMPONENTS AND RARE BIRTH DEFECTS

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Rare Birth Defects

- accepted multifactorial (genes-environment) origin
- so let's focus also on the "environment" (*i.e., potentially preventable*) part
which can be as much as complex as the genetic component
- Food is a major component of our living environment: indeed,
We eat every day
The wholesomeness of food is influenced by the quality of the environment where food are produced
As well as by culture, society and personal choice

Food components: a toxicologist'viewpoint

Consider

***macronutrients* (e.g., proteins, lipids)**

***micronutrients* (vitamins, trace elements),**

***non-essential bioactive* (e.g., phytoestrogens)**

***unavoidable/undesirable* (mycotoxins, heavy metals...)**

- "nutrients" NOT "the more the better":

***both* deficiency and excess may lead to adverse effects (e.g., selenium, vitamin A; upper tolerable levels -UL- defined in Europe)**

- "*Desirable*" and "*undesirable*" may interact, in not simple ways (see our database EDID, at http://www.iss.it/inte/?lang=2 homepage)

Food in rare birth defects

***General knowledge*: Maternal diet is critical to prevent an inadequate and/or unbalanced embryonic nutrition, as well as the transfer of contaminants during organogenesis.**

New concept: "*sustainable food safety*" pivoting on health of the generation to come (Frazzoli et al., 2009)

Consolidated knowledge

- Adequate intake of folates/folic acid prevents 50-70 % of neural tube defects and 20-30% of others

- High doses of vitamin A are teratogenic

But more could be done

Essential trace elements: e.g. ZINC

Critical for embryonic health

e.g., role of zn.finger proteins

in the epigenetics,

in neural development

Is Zn deficiency a problem ? May be YES

(18% of adult males in Spain with low plasma Zn;

***Sanchez et al., J Nutr Biochem, 2009*)**

High Zn: meat, whole grains

Low Zn: dairy, many vegetables

As for Folic acid Sub-clinical deficiency may be detrimental for the embryo because of

Higher biological susceptibility and/or

Enhanced requirements

ZINC poses the interesting problem of

Secondary deficiencies

- enhanced requirements/impaired utilization because of

e.g.

Zn/Cu dietary/metabolic unbalance

Zn/Fe “ “

Co-exposure to toxic/non-essential metals (Cd, Sn)

(*conversely, good Zn intake may protect the embryo against toxic heavy metals through modulation of metallothioneins*)

And

also diet-related metabolic disturbances (diabetes, hypertension..)

Vitamins: some evidences, might be more

e.g., NTD: some evidence for inositol deficiency; vitamin B12 is essential for folic acid metabolism

Gastroschisis: vitamin E and C (low animal proteins and vegetables) (Torfs et al. 1998)
Diaphragmatic hernia: choline, group B and E vitamins deficiencies (Yang et al, 2008).
Omphalocele: Periconceptional multivitamins associated with lower risk (Botto et al, 2002)

All body wall-related defects: something happening there ?

***Vitamins*: *the double role of retinoids.* Morphogenic agents: nuclear receptors (RARs, RXR) and transport proteins differentially expressed in ectoderm- and mesoderm-derived embryonic tissues.**
control *deficiency and excess* (supplements ! Vitamin A is identified as at risk of exceeding UL in Europe)

***Vitamins:* secondary deficiencies/antinutritional factors, e.g., brominated flame retardants: *widespread* lipophyllic pollutants (dairy, fatty fish) interfere with retinoid metabolism (possibly iodine, too)**
fumonisin B1: *mycotoxin* (corn, wheat: might deserve more attention, EFSA 2005): reduced expression of folate receptor in nervous tissue

MACRONUTRIENTS/LIFESTYLES ?

The obesity pandemic impinges also on rare birth defects
diabetes, obesity, excess of food sugars or fats
are risk factors for NTD, holoprosencephaly, gastroschisis and omphalocoele

As for NTD, the critical factor might be
high periconceptional blood sugar leading to increased oxidative stress and apoptosis in neuroepithelium (Zhu et al., 2009; Carmichael et al., 2009)
Involvement of glucose transport polymorphisms (Au et al., 2008)

A case to think about

Inorganic arsenic: food pollutant gaining more and more interest (EFSA 2009: water, rice, also potatoes)

- Metabolism modulated by folic acid, increases oxidative stress: *secondary deficiencies ?*

- Alter glucose metabolism, reduces insulin production: induction of NTD in various mice strains (and can be prevented by insulin): *macronutrient interference ?*

There are areas with high InAs intake (e.g., from natural ground content..and unproper management of water sources)

Are birth defects increasing there ?

Can a targeted prevention with nutrients be envisaged ?

In conclusion

To support primary prevention
is a scientific, public health, ethical duty

when the problem of f*ood security* is overcome,
Societies have to deal with *secondary nutritional deficiencies*
- suboptimal intakes, related to food consumption or lifestyles;
- interference by other factors
- genetic susceptibility enhancing requirements
As well as with *excess*
High amount, low-equilibrium
Or specific excesses (ill-aimed supplements)

- Available evidence identifies gaps and uncertainties, triggers and adresses further studies

But also

priority issues relevant to both
general public health interest and
specific reduction of the malformation burden
adequate intakes of folic acid,
zinc
and vitamin A (adequate = avoid excess, consider subgroups that might be more vulnerable to excess)
as well as prevention of obesity
and control of sugar intake

Translational prevention:
from bench to risk (and benefit) assessment)
That's all Folks…