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ARTICULOS

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INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4.

#1. <http://www.seinap.org>

INTRODUCCIÓN

La obesidad, la diabetes tipo 2 y las complicaciones asociadas son en la actualidad uno de los mayores problemas de salud. Se estima que el 65% de los adultos de los EE.UU. tienen sobrepeso o son obesos, con cifras de mortalidad atribuibles a la obesidad que oscilan entre 112.000 a 280.000 cada año. Si esta tendencia continua, probablemente en un futuro se reducirán las expectativas de vida media. (1)

La diabetes tipo 2 está estrechamente relacionada con la obesidad en humanos y en los roedores. Se estima que en los países desarrollados afecta al menos a un 6% de su población. Este trastorno metabólico durante largo tiempo fue considerado como exclusivo del adulto; sin embargo, en la actualidad se inicia cada vez en épocas más tempranas de la vida, coincidiendo con la “epidemia emergente” de obesidad.

El estudio *NHANES III* comunicaba cifras de obesidad infantil del 11%; en España el estudio *PAIDOS '84* (2) obtuvo cifras del 4,9% en escolares de ambos sexos, cifras que se multiplican en el estudio en *Kid* (3) del año 2000 hasta un 14%. El 80% de estos niños obesos de edades entre 10-13 años, sin no son tratados, serán adultos obesos y, por tanto, susceptibles de presentar las comorbilidades de la obesidad. La mayoría de estos niños con sobrepeso no están bien evaluados y, por tanto, tratados según revela un reciente estudio realizado entre el 1 de julio de 2003 y el 30 de septiembre del 2003, durante cuyo período fueron revisados los documentos clínicos de pacientes de edades comprendidas entre 2 y 18 años de cinco consultas externas de la Stanford</st1:PersonName> University (SU) y de la University of California de San Francisco (UCFS). El grupo de mayor riesgo de infradiagnóstico fue el < 5 años y con IMC entre el 85% y 94%. En este análisis, además, el 28,7% de adolescentes con sobrepeso presentaban criterios diagnósticos de síndrome metabólico. (4)

El descubrimiento de la leptina en el año 1994 abrió camino para la comprensión del sistema que controla la homeostasis energética de los mamíferos. El análisis de las vías centrales neuroendocrinas que regulan este proceso, basado principalmente en la investigación neuroanatómica y en la genética molecular, ha permitido un conocimiento mucho más profundo de la compleja red que interviene en el metabolismo y depósito del exceso de aporte energético en el adiposito; factores humorales, neuropéptidos y circuitos neuronales que incluyen sinapsis y neurotransmisores, están involucrados en la fisiopatología de la obesidad. El adipocito se ha convertido, a su vez, en un auténtico órgano endocrino, como se estudiará a continuación (5,6,7).

En el año 1988 Reaven en la Conferencia Banting denominó “síndrome X” a la agrupación de factores de riesgo cardiovascular y de diabetes mellitas tipo 2 que en la actualidad se conocen en el nombre de síndrome metabólico. (8). Este término es usado para indicar una situación clínica que incluye diferentes grados de hipertensión, intolerancia a la glucosa, dislipidemia aterogénica, obesidad central, resistencia a la insulina y estados proinflamatorios y protombóticos. (9)

El número de publicaciones y de trabajos de investigación sobre el síndrome metabólico es de varios miles en el momento actual, incluidos los que se refieren a niños obesos. La obesidad es la causa más frecuente de resistencia a la insulina en niños.

Recientemente han aparecido en la bibliografía internacional una serie de artículos que ponen en duda el valor clínico del síndrome (10,11,12), incluido uno del propio Reaven (13) que propone “el descanso en paz de su síndrome”. Las críticas se centran en las dificultades para la definición del síndrome con criterios incompletos y puntos de corte de dudosa justificación, etiología no suficientemente aclarada y ausencia de tratamiento farmacológico del síndrome como tal. (4)

La definición de esta entidad en edad pediátrica es aún más problemática, pero el concepto es útil para mejorar las perspectivas del tratamiento de los niños y adolescentes obesos desde las vertientes dietéticas y de cambios en el estilo de vida.

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ABSTRACS SEINAP 06

1. Early and silent lesions in familial hypercholesterolemia. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #2.* <http://www.seinap.org>

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Familial hypercholesterolemia is an inherited disorder of lipoprotein metabolism caused by abnormalities in the cell-surface receptor for LDL. The homozygous state is rare (1 case per million persons), and is characterized by a serum cholesterol concentration between 600 and 1000 mg /dl. Early appearance of xanthomas and onset of coronary artery disease in childhood are common, and death occurs frequently due to myocardial infarction before age 20 years. Patients with homozygous familial hypercholesterolemia are resistant to therapy with diet and drugs. We show the vascular lesions in a boy with homozygous familial hypercholesterolemia. The patient received a double transplant (heart and liver) at age 12 years. Nowadays, 20 years later, he is alive. The vascular pathology of hypercholesterolemia is revised.

2. Hypercholesterolemias. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #3.* <http://www.seinap.org>

P. Sanjurjo. Bilbao

3. Hypocholesterolemias. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #4.* <http://www.seinap.org>

Luis Ros.

Hypocholesterolemias can be primary or secondary. Primary are congenital diseases, produced by alterations of lipoproteins (Analfalipoprotein; Abetalipoproteinemia and Hypobetalipoproteinemia Homozigote o Heterozigote), or due to a failure in the transformation from 7 dehydrocholesterol to cholesterol, (Smith-Lemli-Opitz Syndrome, LOS-II and Nguyen Syndrome). The secondary are due to several causes (hepatic diseases, malabsorption, etc.).

Analfalipoproteinemia is also called Tangier disease. It is an autosomic recessive alteration due to mutations in the ABC1 (9q-31) gene, which codifies the proteins for the passing of the cholesterol to the extracellular components. These patients have orange coloured tonsils, liver and hepatic enlargement and periferic neuropathy, with severe deficiency or HDL cholesterol absence, low levels of cholesterol and APO A1 with high or normal levels of tryglicerides.

Abetalipoproteinemia o Bassen-Kornzweig disease, is an autosomic recessive entity, due to a defect of the synthesis of apolipoprotein B48 (4q22-24), which produce the lack of or low values of very low density lipoproteins, cholesterol, tryglicerides and quilomicrones. The lack of these causes fat

malabsorption and a deficiency of liposoluble vitamins and they can show pigmentary retinitis and acantocytosis. The diagnosis is based on clinical features, laboratory data and intestinal biopsy. Lipid vacuoles can be found inside enterocytes with normal villous. Diet must be supplemented with MCT and high doses of liposoluble vitamins, especially Vitamin E. Parents usually have normal cholesterol values.

Familial Hypobetalipoproteinemia. It is an hereditary dominant condition and it is produced by a great number of mutations in apoprotein B (Apo-B) gene. There is a heterozygote form which is suffered by one in 500 people, but the homozygote is very rare. Heterozygote patients are asymptomatic and show high concentrations of LDL cholesterol and ApoB slightly lower, and they do not need a specific treatment. The homozygote patients have extremely low levels of LDL and cholesterol, with normal levels of HDL. The clinical symptoms are similar to the abetalipoproteinemia and they will need a specific diet and vitamin supplements as the previous. Parents show low cholesterol levels and it allows to distinguish from the abetalipoproteinemia.

Smith-Lemli-Opitz Syndrome (LOS) is a genetic autosomal recessive alteration of the gene which codifies DHCR7 located in 11q12-q13. It causes a failure in 7-DHC reductase which transforms the dehydrocholesterol in cholesterol, causing an important lowering in the value of plasmatic cholesterol with a very high level of 7 dehydrocholesterol. It is characterised by microcephaly, short nose with nostrils in anteversion, ptosis palpebral, cleft palate, finger anomalies, pyloric stenosis, hypogenitalism, syndactylia and hypertension. It affects 1/25000 neonates.

LOS II or severe form of the Smith-Lemli-Opitz Syndrome, has a mortality rate of 75% in the first year of life in comparison to the 20% of the classical form. It is due to a larger frequency of visceral malformations: renal, cardiac etc and the shortening of limbs.

Nguyen Syndrome has clinical manifestations quite similar to the LOS but with less affection and a longer survival.

Secondary Hypocholesterolemias, Lipids and lipoproteins values are low in different inflammatory illnesses, including postoperative period, malabsorption and undernutrition, hepatic insufficiency, hyperthyroidism, pernicious and hemolytic anemia, sepsis, lung tuberculosis and end stage kidney insufficiency, corticosteroid insufficiency, neoplasm, myeloid acute leukemia and others. It also happens in long and intense steroid or hypocholesterolemic treatments. The hypocholesterolemia also has a prognostic value in severely ill patients.

4. THE Endocrine disruptors. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #5. <http://www.seinap.org>*

M. Pombo, L. Castro-Feijóo

THE AMBIOME

It is widely believed that genes define our destiny, and that by identifying the genes responsible we will be able to explain practically all human conditions from cancer to homosexuality. In fact this is not the case: we do not come into the world predetermined. It is more accurate to view ourselves as the product of a continually changing interaction between a unique set of genes and a likewise unique set of experiences in the world. Certainly it is true that individuals may be born with allele combinations or gene mutations that predispose to certain diseases. However, the mere presence of these allele combinations or mutations is often insufficient; expression of most major diseases requires the genes in question to interact with other genes and with the environment that surrounds the individual. From here springs a genuinely revolutionary idea: that we could be freed of our most important diseases if we were able to identify and control these critical determinants. The lifetime set of environmental conditions impinging on a given individual has been termed the ambiome, which together with the genome and the proteome determines each individual's development and construction. Among the most important elements making up the ambiome are endocrine disruptors.

WHAT IS AN ENDOCRINE DISRUPTOR?

An endocrine disruptor is a chemical substance that has adverse effects on an organism or its progeny, via effects on endocrine function. The term endocrine disruptor denotes a diverse group of chemical compounds capable of altering hormonal equilibrium. The number of known endocrine disruptors is large and continuously increasing, and includes both naturally occurring and synthetic substances.

Nowadays, we know that many synthetic substances present in the environment, as well as certain naturally occurring substances, have the potential to alter animal endocrine systems, including of course the human endocrine system. These substances include persistent bioaccumulated organohalides (many used as fungicides, herbicides or insecticides) and industrial chemicals, as well as other synthetic substances and heavy metals. Many animal populations have already been affected by these substances. Reported effects of the endocrine disruption caused by these substances include the following:

1. Alterations of thyroid function (fishes, birds).
2. Reduced fertility (crustaceans, fishes, birds, mammals).
3. Reduced egg hatching rate (fishes, birds, tortoises).
4. Severe congenital deformities (fishes, birds, tortoises).
5. Metabolic abnormalities (fishes, birds, tortoises).
6. Behavioural alterations (birds).
7. Demasculization and feminization (fishes, birds, mammals).
8. Defeminization and masculization (fishes, birds).
9. Immune system alterations (birds, mammals).

HUMAN EXPOSURE TO ENDOCRINE DISRUPTORS

The exposure of living organisms to endocrine disruptors is universal, since many of these substances are found worldwide as a consequence of widespread use. Non-persistent endocrine disruptors can act over short periods of time, during critical periods of development, without subsequently being detectable in tissues. Persistent disruptors accumulate in tissues and may have biological effects even though environmental levels are consistently low. The environmental and tissue persistence of such disruptors is attributable to:

1. Low biodegradability,
2. Transport in water or in the atmosphere
3. Bioaccumulation along the food chain.

In addition, compounds accumulated in the fatty tissues of female animals may be transmitted to offspring during gestation and via milk.

Endocrine disruptors are present in a number of widely used domestic products, including food can linings, the plastics used in baby milk bottles, spermicides present on condoms, white dental fillers, sun screens, cosmetics, certain health products, industrial detergents, and pesticides. The list is very long, suggesting that human beings suffer widespread exposure to endocrine disruptors.

The possible forms and routes of exposure to endocrine disruptors are very diverse, but in view of the accumulation of many of these products in food chains, exposure through food is probably the principal route of exposure in humans. Most of the known endocrine disruptors show increasing body load with age. However, the precise period of exposure may often be critical. These aspects evidently vary among species and among disruptors, but four general points can be made:

1. The effects of a disruptor may differ depending on whether exposure is during the embryo, foetal, perinatal or adult period.
2. The effects of disruptors are manifested more frequently in progeny than in exposed parent animals.
3. In developing animals, the period of exposure is critical for determining the character, course and severity of the effects.
4. In the case of effects occurring during the embryonic period, these effects may not actually be manifested until adulthood.

ENDOCRINE DISRUPTORS AND HUMAN DISEASE

Among the possible alterations caused by endocrine disruptors in the humans are the following:

- Declining semen quality
- Cryptorchidia and hypospadias
- Testicular cancer
- Prostate cancer
- Breast cancer
- Endometriosis
- Effects on fertility
- Effects on the thyroid
- Neuroendocrine effects
- Precocious puberty
- Obesity

CONCLUSIONS

Although it is evident that much important information about endocrine disruptors has been brought together over the last decade, it is also true that it is essential to carry out more research focusing on this problem, allowing us to respond to the numerous questions that remain unresolved. To date we have been involved in a sort of guessing game, with too many hypotheses, and biases reflecting the conflicting interests of different interest groups (industrial and commercial lobbies, environmental movements, academic researchers, etc.). We are convinced that there are certainly genuine problems here, but it is difficult to assess their magnitude and real significance. We would also argue that we have an obligation to confront this issue objectively, to seek out the truth, and to assure a viable future for our children.

5. CLINICAL INDEXES OF SLEEP RESPIRATORY PROBLEMS IN OBESE CHILDREN.

INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #6. <http://www.seinap.org>

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INTRODUCTION.

Sleep disordered breathing is an important risk factor for the metabolic syndrome, obesity is the only reversible risk factor⁽¹⁾.

In light of the increasing prevalence of obesity, it is important to determine the relationship obesity / sleep problems. Based on the clinical series, one third to two thirds of obesity children were found to be suffering from SDB^(2,3). Based in objective measures 47% of obese children had moderate to severe SDB and 39% children had mild SDB. Age, rel BWI, and TG level was found as accounted for 47% of the variance; incorporation of apnea-hipopnea index and SpO₂ nadir failed to improve the strength of the prediction in the linear model (51% of the variance)⁽⁴⁾.

METHODS

Subjects:

Our study cohort consisted of an otherwise typical referral-based pediatric population that required clinical evaluation for suspected sleep problems. 26 obese (weight > 120% of ideal weight for height) children (mean age 10.3 years, range 7-14 years) and 30 normal weight, sex and age matched controls.

Methods:

Children and parents completed sleep questionnaires. Total sleep time was controlled by mean of actigraph.

The height and weight were measured by standard standiometer.

Sizes of tonsils, adenoids and velopharyngeal isthmus examined by RX.

Statistical analysis:

All test were considered significant when $p < 0.05$. The χ^2 , independent t test were used.

Results.

| | OBESE | CONTROL | p |
|---|--|---------|--------|
| Mean IBW | 27.4 | 18-0 | <0.001 |
| Snoring | 32.5% | 15.9 | <0.05 |
| Nocturnal Mounth Breathing | 51.2% | 19.6% | <0.05 |
| Adenoid enlargements and velopharyngeal space | Obesse children had more enlargements and narrower velopharyngeal. The difference did no reach statistical significance. | | |

Using logistic regression, SDB (snoring and mouth breathing plus excessive diurnal somnolence) was significantly related to tonsillar size and IBW (OR 1.19, 95% CI 1.06 to 1.29, $p=0.001$).

Using tonsil size (greater than 2) as screening test for SDB in obese children, positive predictive value for predicting SDB was 82,4 %, negative predictive value was 78 %, sensitivity was 37.6 and specificity was 95.9 %.

Discussion:

The presence of tonsillar enlargement had a much higher odds ratio than obesity alone in predicting SDB in children. However, both were significant and independent risk factors in predicting SDB.

There is a high specificity but low sensitivity in using tonsillar size in predicting the occurrence of obstructive SDB: The results suggest that those obese children with obviously enlarged pharyngeal tissues will have a high chance of suffering from obstructive SDB.

Conclusion.

The secular trends in obesity among children will undoubtedly promote incremental prevalence increases in sleep disordered breathing, such that awareness and vigilance to the presence of snoring, as a tonsillar enlargement symptom, is critical for prevention of snoring-associated morbidity.

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6. "THE NUTRITIONAL IMPORTANCE OF DIVERSE STARCHES IN THE FIRST YEAR OF LIFE" . *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #7. <http://www.seinap.org>*

Dr. Antonio Jurado Ortiz. Málaga.

Starch is the most important polysaccharide in human nutrition and is also the most important carbohydrate (CH) in the plant world, widely present in seeds, cereal grains, vegetables, tubercles, and roots.

The grain contained in cereals represents a fundamental part of bottle-fed babies' nutrition, supplying not just CH and energy but also protein, vitamins (B1), and fat acids.

Starch has two components: amylose, a linear chain of glucose molecules joined by α (1-4) links, and amilopectine with α (1-4) and α (1-6) links in branch-like fashion. The proportion of these two determines the nature of starch contained in each plant species.

Starch presents itself as a granulate, containing relatively dense and insoluble amylose and amilopectine that hydrates poorly in cold water and forms a semi-crystalline structure that is rather insensitive to enzymatic attack. Boiling leads to the granulate's swelling and solubility, particularly in the case of amylose, which mixes to form a gel. This process (gelatinization) facilitates its enzymatic digestion. Cooling down leads to its re-crystallization, making it once again resistant to enzymatic attack (resistant starch) which subsequently leads to colonic bacterial fermentation.

The digestibility of flour is therefore enabled, destroying its crystalline structure through humid, acidic, or enzymatic hydrolysis. This way, polysaccharides can degrade into shorter and sweeter components: dextrose, maltotrioxes, maltose, and glucose.

Starch can be chemically modified to stabilize its structure and to thereby avoid the chain aggregation and retro-gradation. Several diverse modification techniques exist: pre-gelatinization, fluidisation, reticulation, and stabilization. These starches can be added to homogenized products as stabilizer and are useful for the modification of consistency and texture of food to concentrations between 5% and 6.5%. There is no evidence that the residuals of employed chemicals have any toxic effects.

The hydrolysis of CH complexes begins with the saliva amylase, but also involves the mammalian amylase and later the pancreatic amylase, liberating dextrines, maltotrioxes, and maltose. This digestion and absorption is completed by hydroxilases and proteins that form at the edge of the intestinal mucosal cells. CH absorption requires its transport from the intestine to the blood or lymphatic system through the mature enterocyte.

Some time between the age of six to eleven months, the saliva amylase reaches levels similar to those of an adult. In the stomachs of newborns and bottle-fed babies, it is active with a pH above 4 and continues its activity in the duodenum.

The mammalian amylase reaches in human milk an activity 25 times that in cow milk and maintains its activity in spite of gastric pH and pepsin.

The activity of glucoamylase during infancy is 50% less than in an adult and its optimal pH level is 6.

The maltase acts on the α (1-4) links of the glucose chains. The α (1-6) links are hydrolyzed via isomaltase.

The pancreatic amylase is not present in the first months of life, reaching adult levels at the end of the bottle-fed period. Initially its absence can be partially compensated by the intestine glucoamylase and saliva and mammalian amylases.

Therefore, during the first four months, the capacity to digest starch is limited, becoming evident only after six months.

Between 2% and 20% of ingested starch reaches the colon without being digested (resistant starch). Here it goes through an anaerobic bacterial fermentation which produces fat acids and gases.

The starch in food may be digested quickly or slowly, or not digested at all. The starch digestibility depends on its structure, on the mechanics of oligosaccharides liberated after their own hydrolysis, and on the "in vitro" amylases inhibition provoked by other nutrients.

The mixtures of various cereals produce an equilibrated distribution of the diverse amino-acids.

From a nutritional point of view, we can conclude that flour makes a significant caloric contribution without increasing osmolarity (80 kcal/100 gr); accelerates the secretion of pancreatic amylase; decreases gastrointestinal transit while increasing the viscosity of faeces; should start at an age between 3 and 5 months, and without gluten at an age of 7 months; and should start with a dose between 3 and 6 grams, increasing depending on tolerance.

Other non-exclusively nutritional uses of starch are: to treat glycogen storage diseases by maintaining normal glucose levels in the blood and adequate growth; as a thickener in “anti-reflux” milk; as modified starch, to replace fats; and as anti-diarrheic treatment and re-hydrant solution.

Intolerances are not frequent (sacarase, isomaltase, and glycoamylase deficit). Also infrequent is the deficit of amylase or of both amylase and tripsine (F.Q. or Schwachman-Diamond and Pearson syndromes).

7. Obesity Prevention. Individual Intervention in Pediatric population at risk.*INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #8. <http://www.seinap.org>*

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The increase in pediatric obesity prevalence in the developed/developing worlds together with the early development of vascular (endothelial) inflammatory lesions, functional disorders and the progress of these situations towards adulthood require a significant preventive reaction. One of the ways to do this is Individual prevention, carried out by pediatricians, which backs this study. Furthermore, this will be complementary with Global prevention supported by governments and health authorities.

Why start Prevention in pediatric ages? The main reason is that 30% of obese adults began to be so before adolescence (1). Besides, if it is considered that over 1 billion overweight and obese people exist in the world then the above percentage acquires an important preventive dimension. In the world today the pediatric population suffering from overweight is 10% and obesity 2-3% (155 million, 45 million respectively). However, in certain areas of North America or Southern Europe these percentages rise up to 25% and 8% respectively (2).

Another aspect of interest is that this trend began in the 1980s and has been growing ever since and the levelling out of the curve will not be achieved for at least another decade. Furthermore, once obesity is established then the treatment is lengthy, painful and mostly unsuccessful.

The main objectives for individualised intervention are:

- i) Stabilisation of the thermodynamic equilibrium result at a lower level through reduction of energy intake and also through an increase in energy expenditure; ii) Identification and counteraction of obesogenic lifestyles.

In the present work, 317 children and adolescents being overweight (rBMI 111-120%) and attending an outpatient clinic belonging to this centre were followed for 4.11 ± 2.7 years.

The preventive interventions were explained to the parents (and the child) ie: the meaning of being overweight and its consequent risks; food recommendations (respecting satiety sensation, no eating between meals and advising against hypercaloric foods); less concrete was the indication for increasing physical activity. From these 317, 68 achieved a normal rBMI (< 110 %), 72 kept in the range of being overweight (111-120%) and 78 went on to reach obesity ($\geq 121\%$). The remaining 99 children included those with a shorter follow-up, syndromic overweight, and drop-outs. Some data from this sample point out that the early diagnosis of being overweight did not affect their fate with regards to the final rBMI (chi square. 3,97, p:13). Also, the initial rBMI in the three groups although in the range of overweight, was higher in the ----- group.

As a consequence a stricter individualized programme is designed to be carried out by the pediatrician. With the following characteristics:

- i) Prospective, not randomized, no controlled study. Drop-outs.
- ii) Population: child/adolescent from 4-16 years with non-syndromic overweight.
- iii) Methods: stadiometer, fixed to wall, scales (0.1 kg), non-lengthening tape, skin fold calliper, blood pressure set with two different size cuffs. Computer programme (Seinaptracker) for assessing rBMI ($\text{kg/m}^2/\text{kgp}50/\text{m}^2\text{p}50 \times 100$), SD or ZS, growth velocity and clinical/nutritional details obtained in each appointment.

Procedures: clinical and nutritional evaluation, assessing risk factors. Alimentary intervention. Physical intervention. Lifestyle modification. Follow-up evaluation.

In conclusion being overweight at any age but specially from 3 years onwards is a risk situation, for becoming obese. According to this experience with regular preventive action although with an intensity in agreement to the clinical ground, the results show that only one third achieves a normal BMI. Therefore a stricter individual prevention programme would diminish overweight and obesity in pediatric ages and its tracking to adulthood.

8. Novel genomic tools for the quantification and identification of intestinal microbiota in infants.*INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #9. <http://www.seinap.org>*

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The aim of the present study is to review the new molecular techniques of interest in the quantification and identification of intestinal microbiota in infants. We also provide new data on microbiota profiling in healthy and cow's milk proteins allergy (CMPA) children as obtained in the European Project INFABIO by our research group.

Since the pioneering study of Tissier in 1900, several studies have described bacterial succession in infants based on analysis of the microbiota in stools. In full-term vaginally delivered infants, colonization starts immediately after delivery, and enterobacteria and streptococci appear in faeces. The composition of the gut microbiota is profoundly influenced by the diet of the infant. In breast-fed infants, the microbiota is rapidly dominated by bifidobacteria, and a more diverse microbiota develops only after dietary supplementation commences. In contrast, the intestines of formula-fed infants are colonized by members of a variety of bacterial genera, including enterobacterial genera, *Streptococcus*, *Bacteroides*, and *Clostridium*, in addition to members of the genus *Bifidobacterium*. This characteristic succession continues until after weaning, when a dense, complex, more stable microbiota becomes established, similar to that of the adult.

The previous studies, which have relied almost exclusively on the use of culturing methods, have generated our current understanding of gut microbiology and ecology in infants. However, a major proportion of the microbiota in the digestive tract is composed of a large number of diverse anaerobic bacteria that cannot be cultivated on the existing selective or non-selective media. Thus, gastrointestinal microbial ecology is experiencing a revival because of the development of molecular techniques, particularly techniques based on 16S rRNA genes that are used to study complex bacterial ecosystems. It was thought until recently that there were more than 400 different species in the dominant flora but new molecular techniques which measure bacterial DNA or RNA such as fluorescence *in situ* hybridization (FISH), DGGE (Denaturing Gradient Gel Electrophoresis), TGGE (Temperature Gradient Gel electrophoresis) and RTFLP (Terminal Restriction Fragment Length Polymorphisms) have indicated that the number of species is much greater, and many of them cannot be cultured with current media and techniques which makes it hard to study their functionality. The new genomic approaches to bacterial quantification and identification mean that we can now characterise a difference in the pattern of the microbiota without the need to grow the bacteria and then more detailed molecular analysis can pinpoint the exact changes in bacteria.

So far, only a limited number of infant microbiota studies have been performed with those molecular techniques. Quantitative results that are more accurate than classic plate count results have been obtained by using fluorescent *in situ* hybridization (FISH) probes targeting RNA of specific groups of bacteria. However, only bacterial groups recognized by the currently available probes can be detected since the design of probes depends on prior 16S ribosomal DNA (rDNA) sequence information. PCR and DGGE of 16S rDNA amplicons from babies' faeces have been used to investigate the contribution of bacteria not detected by culturing. DGGE and TGGE are molecular fingerprinting techniques that are being used more frequently in microbial ecology. When combined with sequencing of 16S rDNA clones, they permit determination of the taxonomic affiliations of members of the microbial community. Analyses of amplified 16S rDNA fragments by DGGE and TGGE are rapid and efficient approaches for obtaining profiles of the complex intestinal microbial community structure. These methods are especially valuable for monitoring shifts in community structure that occur in response to environmental perturbations, such as diet.

Another molecular approach for quantification of infant's microbiota is the molecular finger printing- method T-RFLP. In this method PCR amplified microbial small 16S rDNA subunits are fragmented using different restriction enzymes and separated by means of capillary electrophoresis. The profile of separated fragments is characteristic of a family, genus or species depending of the specific restriction enzymes used. Our research group is currently investigating the characterization of intestinal microbiota in healthy and CMPA children, using RTFLP. Most of the identified bacterial groups correspond to non cultivable bacteria in both groups of children and the profiles of TRFLP obtained in children with CMPA are significantly different from those observed in healthy children. This last finding suggests an alteration of the intestinal microbiota in CMPA that can be related to the aetiology of the disease

This study was part of the Commission of the European Communities funded project QLRT-2002 02606 Effects of diet and lifestyle on risk of gastrointestinal infections and allergy in early life; consumer knowledge, attitudes and needs (INFABIO) It does not necessarily reflect the Commission's views and in no way anticipates the Commission's future policy in this area.

9. BLOOD LIPID AND LIPOPROTEINS RESPONSES TO EXERCISE AND TRAINING. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #10. <http://www.seinap.org>*

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Physical activity is strongly related to numerous health benefits, among which inducing a favourable lipid profile. Results from cross-sectional studies and training programmes suggest that exercise can increase high-density lipoprotein-cholesterol (HDL-C), and decrease triglyceride (TG) concentrations. However, training effects on total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C) is less clear and warrant further investigations. The changes in lipid profiles are achieved at low training volumes and moderate exercise intensities, although the effects may not be observed until certain exercise thresholds are met. The increase of HDL-C with training is of vital importance since HDL-C is not only involved in the reverse cholesterol transport (RCT), but also in avoiding the development of early and advanced steps of atherosclerosis. Training volumes of 24 to 32 km/week (15-20 miles/week) of brisk walking or jogging eliciting between 1200 to 2200 kcal/week, seem to be sufficient to induce positive changes in HDL-C and TG. TC and LDL-C response to exercise are not as sensitive as HDL-C and TG. Regular exercise appears to induce changes in LDL-C characteristics, as reflected by a small and dense LDL particles concentration, and also a delay in the susceptibility of LDL to undergo oxidation. The role of the key enzymes associated with RCT, and its impact on HDL-C concentrations remains unclear. Regular exercise increases lipoprotein lipase and lecithin cholesterol acyltransferase levels, whereas a decrease or no change in cholesteryl ester transfer protein and hepatic lipase concentrations were reported. The available cross-sectional data suggest that young athletes possess a better blood lipid profile, and the age- and gender-associated variations in blood lipids in young runners are similar to the general population.

10. CHANGES IN BONE REMODELLING MARKERS IN PREPUBERTAL CHILDREN AFTER DIETARY COLLAGEN INTERVENTION. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #11. <http://www.seinap.org>*

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Bone remodelling depends on bone cells activity, osteoblast (bone-forming cells) and osteoclast (bone-destructing cells). The bone is constituted by an inorganic mineral compound, hydroxiapatite, and an organic matrix 90% formed by type I collagen and another non collagen component which contains different proteins, such osteocalcin (Bone Glan Protein-BGP), osteonectin, bone sialoprotein and proteoglicans, bone tissue specifics. The term collagen does not mean only one molecular species, but comprise a family of macromolecules with common structural characteristics, which are synthesised by fibroblast from pro-collagen. Collagen has an important role in the structure of organs such us skin, tendons, cartilages,..., and in bone matrix-cell interactions during development, but also in different pathologies (poliarthritis, artrosis, liver fibrosis,...). The aim of the present study is to determine the influence of continous gelatine dietary intake (Royal®) on bone remodelling biomarkers in healthy prepubertal children. **Study design:** *Subjects:* 71 healthy children (42 boys/29 girls) aged 9.46 ± 1.47 years, Weight: 37.11 ± 9.05 Kg, Height: 140.33 ± 9.38 cm, and Body Mass Index (IMC): 18.74 ± 3.26 ; from 71 children enrolled in the study, 60 finished the study. Under a randomized and double blind study design they were subdivided into three groups depending on the type of gelatine (partially hydrolysed collagen-gelatine Royal®) they received during 3,55±0,67 months: 18 placebo (G-I), 20 gelatine (G-II) and 22 gelatine supplemented with calcium (G-III). *Biochemistry:* The following bone remodelling biomarkers were analysed: *Bone formation:* Total alkaline phosphatase (APt) (UI/L) (cholorimetry), bone isoenzyme of alkaline phosphatase (BIAP-OSTASE) ($\mu\text{g/ml}$) (immunoradiometry), BGP (ng/ml) (RIA), osteoprotegerine (OPG) (ELISA) (pg/ml); *Bone resorption:* Tratrare resistant acid phosphatase (TRAP) (UI/L) (ELISA), type I collagen carboxi-term telopeptide (CTX-Crosslaps) (ng/ml) (RIA). Moreover, determinado it was also determined: Calcium (mg/dl), Phosphorus (mg/dl) and Magnesium (mg/dl) by cholorimetry; Vitamin D-25OH (ng/ml): radioisotopic method, C Somatomedine (IGF-1) (ng/ml): IRMA; TSH ($\mu\text{UT/ml}$), FT4 (ng/dl) and Parathormon intact (PTHi) (pg/ml): Electrochimio-luminiscence Immunoassay (ECLIA). *Biostatistics:* Test of normality and General Lineal Model for repeated measures, with intersubjects factor: T0=initial time; T1=final time after dietary intervention, and intrasubjects factor: types of gelatine gave to the children were performed. Pearson's and Spearman's correlation analysis was done. Minimal level of significance: $p<0.05$. *: G-I vs G-II; **:G-I vs G-III; &:G-II vs G-III. **Results:** Nutritional intervention with placebo, gelatina or gelatina+calcium, did not determine statistically significant differences in the increments (T1-T0) between the different study groups, respect to the plasma concentrations of the following parameters: TSH, FT4, TPHi, BGP, OPG, Vitamin D, Calcium and Phosphorus. IGF-1 increased in plasma in G-III compared to G-II. The increment comparison between the three groups established G-I, G-II and G-III showed the following differences: plasma increase of APt ($-6.59\pm 32.09^{**}$, -0.47 ± 31.86 , 0.20 ± 28.68), and significant decrease of plasma concentrations of CTX-crosslaps ($0.069\pm 0.43^{**}$, $0.028\pm 0.44\&$, -0.20 ± 0.25) in G-III respect to G-II and G-I. Mg plasma leves decreased less in G-III. TRAP concentrations decreased in plasma in G-II vs G-I and in G-III vs G-II ($1.56\pm 4.19^*$, $-1.16\pm 4.01\&$, -1.50 ± 3.43). BIAP showed a significant increase in G-II and less marked decreased in G-III respect to the placebo ($-28.60\pm 29.95^*$, 2.35 ± 42.63 , -5.68 ± 31.98). The increases of Crosslaps were correlated with those from Calcium ($r:0.53$, $p=0.024$) in G-II. TRAP changes between T0 and T1 in G-III were inversely correlated with OPG increments ($r: -0.50$, $p=0.018$) in G-III and ($r: -0.48$, $p<0.05$) in G-I. Other correlations were established between the different bone biomarkers. **Conclusion:** The present pilot study show that prolonged dietary collagen intake, in usual quantities, seems to be a bone formation stimulant role during important periods of growth and development, with influences either on bone formation biomarkers (BIAP), than in bone resorption biomarkers (TRAP). However, long-term and epidemiological studies are necessary to obtain conclusions more sustainable. *Supported by ⁵Dept. Científico de Kraft Foods Europe. Barcelona. Spain.

11. Dyslipidemia and fat distribution in adolescents. The AVENA Study. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #12. <http://www.seinap.org>*

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Introduction

Obesity is often associated with lipid metabolism disturbances even in children and adolescents. The most frequently observed is dyslipidemia (elevated triglycerides and diminished HDL-cholesterol concentrations). In adolescents, it's not well known if these abnormalities are related with body fat distribution, because the studies are scarce and not only controlling for the main confounding factors, like sexual maturation and body fat mass.

Objectives

To assess if abdominal and/or troncular fat determine triglyceride and HDL-cholesterol (HDL-C) serum concentrations, independently of age, sexual maturation and body mass index (BMI).

Population and method

We have studied 284 males and 263 females that participated in a cross-sectional study in a representative sample of the Spanish adolescents aged 13 to 18 years, studied in 5 cities (Granada, Madrid, Santander, Murcia y Zaragoza), in the framework of the AVENA Study (Alimentación y Valoración del Estado Nutricional en Adolescentes). In all the adolescents, total fat and its distribution was assessed by anthropometry. Abdominal fat was estimated by means of waist circumference measurement. Troncular fat by assessing subscapular / triceps skinfolds ratio and the ratio between central / total skinfolds (%). The lipid profile was assessed by means of routine laboratory methods. We established multiple regression models in each sex, adjusted for age, sexual maturation and BMI. Dependent variables were serum triglyceride and HDL-C concentrations and independent variables were the anthropometric indicators of body fat distribution.

Results

In males, age had a significant effect on BMI, waist circumference, subscapular / triceps ratio, the ratio between central / total skinfolds (%) and HDL-C serum concentrations. In females, sexual maturation had a significant effect on BMI and waist circumference. After age, sexual maturation and BMI adjustment for, we observed that HDL-C serum concentrations were determined by subscapular / triceps ratio ($P = 0.027$) and the ratio between central / total skinfolds (%) ($P = 0.001$). In females, triglyceride serum concentrations were determined by waist circumference ($P = 0.025$).

Conclusions

In males, troncular adiposity determine HDL-C serum concentrations and in females abdominal fat determine triglyceride serum concentrations, independently of age, sexual maturation and total adiposity. The AVENA study was supported by the Spanish Ministry of Health, FIS nº 00/0015, the Spanish Ministry of Education (AP2002-2920, AP2003-2128, AP-2004-2745), and grants from Panrico S.A., Madaus S.A. and Procter and Gamble S.A.

12. Alterations of faecal microbiota in Spanish children with cow's milk protein allergy (CMPA).

INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #13. <http://www.seinap.org>

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Introduction: The improvement in environmental hygiene during early life causes retarded contact with microorganisms that stimulate the development of immune system and antigen tolerance. It has been suggested that changes of intestinal microbiota might be related to increased incidence of CMPA in children.

Objective: To evaluate the alterations of the intestinal microbiota in CMPA children.

Material and methods: 22 children with CMPA and 22 healthy children paired by age and sex were selected. Faecal cultures were done at the diagnoses and 6 months later.

Results: At diagnoses CMPA children had significantly higher counts of anaerobes and lactobacilli and a lower count of bifidobacteria. These changes remained after six months although enterobacteria count was diminished, too.

When comparing diagnoses to 6 months, CMPA exhibited a moderate decrease in aerobes, enterobacteria and lactobacilli whereas these bacterial groups increased in the healthy group. We conclude that the intestinal microbiota seems to be different between healthy and CMPA children and may contribute to the aetiology of the disease.

This study was part of the Commission of the European Communities funded project QLRT-2002 02606 Effects of diet and lifestyle on risk of gastrointestinal infections and allergy in early life; consumer knowledge, attitudes and needs (INFABIO) It does not necessarily reflect the Commission's views and in no way anticipates the Commission's future policy in this area

13. GASTRIC EMPTYING STUDY WITH ¹³C ACETATE. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #14. <http://www.seinap.org>*

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The study of gastric emptying (GE) with the administration of a liquid containing ¹³C Acetate, is based on the fact that stable isotope is only metabolized when it passes into duodenum, then it is

absorbed and ^{13}C is joined to CO_2 and $^{13}\text{CO}_2$ is afterwards measured in expired air. The quantification of the time between the administration of the isotope and the measuring of ^{13}C in expired air allows to study the beginning of the emptying, the maximum of the emptying which are parameters not obtained by other study methods as gammagraphy or ultrasonography..

The gastric emptying was studied in healthy infants (Group A) infants suffering from gastroesophageal reflux (Group B) and infants having an antiregurgitation formula with low fat content and added with a thickening agent.(Group C).

METHODS:

Group A.- 9 healthy infants (1- 6 months) with no vomiting problem had ^{13}C acetate (50 mg) in 120 ml of formula, the expired air was collected into special bags before they had the acetate and every 5 minutes during the first 30 minutes and afterwards every 5 minutes to complete two hours and 15 minutes of study. (14 determinations).

Group B.- The same procedure was done on 15 infants suffering from gastro oesophageal reflux. The DOB, speed of metabolization and percentage of accumulated doses were calculated.

Group C: The same was performed in 15 infants who were having an anti regurgitation formula

The DOB, speed of metabolization and percentage of accumulated dosis were measured using an Infra Red Isotop Stable Analyzer (Wagner, Germany).

RESULTS:

Group A (Healthy infants):

- Maximum DOB, average 70,1 (s: 53) between 45 and 60minutes
- Doses metabolized / hour ($\%^{13}\text{C}/\text{h}$): average 15, 3 (s. 2, 44)
- Accumulated metabolized dosis at 2 hours and 15 minutes: average 38,15 % (s: 5,3)

Group B (GER):

- Maximum DOB 33,16 (s: 12,5) between 60 and 90 minutes
- Doses metabolized / hour ($\%^{13}\text{C}/\text{h}$): average 7, 6 (s. 2, 45)
- Accumulated metabolized dosis at 2 hours and 15 minutes: average: 20,01 (s: 6,67)

Group C: (formula AR)

- Maximum DOB, average, 48,1 (s: 53) between 45 and 60 minutes
- Doses metabolized / hour ($\%^{13}\text{C}/\text{h}$) : average 11,3 (s. 2,44)
- Accumulated metabolized dosis at 2 hours and 15 minutes: average 31,25 % (s: 4,3)

Groups A and B : $p < 0,05$.

- Maximum gastric emptying at 45 minutes : group A, and 90 minutes in : group B
- A bigger amount passed to duodenum (DOB 70,1) in group A than in B (33,6);
- A higher metabolized dosis and speed metabolization in group A (15,3 $\%^{13}\text{C}$ dosis /h) than in group B (6,6 $\%^{13}\text{C}$ dosis /hour);
- A higher accumulated metabolized dosis at 2 hours and 15 minutes post administration in group A (38,15, CUM dosis, $\%^{13}\text{C}$) than in group B (19,02% CUM dose, $\%^{13}\text{C}$), meaning a faster gastric emptying in the healthy group.

The results of group C show a significant improvement related to the pathologic group after the administration of anti regurgitation formula

CONCLUSIONS: The study of gastric emptying using ^{13}C Acetate is an excellent method, it is non invasive, measurable and reproducible, and it allows its study in several clinical situations, on different diets and treatments. The administration of an anti regurgitation formula can be of help in lowering the symptoms of vomiting and regurgitation.

14. NUTRITIONAL SURVEY IN PRESCHOOL CHILDREN IN THE CENTRAL NORTH OF SPAIN. INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #15. <http://www.seinap.org>

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GRUPO EBRO DE GASTROENTEROLOGIA Y NUTRICION PEDIATRICA

The preschool age is the period of changing from a mainly milk diet to an adult diet. It is an age where we do not have too much information even having in account that in this period we can observe the nutritional and feeding profile the child is going to choose and this choice will be his nutritional model

MATERIAL AND METHODS

A nutritional survey is done on a representative sample of 814 children aged 2-6 years from the North of Spain (Cantabria, País Vasco, Navarra, La Rioja and Aragón and the province of Soria). The method used was to question the children about the last 24 hours, and the composition was calculated using photographs and standardized models which were formerly validated by Nestle Company. To find out the intake of nutrients the Food Composition Tables of Barcelona University were used and a computer

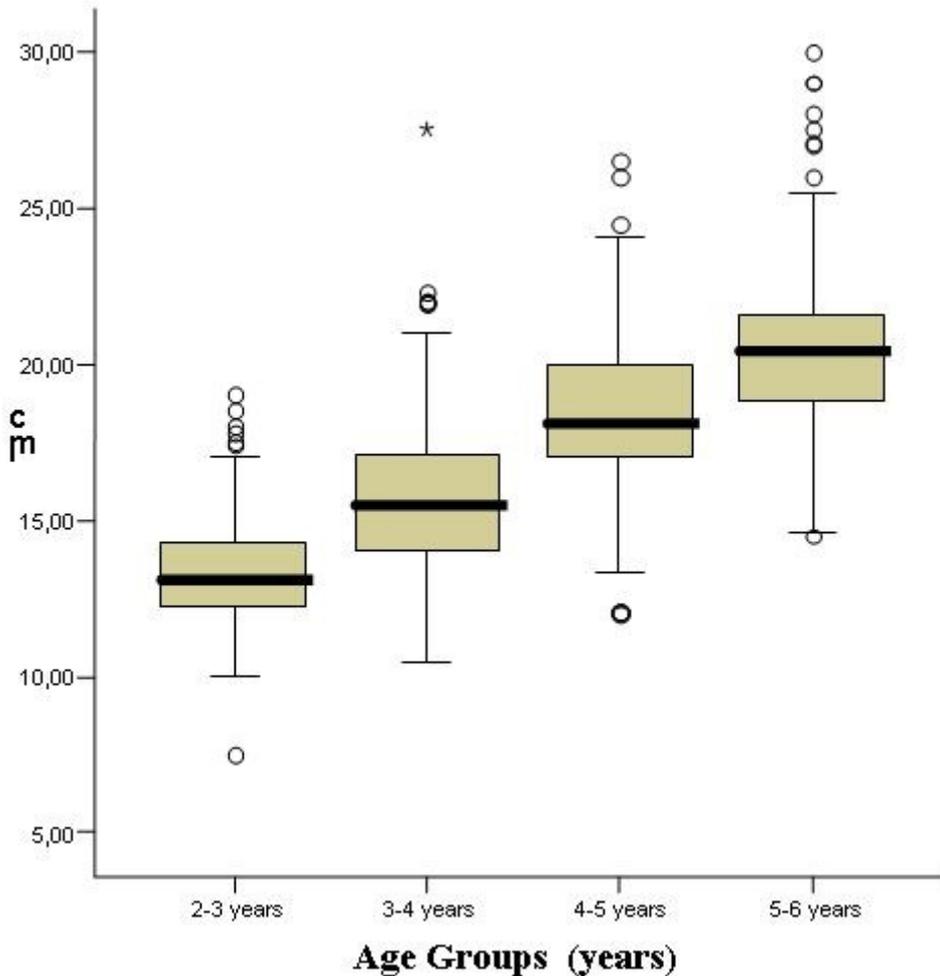
programme with a data base related (FileMaker). Data were exported to statistical study to SPSS 14.0. For Windows.

RESULTS

| | <i>Mean</i> | <i>Sd. Desv.</i> |
|---|-------------|------------------|
| <i>Energy (Kcal)</i> | 1509,3545 | 324,36899 |
| <i>Proteins (grams)</i> | 70,7326 | 19,61547 |
| <i>Carbohydrates (grams)</i> | 157,7448 | 44,71826 |
| <i>Lipids (grams)</i> | 66,7719 | 20,34586 |
| <i>Saturated fats (grams)</i> | 26,0020 | 8,35842 |
| <i>Mono-Unsaturated fats(grams)</i> | 25,5190 | 9,10330 |
| <i>Poli-Unsaturated (grams)</i> | 9,1426 | 5,06437 |
| <i>Cholesterol (miligrams)</i> | 312,4945 | 159,75467 |
| <i>Iron (miligrams)</i> | 11,5929 | 5,25325 |
| <i>Calcium (miligrams)</i> | 882,7822 | 258,20842 |
| <i>Sodium (in food) (miligrams)</i> | 1907,91892 | 902,595605 |
| <i>Fibre (grams)</i> | 12,2380 | 9,64449 |
| <i>Fat on the total energy (%)</i> | 39,5832 | 7,2851 |
| <i>Protein on the total energy (%)</i> | 18,9626 | 4,31116 |
| <i>Carbohydrate on the total energy (%)</i> | 41,7206 | 7,70544 |

Body Mass Index

| Age group | Mean | N | Sd Desv. |
|-----------|---------|-----|----------|
| 2-3 years | 13,2662 | 242 | 1,71324 |
| 3-4 years | 15,6244 | 205 | 2,59291 |
| 4-5 years | 18,3553 | 208 | 2,55125 |
| 5-6 years | 20,4964 | 137 | 2,86905 |
| Total | 16,4638 | 792 | 3,57977 |



The average of energy consumed was 1.509 ± 324 kcal ($1551,96 \pm 1551,96$ boys and $1471,98 \pm 319,50$ girls.) leaving proteins a percentage of $18,96 \pm 4,31$ of the total caloric intake, carbohydrates $41,72 \pm 7,70$ and fats $39,58 \pm 7,28$. The average cholesterol was $312,49 \pm 159,75$ mg, giving an average of 1,89% of the consumed calories. The mean amount

of proteins per kilogram was $4,47 \pm 1,45$ gr., the average intake of calcium was $882,78 \pm 258,20$ mg, iron $11,59 \pm 5,25$ mg, sodium $1907,91 \pm 902,59$ mg and fibre $12,23 \pm 9,64$ gr.

Saturated fats within the total fat consumed was $39,40 \pm 6,13$ %, monounsaturated $37,81 \pm 5,70$ %, and polyunsaturated $13,49 \pm 5,53$ %, being the percentages on the total energy intake $15,4 \pm 3,20$ %, for saturated, $15,13 \pm 4,119$ for monounsaturated and $5,35 \pm 2,44$ % for polyunsaturated.

The average body mass index (BMI) increased clearly (as we can see in the graph). The BMI at 2 years of age was $= 13,26 \pm 1,71$ and at 5 years $= 20,49 \pm 2,86$. For the total of the sample we have found 39,3% of overweight (BMI > p85 according to the Reference Tables for each age in our population Orbeagozo-2005) and a 26,8% of obesity (BMI > p97). These figures have changed from a 19% of overweight at 3 years of age and 87,6% between 5 and 6 years. At 3 years of age 10,7% of the children were obese and between 5 and 6 years 70%. . These percentages were significantly higher in Cantabria and País Vasco than in Soria and Aragón.

CONCLUSIONS

The most outstanding results in our study at this moment are:

1. The feeding model is the habitual one in our society from the preschool age and the main characteristics of the diet were HIPERCALORIC, HIPERPROTEIC, HIPERFAT AND LOW IN CARBOHYDRATES.
2. The most obvious consequences of this diet in our children is the proof of an increasing BMI related to age giving an overweight percentage at 5 years of age of 87%. The more recent standards for our population were used but it is clear that either they are "out of date" or obesity in children is a social emergency.
3. There is an evident correlation between caloric intake and overweight.

15. GENE EXPRESSION PROFILE IN ADIPOSE TISSUE OF PREPUBERTAL OBESE CHILDREN. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #16. <http://www.seinap.org>*

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AIMS: To evaluate changes in gene expression profile of intrabdominal adipose tissue associated to obesity in childhood and to determine changes in expression of some selected genes related to lipid metabolism and insulin resistance in adipose tissue in prepubertal children.

METHODS: We selected 10 children, 5 obese (BMI adjusted for age and sex z score > 2) and 6 controls, all in prepubertal stage. During abdominal surgery, about 400 mg of adipose tissue was taken and immediately immersed in RNAlater solution to avoid RNA degradation. Total mRNA was isolated using the "RNeasy-Lipid tissue Midi" Qiagen kit. We obtained the corresponding cDNA using RT-PCR and cRNA by RNA polymerase. cRNA was hybridized on the human genome U133 Plus 2.0 Arrays (Affymetrix®) according to manufacturer protocol. This DNA arrays contains more than 44,000 oligonucleotide probes. To minimize arrays discrepancies all arrays were scaled up using the Affymetrix GCOS 1.1 software and the results of each array was compared with all the others. Expression gene profiles were classified using the Spearman correlation and the GeneSpring and Affymetrix softwares. GeneSpring algorithms were used to determine significant differences for genes differentially expressed between obese and controls using ANOVA. Cluster analysis with the "Gene Ontology", "Panther" and "Ingenuity Systems" was used to transcripts gene classification and to locate differentially expressed genes in cascade signalling and metabolic pathways implicated. Also, validation of differential gene expression by quantitative PCR for a selected number of genes was done using RNA treatment with Turbo DNase Ambion. For RT-PCR we used the RT High Capacity cDNA Archiv Kit, Taqman Universal PCR Master mix, and Taqman Low density arrays probes. The Abi Prism7900 HT (Applied Biosystems) and the Sequence Detection System Software were used to quantitate cDNA

RESULTS: 10976 sequences were expressed in obese and 11014 in control children. Bidimensional cluster analysis allowed to adequately separate samples by experimental condition (obese and control). 1588 genes at $P < 0.05$, 435 at $P < 0.01$ and 57 genes at $P < 0.001$ were found to be differentially expressed. These transcripts were classified according to Gene Ontology and Panther softwares by biological process (30.5% metabolism, 17.7% cellular physiological processes and 13.5% cell communication) molecular function (14.5% nucleic acid binding, 10.4% protein binding and 8.5% metal ion binding), cellular components (31% intracellular, 14.6% membrane and 2.7% cell fraction) and pathways (2.3% Cytokine signalling, 2.3% Wnt signalling and 2.2% angiogenesis). For the selected genes validated by quantitative RT-PCR we found overexpressed within others: adiponectin, adiponectin R1 and R2 receptors, CD151, diacylglycerol acyltransferase (DAGT), leptin, natriuretic peptide receptor, phosphate dehydrogenase kinase 4, tumour necrosis factor-1 (TNF- α) and uncoupling protein UCP-1. Within those repressed we found the membrane glucose transporter GLUT-4.

CONCLUSIONS: Obesity in early childhood results in a marked alteration of gene expression. Metabolic genes are the most affected ones followed by membrane proteins and transduction signals. Some genes related to lipid metabolism and glucose homeostasis, like leptin, adiponectin, GLUT-4, DAGT and TNF, show marked changes in their expression. These changes appear to have implications in the precocity of metabolic syndrome in childhood.

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16. OPTIMISATION AND CONSOLIDATION OF CIRCADIAN RHYTHMS IN INFANTS. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #17. <http://www.seinap.org>*

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Sleep is important in all stages of life since it is related to multiple functions such as development of the Central Nervous System, cortical homeostasis, memory, and learning and hormone regulation. Sleep is particularly important during the neonatal period when numerous functions and organs are still growing

and maturing and therefore need a balance between periods of wakefulness and sleep for their correct development.

At birth wake-sleep rhythms are ultradian (less than 24 hour cycles) and polyphasic (altering between different wake-sleep periods during the day). These rhythms progressively adapt to produce a longer periods of sleep during the night. This process is strongly affected by external elements, known as "zeitgebers" (time controllers) which the organism uses to establish these rhythms. The universal "zeitgeber" is the alternating cycle of light and dark.

Some nutrients, by nature of their biochemical interrelationship with compounds which participate in the regulation of the wake-sleep cycle, can also act as "zeitgebers". For example, it has been shown that human breast milk shows daily variations in its composition of various nutrients, as is the case of tryptophan¹⁻² whose function is helping the infant to establish the correct circadian rhythms. Tryptophan is the precursor of melatonin, a hormone produced by the pineal gland and which regulates the wake-sleep cycles. The effect of other nutrients on these cycles has also been described³⁻⁵.

Based on this concept together with data available in scientific publications, two infant formulas were designed with differentiated compositions according to the capacity of some nutrients to facilitate sleep or wakefulness. Both formulas complied with the European Directive (91/321) regarding the composition of infant formulas. The formula facilitating wakefulness (Day Formula) contains more protein, the nucleotides cytosine, guanosine and inosine, whilst the sleep facilitating formula contains more tryptophan, carbohydrates, vitamins C and B¹² as well as the nucleotides uridine and adenosine together with more medium chain triglycerides.

The efficacy of both formulas, compared with a standard formula, was evaluated in a double blind clinical trial with 51 infants aged 4 – 20 weeks, preferably with sleep problems, which was carried out by two research teams from the University of Extremadura and University of the Balearic Islands. Sleep analysis was carried out using actimeters (Actiwatch[™]). The infants received the Day formula from 6.00 am to 18.00 hours in the evening and the Night formula from 18.00 hours to 6.00 in the morning or alternatively the control formulas.

Total sleep hours (8,66±0,16h vs. control 7,44±0,12h), sleep efficiency (79,19±1,19 % vs. control 74,15±0,95 %), minutes of immobility (411,52'±13,91' vs. control 327,19'±9,21') and the number of awakenings (14,88 ± 0,69 vs. control 15,48 ± 0,70) improved significantly in the group of infants consuming the combination of Day / Night formulas when compared with the control formula⁶.

In parallel to this clinical study, the gene expression in neonatal rats fed with each of these experimental formulas and control formula was studied. The animals fed with the Night formula showed alteration of the expression of genes related to sleep and similarly the Day formula showed expression of genes related to wakefulness⁷.

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17. Life styles, added sugars and risk for health in adolescents. INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #18. <http://www.seinap.org>

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Consumption of added sugars has increased significantly in last years. On average, intakes of added sugars contribute 20% of total energy intake for adolescents. Added sugars are sugars and sweeteners and syrups, that are eaten separately or used as ingredients in processed and prepared foods. Major sources of added sugars in the diets of U.S. children¹⁻³ are nondiet soft drinks, fruitade drinks, sugars and sweets, sweetened grains, sweetened dairy products and pre-sweetened cereals. Nondiet soft drinks contribute the greatest percentage of added sugars (adolescent females 37% and adolescent males 41%). In Spain⁴, consumption of soft drinks (fruit juices and beverages) has increased by 41.5% from 1991 to 2001 (extract-based drinks by 62.1% and that of juices by 26.7%), with teenagers drinking about 740ml/day.

Several studies show the relation between high intake of added sugars and high body mass index (BMI), obesity, hepatic lipogenesis, glucose and insulin metabolism disturbances and small intake of micronutrients, probably in relation to an increase of energy intake and a change of consumption of solid foods and drinks, especially milk, with high nutritional quality by a consumption of foods with poor nutritional quality and high glucemic index.

The relation between progressive increase of obesity prevalence in early age and obesogenic environmental (diet rich in energy, saturated fat, trans and sugars, poor physical activity and increase of sedentary life style) makes necessary the knowlegment of life-styles in our adolescents^{5,6} with BMI normal (7) to identify risk of obesity development and their comoribilities. So, a questionnaire make in 268 adolescents (136 males 51% and 132 females 49%), age range 15-16 years old and socioeconomic level middle shows that 86 adolescents (32.1%) have small nutritional quality index of their diet, means <5, in 82 of them (30.6%), this index is middle, means 5-9, and only in 37.3% of them the index is high, means >9. 12% go to school without having breakfast and 19% do not eat dairy products, 13% eat proccesed cakes and 24% do not eat fruits. Although, 57% do not eat a second fruit in the day and 22% do not eat a second dairy product. It is important to say that 57% do not consume vegetables once/day, 46% do not consume more than once/week and 13% do not consume fish more than once/week. But 25% say consume candies several times/day and 3% go to fast food restaurant once o more times/week.

According to use of information, communication and knowlegment tecnologies (TICs), all adolescents in the study have TV at home, 25% in their room and 35.3% eat while they are watching it. 47% watch TV more than 2 hours/day, 16.3% use video-games more one hour/day, 12.1% the computer and 49.3% use personal telephone daily. Although, we must resalt that only 36.8% do not use private or public transport to go to the school, but 72.9% live from less of 20 minutes.

Because these results, establishment of preventive strategies that promote in adolescence a healthy diet, in which soft drinks must be consumed occasionally and water and milk are major drinks, a regular physical activity and a control of maluse and abuse of TICs is prioritare

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18. **OLIGOSACCHARIDES.** *INVEST NUTR ALIM PEDIATR (Rev on-line)* 2006; 4. #19. <http://www.seinap.org>

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Oligosaccharides are carbohydrates with a level of polymerization between 3 and 20 molecules of monosaccharides. They can be fructo-oligosaccharides (FOS) and inulin, galacto-oligosaccharides (GOS), xilo-oligosaccharides (XOS) and isomalto-oligosaccharides (IMOS). In infant nutrition FOS and GOS have been the most studied. These substances are fermented by intestinal microflora and they comply the criteria to classify as prebiotic like they are : a) be neither hydrolyzed or absorbed in the upper part of the gastrointestinal tract ;b)be a selective substrate for beneficial comensal bacteria in the large intestine;c)alter the colon environment toward a healthier composition; and d) induce luminal or systemic effects that are advantageous to the host.

Human milk contains more than 130 different oligosaccharides at a concentration of 8-12 g/l in mature milk. The highest amount is reached on the fourth day of life and there is decrease of 20 % and 40 % on days 30 and 120 of lactation. The decrease in oligosaccharides is compensated by an increase in lactose content. There is substantial evidence that the oligosaccharide secretion in mother's milk is a complex, variable and dynamic process. The carbohydrate chains of almost all oligosaccharides in human milk contain lactose at the reducing terminal. Human milk oligosaccharides appear to bind to specific carbohydrate receptors on mucosal cell surfaces and act as competitive receptors on the host cell surface, preventing adhesion of a number of bacterial and viral pathogens. Moreover, part of the undigested oligosaccharides may serve as substrates for colonic fermentation and contribute to stimulation of the growth of Bifidobacteria in the colon. Breast-fed infants have a gastrointestinal flora that is dominated by bifidobacteria and lactobacilli, while the gastro-intestinal flora of formula-fed infants is dominated by anaerobic bacteria such as bacteroides. The flora regulates the gastro-intestinal transit, stimulates migrating motor complexes , intervenes in the deconjugation of bile salts and stimulates entero-hepatic circulation. Finally, the flora hydrolyses proteins and therefore may have a role in decreasing the allergenicity of non digestible proteins.

The rationale for supplementing an infant formula or solid weaning foods with oligosaccharides is to obtain bifidogenic effect and the implied advantages of a "breast-fed-like" flora. The bifidogenic effect of oligofructose,, a long-chain inulin and galactooligosaccharide mixture in term and preterm infants has been shown with dose

dependent effect during the time of their administration but there is no published evidence of other clinical benefits. Although administration of prebiotic oligosaccharides has this potential to increase the total number of bifidobacteria in feces and may also soften stools, there is no published adverse effects, but further evaluation is recommended. A more convincing argument for the benefit of prebiotic supplemented formula will require a large controlled study comparing the frequency of infectious illnesses in supplemented infants

In conclusion, at the present time, there is not a general recommendation on the use of oligosaccharide supplementation in infancy as a prophylactic or therapeutic measure. Probably it seems difficult to mimic the complexity of human physiology and the extraordinary diversity of human oligosaccharides.

19. Diabetes tipo 2 e intolerancia a la glucosa en niños y adolescentes obesos. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #20. <http://www.seinap.org>*

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The rise in the prevalence of glucose intolerance and type 2 diabetes in childhood and adolescence appears related to the increased incidence in obesity.

The presence of glucose intolerance and type 2 diabetes was evaluated after an oral glucose tolerance test (WHO criteria) in 145 obese children and adolescent (4-18 years of age), (BMI > +2 SDS, 3.8±1.4 SDS), (85 girls and 60 boys).

Glucose intolerance was present in 19.2% and no case of diabetes type 2 was observed. However, the percentage of glucose intolerance varies with age (7% in prepuberty, 28.2% during puberty and 26.5% in postpuberty) and with BMI (8.9% for BMI values between +2DE y +3 SDS; 21.9% for BMI values between +3DE and +4 SDS; and 25% for BMI > +4SDS).

These data are similar to others previously reported and show that obesity degree and probably the time of obesity evolution may be involved in the appearance of carbohydrate disorders in obese subjects during childhood and adolescence.

20. ANTIDIABETIC AGENTS IN CHILDHOOD. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #21. <http://www.seinap.org>*

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Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. The vast majority of cases of diabetes fall into two broad etiopathogenetic categories. In one category (type 1 diabetes) the cause is an absolute deficiency of insulin secretion due to an autoimmune process and the treatment is basically the insulin. Type 2 diabetes has dramatically increased throughout the world coincident with the rise on the number of children who are overweight. There has also been a strong association between type 2 diabetes and the onset of puberty, a positive family history and elements of the metabolic syndrome. Lifestyle modifications have been shown to improve insulin sensitivity in overweight and diabetics children. Therefore, most adolescents require initiation of drug therapy. Currently available oral hypoglycemic agents can be divided into 3 groups: (1) agents that improve insulin sensitivity, thereby lowering glucose levels without increasing insulin secretion (metformin and thiazolidinediones); (2) insulin secretagogues (sulfonylureas and meglitinide analogues), and (3) glucosidase inhibitors, which slow carbohydrate absorption (acarbose and miglitol). If treatment goals with nutrition education and exercise are not met, the first oral agent used should be metformin. Metformin has the advantage over sulfonylureas of as similar reduction in overall glucose levels without the risk of hypoglycaemia. In addition, weight is either decreased or remains stable, and

LDL cholesterol and triglyceride levels decrease. Treatment with metformin also may normalize ovulatory abnormalities in girls with ovarian hyperandrogenism. The most common side effects of metformin are gastrointestinal disturbances. If monotherapy with metformin is not successful over a reasonable period of time (3-6 months), several alternatives can be considered. Thiazolidinediones are indicated for monotherapy or for use in combination with a sulfonylurea, metformin or insulin in adults. Clinical trials reported a favorable pharmacokinetic, with glucose-lowering effects, in addition to several powerful anti-atherogenic properties, including anti-inflammatory effects in the vascular endothelium, redistribution of visceral fat and reduction of insulin resistance. This makes the thiazolidinediones ideal candidates for the early treatment of many components associated with the metabolic syndrome. Thiazolidinediones can cause weight gain, fluid retention and hepatotoxicity. Liver function tests should be evaluated before the initiation of therapy. The evidence that thiazolidinediones may slow deterioration of beta-cell function has raised the suggestion that the addition of thiazolidinediones to metformin may be appropriate early in the course of the disorder, rather than waiting until poor glycemic control requires a second agent. The use of sulfonylureas is associated with an increased risk for hypoglycaemia in adolescents, given their generally well-maintained pancreatic insulin secretion. Meglitinide analogues were developed to specifically control meal-related glucose fluctuations by stimulating release of insulin from the pancreatic beta-cells. These agents act on a different binding site than the sulfonylureas and have a quicker response and a shorter duration. They have no significant effect on plasma lipid concentrations. Acarbose and miglitol inhibit the alpha-glucosidase enzymes that line the brush border of the small intestine, interfering with hydrolysis of carbohydrates and delaying absorption of glucose and other monosaccharides. Unabsorbed carbohydrates cause abdominal pain and flatulence and many adolescent patients find them difficult to comply with the therapy for this reason. In conclusion, metformin is an effective medication for the treatment of type 2 diabetes in children, but probably is not sufficient long-term monotherapy. Different studies indicate that management strategies for children with type 2 diabetes will likely be as complex as those with adults.

21. NUTRITIONAL VALUE OF ADAPTED FORMULAE ACCORDING TO STERILIZATION PROCESS AT INDUSTRIAL LEVEL. INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #22. <http://www.seinap.org>

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Nowadays there are a lot of formulae for baby feeding. Although there are some regulations for the preparation, treatment, package and later distribution of the different formulae, it is difficult to know which treatment each presentation has received because it is not printed in the label.

The different thermal treatments which are used with milk have some microbiological and nutritional consequences

Mainly there are two kinds of commercialized milk, powder and liquid. Liquid milk is processed in two different ways which allows us to classify them. The differences lie in the treatment and package. The UHT system consists of bottling sterilised milk and the other system sterilises the milk after its packaging.

The different ways of processing have some effects on formulae composition, being some of them undesirable.

Pasteurization used in preparing both powder and liquid milk, can affect the proteins and inactivate a percentage of some immunoglobulins. The bio availability and antigenicity of proteins can be affected, mainly minority ones as lactoferrin.

Milk carbohydrates can be affected too as we already know as the Maillard reaction which modifies lactose.

Bio availability of minerals depending on the relationship between ionic and non ionic forms. Water-soluble vitamins can be altered because of the different ways of processing in relation to the used temperature and the time. Liposoluble vitamins are less influenced by thermal treatment

There are no randomized studies comparing the nutritional value of the different formulæ according to its presentation. The powder formulæ have been better studied and they are the standard for reference.

There is an unquestionable advantage at a microbiological level caused by the thermal treatments but they are modulated by some nutritional consequences which are difficult to avoid. So, it is recommended to industrialization to minimize as much as possible the accumulation of thermal process and substitute them by non thermal methods. In the same way it is recommended to point out on the label which components have been treated by non thermal methods and by thermal ones and which sort of each one. As a conclusion it is necessary to perform randomized studies in order to establish parameters with relevant scientific evidence at a hospital and domestic level..

22. Home artificial nutrition in children. *INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #23. <http://www.seinap.org>*

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Most industrialized countries have initiated health care system reforms aiming to increase the number and scope of health services delivered on an ambulatory basis and at the patient's home. Although "traditional" home health-care services as nursing or personal care have been available for a long time, this shift is mainly related to the so-called high-tech home care ("methods of diagnosis, treatment or rehabilitation which are embodied in or supported by specialized equipment")

Home artificial nutrition has been an expanding area in home care in many countries over the world for the last 30 years. Home Parenteral Nutrition (HPN) was developed as a life-saving treatment for patients who were unable to ingest food or absorb sufficient amounts of nutrients thus avoiding the problems of chronic undernutrition.

In a large survey done in Montreal in 2002, HPN was the third most frequent home care service provided by local community health centres, after provision of home IV therapy and oxygen therapy.

Four aspects of the development and increased use of HPN require attention:

- a. Weak connection between community-based and specialized, hospital-based home care.*
- b. Delegation to patients and caregivers of increased responsibility.*
- c. Importance of the risks associated with home environment.*
- d. Implementation of home care services despite the lack of evidence about cost-effectiveness.*

Along with the technical aspects regarding the introduction of sophisticated technologies into the home setting, organizational and social dimensions also arise. Social dimensions refer to the capacity of the patients and their relatives to maintain satisfying relationships, to engage in leisure activities, to raise a family, to carry out social roles, etc. Frequently, women in particular suffer the consequences of the burden of home care, since their role as "natural" caregivers is often taken for granted; their careers and health are often affected due to the time and effort devoted to take care of their relatives.

Thus, a complete home care policy should include organizational initiatives that promote collaboration and trusting relationships among organizations, service providers, public health and voluntary organizations.

We will provide information regarding our own experience in HPN during the last 12 years as well as the data from an European survey done in near 1000 patients in 2003. At

the same time the data from the first year of functioning of the Spanish Register on Home Enteral Nutrition (NEPAD) will be presented.

23. DIET and OXYDATIVE STRESS. INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #24. <http://www.seinap.org>

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Reactive oxygen species (ROS) are known to be involved in pathogenic processes of numerous degenerative diseases. Indeed the antioxidant defence has a role to prevent or delay the development of disease states.

Biological antioxidants are defined as “compounds that protect biological systems against the potentially harmful effects of processes or reactions that can cause excessive oxidations”. They inhibit the oxidation of cellular components by directly scavenging reactive oxygen and nitrogen species, by metabolising lipid peroxides to non-radical products and by the chelation of metal ions to prevent generation of oxidising species. A first strategy to balance oxidative damage and antioxidant defence would be to enhance the antioxidant capacity by optimizing the dietary intake of antioxidants. Children may be a particular population that will benefit from enhanced antioxidant intake.

The main antioxidant micronutrients of dietary origin are:

Vitamin E (in particular *d*- α -tocopherol) is a phenolic that is probably the main lipid-soluble antioxidant in human tissues. Major dietary sources of vitamin E are vegetable oils, foods containing such oils and foods that have been prepared using such oils. Other foods such as grains, dairy foods and legumes may also contribute significantly to the total vitamin E intake.

Vitamin C is water soluble and efficiently scavenges a range of reactive oxygen species. It can also chelate trace elements such as Fe and Cu. All fruits and vegetables contain vitamin C: However it is not a stable micronutrient, and vitamin C content can vary widely depending, mainly, on maturity and agronomic conditions. Foods may lose vitamin C as a result of harvesting conditions.

Carotenoids are polyisoprenoid structures very widespread as colourants in the plants and animal kingdoms. The major carotenoids in food plants, dairy products and meats are β -carotene, lutein, lycopene, β -cryptoxanthin and zeaxanthin. β -carotene is particularly effective at scavenging singlet oxygen. The concentration of carotenoids in plant tissues is dependent upon agronomic conditions, especially light exposure and nitrogen supply.

Flavonoids are ubiquitous polyphenolic products of the plants. Several thousand different phenolic compounds have been described. In the human diet, chlorogenic acid (coffee, carrots, potatoes), ferulic acid (cereals, beet and monocotyledonous vegetables), flavones and flavonols (onions, green vegetables, tea, apples), catechins and other flavan-3-ols (tea, apples, grapes, chocolate), isoflavones (legumes) are the main representative compounds.

Selenium is a cofactor of antioxidative enzymes. The main food sources of selenium are seafood, liver, meats and cereal products. The amounts of selenium in foods can vary greatly with production methods and the areas in which crops are grown or animals are reared. The majority of selenium in plant and animal materials consumed by humans will be in the form of selenomethionine.

Glutathione (γ -glutamyl cysteinyl glycine) is a tripeptide whose constituent aminoacids are glutamate, cysteine and glycine.

It is contained in all foods and is also synthesised in the human liver. Avocado has been noted as a particularly rich fruit source of glutathione.

Only a proportion of the types and quantities of antioxidants components in the foods consumed is absorbed and utilised. Crucial is accurate information about food sources, content and bioavailability of antioxidants and also the knowledge of the required level of relevant antioxidants in the diet to provide protective effects.

In various European populations an inverse relationship was found to exist between cardiovascular risk and diets rich in vitamin C, but also β -carotene and vitamin E selected in terms of blood plasma levels. A number of studies have been undertaken to examine the possible link between flavonoid intake and cardiovascular disease, especially focused around the effects of red wine and tea consumption.

The aim of our work was to study the relation between dietary supplementation of a beverage rich in vitamin C and polyphenols, as tangerine juice, and values for serum lipids and lipoproteins in children with hyperlipemia. The status of oxidative metabolism is also evaluated because its impact in atherosclerosis pathophysiology.

24. THE HYPOTHESIS OF BERKER REVISITED. INVEST NUTR ALIM PEDIATR (Rev on-line) 2006; 4. #25. <http://www.seinap.org>

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A series of important papers by A. Lucas et al and D Barker et al posed the problem that alterations in nutrition in intrauterine life, and especially in small for date, could condition at long term on diseases of the adult. Extensive epidemiological studies confirmed the evident relation in a large number of cases and during the last three decades the problem has acquired importance in a worldwide scale. Profound examination concerning this subject has led to the demonstration that long term consequences could not only be limited to intrauterine malnutrition, but also to critical periods in the feeding of small for date and premature infants during the first weeks of life and the type of alimentation they receive. The effects of an acceleration of growth during that postnatal period could also cause adverse consequences at long term and this has motivated the hypothesis of the acceleration of growth of Singal and Lucas and it has even been considered that a relative under-nutrition at the beginning of life in premature babies can have beneficial effects on the non appearance of insulin resistance.

The explosion over the last decades of what can be qualified as an epidemic of obesity on a worldwide scale has also allowed knowledge of the appearance of what is called Metabolic Syndrome and its relation with insulin resistance and Type 2 Diabetes. This form of diabetes and the metabolic syndrome which were considered diseases typical of the adult, have undergone a progressive advance in their time of appearance and now constitute important problems in progression in childhood, above all for adolescents. That is to say, intrauterine malnutrition that affects small for date babies can also initiate stages that will lead to the metabolic syndrome -type 2 diabetes, possible cardiovascular affection and atherosclerosis.

In addition to this matter, and it is very possible in at least an important number of cases, is the fact that genetic factors influence the appearance of the syndrome and that a series of other factors which we will call of provocation linked to the different life styles condition an ever greater exteriorization of the number of cases.

All of this makes us consider that the Hypothesis of Barker has acquired an enormous complexity. A critical analysis of the fetal origin of diseases of adulthood carried out by Sue Y S Kimm points to the fact that greater knowledge of the fundamental understanding concerning the fetal origin of chronic diseases of the adult is still necessary

REVISTA DE REVISTAS

En este número el Dr. A. Sarriá propone la lectura de:

*1) Geier A B, Rozin P, Doros G. (Universidad de Pennsylvania). Unit Bias. A New Heuristic That Helps Explain the Effect of Portion Size on Food Intake. *Psychological Science*, 17(6),2006: 521-525.*