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VITAMIN C ENHANCES HYDROXYL RADICAL FORMATION IN IRON-FORTIFIED INFANT CEREALS

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Cereals are usually fortified with iron to prevent iron-deficiency. To enhance iron-bioavailability, approx. 1mM supplemental Vit.C (AA) is recommended. AA is considered to be an antioxidant in vivo, but has prooxidant effects when exposed to electrolytic iron. We measured radical formation in cereals after addition of AA. Cereals were mixed with either water (wa), infant formula (NAN) or breastmilk and incubated for 1 hour. Hydroxyl radicals were quantified by their ability to convert salicylate to 2,5-dihydroxybenzoic acid (DHBA). Production of 2,5-DHBA increased linearily with increasing AA doses added ($p<0.0001$), and was attenuated by catalase (ca)($p<0.0001$) and deferoxamin (df)($p<0.0001$). Cereals mixed with breast-milk produced less radicals than cereals mixed with water ($p<0.0001$) or NAN ($p=0.003$). Values are given as mean(SD).

solute	AA(added)	2,5-DHBA	solute	AA(added)	2,5-DHBA
wa (n=8)	0mM	0.04(0.02)µM	wa+ca (n=6)	0.4mM	0.04(0.01)µM
wa (n=8)	0.2mM	0.12(0.03)µM	wa+df (n=6)	0.4mM	0.06(0.03)µM
wa (n=8)	0.4mM	0.19(0.02)µM	milk (n=6)	0.4mM	0.07(0.03)µM
wa (n=8)	0.8mM	0.28(0.05)µM	NAN (n=6)	0.4mM	0.50(0.19)µM

CONCLUSION: Vit.C enhances hydroxyl radical formation in iron-fortified cereals. Cereals mixed with breastmilk produce less radicals than cereals mixed with formulas.

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COMPARATIVE STUDY OF LIFE-STYLE AND TIME ACTIVITY PATTERNS OF SCHOOL-AGE CHILDREN ADMITTED TO HOSPITAL FOR ACUTE RESPIRATORY PROBLEMS.

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A sample was studied of 228 children aged 5-14 years, resident in Greater Athens, who were admitted to hospital for acute respiratory problems (laryngitis, asthmatic bronchitis, asthma, pneumonia) between October 1992 and June 1993. The control group consisted of 217 children of the same age and sex distribution admitted the same period for non-respiratory health problems. For each child, a questionnaire was completed covering family information, living conditions and activities of the child in the 24-hours before the onset of symptoms. The control group was similar to the study group in socio-economic status and living conditions, including home exposure to cigarette smoke (70%). There were significant differences between the study group and the controls in their activities in the 24 hours before the onset of symptoms: study children had spent less time at home indoors and more time outdoors; they had used transport more (29% v 16%) and been more involved in athletic activity (56% v 20%). Differences were also recorded between respiratory diagnostic categories: 57% of children with pneumonia and 37% with asthma had spent no time outdoors; 60% with pneumonia but 30% with asthma had not exercised.
Conclusions: There were differences between children admitted to hospital with different acute respiratory problems and other illnesses in activity patterns which may affect exposure to air pollution, in the 24 hour period before the onset of symptoms.

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THE EFFECT OF GASTRIC PH ON THE ABSORPTION OF KETOCONAZOLE BY VERY-LOW-BIRTH-WEIGHT INFANTS. John N. van den Anker, Anja van IJsseldijk, Rob Woestenborghs, Marijke Koster, Pieter J.J. Sauer. University Hospital Rotterdam/Sophia Children's Hospital, Department of Pediatrics, Rotterdam, The Netherlands and Janssen Research Foundation, Beerse, Belgium.

Fungal infections, occurring frequently in VLBW infants, are usually treated by the toxic amphotericin B and flucytosine. Ketoconazole (keto), an oral antifungal agent with broad spectrum activity and low toxicity, might be a good alternative. Data on the gastro-intestinal absorption of keto in preterm infants with a gestational age below 32 weeks are not available. Desired therapeutic levels are between 100-10000 ng/mL and area under the curve (AUC) > 2400 ng/h/ml. We studied the gastro-intestinal absorption of keto in relation to gastric pH in 8 preterm infants (gestational age: 26-32 wks) in the first week of life. All infants were on total parenteral nutrition and received a single oral dose of 10 mg/kg of keto as a suspension. Blood samples were taken before and 1, 2, 4, 8, 12, 24 hrs after the keto administration. Plasma keto concentrations were analyzed by HPLC-assay. Gastric pH was measured at t=0. AUC (ng/h/ml), peak concentration (Cmax in ng/ml) and gastric pH were:

pat.	pH	Cmax	AUC	pat.	pH	Cmax	AUC
1.	1.4	3761	25160	5.	2.4	364	3875
2.	1.6	2433	13525	6.	2.5	834	2587
3.	1.8	2157	12227	7.	2.8	220	1860
4.	1.9	1459	10914	8.	4.0	25	259

Conclusions. 1. Preterm infants can absorb ketoconazole from the gastro-intestinal tract leading to therapeutic levels. 2. However, a gastric pH above 2.5 is associated with insufficient absorption. 3. Continuous oral feeding will cause insufficient keto absorption due to an increase in gastric pH.

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AMOXICILLIN PHARMACOKINETICS IN THE PRETERM INFANT. John N. van den Anker, Janetta J. Huisman-de Boer, Marius Vogel, Wil H.F. Goessens, Rik C. Schoemaker, Ronald de Groot. University Hospital Rotterdam/Sophia Children's Hospital, Departments of Pediatrics and Microbiology, Rotterdam, and Centre for Human Drug Research, Leiden, The Netherlands.

Amoxicillin (AM) is one of the most frequently used antibiotics in the treatment of bacterial infections in the preterm infants. Despite the widespread use of AM in neonatal intensive care units, pharmacokinetic studies in preterm infants are not available. The recommended dosage of AM is 50-100mg/kg/24h. We studied the multiple-dose pharmacokinetics of AM (25 mg/kg q12h) in 17 preterm infants (gest. age 29 ± 1.9 wks) on day 3 of life. Blood samples were taken before (t=0) and 1/2, 1, 2, 4, 8,and 12 hrs after the AM dose and analyzed by HPLC-assay. The glomerular filtration rate (GFR) of all infants was simultaneously studied by means of the 24h continuous inulin infusion technique to investigate the effect of GFR on the clearance of AM. The results were:

	Mean ± SD
Elimination serum half life (h)	6.7 ± 1.7
Volume of distribution (ml)	584 ± 173
Total body clearance (ml/min)	1.0 ± 0.4
Inulin clearance (ml/min)	1.0 ± 0.3
Trough levels (mg/l)	16 ± 5

Conclusions. 1. Amoxicillin 25 mg/kg q12h results in adequate serum levels of AM in preterm infants with a gestational age below 32 weeks on day 3 of life. 2. The total body clearance of AM (1.0 ± 0.4 ml/min) and the GFR (1.0 ± 0.3 ml/min) are equal, indicating that AM is primarily excreted by glomerular filtration in the preterm infant.

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IS INCREASING SERUM TRANSFERRIN AN INDICATOR OF IRON DEFICIENCY, OR OF ACTIVE ERYTHROPOIESIS IN PUBERTAL BOYS?

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During male puberty, hemoglobin increases to adult male level. The growth spurt, with rapid increase in body weight, is associated with a great increase in blood volume. We studied serum transferrin in relation to individual body growth, stage of puberty, hemoglobin and ferritin in 60 prepubertal or early pubertal boys with 3-month intervals for 18 months. We found a positive correlation between the individual 18 month increments of transferrin and hemoglobin ($r=0.55$, $p<0.001$) and estimated erythrocyte iron ($r=0.31$, $p=0.02$). Positive correlations were also observed between transferrin and body weight and weight velocity. In contrast, the increments of ferritin, MCV and transferrin saturation did not correlate with the increments in hemoglobin or erythrocyte iron. We found only poor associations between ferritin and transferrin or growth parameters. Mean serum ferritin decreased significantly during the study, but number of boys with transferrin saturation below 16% and ferritin below 12 µg/l varied from zero to two indicating iron sufficiency in the studied population. Decrease of ferritin may be physiologic and beneficial through stimulation of iron absorption. Role of increasing transferrin by rate of erythropoiesis may be to support iron for growing erythropoiesis rather than to indicate iron deficiency.

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MEGESTROL ACETATE AND CORTISOL RHYTHM IN CHILDREN WITH CANCER

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Megestrol acetate (MA) is a progestagen agent that has been reported to cause increase appetite and weight gain in cancer patients (*). We describe the cortisol rhythm in 27 patients (20 boys, 7 girls), mean age 12,2 years (range: 1-19 years) affected of solid malignant tumours. They have received MA during a mean period of time of 4,2 months, being the mean dose 100 mg/m^2 (range 80-400 mg/m^2). The increase in weight an skinfolds demonstrates, in a statiscally significative way ($p < 0.001$), the efficacy of this drug. We have also assessed the secondary effects of this agent, finding an statiscally significative decrease in serum cortisol levels that correlates with the dose and return to normal values after discontinuing the treatment. We have not observed any detectable effects, secondary to suprarrenal supression. We conclude that MA is a very useful drug to treat anorexia and weight loss in children with cancer. It is necessary to perform further studies to assess the corticosteroid-like action of this drug. The possibility of studying MA efficacy being administered on alternate days, to avoid the encountered cortisol alterations, is suggested.

(*) CL Loprinzi, DJ Schaid, AM Dose, NL Burnham, MD Jensen.. J Clin Oncol 11:152-154; 1993.