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URIC ACID EXCRETION IN ACUTE LYMPHATIC LEUKEMIA (ALL), A FIVE YEAR SURVEY. James A. Stockman III, Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Urinary uric acid, xanthine and hypoxanthine (UXH) were determined following vincristine (VCR) and steroid administration during the induction and remission phases of 37 subjects with ALL in order to determine a possible parameter of disease activity. Average daily UXH (mg/m²) during induction were: Wk1:817, Wk2:577, Wk3:693, Wk4:803 (n.l. range 150-270 mg/m²). UXH excretion was no different for the 86% of subjects who achieved remission (712 mg/m²/day) compared to those who failed (707 mg/m²). The markedly elevated UXH at the time of clinical remission suggests that a longer induction program might achieve greater cell kill. Similar induction UXH excretions were found for those who ultimately relapsed as opposed to those remaining disease free. Induction UXH excretion correlates with clinical evidence of tumor burden (liver-spleen size). During remission, the UXH excretion was significantly lower (259 ± 104 mg/m²/day) but 50% of subjects did excrete mild to moderately abnormal quantities of UXH. UXH excretion demonstrated no tendency to decline over 48-60 mos. for the overall group. Relapses occurred with equal frequency in those with normal or increased UXH during the remission phase suggesting that a normal UXH in a patient who relapses indicates a failure of VCR and steroid to be effective in these subjects. Relapsed patients who did not exhibit elevated UXH with VCR during remission generally failed to achieve a second remission with VCR and steroid. Thus UXH excretion in remission cannot be used to predict relapses in all cases.

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THE NEONATAL PLATELET: EVALUATION OF PROSTAGLANDIN SYNTHESIS. Marie J. Stuart, Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Neonatal platelet prostaglandin synthesis was assessed by evaluating platelet malonyldialdehyde (MDA), a byproduct of the endoperoxide PGG₂. MDA (n moles per 10⁹ platelets) in the presence of N-ethyl maleimide (NEM), or Thrombin, was measured in platelets from 10 normal maternal-neonate pairs, and contemporaneously from 10 donors who had ingested aspirin within 18 hours prior to evaluation. A significant decrease in MDA in the presence of NEM was observed in the neonatal platelets, 2.46 ± 0.61 (1SD) when compared to maternal or adult controls, 3.23 ± 0.31. Thrombin induced MDA was similarly decreased in the neonate to 0.90 ± 0.19, compared to maternal and adult values of 1.30 ± 0.17. A marked decrease in platelet MDA in the presence of NEM and Thrombin was also seen in the aspirin donors (0.25 ± 0.14, and 0.10 ± 0.09). When compared to normal maternal platelets, both the neonate and the aspirin donors demonstrated abnormalities in platelet aggregation in response to ADP, Epinephrine, and Collagen. Mutual correction was obtained when both these abnormal platelets were mixed in varying proportions. No mutually corrective effect was observed when neonatal platelets were preincubated with aspirin in vitro prior to mixing with aspirin donor platelets. The platelet dysfunction in the neonate cannot be attributed to the observed decrease in neonatal platelet prostaglandin synthesis, since the amount synthesized appears sufficient to cause irreversible aggregation of platelets from aspirin donors who were unable to synthesize their own endogenous prostaglandins.

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ASPIRIN (ASA) AND HYDROGEN PEROXIDE (H₂O₂) INDUCED RED BLOOD CELL INJURY, MEMBRANE PROTEIN ALTERATIONS. James A. Stockman III and Stephen Landaw. Depts. of Peds. and Med., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Previous studies have demonstrated that normal intact red blood cells (RBC's) will undergo membrane lipid peroxidation and will hemolyze in vitro in the presence of ASA+H₂O₂ but not with either agent alone (Ped. Res. 9:326, 1975). In order to determine whether ASA+H₂O₂ induced oxidant injury results in RBC membrane protein damage, 5% RBC suspensions were incubated with equal volumes of buffer, ASA (25 mg%), H₂O₂ (1.2%) or ASA (25 mg%)+H₂O₂ (1.2%). Following incubation, RBC membrane proteins were separated on SDS gel. ASA+H₂O₂ resulted in the production of a high M. Wgt. membrane protein complex (M. Wgt. 300,000-600,000) with a decrease in other membrane protein fractions. Similar changes were not observed with ASA alone or H₂O₂ alone. Incubation with ¹⁴C-acetyl and ¹⁴C-carboxyl tagged ASA+H₂O₂ failed to label any membrane protein fraction. Although prior incubation with water soluble α-tocopherol in concentrations as low as 0.01 mg/ml completely prevented hemolysis and membrane lipid peroxidation in the presence of ASA+H₂O₂, no protective effect on RBC membrane protein was found. While in this system lipid peroxidation is more predictive of in vitro hemolysis than is the membrane protein change, such protein change, if it were to occur in vivo, might result in hemolysis. ASA+H₂O₂ induced hemolysis represents an interesting model by which to study the multiple effects of oxidative damage on the normal intact RBC and the mechanism of the protection afforded by antioxidants.

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PLATELET MALONYLDIALDEHYDE (MDA) FORMATION: A NEW TEST FOR PLATELET HYPERFUNCTION. Marie J. Stuart and Pedro A. deAlarcon, Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Methods for identification of enhanced platelet function to date include measurements of spontaneous platelet aggregation, determinations for circulating platelet aggregates, and platelet hypersensitivity to the various aggregating agents. Platelet malonyldialdehyde (MDA) formation in the presence of either N-ethyl maleimide (NEM) or Thrombin was evaluated as a method of identification of platelet hyperfunction. In 13 patients with either spontaneous aggregation (7/13), or enhanced sensitivity to minimal concentrations of ADP or Epinephrine (6/13), platelet MDA formation in the presence of NEM was markedly increased to 3.96 ± 0.16 (1SD) n moles/10⁹ platelets when compared to a value of 3.10 ± 0.25 in 25 normal controls with normal aggregation patterns. Increased values (p<0.0005) were also observed when Thrombin induced MDA values in the patient group (1.82 ± 0.15) were compared to the values obtained in the control group (1.26 ± 0.19). Studies in all 13 abnormal subjects later revealed normal aggregation patterns in 7/13 on follow-up evaluation. Concomitant estimation of platelet MDA induced by either MDA or Thrombin now revealed a significant decrease into the normal range in these 7 patients. Since platelet MDA is a byproduct of the platelet endoperoxide PGG₂, these results suggest that part of the phenomenon of platelet hypersensitivity is intrinsic to the platelet and involves an increase in platelet endoperoxide synthesis.

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MEAN CORPUSCULAR VOLUME (MCV) IN LOW BIRTH WEIGHT INFANTS DURING THE FIRST 7 WEEKS OF LIFE. James A. Stockman III and Frank A. Oski. Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Although changes in rate of fetal hemoglobin synthesis appear to be a function of gestational age rather than postnatal age, changes on other red blood cell (RBC) parameters are undefined in very premature infants during the first weeks of life. RBC indices were determined in 40 preterm infants (mean wt. 1290 g, range 880-1500 g) who were both vitamin E and iron sufficient. Results were:

Day	Hb(g/dl)	MCV(fl)	MCH(pg)	MCHC(%)	RBC(x10 ⁶ /μl)
1	18.2±2.7	115±5	38.9±1.7	33.5±1.2	4.71±0.75
3	16.2±2.9	112±4	39.0±3.4	33.8±1.0	4.40±0.83
7	16.3±2.9	110±5	37.3±1.8	33.9±1.3	4.45±0.83
14	14.5±2.4	106±5	36.3±1.9	33.9±1.0	4.10±0.69
21	12.9±2.0	102±5	35.3±2.2	34.2±1.1	3.71±0.59
28	10.9±1.9	100±5	35.1±1.9	34.4±1.0	3.17±0.60
35	10.0±1.4	98±5	34.4±1.5	34.5±0.7	2.97±0.45
42	9.5±1.5	97±5	32.2±1.7	33.7±0.9	2.92±0.49
49	10.1±1.7	95±5	32.1±1.6	33.5±1.0	3.21±0.59

The MCV falls from the moment of birth thus there is no relationship between cell size and the presence of fetal Hb synthesis. The fall in MCV may reflect an aging RBC population, although the constancy of the MCHC and the continued fall in MCV after a resumption of active erythropoiesis argues against this. The change in cell size may represent another adaptation to extrauterine life.

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INHIBITION OF ADRIAMYCIN (ADR) INDUCED LIPID PEROXIDATION BY α-TOCOPHEROL (α-T) AND ACETYL SALICYLIC ACID (ASA). Marie J. Stuart, Pedro A. deAlarcon and Frank A. Oski. Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

ADR induces cardiac toxicity by peroxidation of cardiac lipids. Cardiac toxicity and lipid peroxidation are reduced by α-T in the animal model. Malonyldialdehyde (MDA) formation was measured in human platelet rich plasma (PRP) as a measure of lipid peroxidation. There was a relationship between the concentration of ADR and the amount of MDA produced, i.e., ADR at 5, 50 and 100 μg/ml produced 1.55 ± 0.13 (1 S.D.), 4.09 ± 0.41, and 5.72 ± 0.76, n moles of MDA per 10⁹ platelets. The addition of α-T to PRP prior to ADR decreased MDA formation, the % inhibition being dependent on the concentration of α-T. At final concentration of α-T of 0.01, 0.05, and 0.1 mg/ml, inhibition of platelet MDA was 14 ± 2%, 27 ± 4%, and 39 ± 5%, and was independent of the ADR concentration. ASA in vivo and vitro caused inhibition of platelet MDA induced by ADR. However, unlike the >90% inhibition of MDA by ASA in the presence of the aggregating agents epinephrine and thrombin, inhibition of ADR induced platelet MDA formation was only 60 ± 4%. α-T (0.1 mg/ml) increased this inhibitory effect of ASA by an additional 24 ± 3%. Platelet lipid peroxidation induced by ADR is inhibited independently by α-T and ASA. Although the effect of ASA appears greater than α-T, both agents are additive. The effect of ASA on ADR induced platelet MDA does not appear to be consistent with its previously known effect on platelet cyclooxygenase.