919 NK CELL ACUTE LYMPHOBLASTIC LEUKEMIA (ALL), A SUBSET OF T-ALL.

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To determine the proportion and subtype of acute lymphoblastic leukemias which have natural killer (NK) phenotype and activity, we examined leukemic blasts from 31 children with ALL (14 with T-ALL, 17 with non-T-ALL) for expression of antigens detected by NK-specific monoclonal antibodies Leu 11b, Leu 7, and 1G2 (an antibody we have developed which cross-reacts with Leu 7). None of the patients had leukemic blasts which reacted with Leu 11b. However, leukemic blasts from 4 T-ALL patients were Leu $7^+/1G2^+$. Blasts from 2 of these had spontaneous lytic activity against standard NK target cell line K562; blasts from one killed K562 only when incubated with interferon; blasts from the other had no lytic activity against K562 but did manifest antibody-dependent cell-mediated cytotoxicity against antibody-coated cells from NK-resistant cell line SB. When leukemic blasts from 6 Leu $7^-/1G2^-$ leukemic patients (2 with T-ALL, 3 with non-T-ALL, 1 with AML) were tested, none had NK activity against K562. Blasts from all 4 Leu $7^+/1G2^+$ patients had L2 morphology. In one, the leukemic blasts had azurophilic cytoplasmic granules similar to those found in NK-enriched normal populations of large granular lymphocytes.

These findings indicate that a significant proportion of subjects with T-ALL have a malignancy of NK cell origin.

● 920 PLASMA PROTEIN C LEVELS IN PATIENTS WITH SICKLE CELL DISEASE (SCD).

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Vitamin-K=dependent protein C (PC) functions as a potent anti-coagulant. Thrombo-embolism has been reported in kindreds with congenitally low PC levels suggesting that PC has an important role in hemostasis and that even a moderate reduction in this plasma protein may be associated with increased risk of thrombosis. Since thrombotic phenomena have important roles in the vaso-occlusive manifestations in SCD, PC was determined in 32 SCD during steady state and in controls (C).

	C	SCD	P Values
Number	32	32	
Age (Years)	8.6 ± 5.6	8.8 ± 5.5	NS
PC Levels (%)	90.3 ± 19.2	63.2 ± 10.5	< 0.001

The SCD had significantly lower PC levels as compared to controls. Six SCD were also studied during vaso-occlusive crisis (VOC). During VOC there was marked decrease in PC as compared to levels during steady state (49.5 ± 6.4 and 66.1 ± 10.0, respectively. $P < 0.01$). Decreased levels of PC during VOC increased to initial levels or higher with clinical improvement. It is postulated that the decreased levels of PC in SCD are probably secondary to increased consumption as well as decreased production because of altered liver functions. This data suggests that decreased levels of PC may increase the risk of thrombosis in these patients.

921 HIGH LEVELS OF INTERLEUKIN 2 IN HEMOPHILIA PERSONS WITH ABNORMAL HELPER-SUPPRESSOR CELL NUMBERS.

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Helper/suppressor (H-S) cell abnormalities are found in more than 70% of hemophilia persons who are receiving factor VIII concentrates. Interleukin 2 (IL2) or T cell growth factor is a lymphokine produced by the helper cell as well as other cells. We studied 12 hemophilia subjects, 7 who received factor VIII concentrates and 5 who received cryoprecipitate. All those receiving factor VIII and 2 of the 5 receiving cryoprecipitate had reversed H-S ratios. IL2 was assayed on the supernates of PHA-stimulated mononuclear cells previously isolated on a ficoll-hypaque density gradient. The target cell was a human IL2 dependent T cell line established by stimulating normal mononuclear cells with PHA for 3 days. The cells were incubated for a further 4 days in media containing 50%, 4x concentrated IL2 previously prepared from PHA stimulated supernates pooled from normals.

	INTERLEUKIN 2 LEVELS (UNITS)		
	CONTROLS (16)	CRYOPRECIPITATE (5)	FACTOR VIII (7)
M ± SD	1.28 ± 0.5	2.03 ± 0.82	1.69 ± 0.37
P	-	0.01	0.03
H/S	1.8 ± 0.6	1.4 ± 0.7	0.9 ± 0.3
P	-	NS	0.008

Significant high levels of IL2 were found in hemophilia persons receiving factor VIII concentrate and cryoprecipitate. It is possible that a receptor defect accounts for the H cell failure.

922 THE INHIBITORY EFFECT OF TIN PROTOPORPHYRIN (SN-P) ON HEME DEGRADATION.

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Sn-P is a potent competitive inhibitor of heme oxygenase, the enzyme which converts heme to bile pigment and carbon monoxide (CO), and has been used to suppress hyperbilirubinemia in experimental animals and man. These experiments were performed to determine which heme pools are affected by Sn-P. Hepatic heme(s) were labeled with delta-aminolevulinic acid (ALA)-5-^{14}C, which does not label hemoglobin heme in the rat. The "free" heme pool was tested by injecting heme prepared in vivo from glycine-2-^{14}C. Adult (300g) rats were injected either with Sn-P (50uM/kg sq) or saline one hour before injection with either 10uCi ALA-5-^{14}C or 0.9mg hemin (specific activity $3x10^4$ DPM/mg in 1ml alkalinized rat plasma). Expired ^{14}CO was then collected over the next 24 hours. Results were:

	Inhibition by Sn-P (Percent)			
Heme Pool	0-12 hours	p	12-24 hours	p
Hepatic heme(s)	61.0 ± 8.8*	.005	- 7.1 ± 16.6	N.S.
Free Heme	45.4 ± 20.0*	.01	33.5 ± 5.3	.05

*Mean ±SD. Results of 4 paired experiments.

These experiments indicate that a single injection of Sn-P significantly inhibits the degradation of hepatic (non-erythropoietic) hemes for 12 hours and exogenous heme for an even longer period. They further suggest that Sn-P may exert different degrees of inhibition of bilirubin (and CO) formation depending upon the heme pool(s) involved.

923 GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY, NEUTROPHIL DYSFUNCTION AND CHROMOBACTERIUM VIOLACEUM SEPSIS.

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A three year old white male with Class I glucose-6-phosphate dehydrogenase (G-6-PD) deficiency developed fever and lethargy. In spite of antibiotics, he developed septic shock and died twelve hours later. Blood and post-mortem liver cultures grew Chromobacterium violaceum. Molecular, kinetic and functional studies were carried out on erythrocytes (RBCs), leukocytes (PMNs) and fibroblasts of his identical twin and mother.

	Twin	Mother	Control
RBC G-6-PD (μm/min/gm Hgb)	<0.02% control	5.0	6.0-7.0
PMN G-6-PD (μm/min/mg protein)	0.011	0.32	0.76
PMN ^{14}C-1-Glucose oxidation (S.I.)	2.2	1.8	5.5
Nitroblue tetrazoleum reduction (O.D. 515, % control)	15	85	100
PMN membrane cytochrome b_{245}	present	present	present

Chemiluminescence was profoundly abnormal in the twin.

G-6-PD isolated from the twin's fibroblasts demonstrated heat lability (27% of initial activity), normal G-6-P Km (56μM) and pH curve, and increased utilization of 2-d-G6P (76% of G-6-P rate); suggesting a new molecular variant (G-6-PD Beaumont).

This is the first reported lethal infection in a child with neutrophil dysfunction due to PMN G-6-PD deficiency. This enzyme defect, like classic chronic granulomatous disease, may cause unique susceptibility to Chromobacterium violaceum.

● 924 IMPROVED SURVIVAL OF CHILDREN WITH GROUP III RHABDOMYOSARCOMA (NON-SPECIAL PELVIC SITES).

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Children with rhabdomyosarcoma who have localized gross residual disease after surgery (Group III disease) are at high risk for disease recurrence and death. In the first national study (IRS-I, 1972-78), 261 Gp III pts were treated with VAC± adriamycin for 2 yrs plus postoperative radiation. At 3 yrs, the relapse-free survival (RFS) rate was 60% and the overall survival rate was 57%. In IRS-II (1978-84), 370 pts were treated with intensive repetitive pulse VAC± adriamycin for 2 yrs and postoperative radiation. Pts. with cranial parameningeal (PM) tumors at risk of CNS extension received, in addition, cranial radiation plus intrathecal methotrexate, hydrocortisone and cytosine arabinoside. The 3-yr RFS and overall survival rates of 72% and 70% on IRS-II were superior ($P < .002$) to IRS-I results. The major reason for improved outcome was the superior results in PM pts who accounted for 37% of Gp III pts in both studies. The 3-yr RFS and overall survival rates for PM patients in IRS-II vs.-I were: 72% vs. 58% (p=.04); 69% vs. 52% (p=.002). Improved outcome for all other pts was less significant (IRS-II vs.-I: RFS-72% vs. 60%; overall survival - 68% vs. 58%; p=.08 for both). We conclude that CNS prophylaxis improves survival in pts. with PM tumors and that intensive chemotherapy for 2 yrs improves the outcome for all Gp III pts.