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†1219 LEAD TOXICITY: INTERACTIONS BETWEEN LEAD (Pb), ZINC (Zn) AND CALCIUM (Ca) IN BONE ORGAN CULTURE. John F. Rosen, Albert Einstein College of Medicine, Montefiore Medical Center, Dept. of Pediatrics, Bronx, New York.

Bone is a major reservoir for Pb (and Zn) and the primary source of Pb mobilized by CaNa₂EDTA. Previous studies have shown that CaNa₂EDTA depleted Pb and Zn from bone explants; and we have reported that Pb-poisoned children evidence a depression in serum Zn post-chelation. This study was undertaken to understand interactions between Pb, Zn and Ca in bone organ culture. Pregnant rats (on day #18 of gestation) were injected IV with ²⁰³Pb and ⁴⁵Ca. On day #19, paired fetal bones were cultured in medium with different concentrations of Zn, as ZnSO₄. After 3-5 days of culture, ²⁰³Pb and ⁴⁵Ca released from bones into the experimental medium (EM) were compared to that released from bones in the control medium (CM). The effects of modifying Zn concentrations in the EM were expressed as cpm EM/CM ratios. The results were:

Zn Concentration, M	EM/CM Ratio for ²⁰³ Pb Release
4 x 10 ⁻⁶ (control)	1.00
10 ⁻⁷	1.79±10*
10 ⁻⁹	3.49±10** *p<.01 vs control
10 ⁻⁵	.81±.14* **p<.001 vs control
10 ⁻⁴	.56±.13**

Parallel rises in ⁴⁵Ca release accompanied the enhanced efflux of ²⁰³Pb in low Zn medium. Conclusions: 1) Low Zn concentrations in medium (ECF) enhance bone resorption and ²⁰³Pb efflux; inhibition of bone resorption was found in high Zn medium; 2) These data may account, in part, for the "rebound" in blood Pb post-chelation in children.

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1220 METHYLCOBALAMIN DEFICIENCY. David S. Rosenblatt, and Bernard A. Cooper. MRC Genetics Group, Division of Hematology, Royal Victoria Hospital, Centre for Human Genetics, and Depts. of Biology, Pediatrics, Physiology, and Medicine, McGill University, Montreal.

Fibroblasts from a patient with homocystinuria and megaloblastic anemia of infancy incorporated labeled cobalamin normally into cells where most of it was bound as observed in control cells. Cobalamin metabolism in these cells differed from that in control cells in the distribution of intracellular cobalamins, most strikingly in a selective deficiency of intracellular methyl cobalamin in the presence of normal levels of intracellular adenosyl cobalamin. Two abnormalities of methionine synthetase activity were observed in this patient's cells. Enzyme activity in extracts of the patient's cells showed resistance to the effect of nitrous oxide on intact cells, suggesting that the methionine synthase in the patient is not active. The patient's enzyme showed a greater sensitivity to thiols in the reaction mixture and showed a greater response to betamercaptoethanol as compared to dithiothreitol. This observation suggests that the methionine synthetase enzyme in extracts of the patient's cells is either more labile to oxidation or is deficient in a reduction step that is required for methionine synthesis. The addition of small quantities of normal extract corrected the defect of methionine synthetase in extract from the patient suggesting that the defect involves a step other than methionine synthetase and one which might be related to the reduction of components during the enzyme reaction.

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1221 PROPIONIC ACIDEMIA, A VARIANT FORM, Claude Sansaricq, Selma E. Snyderman, Fred B. Goldstein, New York University Medical Center, New York City-

A lack of correlation between clinical symptoms and the degree of enzyme activity in propionic acidemia has been reported; siblings of symptomatic patients have had greatly reduced propionyl CoA carboxylase activity without any clinical sequelae. The opposite situation occurred in two sisters who had typical severe symptoms and marked elevation of serum propionic acid levels but lymphocyte enzyme activity was 1/2 normal. Two male siblings had succumbed in infancy with symptoms suggestive of the same disorder. There was neither clinical response nor enzyme enhancement after biotin supplementation. Enzyme activity of the father was normal but that of the asymptomatic mother was in the same range as the two daughters'. This was of particular interest in that we have observed reduced activity of the father and normal activity of the mothers of other patients with propionic acidemia who had minimal enzyme activity. These findings suggest a variant of the disorder with an unusual pattern of inheritance.

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1222 PROPIONYL CoA CARBOXYLASE ACTIVITY OF OBLIGATE HETEROZYGOTE FOR PROPIONIC ACIDEMIA. Claude Sansaricq, Selma E. Snyderman New York University Medical Center, Dept. Peds.

Propionyl CoA carboxylase activity was determined in patients and obligate heterozygotes for propionic acidemia and control subjects. The assay was performed on lymphocytes using ^{14}C sodium bicarbonate. There were 5 males and 5 females in the heterozygotes group and 5 males and 4 females in the control group. The table lists the propionyl CoA activity in picomoles/minute/mg protein.

Enzyme Activity:	Mean	SE	Range
Patients	7.2	$\pm(1.41)$	5.6-10
Controls	376.52	$\pm(14.09)$	289.85-639.95
Male heterozygote	168.03	$\pm(32.77)$	134.9-206.5
Female heterozygote	400.26	$\pm(99.64)$	211.1-789.3

Obligate male heterozygotes demonstrated activity one half of normal. However the activity of female heterozygotes was in the same range as that of controls. Although complementation studies could not be performed it is highly unlikely that any of these patients fell into the PccC group in which the heterozygotes do have normal activity since all the patients' fathers did demonstrate the reduced activity. This difference in activity between male and female heterozygotes has also been observed in MSUD. Although there is no explanations for the sex difference the finding is of interest in that it demonstrates that lymphocyte enzyme activity cannot always be relied on to determine the heterozygous state.

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1223 GLYCOHEMOGLOBIN: COLORIMETRIC VS. CHROMATOGRAPHIC MEASUREMENT. Shirish C. Shah, John L. Malone, Robert C. Harvey, Dept. of Pediatrics, U of So. Fl., Tampa.

Glycohemoglobin (Ghb) is an indicator of long-term glycemic control. Fasting blood specimens were collected from 40 insulin-dependent diabetics. Patients measured fasting and 1 hour post-prandial blood glucose values on 2 days/wk. using a Dextrometer®. Ghb was measured on each specimen in our laboratory after removing labile Schiff base (LSB) by high pressure liquid chromatography (HPLC) and a colorimetric method (CM) using thiobarbituric acid and in a commercial laboratory (CL) using mini columns without removing LSB. Ghb measured by HPLC correlated better with CM ($r=0.7$) than with CL ($r=0.49$). This discrepancy was not explained by the presence of LSB as it was an insignificant component in HPLC results. Freezing the samples immediately increased HbA_{1c} but not HbA_{1c}. Samples sent to CL were frozen at their request and may explain the discrepancy. When an aliquot of the specimens was stored at 25°C, 4°C or -20°C and Ghb was measured at weekly intervals, results of CM remained stable while alteration occurred in HPLC results. Fractions of Hb (A_{1a}+b, A_{1c}, A₀) separated by liquid chromatography were collected. Ketoamine sugar was detected by CM in all fractions. Half of the total ketoamine sugar not measured by either HPLC or CL method was present in the HbA₀ fraction. Ghb measured by each of the 3 methods was compared to the mean blood glucose values during the preceding 4 wks. CM ($r=0.53$) correlated better than HPLC ($r=0.25$) or CL ($r=0.3$) with mean blood glucose values. Ghb measured by CM more accurately predicts long-term glycemic control as it is less subject to handling artifacts and it represents the total Ghb.