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BONE DYNAMICS AND MINERAL METABOLISM IN A PATIENT WITH TURNER SYNDROME AND A CRANIOPHARYNGIOMA TREATED WITH GROWTH HORMONE. D.C. Leach, and L. Weiss. Henry Ford Hospital, Department of Pediatrics, Detroit, Michigan.

Trephine biopsy of tetracycline labeled bone, parathyroid hormone levels and bone densitometry using photon absorptiometry were accomplished in a 14-year-old girl with 45,X karyotype who also has a craniopharyngioma. At the time of the initial studies, she was taking replacement hydrocortisone, 10mg. every morning and 5mg. at night and 150mcg. of Thyroxine daily. The cell and tissue level dynamics of bone remodelling were elevated and slightly above normal compatible with high turnover bone. In retrospect this may have been related to the slightly high thyroxine replacement dose. Following eight months of growth hormone treatment, the dynamics showed further increase in bone activity at both the haversian and endosteal-cortical surfaces. The thyroxine replacement remained constant. She grew three inches, whereas she had previously only grown ½ inch per year. The parathyroid hormone levels did not change significantly. The bone densitometry was 7 standard deviations below normal for age and sex and did not change significantly with treatment.

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CALCIUM DYNAMICS IN INFANCY. Mary O. Lim, James W. Hansen, Larry Moore, and Kevin Rosman (Spon. by Harvey Sharp) NICHD, NIH, Bethesda, Md. and Center for Analytical Chemistry, NBS, Gaithersburg, Maryland.

Calcium (Ca) disorders and therapeutic effectiveness can be assessed by measurements of bone dynamics using stable tracer methods. A pulse of IV Ca-46 is followed by a 9-15 day continuous feeding of Ca-48. Ca isotopic abundances in serum, urine, and feces are determined by thermoionization mass spectrometry (0.5% precision). Kinetic parameters (mg/kg/d) are calculated by nonlinear, weighted least squares analysis and growth is compensated for by using expanding pool sizes. Two infants (Inf.) had Ca turnover rates 12 times that of a control adult (Ad); bone Ca deposition (v_{o+}) and resorption (v_{o-}) were determined with 2 to 5% precision. Two infants with osteogenesis imperfecta (OI) were studied before (B) and while taking ascorbic acid (C).

	v_f	v_u	v_{o+}	v_{o-}	
	2	5	6	9	
Adult					
Infant	8	2	127	59	
Infant	27	1	133	119	
OI(B)	28	3	62	57	
OI(C)	28	1	31	41	(significant loss)

Inf show excessive endogenous fecal (v_f) to urinary (v_u) Ca excretion as compared to adults, suggesting a major role for v_f in regulating Ca balance in Inf. An Inf with OI had similar Ca dynamics except for a decrease in bone Ca fluxes. Ascorbic acid, as suggested for clinical use, had no effect on bone calcium balance.

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SPONTANEOUS TRANSFORMATION OF CULTURED SKIN FIBROBLASTS INTO OSTEOBLASTS IN A CASE OF DYSPLASTIC INTRADERMAL CALCIFICATION. Mary O. Lim, Anil B. Mukherjee, Jean DeB. Butler, Stephen B. Doty, Itzhak Binderman, Leo Liu, and James W. Hansen (Spon. by Joseph D. Schulman), NICHD, NIDR, and NCI, NIH, Bethesda, Maryland

A unique case of spontaneous dysplastic intradermal calcification was identified in a 14 month old child. She presented with a rash at birth which evolved to generalized calcified nodules and plaques. Extensive investigation ruled out known causes of dystrophic calcification. Skin biopsy revealed osteoblast-like cells (OB) surrounding an osteoid layer at the surface of dysplastic woven bone containing osteocytes (OC). Electron microscopy (EM) showed that the OB more closely resembled fibroblasts and the OC appeared to be non-functional. Alkaline phosphatase (AP) was identified by EM techniques in the outer surface of the fibroblast cell membrane 5 microns from the mineralizing front of fibrous bone and along collagen fibers. X-ray microanalysis of the woven bone revealed mineral composition (Ca 41%; P 19%) similar to normal bone but less dense. Skin fibroblasts in vitro apparently transformed to OB after the 4th passage as evidenced by positive Von Kossa staining, high AP activity (201 units/mg protein with 70% heat labile), and morphological appearance. Cyclic-AMP phosphodiesterase activity was markedly elevated in the patient's fibroblasts (mean 708 p moles/mg/min) compared to controls (mean 212 pmole/ mg/min). This patient may provide a unique model for studying OB differentiation in vivo and in vitro.

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INSULIN RECEPTORS IN CYSTIC FIBROSIS (CF): INCREASE IN RECEPTOR NUMBER MAY EXPLAIN INSULIN SENSITIVITY. Barbara M. Lippe, Naomi D. Neufeld, Marilyn Scott, Solomon A. Kaplan. UCLA School of Medicine, Department of Pediatrics, Los Angeles.

Specific ^{125}I insulin binding to circulating monocytes was studied in a group of 13 patients with CF, 4 of whom were insulin dependent. Nine untreated patients had mild carbohydrate intolerance in response to oral glucose as compared to controls (201±26mg/dl vs.103±6 M±SEm at 2h; 144±26 vs.92±5 at 3h). The peak insulin response was delayed to 2 hours in CF and lower than the one hour peak of normals (44mIU/ml vs.66mIU/ml). Calculated insulinogenic index, II ($\Sigma\Delta$insulin/$\Sigma\Delta$glucose) was lower for CF than controls (0.21±0.05 vs.0.37±0.04 $p<0.01$), indicating enhanced insulin sensitivity. Scatchard analysis of insulin binding revealed a marked increase in receptor sites in untreated CF patients as compared to controls; 44,000 sites/cell vs. 25,000 sites/cell. Specific insulin binding at tracer concentrations (0.3ng/ml) was lower in CF 3.14% vs.5.14%, and the calculated affinity constant for binding (Ke) was reduced, 0.8×10^8 M^{-1} vs. 2.5×10^8 M^{-1}. Insulin treated patients did not have lower receptor numbers or altered affinity as compared to the untreated. Thus 1) in CF diminished insulin secretion is associated with an increased number of receptor sites 2) increased binding sites would explain sensitivity to endogenous insulin, as demonstrated by the decreased II as well as to exogenous insulin (reported by others) 3) the consequences of the substantial increase in receptor number may be offset somewhat by reduced receptor affinity.

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ZINC THERAPY IN MANNOSIDOSIS. Ira T. Lott, Richard Dickersin, Ann B. Dvorak, and Edwin H. Kolodny. (Spon. by Aubrey Milunsky) Harvard Medical School, E. Kennedy Shriver Center, Massachusetts Gen. Hosp., Depts. of Neurology and Pathology, Boston.

Our previous observation that $ZnSO_4$, added in vitro, both stimulated and stabilized residual leukocyte acidic α-mannosidase activity in two patients (Arch. Neurol. 34, 45, 1977) prompted a therapeutic trial of the metal. Oral $ZnSO_4$ in doses ranging from 13-45 mg/kg over a 12-week period raised serum Zn levels to a maximum of twice normal. Average leukocyte acid α-mannosidase activity during the treatment period ranged from 2-5% of control values, showing no significant difference from baseline levels. No treatment related change occurred in the 11 band thin layer chromatographic profile of mannose containing neutral oligosaccharides excreted in a 24-hour urine. Because Zn is known to have a high affinity for tissue uptake, 1 ml containing 10 mg $ZnSO_4$ was injected into the gingiva of patient 1, which had become hyperplastic with PAS-positive storage material. A control site was injected with an equal volume of saline. Biopsies before and one month after the injections showed no change in the ultrastructural characteristics of membrane bound cytoplasmic vacuoles. The Zn injected tissue had a moderately increased amount of collagenous stroma, which was not seen in either the saline or pre-injection controls. This may reflect a positive effect on wound healing. Otherwise, $ZnSO_4$ does not appear to have specific therapeutic efficacy in ameliorating storage material in mannosidosis under the above conditions.

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DECREASED POLYAMINE CONTENT IN CON A STIMULATED LYMPHOCYTES FROM DOWN'S SYNDROME. Ernest E. McCoy, Ken Strynadka and Henry Pabst. Dept. of Pediatrics, University of Alberta School of Medicine, Edmonton, Alberta.

The present study was done to determine if polyamine content of Concanavolin A (Con A) stimulated lymphocytes was decreased in cells from D.S. patients. Increased polyamine content or synthesis has been associated with increased rates of growth in a number of tissues in many animal species. Down's syndrome fibroblasts have a lengthened doubling time and PHA stimulated lymphocytes have decreased DNA polymerase activity and 3H thymidine uptake. Lymphocytes were isolated and cultured in RPMI-16 media with 15% v/v autologous plasma for 4 or 5 days in presence or absence of Con A. Polyamines were extracted, quantitated with an amino acid analyzer and the net increase between non-Con A and Con A stimulated lymphocytes compared in D.S. and control subjects. The net spermidine content of cells stimulated 4 days was 814.4±115.5 nM/10^9 cells in controls compared to 410.8±107.9 nM/10^9 cells in D.S. ($p<.025$). The spermine content was 858.9±150.4 nM/10^9 cells in controls compared to 329.4±78.8 nM/10^9 cells in D.S. ($p<.01$). In cells stimulated 5 days by Con A net spermidine content was 700.8±77.8 nM/10^9 cells in controls and 379.2±67.1 nM/10^9 cells in D.S. ($p<.01$). Spermine content was 825.3±131.5 in control cells compared to 372.3±68.5 nM/10^9 cells in D.S. ($p<.01$). The decreased content was not due to increased leak of polyamines into the medium or to differences in time of peak content of polyamines in the D.S. cells. Decreased polyamine content in D.S. tissues may be a factor in the slow growth rates seen in D.S. subjects.