Oral presentations

**001 Vitamin D insufficiency and chronic diseases: Facts and fictions**
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Abstract: It is a myth that vitamin D is a panacea for any kind of disease. In reality recent studies that had been inadequately controlled for confounding factors found no association between vitamin D insufficiency and, for instance, obesity, metabolic syndrome, diabetes mellitus type II, arterial hypertension, multiple sclerosis and cognitive dysfunction. An effect of vitamin D on autoimmune diseases, though evident in animal models, has not yet been observed in humans. However, there is convincing evidence from multiple epidemiological, clinical and experimental studies, that vitamin D insufficiency plays a significant role in the pathogenesis of osteoporosis, colorectal and breast cancer as well as cardiovascular disease.

Another myth is that serum vitamin D concentrations are independent of season and latitude. Vitamin D insufficiency estimates based on serum 25 hydroxy-vitamin D (25OHD) thresholds, currently recommended for maintaining optimal bone health, is a myth. A more accurate estimate of desirable 25-(OH)D serum concentrations can be because they were calculated from pooled odds ratios reported by largely uncontrolled studies. A more accurate estimate of desirable 25-(OH)D serum concentrations can be obtained from plots of multivariate risks vs. 25-(OH)D in serum. It becomes evident that raising 25-(OH)D to >50 nmol/l has no additional effect on the reduction of risk of osteoporotic fractures, cancer of the colorectum and the breast, and of cardiovascular disease. One must not ignore the fact that the potential of vitamin D to reduce the risk of chronic diseases depends to a great extent on adequate calcium nutrition. I will summarize the evidence that efficient disease prevention does not require intake of more vitamin D and calcium than currently recommended for maintaining optimal bone health.

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**002 Searching for a biochemical definition of vitamin D deficiency in children**
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Abstract: Objective: Currently, a variety of guidelines use differing definitions of vitamin D deficiency based on serum 25 hydroxy-vitamin D (25OHD) thresholds, which complicates clinical decision making on Vitamin D doses used for prevention and treatment. This study examined the relationship between serum 25OHD levels, parathyroid hormone (PTH) and other markers of bone metabolism in children and adolescents. Study design: Audit of children and adolescents presenting to a large children’s hospital, who had simultaneous measurements of serum 25OHD, PTH, plasma calcium, phosphate and alkaline phosphatase. The inter-relationship between these metabolites was examined to determine which 25OHD level is associated with abnormal bone metabolism. A two-phase linear spline was used to model the relationship between 25OHD and PTH. Results: Blood results of 214 children (median age 9.5 years [range 0.1–19.2]) were included. 65.4% of children had 25OHD levels below 50 nmol/L. The deflection of the spline where PTH levels started to rise occurred between 31 and 37 nmol/L, with best fit at 34 nmol/L (R2 = 0.454). 74.3% and 82.3% of children demonstrated some bone metabolic abnormality below 25OHD levels of 37 nmol/L and 31 nmol/L, respectively. 16 of 17 children with radiological confirmed Vitamin D deficiency rickets had 25OHD levels below 31 nmol/L. Results from the 17th rickets patient (25OHD 32.5 nmol/L) and an additional case (25OHD 50.0 nmol/L), both pre-treated with vitamin D, demonstrated that 25OHD can normalize long before other biochemical and skeletal signs do. Conclusion: Vitamin D deficiency in children, based on PTH suppression, was best defined by a 25OHD level of below 34 nmol/L. The slow biochemical and skeletal response to changes in vitamin D levels and high prevalence of low calcium intake impede researchers’ attempts to determine a threshold for the skeletal effects of vitamin D based purely on 25OHD levels.

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**003 FGF23 regulates renal sodium handling and blood pressure**
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Abstract: Fibroblast growth factor-23 (FGF23) is a bone-derived endocrine signal regulating renal phosphate reabsorption and vitamin D synthesis. In patients with chronic kidney disease (CKD), FGF23 serum levels are associated with cardiovascular risk and mortality for unknown reasons. In earlier studies, we found that FGF23 signaling in distal renal tubules involves serum/glucocorticoid-regulated kinase 1 (SGK1) and with-no lysine kinase-4 (WNK4) which are both involved in renal sodium (Na) handling. Here, we examined the role of FGF23 in the regulation of renal Na reabsorption in gain- and loss-of-function models. Nine-month-old compound mutant mice deficient in both Fgf23 and vitamin D receptor (VDR) function revealed increased urinary loss of Na, relative to wild-type (WT) and VDR mutant mice. Serum aldosterone was elevated in compound mutants. Compound mutants showed reduced membrane expression of the Na-chloride cotransporter (NCC), but upregulated expression of the epithelial Na channel ENaC, as measured by immunoblotting of renal membrane preparations. Treatment of WT mice with recombinant FGF23 (rFGF23) profoundly upregulated NCC membrane expression, and decreased ENaC membrane abundance as well as serum aldosterone, 8 h post-injection. After 5 days of treatment, urinary Na excretion and urine volume were decreased, whereas systolic and diastolic blood pressure, and heart-to-body weight ratio were increased in rFGF23-treated animals. In vitro experiments with isolated distal tubular segments showed that rFGF23 increased NCC and decreased ENaC protein expression in an ERK1/2-dependent fashion. Taken together, our data have uncovered a previously unknown function of FGF23 in distal renal tubular Na reabsorption. Gain of FGF23 function results in renal Na retention and volume overload due to increased NCC membrane abundance, leading to hypertension and heart hypertrophy. Our data may explain why serum FGF23 is associated with cardiovascular risk and mortality in patients with CKD.

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