ABNORMAL TUBULAR Pi ADAPTATION TO DIETARY Pi RESTRICTION AND DECREASED CALCIUM REABSORPTION IN X-LINKED HYPOPHOSPHATEMIC (HYP) MICE

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The renal transport of Pi is under a powerful parathyroid hormone-independent adaptation mechanism (1,2). It has been suggested (3) that this adaptation mechanism could be defective in X-linked hypophosphatemia, a disease characterized by vitamin D-resistant rickets and decreased tubular reabsorption of Pi (4).

HYP mice first described by Eicher et al. (5) are considered as animal model of the human X-linked hypophosphatemic rickets. In a recent study (6) we have tested the hypothesis whether the renal leak of Pi might be caused by a defect in the adaptation mechanism which adjusts the renal handling of Pi according to the dietary Pi intake. Male HYP mice (HYP/Y) and normal littermates (+/Y) were submitted to high (0.75 %) or low (0.25 %) phosphorus diets for periods varying between 1 and 20 days. Then the urinary fractional excretion of Pi (FEPi) at endogenous plasma Pi [Pi] was measured. Furthermore, Pi excretion was measured in all animals at increasing [Pi] during an acute Pi infusion. The overall tubular Pi transport capacity was assessed by determining the maximal net Pi reabsorption per unit volume of glomerular filtrate (max. TRPi/ml GF). As shown in the upper panels of Fig. 1, in both +/Y and HYP/Y mice a dramatic fall in FEPi was observed already after 1 day of Pi restriction. In the left lower panel the progressive and marked enhancement of max. TRPi/ml GF beyond the first day of feeding low Pi diet in +/Y mice is shown. The results obtained in HYP/Y mice are depicted in the right lower panel. In sharp contrast it can be seen that HYP/Y mice are unable to increase significantly their

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Fig. 1. Upper panels: Fractional excretion of phosphate in control +/-Y (left) and hypophosphatemic HYP/Y (right) mice fed either a high (●) or a low (○) phosphate diet for various periods of time.

Lower panels: Maximal phosphate reabsorption per ml GF in +/-Y (left) and HYP/Y (right) mice fed low (○) phosphate diet for various periods of time. (●) and dotted lines indicate the values obtained in animals fed the high phosphate diet.

The values represent means ± SEM. NS = not significantly different, ** p < 0.01, *** p<0.001 as compared to the corresponding high phosphate group. Adapted from (6).