thromboxane synthesis in the following manner: ADP < EP < AA. Our previous work[11] agrees with this, if in fact CO inhibits thromboxane synthesis, since CO inhibits platelet aggregation as follows: ADP < EP < AA.

Our in vitro experiments may, however, not be directly comparable to the in vivo situation possibly due to the synergistic actions of many aggregating agents with ADP[22] since ADP release, although inhibited in the presence of CO and in smokers is not absent. Also important is that serotonin release by AA is unaffected. Rao and White's finding[23] that drug-induced defects in platelet prostaglandin synthesis may be compensated for by membrane modulation and receptor cooperativity also complicates the extrapolation of in vitro obtained data to in vivo situations.

The presence of deaggregating agents as well as the alteration of platelet sensitivity towards them is another complication. Recently Pittilo et al.[24] have shown that prostacyclin production in vitro is decreased in smoking rats. Diminished prostacylin formation has also been shown in umbilical arteries of babies born to smoking women[25]. Our data showing that serotonin release is inhibited in smokers may support this, since serotonin can act as a coenzyme for prostaglandin biosynthesis[26]. Recent data from other workers have suggested that smokers' platelets may be less sensitive to prostacyclin[27].

Therefore, although platelet aggregation and the release reaction are generally decreased in the presence of CO and in smokers, they may not reflect the in vivo situation. Atherosclerosis in smokers probably occurs due to a combination of interacting factors for which no one in vitro experiment can give a clear understanding.

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Metabolic implications in the elevation of serum activity of intestinal alkaline phosphatase in chronic renal failure

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Summary. The activity of intestinal isoenzyme of serum alkaline phosphatase was evaluated in 21 non-dialyzed patients with advanced renal failure and in 52 patients on regular hemodialysis. In patients without hepatopathy, a significant inverse correlation was found between the enzyme activity and serum calcium levels. Hepatopathy was the most significant variable influencing the enzyme activity in patients on dialysis. Secondary hyperparathyroidism and a decreased rate in enzyme elimination should be assessed for the above-normal activities of intestinal ALP in serum in chronic renal failure.

Elevation in the serum activity of intestinal isoenzyme of alkaline phosphatase (EC 3.1.3.1) has been described in patients on regular hemodialysis[1-3]. The present investigations were designed to determine the factors which influence the changes in the enzyme activity in chronic renal failure.

Patients and Methods. Measurements were made in 21 non-dialyzed patients with advanced renal failure (creatinine clearance mean ± 2 SD range, 35 ml/min, and 13–85 ml/min, respectively) and in 52 patients on regular hemodialysis. No patients received phosphate binders, vitamin D or its derivatives, anticonvulsants or corticosteroids (except for the transplant patients and patients with an active hepatitis). In 37 patients (35 on dialysis), a chronic hepatopathy was documented by a previous history of acute hepatitis and serial evaluation of liver tests. The dialysis calcium concentration was 2.3 mmol/l. Nine patients had a previous history of a non-successful renal transplantation. The control group consisted of 40 adults without evidence of renal, hepatobiliary, or bone disease. Blood samples were drawn in the morning after a fasting period of approximately 8 h, in patients on dialysis before the dialysis. Informed consent was obtained from all the patients.

The activity of the intestinal, liver and bone isoenzyme of serum alkaline phosphatase (ALP) was determined with 4-nitrophenyl phosphate as substrate[4]. The total concentration of calcium in the serum was determined with methylthymol blue and

corrected for individual variations in serum albumin concentration[5], inorganic phosphate in the serum was determined photometrically[6]. In all patients, determinations of the serum activity of alanine aminotransferase (EC 2.6.1.2), gamma-glutamyl transferase (EC 2.3.2.1, GMT) cholinesterase with butyryl thiocholine as substrate (EC 3.1.1.8), albumin, creatinine, and clearance of endogeneous creatinine, were performed. The serum immunoreactive parathyroid hormone (iPTH) was determined by radioimmunoassay, using Human Parathyroid Hormone PTH II and Human N-Terminal Parathyroid Hormone Kits (Immuno Nuclear Corp., MN, USA). The kits were kindly provided by DRG International, NJ, USA. Statistical analysis of the results was performed by commonly accepted methods using BMDP 1V, 1R, 6R, 9R, 6M and 7M programs of the Health Science Computing Facility, University of California, Los Angeles, USA[7].

Results. Mean values for the variables are shown in the table. The intestinal isoenzyme activity in patients without biochemical and clinical evidence of hepatopathy was most significantly influenced by serum calcium level (fig.). Accordingly, in these patients a significant positive correlation was found between serum iPTH and intestinal ALP activity (log intestinal ALP activity (log intestinal ALP = 0.21+0.72 log iPTH, $r = 0.61$, $n = 19$, $p < 0.01$).

The figure shows that the activity of the intestinal isoenzyme of serum ALP in 44% of the patients with hepatopathy fell out of the 95% confidence limits of the regression observed in patients without hepatopathy. No significant correlation was found between iPTH values and intestinal ALP activity in patients with hepatopathy. The multiple regression analysis showed that the activity of the intestinal ALP in serum of patients with hepatopathy was significantly influenced by blood group, liver ALP activity in serum and serum GMT activity.

Discussion. The results of the present study indicate that the liver functional state and the role of serum calcium should be considered as being involved not only in an increased entrance rate of the enzyme into the blood, but also in the removal of intestinal ALP from the circulation. In our patients who had normal liver function tests and normal serum calcium level, a normal activity of intestinal ALP was found.

In contrast to the other organ-specific forms of ALP, the adult intestinal ALP is an asialoglycoprotein[8]. A damage to the hepatocyte plasma membrane is known to interfere with the hepatic uptake of circulating desialylated glycoproteins and lead to their accumulation in serum[9], especially if the patients blood group is type O[10]. The binding activity of the asialoglycoprotein receptor of hepatocytes has been shown to depend on calcium ions[11]. However, hypocalcemia and a consequent secondary hyperparathyroidism might lead to an increased rate of entrance of the enzyme into serum as well. Birge and Gilbert[12] identified an ALP in rat intestine that was stimulated by parathyroid hormone. An augmented catalytic efficiency of the intestinal ALP could also account for its increased activity[13].

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