Abstracts

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Increased calcitonin plasma concentrations in chronic and early acute renal failure. R. Ardaillou, R. Isaac, M. Beaufils and M. P. Nivet. INSERM, U64, Hopital Tenon, Paris, France. Plasma calcitonin (CT) and parathyroid hormone (PTH) concentrations were compared before and after calcium infusion (4.5 g of calcium gluconate over 12 min) in both recurrently hemodialyzed patients and control subjects. Concentrations of both hormones were significantly higher in patients with chronic renal failure (mean ± SEM = 1.5 ± 0.3 and 3.5 ± 0.6 ng/ml for CT and PTH, respectively) than in control subjects (mean ± SEM = 0.15 ± 0.06 and 0.7 ± 1 ng/ml for CT and PTH, respectively). In the uremic group, calcium infusion inhibited PTH secretion but did not affect CT. High plasma CT levels were also observed in 10 of 11 patients with acute renal failure particularly in the oliguric phase. A large dispersion was observed in these patients, plasma CT ranging between 0.98 ± 0.42 and 16.08 ± 0.22 ng/ml (mean ± SEM of serial daily samples). CT levels decreased progressively with time independent of renal function recovery. High plasma CT values were found whatever the anti-CT antibody used (four different antibodies), and plasma CT was completely removed using charcoal extraction. Multiples dilutions of plasma with high CT levels gave a radioimmunossay curve superposed to that obtained with synthetic human CT indicating same immunological reactivity of both peptides. Calcium plasma concentration was inversely correlated to PTH serum levels. In the early group, bone histomorphometric analysis showed a rather rapid disappearance of uremic bone lesions. A significant correlation was found among serum PTH, renal function and bone changes. In long-term dialysis patients, remarkable differences have been found in "true" dialysis starting-time (mean value of creatinine clearance at the beginning of treatment, 2.04 ± 1.7) with respect to "early" starting-time (mean value, 13.1 ± 3.9). In the late group, bone histomorphometry showed quite evident signs of secondary hyperparathyroidism and hyperosteoedidism which remarkably worsened three to four years after dialysis. The amino acid composition of the bone showed an increase in the total amount of amino acids during dialysis, especially for proline, hydroxyproline and glycine. In the early group, both basic values and progression rate of bone lesions were less severe. In transplanted patients with good renal function (serum creatinine <1.4 mg/100 ml) bone histomorphometric analysis showed a rather rapid disappearance of uremic bone lesions. A significant correlation was found among serum PTH, renal function and bone histology. On some occasions signs of secondary hyperparathyroidism were documented even after 16 months. A good correlation between inactive bone surfaces and immunosuppressive regimen was found.

Histological, hormonal, biochemical and radiological evaluation of vitamin D therapy in osteodystrophic patients on RDT. D. Brambilla, G. Graziani, J. M. Vaccari, G. Bonfi, G. Podoia and L. Watson. Sezione di Nefrologia e Dialisi, Ospedale Policlinico, Milano, Italy; University College Hospital Medical School, London, England; Instituto di Radiologia, Ospedale S. Carlo Borrromeo, Milano, Italy; and University College Hospital, London, England. Five patients of our Unit on long-term RDT showing clinical and radiological signs of well-established long-standing osteodystrophy were studied. For almost two years the schedule of RDT was: Gambio LN 13.5 U, 5 hr × 3 × week; bath Ca, 8 mg/100 ml. All patients were treated with high doses of vit D3 (600,000 U weekly for six months); at the beginning and at the end of therapy the patients were checked for blood PTH levels, bone biopsies (evaluated by an image analyzing computer), bone X-ray; blood Ca, P, alkaline phosphatase were estimated weekly. Evident improvement of PTH levels and X-ray findings were observed after six months of therapy, continued as far as hypercalcemic crisis appeared. The results show: high doses of vit D3 can reverse uremic long-standing osteodystrophy; no difference between anephric and nephric patients was observed; vascular calcifications seem to improve; since hydroxylate vit D metabolites are not available, high doses of vit D3 can be suggested in the treatment of uremic osteodystrophy.

Microtubule disrupters and secretion of parathyroid hormone in vivo J. Chunard, S. Klair and E. Slaiopolsky. INSERM U 90 Hopital Necker, Universite Paris, France, and Washington University, St. Louis, Missouri, U.S.A. Colchicine (C) and vinblastine (V) have been shown to interfere with the secretory process of several hormones and neuro-transmitters. The inhibitory effect of these drugs is related to their microtububle-disrupting action. In the parathyroid gland (PTG) C and V induce a total disappearance of microtubules that suggests inhibition of immunoreactive parathyroid hormone (iPTH) secretion. To investigate this hypothesis we have measured serum iPTH release three hours after injection of these drugs, either intraperitoneally (i.p.) or intravenously (i.v.). The decrease in ionized calcium (ICa) and the corresponding increase in iPTH were:

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>ICa, mg/100 ml</th>
<th>iPTH, pg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>4.51 ± 0.08 (SEM)</td>
<td>80 ± 10</td>
</tr>
<tr>
<td>C 2.5 mg/kg i.p.</td>
<td>6</td>
<td>3.09 ± 0.19*</td>
<td>210 ± 25*</td>
</tr>
<tr>
<td>C 2.5 mg/kg i.v.</td>
<td>8</td>
<td>3.61 ± 0.24*</td>
<td>287 ± 23*</td>
</tr>
<tr>
<td>V 1 mg/kg i.p.</td>
<td>6</td>
<td>4.44 ± 0.05</td>
<td>80 ± 12</td>
</tr>
<tr>
<td>V 10 mg/kg i.v.</td>
<td>6</td>
<td>4.20 ± 0.07*</td>
<td>257 ± 50*</td>
</tr>
</tbody>
</table>

* P < 0.001.

The increased iPTH secretion induced by C was suppressed by calcium gluceptate injection preventing the drop in ICa. Three hours after injection of C or V, the PTG retained its ability to secrete more iPTH when stimulated by a further decrease in ICa induced by disodium EDTA injection. These results indicate that: 1) high doses of C or V induced a decrease in ICa related to a direct effect at the bone level; 2) iPTH-increased secretion in response to a decrease in ICa was not suppressed by the microtubule disrupters; 3) iPTH secretion could be possible without requirement of tubulin polymerization.
Defective calcium absorption in the proximal small intestine in uremic man: Effect of dihydrotachysterol. G. Coen, M. Di Segni, G. Stitrati, and G. A. Cinotti, 2nd Clinica Medica, University of Rome, Italy. Intestinal absorption of calcium was determined in uremic patients (GFR, 6 to 20 ml/min) and in normal controls. Absorption was evaluated at ten-minute intervals over a four-hour period after oral administration of radioactive calcium in 100 mg Ca++. Fractional absorption of the oral dose as a function of time was calculated by deconvolution from the experimental serum activity curves obtained following oral and i.v. radioactive calcium administration. In normal subjects intestinal absorption occurred primarily within the first two hours, with a maximum rate of transport (% dose/min) of 0.579 ± 0.08 (mean ± SE) at about 40 min after ingestion of the isotope, while absorption was markedly impaired in the patients with uremia, the maximum rate of transport being 0.268 ± 0.03. At the end of the four-hour period the mean integrated fractional absorption of the test load in normal controls and uremic patients was, respectively, 49.9 and 29.9%. Oral administration of dihydrotachysterol, 0.66 mg/day for 6 to 10 days, completely reverses the absorption defect. Absorption was only slightly improved following administration of 0.33 mg/day. The following conclusions are presented: 1) Defective calcium transport in uremic patients appears to be due to impaired absorption in the proximal part of the small intestine, where a vit D-dependent active transport normally occurs. 2) Dihydrotachysterol reverses the absorption defect, and its effect is not different from that of 1,25-dihydroxycholecalciferol. The activity ratio of these substances [1,25(OH)2D3/DHT], based on a comparison with published data on the dihydroyxlated compound, is about 1/300—1/600. 3) The present method of study giving detailed information on proximal intestinal absorption of calcium is preferable to the mere determination of percent absorption after 24 hr, in establishing the sensitivity to vit D metabolites and analogues in man and in defining the dose-effect relationship.

Parathyroidectomy for secondary hyperparathyroidism in chronic renal insufficiency. J. Corvilain, M. Fuss, P. Kinnaert, J. P. Meurmans, C. Toussaint, J. Van Geertruyden and P. Vereestraeten. Hôpital Brugmann, University of Brussels, Belgium. Among 304 patients hemodialyzed for chronic renal failure, 12 developed symptoms of secondary hyperparathyroidism (11 under hemodialysis, one before dialysis treatment was undertaken). Indications for parathyroidectomy were clinical symptoms (nausea and vomiting, pruritus, bone pain, joint tenderness and swelling) and radiologic signs (osteolysis and para-articular calcifications), biological data (serum Ca, P, alkaline phosphatase and parathyroid hormone) being of no value. Eleven patients were submitted to subtotal parathyroidectomy. Nine have been followed for at least one year. In five cases, a subtotal parathyroidectomy was done, leaving a glandular volume equivalent to one normal parathyroid: these five patients are cured. In the four other patients, the amount of parathyroid tissue removed was less important (14 to 33% parathyroids): one is cured; one is improved; in the two others, who had not been improved by parathyroidectomy, hyperparathyroidism disappeared after renal transplantation.

Interaction between secondary hyperparathyroidism in uremia and the beta-adrenergic system at the cardiac level: In vitro and in vivo studies. T. Breike, F. Lhoste, A. Ulmann, S. Lanno, N. K. Man, J. Zingraff, P. Jungers, J. B. Boissier, and J. Crosnier. C.H.U. Necker-Enfants Malades, Paris, France. 1) In vitro study. The effect of d-l propranolol on isolated guinea pig auricles has been studied in the presence of hyperparathyroid plasma ultrafiltrates (UF) sampled in two patients on chronic hemodialysis, before and after subtotal parathyroidectomy (PTx). The depressant action of UF of 1.35 × 10-8 M d-l propranolol on cardiac contractile strength at five minutes (25.79 ± 2.62%, mean ± SEM, N = 6) has been found to be significantly inhibited in the presence of pre PTX-UF (16.26 ± 1.44%, N = 6, P < 0.01 for patient J. B., and 17.38 ± 0.83%, N = 6, P < 0.02 for patient Z. J.). No such inhibition was found in the presence of post PTX-UF. 2) In vivo study. The effect of isoproterenol (ISO) on cardiac rhythm has been studied in four severely hyperparathyroid patients on chronic hemodialysis in whom an i.v. perfusion of ISO was performed before and after PTX. Stepwise increments of the i.v. dose at five-minute intervals were realized until cardiac rhythm was increased by 20 beats/min. To obtain this effect, a mean (range) cumulative dose of 291 (112 to 571) ng/kg body wt ISO was needed before PTX, whereas it was reduced to 116 (67 to 179) ng/kg body wt after PTX. This difference of cardiac responsiveness to ISO was observed in the absence of significant changes in total plasma calcium concentration. 3) In conclusion: The cardiac effects of d-l propranolol and isoproterenol in the uremic patient appear to be modified by high plasma parathormone concentrations.

Hypercalcemia with oral calcium carbonate in patients on chronic hemodialysis—Assessment of plasma gastrin and parathyroid hormone. A. Fournier, C. Ferrière, J. Guert, J. L. Sebert, J. Quichaud and P. Border. CHU d'Amiens and Hôpital Lariboisière, Paris, France. Unexpected hypercalcemia occurred in four out of ten patients undergoing chronic hemodialysis with a dialysate calcium of 6.5 mg/100 ml. All patients were taking 3.2 g of CaCO3, 2000 IU of vitamin D2, 3 g of aluminum hydroxide. Cumulative dose of vitamin D2 was lower in the hypercalcemic group. Normophosphatemia was present in 2/6 of the normocalcemic and in 3/4 of the hypercalcemic patients. In one patient, hypercalcemia promptly followed lowering of plasma phosphate by aluminum hydroxide. Increase of CaCO3 in another patient induced a further increase of plasma calcium (Pca). Discontinuation of CaCO3 was followed by a prompt return of PCA below 10.0 mg/100 ml. To investigate the pathophysiology of the hypercalcemia, plasma concentrations of parathyroid hormone (PTH) and gastrin (G) were measured by radioimmunoassay, and bone biopsies were performed for measuring the active resorption surface. Mean PTH (± SD) was significantly lower (P < .05) in the hypercalcemic group than in the normocalcemic group: 49 (± 16) vs. 86 (± 9) ng of protein/ml (normal range, 4.5 to 9.5). Sequential measurement of PTH and G in one patient after CaCO3 discontinuation revealed that PCA was negatively correlated with PTH (r = −.85, P < .01) and positively with gastrin (r = .77, P < .05). It is concluded that 1) a moderate oral supplement of CaCO3 may induce severe hypercalcemia; 2) phosphate binders may potentiate this hypercalcemic effect; 3) hyperparathyroidism can be reduced but not completely suppressed by this chronically induced hypercalcemia and normophosphatemia; 4) a more severe hyperparathyroidism is not the explanation for the hypercalcemia; 5) hypergastrinemia is the consequence but not the cause of hypercalcemia.

Variation of parathyroid hormone, calcitonin and calcium blood concentrations in acute renal failure. M. Fuss, E. Dupont, J. Bagon and J. Corvilain. Université Libre de Bruxelles, Hôpital Brugmann, Brussels, Belgium. Parathyroid hormone (PTH), creatinine, calcium (Ca) and phosphate (P) blood concentrations were repeatedly measured in five patients with acute renal failure (ARF), before hemodialysis and during the recovery phase of the illness. Plasma calcitonin (CT) was measured in one of these patients; one of them developed transient hypercalcemia during the recovery period. PTH and CT concentrations were elevated before starting hemodialysis treatment. After completion of the treatment PTH and CT varied in parallel to creatinine. In the patient with transient hypercalcemia there was an inverse correlation between PTH and Ca concentrations, whereas no relationship was found between CT and Ca. Our data show that parathyroid function in ARF is closely related to changes in renal function and that hypercalcemia, when occurring, is not necessarily due to parathyroid hyperactivity.

Nodul calcifications in a patient on chronic maintenance hemodialysis—Survival during 27 months under cardiac pacemaker. C. P. Giudicelli, T. Kamaladun, Ch. Lombard, P. Laroque, Ch. Hiltbrand and A. Matherne. Hôpital d'Instruction des Armées du Val-de-Grace, Paris, France. Nodular calcium deposits in a patient on chronic maintenance hemodialysis with secondary hyperparathyroidism led the authors to attempt a review of the common features of the reported cases. Although myocardial calcifications
could be found on necropsy in 2.5% of the patients with chronic renal insufficiency, calcium deposits in the conduction system are seemingly infrequent: only eight cases were found in the literature. Atrioventricular and/or ventricular conduction disturbances, in certain cases with atrial fibrillation or ventricular tachycardia, supervened after a variable duration of hemodialysis (9 to 26 months), following a mostly long-standing renal insufficiency. In all the patients an adenomatous or hyperplastic hyperparathyroidism could be pathologically confirmed. In six of them a high calcium-phosphorus product above 75 had been noted. This reported case is remarkable through the 27 months survival of the patient under cardiac pacemaker before her death due to gastrointestinal bleeding.

A study of the variations of phosphoremia in persons undergoing a treatment of hemodialysis. B. Guittienne M. Kessler and C. Huriet. Centre Hospitalier Regional, Nancy, France. From the very beginning of the application of an artificial kidney with an acrylonitrile membrane (R.P. 3 x 4 hours/week), a significant increase in phosphoremia was revealed in the majority of the patients. There are three possible explanations for this: 1) the technique of the closed circuit (the phosphorus concentration of the dialysate at the end of the purification process reaches a maximum of 12 mg/liter); 2) the special permeability of the membrane AN 69 with respect to phosphorus; 3) the duration of dialysis treatment. The same phenomenon is noted if the length of sessions is reduced with cuprophane in an open circuit, even if the surface area is increased in order to maintain the same m² per hour (7.5% per week). Hyperphosphoremia appears therefore to be the result of a reduction in the length of the sessions of dialysis treatment. The authors believe that the purification of phosphorus by the artificial kidney depends neither on the type of dialyzer used nor on the membrane, but exclusively on the duration of dialysis treatment; the number of m² per hour per week plays no part in it.

Heterogeneity of Ca-P regulation in hemodialyzed patients. G. Heynen, G. Rorive, and P. Franchimont, Dept. of Medicine and Treatment of Hemodialysis. B. Guittienne M. Kessler and C. Huriet. Centre Hospitalier Regional, Nancy, France. From the very beginning of the application of an artificial kidney with an acrylonitrile membrane (R.P. 3 x 4 hours/week), a significant increase in phosphoremia was revealed in the majority of the patients. There are three possible explanations for this: 1) the technique of the closed circuit (the phosphorus concentration of the dialysate at the end of the purification process reaches a maximum of 12 mg/liter); 2) the special permeability of the membrane AN 69 with respect to phosphorus; 3) the duration of dialysis treatment. The same phenomenon is noted if the length of sessions is reduced with cuprophane in an open circuit, even if the surface area is increased in order to maintain the same m² per hour (7.5% per week). Hyperphosphoremia appears therefore to be the result of a reduction in the length of the sessions of dialysis treatment. The authors believe that the purification of phosphorus by the artificial kidney depends neither on the type of dialyzer used nor on the membrane, but exclusively on the duration of dialysis treatment; the number of m² per hour per week plays no part in it.

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Parameter of uremic osteodystrophy are heterogeneously distributed. The Ca dialysate concentration was 3.75 mEq/liter. As compared to normal subjects, this population was characterized by lower Ca and higher P, A.P., PTH and CT levels. However, frequency distribution of these parameters showed a marked heterogeneity except for A.P. values, which were clearly distributed in two populations: normal levels (group 1) and high levels (group 2). While Ca and P concentrations were not significantly different in both groups, CT values (mean ± SEM in ng/ml) were higher in group 1 (2.6 ± 0.35) than in group 2 (2.6 ± 0.35; P < 0.01), whereas PTH levels (ng/ml) were higher in group 2 (3.53 ± 2.23) than in group 1 (1.91 ± 0.2; P < 0.001). In group 1, CT levels were correlated to PTH, to Ca and to P, and PTH was correlated to P. These correlations were no more apparent in group 2. These results show: 1) Parameters of uremic osteodystrophy are heterogeneously distributed in hemodialyzed subjects. 2) There are at least two populations, one with normal A.P. and one with high A.P. 3) When A.P. is normal, Ca-P regulation is achieved in the presence of higher CT levels and lower PTH levels than when A.P. is high. 4) The relationship between PTH, Ca or P levels and CT levels is observed only when A.P. is normal. This heterogeneity should be taken into account when investigating treatment of "uremic bone disease."

Quantitative study of bone biopsy in 81 uremic patients. S. Latorr-zeff, D. Durand, D. Durroux, H. Ton That, J. Arlet, J. M. Sue. Service de Nephrologie, Pavillon Rayer, Hopital Purpan, Toulouse, France. A quantitative histological study of iliac bone biopsy is performed in 81 patients with chronic renal failure. Material and methods. These patients are separated into two groups according to the serum creatinine levels. Group 1: 14 patients with a mild renal failure (serum creatinine between 1.8 and 3.5 mg/100 ml). Group 2: 67 patients with a more advanced renal failure (serum creatinine between 6 and 14 mg/100 ml); 12 of them are maintained on hemodialysis. Quantitative study is realized with P. Meunier's technique. In 21 patients previous labeling by demethylchlortetacycline is used. Four uncalcified and six non-uncalciﬁed bone sections are performed on each biopsy. The six following parameters are studied: bone trabecular volume, resorptive surface, periosteocytic lacunae, relative osteoid volume, osteoid surface and index of osteoid thickness. The latter parameter associated to calcification front study allows to distinguish hyperparathyroidism osteoid tissue from osteomalacic osteoid tissue. Results. Group 1: 11 patients from the first group (mild renal failure) already show signs of slight and alone hyperparathyroidism. Group 2: In the more advanced renal insufficiency patient group, the two abnormalities are found, together or separate. Five patients show obvious and isolated osteomalacia signs. Sixty-two patients show hyperparathyroidism pattern: in 48 of them hyperparathyroidism is alone and of various degrees (11 most typical hyperparathyroidism, 27 obvious hyperparathyroidism and 10 mild hyperparathyroidism); in 14 others, bone volume increase suggests the addition of osteomalacia to hyperparathyroidism. The study of these 81 patients leads to the following conclusion: Hyperparathyroidism stigmata occur commonly (90% of patients) and early, whereas osteomalacia is seldom seen and associated with the latter in 19% of patients. Osteomalacia is only found in end-stage renal failure. Osteomalacia lesions are superimposed secondarily in natural evolution of renal osteodystrophy.

Treatment of severe renal osteodystrophy by 25-hydroxycholecalciferol. A. Meyrier, Ph. Border, C. Pages and R. Ardailou. Hopital Tenon, Paris, France. Four Nondialyzed patients with chronic renal failure (GRF between 4 and 9 ml/min) and clinical and radiological evidence of osteodystrophy were studied. Before treatment the average serum concentrations for calcium, phosphate and magnesium were 7.6 mg, 4.5 mg and 2.05 mg/l00 ml respectively; alkaline phosphatase was 205 IU, parathormone (PTH) 10.3 ng/ml and calcitonin (CT) zero. Calcium and phosphate excretion rates were 49 mg and 415 mg/24 hr. Bone biopsy showed osteomalacia in all four cases with associated osteoclastic resorption (moderate in two cases and severe in two). After a control period of one month on a 500 mg/day calcium diet, 50 µg of 25-hydroxycholecalciferol (25-OH D3) was given daily for one month, then increased to 100 µg/day till the end of the study. Aluminum gels were prescribed whenever the serum phosphate concentration exceeded 6.0 mg/100 ml. The following results were obtained: a moderate rise in serum Ca concentrations (maximum: 8.3 mg/100 ml) was noted only from week 27 onwards. Serum phosphate concentrations rose above 6.0 mg/100 ml at week 25 and were difficult to control with aluminum gels. The calcium and phosphate excretion rates showed parallel changes. Plasma PTH levels showed three phases: an initial increase until week 12, a fall between weeks 12 and 17, and then a second larger rise. Serum magnesium showed similar changes. CT was unmeasurable until week 12 and then rose rapidly. The alkaline phosphatase levels fell progressively from week 15 onwards, becoming normal at week 30. The second bone biopsy, performed at the end of the study, showed osteoid remineralization, reappearance of the calcification front and diminution of osteoclastic resorption and of fibrosis. We conclude that: 1) 25-OH D3 modified favorably the renal osteodystrophy of the patients studied; 2) serum calcium changes were, however, not pronounced during the treatment period; 3) 25-OH D3 appears to play an important role in phosphate intestinal absorption and/or mobilization from bone; 4) variations in PTH concentrations seem to be linked to concomitant changes in serum phosphate and/or magnesium concentrations; 5) the reappearance of CT secretion, not correlated to the serum calcium concentration, could be an important factor in the diminution of osteoclastic activity.

Comparative study of the different calcium intestinal absorption tests: Determination by using a double radiotracer technique with simultaneous measurement of the urinary excretion rate of calcium. J. Mirouze and L. Monnier. Department of Endocrinology and
Metabolism, Hospital Saint-Eloi, Montpellier, France. Fifty-three determinations of the intestinal absorption rate of radioisotope calcium were performed by giving simultaneously two radioisotopes, one via an oral route (44CaCl2) and the second i.v. (45CaCl2). A mathematical procedure of inverse convolution was applied to the time courses of the oral and i.v. plasma activities. By this calculation, the transit time curve of radioisotope across the intestinal barrier was determined and provided an accurate measurement of the total fractional absorption rate of calcium (TFACa) and of many other parameters. A good correlation was found between the TFACa measured by the inverse convolution method and a simple estimation by the oral/i.v. plasma activity quotients. On the contrary a poor correlation was observed when the 44Ca plasma concentration at the third hour was plotted vs the TFACa determined by the inverse convolution analysis. The TFACa can be measured by using single radiotracer methods. However, they provide less accuracy and information about absorption than the double radiotracer technique. By applying this latter method to a group of seven diabetic patients, we observed that calcium transfers across the intestinal and renal tubular cells were stimulated by an oral glucose load. In three primary hyperparathyroidisms, we noted that intestinal absorption remained elevated a few months after the patients had been surgically cured.

Interactions between propranolol and the renin-angiotensin system. L. Peters-Haefeli and E. J. Kircherz (Introduced by G. Peters). Institut de pharmacologie de l'Université de Lausanne, Lausanne, Switzerland. In pentobarbitol-anesthetized rats, D,L-propranolol (PR) (0.04 to 5 mg/kg i.v.) depressed the basal plasma renalin level (PRL) by 35 to 60%, but did not interfere with the rise of PRL induced by bleeding. In urethane-anesthetized rats, i.v. D,L-PR (0.25 to 0.50 mg/kg) induced 1) an initial rise of blood pressure (BP) by +14 ± 2 mm Hg lasting 1 to 2 min, 2) a sustained rise of BP (+7 ± 1 mm Hg) lasting for more than 30 min, and 3) an increase of the pressor potency of vas-angiotensin II amide (AT II) by a factor of 2 to 4. These effects were abolished in D,L-PR-treated rats. D-PR caused an initial rise of BP (I), but neither effects (2) nor (3). It was concluded that the initial rise of BP (I) is presumably due to a PR-induced release of catecholamines for the adrenal medulla, while the increased potency of AT II (3) is due to a blockade of vasodilatator beta receptors. Since D,L-PR does not depress rises of PRL after hemorrhage, and since its depressor effect on basal PRL would be compensated by an increased response to AT II, its antihypertensive action appears to be independent of the renin-angiotensin system.

Thyroid lymphography: A new method for preoperative localization of the parathyroid glands and for the study of secondary hyperparathyroidism in uramic patients. R. Rossi, A. Farina, G. C. Cairoli, G. Casaratti, M. I. Quarenghi, M. Dassi, F. Muggli and G. Colantonio. Department of Surgery A and Department of Ne- phrology. S. Anna Hospital, Como, Italy. Thyroid lymphography, suggested by Tomoji Kato et al (Annals of Surgery, vol. 107, no. 8, March 1974) as a useful method for preoperative localization of primitive parathyroid adenomas, was performed by the authors on patients undergoing regular hemodialytic treatment for preoperative localization and size evaluation of hyperplastic parathyroid glands. Methods: Bilateral injection of contrast liquid (1 to 1.5 ml of Lipiodol Ultrafluid) in thyroid parenchyma. Roent- genograms were taken as follows: antero-post and laterolateral projection 15 min, 30 min, 60 min, 80 min and 24 hr after injection of Lipiodol. Results: Thyroid lymphography was performed on ten patients showing altered Ca/P metabolism and high concentrations of serum alkaline phosphatase. Some patients showed metastatic calcifications at X-ray investigation. PTH serum concentrations were determined in all patients. All patients had hyperplastic parathyroids of various sizes and two of them underwent surgery. Operative findings confirmed the radiological localization performed with our method. Conclusions: We have shown that thyroid lymphography is one of the most useful methods for the localization of hyperplastic parathyroids prior to surgery as well as for the evaluation of secondary hyperparathyroidism in uramic patients.

Plasma ionized calcium: From sampling to ion measurement. C. E. Sachs and A. M. Bourdeau. Laboratoire d'Exploration Fonctionnelle chez l'Enfant, Hôpital des Enfants Malades, Paris, France. Ionized calcium evaluation gained recently in both fields of blood sampling and ion measurement. The main purpose of the described sampler is to ensure a strictly anaerobic blood handling throughout the process. Blood is sampled with a double-edged needle into a thermoplastic supple tube placed under vacuum in a rigid carrying container. After centrifugation the supple tube is squeezed and heat-sealed just above the red blood cells–plasma interface with heat-sealing cutters. The upper compartment, thus separated, contains the supernatant of the plasma, which can be directly fed into the apparatus with the above-mentioned needle, just by squeezing the supple tube. It can also be stored at 4°C or deep-frozen. The last liquid membrane electrode system developed (SS-20 ORION model) operates with a 300-μl sample. It combines several advantages: it works by a discontinuous fully automated procedure, displays the final result in mEq/liter, and requires simplified maintenance. Nevertheless right now, the ready-to-use electrodes, expected to last two to three months, have too short a life span (five days). This represents a last handicap that has to be overcome. Plasma ionized calcium (anticoagulant: 100/μl sodium heparinate) measured under these conditions in 60 blood donors was found to be of 1.95 ± 0.07 mEq/liter.

Cytosol binding of 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol in the rat duodenal mucosa. A. Ulmann, M. Brani, J. D. Moner, C. Bader and J. L. Funck-Brentano. I.N.S.E.R.M. U.90, Hôpital Necker, Paris, France. In order to study the mechanism of action of vitamin D metabolites on the intestinal absorption of calcium, the cytosol binding of labeled 25-hydroxycholecalciferol (25-OH D3) or 1,25-dihydroxycholecalciferol (1,25-(OH)2D3) was studied in the duodenal mucosa of vitamin D-deficient and vitamin D- sufficient rat. Sucrose gradient analysis show that 25-OH D3 and 1,25-(OH)2D3 bind to a 5.5-6 S protein; nevertheless, whereas a 100-fold excess of unlaabeld 25-OH D3 completely abolishes the binding of 1,25-(OH)2D3, a similar excess of unlaabeld 1,25-(OH)2D3 does not prevent tritiated 25-OH D3 from its binding site. The quantification of this binding was performed with a dextran-coated charcoal assay: tritiated 25-OH D3 binds with an apparent dissociation constant at 4°C of 1.2 × 10-10 M, and a binding capacity of 6.5 × 10-18 m/g of protein; tritiated 1,25-(OH)2D3 binds with a Kd = 2 × 10-8 m (4°) and a binding capacity of 2.3 × 10-18 m/g of protein. Competition experiments with unlabeled sterols show that neither progesterone nor dexamethasone nor vitamin D3 can displace tritiated 25-OH D3 or 1,25-(OH)2D3 from their binding sites; they show that when aliquots of cytosol are incubated with 10-6 M tritiated 25-OH D3, a 100-fold excess of unlaabeld 25-OH D3 displaces the binding by 80%, whereas a similar excess of unlabeled 1,25-(OH)2D3 displaces this binding by only 40%. Conversely, when aliquots of cytosol are incubated with 10-6 M tritiated 1,25-(OH)2D3 a 100-fold excess of unlabeled 1,25-(OH)2D3 displaces the binding by 66%, whereas the same amount of 25-OH D3 decreases the binding by 74%. Thus, both 25-OH D3 and 1,25-(OH)2D3 bind to the duodenal cystosol of vitamin D-deficient rats. The binding capacity for 1,25-(OH)2D3 is lower than that for 25-OH D3. Competition studies and Kd measurements suggest that among the 25-OH D3 binding sites, some are specific for this sterol, and a small number can bind 1,25-(OH)2D3 with a lower affinity. Kinetic studies of these sites are in progress; they will perhaps provide some information about their functional significance.

Treatment of renal osteodystrophy with high doses of vitamin D3. R. Verberckmoes, R. Boudillon and B. K. Krempien. A. Z. St. Rafail, University of Brussels, Belgium. Thirteen dialyzed patients with renal osteo- dystrophy were treated with high doses of vit D3. All patients had one or more of the following radiological signs: subperiostal and endostal resorption in several phalanges, ground-glass appearance of the skull, resorption of the lateral ends of the clavic- ulae and/or of the symphysis pubis. Luenser-Mikman pseudofractures. Histological examination showed one or more of the following signs: increased osteoclast activity, broadened osteoid

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seams, periosteocytic osteolysis, endosteal and narrow fibrosis. Serum PTH and serum alkaline phosphatase levels were elevated. Vit D₃ was given orally in doses of 15 mg once to thrice weekly. Al(OH)₃ treatment was adjusted to the predialysis P concentration. The vit D₃ treatment was continued until the serum alkaline level was normal. At this time usually some degree of hypercalcemia was seen. The total doses of vit D (120 to 2000 mg) and the duration of the treatment (60 to 450 days) were inversely correlated with the dialysate calcium concentration (5.6 or 7.5 mg/100 ml). At the end of the treatment in all patients a marked improvement or total disappearance of the radiological abnormalities was observed, which was confirmed by the histological controls. Serum PTH levels measured with a N-specific antiserum were normal or nearly normal; whereas the decrease of PTH levels obtained with a C-specific antiserum was less pronounced, these values remaining highly elevated, even in a patient who was successfully transplanted after treatment with vit D₃. We therefore postulate that the hypertrophic parathyroid glands continue to secrete inactive PTH fragments (measured with the C-specific antiserum) even when the secretion of active PTH (measured with the N-specific antiserum) was inhibited. During treatment 25 OH-CC levels reached values between 200 and 500 ng/ml. The t/2 after the end of the treatment determined in three patients was 40, 63 and 110 days. Adverse reactions during and after treatment were minimal. Permanent hypercalcemia necessitated PTX in one patient. Preexisting vascular calcifications regressed markedly during treatment in two patients. Long-term results indicate that permanent suppression of the parathyroid glands was not obtained: serum PTH (measured with the N-specific antiserum) returned to high levels some months after the end of vit D₃ treatment. Massive hypertrophy of the parathyroid glands was found on PTX in three patients after vit D₃ treatment.

Body calcium measurement by a local neutron activation method using Californium 252 in renal bone disease. P. Zech, A. Guey, Ph. Leitienne, M. F. Meary, N. Pozet, J. F. Moskovtchenko and J. Traeger. Clinique de Néphrologie et des Maladies Métaboliques, Hospital Edouard Herriot, Lyon, France. Uremic bone disease is a common cause of morbidity in chronic renal failure. However, it is not always able to halt the development of osteitic lesions, which sometimes require parathyroidectomy.

Phosphate, alkaline phosphatase and immunoreactive PTH (iPTH), and on repeated quantitative bone histology. The 1-hydroxy analogues (1α (OH) D₃, three cases, and 1-25 (OH)₂D₃, 3 cases, at a dose of 5 µg thrice weekly) have a frank effect on serum calcium that increases and on serum iPTH that decreases. The increased bone cell activity is expressed mainly by an increase in the resorption surface and an increased number of osteoclasts; marrow fibrosis regresses. The calcification front increases; osteoid volume decreases or remains unchanged. The 25-hydroxy-analogue, low dose (5-6 trans 25 (OH) D₃, 8 cases, 20 µg thrice weekly), does not change serum calcium or serum iPTH; bone histology is not modified uniformly except that the calcification front increases in six out of the eight patients. Administered at high doses, the 25 (OH) D₃ (three cases, 200 µg thrice weekly) increases serum calcium in only one of the three patients, with serum iPTH lowered in this one. This calcification front increases in the three patients; the osteoid volume decreases. The active resorption and the number of osteoclasts diminish only slightly. Marrow fibrosis decreases in all the three cases. The interpretation of the results obtained with these different vitamin D₃ analogues will be discussed.

Evolutionary aspects of renal osteodystrophy in patients on periodic hemodialysis. P. Zucchelli, M. Fusaroli, L. Fabbrì, P. Pavlica, G. Viglietta, L. Catizone and S. Casanova. Hospital M. Malpighi, Bologna, Italy. The development of osteodystrophic lesions and the influence of therapy with calcium, aluminum hydroxide and DHT was studied in 25 patients on periodic treatment for more than three years. All patients underwent repeated investigations, including percutaneous biopsy of the iliac crest with undecalcified samples evaluated according to Bordier, X-ray examination of the skeleton, radiography of the hands with industrial films, bone densitometry, scanning of the skeleton with 99 mTc-pyrophosphate and PTH dosage. Thus: 1) radiological examination reveals a turn for the worse of the lesions in 24% of the patients and a delayed appearance of changes of sacro-iliac junctions, of temporo-mandibular joint and of phenomena of periosteal neostisis; 2) therapy exerts a beneficial influence over osteomalacic lesions, while it is not always able to halt the development of ostetric lesions, which sometimes require parathyroidectomy.