Pediatr Nephrol (2000) 14:342–346

INVITED REVIEW

Paulo C. Koch Nogueira · Louis David · Pierre Cochat

Evolution of secondary hyperparathyroidism after renal transplantation

Received: 16 April 1999 / Revised: 27 September 1999 / Accepted: 5 October 1999

Abstract Renal osteodystrophy is an important problem in children with chronic renal failure, leading to skeletal deformities. The most-frequent type of renal osteodystrophy is secondary hyperparathyroidism, and the main factors contributing to the pathogenesis of this condition are completely or partially corrected after successful renal transplantation. The present paper reviews data on the evolution of secondary hyperparathyroidism after transplantation. Studies in both adults and children suggest that secondary hyperparathyroidism and increased bone remodelling activity may persist months after transplantation. The severity of secondary hyperparathyroidism prior to transplantation, the duration of dialysis, and the development of nodular and/or monoclonal hyperplasia of parathyroid glands are the most-important factors that determine the phenomenon. Important issues, which still need to be answered, are the possible roles of growth factors, cytokines, VDR gene polymorphism (*B/b* allele), and type of immunosuppressive regimen in the skeletal abnormalities observed.

Key words Renal osteodystrophy · Secondary hyperparathyroidism · Kidney transplant

Introduction

Renal osteodystrophy is an important problem in children and adolescents with chronic renal failure (CRF), leading to skeletal deformities and growth retardation, which are major determinants of CRF morbidity. It includes a broad spectrum of bone remodelling disorders, ranging from high-turnover lesions (osteitis fibrosa, mild lesions, and mixed lesions) to low-turnover lesions (adynamic bone disease and osteomalacia) [1].

The most-frequent type of renal osteodystrophy, secondary hyperparathyroidism (2HPT), results from an increase in the synthesis and secretion of parathyroid hormone (PTH), which usually gives rise to high-turnover lesions. Induction of 2HPT is the consequence of both hypertrophy and hyperplasia of parathyroid glands. The main factors in the pathogenesis of 2HPT are hypocalcemia, a reduced concentration of serum calcitriol, and an increased concentration of serum phosphate. The first two factors are both present as soon as the glomerular filtration rate (GFR) falls below 80–60 ml/min per 1.73 m^2, while phosphate retention appears only when the GFR is less than about 30 ml/min per 1.73 m^2. After successful renal transplantation (RT), these abnormalities are completely or partially corrected; nevertheless 2HPT may persist. In addition to persistence of 2HPT after RT, other bone disorders induced by graft tubular dysfunction and/or immunosuppression-related bone disease may supervene [2]. As a consequence the occurrence of bone disorders, such as osteopenia, fractures, calciphylaxis, and avascular necrosis of bone, are major problems in pediatric RT recipients [3–5]. The aim of the present paper is to review data on the evolution of 2HPT after RT.

P.C. Koch Nogueira · L. David · P. Cochat
Department of Pediatrics,
Hôpital Edouard Herriot and Université Claude Bernard,
Lyon, France

P.C. Koch Nogueira
Department of Pediatrics,
Faculdade de Ciências Médicas de Santos, Brazil

P. Cochat (✉)
Unité de Néphrologie Pédiatrique, Hôpital Edouard Herriot,
F-69437 Lyon Cedex 03, France
e-mail: cochat@univ-lyon1.fr
Tel.: +33-4-72110346, Fax: +33-4-72110343

Evolution of 2HPT after RT

Studies in adults

Since the 1970s it has been known that 2HPT may persist months or years after successful RT [6–9]. Since then various reports with comparable results in adult patients have been published. In order to summarize representative results, we pooled the data from two studies in

Table 1 Demographic data and comparison of parameters of secondary hyperparathyroidism (*2HPT*) in adult renal transplant (*RT*) recipients and controls (*WMD* weighted mean difference, *CI* confidence interval, *PTH* parathyroid hormone)

Parameter	Study	RT recipients	Controls	WMD (95% CI)	*P*
n	[a]	30	30	–	–
	[b]	82	82	–	–
	Total	112	112	–	–
Gender	[a]	17 females	17 females	–	–
	[b]	35 females	35 females	–	–
Age (years)	[a]	50±14	49±12	–	–
	[b]	44±1	44±2	–	–
Time after RT (months)	[a]	2–61	–	–	–
	[b]	6–73	–	–	–
PTH (pg/ml)	[a]	98±175	27±11	71.000 (8.253, 133.747)	
	[b]	69±5	30±1	39.000 (37.896, 40.104)	<0.05
	Total			39.010 (37.906, 40.113)	(RT>controls)
Calcium (mg/dl)	[a]	9.60±0.40	9.60±0.40	0.000 (-0.202,0.202)	
	[b]	9.39±0.05	9.32±0.03	0.070 (0.057, 0.083)	<0.05
	Total			0.070 (0.057, 0.083)	(RT>controls)
Phosphate (mg/dl)	[a]	3.10±0.60	3.40±0.60	–0.300 (–0.604,0.004)	
	[b]	2.94±0.06	3.31±0.05	–0.370 (-0.387,-0.353)	<0.05
	Total			–0.370 (–0.387,-0.353)	(RT<controls)
Osteocalcin (ng/ml)	[a]	15.8±7.8	7.3±1.9	8.500 (5.627, 11.373)	
	[b]	16.6±0.8	8.0±0.3	8.600 (8.415, 8.785)	<0.05
	Total			8.600 (8.415, 8.784)	(RT>controls)
Creatinine (mg/dl)	[a]	1.30±0.30	1.00±0.20	0.300 (0.171, 0.429)	
	[b]	1.25±0.20	0.90±0.01	0.320 (0.277, 0.363)	<0.05
	Total			0.318 (0.277, 0.359)	(RT>controls)

[a] Pietschmann et al. [10]
[b] Dumoulin et al. [11]

Table 2 Comparison of parameters of 2HPT in adult RT recipients and controls, considering only subgroups of individuals matched for normal renal function (*NS* not significant)

Parameter	Study	RT recipients	Controls	WMD (95% CI)	*P*
n	[a]	8	23	–	–
	[b]	25	25	–	–
	Total	33	48	–	–
PTH (pg/ml)	[a]	56±39	28±8	28.000 (0.777, 55.223)	
	[b]	52±5	28±3	24.000 (21.714, 26.286)	<0.05
	Total			24.028 (21.750, 26.306)	(RT>controls)
Calcium (mg/dl)	[a]	9.60±0.40	9.60±0.40	0.000 (–0.322, 0.322)	
	[b]	9.37±0.09	9.36±0.04	0.010 (–0.029, 0.049)	NS
	Total			0.004 (–0.028, 0.048)	(RT=controls)
Phosphate (mg/dl)	[a]	3.40±0.90	3.40±0.60	0.000 (–0.670, 0.670)	
	[b]	2.87±0.12	3.24±0.09	–0.370 (–0.429, –0.311)	<0.05
	Total			–0.342 (-0.534,-0.149)	(RT<controls)
Osteocalcin (ng/ml)	[a]	12.3±3.6	7.3±1.9	5.000 (2.387,7.613)	
	[b]	14.9±1.8	8.1±0.5	6.800 (6.068,7.532)	<0.05
	Total			6.355 (4.833,7.877)	(RT>controls)

[a] Pietschmann et al. [10]
[b] Dumoulin et al. [11]

which RT recipients were compared with controls [10, 11]. Although we did not perform a systematic review, some techniques common to meta-analyses were adopted for pooling the data. For comparison of the results the weighted mean difference and 95% confidence interval were used; all calculations were performed using a random effects model, since we did not evaluate heterogeneity in the analysis of outcomes among the studies [12]. Results of this analysis are shown in Tables 1 and 2.

From these data it is apparent that RT recipients exhibited significantly higher levels of serum PTH, calcium (Ca), and osteocalcin than controls, along with reduced levels of serum phosphate, which is consistent with the persistence of 2HPT and increased bone remodelling activity months after RT. These abnormalities might be explained by the reduced renal function of the recipients (Table 1). However, both studies [10, 11] compared subgroups of patients in which recipients and controls were matched for normal renal function, but increased serum concentrations of PTH and osteocalcin, and reduced levels of phosphate, were still present in the recipient subgroup (Table 2).

This suggests that a factor(s) other than reduced renal function may participate in the 2HPT persistence of RT recipients. These might include (1) a less suppressible PTH secretion, which could be related to the duration of dialysis treatment and to the size of the parathyroid glands before transplantation [13, 14], (2) a slow involution of hyperplastic glands due to an alteration in the clearance of excess cells by reduced apoptosis [15], and (3) the type of tissue growth, since nodular rather than diffuse hyperplasia is associated with less uniform distri-

Table 3 Vitamin D receptor genotype (intron 8 *Bb* allele) and serum PTH levels at the time and 1 year after RT

	Genotype (*n*)			*P*
	BB (13)	*Bb* (40)	*bb* (28)	
PTH at time of RT (pg/ml)	70.7±46.8	412.0±617.0	388.0±107.7	<0.01 *BB* vs. *Bb+bb*
PTH 1 year after RT (pg/ml)	53.7±20.3	127.6±93.7	114.1±87.9	<0.05 *BB* vs. *Bb+bb*

Modified from Messa et al. (1998) Kidney Int 54:1704–1713

bution of calcitriol receptors, resulting in a lower inhibitory feedback of vitamin D [16, 17]. Studies in uremic patients have also shown a high prevalence of monoclonal growth of parathyroid glands, regardless of the presence of nodular or diffuse hyperplasia [18, 19]. Should the progression to monoclonal growth of parathyroid tissue occur, it is logical to postulate that the involution of the glands would not occur even after removal of the factors that induced 2HPT.

Messa et al. [20] recently suggested another potential cause of persistent 2HPT after RT. They studied the role of the vitamin D receptor (VDR) gene polymorphism in intron 8 (*B/b* allele) in the evolution of 2HPT after RT in 81 consecutive adult RT recipients, and observed that individuals with the *BB* polymorphism had lower serum PTH levels both at the time of RT and 1 year later (Table 3). In addition, among 8 RT recipients who needed a parathyroidectomy after RT, none expressed the genotype *BB* (6 were *Bb* and 4 *bb*), and all exhibited nodular hyperplasia in the removed glands. These findings are consistent with the hypothesis that the *b* allele is associated with lower transcriptional activity and/or mRNA stability, thus producing a lower degree of VDR expression that would decrease the inhibitory effect of calcitriol on parathyroid tissue [20]. However, when RT recipients were divided into two groups according to the PTH serum concentration 3 months after RT (group A PTH <80 pg/ml and group B PTH >80 pg/ml), group A patients, who had a greater prevalence of the *BB* genotype (group A=10/40, group B=3/41), were younger (group A=39.9±11.5 years, group B=48.7±11.7 years) and had a significantly shorter duration of dialysis before RT (group A=23.8±14.4 months, group B=44.6±37.2 months) [20]. It is therefore possible that the less-severe form of 2HPT in group A patients than group B patients was simply due to a shorter duration of end-stage renal disease. More studies are necessary to better define the possible role of the *B/b* allele.

Another point that must be considered is that bone remodelling is not exclusively controlled by PTH; calcitriol, growth factors, and cytokines are also involved. Factors such as tumor necrosis factor α (TNFα) and interleukin-1 (IL-1) induce the osteoblasts on bone surfaces to produce IL-6, IL-11, granulocyte-macrophage colony-stimulating factor, macrophage colony-stimulating factor, and stem cell factor. These molecules stimulate the differentiation of preosteoclasts to osteoclasts, leading to the development of the ruffled borders, which are specialized bone resorption areas of osteoclast plasma membranes. On the other hand, the products of bone resorption together with Ca and transforming growth factor β limit osteoclast function and serve as growth factors for osteoblasts, resulting in the deposition of new bone in the resorption lacunae. Insulin-like growth factor-1 production is increased by PTH and may also promote osteoblast proliferation. In CRF the expression of TNF-α, IL-1, IL-6, and IL-11 and their receptors are increased, which might contribute to the augmented bone remodelling cycle [21, 22], but their role in the pathophysiology of renal osteodystrophy after RT has not been evaluated.

Studies in children

Studies in children are far more scarce than in adults. Koch Nogueira et al. [23] compared two groups of children who received a first RT, according to the duration of end-stage renal disease [group I, pre-emptive RT (*n*=17) and group II, RT after 6.1±7.3 months on dialysis (*n*=24)]. The groups were matched for age, gender, causes of renal insufficiency, duration of ischemia time, type of donor, and immunosuppressive treatment. There were no significant differences in the serum levels of Ca, phosphate, 25-hydroxyvitamin D, and magnesium between the two groups; however serum PTH levels were significantly higher in the dialyzed group, both before (group I=95±150 pg/ml, group II=253±346 pg/ml, *P*=0.03) and 90 days after RT (group I=40±20 pg/ml, group II=69±42 pg/ml, *P*=0.01), despite the fact that graft function was identical at the end of the follow-up period. On day 90, 13 of 24 (54%) children from group II had serum PTH concentrations above the normal range compared with only 3 of 17 (18%) children from group I, thus suggesting that the severity of 2HPT is related to the duration of end-stage renal disease prior to RT. Moreover, although some involution of the parathyroid glands may be anticipated in children after RT, recipients who have developed a more-severe form of 2HPT may exhibit a lower regression rate. The slow cell involution once 2HPT has occurred is in agreement with the work of Parfitt [24], who observed that cells of human parathyroid glands have a low turnover, the normal rate of parathyroid cell renovation being around 5% per year, which corresponds to a cell life span of 20 years.

In a more-recent study, Sanchez et al. [5] performed iliac crest bone biopsy to evaluate the extent and severity of renal osteodystrophy in 47 patients 3.2±1.7 years after RT; 11 of 47 (23%) had mild hyperparathyroidism, 31 of

Table 4 Evolution of type of bone disease before and after RT in children (*n*=24)

Pre RT biopsy	Post RT biopsy
2HPT (*n*=14)	Normal bone formation rate (*n*=8) 2HPT improved (*n*=5) Adynamic lesion (*n*=1)
Normal bone formation rate (*n*=7)	Normal bone formation rate (*n*=7)
Adynamic lesion without aluminum (*n*=3)	Normal bone formation rate (*n*=1) Adynamic lesion (*n*=1) 2HPT (*n*=1)

Modified from Sanchez et al. (1998) Kidney Int 53:1358–1364

47 (66%) had normal bone formation, and 5 of 47 (11%) had adynamic lesions; the three groups were matched for graft function. In 11 of the 47 patients, serum PTH levels were higher than the reference value for normal individuals (i.e., ≤65 pg/ml) and 4 of 47 had values greater than 100 pg/ml; 3 of these had a normal rate of bone formation and 1 had a mild osteitis fibrosa [5]. It is noteworthy that the serum PTH level could not distinguish the three groups of patients and that there was no significant correlation between the rate of bone formation and PTH level [5]. This study demonstrates that even after a long post-RT follow-up there may be a considerable number of patients who still exhibit mild 2HPT, although some improvement is to be expected in the majority of children. Furthermore, an isolated serum PTH determination alone does not appear to be a sufficiently specific marker of the type of renal osteodystrophy. In the same study [5] 24 of 47 patients had a previous bone biopsy performed 4.7±3.2 years previously; the evolution of renal osteodystrophy prior to and after RT is shown in Table 4.

The severity of post-transplant 2HPT may range from an asymptomatic state of "inappropriate PTH secretion," such as the cases described above [5, 23], to a more-critical situation of refractoriness of parathyroid glands to any form of medical treatment, know as tertiary hyperparathyroidism (3HPT). In a recent report, Nieto et al. [25] described three children in whom 3HPT was noted 1 month to 3 years after RT; in all children hemodialysis was of long duration (7–11 years) and two had undergone more than one transplant (one had 2 RT and the other had 3 RT). These three patients underwent subtotal parathyroidectomy and pathological examination revealed adenoma transformations in the affected glands. The authors suggested that this might be the result of monoclonal parathyroid growth by inhibition of the tumoral suppression factor of chromosome 11 [25].

Effects of immunosuppressive drugs on post-transplant 2HPT

Among the commonly used drugs for immunosuppression after RT, cyclosporine A (CyA) is known to induce a state of high-turnover osteopenia in rats [26], and there are in vitro data suggesting that CyA inhibits bone resorption of cultured mouse calvaria [26]. Although one study in humans has shown a rise in serum alkaline phosphatase activity in CyA-treated patients, suggesting a high-turnover osteopathy [27], two more-recent reports failed to confirm any deleterious effect of CyA on bone and Ca metabolism after RT [28, 29]. The direct effect of CyA on parathyroid gland function, if any, has not been assessed to date, to the best of our knowledge.

To review the extensive data on the role of glucocorticoids on bone metabolism is not within the scope of this paper. It is well known that patients treated with these drugs develop osteopenia, mainly secondary to impaired intestinal absorption of Ca, inhibition of osteoblast function, and increased urinary Ca excretion [28]. All these actions promote a state of negative Ca balance that might contribute to indirect stimulation of parathyroid function after RT. Furthermore, in vitro data suggest that glucocorticoids may have a direct dose-dependent stimulatory effect on PTH secretion in both bovine [30] and human [31] cultured parathyroid cells.

Conclusions

From the data reviewed here it is apparent that persistence of 2HPT after RT is a significant problem that may occur in up to 50% of recipients. A possible increase in the risk of acute tubular necrosis following RT, hypercalcemia, hypophosphatemia, and the extension of renal osteodystrophy after RT are expected clinical consequences [28, 32].

The severity of 2HPT prior to RT, the duration of dialysis treatment, and the development of nodular and/or monoclonal hyperplasia of parathyroid glands are the most-important factors that determine the degree of 2HPT after RT. Important issues which still need to be answered are the possible roles of growth factors, cytokines, VDR gene polymorphism (*B/b* allele), and type of immunosuppressive regimen in the genesis of skeletal abnormalities observed after RT.

These conclusions may have implications for clinical practice, since the data suggest that assessment of bone metabolism parameters should be performed systematically after a successful RT. We do not know at present what is the optimal PTH serum level after RT; it is likely that normal values obtained from healthy individuals are not adequate in this situation. Furthermore, based on the existing evidence it is reasonable to speculate that patients could benefit from continued efforts to control 2HPT after RT.

References

1. Hory B, Druëke TB (1997) The parathyroid-bone axis in uremia: new insights into old questions. Curr Opin Nephrol Hypertens 6:40–48
2. Massari PA (1997) Disorders of bone and mineral metabolism after renal transplantation. Kidney Int 52:1412–1421

3. Feber J, Cochat P, Braillon P, Castelo F, Martin X, Glastre C, Chapuis F, David L, Meunier PJ (1994) Bone mineral density after renal transplantation. J Pediatr 125:870–875
4. Apel DM, Millar EA, Moel DI (1989) Skeletal disorders in a pediatric renal transplant population. J Pediatr Orthop 9:505–511
5. Sanchez CP, Salusky IB, Kuizon BD, Ramirez JA, Gales B, Ettenger RB, Goodman WG (1998) Bone disease in children and adolescents undergoing successful renal transplantation Kidney Int 53:1358–1364
6. Geis WP, Popovtzer MM, Corman JL, Halgrimson CG, Groth CG, Starzl TE (1973) The diagnosis and treatment of hyperparathyroidism after renal homotransplantation. Surg Gynecol Obstet 137:997–1010
7. Kleerekoper M, Ibels LS, Ingham JP, McCarthy SW, Mahony JF, Steward JH, Posen S (1975) Hyperparathyroidism after renal transplantation. BMJ 3:680–682
8. Bernheim J, Tourraine JL, David L, Faivre JM, Traeger J (1976) Evolution of secondary hyperparathyroidism after renal transplantation. Nephron 16:381–387
9. Pletka PG, Strom TB, Hampers CL, Griffiths H, Wilson RE, Bernstein DS, Sherwood LM, Merrill JP (1976) Secondary hyperparathyroidism in human kidney transplant recipients. Nephron 17:371–381
10. Pietschmann P, Vychytil A, Woloszczuk W, Kovarik J (1991) Bone metabolism with functioning kidney grafts: increased serum levels of osteocalcin and parathyroid hormone despite normalisation of kidney function. Nephron 59:533–536
11. Dumoulin G, Hory B, Nguyen NU, Bresson C, Fournier V, Bouhaddi M, Chalopin JM, Saint-Hillier Y, Regnard J (1997) No trend toward a spontaneous improvement of hyperparathyroidism and high bone turnover in normocalcemic long-term renal transplant patients. Am J Kidney Dis 29:746–753
12. Mulrow CD, Oxman AD (eds) Cochrane Collaboration Handbook (updated 9 December 1996). Available in The Cochrane Library (database on disk and CDROM). The Cochrane Collaboration; issue 1. Update Software, Oxford, 1997. Updated quarterly
13. Gonzales MT, Gonzales C, Griñó JM, Castelao AM, Mariñoso ML, Serrano S, Bonnin R, Carreras L, Alsina J (1990) Long-term evolution of renal osteodystrophy after kidney transplantation: comparative study between intact PTH levels and bone biopsy. Transplant Proc 22:1407–1411
14. Torres A, Rodríguez AP, Concepcíon MT, García S, Rufino M, Martín B, Pérez L, Machado M, Bonis E, Losada M, Hernandéz D, Lorenzo V (1998) Parathyroid function in long-term renal transplant patients: importance of pre-transplant PTH concentrations. Nephrol Dial Transplant 13 [Suppl 3]:94–97
15. Uda S, Yoshimura A, Sugenoya Y, Inui K, Iwasaki S, Taira T, Ideura T (1996) Role of apoptosis in the progression of secondary hyperparathyroidism. Nippon Jinzo Gakkai Shi 38: 323–328
16. Fukuda N, Tanaka H, Tominaga Y, Fukugawa M, Kurokawa K, Seino Y (1993) Decreased 1,25-dihydroxyvitamin D3 receptor density is associated with a more severe form of parathyroid hyperplasia in chronic uremic patients. J Clin Invest 92:1436–1443
17. Druëke TB (1995) The pathogenesis of parathyroid gland hyperplasia in chronic renal failure. Kidney Int 48:259–272
18. Arnold A, Brown M, Ureña P, Gaz RD, Sarfati E, Druëke TB (1995) Monoclonality of parathyroid tumors in chronic renal failure and in primary parathyroid hyperplasia. J Clin Invest 95:2047–2053
19. Tominaga Y, Namii Y, Haba T, Uchida K, Numano M, Tanaka Y, Takagi H (1995) Monoclonal proliferation of nodules in parathyroid hyperplasia due to chronic renal failure (abstract). J Am Soc Nephrol 6:972
20. Messa P, Sindici C, Cannella G, Miotti V, Risaliti A, Gropuzzo M, Di Loreto PL, Bresadola F, Mioni G (1998) Persistent secondary hyperparathyroidism after renal transplantation. Kidney Int 54:1704–1713
21. Jehle PM, Jehle DR, Mohan S, Keller F (1998) Renal osteodystrophy: new insights in pathophysiology and treatment modalities with special emphasis on the insulin-like growth factor system. Nephron 79:249–264
22. Hruska KA, Teitelbaum SL (1995) Renal osteodystrophy. N Engl J Med 333:166–174
23. Koch Nogueira PC, Rey N, Saïd MH, Cochat P (1997) Evolution of hyperparathyroidism in children – effect of pre-emptive transplantation and duration of dialysis. Nephrol Dial Transplant 12:984–987
24. Parfitt AM (1997) The hyperparathyroidism of chronic renal failure: a disorder of growth. Kidney Int 52:3–9
25. Nieto J, Ruiz-Cuervas P, Escuder A, Regas J, Callis L (1997) Tertiary hyperparathyroidism after renal transplantation. Pediatr Nephrol 11:65–68
26. Singer GG, Delmez JA (1998) Effects of renal transplantation on bone and mineral metabolism. In: Bushinsky DA (ed) Renal osteodystrophy. Lippincott-Raven, Philadelphia, pp 473–498
27. Graziani G, Aroldi A, Castelnovo C, Bondatti F, DeVecchi A, Ponticelli C (1991) Ciclosporin and calcium metabolism in renal transplanted patients. Nephron 57:480–497
28. Dumoulin G, Hory B, Nguyen NU, Henriet MT, Bresson C, Regnard J, Saint-Hillier Y (1995) Lack of evidence that cyclosporine treatment impairs calcium-phosphorus homeostasis and bone remodelling in normocalcemic long-term renal transplant recipients. Transplantation 12:1690–1694
29. Aroldi A, Tarantino A, Montagnino G, Cesana B, Cocucci C, Ponticelli C (1997) Effects of three immunosuppressive regimens on vertebral bone density in renal transplant recipients. Transplantation 3:380–386
30. Sugimoto T, Brown A, Ritter C, Morrissey J, Slatopolsky E, Martin KJ (1989) Combined effects of dexamethasone and 1,25-dihydroxyvitamin D3 on parathyroid hormone secretion in cultured bovine parathyroid cells. Endocrinology 125:638–641
31. Peraldi MN, Rondeau E, Jousset V, M'Selmi A el, Lacave R, Delarue F, Garel JM, Sraer JD (1990) Dexamethasone increases preproparathyroid hormone messenger RNA in human hyperplastic parathyroid cells in vitro. Eur J Clin Invest 20: 392–397
32. Traindl O, Längle F, Reading S, Franz M. Watschinger B, Klauser R, Woloszczuk W, Kovarik J (1993) Secondary hyperparathyroidism and acute tubular necrosis following renal transplantation. Nephrol Dial Transplant 8:173–176