# HYPERTENSION

**193** LONG TERM MINOXIDIL THERAPY IN CHILDREN WITH REFRACTORY HYPERTENSION. Puri, H.C. and Potter, D.E. University of California San Francisco, California USA

Fifteen children, 1-16 years of age, with severe hypertension uncontrolled by other drugs were treated with minoxidil (Mn) for periods of 1 to 69 months (mean 14.7 mo.). Hypertension was associated with transplant rejection in 6, dialysis in 5, glomerulonephritis in 3, and hemolytic-uremic syndrome in 1. The mean maintenance dose of Mn was 0.29 mg/kg/day (range 0.05 to 1.88 mg/kg). All patients received propranolol and those with appreciable renal function also received furosemide. Before Mn therapy the mean blood pressure (BP) level was 160/112 with Mn therapy the mean BP level was 135/92. (difference in systolic BP, $p < 0.001$; difference in diastolic BP $p < 0.001$). In 13 patients, there was a fall in diastolic BP of 9 to 33 mm Hg whereas in 2 patients there was no response due to inadequate dose of drug in one and progressive transplant rejection and high plasma renin activity (PRA) in the other. In 10 patients treated for a mean of 21 months, the BP levels were significantly lower than the pre-Mn level at 6, 12, 18, 24 and 30 months. Four dialysis patients with severe hypertension and high PRA responded and were able to avoid bilateral nephrectomy. Side effects included hirsutism in all patients treated longer than one month; one patient developed congestive heart failure, one developed pericarditis (a dialysis patient), and one had precipitous decrease in renal function with achievement of normotension. It is concluded that Mn is a highly effective and valuable drug in the treatment of severe hypertension in children with renal disease.

**194** ANTIHYPERTENSIVE EFFICACY OF CAPTOPRIL IN A 7 YEAR OLD BOY INADEQUATELY CONTROLLED BY MINOXIDIL. Warshaw, B.L. and Pruitt, A.W.; Emory Univ. Sch. of Med., Dept. of Ped., Atlanta, GA., USA

Minoxidil (M) has obviated the need for bilateral nephrectomy in patients with severe hypertension (HBP) unresponsive to conventional drugs. However, use of this agent is accompanied by significant side effects including hirsutism and fluid retention. Captopril (C) has recently been shown to be useful for treatment of severe HBP and may offer an effective alternative to M. Experience with a 7 y.o. boy with HBP afforded the opportunity to assess the efficacy of C for HBP inadequately controlled by M. HBP followed an episode of crescentic glomerulonephritis with subsequent chronic renal insufficiency. In 1976, maximum blood pressure (BP) was 240/190 despite multiple drug therapy. M was initiated and adequate BP control was attained on 25 mg/day as well as Furosemide 400 mg/day and Propranolol 160 mg/day. Complications included transient pericardial effusion, episodes of congestive heart failure, and progressive cardiomegaly. In Jan., 1980, BP was 160/100-110 despite increase of the M to 50 mg/day. Creatinine clearance was 25 cc/min/1.73 sq.m.; serum creatinine = 2.1 and BUN=200 mg/dl; peripheral renin=60 ng/ml/hr. M and Propranolol were discontinued and C was initiated. Following 3 weeks of C, BP was 120/70 on a dose of 37.5 mg tid (2 mg/kg/dose), as well as Furosemide 80 mg/day and Metoprolol 100 mg/day. Renal function and BUN were essentially unchanged. No adverse effects were apparent. The initial results indicate that C was an effective hypotensive agent in a child inadequately contolled on M.

**195** CAPTORIL (C) -SUCCESSFUL USE IN SEVERE HYPERTENSION, Friedman,A.L., Chesney, R.W., Ball, D. and Goodfriend, T. University of Wisconsin Health Center, Madison, Wisconsin,USA.

(C) is an orally active anti-hypertensive which inhibits the conversion of angiotensin I (AI) to angiotensin (( (AII). We report 6 patients: 3 with renal failure on dialysis; 2 with vasculitis and 1 chronic renal transplant rejection. All were unresponsive to conventional therapy. Plasma renin activity (PRA) (ng/ml/hr), AI (pg/ml) and AII (pg/ml) levels were measured pre and post therapy.

| | Cases | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| PRA | pre | 23.8 | 39.2 | 0.5 | >40 | 4.8 | >40 |
| | post | 31.8 | 23.6 | 0.7 | >40 | 5.6 | >40 |
| AI | pre | 237 | 1113 | 80 | 2100 | 480 | 370 |
| | post | 2020 | 3070 | 2420 | 5370 | 390 | 390 |
| AII | pre | 53 | 143 | 55 | 3530 | 124 | 1240 |
| | post | 0 | 10 | 72 | 118 | 93 | 700 |
| BP | pre | 170/130 | 188/120 | 200/160 | 184/114 | 240/170 | 190/130 |
| | post | 100/62 | 120/84 | 130/78 | 138/84 | 138/78 | 130/80 |

In cases 1,2,4 (C) alone served to reduce blood pressure (BP). (C) decreased BP in 3 despite low renin levels, indicating at least 2 modes of action for (C). No significant side effects were noted. (C) is an effective, well-tolerated anti-hypertensive agent in children.

**196** SHORT TERM RESPONSE AND LONG TERM MANAGEMENT WITH CAPTOPRIL IN SEVERE HYPERTENSION (HT) OF CHILDREN. BACRI J.L., DECHAUX M., GAGNADOUX M.F., GUILLOT M. BROYER M. HOPITAL ENFANTS MALADES, PARIS, FRANCE.

Short term response to single dose of Captopril has been studied in 15 severe HT children at least 24 h after cessation of anti HT drugs. Blood pressure (BP) fell significantly ($p < 0,001$) PRA rose ($p < 0,01$) plasma aldosterone fell ($p < 0,02$) in the 6 first hours. Sequential measurement of plasma converting enzyme activity (PCEA) in 6 cases shows significant inhibition. Decrease in PCEA does not constantly parallel the decrease of BP suggesting intervention of other (s) mechanism (s). A positive poor correlation was found between fall of BP and increase of PRA ($r = 0,45$), a negative one was found between fall of BP and inuline distribution volume ($r = 0,52$). Long term treatment with Captopril (7days to 12 months, average 101 days) has been performed in 10 patients with resistant HT. 4 of them had a chronic renal failure (mean inulin clearance 25 ml/mn/1.73 sq.m) and 3 were haemodialysed. Maximal dosage was 200 mg/1.73 sq/m/day ; low salt diet was maintained. BP was normalized in 9 cases. In the last patient partially uncontrolled BP and dialysis hypotensions led to bilateral nephrectomy. In one patient with graft artery stenosis Captopril induced a dramatic fall of BP and a consecutive acute reversible tubulopathy leading to cessation of the drug. 5 patients are still treated ; GFR improved in 2 cases. No "allergic" side effect has been observed. Since this side effect is dose related it is fully recommended to obtain the lowest dosage by associating salt depletion.

**197** REVERSAL OF ADVANCED RENAL FAILURE WITH CONTROL OF MALIGNANT HYPERTENSION. McVicar, M. and Chandra, M., North Shore University Hospital, Cornell University Medical College, Manhasset, N.Y., U.S.A.

Recovery from advanced renal failure associated with malignant hypertension is rare. We report a 17 y.o. girl with N.S. and hypocomplementemic MPGN (Type I) who on two occasions developed advanced renal failure associated with malignant hypertension and recovered adequate renal function to remain off dialysis when the hypertension was controlled. Four years after onset, her serum creatinine was stable between 4-4.8 mg/dl. She then developed malignant hypertension with BP 170/120 and grade IV retinopathy and a s.creat of 9.6 mg/dl. Plasma renin was 0.4 ng/ml/hr. Removal of 5 kg of fluid by dialysis and aggressive antihypertensive therapy resulted in normalization of BP. This was followed by a gradual decrease of s creat over a period of 4 mos to the former mean of 4.5 mg/dl. Nine mos later, after failing to take meds, she had a second episode of malignant hypertension with BP 180/115 and s creat 12.9 mg/dl. Dialysis resulted in the loss of 7 kg excess fluid but BP continued abnormally high until vigorous antihypertensive therapy consisting of propranolol 720 mg, prazosin 20 mg, furosemide 160 mg and metolazone 10 mg daily was used. The s creat then dropped to 8.0 mg/dl. Over the next 6 mos s creat stabilized at 4.7 mg/dl and the BP has remained normal. Our experience indicates that some patients with severe hypertension and advanced renal failure require at least 4 weeks of observation with normal BP to determine whether chronic dialysis should be initiated.

**198** EFFECTS OF PRORENIN ON NEWBORN BLOOD PRESSURE AND THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM (RAAS). Siegel, S.R., and Parkhill, T., UCLA Hospital and Clinics, Div. of Nephrology, Los Angeles, Calif., U.S.A.

Large molecular weight (M.W.) renin (prorenin) has been isolated from human and animal blood, kidneys, brain, and amniotic fluid. The purpose of this study is to define the biological effects of prorenin. Prorenin (M.W. 56,000) was purified from human cord or newborn blood by four chromatographic methods: 1) ammonium sulfate fractionation 2) gel filtration 3) ion exchange chromatography and 4) affinity chromatography. In vitro trypsin activation of prorenin producing PRA did not decrease the M.W. to renin (44,000). One ug of prorenin was infused as an I.V. bolus in 6 newborn puppies 1-2 wks. old. Mean aortic blood pressure (B.P.) was monitored continuously. Blood samples for PRA, plasma aldosterone (pA), Na, and creatinine were measured at 15, 30, 60, 90, and 120 min post-infusion; 30 min urine collections were measured for creatinine, Na, and K. PRA increased from a baseline of 23.7 ± 3.8 ng/ml/hr to 36.9 ± 4.3 (M and SEM), $p < .05$, at 15 min and remained high; pA levels increased from 48.0 ± 7.3 ng/dl to 67.8 ± 14.6 and 73.9 ± 14.2 (M and SEM) at 90 and 120 min, but it was not statistically significant. B.P. decreased initially 8-12 mmHg for 3-6 min and then increased 8-16 mmHg between 30 and 60 min in 4/6 puppies. There was no change in Ccr, urinary Na or K excretion. Summary and Conclusion: 1) Large M.W. prorenin can cleave renin substrate in vitro and in vivo to produce angiotensin 1. 2) Big renin (prorenin) may regulate B.P. and RAAS levels.