have shown that hypertensive subjects with microalbuminuria are at increased cardiovascular risk. However, the criteria for the diagnosis of microalbuminuria are not clear. This study investigated hypertensive non-diabetic subjects with a normal urinary albumin:creatinine ratio (ACR < 3.5 mg/mmol/l) to determine whether BP influenced the level of albuminuria within the normal range.

Demographic data including office BP and urinary ACR values (analysed by immuno-turbidimetric test) from 426 subjects (Mean age 41.2 y, Female 51%, Treated 68.8%, White 82.9%) was analysed. Subjects were stratified according to office systolic BP into 3 discrete groups (A: 130-149 mmHg, B: 150-169 mmHg and C: 170+ mmHg) for comparison. Mann-Whitney and Kruskal-Wallis ANOVA statistical analyses were used.

Female subjects have significantly raised ACR values with similar BP and treatment status (ACR (all subjects): 1.00 (Female) v. 0.83 (Male) p=0.0002; ACR (untreated): 0.86 (F) v. 0.72 (M) p=0.0342). There were no differences between ethnic groups or specific anti-hypertensive therapy. Subsequent analysis was therefore gender-specific. There was significantly greater mean ACR in both male and female subjects at higher levels of BP (Female ACR: A: 0.88; B: 0.88; C: 1.23 p=0.0016. Male ACR: A: 0.64; B: 0.76; C: 1.05 p=0.0004).

Diabetic subjects with microalbuminuria, irrespective of BP, are treated specifically with ACE inhibitors to delay the onset of nephropathy. In non-diabetic hypertensive patients, this issue is currently unresolved. Our study highlights the important observation that the positive correlation of albuminuria to blood pressure continues into the normal range. Although these subjects clearly do not have overt albuminuria, this highlights the difficulty in determining an arbitrary value for microalbuminuria and thus a guide for drug-specific therapy.

Key Words: Albuminuria, Essential Hypertension, Kidney

P-396

D5 DOPAMINE REGULATION OF PHOSPHOLIPASE D AND BLOOD PRESSURE IN MICE
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D1-like receptors inhibit the proliferation and hypertrophy of vascular smooth muscle cells by suppressing phospholipase D (PLD) activity. We hypothesize that the D5 receptor is the D1-like receptor that inhibits PLD activity and serves to regulate blood pressure via this mechanism. Thus, sytolic, diastolic, and mean (MAP) blood pressures were higher in D5 receptor-deficient (MAP, mm Hg = 114±4, n = 70) than in wild type mice (MAP = 85±1, n = 67, p < 0.05). The renal tubular and vascular distribution of PLD was similar in both strains but expression (units) was 2-fold higher (D5-/−:66±2; D5+/+:34±2; n = 3, P < 0.05) and activity (units) was 70% greater (D5-/−:5.5±0.5; D5+/+:3.2±0.6; n = 3, P < 0.05) in D5−/− than in D5+/+ mice. In CHO cells expressing D5 receptors but not in control cells, the D1/D5 agonist, fenoldopam (FEN) decreased PLD expression (10 μM, 2 hr) (vehicle = 40.2±8.1, FEN = 12.9±2.9, n = 4, P < 0.05) and activity (1 μM, 30 min) (vehicle = 0.21±0.02, FEN = 0.13±0.01; n = 4, P < 0.05). In the basal state, D5 F173L, a D5 receptor that cannot stimulate adenylyl cyclase, produced more reactive oxygen species, ROS (units), (131±27, n = 3) than the wild type D5 receptor (81±27, n = 3, P < 0.05). FEN (5 M, 30 min) transiently increased ROS production to a greater extent in D5 F173L (1041±130, n = 3) than in wild type D5 receptor (585±78, n = 3, P < 0.05). We suggest that the hypertension in the D5−/− mice is caused, in part, by increased PLD expression and increased generation of ROS.

Key Words: Phospholipase D, Reactive Oxygen Species, Dopamine Receptor

P-397

CYSTATIN C VERSUS CREATININE IN RENOVASCULAR DISEASE
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Objective: We investigated if cystatin C, a reliable marker of GFR, may serve as a more sensitive discriminator than creatinine in a rule-out strategy in the diagnostic work-up for renovascular disease (RVD).

Design: Cystatin C was measured in 150 hypertensive patients with an intermediate to high index of clinical suspicion of RVD and slightly impaired renal function (creatinine concentration < 177 micromol/L). In order to define the normal range of cystatin C, it was also measured in 128 sex-matched normotensive subjects (age interval 19 to 78 years) free of any drugs.

Methods: Cystatin C was measured by particle-enhanced nephelometric immunoassay. RVD diagnosis was established by renal angiography (RVD n=65, RVD-free n=85). To define RVD diagnostic accuracy of both cystatin C and creatinine, Receiver operating curves (ROC) curves were calculated. As decision thresholds, values corresponding to 90th and 95th percentiles of the distribution in healthy normotensive population were used.

Results: Cystatin C and creatinine were higher in RVD than in RVD-free patients. ROC curves for the two assays resulted quite similar (AUC 0.73 with 95% CI 0.64-0.8 and 0.74 with 95% CI 0.66-0.82 for cystatin C and creatinine, respectively). However, considering the values corresponding to 90th or 95th percentiles of normotensive population as decision thresholds (0.90-0.93 mg/L for cystatin C and 92.9-97.2 micromol/L for creatinine), cystatin C showed better sensitivity (87.7-92.3%) and negative predictive value (82.2-87.2%) for RVD diagnosis than did creatinine (sensitivity 70.8-72.3%; negative predictive value 74.3-76.5). Odds ratio against the occurrence of true RVD in case of cystatin C <0.90 mg/L was 4.26.

Conclusion: Cystatin C is a more sensitive discriminator than creatinine in a rule-out strategy in the diagnostic work-up for renovascular disease. Accordingly, hypertensive patients presenting cystatin C <0.90 mg/L have a low probability of RVD and may reasonably be excluded from any other complex diagnostic investigations.

Key Words: Cystatin C, Renovascular Disease, Renal Function

P-398

LOSS OF RENAL RESERVE IN OBESE HYPERTENSIVE PATIENTS

To demonstrate the effects of obesity on renal hemodynamics and the role of renal kalikrein (kAl) and nitric oxide (NO) on renal response to oral protein load (renal reserve, RR), we studied 14 obese (BMI: 32.9 ± 1.1, age: 50.5 ± 2.9 yrs, SBP: 152.8 ± 2.4 mmHg, DBP 96.2 ± 2.2 mmHg, 5 males and 9 females) and 9 non obese hypertensive patients (BMI = 22.9 ± 1.1, age: 50.6 ± 2.7 yrs, SBP = 151.2 ± 2.8 mmHg, DBP = 97.9 ± 2.1 mmHg, 4 males and 5 females). Hemodynamic and metabolic evaluations were conducted at basal conditions and after protein challenge moment (1g/kg of weight). Glomerular filtration rate (GFR) was estimated by clearance of inulin, and renal plasma flow (RPF) was
calculated by the clearance of 131 orthoiodohippurate. We measured the levels of serum NO by the Griess reaction modified, and the urinary excretion of Kallikrein (Kal) by chromogenic substrate.

After protein load there were significant increases of urinary Kal/Creat in both obese individuals (0.12±0.04 vs 0.29±0.06, p=0.002) and lean subjects (0.052±0.008 vs 0.22±0.02, p<0.05) with no differences in response between groups. RPF significantly increased in both groups (374.2±25.5 vs 438.8±27.2 ml/min, p=0.02 in obese, and 496.1±19.9 vs 637.1±40.4 ml/min p=0.001 in lean subjects) accompanied by increases in GFR (130.9±3.3 vs 138.5±3.5ml/min, p<0.001 in obese and 101.4±3.6 vs 112.9±3.5ml/min, p<0.001 in lean subjects). Serum NO increased in lean subjects but not in obese individuals (19.5±1.2 vs 23.4±3.4 μM, p=0.04 and 23.2±0.9 vs 221±1.2 μM, respectively). The NO change after protein challenge correlated significantly to RR (r=0.51, p<0.03). The mean RR was lower in obese (7.1±0.9) compared to lean hypertensive individuals (11.3±0.8, p=0.005).

In our group of obese hypertensive individuals renal reserve is determined compared to lean hypertensive individuals, which appears to be related to differences on vasodilator capacity of renal vasculature after protein load. This effect may be mediated by renal kallikrein and NO, pointing out a deleterious role of obesity on renal reserve.

Key Words: Renal Reserve, Obesity, Kallikrein

P-399
METABOLIC DISORDERS IN HYPERTENSIVE PATIENTS: PROSPECTIVE COHORT STUDY
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The relationships of metabolic risk factors (dyslipidemia, hyperuricemia, hyperuricosuria, insulin resistance, obesity) in subjects with high (>140/90 mm Hg) -HBP and normal blood pressure were evaluated.

Cohort of men and women (n=253) aged 20-75 years from Moscow organized population was examined. Height, weight, waist/hip ratio, blood pressure, heart rate were measured. Biochemical test included blood lipids, fasting glucose, fasting insulin, uric acid, 24-hour urine excretion of uric acid. Insulin resistance was defined as glucose/insulin ratio<6. HBP was diagnosed in 50.2 percent.

The incidence of new HBP cases was 52.3 percent (in 90 out of 172 subjects with normal BP level at the first screening).

Hyperglycemia or insulin resistance was more prevalent in hypertensives (66.7%) compared to normotensives (45.7%, p<0.006). Dyslipidemia was also significantly higher in hypertensives (60.8% vs 23.6%, p<0.001). Similar pattern was true for uric acid disorders: 59.5% vs 43.3%, p<0.001. Obesity was present in 76.8% subjects with high blood pressure compared to 34.2% subjects with normal blood pressure (p<0.001). The prevalence of high BP in presence of 3 metabolic risk factors was 82.6%, for more then 3 factors - 91.1% while for subjects with less then 3 factors - 29.6 (p<0.001). While using BP cut off point >160/95 mm Hg the prevalence of high BP in those groups was 56.5%, 86.7% and 10.5% respectively (p<0.001). It was shown also the elevation of uric acid excretion in 100 mg increased the HBP new cases risk in 1.27 (CI: 1.10, 1.48).

Thus large proportion of subjects with high BP (80-90%) has the modified metabolic risk factors. Not only lowering of high BP, but correction of metabolic disorders is emerging for control of hypertension.

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Key Words: Hypertension, Uric Acid, Metabolism

P-400
BASELINE CHARACTERISTICS OF ALLHAT PARTICIPANTS WITH IMPAIRED RENAL FUNCTION: ASSOCIATION WITH COEXISTENT CARDIOVASCULAR DISEASE
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Objective: a) To determine the prevalence of decreased glomerular filtration rate (GFR) and chronic kidney disease (CKD) at baseline in ALLHAT participants b) describe the association between GFR at baseline and history of cardiovascular disease (CVD) and c) describe the association between GFR and left ventricular hypertrophy (LVH) on ECG.

Methods: The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) is a practice based, randomized, multicenter clinical trial of antihypertensive pharmacologic treatment with 42419 participants aged 55 or older with one additional risk factor for CVD. Since there was limited general acceptance of equations to estimate GFR when the study was designed, a serum creatinine >2 mg/dl by history was used as the criterion to exclude patients with advanced renal dysfunction. Baseline serum creatinine was measured in a central lab with calibration allowing for application of the simplified MDRD equation to estimate GFR. Decreased GFR and CKD were defined according to the NKF-K/DOQI CKD clinical practice guidelines (unpublished draft). The Minnesota code was used to define LVH on the baseline ECG. History of CVD was as reported by the physician at the clinical center.

Results: After adjustment for age, race, gender, body mass index, baseline blood pressure, LDL, HDL, triglycerides, diabetes and smoking by multiple logistic regression, lower estimated GFR was independently associated with a 6% higher history of cardiovascular disease (OR 0.94 per 10 ml/min/1.73 m² p<0.0001), and a 10% higher prevalence of ECG-LVH (OR 0.90 per 10 ml/min/1.73 m², p<0.0001).

Conclusions: 1) The prevalence of decreased GFR (61-90 ml/min/1.73 m²) and CKD with moderate decreased GFR (31-60 ml/min/1.73 m²) is very high in hypertensive patients older than 55 years with one or more risk factors for CVD.

2) Patients with CKD with moderate or severe decreased GFR are more likely to have a history of CVD, ischemic ST-T wave changes, and LVH on ECG.

3) Estimated GFR is independently associated with a history of CVD and the presence of ECG-LVH.

Key Words: Left Ventricular Hypertrophy, Chronic Renal Insufficiency, Cardiovascular Disease