ISOLATED RENAL THROMBOTIC MICROANGIOPATHY AS AN INITIAL PRESENTATION OF SCLERODERMA WITHOUT OTHER SYSTEMIC MANIFESTATIONS OF THE DISEASE. Sri Ranga Bonam, Sirisha Chalasani, Sashidhar Bollini, Robert Grunberg, Richard Snyder

The thrombotic microangiopathies (TMA) share a common pathway of vascular endothelial injury and thrombus formation. Scleroderma is an autoimmune disease and histologically, scleroderma renal crisis (SRC) is indistinguishable from a TMA. To our knowledge, there are only several cases describing an association between the two. In those cases, patients with a TMA initially presented with either limited or diffuse scleroderma. We believe that this is the first time that an association between a TMA and scleroderma has been described in a patient without a pre-existing laboratory or clinical diagnoses of scleroderma.

A 70 year old white male with past medical history significant only for hypertension and coronary artery disease presented with acute kidney injury (AKI). The patient was normotensive at this time, and prior had normal renal function. Serologic evaluation for connective tissue diseases was non-diagnostic. A renal biopsy demonstrated a TMA. The patient had no thrombocytopenia and no antiphospholipid antibodies. Because of the diagnostic dilemma concerning the etiology of the TMA, plasmapheresis and hemodialysis(HD) was started. The patient was transferred to a tertiary center where a repeat diagnostic evaluation was inconclusive. The patient was maintained on HD, and after a period of four months developed skin changes consistent with scleroderma. While the ANA was only mildly positive, and antibodies specific for scleroderma were negative. A skin biopsy demonstrated scleroderma-type changes. The skin manifestations quickly worsened, and the patient was started on D-Penicillamine and continued on HD. This case represents a rare presentation of a TMA that we think may have been a SRC with delayed onset of generalized scleroderma. A vWf cleaving protease assay may have helped in distinguishing between the SRC and TMA, as the treatment of each is different. If this was a SRC, it is also unusual that it preceded the skin manifestations. While not a leading diagnosis, scleroderma should be considered in the differential diagnosis of a TMA with AKI.

ACUTE TUBULAR NECROSIS DUE TO OXALIPLATIN

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The platinum based compounds are commonly used chemotherapeutic agents. Many agents in this class, such as Cisplatinum, are nephrotoxic. Oxaliplatin, a third generation based platinum compound, is a cytotoxic agent used in the treatment of recurrent colon and rectal cancers. We report a rare case of acute tubular necrosis (ATN) due to Oxaliplatin.

An 82 year old female with a past history significant for recurrent rectal carcinoma and hypertension received four cycles of Folfox (Oxaliplatin/Leucovorin/5FU) at a dose of 85mg/$m^{2.}$ She experienced significant improvement in her cancer burden. One week after her fourth cycle of chemotherapy she presented to the hospital with increasing shortness of breath and lower extremity edema. She denied any nausea, vomiting, or diarrhea. Labs showed acute kidney injury (AKI) with a creatinine of 4.5mg/dl. Prior to beginning the chemotherapy, she had a creatinine of 0.8 mg/dl.

During the hospitalization, her renal function worsened and with a creatinine of 7.5mg/dl hemodialysis was initiated. A 24 hour urine protein showed tubular range proteinuria of 141mg. Serologic workup including complements was negative, and there was no peripheral or urine eosinophilia. A renal ultrasound showed parapelvic cysts, mild cortical thinning, and no hydronephrosis. A triple- phase renal flow scan with technetium showed diminished perfusion of both kidneys with moderately reduced function of both kidneys in a symmetrical pattern consistent with ATN. Over the next two weeks, she improved and dialysis was discontinued. Her creatinine has decreased so far to a value of 1.3mg/dl.

An extensive review of the literature only shows two case reports of oxaliplatin induced AKI. Based on the above , we believe that her AKI was due to the Oxaliplatin.. We wonder if there may be a circulating metabolite that may be nephrotoxic given that the cumulative dose of four cycles is significantly less than other described regimens, and that each individual dose was calculated based on ideal body weight. We feel that Oxaliplatin should be considered as a nephrotoxic agent along with the other platinum based compounds.

INCIDENCE AND PREDICTORS OF ACUTE RENAL FAILURE IN PATIENTS HOSPITALIZED FOR CONGESTIVE HEART FAILURE

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Congestive heart failure (CHF) is a common cause for hospital admission. Patients often develop acute renal failure which may lengthen hospital stay and increase risk for adverse outcomes. The purpose of this study was to describe the incidence of acute renal failure (ARF) in hospitalized patients with CHF, and to determine predictors for its occurrence. Chart review was conducted of 508 consecutive admissions to a community hospital with principal discharge diagnosis of CHF from 2004. A variety of demographic, clinical and echocardiographic parameters were studied. Increase in serum creatinine (SCr) of ≥0.5 mg/dL occurred in 106/508 (20.8%) of patients, SCr increase of ≥1.0 mg/dL in 21 (4.1%) patients, ≥2.0 mg/dL in 7/508 (1.4%). ARF (SCr increase 0.5 mg/dL) developed on day 2-(10.3%), day 3- (19.8%), day 4- (18.8%), day 5- (24.5%), day 6- (25.4%). The risk of ARF (defined as increase SCr 1.0 mg/dL) was increased among patients with lower admission sodium (133.5±6.1 meq/L vs. 138.6±4.5 meq/L, $p<0.0001$), higher admission serum creatinine (1.7±0.9 mg/dL vs. 1.4±0.6 mg/dL, $p<0.0001$), and patients with echocardiographic diastolic dysfunction (52.3% vs. 18.0%, $p=0.006$). Other variables close to reaching statistical significance included IV diuretic use day 1, (95.2% vs. 81.7%, $p=0.14$) and diabetes mellitus (52.3% vs. 34.3%, $p=0.10$). Use of ACEI/ARB after admission did not increase the risk of ARF (52.3% vs. 53.5%).

In conclusion, acute renal failure is a common complication in patients hospitalized for CHF. Its risk is increased among patients with diastolic dysfunction who are hyponatremic and have elevated serum creatinine at admission.

ROLE OF BNP LEVEL IN THE ASSESSMENT OF VOLUME STATUS IN PATIENTS WITH ADVANCED LIVER DISEASE AND ACUTE RENAL FAILURE

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Most patients with advanced liver disease have clinical evidence of volume overload but they may be intravascularly volume depleted. Assessment of the volume status is challenging in this clinical setting. Blood BNP levels are being used for determination of volume status increasingly. This study was performed to determine the correlation between BNP levels and urine parameters in the assessment of the volume status in patients with advanced liver disease and acute renal failure. This is a retrospective study conducted between December 2004 and September 2005. Patients with anuria, requiring emergent dialysis, creatinine < 1.4 mg/dl, recipients of liver and/or kidney transplant and without complete laboratory data were excluded. Thirty-two patients met the inclusionary criteria (age 18-70 yrs). Initial volume status was determined based on clinical findings: neck veins, edema, skin turgor and mucus membranes characteristics. Demographic and laboratory data were collected at the time of initial evaluation. Patient's outcome was recorded: improvement of renal function, no change, requirement of dialytic therapy and death. Results were analyzed by Pearson Correlation and Chi-square using SPSS software.

Patients were stratified as prerenal (n=9), hepatorenal (n=15) and acute tubular necrosis (n=8) Mean FeNa was 0.37, 0.42 and 2.08; Mean FeUrea was 19.68, 24.02 and 43.64; Mean BNP level was 155.67, 390.47 and 390.01 respectively. Based on the clinical assessment, the patients were divided into three groups: volume depleted (n=16), euvolemic (n=11) and volume overloaded (n=5). BNP levels did not correlate with the clinical assessment of the volume status (P = 0.09) nor with FeNa and FeUrea (P = 0.84 and 0.96 respectively) nor patients' outcome (P =0.43). These data suggest that BNP has limited value for assessment of volume or outcome in patients with advanced liver disease and acute renal failure. Urinary indices with clinical response to hydration may help differentiate amongst different etiologies for the ARF.

STILL CONSIDER POSTPARTUM URINARY RETENTION DESPITE NO CHANGE IN URINE OUTPUT

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Postpartum urinary retention is a common complication in the early puerperium. There is no standard definition, but it is usually not associated with spontaneous micturation within 6 hours of vaginal delivery, or post-foley removal after C-section. We report a case of postpartum urinary retention which reportedly had no change in voiding pattern or urine volume. Case Report: A 24 y/o Asian female (G2P2) with no past medical history and a normal pregnancy had an uneventful C-section. She received epidural anesthesia, and per protocol, the bladder catheter was removed 12 hours post surgery. She received IV ketorolac for pain. The next day she presented with abdominal discomfort and distention. There was no reported change in urinary volume or pattern. Serum creatinine rose from 1mg/dL to a peak of 5mg/dL. Urinalysis was unremarkable. CT of the abdomen revealed anasarca. Ultrasound was negative for hydronephrosis and doppler showed intact blood flow. Initial diagnosis was acute renal failure contributed by IV NSAIDS and possible volume depletion. Intravenous hydration was instituted without improvement in serum creatinine. A bladder catheter was reinserted. Within a few hours, the patient's urine output improved. Renal function returned to baseline within 24 hours. Discussion: Risk factors for urinary retention include nulliparity, instrument assisted delivery, prolonged first and second stages of labor, caesarean delivery, and possibly epidural anesthesia. Urinary retention is easily diagnosed if there is a decrease in urine output or symptoms of voiding dysfunction. Our patient did have the classic signs and symptoms of urinary retention. In the setting of IV NSAID use, the diagnosis was delayed and the patient was subjected to a multitude of costly radiological tests; causing additional emotional trauma. It is important to think of urinary retention as a cause of postpartum renal failure despite a normal urine volume and pattern. Placement of a bladder catheter early in the therapeutic course may avoid unnecessary testing.

THE EVALUATION OF EFFECTS OF DEMOGRAPHIC FEATURES, BIOCHEMICAL PARAMETERS AND CYTOKINES ON CLINICAL OUTCOMES IN PATIENTS WITH ACUTE RENAL FAILURE

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Our aim was to investigate the effects of cytokines, biochemical parameters and demogra-phic features of patients with acute renal failure on clinical outcomes.

59 patients with acute renal failure (28 Men, 31 Women) that were hospitalized in Department of Nephrology, in Dicle University Medical Faculty were enrolled to the study. For patients with no prior history of kidney disease or baseline creatinine values of <1,5 mg/dl, ARF was defined by an increase in creatinine of at least 0,5 mg/dl occuring over a 48 hour period. For patients with preexisting renal disease that creatinine values >1,5 mg/dl, ARF was defined by a increase in creatinine of >1 mg/dl. Demographic features were recorded by reviewing with patient and relatives or examining patient's files. Cytokines, biochemical parameters, and complet blood count were measured after 12 hours fasting period. Patients were divided into 2 groups; such as survivors (group 1: n=46) and nonsurvivors (group 2: n=13)

Mean age of patients (± SD) were 52,3±17,9 years (range from16 to 78 years). 46 patients survived (%77,9) and 13 patients died (%22,1). Male gender was dominant in nonsurvivors group (p=0,016). There was a statistically significant relationship between IL-2, TNF-α levels and mortality rates (p=0,002 and p=0,020, respectively). Also a significant relationship was found between TC, HDL-C, LDL-C levels and mortality rates (p =0,042 and p= 0,020, respectively). In multipl lineer regression analysis the effects of proinflamatory cytokines (IL1β, IL2R,IL6,TNFα,CRPand ESR) on the clinical outcomes in ARF was observed statistically significant (r square =0,341, p=0,005). There was an association between prolonged hospitalization and mortality rate (p = 0.016).

Male gender, prolonged hospitalization, inflamatuar cytokines such as IL-2R and TNF-α, and low cholesterol levels has a prognostic and predictive importance on the clinical outcome of ARF.

FILTER SURVIVAL IN HIGH RISK PATIENTS ON CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

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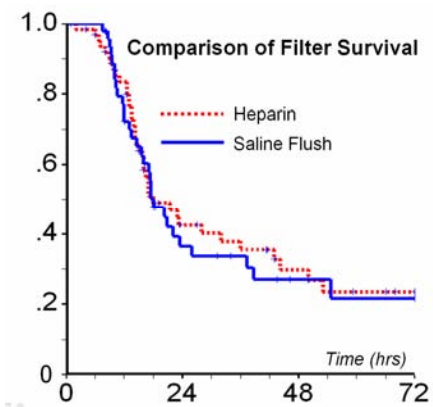
Systemic anticoagulation is used in patients (pts) receiving CRRT to prevent clotting and prolong the survival of filters. Systemic anticoagulation is contraindicated in pts with recent surgery, hemorrhage, or other risks for bleeding. Regional anticoagulation with citrate has been used with some success in such pts. Unfortunately, citrate is unavailable in many hospitals. Hourly saline flush is routinely used to avoid anticoagulation in pts receiving intermittent hemodialysis and may be an alternative to systemic anticoagulation in patients receiving CRRT. We compared filter survival in pts at high risk of bleeding (grp 1, n=13) on hourly saline flush to pts on heparin anticoagulation (grp 2, n=16). Data were analyzed retrospectively from 112 filters used on 29 consecutive pts who received CRRT from 12/04-11/05 at Harlem Hospital Center. All filters were primed twice with 5000U of heparin in 1L of saline. Grp 1 received 100ml saline flush every hour; grp 2 received heparin. Baseline aPTT was significantly higher in grp 1 compared to grp 2 (56.9 v. 40.4s); there was no difference in age (56.7 v 57.2 yrs), Hb (9.6 v 9.1 g/dL), Wt (84.1v. 92.2±20.0 kg), filtration fraction (15.7 v 14.1%), prevalence of diabetes, hypertension, CHF, sepsis, intubation, the presence of oliguric renal failure or the location of the catheter. There was no difference in mean filter survival (24 v. 25.6 hrs, *p=ns).* The log rank test showed no difference in the Kaplan Meier survival curves between the two grps (log rank statistic=0.12, *p=ns*). Our results show that saline flush is a simple and effective alternative to systemic anticoagulation in high-risk pts.



ALTERNATIVES TO HEPARIN USE DURING SLOW EXTENDED DAILY DIALYSIS IN THE ICU

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Slow Extended Daily Dialysis (SLEDD) is well tolerated by ICU patients. Although, in many critically ill patients, heparin use to maintain dialysis circuit is contra-indicated. We reviewed our use of alternatives to heparin during SLEDD in the critically ill.

All patients with contra-indications to heparin, on SLEDD during past year were reviewed. We compared 2 alternatives to our standard practice of saline flushes (SF) every 30-60 minutes. The first was citrate-based dialysate (CD) plus hourly SF, the other was Regional Citrate (RC). We defined clotting as discontinuation of dialysis, >30 minutes prior to prescribed treatment time, due to clots in lines, chambers or dialyzer, or when prompting the need for a new set up.

Overall there were 349 receiving SF, 64 received CD, and 84 on RC. Mean (±SD) age was 57 yrs (±16); 60% were men; access was via catheter in 95%; and an overall clot rate of 24 %. When comparing groups, we used ANOVA with Bonferroni corrections, and considered the SF group as the reference. The CD group was younger than the other groups, with mean age of 50 (±13) vs SF 58 (±13) yrs and RC 57 (±14), $p<0.001$. There were more women in the CD (83%), than in SF (36%) or RC (26%) $p<0.001$ for difference. Comparing SF to RC, there were no differences in mean ages, or % women. In all groups the percent using catheters (SF 95%, CD 98%, and RC 91%) or the mean duration of SLEDD (SF 5.8, CD 5.9, and RC 5.7 hrs) was not different ($p=0.29$, and $p=0.84$ respectively). SF had the highest clotting at 30%, compared to 16% for CD group, and 5% for the RC group. Both CD and RC had fewer clotting events compared to SF ($p=0.042$, and $p<0.001$, respectively). However, there were no statistically significant differences between CD and RC ($p=0.34$).

In ICU on SLEDD, both CD and RC were superior to SF alone. Of the 2 options, there were no differences in clotting, but this may be due to sample sizes.

RHABDOMYOLYSIS AND ACUTE RENAL FAILURE DUE TO COMBINATION THERAPY WITH LOVASTATIN AND WARFARIN

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Lovastatin, an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors has been in clinical use for almost 2 decades. There is an increased risk of myositis including rhabdomyolysis with concomitant administration of certain medications with HMG-CoA reductase inhibitors. We report a case of rhabdomyolysis and acute renal failure occurring in a patient taking lovastatin and warfarin.

A 38 year-old female with a past medical history of spina bifida, adrenal insufficiency, and chronic renal insufficiency was admitted for acute right leg pain and swelling. Her medications included lovastatin, zolpidem, buspirone, hydrocortisone, venlafaxine, fludrocortisone, glipizide, lansoprazole, verapamil. Four days prior to hospital admission, she was switched over to lovastatin from atorvastatin due to diarrhea. A Doppler ultrasound of the right lower extremity revealed a venous thrombosis involving the right popliteal vein extending up to the mid femoral veins. The patient was started on unfractionated heparin and warfarin, and continued on her previous medications. Laboratory investigations on day 2 showed a creatine kinase (CK) of 73, constant from the time of admission; but her creatinine was up to 2.2 from a value of 1.5 at admission. On day 3 her CK rose to 411 and creatinine rose to 2.8 despite adequate hydration. She was evaluated for rhabdomyolysis, and was found to have elevated serum lactate and aldolase. She also had positive urine myoglobin. Warfarin was stopped after 2 doses (10mg/day) as her INR was 3.4 and continued to rise peaking at 8.4 despite cessation of therapy. Lovastatin was also stopped. On day 5 her creatinine dropped to 1.4. Her elevated INR was most probably due to the interaction of warfarin and lovastatin.

The most likely cause for the rhabdomyolysis seen in this patient was an interaction of warfarin and lovastatin. A close monitoring of INR is warranted for patients who are on a combination of warfarin and statins. We recommend careful monitoring for rhabdomyolysis when warfarin is given to patients receiving statins.

METHAMPHETAMINE: CAUSE FOR ACUTE RENAL FAILURE IN A YOUNG MAN

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An estimated 12.3 million Americans, or 5% of the adult population, have used methamphetamine at least once and an estimated 600 000 people are weekly users of the drug. Renal adverse effects have been anecdotally reported with amphetamine derivatives. Amphetamine derivatives precipitate renal failure through different mechanisms such as hyperpyrexia, DIC, rhabdomyolysis, necrotizing angitis and interstitial nephritis. An 18-year-old man was brought to the emergency department by police, who found him trying to break into a stranger's house. On admission he was disoriented to time, place, and person and had paranoid delusions. He was afebrile and his vitals were stable. A toxicology screen in the urine was positive for methamphetamine. His serum creatinine at admission was 1.4 mg/dL. His confusion resolved over next few days. A detailed history elicited at this point revealed that the patient had been smoking meth amphetamine for 3 days continuously. On day 3 his creatinine went up to 3.9 mg/dL. He was non oliguric during the hospitalization. He had no past history of kidney disease or any other medical conditions. Serology for Hepatitis B and C was negative.

At this time he was evaluated for possible rhabdomyolysis, however his laboratory data showed normal creatinine kinase and absent myoglobin in the urine. The ultrasound of the kidneys was normal. His fractional excretion of sodium was 0.8% suggesting a pre-renal cause for his renal failure. After vigorous hydration his creatinine level reverted to normal. The possible cause for his renal failure was either ischemic acute tubular necrosis (ATN) or pre renal failure due to poor fluid intake. The former was the likely cause, as his creatinine at admission was within normal limits. The possible mechanism would be methamphetamine causing vascular spasm of the renal artery or its branches causing ischemic ATN leading to renal failure in this patient.

ACUTE TUBULAR NECROSIS: NOT JUST AN ICU RELATED DIAGNOSIS

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Acute Tubular Necrosis (ATN) is considered in the differential diagnosis of Acute Kidney Injury (AKI), especially in the Intensive Care Unit (ICU) in the setting of profound hypotension and shock. In the outpatient setting, or in patients presenting to the hospital with AKI, pre-renal and post-renal causes are most often considered. We present two cases of biopsy proven ATN where initially it was not thought of a leading diagnosis.

A 68 year old white male with a past medical history of diabetes, hypertension, dyslipidemia, coronary disease, and chronic kidney disease (CKD)with a baseline creatinine (Cr) of 2.2 mg/dl presented with abdominal discomfort. Ten days prior to admission, he had begun doing outside construction in the middle of the summer. Labs showed a BUN of 101, and Cr of 14.4 mg/dl. Biopsy showed diabetic glomerulosclerosis, and diffuse proximal tubular degenerative and regenerative changes, consistent with ATN. The patient was dialyzed twice, and in several months his function returned to baseline.

A 47 year old black male with a past medical history significant for drug use, hepatitis B, and CKD with a baseline Cr of 1.5 mg/dl presented with vomiting and abdominal discomfort. On admission was found to have a BUN of 75 and Cr of 13.5 mg/dl. Biopsy showed only tubular degenerative and regenerative changes and mild arteriosclerosis. The patient was maintained on hemodialysis for one week, and his Cr returned to baseline.

Ischemic ATN is often described in the ICU, where hypotension and shock cause dramatic changes in renal perfusion. In an outpatient setting, or in patients admitted to the hospital with AKI, ATN is often an overlooked diagnosis. In patients with underlying chronic kidney disease, especially those with diabetes, hypertension, and renovascular disease (large vessel or small vessel), subtle decreases in renal perfusion, if prolonged, can lead to an ischemic ATN. Both patients had a history of CKD. We feel that in a patient with CKD, ATN should be definitely considered in the differential diagnosis of ARF when presenting to the hospital or in an outpatient setting.

ACUTE KIDNEY INJURY (AKI) FOLLOWING GASTRIC BYPASS SURGERY. Charuhas V. Thakar, Varsha Kharat, Sheila Blanck, Melissa, Schnell, Anthony Leonard. University of Cincinnati, Cincinnati, Ohio

Gastric bypass surgery is an increasingly common treatment for morbid obesity. However, the incidence, risks and outcomes in post-op AKI are not well studied.

506 patients (year 2003, 2004) underwent gastric bypass surgery our institution. Post-op AKI was defined as 50% increase in baseline serum creatinine or requirement of dialysis. Secondary outcomes were mortality and length of hospitalization. Demographic, laboratory, co-morbid, and intra-operative, variables were tested along with pre-op medication use including angiotensin converting enzyme inhibitors (ACE) /Angiotensin receptor blockers (ARB), diuretics, and non-steroidal anti-inflammatory agents. Chi-square test and paired t test were used for comparison.

Two patients were excluded due to missing data (n, 504). There were 83.3% females and 90.7% whites. 31% had diabetes, 69% had hypertension, and 32.8% had hyperlipidemia. Overall frequency of post-operative AKI was 7.94% (n, 40, two of which required dialysis). The risk factors for developing AKI included, higher BMI ($p = 0.03$), presence of hyperlipidemia ($p = 0.001$), pre-operative use of ACE/ARB ($p = 0.002$), Oral antidiabetic or insulin use ($p = 0.05$), and higher baseline creatinine ($p = 0.04$). The overall mortality rate was low (0.54%; n, 2) and was similar in AKI versus no AKI group. The mean hospital stay was significantly greater in AKI group (3.9 days versus 2.7 days, $p < 0.001$).

AKI is not infrequent after gastric bypass. Pre-operative use of ACE/ARB is associated with greater frequency of AKI; temporary avoidance of which may offer renal protection. AKI increased the length of hospital stay but did not affect post-operative mortality.

CYANIDE TOXICITY FROM NITROPRUSSIDE IN A PATIENT WITH CHRONIC KIDNEY DISEASE

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We report a case of a 48-year old female who presented with altered mental status for 1 day. Blood pressure was 265/102 mm Hg with right-sided weakness. A CT scan showed a left basal ganglionic hemorrhage with intraventricular decompression. The patient was started on a nitroprusside drip at 1.5 mcg/kg/min. While initially the nitroprusside provided good blood pressure control, higher doses were required after 24 hours. After 36 hours the patient become bradycardic, developed respiratory distress. Afterwards she went into cardiac arrest. The nitroprusside was discontinued and the patient was resuscitated. Labs showed the presence of a new metabolic acidosis with a widened anion gap. The cyanide level was 391 mcg/dl. A CT scan had been done just prior to and after the event that showed no change in the intracranial bleed.

Nitroprusside spontaneously reacts with hemoglobin to form cyanide and cyanmethemoglobin. A healthy individual can detoxify 50 mg nitroprusside to thiocyanate using existing sulfur stores. Patients at high risk for cyanide toxicity include patients following surgery, liver disease, renal disease, malnourishment, and tobacco users. Our patient had significant chronic kidney disease with a calculated GFR of 20 ml/min. Our patient experienced tachyphylaxis to the nitroprusside, bradycardia, acidosis and increased anion gap all of which are consistent with cyanide toxicity. In the presence of chronic renal disease, patient’s receiving Nitroprusside require more vigilant monitoring of doses and cyanide levels to avoid toxicity.

ATRIAL NATRIURETIC PEPTIDE (ANP) CHANGES IN STREPTOZOTOCIN (STZ) INDUCED DIABETIC RATS

Enyioma Obineche, Michael G Nicholls, Sheela Benedict, Irwin Chandranath, Mohamed Fahim, Ernest Adeghate, Abdu Adem

Diabetes mellitus (DM) shows a markedly increased incidence of cardiovascular pathology that leads to hypertension, endothelial micro and macroangiopathy, diabetic nephropathy and myocardial infarction. Atrial natriuretic peptide (ANP), a 28 amino acid peptide hormone is mainly synthesized by the atria and heart ventricles with potent diuretic and natriuretic properties. In this study the effect of long term diabetes mellitus on plasma, kidney and heart atrial and ventricular ANP concentrations were evaluated in STZ induced 8 months diabetic and control rats by using radioimmunoassay (RIA). Moreover ANP receptors (ANP-Rs) in STZ induced 8 months diabetic rat kidneys were studied by receptor autoradiography. In addition, the expression of ANP concentrations in the kidney of diabetic and control rats was evaluated by means of immunohistochemistry. Body weight loss and increased glucose levels were used as indices of diabetes mellitus in the STZ induced diabetic rats.

Our results showed that significantly higher ANP concentrations were observed in diabetic plasma (P0.05) kidney ($P<0.01$) heart atria, ($P<0.05$) and ventricles ($P<0.01$) compared to controls. We also demonstrated a significant decrease in ANP-Rs in the outer cortex ($P<0.05$), juxtaglomerular medulla ($P<0.05$) and papilla ($P<0.05$) in the 8 month diabetic rat kidneys compared to controls.

The observed increase in ANP levels in plasma and kidney could be contributory to the development of diabetic nephropathy: probably by reducing the levels of ANP receptors in the diabetic kidney. Furthermore, the role of ANP in the STZ induced diabetic heart merits additional study.

HYPOKALEMIC MYOPATHY SECONDARY TO EXCESSIVE CONSUMPTION OF A CAFFEINATED SOFT DRINK.

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Caffeine is a substance with stimulant, diuretic and anorectic properties, which is widely consumed in coffee, and other caffeinated soft drinks. While caffeine has been demonstrated experimentally to lower serum potassium, this effect is not significant with regular caffeine consumption. High dose ingestion of caffeine can cause hypokalemia and can lead to myopathy and/or paralysis. Profound hypokalemic myopathy secondary to excessive ingestion of caffeinated beverages is very rare: a comprehensive literature search revealed only three cases. Our patient is a 43-year-old female who presented with progressive worsening of muscular pain and lower extremity numbness and weakness. She vomited twice on the day of presentation.She denied diarrhea, laxative or diuretic use or abuse. There was no history of bulimia or anorexia. Further history revealed that the patient had been consuming three to four liters of cola on a daily basis for over a year. The patient was normotensive at time of admission and throughout the hospitalization. On admission she had severe hypokalemia with an undetectable K of < 1.5 mmol/L. Initial labs revealed CPK 4640 U/L, Na 138 mmol/L, Cl 83 mmol/L, HCO3 41 mmol/, BUN 3 mg/dL, creatinine 0.6 mg/dL and Mg 2.5 mg/dL. Her arterial blood gas (7.57/50.4/70) revealed primary metabolic alkalosis, with respiratory compensation. Additional labs include a 24 hour urine potassium of 30.6 which was associated with a serum K of 3.4 mmol/L after patient received 240 mEq of KCl. Her serum and urine diuretic screens were negative. TSH (2.14 microIU/mL), renin (2.7 microU/ml) and aldostrerone (4ng/dL) levels were within normal limits. With cessation of cola consumption and aggressive potassium replacement, the symptoms rapidly resolved. The patient was subsequently discharged, has abstained from caffeinated soft drinks and remained normokalemic with K in the 4-4.5-mmol/dL range a year after discharge from hospital. Based on our case and other case reports we conclude that excessive consumption of caffeine should be considered in the differential diagnosis in any patient presenting with hypokalemia and myopathy.

ON THE MECHANISM OF LITHIUM (Li^+) INDUCED HYPERCALCEMIA.

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Hypercalcemia is usually accompanied by Hypercalciuria. A notable exception is the syndrome of Familial hypocalciuric hypercalcemia (FHH), which may result from an inactivating mutation of the calcium sensing receptor (CaSR). Lithium (Li) associated hypercalcemia can be a challenging clinical dilemma as it has features of primary hyperparathyroidism (PHP), leading to unnecessary parathyroid surgeries. We describe a patient, who after chronic Lithium therapy developed hypercalcemia, hyperparathyroidism and hypocalciuria and propose an explanation for this unique constellation of findings. She had been on Li therapy for bipolar disorder for over 30 years. She had an elevated serum ionized Calcium 1.53 M mol/l (1.15-1.35 M mol/l) and intact PTH 216 pg/ml(10-65 pg/ml). Her plasma Cr was 2.2 mg/dl, and plasma Li level 0.4 meq/l. Serum Mg and phosphorus were normal, while 24-hour urine Calcium was reduced. (26 mg/ 24 hours)(Normal 100-300 mg/24 hr). The Ca:Cr clearance ratio was also very low (0.008)(Normal 0.01-0.02). Thus, Li induced hypercalcemia is associated with hypocalciuria, a feature that distinguishes it from primary hyperparathyroidism, but that resembles FHH (Table).

Characteristic	**Primary Hyperparathyroidism**	**Familial Hypocalciuric Hypercalcemia (FHH)**	**LithiumInduced Hyperparathyroidism**
Serum Calcium	High	High	High
Serum PTH	High	Normal or Mild increase	High
UrineCa Excretion	Normal to high	Low	Low

Hypercalcemia in Li treated subjects has been ascribed to an alteration in the “set point”, whereby a higher Ca level is needed for PTH inhibition, shifting the Ca-PTH response to the right. Because Li does not directly affect the CaSR, we surmise that, by persistently inhibiting intracellular cAMP in parathyroid and renal tubular cells, Li alters CaSR signaling. This way, the stimulatory effect of high Calcium on the CaSR, does not result in inhibition of PTH release by the parathyroid glands or inhibition of renal tubular Calcium reabsorbption.

LACTIC ACIDOSIS CANNOT BE USED TO EXPLAIN AN OSMOLAL GAP IN PATIENTS WITH POTENTIAL ETHYLENE GLYCOL TOXICITY. A CASE REPORT AND REVIEW OF THE LITERATURE.

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The finding of an *unexplained* osmolal gap in the presence of an anion gap metabolic acidosis (AGMA) suggests ethylene glycol or methanol ingestion. In many hospitals specific assays for these toxic alcohols are not available in a timely manner and definitive therapy must be initiated based on clinical suspicion. Separating an *explained* from *unexplained* osmolal gap focuses on ruling out sepsis, ketoacidosis and lactic acidosis as the etiology for the osmolal gap. Though lactic acidosis can cause an osmolal gap with an AGMA, the lactic acid assay is unreliable during ethylene glycol intoxication.

We report a case where a patient had an elevated osmolal gap (22 mOsm/kg), severe metabolic acidosis (pH 6.9) and an elevated anion gap (37 mmol/L). His osmolal gap was completely explained by a lactic acid level of 27 mmol/L. While this should rule out a toxic alcohol as the etiology of his osmolal gap and acidosis, subsequent lab results revealed an admission ethylene glycol level of 11 mg/dL. We believe the elevated lactic acidosis was due to a previously documented artifact where the enzymatic lactic acid assay non-specifically mistakes glycolate for lactic acid.

Ethylene glycol toxicity can cause artificially elevated lactic acid which can erroneously explain an osmolal gap. Lactic acid should not be used to explain an otherwise suspicious osmolal gap in patients where a toxic alcohol is a consideratio

CAUSES OF DELAYED REFERRAL TO NEPHROLOGSTS IN CHRONIC KIDNEY DISEASE PATIENTS: A SYSTEMATIC REVIEW

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Despite guidelines recommending earlier referral of chronic kidney disease patients to nephrologists for preparation for renal replacement therapy, late referral is still a major problem. This results in substantial economic and patient related burden. We systematically identified the factors that resulted in late referral to nephrologists.

We searched MEDLINE, EMBASE, and CENTRAL using the appropriate search terms. Two reviewers individually reviewed a total of 63 potential studies and 9 studies were included in the final review. We defined late referral as studies that included patients referred to nephrologists within 6 months prior to initiation of dialysis. We stratified the causes of delayed referral into 2 groups: 1) Patients related factors and 2) Health care related factors.

Several patient and health care related factors that resulted in delayed referral to nephrologists were identified. Most studies identified older age, race other than caucasian and insurance status as the patient related factors impeding earlier referral. Other potential patient related factors include lower socioeconomic status, lower level of education, and presence of other comorbidities. Health care related factors include the lack of communication between the physicians of different specialties, lack of referring physician knowledge about the appropriate timing of referral and patients cared for in tertiary medical centers.

Both patient and healthcare related factors can affect the timing of referral of patients with CKD to nephrologists. More education for the referring physicians about the appropriate timing to refer these patients with particular emphasis on older non-caucasian patients may result in appropriate referral rates.

LEISURE TIME PHYSICAL ACTIVITY STATUS AND MORTALITY IN CHRONIC KIDNEY DISEASE: PRELIMINARY FINDINGS FROM THE MDRD STUDY

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Chronic kidney disease (CKD) is an important risk factor for cardiovascular disease and all-cause mortality. In the general population, physical activity is associated with reduced mortality. We examined physical activity status in CKD patients and its relation to all-cause mortality.

The Modified Diet in Renal Disease (MDRD) Study was a multi-center trial that randomized 840 CKD patients between 1989 and 1993 with mortality determined through the end of 2000. We analyzed baseline self-report data from the MDRD/Leisure Time Physical Activity Questionnaire on 834 patients. Based on the Surgeon General's Recommendations, patients were divided into four patterns of physical activity: 1. regular and intensive; 2: regular and not intensive; 3: irregular; 4: no physical activity.

The mean age was 52 years and 61% were male among the study sample. 19%, 19%, 24%, and 38% of patients were identified to have exercise patterns 1-4 respectively. The mean energy expenditure in patterns 1-4 were 12655, 7507, 3976, and 0 KJ/week respectively. Although patients with physical activity pattern 1 were significantly older, had more prior cardiovascular disease and higher blood pressure, there was no significant difference among the groups in GFR, albumin and other cardiovascular diseases factors. A total of 205 patients (24.6%) died during follow up. The unadjusted hazard ratio for all-cause mortality for Pattern 1 was 1.2 (95% CI 0.8-1.7); Pattern 2: 0.7 (0.4-1.2), and Pattern 3: 0.8 (0.6-1.2), in reference to Pattern 4. After adjusting for age, gender, GFR, albumin, prior cardiovascular disease, and BMI, the adjusted hazard ratios for patterns 1–3 , in reference to pattern 4, were 0.8 (0.6-1.2), 0.9 (0.6-1.5), and 1.1 (0.8-1.6).

The majority of CKD patients do not participate in any leisure time physical activity. We did not find significant differences among the physical activity and 10 year outcomes. Given the benefit of physical activity in general population, the role of physical activity in health outcomes in CKD requires further study.

OVERSHOOT OF THE TARGET HEMOBLOBIN RANGE OCCURS IN MAJORITY OF NEW DIALYSIS PATIENTS

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Initiation of anemia treatment in dialysis patients (pts) targets a hemoglobin (Hb) level of 11-12 g/dl. Little is known about how rapidly pts reach the target and how likely they are to exceed the target range.

We followed 23,337 incident ESRD, EPO-treated pts in 2002 for the first nine months of dialysis. All pts were 65 years of age or older, and were categorized into Hb levels of <9, 9-<10, 10-<11, 11-<12, & 12+ at initiation based on the Medical Evidence Form (2728).

After 4 months, approximately 90% of all pts reached Hb >=11 g/dl at least once. The table below shows the likelihood of reaching a Hb >12, >12.5 & >13 g/dl in the first three months after the first Hb >=11 g/dl. Roughly 85% will exceed 12 g/dl, 70% will exceed 12.5 g/dl, and over half will exceed a Hb level of 13 g/dl, regardless of Hb at initiation.

Patients who have lower Hb at initiation take longer to get to target. However once reaching the target, they are equally likely to go past 12, 12.5, & 13 g/dl.

Correction of anemia appears to be highly associated with overshooting the target, which may reflect increased sensitivity of the patients to treatment. Exceeding the target may contribute to dosing changes and subsequent instability in patients' Hb levels.

		Cumulative probability of exceeding a Hb (g/dl) of 12, 12.5, and 13 within 3 months after the first claim with Hb 11+; by initial Hb				
Year	Hb (g/dl)	<9	9-<10	10-<11	11-<12	12+
2002	12+	85.4	84.8	85.3	83.2	84.9
	12.5+	71.0	71.1	70.8	68.8	67.7
	13+	55.0	55.0	54.4	51.6	50.8

THE EFFECT OF HEMOGLOBIN LEVELS BELOW 11 G/DL ON FUTURE HOSPITALIZATIONS AND MORTALITY AMONG INCIDENT HEMODIALYSIS PATIENTS

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Studies of the effect of hemoglobin (Hb) level on patient outcomes suggest that a level below 11 g/dl is associated with poor outcomes. More recent research suggests that variability of Hb levels over time, and cumulative time with Hb <11 g/dl in particular, shows the strongest association with poor outcomes. This study assessed the effect of cumulative time with Hb <11 g/dl during a 6-month entry period on hospitalization and mortality.

Incident ESRD patients were identified by first service date in 2002. Those who survived at least 9 months were followed, from month 10, for one year for hospitalizations and mortality. Months 4-9 were used to characterize comorbidity from claims, and to assess the patient-level number of months with Hb <11 g/dl. Patients were classified into 2 groups: those with Hb <11 g/dl for 0 or 1 month, and those with 2-5 months below 11 g/dl. A propensity model based on comorbidity predicted the probability of having greater than the mean time with Hb <11 g/dl. A proportional hazards model assessed the independent effect of time with Hb < 11 g/dl on time to first hospitalization and time to death.

29,131 patients were studied. The mean number of months with Hb <11 g/dl for this group was 1.3. 10,468 (36%) patients had a cumulative number of months with Hb <11 g/dl greater than the mean (2-5 months). These patients were 1.15 times more likely to be hospitalized (P value < 0.0001, 95% CI: 1.12-1.19) and 1.26 times more likely to die (P value < 0.0001, 95% CI: 1.20-1.33). Results across propensity strata showed relatively consistent results.

These results suggest that patients with Hb <11 g/dl for prolonged periods of time (>1.3 months out of 6) have significantly greater risk of hospitalization and death, regardless of comorbidity status.

RELATIONSHIP BETWEEN KIDNEY DISEASE AND MORTALITY IN CHRONIC SPINAL CORD INJURY

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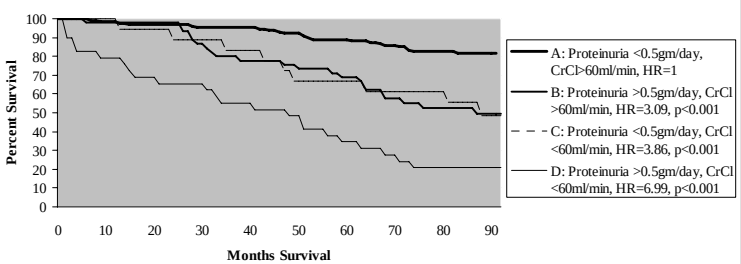
The purpose of this study was to evaluate the relationship between kidney disease (as determined by creatinine clearance (CrCl) and proteinuria, both measured from 24-hour urine samples between 1993 and 1998) and mortality in chronic spinal cord injury (SCI) patients (n=219). Computerized medical records were reviewed in 2004 (follow-up period of 6-11 years) to determine overall mortality. Patients were placed in one of four groups depending on their level of proteinuria and CrCl (Group A: proteinuria<500mg/day, CrCl>60 ml/min, n=127; Group B: proteinuria>500mg/day, CrCl>60ml/min, n=45; Group C: proteinuria<500mg/day, CrCl<60ml/min, n=18; Group D: proteinuria>500mg/day, CrCl<60ml/min, n=29). Long-term survival was assessed by Kaplan-Meier analysis and hazard ratios were calculated. Patients with either significant proteinuria and/or reduced CrCl had significantly decreased survival when compared to those with preserved renal function (Figure 1). There was no difference in survival when comparing Groups B and C (p=0.614). However, there was a significant reduction in survival in Group D compared with Groups B and C (p<0.05). In conclusion, proteinuria>500mg/day and CrCl<60ml/min are both associated with increased mortality in the spinal cord injury population. There appears to be an additive effect of proteinuria and reduced CrCl on this association.

Figure 1: Kaplan Meier Survival Curve



IMPLEMENTATION OF THE K/DOQI GUIDELINES USING A CLINICAL REMINDER SYSTEM

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Background: The National Kidney Foundation developed the Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines to help guide the management of patients with chronic kidney disease (CKD). However, because of evidence of sub-optimal uptake of the K/DOQI recommendations, there is currently a major effort to disseminate this information to primary care physicians to identify patients with CKD who lack recommended services and interventions. Methods: We developed a claims-triggered clinical alert and reminder system to communicate potential clinical opportunities to the primary care provider. These messages were derived from the recent K/DOQI guidelines (e.g. ACE-inhibitor in patients with microalbuminuria). Compliance with the alerts was measured using claims-based data during a pre-established evidence time window following communication. Results: The implementation rates averaged 27% across commercial, Medicare and Medicaid populations. Conclusion: A technology-driven claims-based clinical alert system can produce a measurable change in adherence to a guideline. Future directions: A randomized, controlled trial.

FACTORS CONTRIBUTING TO CHANGE IN EMPLOYMENT STATUS AT INITIATION OF RENAL REPLACEMENT THERAPY

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Many factors limit job retention of people with kidney failure. Yet some patients continue to work. We hypothesized that patients with better access to health care were likely to remain employed. We analyzed the1992-2003 USRDS database for incident patients ages 15-64 who reported full or part-time employment 6 months prior to initiation of renal replacement therapy (RRT) and had a Change in Employment Status (ΔEMS) at RRT. We analyzed co-morbid conditions and demographic factors using univariate and multivariate analyses to calculate odds ratios for ΔEMS. Patients on PD , who had pre-RRT Epo treatment (OR =1.30), cystic renal disease (OR=2.11) or glomerulonephritis (OR=1.26), or employer group or other health insurance (OR =1.66) were significantly more likely to be employed at the start of RRT. Those with a history of Etoh dependence, cardiac arrest, cancer, cerebrovascular disease, COPD, CHF, inability to ambulate, and tobacco use were less likely to be working at the start of RRT. Conclusion: Better access to healthcare may allow patients to remain employed with advanced stages of renal failure.

Insurance and Change in Employment Status					
Insurance Type	No change in EMS	Change in EMS	Odds ratio	Confidence interval	P-Value
Medicaid	2561	5473	040	0.37 - 0.43	<0.000001
Medicare	4373	3383	0.90	0.85 - 0.95	<0.0002
Employer insurance	42325	19469	1.66	1.55 - 1.78	<0.000001
No Medical insurance	4960	9412	0.45	0.42 - 0.49	<0.000001

Multivariate analysis with OR < 1.0 meaning increased risk of lower level of employment.

ELEVATED INTACT PARATHYROID HORMONE LEVELS AND HEALTHCARE COSTS AND UTILIZATION: RETROSPECTIVE COHORT OF PATIENTS WITH CHRONIC KIDNEY DISEASE

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The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative Guidelines (K/DOQI) recommend that physicians monitor intact parathyroid hormone levels (iPTH) among patients with chronic kidney disease (CKD) whose GFR falls between 15 and 59 mL/min/1.73m^2. The target ranges for iPTH levels in CKD are based on expert opinion: patients in stage 3 should not exceed 70 pg/mL; patients in stage 4 should not exceed 110 pg/mL. We investigated the shape of the relation between iPTH levels and healthcare costs to offer evidence.

We assembled a cohort of 830 patients with stage 3 or 4 CKD (using K/DOQI criteria) and an iPTH test to measure their healthcare costs in the year following their index iPTH test. Patients were members (1998 to 2004) of an HMO. Costs were assigned by applying standard unit costs to utilization. We compared the ratio of costs (geometric means) for quintiles of iPTH using natural log-transformed, linear regression.

Costs increased for patients who exceeded one of the K/DOQI cut-offs for "elevated" iPTH (110 pg/mL), but costs in the highest quintiles of iPTH were comparable to those in the lowest quintiles. Compared with patients ≤20th percentile of iPTH (3 to 55 pg/mL), we identified the following levels of relative excess (or lower) cost:

- 21st to 40th percentile (56-99), +25% 95% CI, -18% to +89%
- 41st to 60th percentile (100-144), +50% 95% CI, -2% to +131%
- 61st to 80th percentile (145-228), +1% 95% CI, -35% to +56%
- >80th percentile (229-1700), -17% 95% CI, -47% to +30%.

Our estimates controlled for age, sex, most recent estimated GFR (MDRD), annual cost before the index iPTH value, and mortality.

iPTH levels predict cost, but not in the expected dose-response relation; future studies should explore why the rates of utilization were lower among patients with the highest levels of iPTH.

PREVALENCE OF UNRECOGNIZED CKD IN AMBULATORY ELDERLY PATIENTS

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CKD is often unrecognized in elderly patients. A field for GFR estimate was added to the electronic medical record of an academic geriatrics clinic. We assessed the prevalence of unrecognized CKD after implementation of this reminder.

All patients seen from August 1, 2004 to August 1, 2005 with a stable creatinine were included. Patients with a creatinine greater than 0.2 mg/dl above their most recent baseline value or with only one recorded creatinine were excluded. Patients on dialysis were excluded. The 4-variable MDRD equation was used to estimate GFR. Charts were reviewed for the diagnosis of CKD and CKD risk factors.

Of 1,990 eligible patients, 1,424 had complete data to compute an MDRD GFR. The average age was 81.7 (+/-7.5) years, and 80% were female. 26% reported their race as black, and 30% as Hispanic. 59% of subjects had hypertension and 17% had diabetes. The mean GFR was 77.7 (+/-28.2). 346 subjects (24.3%) had a GFR<60, including 320 patients (22.5%) with a GFR between 30-59 and 26 patients (1.82%) with a GFR < 30. Only 62 patients with GFR<60 (17.9%) had a documented diagnosis of CKD, including 54% of patients with GFR<30. CKD patients with hypertension or diabetes were more likely to have recognized CKD.

Unrecognized CKD remains common in ambulatory elderly patients despite increased awareness. This has implications for medication prescribing, risk factor modification, and management of complications of CKD.

EPOETIN ALFA AND DARBEPOETIN ALFA DOSING PATTERNS AND DRUG COSTS IN PATIENTS WITH PRE-DIALYSIS CHRONIC KIDNEY DISEASE

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Epoetin alfa (EPO) and darbepoetin alfa (DARB) are approved for the treatment of anemia in patients with chronic kidney disease (CKD). The objective of this analysis was to compare recent dosage patterns and associated drug costs of EPO and DARB in patients with pre-dialysis CKD (pCKD).

A retrospective analysis was conducted using medical claims from approximately 35 health plans. To be included in the analysis, patients were required to be ≥18 years old, be newly initiated on EPO or DARB therapy, and have ≥2 EPO or DARB claims from October 2002 through December 2004 for anemia of pCKD. Patients diagnosed with cancer or who had undergone chemotherapy in the time period from 90 days prior to treatment initiation or during treatment were excluded. 2005 wholesale acquisition costs (WAC – EPO: $0.01217/Unit, DARB: $4.36/mcg) were used to calculate drug costs.

Among the 595 EPO and 260 DARB study patients, EPO patients were slightly older (years; EPO 63.5±13.3; DARB 61.2±13.5, p=0.0202), with gender distribution similar between groups (EPO 51.6% female; DARB 50.4% female, p=0.7443). Weekly and extended (≥Q2W) dosing frequency during treatment was observed in both treatment groups (EPO – QW: 36.8%, Q2W: 43.7%, Q3W: 9.9%, ≥Q4W: 9.6%; DARB – QW: 9.2%, Q2W: 55.0%, Q3W: 20.0%, ≥Q4W: 15.8%). The average weekly dose weighted by the therapeutic duration was EPO 11,527±10,267 Units and DARB 42.6±31.8 mcg, corresponding to an average weekly erythropoietic drug cost of $140 for EPO and $186 for DARB (p<.0001).

Extended dosing frequency (≥Q2W) was observed in both EPO and DARB patients. Based on 2005 WAC, DARB was found to cost 33% more than EPO based on the average weekly dose administered.

RESULTS OF A PILOT STUDY OF SULODEXIDE IN TYPE 2 DIABETIC NEPHROPATHY WITH MICROALBUMINURIA.

Edmund J. Lewis,., Julia B. Lewis, Lawrence G. Hunsicker for the Collaborative Study Group, Chicago, IL

We studied the effect of sulodexide, a low molecular weight heparin (mean MW 9000d) preparation which is administered orally, upon urine albumin excretion rate (UAER) in patients with type 2 diabetes mellitus and UAER >20 - <300 mg/G creatinine per day. This multicenter, placebo-controlled, double blinded study was designed to determine whether 6 months of sulodexide therapy (at doses of 200 mg or 400 mg per day) decreased UAER. 149 patients were enrolled. The primary endpoint of the study was either the achievement of normal UAER (<20 mg albumin/G Cr) plus a decrease of at least 25% or a 50% decrease in the initial UAER. All patients received maximum FDA approved ACE inhibitor or angiotensin receptor blocker therapy prior to randomization. Stable BP was maintained throughout the study. Achievement of the primary end point occurred in 26% of sulodexide patients vs. 10.5% of placebo. Normalization of UAER occurred in 15% sulodexide vs 11.5% placebo. A 50% decline in albuminuria was found in 23% sulodexide vs 8% placebo. Most patients achieving the primary end point did so in <2 months. Patients receiving 200 mg sulodexide performed best of the 3 randomized groups. The decrease in albuminuria observed in patients achieving a primary end point was maintained for 2 months after cessation of therapy. The safety profile was benign. We report the effectiveness of sulodexide as an agent which lowers UAER in type 2 diabetic nephropathy and is capable of normalizing UAER.

CORRELATES OF HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN CKD: RESULTS FROM CRIOS

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The impact of CKD on HRQOL has hitherto been evaluated only in small series. Evaluation of HRQOL is crucial to understand the impact of CKD and to assess interventions designed to alleviate disease burden.

We evaluated the predictors of HRQOL in 987 patients with CKD in 7 North American nephrology practices as part of a prospective cohort study using advanced informatics (CRIOS). HRQOL was evaluated using the validated Kidney Disease Quality of Life (KDQOL) instrument. The population had a mean age of 65, a mean albumin of 3.76 g/dL, a mean hematocrit of 36.6%, with 45% diabetics, and predominant distribution in CKD stages III and above (III 29%; IV 45%; V 18%). Physical composite scores (PCS) declined with age ($p<0.001$), female gender ($p<0.001$), higher CKD stage ($p<0.05$), and presence of diabetes ($p<0.001$). Mental composite scores (MCS) were independent of CKD stage, and worse in females ($p<0.001$) and increased with age ($p<0.05$). Age had a bidirectional effect on HRQOL, negative on physical measures and positive on mental measures. Female gender and requiring EPO were consistently associated with worse HRQOL. Diabetes, low albumin and CKD stage had a physical domain limited effects on HRQOL. Patients with CKD have worse HRQOL than the general population, and the effects of CKD on HRQOL are complex and require a more detailed scrutiny than monolithic examination of composite scores.

RACIAL DIFFERENCES IN THE PROGRESSION OF DIFFERENT STAGES OF DIABETIC NEPHROPATHY

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We conducted this study to determine whether there were any differences in the rate of decline of GFR between Blacks and Whites at different stages of diabetic nephropathy.

We followed 183 patients with diabetic nephropathy over a year period (Black, n=95, White, n=88, mean age 66±10 vs. 70±11 years respectively) at three different time points (initial creatinine, 6 months and 12 months). GFR (ml/min) was calculated by MDRD formula and the baseline (initial) GFR categorized into stage 1&2 (≥60 ml/min) stage 3 (30-60 ml/min) and stage 4 (<30 ml/min). Time dependent changes in GFR for each stage was determined.

For stage 2 patients, mean baseline GFR was 67.1±28.0 vs. 69.3±26.7, p=ns, 6 months 67.8.0±20.0 vs. 65.3±19.1, p=ns and at last clinic visit was 67.1±27 vs. 69.3±26.0, p=ns between Blacks and Whites respectively. For stage 3 patients, mean baseline GFR was 47.9±8.1.0 vs. 49.4±7.2, p=ns, 6 months 46.8±12.9 vs. 49.2±9.7, p=ns and at last clinic visit was 47.7±15.0 vs. 50.9±11.9, p=ns between Blacks and Whites respectively. For stage 4 patients, mean baseline GFR was 22.1±5.2 vs. 21.1±4.0, p=ns, 6 months 22.1±5.2 vs. 21.1±4.0, p=ns and at last clinic visit was 28.4±12.9 vs. 27.4±16.9, p=ns between Blacks and Whites respectively. There were no differences in demographic variables including age and mean HbA1c between Blacks and Whites.

These data demonstrate a lack of differences in changes in GFR over a year period between Blacks and Whites at each stage of diabetic nephropathy. A longer follow up would be needed to validate these findings.

BARRIERS TO ACCESS TO RENAL TRASNPLANTATION AMONG AFRICAN AMERICANS IN THE US- A SYSTEMATIC REVIEW

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African-American patients with end-stage renal disease are much less likely than white patients to undergo renal transplantation. We systematically reviewed the barriers that impede access to renal-transplantation among African-Americans in the United States.

We searched MEDLINE, EMBASE, and CENTRAL for articles that identified the barriers that impeded African Americans access to renal transplantation. Two reviewers independently extracted relevant data from the included studies. Barriers were broadly divided under two categories: 1) Patients related barriers 2) Health care related barriers.

We obtained fifty-nine potentially relevant articles of which only twelve studies were included in the final review. Several patient related barriers and health care related barriers at different stages of the transplantation process were identified. Five studies addressed both patient and health care related barriers whereas two studies addressed health care related barriers alone and four studies addressed patient related barriers alone. Patient related barriers identified included personal beliefs about transplantation, cultural beliefs, lower socioeconomic status and level of education. African Americans personal and cultural beliefs were consistently identified barriers among several studies. Health care related barriers identified at different stages of the transplant process included referral delays by general nephrologists, inadequate transplant workup despite being referred, HLA-mismatching and physician perceptions about African Americans post transplantation survival. Delayed referral by general nephrologists is the consistently identified health care related barrier among these studies.

A wide spectrum of patient-related barriers especially their personal and cultural beliefs about transplantation and several health care related barriers at different stages of the transplant process impede access to renal transplantation among African Americans in the US. Reducing disparities in renal transplantation will require a comprehensive multisectoral approach to these barriers.

SEVELAMER HYDROCHLORIDE VERSUS CALCIUM SALTS AS PHOSPHATE BINDER IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW

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Bone disease occurs secondary to the disturbances of calcium, phosphorus and vitamin D metabolism in kidney disease patients. We evaluated the effects of sevelamer hydrochloride and calcium salts on electrolytes, bone and cardiovascular outcomes in these patients.

MEDLINE, EMBASE, and CCTR were searched for randomized controlled trials comparing sevelamer hydrochloride versus calcium acetate, calcium carbonate and calcium ketoglutarate. Two reviewers independently assessed trial quality and extracted data. Results were expressed as weighted mean difference (WMD) for continuous and as relative risk (RR) for dichotomous outcomes with 95% confidence intervals (CI) using a random effects model.

Eight head to head randomized clinical trials were included in this review. Use of sevelamer hydrochloride had similar impact on serum phosphorus levels and Ca X P product in comparison to calcium salts. However, the incidence of episodic hypercalcemia (serum calcium>11 mg/dl) was lower with sevelamer (6 Studies, 553 patients, RR- 0.27 (CI 0.15, 0.47) along with reduced cholesterol levels and lower hospitalization rates (2 studies, 308 patients, RR-0.65 (CI 0.41, 1.02). Sevelamer hydrochloride reduced coronary calcification scores in comparison to calcium salts (3 studies, 375 patients, WMD: -223.18, (CI -332.18,-114.19).One study showed that the use of calcium salts resulted in lower bone attenuation of thoracic spine.

Calcium salts and sevelamer had similar impact on mineral metabolism except for hypercalcemia.Even though sevelamer use resulted in decreased calcification scores and better bone outcomes, its impact on patient centered end points such as fracture and mortality rates are still not established.

CHANGES IN HEMODIALYSIS (HD) PATIENTS' HEMOGLOBIN (HGB) LEVELS BEFORE AND AFTER HOSPITALIZATION Norma Ofsthun, Fresenius Medical Care, Lexington, MA, USA and Gerard Smits, CSC, Inc., Santa Barbara, CA, USA

Introduction: Hospitalization is common in end-stage renal disease (ESRD) patients on HD and the length of stay is 3-fold higher than non-ESRD patients. Changes in HD patients' level of anemia, that occur before and after hospitalization are not well described. A recent report showed a ↓ in hemoglobin (Hgb) over the peri-hospitalization period (11.4 pre- to 10.7 post-hospitalization, $p<0.0001$; Yaqub, 2001). The purpose of this retrospective analysis was to determine the distribution of peri-hospitalization and post-hospitalization Hgb changes in a large randomly selected sample of HD patients, and to determine the length of time required to restore the Hgbs to pre-hospitalization levels. Methods: Treatment-level data from a large dialysis provider (FMC-NA) was reviewed for the period 7/1/2000 through 6/30/2002 and 60,000 patients were randomly selected. Data included Hgb values pre- and post-hospitalization. Selected patients had to have at least one hospital stay of 4-27 days, with Hgb values in the 60 days pre-hospitalization and post-hospitalization, but ≤ 5 hospitalizations in the two-year period. Results:

Variable	N	M ± SD
Δ Hgb pre to post hospitalization, g/dL	30,557	-0.62 ± 1.68
Δ Hgb Month 1 to Month 2 post-hospitalization, g/dL	30,557	+0.51 ± 1.17

Change in Hgb 1 month pre- to 1 month post-hospitalization

Δ Hgb, g/dL	% of Hospitalizations
< 0	23.14
> 0 to 1	41.54
> 1 to 2	25.79
>2	9.52

Conclusions: Hospitalization in HD patients is associated with a drop in mean Hgb and return to pre-hospitalization Hgb levels is delayed by an average of > 2 months.

PREVALENCE OF VITAMIN D DEFICENCY/ INSUFFIENCY IN NONDIALYZED (ND) HISPANIC PATIENTS (HP) WITH CHRONIC KIDNEY DISEASE (CKD)

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25- hydroxyvitamin D (25OHD) deficiency may be associated with secondary hyperparathyroidism (SHPT), reduced bone mineral density, and increased hip fractures. Low 25OHD levels have been documented in ND-CKD patients. However, similar data are not currently available in nondialyzed HP with CKD. We routinely obtain intact PTH, calcium, phosphorus, and vitamin D levels in our ND-CKD patients in the renal clinic at Texas Diabetes Institute. In this study, we reviewed medical records and laboratory data of 196 patients to determine the prevalence of vitamin D deficiency/insuffiency and high PTH levels. GFR estimated by simplified MDRD equation. Patients receiving vitamin D or phosphate binders were excluded Of the 196 CKD patients, 156 were HP. Mean age 57 years. 42% males.

	Stages 1& 2	**Stage 3**	**Stage 4**	**Stage 5**
25OHD (ng/ml) **< 30** **<15**	 **81%** **38%**	 **82%** **27%**	 **80%** **48%**	 **100%** **65%**
1,25(OH)2D (ng/ml) (< 35)	**56%**	**87%**	**92%**	**92%**
PTH (pmol/ml)	**(>65) 13%**	**(> 70) 56%**	**(> 110) 58%**	**(> 300) 24%**
Calcium < 8.4 mg/dl	**0.6%**	**1.7%**	**17%**	**2%**
Phosphorus > 4.6 mg/dl	**0%**	**2%**	**7%**	**(>5.5) 24%**

Conclusions: Vitamin D deficiency/ insufficiency and SHPT are common in all stages of CKD in HP despite living in Southern geographical location. In contrast, hyperphosphatemia and hypocalcemia are not common suggesting that low vitamin D levels may represent the initial stimulus for PTH secretion in CKD.

UNDER-RECOGNITION OF CHRONIC KIDNEY DISEASE IN HOSPITALIZED PATIENTS

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Timely identification of chronic kidney disease (CKD) is crucial in reducing cardiovascular risk, medical errors, and delaying progression to end stage renal disease. Under-recognition of CKD in the hospital setting may be an important impediment to achieving this goal. We sought to quantify the frequency with which CKD is properly identified in an inner-city teaching hospital.

Serum creatinine values were screened in adult patients during November 2004, adult out patients with CKD were identified and patients with ESRD, renal transplant and acute renal failure (ARF) were excluded. Primary and secondary discharge diagnosis were matched to ICD-9 codes.

1345 patients were screened and 105 patients with CKD form the study group. Mean age 65, males - 62%, Caucasians 36%, African-Americans 24 % Hispanic 27% There were 2.5 hospitalizations per patient,6 secondary diagnoses per hospitalization(range 1-16). Mean serum creatinine was 2.7(SD 1.6) and MDRD GFR was 32 ml/min (SD 14, range 6-58). 48% of patients had CKD ICD codes.

Kidney disease was not recognized in more than half of hospitalized patients with CKD. Nephrologists should take the lead in their respective institutions to assure improved recognition of CKD during hospitalizations.

PLASMA ADIPONECTIN AND CLINICAL OUTCOMES AMONG HEMODIALYSIS PATIENTS

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Low adiponectin (ADPN) levels may be associated with insulin resistance, inflammation and adverse cardiovascular outcomes among hemodialysis patients. We measured plasma adiponectin levels in 182 hemodialysis (HD) patients enrolled into the baseline phase of the NIH-HEMO study with a mean±SD age 62±12 years, duration on HD of 3.7±4.2 and serum albumin 3.6±0.4 g/dL; 47% were male, 41% diabetic, 42% African American and 67% had pre-existing vascular disease. Plasma ADPN was normally distributed, with a mean±SD of 17.2±8.8 and median of 16.7 mcg/mL. In contrast to previous observations, plasma ADPN was not lower in men or diabetics and did not show a relationship to age, race or duration of HD. Lower ADPN levels were seen with pre-existing vascular disease (18.9±10.1 vs 16.3±7.9 mcg/mL; $p=0.06$) and extremely low Karnofsky index (KI) scores (KI<50: 9.8±6.1 vs KI≥50: 17.6±8.8 mcg/mL; $p<0.01$). There was an inverse correlation with body mass index (BMI) ($r=-0.16$, $p=0.04$) and (log) CRP ($r=-0.14$, $p=0.06$). The inverse relationship with CRP was stronger among diabetic patients ($r=-0.29$, $p=0.01$) and those with higher comorbidity (index of coexistent disease score of 3; $r=-0.33$, $p=0.01$). However, plasma ADPN was not an independent predictor of overall mortality or cardiovascular mortality in either the entire cohort or within high-risk subsets (diabetics, high comorbidity).

In summary, plasma ADPN is not a predictor of clinical outcomes in stable HD patients unlike established markers such as CRP, although its significance among higher risk patients needs further investigation.

IS CHRONIC KIDNEY DISEASE COMPARABLE TO DIABETES AS A CORONARY ARTERY DISEASE RISK FACTOR? EVIDENCE BASED ON WHITEHALL ECG CRITERIA FOR ISCHEMIA IN A LARGE SCREENING POPULATION

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Background. Chronic Kidney Disease (CKD) is one of the known risk factors for coronary heart disease (CHD). Though ECGs have limited accuracy for determining true prevalence of CHD, we wondered whether CKD and DM controlled for hypertension (HTN), had similar prevalence of ECG abnormalities that could reflect underlying coronary heart disease.

Method. Data were collected for 5942 men and women aged 30-69 years in the Tehran Lipid and Glucose Study (TLGS), a cross-sectional phase of a large epidemiological study first initiated in 1999. ECG findings of all subjects were coded according to Minnesota ECG coding criteria. The Whitehall criteria for abnormal ECG findings that could represent ischemia were utilized. GFR was estimated using the Cockroft-Gault equation. Subjects with moderate CKD and without DM were compared to the patients with DM without CKD. The analysis was performed for all Whitehall ECG ischemia abnormalities combined, and separately for pathologic Q waves.

Results. In spite of an overall similar prevalence of smoking, and a lower incidence of dyslipidemia and HTN, and in an aged matched group, the prevalence of ECG abnormalities was 19.3%, in patients with DM and no CKD and it was similar to the patients with moderate CKD and no DM (19.7%) (p=0.9). The prevalence of pathologic Q waves was 11.45% compared to 11.5%, respectively.

Conclusion. Moderate CKD is a major risk factor for the development of the Whitehall ECG criteria which have been associated with ischemic heart disease. The importance of CKD as a risk factor for ECG abnormalities is comparable with DM. Patients with moderate CKD probably are candidates for aggressive CHD risk modification.

CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH PULMONARY HYPERTENSION AND RIGHT HEART DYSFUNCTION

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The aim of this study was to assess the association of CKD with abnormal right heart hemodynamics and pulmonary arterial hypertension (PAH).

We identified 193 consecutive ambulatory patients who had undergone right heart catheterization. Hospitalized patients and patients with acute kidney injury were excluded. Data abstracted from patient medical records included: demographics; history of diabetes mellitus, hypertension, and smoking; laboratory data; and cardiac catheterization data. Serum creatinine was used to calculate GFR using the MDRD equation. CKD was defined as a calculated GFR < 60 mL/min/1.73m^2. Demographic, clinical, and hemodynamic data were compared between patients with and without CKD. Logistic regression was used to determine odds ratios (OR) for CKD in patients with PAH with and without adjustment for age, gender, and cardiac index.

CKD was present in 91 of 193 (47%) patients. CKD was associated with male gender (p=0.03) and older age (p=0.01) but was not associated with body mass index, hyperlipidemia, hypertension, diabetes mellitus, or smoking. By univariate analysis, CKD was associated with higher right atrial mean pressure (p=0.02), right ventricular (RV) systolic pressure (p=0.007), RV end diastolic pressure (p=0.05), pulmonary artery (PA) mean pressure (p=0.01), PA systolic pressure (p=0.03) and lower PA oxygen saturation (p=0.03). There was no association between CKD and cardiac index (p=0.16) or aortic systolic pressure (p=0.08). PAH, defined as PA mean pressure > 25 mmHg, was present in 117 of 193 (61%) patients and was associated with CKD (odds ratio 2.6, 95% confidence interval, 1.5 to 4.9, p=0.002). After adjustment for age, gender, and cardiac output this association persisted (OR 2.3, 95% CI 1.1-4.9, p=0.04).

In conclusion, PAH and right heart dysfunction are associated with CKD. The association of PAH with CKD appears to be independent of left heart function.

ANEMIA, HOSPITALIZATIONS, AND FALLS IN NURSING HOME POPULATION WITH CHRONIC KIDNEY DISEASE

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This study was undertaken to determine if a relationship exists between history of falls, hospitalizations, and anemia in nursing home residents who have chronic kidney disease (CKD).

Retrospective chart review of 148 nursing home patients with history of anemia and CKD was undertaken.

Patient demographics were collected, including age, sex, race, and smoking history. History of co-morbidities including history of heart disease, COPD, and cerebrovascular disease, were noted. Use of certain antihypertensive medications, baseline blood pressure, hemoglobin (Hgb) and serum creatinine were also noted. There was no significant correlation between a history of falls and anemia defined as Hgb levels<13mg/dl for males and <12mg/dl for females (13% in non-anemic vs. 7.7% in anemic. P=0.65). There was a lower prevalence of falls among patients on ACE-inhibitors or ARB therapy, though this result was not statistically significant (11%vs 20%, p=0.42). There was also no significant difference in the mean systolic and diastolic blood pressures between the groups.

Our preliminary data were unable to demonstrate a statistically significant correlation between anemia, anti-hypertensive medication use, and a history of falls in nursing home patients with CKD.

RACIAL DIFFERENCES IN PROGRESSION OF DIABETIC NEPHROPATHY UNDER EQUIVALENT GLYCEMIC CONTROL

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Although diabetes is the leading cause of End Stage Renal Disease in the USA and more prevalent in Blacks than Whites, the impact of race and glycemic control on rate of decline of glomerular filtration (GFR) in diabetic nephropathy is unclear.

We followed 183 patients with diabetic nephropathy over a year period (Black, n=95, White, n=88, mean age 66±10 vs. 70±11 years respectively) at three different time points (initial creatinine, 6 months and 12 months), to determine differences in GFR decline. GFR (ml/min) was calculated by MDRD formula and glycosylated haemoglobin A1C (HbA1c) was categorized into tertiles (<7%, 7-8% and >8%) at each time point. The two racial groups were compared for GFR at each tertile of HbA1c and other continuous variables using T-test and Chi square as appropriate.

Mean initial GFR was 47.0±20.9 vs. 54.1±20.2, p=0.045, 6 months 45.0±19.0 vs. 51.5±17.1, p=0.018 and at last clinic visit was 47.1±22 vs. 53.5±21.0, p=0.022 between Blacks and Whites respectively. Mean change in GFR over the 12 months was not significantly different between the two groups (-0.3±17.3 vs. -0.3±15, p=0.88). No significant differences at any time point were noted when the two groups were compared for mean GFR at each tertile of HbA1c. Similarly, within each racial group, GFR was not significantly different at each tertile of HbA1c.

Our data suggest that under equivalent glycemic control, although baseline GFR appeared to be slightly higher in Whites, no differences in GFR decline over one year period could be detected.

A PROSPECTIVE OBSERVATIONAL REGISTRY ASSESSING THE MANAGEMENT AND PROGRESSION OF SECONDARY HPT IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD): METHODS AND OBJECTIVES

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Disturbances in bone mineral metabolism are associated with increased morbidity and mortality in CKD patients (pts). Currently there are limited prospectively collected long-term pt data that can provide insight regarding treatment practices, disease progression, and clinical outcomes for CKD pts across the continuum of disease. Thus, a 5-year, prospective, observational registry to assess these interactions in a real-world setting was initiated. The 1000 pt population will be derived from 4 CKD strata: stage 4 with bio-intact PTH (biPTH) <59 pg/mL (n=100) or ≥59 pg/mL (n=300), or stage 5 on dialysis with biPTH <160 pg/mL (n=200) or ≥160 pg/mL (n=400). Pts will be enrolled over 12 months (mo) and followed for 60 mo. Currently 796 pts have enrolled over 11 mo. Primary study objectives are to describe current and evolving patterns of secondary HPT management; to assess KDOQI™ bone and mineral metabolism target achievement over time; to determine the relationship of practice patterns and target attainment to clinical outcomes (CO), health resource utilization (HRU), and pt-reported outcomes (PRO); and to evaluate the effect of the calcimimetic cinacalcet HCl on KDOQI™ target attainment, CO, HRU, and PRO. Key data being collected include biPTH, Ca, P, and Ca x P; secondary HPT therapies; CO, eg, dialysis status changes, bone and cardiovascular (CV) disease, parathyroidectomy, fractures, all-cause and CV mortality; HRU, eg, all-cause and CV hospitalizations, length of stay, and emergency room and outpatient visits; and pt-reported quality of life. Assessments will be collected quarterly for the first 24 mo and semi-annually thereafter. This CKD registry will provide a comprehensive insight into clinical management, disease progression, and CO in pts with secondary HPT, thereby providing the nephrology community with an important new source of clinical information.

ACHIEVMENT OF KDOQI GUIDELINES FOR BONE METABOLISM IS MORE FREQUENT AMONG HD PATIENTS RECEIVING DOXERCALCIFEROL (D) AND PARICALCITOL (P) VERSUS CALCITRIOL (C)

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Intravenous vitamin D (IVVD) is standard therapy for secondary hyperparathyroidism among HD patients. We postulated that achievement of KDOQI guidelines for PTH, calcium and phosphorus is more frequent among D- and P- vs. C-treated patients. To explore this hypothesis we studied incident HD patients in DCI facilities between 1999 and 2004 who received D (n=1,354), P (n=1,129) or C (n=1,655) for ≥ 180 days. The percentage (%) of patients achieving KDOQI guidelines was calculated at baseline and after six months on IVVD. Overall, achievement of targets was more common in DCI study population compared to the US DOPPS cohort.

% achieving target	Baseline			After 6 mo on IVVD		
	D	P	C	D	P	C
Calcium	**56.6**	**57.7**	**44.2***	**62.1**	**59.6**	**59.5**
Phos	**56.0**	**56.3**	**54.1**	**48.4**	**46.7**	**48.7**
iPTH	**31.7**	**34.7**	**38.6***	**35.3**	**35.1**	**28.9***

*$p<0.05$ for C vs. D and P

In summary, achievement of the PTH but not the calcium and phosphorus guidelines was more common among D- and P- vs. C-treated patients. Mechanisms other than direct effects on calcium-phosphorus metabolism are likely to contribute to the improved control of PTH levels among D- and P-treated patients. Further studies are needed to assess what seem to be vitamin D2-specific mechanisms of action.

THERAPY WITH DOXERCALCIFEROL (D) AND PARICALCITOL (P) RESULTS IN SIMILAR CHANGES IN SERUM PTH, CALCIUM (CA) AND PHOSPHOROUS (PHOS)

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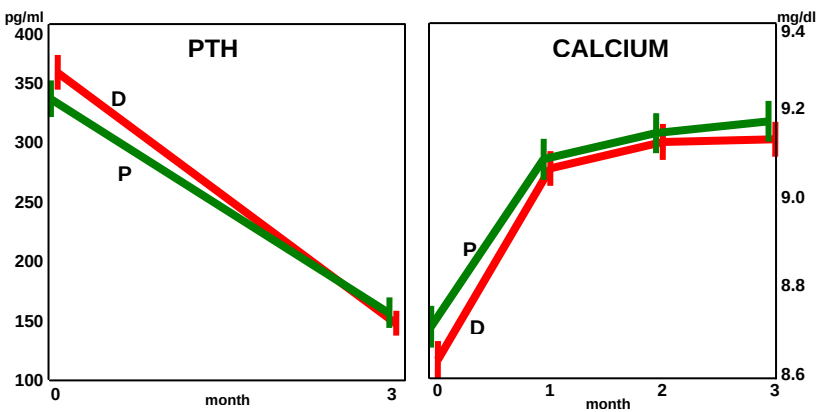
Compared to calcitriol, P has been reported to induce greater reductions in serum PTH and smaller changes in Ca and Phos. A direct comparison of the effects of D - the other widely used vitamin D2 analog- with P has not been reported.

We postulated that D and P have similar effects on serum PTH, Ca and Phos. To explore this hypothesis we studied incident patients treated in DCI facilities between 1999 and 2004 who received D (n=2,010) or P (n=1,697) for ≥ 90 days. D and P were equally effective in reducing PTH and produced similar changes in serum Ca (figure). Incidence of hypercalcemia did not differ between the two groups. Serum Phos was similar among D- and P-treated patients at baseline and at months1, 2 and 3.

In conclusion, D and P produce similar effects on serum PTH, Ca and Phos



SUPERIORITY OF CREATININE CLEARANCE IN PREDICTING SURVIVAL AFTER LOWER EXTREMITY BYPASS SURGERY

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Purpose: To examine the predictive power of serum creatinine, estimated creatinine clearance, and other patient characteristics for long-term survival after major vascular reconstruction. **Methods:** A retrospective review of this institution's vascular registry was performed. Logistic regression analysis was conducted to determine independent predictors of postoperative mortality. Creatinine clearance was estimated as [[140 -age (yr)] * weight (kg)] / [72 * serum Cr (mg/dL)] (multiplied by 0.85 for women).] **Results**: 252 patients underwent infrainguinal bypass procedures between August 1999 and May 2000. Demographics included average age 68 years, 65% male, 74% diabetic, 12% dialysis-dependent, 23% history of CHF, 12% history of stroke, and 20% serum creatinine greater than 2.0 mg/dL. One-year mortality was 16% (n=40), 2-year mortality 25% (n=64), and 3-year mortality 35% (n=88). There was no difference in serum creatinine values between survivors and no-survivors at one (1.8 vs 1.9, p=0.802), two (w.8 vs 2.0, p=0.618), or three years (1.8 vs 2.0, p=0.241). Serum creatinine greater than 2.0 mg/dL did not predict long-term adverse outcomes. In contrast, reduced creatinine clearance (≤ 60 mL/min) was an independent predictor of mortality (1-yr: OR=2.53, p=0.014; 2-yrs: OR=2.46, p=0.004; 3-yrs: OR=2.45, p=0.001), and creatinine clearance was higher for survivors at all three time points (1-yr; 70.2 vs 49.5, p=0.003; 2-yrs: 72.3 vs 51.2, p<0.0001; 3-yrs: 74.7 vs 52.6, p<0.0001). Other independent predictors of mortality included a prior history of stroke and CHF. **Conclusions:** Independent of dialysis status, a decreased creatinine clearance, but not elevated serum creatinine alone, is an independent predictor of mortality after lower extremity arterial reconstruction. Determination of creatinine clearance should be included in all preoperative risk evaluations of such patients.

CAN DECREASES IN RENAL TRANSPLANTATION HEALTH DISPARITIES FOR MINORITIES BE ACCOMPLISHED BY INCREASING RENAL TRANSPLANTATION HEALTH LITERACY?

Carlumandarlo Zaramo, Andrew Novick, Charles S. Modlin Jr.

In accordance with the US Department of Health statistics substantiating that kidney disease affects African Americans(AA) disproportionately, the rate of end stage renal disease (ESRD) and renal failure in AA outnumbers that of their non-minority counterparts by 4 to 1. Several explanations have been theorized for this type of disparity in disease prevalence between each group.We hypothesize that the ability to read, write, and comprehend health information inevitably has a significant effect on an individual's ability to manage their renal illness.We hypothesize that racial disparity in the rate of defined renal failure/transplantation correlates to disparities in renal health literacy. To effectively decrease renal transplantation health disparities for patients at the Cleveland Clinic Foundation Minority Men's Health Center (MMHC) the need exists to increase "Renal Failure-Transplantation Health Literacy "(RTx-HL). To consistently identify and assess the renal failure-transplantation health literacy among these patients (RTx-CCF). AA's N=36 and Caucasian-Americans (CA's) N=36(Mean ages= 52) were asked to complete the "newly" modified transplantation version of the Rapid Estimate of Adult Literacy in Medicine (REALM),referred to as the Rapid Estimate of Adult Kidney Literacy in Medicine (K-REALM), prior to Educational Assessment and "Novel" Tool Kit. The K-REALM is simple 2 min., 66 medical kidney disease/transplantation word pronunciation test. After administration of the K-REALM , a pilot study of N=71 of the same patients were assessed with K-REALM Toolkit and renal transplantation education intervention to improve renal health literacy. **Figure 1.** shows the K-REALM® scores for AA were 45 and 54 for CA. After "the novel-REALM Health Literacy Tool Kit" and Educational intervention, Health literacy scores improved significantly to 56 for AA to 60 for CA's. Our hypothesis shows the need to implement educational policies that will help reduce renal failure-transplantation health literacy disparities in this specific cohort of minority patients.

RACIAL DIFFERENCES IN ALBUMINURIA AND DECREASED KIDNEY FUNCTION: A COMPARISON BETWEEN A CHINESE COMMUNITY BASED SCREENING STUDY AND THE NHANES 1999-2002

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Purpose: It is unknown whether the epidemic of unrecognized chronic kidney disease (CKD) seen in the US general population is as marked in other countries. We compared the prevalence of CKD in general population samples from the US and Mainland China to address this question.

Methods: We selected White and African-American participants, ≥ 40 years from the US NHANES 1999-2002 survey (N = 6,475, including 3,509 Whites 1,236 African-Americans and 1,730 Hispanics) and compared them with participants from a Chinese sample, studied in 2004 (N = 2,310). Serum creatinine was directly calibrated at the Cleveland Clinic Laboratory in both studies, and the abbreviated Modification of Diet in Renal Disease (MDRD) equation was used to estimate GFR.

Results: In spite of similar age distributions, eGFR < 60ml/min/1.73m^2 was less prevalent in Chinese participants (3.0% Vs 4.9% in [US] Whites, 4.9% in African-Americans, and 3.4% in Hispanics, P =0.0007). Urinary albumin/creatinine ratios (UACR) > 30mg/g were also less prevalent in the Chinese populations (6.2 Vs 13.3 Vs 18.5 Vs 17.1, P < 0.0001). These disparities persisted when adjustment was made for age, gender, body mass index, education, smoking, diabetes, hypertension, disease duration of DM and medication.

Conclusion: CKD appears to be at least as common in China as in the US, and is characterized by much less proteinuric disease and decreased kidney function. These findings may have implications for population screening strategies.

HIF1 AND VHL IN MURINE PODOCYTES ARE DISPENSIBLE FOR NORMAL GLOMERULAR DEVELOPMENT

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The role of hypoxia in podocyte biology has not been thoroughly elucidated previously, despite extensive knowledge about significance and mechanism of hypoxic injury to the tubular nephron segments. Hypoxia-inducible factors (HIFs) mediate the cellular transcriptional response to hypoxia, resulting in upregulation of target genes. Under normoxia, von Hippel-Lindau tumor suppressor protein (pVHL) targets HIF α subunits for destruction in the proteasome. Mouse models with podocyte-specific conditional HIF1α and VHL inactivation via the cre/loxP technology were created with cre recombinase expression under the NPHS2 promoter. Mice of mixed background remained viable and healthy in the VHL, HIF1α, and combined VHL / HIF1α deletion models. The lack of a prominent murine phenotype in podocyte VHL deficiency with subsequent HIF1 upregulation under physiologic conditions is in accordance with the absence of a susceptibility to significant glomerular abnormalities in human VHL disease. HIF1 is also functional in podocytes under exposure to hypoxia in vitro, with HIF1 protein stabilization and increased transcription of target genes relevant for angiogenesis and metabolism, such as VEGF, PGK, and Glut1. A novel podocyte cell line bearing simian virus 40 large T antigen and VHL 2lox alleles was established and exhibited typical podocyte markers such as Wt1, nephrin, and synaptopodin. Treatment with cre recombinase adenovirus and ensuing VHL loop-out mimicked hypoxic conditions by HIF1 stabilization and target gene transcription. VHL deletion also lead to attenuated proliferation of undifferentiated and reduced survival of differentiated podocytes. The contribution of HIF1 and VHL in podocytes as part of the glomerular filtration barrier is therefore not required for the development and maintenance of glomerular capillaries, but HIF pathway components participate in podocyte metabolism and cell cycle regulation.

CORTICOSTEROID THERAPY IN HUMAN IMMUNODEFICIENCY VIRUS-ASSOCIATED NEPHROPATHY

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Untreated human immunodeficiency virus-associated nephropathy (HIVAN) progresses to end-stage renal disease over weeks to months. We examined the effect of corticosteroids in HIVAN therapy in the era of highly active antiretroviral therapy.

One hundred forty five HIV-infected patients who had a kidney biopsy at our institution between the years 1995 and 2004 were identified. The kidney biopsy reports were examined including electron microscopy and immunofluorescence and patients with the diagnosis of HIVAN were selected. Sixty two patients were eligible for inclusion. The follow-up period was defined as the time from kidney biopsy to the time of doubling of serum creatinine, initiation of dialysis or death.

In univariate analysis the use of antiretrovirals, corticosteroids and ACEI/ARB was significantly associated with better renal survival (RR 0.42, 95%CI (0.22-0.82), p=0.01, RR 0.36, 95%CI (0.18-0.69), p=0.002, RR 0.48, 95%CI (0.24-0.02), p=0.02, respectively). The median survival time was 52 months for patients with HIVAN who received corticosteroids compared to 10 months in the group that did not receive corticosteroids (adjusted for serum creatinine, proteinuria, CD4 count, hepatitis C, hypertension, ARV, and ACEI/ARB). In multivariate Cox proportional hazard model including serum creatinine, proteinuria, CD4 count, hepatitis C antibody status, and the use of corticosteroids, ARV, and ACEI/ARB, only corticosteroid therapy was significantly associated with better renal survival (risk ratio 0.32, 95% CI 0.13-0.82, p=0.01).

In this retrospective analysis, the use of corticosteroids in patients with HIVAN was associated with better renal survival.

RESOLUTION OF NEPHROTIC-RANGE PROTEINURIA WITH BEVACIZUMAB-BASED CHEMOTHERAPY IN A CASE OF SECONDARY MEMBRANOUS NEPHROPATHY

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Underlying malignancy is thought to be responsible for 5-10% of cases of membranous nephropathy. Bevacizumab (Avastin ®) is a humanized recombinant monoclonal antibody against vascular endothelial growth factor (angiogenesis inhibitor) recently approved for the treatment of metastatic colorectal cancer. One of its complications is proteinuria and nephrotic syndrome, making the treatment decisions challenging for patients who already have proteinuria.

We report a case of a 26-year old Caucasian female who was found to have proteinuria in the setting of metastatic colorectal cancer. She had undergone a hemicolectomy and received one cycle of FOLFOX-6 (oxaliplatin and short term infusional 5-flourouracil and leucovorin) and bevacizumab. Prior to these, she was found to have 4 plus protein on dipstick urine. At formal nephrology evaluation, she had 6.8gm protein/24 hour urine. Serologic studies and renal biopsy were consistent with a diagnosis of secondary membranous nephropathy. Bevacizumab based chemotherapy was resumed. Still her proteinuria improved. At 4 months, she had only 325mg of protein/24 hour urine collection. Her renal function remained normal.

30-40% of patients with colorectal cancer have metastasis at the time of diagnosis and as such surgery is not curative. Bevacizumab has been shown to improve survival in metastatic colorectal cancer when added to standard chemotherapy. However, the safety of continued treatment in patients with proteinuria is undetermined. To our knowledge this is the first case report of resolution of nephrotic proteinuria while undergoing treatment with bevacizumab. This may be due to reduction of tumor mass and disappearance of tumor related factors (antigens) which had been deposited at subepithelial space. Based on our experience, we proposed that the use of bevacizumab may be justified, despite manufacture’s warning, in a patient with pre-existing proteinuria, provided that the proteinuria is closely monitored and improving

MINIMAL CHANGE DISEASE WITH INCIDENTAL MESANGIAL IGA DEPOSITS PRECEDING HODGKIN'S LYMPHOMA Dijana Jefic, Joel Topf; St.John Hospital and Medical Center, Detroit, MI, USA

IgA nephropathy presents with nephrotic syndrome in up to 13% of cases. This presentation is associated with severe focal proliferative glomerulonephritis and significant sclerosis. Minimal change disease (MCD) is a cause of nephrotic syndrome in 10-15% of adults. Most commonly it is associated with hematologic malignancies, such as Hodgkin's lymphoma (HL). The onset of nephrotic syndrome is typically simultaneous with the diagnosis of lymphoma.

We are reporting a case of MCD with mesangial IgA depositions preceding the presentation of HL. The patient is a 23-year-old white male with no significant past medical history who was presented to the ER with lower extremity edema. The patient had a one-week history of generalized body aches and weakness. He also noted a 25-pounds weight gain. Initial labs: urinalysis > 300 protein, 1 RBC, 2 WBC per HPF, no casts. BUN 19, creatinine 1.4, total protein 3.4, albumin 1.3. Random urine spot protein to creatinine ratio: 10.1. Total cholesterol 384, HDL 39, LDL 276. Hemoglobin 17.1 plts 270. Total complement, C3, and C4 normal. Hepatitis B, C, ANA, dsDNA, HIV negative. Kidney biopsy was preformed. Light microscopy showed mild segmental increase in mesangial cellularity. IF was positive for mesangial IgA and C3 staining. EM revealed diffuse epithelial foot processes fusion. Diagnosis of IgA nephropathy was made. He was treated with prednisone 60 mg per day for 2 months. Proteinuria ceased and steroids were tapered off over the ensuing couple of months. Six months later he developed cervical lymphadenopathy. Bone marrow biopsy showed Hodgkin's lymphoma. Patient is undergoing chemotherapy at this time. Nephrotic syndrome is in remission to date.

We conclude the patient has a MCD with incidental mesangial IgA deposits. The phenomenon of mesangial IgA deposits in patients with MCD is reported to be 23.8%. The IgA deposits have neutral influence on the course of MCD and disappear with successful treatment. Rapid response to steroid therapy and the later diagnosis of HL support diagnosis of MCD. The diagnosis of HL following the diagnosis of MCD has rarely been reported in the literature.

AUTOSOMAL DOMINANT MULTIPLE LIPOMATOSIS, RENAL CELL CARCINOMA, SPINAL ARTERIOVENOUS MALFORMATION IN A YOUNG MAN: A NEW SYNDROME?

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Renal cell carcinoma (RCC) is rarely associated with inherited syndromes. We report a 31 year old male who was referred from out side center for the evaluation of glomerulonephritis in January 2004. He underwent intermittent hemodialysis (IHD) for 3 months prior to presentation. There was no family history of any kidney disease, but the patient reported multiple lipomas in several of his family members. On examination he was hypertensive 160/98 mm Hg, and skin examination showed multiple lipomas in the extremities and trunk, with sizes ranging from .5cm x 1cm to 1.5cmx 1cm. His renal biopsy showed membranoproliferative glomerulonephritis, and electron microscopy showed dense deposits in sub endothelial and sub epithelial spaces. A work up for vasculitis and autoimmune disorders was negative. He was started on prednisone and mycophenolate mofetil and continued with IHD. In June 2004, he developed hematuria and non specific abdominal pain. An ultrasound done at that time showed a mass in the right kidney measuring 3.5x 2.8 cm. He underwent right nephrectomy, which showed grade 2 renal cell carcinoma clear cell type. In November 2004, he developed lower back pain and marked weakness of his lower extremities. An MRI done at that time showed herniation of lumbar disc. He underwent lumbar diskectomy . After surgery his weakness improved and he was able to ambulate with support. In February 2005, he had progressive weakness and numbness of lower extremities, MRI of the spine was suggestive of arterio venous fistula (AVF) of spine in thoracic vertebra. A conventional catheter spinal arteriogram confirmed the diagnosis of dural AVF, at right T5 pedicle. He underwent T5 laminectomy and disconnection of AVF. Followng surgery there was improvement of muscle strength in his lower extremities. His dialysis requirement went up to four times a week because of poor compliance with diet. Autosomal dominant multiple lipomatosis is an extremely rare entity and a combination of this with RCC and spinal AVF could represent a new syndrome.

ALBUMIN PERMEABILITY (Palb) IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS) IS ASSOCIATED WITH RAPID PROGRESSION TO END-STAGE RENAL DISEASE (ESRD)

Sudhindra Pudur, Virginia J. Savin, Ellen T. McCarthy, Mukut Sharma

Background: A circulating factor in serum or plasma of patients with FSGS increases glomerular macromolecular permeability during *in vitro* testing. Permeability activity has been verified in functional assays and defined by P_{alb}. This study was done to determine if high levels of P_{alb} activity are associated with severe disease as defined by rapid progression to ESRD.

Methods: P_{alb} activity was determined on samples submitted to our laboratory in the course of clinical evaluation of FSGS from 1/00 to 12/04. Samples analyzed were those of patients with biopsy diagnosis of FSGS in native kidney or renal allograft (recurrent FSGS). We defined the date of diagnosis as the biopsy date, and the date of progression to ESRD as the date of first renal replacement therapy (dialysis or transplantation) or date when GFR was less than 15 ml/min as estimated by MDRD formula. Post-plasmapheresis specimens were excluded. Rapid progression was defined as development of ESRD < 3 years from diagnosis of FSGS. P_{alb} value ≥ 0.5 was considered high.

Results: Complete data were available on 80 samples. Patients ranged in age from 1 to 63 years; 35 patients were male, 53 were Caucasian. The relationship between time of diagnosis and time to ESRD and P_{alb} was compared using chi-square analysis. There was a significant relationship between rapid progression and high P_{alb} ($P<0.0167$). Odds ratio for rapid progression was 3.37 (95 % CI 1.13-10.29) in patients with $P_{alb} \geq 0.5$ vs $P_{alb} < 0.5$.

Conclusions: High P_{alb} is associated with rapid progression to ESRD in FSGS. Odds of rapid progression were 3-fold greater when $P_{alb} \geq 0.5$ compared to $P_{alb} < 0.5$. P_{alb} may be useful to predict progression to ESRD and may identify patients at risk for rapid progression who would benefit from aggressive treatment and/or novel therapies to prevent progression.

MYCOPHENOLATE MOFETIL TREATMENT FOR GLOMERULAR DISEASE

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This study assessed the clinical efficacy of mycophenolate mofetil (MMF) treatment in primary and secondary glomerular disease (GN) .Between December 1999 and July 2004, we studied 22 patients who had biopsy proven GN complicated by renal insufficiency and/or nephrotic proteinuria. There were 12 male and 10 female patients. Mean age was 43.8±16.7 years. Acute GN included IgA GN (n=2): FSGS (n=7): polyarteritis nodosa (n=1): Lupus nephropathy (n=6): membranoproliferative GN (n=3): and membranous nephropathy (n=3).Mean duration of MMF treatment was 20.8 months. Mean 24 hour urine protein before and after MMF was 3.65±2.89gm and 2.77±3.25gm (p=0.343). Mean Serum creatinine before and after MMF was 2.13±1.42mg/dl and 2.19±1.26mg/dl (p=0.805).Creatinine clearance before and after MMF was 63.9±39ml/min and 54.8±35.7ml/min (p=0.211). Mean Albumin before and after MMF was 3.47±0.75g/dl and 3.83±0.53g/dl (p=0.005). Empirical MMF therapy in acute GN complicated by renal insufficiency and/or nephritic proteinuria was well tolerated and achieved the goals of steroid withdrawal, improvement of proteinuria and stabilization of renal function. No significant side effects was encountered during more than 24 months of follow-up.

CASE OF IGA NEPHROPATHY IN A PATIENT WITH BEHCET'S SYNDROME

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Renal involvement is not common in Behcet's syndrome (BS) and consists of occasional reports of patients having glomerulonephritis, renal amyloidosis and renal vein thrombosis. We report on a patient with rare association of BS and IgA nephropathy (IgAN).

An 18 year old Japanese male had history of multiple recurrent oral and genital ulcers, erythema nodosum, folliculitis, and intermittent arthritis of the knees. He was clinically diagnosed with BS about a year ago, followed by a positive pathergy reaction. He also carried HLA B5. Patient had no history of any vision problems and his recurrent oral and genital ulcers are being treated with pain medications and topical steroids.

Patient was referred to the nephrology clinic because of an incidental finding of proteinuria on routine urine analysis which is confirmed by 24 hour urine showing 2.6 g/day of proteinuria. On physical examination, the patient had oral ulcers and multiple scars in scrotal area of previously healed genital ulcers. Erythema nodosum and mild painful swelling of the ankles were also noted. An ophthalmologic examination was unremarkable. The blood pressure was 126/78 mm/Hg and pulse of 68. The patient had no fever, JVD and peripheral edema. Laboratory data showed Scr of 0.9 mg/dl and BUN of 20 mg/dl, with normal electrolytes and albumin. Serological tests for complement levels, rheumatoid factor, antinuclear and anticytoplasmic antibody, immunoglobulin levels, syphilis, hepatitis serology, HIV, serum and urine immunofixation and cryoglobulin were negative.

The renal biopsy showed features of mesangiocapillary glomerulonephritis. Immunohistology revealed membrane deposits of IgA and staining for C1q along the capillary wall. Staining for IgG, IgM, C3, kappa and lambda were negative. Staining with congo red showed no evidence of amyloidosis.

Patient was started on angiotensin receptor blocker, and at his 6 month follows up, the 24 hour urine showed decrease in proteinuria to 1.4 g/day with normal kidney functions.

The co-occurrence of IgAN and BS has only been reported twice to our knowledge. IgAN is the most common form of glomerulonephritis. There might be a relationship between IgAN and BS but simple coincidence cannot be excluded.

AMELIORATION OF PODOCYTE DAMAGE IN THE TG(REN2)27 (REN2) TRANSGENIC RAT WITH AT1 RECEPTOR BLOCKADE

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TG(mRen2)27 (Ren2) transgenic rats are used to study overexpression of renin-angiotensin-system with elevated tissue levels of angiotensin-II (Ang-II) and hypertension (HTN). HTN can lead to proteinuria. Integral to the filtration barrier are podocytes and changes characteristic of nephropathy include effacement and loss of slit-pore diaphragm. Treatment with an AT_1 receptor (AT_1R) blocker (Valsartan) is known to reduce proteinuria but it is not known what effects Valsartan treatment has on structural changes of podocytes. Sprague-Dawley (SDC), Ren2 (RC), and Ren2 rats were treated with Valsartan (RV) (30mg/kg) given in their drinking water for 3 weeks. Proteinuria was measured following treatment and normalized to creatinine level. We evaluated 3 glomeruli/rat via electron microscopy using five 10k and 60k images. The 10k images were used to measure the number of slit-pores per 100μm of basement membrane (BM) and 60k images for thickness of the BM, width of the slit-pore diameter and each foot process base. Evaluation of the 10K images demonstrated a decrease in the number of slit-pores in the controls (RC and SDC), and a 12% increase in RC compared to RV. Similarly, evaluation of the 60K images demonstrated a difference between the controls and after AT_1R blockade in slit-pore diameter (increase of 22%), foot-process base width (decrease 12%), and BM thickness (decrease 16%). Proteinuria and blood pressure were also significantly reduced in the RV vs RC. Treatment with AT_1R inhibition resolved the effects of elevated Ang-II in the kidney as measured by four variables on electron microscopy of the podocyte and BM. Furthermore, improvements in proteinuria and BP correlated with improvement in podocyte injury.

THE COST SAVINGS OF DIALYZER REUSE COMPARED TO NON-REUSE DIALYZER

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Dialyzer reuse was practiced by more than 81% of dialysis centers in the United States. To evaluate the cost savings by adopting reuse dialyzer versus single use dialyzer strategy, we reviewed charts of 120 patients receiving hemodialysis in a center that practiced dialyzer reuse (Center A). The results were compared with another non reuse urban dialysis center (Center B). The costs of staff, reprocessing machine (Renatron), maintenance, renalin, and test strips, were included. The total number of dialysis treatment sessions during the 12 months was 11983. Average treatment cost varied from $1.79 to $5.11, depending on dialyzer type. Average reuse rate was 10.65. Annual cost of the reuse program was $104,054, using unlimited choices of different types of HF and HE dialyzers. Based on number of dialysis treatments and dialyzer costs, annual cost of non reuse program (Center B, which exclusively uses C121 and HF 400/500) was estimated to be $114,209 using C121 dialyzer; the annual cost was estimated to be $169,510 using HF 400/500 series dialyzer. The estimated cost would be $250,950 in center A if we follow a non reuse protocol. Based on these estimates, the annual savings of the reuse program was $10,155 (8.9%) compared to using C121 Dialyzer non reuse program; $65,456 (38%) compared to using HF400/500 non reuse program; $146,896 (59%) compared to using same patient's dialyzer type in a non reuse program.

	Re-use program	Center B: Non reuse (C121)	Center B: Non reuse (HF400/500)	Center A: Non reuse, current dialyzer type
Annual $	104,054	114,209	169,510	250,950
Savings $	----------	10,155(8.9%)	65,456(38%)	146,896(59%)

Our study shows that the reuse dialyser program is associated with significant cost savings. Randomized controlled trials are needed before recommending this strategy.

USE OF CEFAZOLIN IN STAPHYLOCOCCUS AUREUS INFECTION IN HEMODIALYSIS PATIENTS

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Staphylococcus aureus bacteremia and or line sepsis can be result in significant morbidity and mortality in dialysis patient. Early diagnosis and adequate treatment is required to prevent complications. The choice of treatment is Nafcillin in Methicillin sensitive Staph. Aureus bacteremia (MRSA). Nafcillin is very inconvenient for long term treatment for dialysis patient since it needs to be given every 4 hours interval at home with an additional PICC line placement. Vancomycin is used empirically before the status of Methicillin sensitivity is identified. Vancomycin can be used in convenient interval after each dialysis but is not as effective in MSSA.

We have tried Cefazolin as an alternative to Nafcillin in an anuric dialysis patient with MSSA bacteremia to evaluate the efficacy and dosing strategy.

The Patient 65 year old weigh 69 kg with history of ESRD due to diabetes with Staphylococcus. aureus bacteremia followed by a wound infection was given 2 gm of Cefazolin after each dialysis for 6 weeks. Five trough levels and 1 peak level were drawn. Patient was followed by set of blood cultures after each dialysis.

The average trough Cefazolin level was 11.4 µgm/ml (Range 7.7 to 16.6 microgram/ml) on regular days (Wednesday and Friday) and 3.5 µgm/ml (3.4, 3.6) on Mondays (after weekends). The peak Cefazolin level was 280 µgm/ml. Blood cultures were negative after the first dose of Cefazolin and remained negative through out the treatment. Patient's infection resolved without any events.

Cefazolin may be useful in methicillin sensitive Staph aureus infection in dialysis patient even if it is given every post dialysis period for few weeks. This will avoid insertion of any new line for frequent Nafcillin usage at home and ensure the compliance in the treatment of serious Staphylococcus aureus bacteremia in dialysis patients.

C-REACTIVE PROTEIN (CRP) IN HEMODIALYSIS (HD) PATIENTS (PTS)

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C-reactive protein, an acute-phase reactant and a marker of inflammation, is elevated in dialysis pts, and has been associated with cardiovascular morbidity and mortality in this population. We enrolled 48 HD pts treated at the Long Island College Hospital's outpatient facility from April 2003. Enrollment demographic, clinical and biochemical data were collected. High sensitivity (hs) CRP was assayed by immunoturbidimetric method. Pts were followed to November 2005. The mean age was 59 ± 14 (SD) years. Fifty-eight percent were women, and the majority were African- American (79%). Mean dialysis vintage at enrollment was 74.6 ± 72.9 (SD) months (range: 3.8 to 290 months). Mean and median enrollment hs-CRP were 7.39 ± 6.89 (range 0.2-29.3) and 5.6 mg/L, respectively. Hs-CRP was ≥10mg/L in 12 pts (25%). Pts with a history of congestive heart failure (9.54 vs. 6.89), coronary artery disease (8.35 vs. 6.98), myocardial infarction (9.4 vs. 7.0), and cerebrovascular accident (10.5 vs 6.86) had higher levels of hs-CRP compared to those without. The results, however, did not reach statistical significance. Hs-CRP was inversely correlated with hemoglobin (Hgb) (r=-0.26, p=0.07), serum iron (r=-0.28, p=0.05, and transferrin saturation (Tsat) (r=-0.36, p=0.013), as well as with urea reduction ratio (URR) (r=-0.30, p=0.04) and Kt/V urea (r=-0.27, p=0.07). During the study period, 15 pts (31%) died, 6 of whom (40%) had hs-CRP≥10 mg/L. Although the observed 2.5 year cumulative survival (Kaplan Meier) of pts with hs-CRP<10mg/dL was better than those with hs-CRP≥10 mg/L (75% vs.50%, respectively), the difference did not reach statistical significance (p=0.06). The inverse correlations of hs-CRP with Hgb, serum iron, Tsat, URR, and kT/V urea may imply an association of inflammation with anemia and with dialysis adequacy in HD pts. Large prospective trials are required to confirm the prognostic utility of routine hs-CRP measurement in HD pts.

IMPACT OF ENTERAL NUTRITION SUPPLEMENTATION DURING HEMODIALYSIS SESSION IN MALNOURISHED PATIENTS

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Maintaining adequate nutritional status in hemodialysis (HD) patients is a continuous challenge. Several factors such as inadequate dialysis dose, endocrine disarrangements, activation of the inflammatory response, dialysis-related nutrient losses, among others, contribute to the high prevalence of malnutrition in this population. Our objective was to study the impact on nutritional status of a malnourished population on regular HD underwent to hipercaloric and hiperproteic commercial enteric formula during dialysis session. Fifteen patients (8 women and 7 men) with mean age 72.5 ± 12.5 years and mean height 162 ± 7.04 cm, on regular HD for more than 6 months without acute illness, who maintained a serum albumin< 3.3g/dL for more than 12 weeks, were studied. The following parameters were evaluated at baseline (T0), at the end of month 1 (T1) and month 3 (T3): dry body weight (DBW), body mass index (BMI), serum phosphorus (PO4), serum albumin (Alb), serum creatinine (Cr), normalized protein nitrogen appearance (nPNA). Statistical analysis was performed using SPSS 12.0 for Win. Xp, paired samples T-test and Wilcoxon test were used accordingly. At T0 the mean DBW was 62.7 ± 10.91Kg, BMI 23.8 ± 3.9 Kg/m^2, Alb 3.17 ± 0.244g/dL, PO4 3.2 ± 1.4mg/dL, Cr 6.7 ± 2.3mg/dL, nPNA 0.96 ± 0.25g/Kg/day. At T1 comparing with T0 there was an increase in Alb (p=0.017), and nPNA (p=0.023). At T3 comparing with T0, there was an increase of Alb (p=0.011), nPNA (p=0.036) and serum phosphorus (p=0.015). Comparing T1 with T3 we observed only a marginal increase of serum phosphorus (p=0.048). None of the patients reported intolerance to the product. We conclude that the administration of a commercial dietary supplement during HD session improves the patient's biochemistry nutritional markers.

IMPROVED SURVIVAL IN PATIENTS ACUTE RENAL FAILURE STARTING EARLY ON CRRT

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Background: Mortality rates with Continuous Renal Replacement Therapy (CRRT) remain high. Issues that remain unanswered include the timing of initiation, the dose of CRRT, and patient characteristics that predict mortality.

Objective: To compare survival of patients started on CRRT within 24hrs ,48hrs and 48hrs to 240 hrs from time of Nephrology consultation.

Design: We carried out an observational study of 83 consecutive CRRT patients at our institution from Jan 2003 to June 2004. We split our database into 3 groups depending on time of initiation of CRRT and compared survival using Kaplan Meier survival analysis. Group-1 consisted of patients in which CRRT was started within 24 hrs(n-27), Group-2- within 48 hrs but not in first 24 hrs(n-42) and Group 3- more than 48 hrs up to 240 hrs(n-14). We compared the age; Apache II score; acidosis; BUN and Scr change; dose of dialysis in each group; URR; UF; urea clearance; time on CRRT. Data was analyzed using SPSS-13 for Hazard function, Kaplan Meier survival analysis, ANOVA and descriptive statistics.

Results: Overall survival at 30 days post-initiation of CRRT was approximately 48%. Survival in group 1 was 77%, group 2 was 45% and group 3 was 29% ($p<.05$) Kaplan Meier survival analysis and hazard function showed a better survival in early initiation on CRRT. There was no statistically significant difference in age; Apache II score; acidosis; BUN and serum creatinine change; dose of dialysis in each group; URR; UF; urea clearance; time on CRRT.

Conclusion: Timing from renal insult to initiation of CRRT plays a role in predicting survival of patients in our CRRT database. Patients with acute renal failure who were started early on CRRT had better survival as compared to those who were started late.

PATIENTS WITH PRE-EXISTING RENAL DISEASE HAVE BETTER SURVIVAL ON CRRT.

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Objective: To compare survival of patients with acute renal failure (ARF) with or without pre-existing renal dysfunction on admission.

Design: Observational study of 96 consecutive CRRT patients. There were 2 arms of the study: those without pre-existing renal disease who developed acute renal failure after admission (Inpt-ARF; defined as a Serum creatnine (Scr) of less than 1.3mg/dl prior to ARF and CRRT) (n-56) and those with renal dysfunction on admission (CKD-ARF; Scr of greater than or equal to 1.3mg/dl prior to ARF and CRRT) (n-40). We compared the survival of the two groups (Inpt-ARF versus CKD-ARF- time waited for the initiation of CRRT ; age; Apache II score; acidosis; BUN and Scr change; dose of dialysis; URR; UF; urea clearance; time on CRRT. Survival analysis was done in 3 groups. Group-1 -patients in which CRRT was started within 24 hrs, Group-2- within 48 hrs but not in first 24 hrs and Group 3- more than 48 hrs. Data was analyzed using SPSS-13 for Hazard function, Kaplan Meier survival analysis, ANOVA and descriptive statistics.

Results: Survival in CKD-ARF group 1 - 78%, group 2 - 57% and group 3 - 35% (p-value 0.039).Kaplan Meier survival analysis and hazard function showed a better survival in early initiation on CRRT. Survival in ARF group was Group1-44%, group 2 - 33% and group 3 - 40%. However it did not reach statistical significance (P 0.84).No statistically significant difference in age; Apache II score; acidosis; BUN and Scr change; dose of dialysis in each group; URR; UF; urea clearance; time on CRRT. Overall survival in Inpt-ARF group was 37% while the CKD-ARF was 57%. The percentage of survivors needing dialysis support at 30 days post initiation of CRRT was lower in the CKD-ARF group than in the Inpt-ARF group.

Conclusion: Patients on CRRT with pre-existing renal disease who were started early had better survival; however, the same cannot be said about the ARF group, as it did not reach statistical significance.

HEMODIALYSIS SUBJECTS WITH DEPRESSION HAVE LOWER SERUM FOLATE AND COBALAMIN LEVELS

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Depression is very common in dialysis patients. Elevated plasma levels of total homocysteine (tHcy) and/or lower plasma folate or vitamin B-12 have been associated with an increased risk of depression in the general population but little information is available regarding subjects on hemodialysis. The purpose of this study was to evaluate if there was a significant difference in serum and RBC folate or serum cobalamin levels in depressed versus non-depressed subjects on hemodialysis.

A cross sectional study design was used and 75 individuals undergoing hemodialysis for at least 6 months had serum folate and cobalamin and RBC folate measured using radioisotope dilution. The Beck Depression Index II (BDI) was used to assess for depression and subjects with scores of 10 or greater were considered depressed. Other laboratory, anthropometric, and demographic data were obtained from the subjects' medical records. T tests were performed to assess for significant differences ($p \leq 0.05$) in group mean values using SPSS.

Of the subjects in this study, 44% had BDI scores > 10 indicating depression. The non-depressed subjects had significantly higher mean serum folate (281±649 vs 52±137 ng/mL), RBC folate (1433±1757 vs 810±654 ng/mL), and serum cobalamin (1162±1014 vs 757±463 pg/mL) than did depressed subjects. In the non-depressed group, 39% of subjects were taking a supplement containing 35-42 mg folacin and 7 mg cobalamin per week while only 9.1% of depressed subjects were taking a vitamin containing these levels of B vitamins. The group means were not significantly different for age, mo on HD, BMI, EPO/kg body wt, tHcy, Hgb, albumin, or ferritin

As with the general population, lower serum folate, RBC folate, and serum cobalamin levels were found in depressed as compared to non-depressed subjects on hemodialysis. Plasma levels of these vitamins may be one of many factors related to depression but larger studies with stronger designs are needed to confirm results of this study.

INTRAVENOUS (IV) IRON DOES NOT AFFECT HOMOCYSTEINE (Hcy) LEVELS IN HEMODIALYSIS (HD) PATIENTS WITH ELEVATED SERUM FERRITIN (SF) AND LOW TRANSFERRIN SATURATION (TSAT): PRELIMINARY DATA FROM THE DRIVE STUDY.

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The **D**ialysis patients **R**esponse to **IV** iron with **E**levated ferritin **(DRIVE)** study is the first prospective, multi-center randomized controlled trial, to evaluate the effect of IV iron therapy on Hgb of anemic HD pts with higher SF. Pts with SF 500-1200ng/mL, TSAT≤ 25%, Hgb ≤ 11g/dL, baseline epoetin alfa (EPO) dose ≥ 225 IU/Kg/wk or 22,500 IU/wk, and not on antibiotics are randomized to IV iron or control. All pts receive a 25% increase in EPO dose at the beginning of week 1. The control group receives no IV or oral iron. The IV iron group receives 1g IV sodium ferric gluconate complex (SFGC) (125 mg QHD session X 8 doses). Hematology and serum chemistry (including Hcy levels) are collected at baseline and at wk 6. Changes in EPO doses are not permitted except for safety reasons. Since elevated Hcy levels are a marker of poor cardiovascular outcomes, we performed a preliminary analysis on the data of the first 56 pts enrolled in this 150-pt study in order to assess the effect of IV iron administration on Hcy levels of this sub-population of HD pts. At baseline, the control and SFGC groups had similar EPO doses (37,379 vs. 38,243 IU/wk), Hgb (10.2 vs. 10.3 g/dL), SF (708 vs. 713 ng/mL), TSAT (19% vs. 19%), C-reactive protein (28.5 vs. 36.8 mg/L), respectively. Both groups had elevated Hcy levels (control 26.7 vs. FSGC 24.5 mcmol/L). By wk 6, iron indices had changed significantly in both groups (control TSAT 21% and SF 556 ng/mL; SFGC TSAT 25% and SF 757 ng/mL). However, Hcy levels did not change significantly in either group (Control 27.3 mcmol/L, p=0.32; SFGC 25.5 mcmol/L, p=0.21).

We conclude that although administration of IV iron in HD patients with elevated SF and low TSAT results in clinically significant increases in TSAT, it has no effect on Hcy levels.

ELEVATION OF CYTOKINE LEVELS AMONG HEMODIALYSIS PATIENTS

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The risk of mortality among patients receiving maintenance hemodialysis (HD) for the treatment of end-stage renal disease is approximately 23% per year, due in large part to complications of cardiovascular disease. In contrast to those with normal renal function, non-traditional risk factors such as elevated levels of C-reactive protein (CRP) are stronger predictors of mortality among HD patients than are traditional risk factors such as hypercholesterolemia. We sought to characterize distributions of cytokine levels and persistence of elevated cytokine levels among HD patients.

The study population consisted of 449 HD patients at one of several dialysis facilities between November 2004 and July 2005. Subjects must have been receiving HD for ≥3 months but not using a venous catheter access, be ≥18 years of age, and not receiving antibiotic or immunosuppressive therapy. Blood samples, drawn before beginning dialysis, were obtained at three consecutive monthly visits for the assessment of CRP, IL-6, IL-8, IL-1B, IL-10 and IL-12. CRP and cytokine levels were evaluated at a central laboratory. Of the 449 subjects, 435 had baseline samples evaluable for CRP, of which 228 (52.4%) had levels ≥6.0 mg/L and 102 (23.4%) had levels ≥15.0 mg/L (median, 6.3; interquartile range, 2.7-13.9 mg/L). Although subjects with high (≥15.0 mg/L) as compared to lower CRP levels were similar with respect to gender (63% *vs*. 60% male) and time since initiating dialysis (72.5% *vs*. 75.6% >2 years), they were more likely to be older (44% *vs*. 33% ≥65 years of age; p=0.05), and white (59% *vs*. 45%; p=0.03). Of 401 subjects with CRP samples at each of the 3 monthly visits, 144 (35.9%) had values ≥6.0 mg/L and 50 (12.5%) had values ≥15.0 mg/L at all 3 visits. A very high percentage of subjects had transiently elevated CRP values: 288 (71.8%) and 162 (40.4%) had at least one value ≥ 6.0 mg/L and ≥ 15.0 mg/L, respectively. Baseline samples from 444 subjects were available for analysis of cytokines. IL-6 was detectable in 356 (80.2%) subjects. Among those with IL-6 detected, the 25^{th}, 50^{th} and 75^{th} percentiles corresponded to 4.3, 7.2 and 13.7 pg/mL, respectively. IL-8 was detectable in all but one subject; the 25^{th}, 50^{th} and 75^{th} percentiles corresponded to 24.1, 36.3 and 53.5 pg/mL, respectively. IL-10, IL-12 and IL-1B were detected in only 3.4%, 2.3% and 0.9% of subjects, respectively. These data suggest that chronic inflammation is common among maintenance hemodialysis patients not using a venous catheter access. Assessment of the clinical implications of these findings is warranted.

PREDIALYSIS NEPHROLOGIST CARE: SURVIVAL IMPACT ON PATIENTS WITH END-STAGE RENAL DISEASE INITIATING HEMODIALYSIS

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Early referral to a nephrologist of patients with chronic kidney disease aiming to achieve better control of blood pressure, anemia, calcium/phosphorus metabolism and nutritional status appears to delay the progression of renal disease and to reduce the mortality and morbidity associated with renal failure. Our aim was to evaluate the impact of nephrologist referral in a group of patients with end-stage renal disease (ESRD) initiating hemodialysis (HD).

This is a retrospective study based on 92 patients [(male 57, female 35), age 61,4±16,4 years, 100% caucasians, 24% diabetics] with ESRD initiating HD at a dialysis unit from 1-01-2003 to 31-12-2004. We performed an analysis of the group of patients referred to nephrologist care (n=54) versus no referral (n=38) comparing: type of dialysis access; acute/programmed HD initiation; glomerular filtration rate (GFR) and co-morbidity at initiation; hospitalizations and deaths until 31-06-2005. Blood pressure control, nutritional status, anemia and calcium/phosphorus metabolism were also evaluated by the time of HD start, 6 and 12 months later.

We found no differences between groups regarding gender, age, ESRD etiology and co-morbidity. The patients who had nephrologist care showed significant differences in pre-dialysis prescription of anti-hypertensive drugs (90% vs 44%, $p<0,001$), EPO (32% vs 0%, $p=0,002$), iron (45% vs 8%, $p=0,002$) and vitamin D (37% vs 0%, $p<0,001$). Those patients initiated HD with higher GFR (8,8 vs 6,1 ml/min, $p=0,04$), hemoglobin (10,4 vs 8,6 gm/dl, $p=0,01$) and albumin levels (3,7 vs 3,4 gm/dl, $p=0,01$). The initiation was planned in 59% vs 18% ($p<0,001$) of patients and using an arteriovenous fistula (AVF) in 35% vs 8% ($p=0,003$) of cases. The overall mortality rate was 15% vs 26% and the rate of overall survival 85% vs 78% at 1 year and 83% vs 60% at 2,5 years.

We concluded that patients referred to nephrologist: 1) presented better control of blood pressure, anemia, calcium/phosphorus metabolism and nutritional status; 2) initiated HD earlier and more often in a planned fashion using an AVF; 3) presented less mortality during the follow-up period.

CONVERTING PATIENTS FROM PARICALCITOL TO DOXERCALCIFEROL: A STUDY OF DOSE EQUIVALENCY AND TITRATION

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In vitro studies indicate similar Vitamin D receptor binding for doxercalciferol (DOX) and paricalcitol (PAR), but minimal information on the relative doses to be used in humans is available. The objectives of this study were to define the equivalent dose required when converting patients from IV PAR to DOX and to examine the effect of titrating DOX. After a 4-wk PAR fixed dose period (FDPAR), 42 adult hemodialysis patients were switched from PAR to DOX using a conversion factor of either 0.50 or 0.65. A 4-wk fixed DOX dose period (FDDOX) was followed by a 12-wk DOX titration period (TDOX) where DOX was titrated to reach goal (iPTH 150-300 pg/mL).

The mean age was 59 years, 69% were male, and 55% were African-American. The mean ± SD dose was 4.3 ± 2.3 mcg during FDPAR, 2.3 ± 1.5 mcg at the start of FDDOX and 2.9 ± 1.8 mcg at the end of TDOX. In the 0.50 group, mean iPTH increased significantly from baseline during FDDOX (p=0.02), but was not significantly different from baseline following titration (p=0.29). There was no difference in iPTH from baseline during FDDOX or TDOX in the 0.65 group. The overall proportion of patients with iPTH levels within the target range was similar for DOX and PAR during the fixed dosing periods (78% for both), but all patients were able to achieve an iPTH level within the target range with titration. Mean serum calcium, phosphorus and Ca*P product levels were similar during FDPAR and FDDOX.

In this study, the 50% dose of DOX relative to PAR did not achieve similar iPTH control while the 65% dose showed no difference. Once converted from PAR at either rate, patients could be safely and effectively managed with dose titration of DOX.

RIGHT ATRIAL THROMBOTIC COMPLICATIONS OF CENTRAL VENOUS CATHETERS IN HEMODIALYSIS

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Central venous catheters (CVCs) are frequently used for hemodialysis (HD) access. Their role in the pathogenesis of right atrial thrombus (RAT) has been demonstrated experimentally. We reviewed nine bacteremic HD patients who developed infected right atrial thrombi with the use of central venous catheters.

Right atrial thrombi were diagnosed by transesophageal echocardiography (TEE). Medical records were reviewed to obtain demographic information, clinical history, laboratory evaluation, echocardiographic findings and treatment outcomes.

9 cases of infected right atrial thrombi were identified from 2002 to 2005 in a single center. Prior to echcardiography only 2 patients had clinical events suggestive of the presence of RAT. Fatal pulmonary thromboembolism was observed in 1 patient. One patient had tricuspid valve regurgitation. The rate of recurrent bacteremia was 78 %. Transthoracic echocardiography failed to identify infected right atrial thrombi in 3 cases.

Infected right atrial thrombi occur in hemodialysis patients using CVCs for access, but cannot be predicted by clinical findings alone. Our observations suggest a frequently missed right heart complication of central venous catheter use in dialysis patients. Catheter-related bacteremia warrants investigation by TEE in hemodialysis patients.

MEDICATION USE IN PATIENTS TREATED WITH DAILY NOCTURNAL HOME HEMODIALYSIS (DNHHD): TRENDS OVER TIME

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Hemodialysis patients take an average of 12 medications. Trends of medication use over time and indications in DNHHD patients are unknown.

Medication prescription data were obtained for all our DNHHD patients (4/23/1998 to 01/25/2005). Medications were categorized as: analgesics (ALG); anemia; cardiovascular (CV), endocrine (endo), gastrointestinal (GI), psychotropics (PS), bone disease (bone), and other (data not shown). Number of medications/patient and indication were calculated at start and at 6, 12, 18, and 24 months of DNHHD.

We analyzed 1700 medication orders for 42 patients (37 white, 2 black, 2 Hispanic, 1 Turk), aged 53 $\pm$ 11 years, DNHHD vintage 2.25 $\pm$ 1.68 years. The mean $\pm$ SD number of medications/patient/indication at different time points is provided in the table. Overall use decreased from baseline to 24 months by 42%. Medication use decreased from baseline to 24 months for all indications: ALG (68%), anemia (76%), CV (61%), endo (25%), GI (40%), PS (57%), bone (86%).

vintage (mo)	ALG	anemia	CV	endo	GI	PS	bone	Overall use
start	0.83	0.93	2.33	0.69	0.86	0.60	1.17	9.6$\pm$5.0
6	0.62	1.24	1.97	0.89	0.92	0.59	0.86	10.2$\pm$4.5
12	0.68	0.77	1.74	0.77	1.10	0.55	0.39	9.2$\pm$4.5
18	0.48	0.33	1.30	0.52	0.78	0.30	0.22	6.6$\pm$4.0
24	0.35	0.22	1.13	0.52	0.52	0.26	0.17	5.6$\pm$4.1

DNHHD was associated with major reductions in use of medications overall and within specific indications.

POST-DIALYSIS USE OF PHENYTOIN SODIUM TO CONTROL SEIZURE IN A DIALYSIS PATIENT

Navin Gupta, Vicky Largosa, Devasmita Dev, Jean Lee, Ziauddin Ahmed

Non compliance to medications is a common problem in dialysis patients. When they are asked to take multiple medications, it is not easy to determine which medications they are actually taking. Frequently they miss the important medications that can result in significant morbidity and mortality. Administration of some important medications (Erythropoietin, Vitamin D analogs, Intravenous iron, Vancomycin, Gentamycin, etc) in dialysis units resulted in significant improvement of patient care. Still many comorbid conditions are needed to be treated by home medications. It is unknown in order to reduce pill burden how many medications can be given effectively after dialysis in out patient dialysis center. We had to try post dialysis phenytoin sodium in a patient to control her seizure despite its known pharmacokinetics unfavorable to such dosing.

A 67-year-old African American female patient on hemodialysis with history of Diabetes, CVA with right hemepheresis, aphasia, and dementia was frequently visiting emergency room because of uncontrolled seizures. Among other medications she was supposed to take 300 mg of phenytoin a day. Every time her phenytoin levels were low and the care giver could not be trusted with administration of her medications. During the process of arranging an alternating residence we have begun administering 500 mg of phenytoin sodium after each dialysis and drew 4 trough phenytoin levels before next dialysis. Patient did not have history of liver disease or known drug interactions which can result in increased drug level.

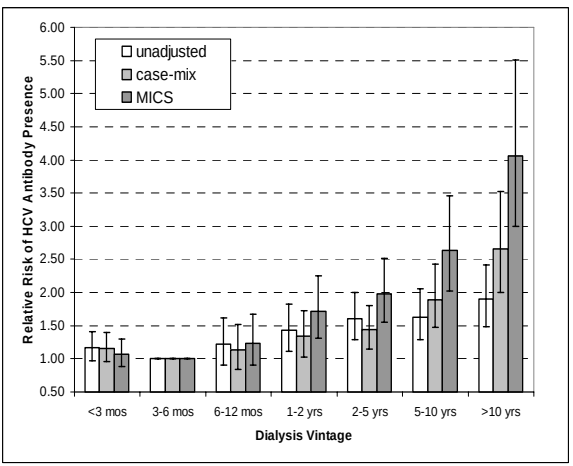
Pre-dialysis average phenytoin levels were 12 mcg/ml and patient's seizures were controlled. No phenytoin toxicity was noted. Patient was not removed from her family and the treatment was continued for 2 years without any seizures until she died of a cardiac arrest.

Seizures in dialysis patient may be treated with post dialysis phenytoin dosing with effective control of seizure. Larger studies are needed to confirm the findings.

DIALYSIS VINTAGE AND RISK OF HEPATITIS C VIRUS INFECTION.

Kamyar Kalantar-Zadeh[1], Charles J McAllister[2], Ryan D Kilpatrick[1], Loren G Miller[3], Eric S Daar[4], David W Gjertson[5], Joel D Kopple[1], Sander Greenland[5]. [1]Divisions of Nephrology, [3]Infectious and [4]HIV Disease; LA BioMed at Harbor-UCLA, Torrance, CA; [5]UCLA School of Public Health, and [2]DaVita, Inc, El Segundo, CA

Hepatitis C virus (HCV) infection is common in maintenance hemodialysis (MHD) patients. We hypothesized that HCV infection is associated with selective clinical and laboratory characteristics and, in particular, longer dialysis vintage in MHD patients. We analyzed a national database of over 82,958 MHD patients, 13,664 of whom underwent HCV enzyme immunoassay (EIA) testing at least once over a 3 year interval (7/2001-6/2004). The HCV EIA was reported positive in 1,590 MHD patients (12%). In a multivariate logistic regression models that adjust for case-mix and available surrogates of malnutrition and inflammation, the predictors of HCV infection were younger age, male gender, African American race, Hispanic ethnicity, Medicaid insurance, longer dialysis vintage time, unmarried status, HIV disease, and history of smoking. In particular, an increased HCV risk was observed across longer vintage intervals (Figure).

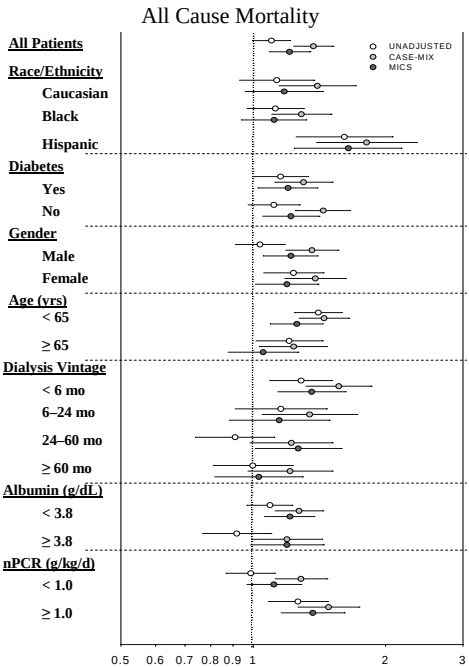


Hence, HCV infection, as diagnosed by EIA, has distinct demographic, clinical and laboratory predilections in MHD patients and is associated with longer time on dialysis. More diligent HCV detection and treatment may improve cardiovascular survival in MHD patients.

HEPATITIS C VIRUS AND DEATH RISK IN HEMODIALYSIS PATIENTS.

Kamyar Kalantar-Zadeh[1], Charles J McAllister[2], Loren G Miller[3], Eric S Daar[4], David W Gjertson[5], Joel D Kopple[1], Sander Greenland[5], and Ryan D Kilpatrick[1]. [1]Divisions of Nephrology, [3]Infectious and [4]HIV Disease; LA BioMed at Harbor-UCLA, Torrance, CA; [5]UCLA School of Public Health, and [2]DaVita, Inc, El Segundo, CA

Hepatitis C virus (HCV) infection is common in maintenance hemodialysis (MHD) patients. We hypothesized that HCV infection is associated with an increased all-cause and cause specific death risk in MHD patients. We analyzed survival in a 3-year (7/2001-6/2004) national cohort of 82,958 MHD patients, 13,664 of whom underwent HCV enzyme immunoassay (EIA) testing. The HCV EIA was reported positive in 1,590 MHD patients (12%). In fully adjusted survival models, HCV infection associated death hazard was 1.25 (95% confidence interval: 1.12-1.39). This death risk was more prominent among incident (vintage <6 mos) than prevalent MHD patients. Subgroup analyses showed tendency towards death risk across almost all clinical, demographic and laboratory subgroups of MHD patients (Figure). Hence, HCV infection, as diagnosed by EIA, is associated with significantly higher mortality risk. More diligent HCV detection and treatment may improve survival in MHD patients.



VALUE OF ACCESS FLOW SURVEILLANCE BY CONDUCTIVITY DIALYSANCE AS A SCREENING TOOL

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This study reports the clinical utility of access flow (Qa) surveillance using conductivity dialysance (Fresenius 2008H/K dialysis machines) as a screening tool for hemodialysis access dysfunction. For screening tests, high sensitivity and positive predictive value are desirable.

A group practice with over 600 hemodialysis patients in 8 facilities that refers solely to one vascular access center initiated the Fresenius Qa surveillance program in Feb, 2004. 10-months of follow-up data (Mar-Dec, 2004) are available for analysis. Arteriovenous fistulae (AVF) and grafts (AVG) were referred for Qa <400 ml/min and <600 ml/min, respectively, and for any decline of >25% from baseline. 444 referrals were noted in 275 patients. 226 unique patients' records of their first referral were available for analysis.

156 of 226 (69%) had >50% stenosis requiring intervention or had clotted before evaluation. 157 of 226 referrals (69%) were triggered by Qa. 124 of 157 (79%) had significant stenoses/clotting. There were 171 AVG (76%) and 55 AVF (24%). A summary of the results are shown:

Total N=226	**All**	**AVF**	**AVG**
Sensitivity	79%	79%	80%
Specificity	53%	59%	49%
(+) Predictive Value	79%	67%	82%
(-) Predictive Value	54%	59%	45%

For AVG, Qa<600 ml/min was predictive in 62/66 (93.9%) and >25% decline was 37/53 (69.8%). For AVF, Qa<400 ml/min was predictive in 9 of 12 (75%) and >25% decline was 12/20 (60%). 4 accesses (3 AVG and 1 AVF) had a mean Qa of 376 ml/min but had delayed evaluation (averaging 25 days) and presented with thromboses.

The Qa surveillance by conductivity dialysance in the Fresenius 2008H/K machines is a good screening tool for identifying accesses at-risk for significant stenoses/clotting. It was successfully implemented in 8 dialysis facilities in this study without hiring dedicated personnel. This tool is an affordable alternative to more complex technologies.

IMPACT OF OBESITY ON VASCULAR ACCESS OUTCOMES IN HEMODIALYSIS PATIENTS. Mark Kats, Alan Hawxby, Jill Barker, Michael Allon, Univ of Alabama at Birmingham, Birmingham, AL and Montana State University, Bozeman, MT, USA.

Although AV fistulas are preferred over grafts, fistulas are less frequent among obese than non-obese patients. This discrepancy may be due to a lower rate of fistula placement in obese patients, a higher primary failure rate (fistulas that are never usable for dialysis), or a higher secondary failure rate (fistulas that fail after being used successfully for dialysis). Using a prospective, computerized vascular access database, we identified all patients receiving a new fistula or graft at our institution during a 2-year period. The access outcomes were compared between obese (BMI >=30) and non-obese (BMI 18.5 to 29.9) patients.

Fistula placement was equally likely between obese and non-obese patients (47.4 vs 47.1%). Among those receiving a fistula, obese (N=54) and non-obese (N=129) patients were comparable in age, sex, race, CAD, PVD, and fistula location. However, the obese patients were more likely to have diabetes (76 vs 49%, P=0.0007). The primary failure rate of fistulas (technical failure, early thrombosis, or failure to mature) was similar in both groups (46 vs 41%, P=0.45). Among fistulas that were usable for dialysis, the long-term survival was worse in obese patients (hazard ratio 2.74, 95% CI 1.48 to 7.90, P=0.004). Fistula survival was 68 vs 92% at 1 year, 59 vs 78% at 2 years, and 47 vs 70% at 3 years.

Among patients receiving a graft (60 obese, 145 non-obese), thrombosis-free survival was similar (hazard ratio 1.21, 95% CI 0.84 to 1.76, P=0.28). Likewise, the cumulative graft survival (time to permanent failure) was comparable in both groups (hazard ratio 1.14, 95% CI 0.72 to 1.82, P=0.57). The proportion of grafts failing due to infection was similar in both groups (25 vs 29%).

In conclusion, long-term fistula survival is worse in obese than non-obese patients, due to a higher secondary failure rate. In contrast, graft survival is similar in obese and non-obese patients.

A COMPARITIVE ANALYSIS OF TREATMENT OF HYPERPHOSPHATEMIA WITH SEVELAMER HYDROCHLORIDE VS CALCIUM ACETATE IN HEMODIALYSIS PATIENTS

Fauzia Khalid, Knoxville, TN, USA, Mohammad Shafi, Knoxville, TN, USA, Naseem Siddiqi, Knoxville, TN, USA, Yaqub Ali, Knoxville, TN, USA

Hyperphosphatemia has been associated with hyperparathyroidism and renal osteodystrophy leading to significant morbidity and mortality among hemodialysis patients.

To compare the effectiveness of two different types of phosphate binders in controlling hyperphosphatemia among hemodialysis patients.

Retrospective study of a dialysis unit, involving 30 dialysis patients receiving either Sevelamer or Calcium Acetate. The total duration of followup was one year.

Results: There was a significant decrease of serum phosphorus level in Sevelamer group(1.1 mg/dl difference) compared with Calcium Acetate group(0.1 mg/dl difference) after one year of therapy. The incidence of hypercalcemia was similar in both groups. Both agents reduced the total cholesterol. It was also noted that Sevelamer recipients had lower Ca x P product than calcium acetate recipients ($P < 0.001$). Serum intact parathyroid hormone levels decreased in both groups, but to a greater extent in patients receiving calcium acetate.

In conclusion, Sevelamer is more effective than Calcium Acetate for the treatment of hyperphosphatemia in hemodialysis patients. Incidence of hypercalcemia appears to be similar in both groups.

PARICALCITOL VERSUS 1α-HYDROXYVITAMIN D2 FOR THE TREATMENT OF SECONDARY HYPERPARATHYROIDSM IN HEMODIALYSIS POPULATION

Fauzia Khalid, Knoxville, TN, USA, Mohammad Shafi, Knoxville, TN, USA, Naseem Siddiqi, Knoxville, TN, USA, Yaqub Ali, Knoxville, TN, USA

Secondary Hyperparathyroidism is a major component of renal osteodystrophy. Several vitamin D analogs are currently available for the treatment of secondary hyperparathyroidism. The purpose of this study was to compare the effects of Paricalcitol and 1α-Hydroxyvitamin D2 on parathyroid hormone (PTH) suppression and serum level of calcium, phosphorus and calcium- phosphorus product (Ca x P) in hemodialysis patients.

Retrospective study of a dialysis unit where a total of twelve patients received treatment for secondary hyperparathyroidism. Of these twelve patients five patients received paricalcitol while the remaining seven received 1α-Hydroxyvitamin D2. The total duration of follow-up was 18 months. Initial baseline characteristics included serum Ca x P < 75 and a PTH level >300 pg/ml. Dose adjustments were based on PTH level, serum calcium and Ca x P product.

Mean plasma PTH level decreased by 46% from baseline after 22 weeks of Paricalcitol treatment (P <0.001) with a mean reduction of PTH into a desired therapeutic range (100-300 pg/ml) whereas the 1α-Hydroxyvitamin D2 treated patients achieved 47% reduction in PTH levels after 24 weeks of treatment(P <0.001). Paricalcitol treated patients had more episodes of hypercalcemia, hyperphosphatemia and/or increased Ca x P product than 1α-Hydroxyvitamin D2 group.

In conclusion, Paricalcitol and 1α-Hydroxyvitamin D2 are both equally effective in the treatment of secondary hyperparathyroidism. The incidence of hypercalcemia, hyperphosphatemia and/or increased Ca x P product was more in the Paricalcitol group versus 1α-Hydroxyvitamin D2 group.

THE PREVALENCE TRIAL – AN INTERNATIONAL, NON-INVASIVE STUDY TO DETERMINE THE PREVALENCE OF VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE SUBJECTS ON HEMODIALYSIS

Mark Kraus, Adeera Levin, James Cotton, Jeffrey Hoggard, Nicole Stankus, Chika Oguagha, Jose Cangiano, Francisco Maduell, Jose Hervas, Philp Kalra, Judith Stevens, Deirdre Harrington, José A. Menoyo; John H. Stroger Jr. Hospital, Chicago, IL; Saint Paul's Hospital, Vancouver, CA; Tyler Nephrology Associates, Tyler, TX; Eastern Nephrology Associates, Greenville, NC; University of Chicago; Chicago, IL; Nephrology Foundation of Brooklyn, Brooklyn, NY; Jose Cangiano Nephrology, San Juan, PR; Hospital General de Castellón, Castellón, Spain; Hospital Clínico Universitario San Cecilio, Granada, Spain; Hope Hospital, Salford, UK; Queen Alexandra Hospital, Portsmouth, UK; Genzyme Corporation, Cambridge, MA

Mortality of patients with Chronic Kidney Disease (CKD) on hemodialysis (HD) remains around 20% per year and is driven primarily by cardiovascular deaths. In addition to classic cardiovascular risk factors, novel risk factors have been identified in this population. Both hyperphosphatemia and vascular calcification are important factors contributing to the increased cardiovascular morbidity and mortality in patients receiving maintenance hemodialysis. However, despite the validated utility of Electron Beam Tomography (EBT) for early detection of vascular calcification, the causal interpretation of the positive correlation between vascular calcification and cardiovascular disease burden remains controversial. In addition, EBT is not widely available thereby limiting its utility as a screening tool. Therefore, we conducted an international, multi-center study at 11 sites to determine the prevalence of vascular calcification in CKD patients on HD utilizing simpler and more readily available tools. 269 patients were enrolled. Each patient underwent pulse pressure measurement as well as an echocardiogram and a lateral lumbar x-ray to measure valvular calcification and abdominal aorta calcification respectively.

Findings of the trial at the time of the abstracts submission deadline were not yet available, but will be available at that time of the National Kidney Meeting Spring Meeting in 2006.

CHOREA WITH BILATERAL BASAL GANGLIA LESIONS IN A DIABETIC PATIENT ON HEMODIALYSIS.

Sarat Kuppachi , Lin Lwin , Naqi Idris , Hugo Villanueva , Jyh Haur Lu , Jinil Yoo .
Our Lady Of Mercy Medical Center, Bronx NY.

A 58 year old Hispanic lady presented with a complaint of slurring of her speech of acute onset. Her medical history included having hypertension for 29 years, diabetes for 20 years, and suffering from end stage renal disease for 4 years for which she was on hemodialysis. Initial CT scans to asses for neurologic lesions showed lucencies in both basal ganglia. She progressed to develop chorea and gait instability. An MRI showed the presence of increased T2 signal intensity within both basal ganglia. Her symptoms resolved only marginally with symptomatic management.

Acute extrapyramidal movement disorders have been rarely reported in patients undergoing hemodialysis. Movement disorders with basal ganglia lesions have been described in relation to uremia though, the etiology of this entity remains unclear. F-18 fluorodeoxyglucose positron emission tomography performed in 2 such patients with diabetic uremia showed markedly reduced glucose metabolism in the basal ganglia and in another report in patients on hemodialysis chorea was associated with thiamine deficiency. These examples relate the disease to a metabolic phenomenon. The disease has also been reported in patients with arterial hypotension and hypoxemia suggesting that vasculopathic or hemodynamic abnormalities may also be involved. We propose that this disorder can be of multifactorial origin and the cause of these rare lesions needs further evaluation.

NEEDLE INFILTRATIONS OF ARTERIOVENOUS FISTULAS IN HEMODIALYSIS: RISK FACTORS AND CONSEQUENCES.

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Needle infiltration of arteriovenous fistulas is a common problem in U.S. hemodialysis units. Needle infiltrations of fistulas may result in the temporary inability to use the fistula for dialysis and may lead to fistula thrombosis, necessitating tunneled catheter use for maintenance hemodialysis. The purpose of this study was to evaluate the risk factors for fistula infiltrations, and the clinical consequences arising from this complication

Using a prospective, computerized vascular access database, we identified all hemodialysis patients who suffered a fistula infiltration during a 5-year period (1/1/00-12/31/04) severe enough to require a follow-up diagnostic test, surgery appointment, or an intervention. This patient group was compared to a control group without fistula infiltrations. We also quantified subsequent access outcomes in patients with infiltrations.

During a five-year period, we identified 62 patients with fistula infiltrations, representing a 7% annual rate. Patients with fistula infiltrations were significantly older than those without infiltrations (62±14 vs 55±15 years, P=0.004). Fistula infiltration was not associated with sex, race, diabetes, presence of peripheral vascular disease, location of fistula, or body mass index. On multiple variable regression analysis, the likelihood of fistula infiltration was strongly associated with patient age (odds ratio 1.038 per each year increment, 95% CI 1.014 to 1.063, p=0.001). New fistulas ($\leq$ 6 months in age) were more likely among patients with infiltrations, as compared to a cross-section of patients without infiltrations (43.5% vs 20.5%; odds ratio 2.98, 95% CI 1.61 to 5.54, p=0.0004). The 62 infiltrations resulted in 128 procedures or appointments. Fistula thrombosis occurred in 12 patients (or 19%). Prolongation of tunneled catheter-dependence occurred in 48 (or 77%) of patients with infiltrations, for a median of 97 days.

In conclusion, needle infiltration of fistulas occurs more commonly in older patients and in new fistulas. These infiltrations result in numerous procedures, and prolongation of catheter-dependence.

DOES STENOSIS LOCATION AFFECT GRAFT OUTCOMES FOLLOWING THROMBECTOMY?

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Thrombosis is a common complication of AV grafts, and is usually superimposed on an underlying stenotic lesion at the venous anastomosis, peripheral vein, or central vein. Clotted grafts are treated with mechanical thrombectomy, in conjunction with angioplasty of the underlying lesion. It is not known whether the site of stenosis affects graft patency following thrombectomy.

To evaluate this question, we used a computerized vascular access database to identify all patients undergoing mechanical thrombectomy at our institution during a five-year period. Stenosis of the central vein (CV) was present in 60 patients, and isolated stenosis of the venous anastomosis (VA) in 120 patients. Both groups were comparable in terms of age, sex, race, diabetes, HTN, PVD, CAD, and graft age.

The primary (or unassisted) graft patency (time from initial treatment to next intervention) was similar in the CV and VA stenosis groups (median survival, 102 vs. 79 days, P= 0.50). Primary patency at 30 days was (67 vs 72%), 60 days (60 vs 57%), 90 days (54 vs 49%), and 180 days (33 vs 35%). The hazard ratio for graft failure was 1.13 (95% CI, 0.79 to 1.63). The secondary (or assisted) graft patency (time from initial treatment to permanent failure) was similar in both groups (median survival, 333 vs 386 days, P=0.42). The secondary patency at 90 days was (69 vs 70%), 180 days (62 vs 63%), and 360 days (48 vs 55%).

In conclusion, treatment of thrombosed AV grafts with standard mechanical thrombectomy plus angioplasty, offers short-lived patency before a subsequent intervention is required. However, the unassisted and assisted graft patency following thrombectomy is not affected by the location of the underlying stenosis.

PHARMACOECONOMIC (PE) AND MEDICATION BURDENS IN PATIENTS TREATED WITH DAILY NOCTURNAL HOME HEMODIALYSIS (DNHHD).

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Hemodialysis patients take an average of 12 medications costing nearly $16,000/patient/year. Changes in PE and medication burden in DNHHD patients are unknown.

Medication prescription data were obtained for all our DNHHD patients (4/23/1998 to 01/25/2005). Medications were categorized as: analgesics (ALG); anemia; cardiovascular (CV), endocrine (endo), gastrointestinal (GI), bone disease (bone), and other (data not shown). Doses per day (medication burden) and average medication cost (using NACDS 2004) (PE burden) were calculated at start and at 6, 12, 18, and 24 months of DNHHD.

We analyzed 1700 medication orders for 42 patients (37 white, 2 black, 2 Hispanic, 1 Turk), aged 53 ± 11 years, DNHHD vintage 2.25 ± 1.68 years. The mean PE burden/therapeutic class/patient/month at different time points are provided in the table. PE burden altered from baseline vs. 24 months: CV (21% vs 14%), GI (8.6% vs 14.8%), bone (14% vs 6.8%), and anemia (11.6% vs 8.4%). By 24 months, the total cost had decreased by 65% from baseline. The medication burden decreased during treatment: 11.3 ± 7.1 doses/day (at start), 9.6 ± 4.5 (6 mo), 8.5 ± 4.4 (12 mo), 6.4 ± 4.8 (18 mo) and 5.2 ± 4.2 (24 mo, 46% of baseline).

vintage (mo)	ALG	anemia	CV	endo	GI	bone	Total cost
start	54.16	82.35	149.73	61.19	61.21	109.87	708.28
6	44.94	111.55	121.67	77.99	69.73	82.63	743.31
12	47.47	71.81	101.75	67.50	89.70	36.98	657.23
18	36.10	29.37	71.87	39.64	64.41	21.23	458.01
24	16.41	20.77	35.67	35.52	37.39	16.62	250.48

DNHHD was associated with major reductions in PE and medication burdens.

A SURVEY OF THE TREATMENT AND PERCEPTION OF UREMIC PRURITUS BY UNITED STATES NEPHROLOGISTS

Vandana Mathur[1], Sarbani Bhaduri[2], Jere Fellmann[2], David Rosen[2]
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Although patient-based surveys have suggested that prevalence of pruritus amongst dialysis patients remains high, neither the perception of this condition nor its management by nephrologists has been well characterized.

To address the above questions, we conducted a web-based survey of 102 United States nephrologists who had been in practice between 4 and 35 years, spent $\geq$ 20% of their time in the direct or indirect care of hemodialysis (HD) patients, and who personally managed at least 30 HD patients.

The nephrologists surveyed, 71% of whom had served as a dialysis unit medical director, personally managed a mean of 115 HD patients. The mean percentage of patients who had any degree of pruritus was 34.8% and a similar proportion, (32.0%) were specifically treated for pruritus. Of patients with pruritus, the disease adversely affected quality of life or health in 38.5%. Scratching was directly responsible for non-access skin infections in 17%, access site infections or thrombosis in 15%, and systemic infections in 5%. The etiology of pruritus was most commonly attributed to: 1) Sub-optimal control of Ca, PO4, or PTH (48%); 2) Inadequate use of dialysis-related medications (18%); and, 3) Under-dialysis (15%). The pruritus was more likely to be brought to the attention of the physician by a direct patient complaint (62%) than by physician solicitation (15%), by nurse reporting (14%), or via direct patient observation (8%). The first-line management of pruritus was variable: Oral antihistamines (27%), topical treatment (23%), increasing dialysis dose (22%), change in dialysis medications (21%), and intravenous antihistamines (5%). In the majority (52%), pruritus was not well controlled and this was due to lack of effective pruritus therapies (64%), non-compliance with treatment (24%), and development of refractoriness to therapy (18%).

In conclusion, uremic pruritus is common and associated with significant medical complications. Current therapeutic options have limited efficacy.

DIFFERENCES IN PERCEPTION OF UREMIC PRURITUS BETWEEN HEMODIALYSIS PATIENTS AND NEPHROLOGISTS Vandana Mathur[1], Sarbani Bhaduri [2], Jere Fellmann[2] [1]Mathur Consulting, Woodside, CA, USA, [2]Acologix, Hayward, CA, USA[2]

Medical conditions with manifestations that are subjective (i.e. pain) are often under-recognized and under-treated by physicians.

To determine if a significant disparity exists between the perspectives of hemodialysis (HD) patients and nephrologists (Nephs) on uremic pruritus, a survey of 101 HD patients and 102 Nephs was conducted. Patients were selected if they had been on HD for $\geq$ 6 months, 2 – 4 times per week, and had pruritus from "time to time". 3 patient profiles were developed. Patients were asked to classify themselves into the profile that best fit their clinical condition. Nephs were also asked to predict the percentage of pruritic patients who would classify themselves into each profile (**Table**). When asked to rank from a list of medications commonly used by dialysis patients, the 3 "most important" drugs chosen by patients were sleeping medications, oral and intravenous anti-histamines. Nephs chose erythropoietin, phosphate binders, and intravenous iron.

Profile	Nephs	Patients
A: I do not generally have scratch marks on my skin. I do not generally have a problem sleeping because of itching. My itching does not generally make me feel agitated or sad.	39%	5%
B: I sometimes have scratch marks on my skin. I sometimes have a problem sleeping because of itching. My itching can make me feel agitated or sad from time to time.	37%	68%
C: I often have scratch marks on my skin that may or may not bleed or get infected. I often have a problem sleeping because of itching. My itching often makes me feel agitated or sad.	24%	27%

In conclusion, patients and their doctors showed differences in regards to the clinical impression of excoriation, mood and sleep. It is likely patients ranked Benadryl and Atarax as significant medicines for their care since they are at risk from pruritus. Uremic pruritus was associated with negative consequences on mood, sleep, and skin integrity. Nephs greatly under estimated the frequency of these consequences.

UNDER-RECOGNIZED PERSISTENCE OF UREMIC PRURITUS IN THE MODERN DIALYSIS ERA: A NATIONAL SURVEY

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Recent reports suggest a decrease in the prevalence of uremic pruritus due to improved dialysis techniques and metabolic control (R Twycross. QJ Med 2003). To assess the clinical impact of pruritus in a US-based hemodialysis (HD) population, we conducted a web-based survey of HD patients experiencing symptoms of pruritus, maintained on HD for $\geq$ 6 months and receiving HD 2 to 4 times weekly. Of 255 patients initially screened, 87% (n = 222) of patients reported suffering from itch intermittently, not related to local skin irritation. 101 HD patients met the inclusion criteria and are reported. The mean age was 36 $\pm$ 9 yrs, 51% were male, and mean time on HD was 14 $\pm$ 9 months. Despite use of anti-pruritic medications by 76%, worst itching experienced in the past 7 days was 63 $\pm$18.6 mm on a visual analogue scale (0: no itching, 100: worst imaginable itching). Although 63% were on sleep medications, pruritus reduced the number of hours of sleep from 6.9 hours of expected sleep time to 4.6 hours.

Parameter	**%**
Pruritus is generalized in location	88%
Pruritus is present most days of the year	81%
"Very Much" or "Extremely" bothered by pruritus	67%
Inhibited from going out in public due to appearance of skin or need to scratch	79%
Pruritus affected the ability to sleep on $\geq$ 3 nights per week	39%
"I often have scratch marks on my skin that may or may not bleed or get infected. I often have a problem sleeping because of itching. My itching often makes me feel agitated or sad"	27%

Despite modern day dialysis guidelines and drugs, uremic pruritus is a highly bothersome symptom occurring in the majority of HD patients assessed in this survey. Pruritus had a notable negative impact on QOL measures, including major consequences on sleep, mood and socialization.

RETROSPECTIVE EVALUATION OF CENTRAL VENOUS STENOSIS TREATMENT: STENTS VS ANGIOPLASTY.

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Central venous stenosis is a common complication of tunneled dialysis catheters, and may present with ipsilateral upper extremity edema. Although central vein stenotic lesions can be treated with angioplasty, they frequently recur. It is not known whether stent deployment prolongs the intervention-free survival of such lesions, as compared with angioplasty alone.

To evaluate this question, we retrospectively reviewed the outcomes of patients with central vein stenotic lesions treated during a 7-year period (6/1/1998 to 5/31/2005). Fifty-one patients were treated for severe (>50%) stenotic lesions of the central venous system by either angioplasty alone (N=32) or in combination with stent placement (N=19). Both groups were comparable in terms of age, sex, race, diabetic status, HTN, PVD, CAD, and age of the vascular access. Stenotic lesions were found as follows: 32 brachiocephalic, 18 subclavian, 1 superior vena cava. Thirty-five patients had AV grafts and 16 patients had AV fistulas.

An immediate technical success after the initial intervention was achieved in all cases. The primary vascular access patency (time from initial treatment to next intervention) was similar in the stent and angioplasty groups (median survival, 138 vs 147 days, P=0.75). Primary patency at 30 days was (89 vs 94%), 90 days (63 vs 67%), and 180 days (38 vs 40%). The assisted or secondary patency (time from initial treatment to permanent access failure) was also similar (median survival, 618 vs 586 days, P=0.49). Secondary patency at 90 days was (95 vs 94%), 180 days (76 vs 84%), and 360 days (69 vs 59%).

In conclusion, central venous stenosis treated by angioplasty, with or without stent placement, offers short-term clinical and symptomatic relief. However, stent deployment does not improve the clinical outcomes (primary and secondary patency), as compared with angioplasty alone. Multiple subsequent interventions are required in both groups to treat recurrent central vein stenosis and achieve long-term symptomatic relief.

CORRELATION OF SERUM PHOSPHORUS AND Ca x P PRODUCT IN DIALYSIS PATIENTS

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Control of serum phosphorus (P) levels is an important goal in Dialysis patients. Hyperphosphatemia leads to an increased calcium-phosphorus (Ca x P) product which can result in vascular calcification, cardiovascular disease, calciphylaxis and increased mortality in dialysis patients. The mechanism of morbidity and mortality due to hyperphosphatemia is not known but is largely ascribed to vascular calcification when the Ca x P is elevated. Analysis of two special studies of the United States Renal data System revealed that the adjusted risk of death by serum P levels was not uniform but being constant below a level of 6.5 mg/dl and increasing significantly above this level. The relative risk of death for those with a serum P levels greater than 6.5 mg/dl was 1.27 relative to those with serum phosphorus of 2.4 to 6.6 mg/dl. The relative risk of mortality with Ca x P product greater than 72 mg2/dl2 was 1.34 relative to those products of 42 to 52 mg2/dl2. Ca level was not found to correlate with mortality in dialysis patients. Ca x P product also depends upon serum Ca levels. The guidelines and goals are adopted after KDOQI recommendation that serum P levels and Ca x P product of dialysis patients be maintained between 3.5 to 5.5mg/dl and less than 55mg2/dl2 respectively. We decided to review the correlation of P levels and Ca x P product in one urban dialysis unit.

We have reviewed the monthly laboratory values of 129 dialysis patients. Our dialysis unit had adopted a minimum goal to achieve 60% of patient for P control and 55% of patients for control of Ca x P product. The desired P levels were achieved in 64/129 (49%) patients but in the same population. Ca x P level goal was achieved in 91/129 (70%) patients.

The serum P levels did not correlate with Ca x P product in our dialysis patients. It is not known which level is more important to avoid vascular complications in management of dialysis patients. A larger study is required to address the importance of Ca x P product over serum Phosphorus control in clinical practice.

AN ANALYSIS OF TUNNEL-CUFFED CATHETER SURVIVAL AND INFECTION RATES IN HIV-POSITIVE DIALYSIS PATIENTS

Dana Mitchell, Zipporah Krishnasami, Michael Allon, University of Alabama at Birmingham, Birmingham, Alabama, USA.

Tunnel-cuffed catheters are used for dialysis in about 25% of the prevalent HD population. Catheters are a major risk factor for infection, perhaps even more so in immunocompromised patients as previously reported. In this study, we compared the time to catheter-related bacteremia and cumulative permcath survival between HIV and non-HIV patients.

Using a prospective, computerized vascular access database, we identified all hemodialysis patients who were HIV positive and had permcaths placed during a 6 year, 7month period (12/1/1998 – 6/30/2005). This patient group was compared to an age-, sex-, and access date- matched control group. We evaluated incidence of bacteremia and overall catheter survival in both sets of patients.

During this period, we identified 33 patients with HIV who had permcaths placed. There was no increased incidence of catheter-related bacteremia (CRB) between HIV and non-HIV patients (52% vs 49%, respectively). However, HIV positive patients were more likely to have two different organisms as the cause of bacteremia (41% vs 15%, p=0.049). Furthermore, HIV positive patients were more likely to be hospitalized for treatment of CRBs than HIV negative patients (29% vs 7%, p=0.05). There was no difference noted in time to infection or cumulative permcath survival between the two groups.

There is no difference in the incidence of CRB between HIV positive and negative patients, however, bacteremia secondary to two organisms occurred more frequently in HIV positive patients. In addition, HIV positive patients are more frequently hospitalized for treatment of CRBs than their HIV negative counterparts.

AV GRAFT AND FISTULA SURVIVAL IN HIV-POSITIVE HEMODIALYSIS PATIENTS.

Dana Mitchell, Zipporah Krishnasami, Michael Allon, University of Alabama at Birmingham, Birmingham, Alabama, USA.

AV grafts have a lower primary failure rate (access never usable for dialysis) than fistulas. Conversely, grafts have a higher complication rate (due to thrombosis or infection), once they are used for HD. There is limited information on vascular access outcomes in HIV-positive patients. Using a prospective, computerized vascular access database, we identified all HIV-positive HD patients having a fistula or graft placed during a 6.5-year period. This group was compared to an age-, sex-, and access date-matched HIV-negative control group.

Among 15 HIV-positive patients receiving an AV graft, thrombosis-free graft survival was substantially worse than in the 30 HIV-negative controls (1-year survival, 17 vs 62%, P=0.002). Infection-free graft survival was also lower in HIV-positive patients (1-year survival, 61 vs 88%, P=0.025). Finally, cumulative graft survival (until permanent failure) tended to be lower in HIV-positive patients (1 year survival, 41 vs 65%, P=0.07).

Among 23 HIV-positive patients with AV fistula placement, the primary failure rate was similar to that observed among the 32 HIV-negative controls (44 vs 41%, P=0.83). Similarly, the cumulative fistula survival (after excluding primary failures) was similar in HIV positive and control patients (P=0.18).

In summary, HIV-positive patients are more likely to have graft infection and thrombosis as compared to HIV negative patients. In contrast, fistula outcomes are comparable in both groups. Thus, the disadvantage of grafts vs fistulas is greater in HIV-positive patients, as compared with HIV-negative controls.

COOL DIALYSATE DECREASES PRE-HEMODIALYSIS BLOOD PRESSURE - A NEW LOOK AT AN OLD PROBLEM

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The purpose of our study was to test the effect of decreasing dialysate temperature on blood pressure and cytokines, as endothelial dysfunction (measured by cytokines, which are temperature-sensitive) is implicated as the underlying abnormality in hypertension. The sample included 24 stable hemodialysis (HD) subjects randomized to either a control (n = 13) or experimental (n = 11) group. Each individual patient was followed in the study for 9 months (three 3-month phases). In Phase 2, the patients were randomized to treatment with either **standard dialysate** (37°C) or **cool dialysate** (1°C lower than the mean pre-HD oral body temperature at baseline); both groups received standard treatment during Phases 1 and 3. HD flow sheets and monthly lab data were collected throughout the study period. Serum samples for IL-1 beta, IL-2, IL-6, IL-10 and TNF-alpha were collected for 9 subjects pre-HD at the end of each phase and were measured in duplicate by using a multiplex assay (R&D). There was a marked improvement in both **pre-HD systolic** (p=0.04*, repeated measures ANOVA) and **diastolic** (p=0.06) **blood pressures** in Phase 2 in the experimental group. The mean pre-HD **IL-1 beta** (3.02 $\pm$ 1.6 vs. 1.24 $\pm$ 0.26, p=0.06) and **TNF-alpha** (21.11 $\pm$ 30.21 vs. 7.39 $\pm$ 3.62, p=0.06) were also lower in the experimental group. Our hypothesis was further supported by the observation that there was a decrease in **serum ferritin** (709.2 $\pm$ 299.6 vs. 579.7 $\pm$ 212.9) in the experimental group that could possibly be related to improvement in inflammatory changes. These data suggest that using cool dialysate during HD decreases pre-HD systolic and diastolic blood pressure. This effect may be mediated by an improvement in endothelial function, as measured by a decrease in selected markers of inflammation. Further study is warranted to explore the long-term beneficial effects of these changes on outcomes related to cardiovascular morbidity and mortality.

CHARECTARISTICS AND MORTALITY OF PATIENTS WITH PRIMARY SYSTEMIC AMYLOIDOSIS RECEIVEING RENAL REPLACEMENT THERAPY, DURING THE POST-STEMCELL TRANSPLANT ERA

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Previous studies have described the high mortality of patients with primary systemic (AL) amyloidosis on renal replacement therapy (RRT). These studies were conducted in the pre-stem cell transplant era. The goal of this study was to provide a more recent characterization of this patient population, specifically to identify factors associated with early mortality and evaluate the influence of autologous peripheral blood stem-cell transplantation and renal transplantation.

At a single center, 46 patients were identified with AL amyloidosis and who also received RRT from January 1997 to October 2005. Thirty-eight met inclusion criteria. A retrospective medical record review was done to extract patient clinical information. Survival analysis was performed using Kaplan-Meier estimation.

The study group included 19 females (39%) and 28 males (61%). Median age at diagnosis of AL amyloidosis was 58 years. Median time from diagnosis to start of RRT was 8 months. Two patients used peritoneal dialysis (PD), the remaining 36 used hemodialysis (HD). Six patients (15.8%) underwent renal transplantation, and 12 (31.6%) had stem cell transplantation. Overall, the median survival after diagnosis of AL amyloidosis was 60 months and after initiation of RRT was 33 months. No statistical difference in survival was found between patients with definite, indeterminate, or lack of cardiac involvement. Using log rank testing, there was significantly longer survival after RRT in patients who underwent stem cell transplantation compared to those who did not ($p=0.0149$). Likewise, there was significantly longer survival after RRT for patients that underwent renal transplantation compared to those who did not ($p=0.009$).

Compared to previous studies of this patient population, our cohort had longer median survival times after diagnosis of AL amyloidosis and start of RRT. Both stem cell transplantation and renal transplantation seemed to be associated with improved survival.

IMPACT OF NUTRITIONAL SUPPLEMENTS ON ALBUMIN LEVELS OF DIALYSIS PATIENTS

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Albumin is a known marker for adequacy of nutrition. There is an increase in morbidity and mortality in dialysis patients with albumin level less than 4 mg/dl. We studied the impact of nutritional supplements on albumin levels of dialysis patients.

Applications were submitted to our nutritional supplement assistance program based on financial criteria (lack of Medicaid coverage, annual income <$24,000). Qualified patients were observed for 3 months (A). Patients with albumin < 3.5 mg/dl and/or significant weight loss during that period were eligible. Patients received a 3 month supply of non-renal specific liquid nutritional supplements ordered at 2 cans/day or powdered protein supplements ordered at 6 scoops/day (B). Patients were followed for an additional 3 month washout period without supplements (C). Monthly albumin and weight were tracked.

One hundred thirty patients, 65 males and 65 females, completed 9 months of study. Mean age was 62.3 years. Ninety-nine patients were on hemodialysis and 31 were on peritoneal dialysis. Enrolled for low albumin were 116 patients, 43 for weight loss, and 29 for both. There was a statistically significant increase in albumin level starting in the first month of supplement use that persisted through the whole follow up period even after the supplement was stopped. No significant weight change was found.

	Observation A- mo 1,2,3	Supplement B-mo 4,5,6	follow up(C)	P value A vs B or C
Albumin mg/dl	2.9±.4	3.45±.42	3.49±.4	< .004
weight kg	69.4±21	67.2±16	68.5±17	.3

Nutrition supplements in dialysis patients significantly improved albumin levels. Improvement persisted even after supplements were stopped. Due to the strong inverse relation between albumin level and morbidity and mortality, use of supplements would have beneficial effects.

THE EFFECT OF EXERCISE ON HEMODIALYSIS PATIENTS IN A VETERANS ADMINISTRATION MEDICAL CENTER

Megan Rizzi, Arianna Aoun, Alison Steiber.

Exercise can affect quality of life and comorbities in renal disease. The purpose of this study is to determine if exercise improves functioning capacity, and perceived quality of life in Hemodialysis (HD) patients. This was a prospective clinical trial conducted at a VA Medical Center in which HD patients either chose to participate in a four month exercise program (experimental group) or not (control group). Data were collected on the Medical Outcomes Short Form-36 (SF36), and Sit-to-Stand test (S-S) from patient interview and medical chart review. Data were analyzed using SPSS vs 13.0. 88% (n=24) of the patients were African American, 13% were Caucasian, and 96% were male. The mean age was 59±8 years. Within the treatment group, the S-S time significantly decreased from baseline to month 2 (mean±SD: 39±16 to 32±10 sec; p=0.009) and then to 30±10; (p=0.007) after 4 months of exercise. There was a significant increase in time spent exercising between months 0 and 4 (702±543 to 1281±1187 min) within the treatment group. The SF36 domain, physical functioning, increased significantly from baseline to the end of the intervention (p=0.024). The SF36 domain, mental health, significantly correlated with time spent exercising at months 1 and 2 (r=0.85, r=0.94). Role Physical, an SF36 domain, was significantly correlated with the amount of time spent exercising at months 1 and 3 (r=0.898, r=0.93). The midpoint SF36 domain, social functioning, was significantly correlated with the amount of time spent exercising at month 1 (r=0.81). Subjects who spent more time exercising month 1 were significantly more likely to exercise at month 3 (r=0.98). No significance was seen when comparing post-SF36 between the groups. This study illustrates that initiating a low intensity exercise program significantly decreases patient's S-S time, subjects increase the time spent exercising once a program is started, and exercise intervention is strongly related to specific SF36 domains (social function, mental health, and physical role).

ARTERIOVENOUS FISTULA: SURVIVAL IMPACT ON PATIENTS WITH END-STAGE RENAL DISEASE INITIATING HEMODIALYSIS

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Early referral to nephrologist of patients with chronic kidney disease is associated with a decreased morbidity and mortality after initiation of renal replacement therapy. Survival among hemodialysis (HD) patients is influenced by a number of factors and timely construction of a permanent dialysis access predicts a good outcome.

The aim of the study was to evaluate the impact of HD start with arteriovenous fistula (AVF) *vs* venous catheter (VC)- including temporary and cuffed catheters.

Retrospective study based on 93 patients with end-stage renal disease (ESRD) initiating HD at a dialysis unit from 1-01-2003 to 31-12-2004. Analysis of the groups of patients beginning HD with AVF *vs* VC, comparing: pre-dialysis medical care; acute/programmed HD start; glomerular filtration rate (GFR) by MDRD fomula, comorbidity, hospitalizations and deaths. Blood pressure control, nutrition, anemia and mineral metabolism were also evaluated by the time of HD start and 6 months later.

Of the enrolled patients, 25% (n=23) had a functioning VAF at HD start, whereas 75% (n=70) needed VC placement. The mean age was 60,0±15,3 *vs* 62,1±16,8 years, without significant difference regarding gender and ESRD etiology between the two groups. 86% of the patients presenting VAF had had nephrologist medical care pre-dialysis with programmed HD start *vs* 50% of those with VC. Significant statistic difference was found: GFR 9,5±2,6 vs 7,3±3,9 (p=0,048), comorbidity 4,5±1,8 *vs* 5,9±2,5 (p=0,012), albumine 3,9±0,4 *vs* 3,5±0,5 (p<0,001), Hemoglobin at start 11,5±1,8 *vs* 9,1±2,4 (p=0,001) and after 6 months 13,2±1,1 *vs* 12±1,7 (p=0,003) and phosphatemia at start 3,3±1,6 *vs* 5,5±1,2 (p=0,023) and after 6 months 5,3±1,3 *vs* 4,2±1,4 (p=0,003). 4% (n=1) of patients with VAF died during the first year on HD *vs* 22% (n=13) of the CVC group (p<0,05) with significant difference on cumulative survival.

Our data demonstrated that timely construction of a permanent dialysis access, among other factors, was associated with substancial survival benefit after initiation of dialysis.

QUANTITATIVE RELATIONS OF SOLUTE SIZE AND FILTRATE VOLUME ON CLEARANCE IN HEMODIAFILTRTION (HDF)

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Amyloidosis and cardiovascular morbidity are long-term complications of chronic hemodialysis and presumed to be secondary to the accumulation of "middle-molecules" such as ß$_2$-microglobulin. Convective clearance appears to be the only means of removing meaningful amounts of "middle-molecules" during treatment, but quantitative data are lacking. The Aksys PHD can produce injectable quality dialysate and use this as a replacement fluid for hemodiafiltration.

Methods: 18 HDF treatments were performed in-vitro using the PHD and a Fresenius F80 filter. The removal of urea, phosphorus, creatinine, vancomycin (MW 1.48kD), inulin (MW 5kD) and myoglobin (MW 17.4kD) from a 50-liter tank were studied. Treatment time varied from 3 to 8 hr and the HDF rate from 0 to 3.6 L/hr, for a total of up to 28.8 L/treatment. The HDF fluid was pushed into the blood compartment of the filter across the filtering membrane in 200–300mL aliquots over a minute's time every 5-15 min. The volume was then removed over the next 4–14 min. Clearance, removal rates, and mass balance were studied.

Results: There was no enhancement of removal of molecules < 5kD with any HDF volume used. However, removal of myoglobin was greatly enhanced in a convective volume-dependent manner.

Removal Efficiency as % of a Standard PHD Dialysis Session with an HDF of 0.8 L/hr

Solute:	Urea		Vancomycin		Inulin		Myoglobin	
Duration hrs:	3	8	3	8	3	8	3	8
HDF 3 L/hr:	93	99	96	93	75	84	118	123
HDF 3.6 L/hr:	91	96	100	93	87	93	137	147

Conclusion: With high-efficiency dialysis filters, HDF does not enhance removal of molecules < 5kD but greatly enhances removal of "middle-molecules' in a volume-dependent fashion. With 28 liters of HDF, the removal of myoglobin was increased 47%.

NICOTINIC ACID EXERTS POWERFUL HYPOPHOSPHATEMIC EFFECT IN DIALYSIS

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The existing calcium containing Phosphate (P) binders increase the vascular calcification with myriad cardiovascular implications.Newer agents like sevalemer hydrochloride and lanthanum carbonate have high tablet load and are costly. Recent animal studies show that nicotinamide inhibits the Na-Pi 2b transporter in the rat jejunal mucosa and thereby controls the hyperphosphatemia of renal failure.We undertook a prospective study of its prodrug,Nicotinic acid to test its efficacy and safety in our hemodialysis population.

It was a prospective controlled study from April-September 2005.ESRD patients who were on maintenance HD were enrolled in to the study if their predialysis S.Phosphorus was more than 6 mg%.We Excluded patients with liver disease,malignancy and gout.During the run in period of 1 week all P binders were stopped. A singledose of 375 mg extended release nicotinic acid tablet was given with meal.The dose was titrated to achieve phosphate control.Repeat measurements were carried out after 8 weeks.Statistical analysis was performed.

There were 34 patients.Male;Female-30;4.Age-48 $\pm$ 13 yrs.Etiology of ESRD-CGN(14),DN(8)and HT(8), Others (4).They were on HD for mean period of 8.6 months.

	Pre study	**post study**	**p (2 tailed t)**
Phosphorus. mg %	7.7 $\pm$ 1.5	5.6 $\pm$ 1	< 0.001
Calcium. mg%	8.1 $\pm$ 1	8.5 $\pm$ 1	< 0.015
S.Alk.P.IU/L	107 $\pm$ 66	82 $\pm$ 46	<0.001
Ca X P $mg^2/\%^2$	59 $\pm$ 14	45 $\pm$ 9.8	<0.001

Oral nicotinic acid was well tolerated.Mild pruritus was encountered in 2 patients.30 patients required only 375 mg whereas 4 patients required 750 mg /day .

Oral nicotinic acid significantly reduced the serum Phosphorus, Alkaline Phosphatase and Ca X P product at the end of 8 weeks with good tolerability profile.It may emerge as a powerful yet low cost agent for control of hyperphosphatemia in hemodialysis.

THE RELATIONSHIP BETWEEN BONE MINERAL DENSITY AND BIOCHEMICAL BONE TURNOVER MARKERS IN HEMODIALYSIS PATIENTS

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In recent time osteoporosis is becoming more important among the HD patients. We aimed to evaluate the relationship between BMD and biochemical markers of bone turnover among the HD patients. Seventy uremic patients for at least one year on maintenance HD programme were enrolled to the study. All the patients were treated by conventional bicarbonated HD for 5 hours by using low-flux hollow fiber dialysers. BMD was measured by DEXA in lumbar spine (LS) and femoral neck (FN). Biochemical bone turnover markers such as Ca, P, ionized Ca, iPTH, and ALP levels were measured before the HD session. The patients were divided into two groups as group 1: Male, group 2: Female.

Thirtythree (47.1%) of the 70 patients were female and 37(52.9%) were male with mean age 44,0±13,1 and 46,2±17,0 respectively. Mean duration of HD treatment was 33,7±28,5 in females and 33,0±26,0 in males. According to BMD measurements in FN T score 7.1%(n=5) of patients were osteoporotic, 51.4%(n=36) osteopenic and 41.4%(n=29) normal, on the other hand in LS T score the results were 47.1%(n=33) osteoporotic, 31.4%(n=22) osteopenic and 21.4%(n=15) normal. No statistically significant association was found in osteopenia/osteo-porosis between genders according to FN and LS T score (p=0.604, p=0.470, respectively). There was no significant relationship between BMD and biochemical markers of bone turnover. A positive correlation was found between BMD T score of FN and age (r=0.413, p=0.000).

The osteopenia/osteoporosis is still frequent among HD patients. BMD T scores in the osteopenia/osteoporosis range were observed at the LS in 78.5 % of these patients and at the FN in 58.5 %. There were no correlations between bone turnover markers and BMD measurements at the both skeletal regions.. There is no biochemical marker that can be used instead of DEXA in HD patients as in normal population.

MAGNESIUM CARBONATE- AN EFFECTIVE PHOSPHATE BINDER

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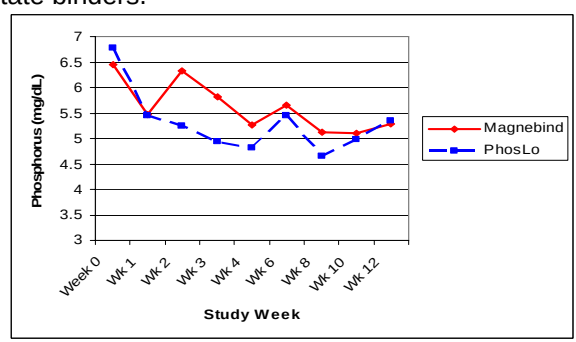
Phosphorus (Phos) control remains a great challenge for patients (pts) on hemodialysis (HD). Magnesium (Mg) carbonate is a dietary supplement and binds dietary Phos. Its use in HD pts is limited out of concerns for hypermagnesemia. This prospective randomized trial was designed to evaluate the efficacy and safety of Mg carbonate as a Phos binder in HD pts.

Pts on HD for > 3 months and without a history of frequent diarrhea were enrolled. Randomization was 2:1 Mg vs. Ca. All pts underwent a binder washout period. Pts randomized to Ca acetate were started on 2-3 tabs AC based on their prior binder dose. Pts randomized to Mg carbonate were started on 1- 300 mg tab AC. Doses of both binders were titrated as needed. All pts were treated with a 0.75 meq/L Mg, 2.5 meq/L Ca bath. Preliminary data (n=16) shows that Magnebind was equally effective as Ca acetate in controlling the Phos (fig). No pt developed a Mg level > 3.5 meq/L. Pts receiving Ca acetate ingested significantly greater amounts of elemental Ca (1597±51 mg/d) than the magnebind tx'ed group (930±136 mg/d).

Magnebind is an effective Phos binder and significantly decreases pts' exposure to elemental Ca compared with Ca acetate binders.



A MULTICENTER STUDY OF SUBJECTIVE GLOBAL ASSESSMENT (SGA) VALIDITY AND RELIABILITY IN THE HEMODIALYSIS (HD) POPULATION.

Alison Steiber, Janeen Leon, Ash Sehgal, Donna Secker, Maureen McCarthy, Kamyar Kalantar-Zadeh, Linda McCann.

SGA is a nutritional assessment tool recommended by the NKF K/DOQI guidelines. However, the validity and reliability of this tool have not been established in HD patients. The purpose of this observational study was to determine the reliability and validity of SGA in HD patients. Renal dietitians (RD) were recruited to perform SGA (7-point scale version) and collect data from 3 HD patients at 0 and 6 months on demographics, clinical status, biochemistries, dietary intake, and quality of life (Medical Outcomes Short Form-36, SF36). To test inter-rater reliability, SGA was performed by a 2nd RD (RD #2) at baseline and to test intra-rater reliability, the original RD (RD #1) repeated SGA at 1 month. RDs were trained for data collection via an SGA website created for this study. RDs (n=54) collected data at HD facilities in the US (109 patients), Canada (35 patients) and New Zealand (9 patients). Of the 155 patients, 46% were female, 64% were Caucasian, 6% Hispanic, 21% African American, and 6% Asian. The primary etiologies were: 10% type 1 diabetes mellitus (DM), 27% type 2 DM, 33% hypertension, and 10% glomerular nephritis; and 59% had documented cardiovascular disease. The mean age, BMI, serum albumin, and duration on HD were: 64±14 years (mean±SD), 28±7kg/m^2, 3.7±0.4 mg/dL, and 41±34 months, respectively. SGA scores were: well nourished (7)-30%, mildly malnourished (MN-6)-41%, moderately MN (5-3) 5-21%, 4-7%, and 3-2%, severely MN (2&1)-0%. Inter-rater reliability had a weighted Kappa of 0.5 and Spearman's Rho of 0.7, and inner-rater reliability had a weighted Kappa of 0.7 and Spearman's Rho of 0.8, all at $p<0.001$. Validity determined using BMI and serum albumin was statistically significant for the 5 categories of SGA documented (7-28±7, 6-29±7, 5-28±8, 4-21±4, and 3-24±2-$p<0.05$ and 7-3.8±0.3, 6-3.8±0.4, 5-3.7±.05, 4-3.4±.07, 3-2.9±1.2-$p<0.001$, respectively). SGA did not differ significantly by ethnicity or nationality but did by gender ($p<0.05$). In conclusion, the 7 point scale SGA is a reliable and valid tool for nutritional assessment in adults on hemodialysis.

A COMPARISON OF SEXUAL DYSFUNCTION IN HEMODIALYSIS (HD) AND RENAL TRANSPLANT PATIENTS (RTP).

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Sexual dysfunction in ESRD patients is multifactorial. We used two questions from KDQOL SF 36 to measure sexual dysfunction (SD). (How much of a problem was each of the following in past 4 weeks? 1. Enjoying sex? 2. Becoming sexually aroused?) Answers were recorded on a scale of 1 (None) to 5 (Severe). A SD score of $\geq$ 6 was considered indicative of sexual dysfunction. 50 RTP and 50 HD patients were interviewed using SD, Illness Effects Questionnaire (IEQ), Quality of life Scale (QLS), Beck Depression Inventory (BDI), Satisfaction with life Scale. Time since transplant / HD, age, hemoglobin and albumin levels were measured in both patient groups. $p < 0.05$ considered significant.

RTP were younger than HD patients (49 ± 11.8[SD] vs. 60.3 ± 14). Average time since transplant or initiation of HD, Hemoglobin (~12 g/dl), quality of life perception, burden of illness, satisfaction with life/depression were comparable in two populations. Serum albumin was higher in RTP (4.1 ± 0.4 vs. 3.8 ± 0.5). Comparison of psychosocial variables is listed in table below.

96% of patients were African American, 52% were women. Only 36% of RTP versus 72% of HD patients had a SD$\geq$ 6. Greater perception of sexual dysfunction correlated with greater perception of depression ($r=0.34$, $p=0.01$) and burden of illness ($r=0.37$, $p=0.01$) and lesser perception of quality of life, social support and satisfaction with life in each population.

We conclude that the perception of better sexual function of renal transplant patients may be due to better clearance of uremic toxins and younger age. These studies need to be replicated and expanded in larger multiethnic populations.

	HD patients	Transplant patients	p value
BDI	9.1 ± 5.3	8 ± 7.8	NS
QLS	7.7 ± 1.4	7.5 ± 2.3	NS
IEQ	65.2 ± 29.7	53.5 ± 34.0	0.07
SD	6.9 ± 3.5	4.4 ± 2.7	<0.01

EFFECT OF SERUM FERRITIN LEVEL ON EPOETIN DOSE REQUIREMENT IN HEMODIALYSIS PATIENTS

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Purpose: The purpose of the study is to determine the relationship between serum ferritin levels and epoetin dose requirements in a cohort of outpatient hemodialysis patients. *Methods*: Outpatient laboratory values for 117 chronic hemodialysis patients were reviewed. Values for ferritin, transferrin saturation, reticulocyte count, MCV, hemoglobin, and per treatment epoetin dose were extracted. The data were then analyzed to determine the relationship between serum ferritin and epoetin dose requirement. Anemia management was carried out during the study period using the dialysis unit's standard protocol. *Results*: There was a negative correlation between serum ferritin level and erythropoetin dose (Pearson's correlation coefficient –0.194, $p<0.05$). Mean hemoglobin levels were >11g/dL in 86% of patients studied. Mean ferritin levels were >800ng/mL in 51% of the study population. Mean values for transferrin saturation (Tsat), hemoglobin (g/dL), serum ferritin (ng/mL), and per treatment epoetin dose (units) are shown in table 1 below. Group 1 represents those patients with ferritin <800ng/mL, Group 2 are those with ferritin >800ng/mL. Age, demographics, Kt/V, weight, biointact PTH, and transaminase levles were similar between groups. *Conclusions*: Patients with higher serum ferritin levels required, on average, lower erythropoetin doses to maintain target hemoglobin levels >11g/dL. Higher serum ferritin levels may not be indicative of increased epoetin resistance in this population. This contradicts the commonly held notion that elevated serum ferritin is an indication of epoetin resistance.

TABLE 1

Group	n	Ferritin (ng/mL0	Tsat (%)	Hemoglobin (g/dL)	Epoetin Dose*
1	57	420	28	11.8	9949
2	60	1303	30	11.8	8172

*$p<0.05$ for overall analysis

REDUCING BLOOD TRANSFUSION IN DIALYSIS UNIT

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Blood transfusions are generally detrimental to dialysis patients and should be avoided when possible (Daugirdas J 1994). The risks for patients, including: ABO incompatibility; anaphylactic reaction; transmission of virus infection such as hepatitis B,C or HIV; jeopardy of a prospect for renal transplantation.

The dialysis unit has 110 patients. In 2002, 386 blood transfusion units were used. In 2003,we introduced a blood transfusion recording system aiming to monitor and reduce blood transfusion for the dialysis patients. It includes: 1) Introduction of Blood Transfusion Request form filled by doctors. It indicates the reason to prescribe. 2) Introduction of Blood Transfusion Record form filled by nurse for each transfusion. It includes date, patients name, HB, blood units and name of the doctor who prescribes. 3) Introduction of Blood Transfusion Folder. Both forms above are kept in it. The Anaemia co-ordinator produces an on going monthly audit of blood transfusion according to the data.

A monthly anaemia review meeting is held between the nephrologists consultants, dialysis unit registrar and anaemia co-ordinator by using 1) a chart of all dialysis patients' current Epo dose, monthly HB, MCV, HCT, reticulocyte count, fe, IBS, ferritin and CRP; 2) a trend record of HB and Epo dose for every patient on a monthly basis; 3) a chart with a graph indicating continuing Hb results according to the UK Renal Association, European Best Practice Guide and K/DOQI standards; 4) a chart with a graph indicating a correlation between average HB, average Epo dosage and blood transfusion each month. The result appeared encouraging. Blood transfusion has reduced by 62% in two yeas.

Time	Blood Transfusion units	
2002	384	100%
2003	225	58%
2004	146	38%
2005	140	36%

Average HB has increased from 10.9g/dl (Dec 2002) to 12 g/dl (Nov 2005). Since Sept 2003, each month average HB has achieved the European Best Practice Guide and DOQI target 11g/dl, but blood transfusion has been reduced largely by 62% in 2 years. A medical-nursing team works well. We believe that blood transfusion recording in dialysis unit is a good clinical practice as a part of the anaemia management for the patients.

ASSESSMENT OF KNOWLEDGE IN PATIENTS WITH END-STAGE RENAL DISEASE TREATED WITH HEMODIALYSIS

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Although many potential sources of disease-related information are available to end stage renal disease (ESRD) patients, not many studies have looked at the level of knowledge of ESRD patients on long-term hemodialysis (HD). We wished to assess the level of knowledge in a group of patients with ESRD treated with long-term HD and to determine its correlation with demographic and clinical factors.

This was a cross-sectional study undertaken in two ambulatory dialysis centers in Milwaukee, Wisconsin. Eighty-eight ESRD patients on long-term HD completed a validated self-administered questionnaire (the kidney disease questionnaire) during the first hour of their dialysis session. A Poisson generalized linear model with log link function was used to test for the effects of race, gender, age, employment status, educational level and duration of dialysis on percentage of correct responses.

The mean age was 53 years. 55 were men (63%), 63.5% were black, 32% were white and 4.5% were from other races. The mean duration of dialysis was 4.27 years. The
patients had a high level of knowledge [the median score was 63% (range 30%-100%)]. After adjustment for all covariates, only educational level and duration of dialysis were associated with higher level of knowledge. Using college graduate and professional level education as reference, patients with intermediate level of education (high school graduate and some college) and those with lower level of education (less than high school graduate) scored 15% (95% CI: 3% to 26%) and 28% (95% CI: 16% to 39%) fewer correct responses respectively. Each increase of two years of dialysis increased the average number of correct responses by 2.9% or approximately one question.

ESRD patients with lower educational attainment have lower level of knowledge about their condition. This information should guide healthcare staff when educating ESRD patients. Prospective studies are required to ascertain whether improvement in disease-related knowledge will decrease hospitalizations and other poor outcomes in ESRD patients.

RACIAL AND GENDER DIFFERENCES IN HYPERTENSION CONTROL IN CHRONIC KIDNEY DISEASE: RESULTS FROM THE KIDNEY EARLY EVALUATION PROGRAM (KEEP)

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Poorly controlled hypertension (HTN), black race, and male gender are all risk factors for the development and progression of chronic kidney disease. The relationship between race, gender, and HTN control across stages of chronic kidney disease (CKD) is not known.

We examined rates of HTN control (<130/80mmHg) across stages of CKD, 1-2 (early) vs. 3-5 (advanced) among black men (n=1162), black women (n=3008), white men (n=1461), and white women (n=2625) in the KEEP study who reported a history of HTN. KEEP is a CKD screening program enrolling individuals ≥18 years with diabetes or HTN, or a family history of CKD, diabetes or HTN. Stages of CKD were determined by calculated glomerular filtration rate and urinary dipstick estimation of albuminuria. We used cross-sectional logistic regression models to estimate the odds of hypertension control, and 95% confidence intervals, for each race/gender group by severity of CKD. We adjusted for education, insurance, BMI, diabetes, and age.

Among participants with early CKD, black men (0.54, 0.41-0.72), and to a lesser extent black women (0.79, 0.63-0.995), had lower odds of HTN control than did white men. HTN control among white women (0.91, 0.71-1.17) did not differ from white men. Similar patterns were seen for advanced CKD, with lower odds of HTN control for both black men (0.60, 0.40-0.91) and black women (0.70, 0.53-0.995), but not for white women (1.0, 0.79-1.27), when compared to white men.

Our findings show that both black men and women with HTN and CKD are at particular risk of poor HTN control. Efforts to improve blood pressure control for these groups may help to narrow both racial and gender disparities in progression to end-stage renal disease.

ASSOCIATION BETWEEN ENaC, SGK1 and CYP11B2 SNPs AND HYPERTENSION

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Purpose: Single nucleotide polymorphisms (SNPs) of the amiloride sensitive epithelial sodium channel (ENaC) have been reported in hypertensive adults.

Methods: We performed a case control study to examine the association between ENaC SNPs and hypertension in two black populations. SNPs were selected from the three genes which encode ENaC subnunits: (SCNN1A), (SCNN1B) and (SCNN1G) and two ENaC regulator genes aldosterone synthase (CYP11B2) and serine threonin kinse (SGK1). Cases and controls were U.S. or Nigerian participants of the International Collaborative Study of Hypertension in Blacks. Hypertension was defined as blood pressure $\geq$ 130/80 mm Hg and/or use of anti-hypertensive medications and controls were normotensive (BP < 130/80 mm Hg). Corrected chi-square and quasi likelihood statistical tests were used to examine the association between each SNP and hypertension while adjusting for relatedness.

Results: From the Nigerian population, 374 cases (mean age 54.3 years) and 376 controls (mean age 55.0 years) were selected. In the U.S. population, 375 cases (mean age 46.9 years) and 376 controls (mean age 37.1 years) were selected. A total of 35 SNPs were examined (10 in SCNN1A, 7 in SCNN1B, 9 in SCNN1G, 4 in CYP11B2, and 5 in SGK1). No ENaC SNPs were consistently associated with hypertension in both populations. No SGK1 SNPs were associated with hypertension in either population. One non-synonymous SNP (C/T) in CYP11B2 showered borderline significance in both the Nigerian and U.S. populations (P = 0.08 for both populations). This SNP was in linkage disequilibrium (r^2 = 0.14 in Nigeria and 0.13 in Maywood) with -344C/T, a CYP11B2 SNP associated with hypertension in previous studies.

Conclusions: A consistent association of borderline significance was noted between the rs4544 CYP11B2 SNP and hypertension in both study groups. These findings should be repeated in larger study populations.

OUTPATIENT MANAGEMENT OF DIABETIC NEPHROPATHY IN AN ACADEMIC INSTITUTION: RESIDENTS (R) VS. FACULTY(F) Michael Levin, Ajay Manchandia, Alin John and Allan B. Schwartz Drexel University College of Medicine Phila, Pa. USA

Introduction: 658 recognized diabetic pts charts were reviewed in alphabetical order from the Clinics; R vs. F. Type 1 diabetics, Type II without documented albuminuria/proteinuria, or not seen in 3 years were excluded. This led to 74 charts evaluated. Methods: Charts were analyzed: 1) systolic and diastolic blood pressure (SBP)(DBP), 2) number/class of anti-hypertensive drugs (AHBP), 3) albuminuria: creatinine ratio (ACR) (Micro: 20-515 mg/G) and proteinuria:creatinine ratio (PCR) (Macro: ≥ 650), 4) MDRD GFR. Therapeutic results and classes of AHBP of the R & F groups were compared by unpaired t-tests, with attention to RAAS. Results: R & F Micro DN pts BP were not significantly different: 133/78 vs. 136/83. R & F Macro DN patients BP were not significantly different: 151/79 vs. 159/78. Macro DN SBP was consistently > than Micro DN pts in both R and F: 151 vs. 133 and 159 vs. 136. Number of AHBP drugs for Micro DN pts was 2.4 by R and 2.8 by F (ns), and for Macro DN pts 2.3 by R and 3.4 by F (ns). ACE-I were used for Micro DN in 68 % by R and 45% by F (p=0.08). ACE-I were used similarly for F & R Macro DN pts. F Macro DN pts. PCR was reduced to 2,571 vs. R to 3,524. GFR was similar in F & R: 70-72 ml/min for Micro: 33-46 ml/min for Macro.

	Residents Clinic	Faculty Practice	X^2 P-value
ACE-I	Micro 68.1% Macro 100%	Micro 44.7% Macro 90%	p =0.0794 NS
ARB	Micro 22.7% Macro 25%	Micro 55.2% Macro 40%	p= 0.0143 NS
Diuretics	Micro 36% Macro 50%	Micro 71% Macro 70%	p=0.0086 NS

Conclusion: PCR of the Macro DN pts, having lower GFR, was reduced to even lower values by F at 2,571 vs. 3,524 by the R. F trended toward using more AHBP drugs than R: 3.4 vs. 2.3. ACE-I and NDHPCCB were used >by R in all DN. ARB and DHPCCB were used > by F. β Blocker use was equal. Diuretics were prescribed > by F than R in both populations (p=0.0086), and a lower PCR was noted in Macro DN pts. Even with aggressive treatment, goal BP of <130/80 was not achieved in either R or F, Macro DN or Micro DN.

PREDICTION OF TOTAL URINARY PROTEIN EXCRETION IN HYPERTENSIVE DISORDERS OF PREGNANCY WITH RANDOM URINARY PROTEIN-CREATININE RATIO

Enyioma Obineche[3], Diaa Rizk[1], Mukesh Agrawal[2], Javed Y. Pathan[3] Department of Obstetrics and Gynecology[1], Department of Pathology[2], Department of Internal Medicine[3], Faculty of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates.

Measure spot urinary protein-creatinine concentration and compare this with total urinary protein excretion in hypertensive pregnancies.

Protein and creatinine levels were measured in a voided random urine sample obtained before 24- hour urine collection for routine quantification of proteinuria. Subjects were all consecutive pregnant women with a viable fetus who were admitted with hypertension after 20 weeks gestation during 4 months (n=86).

Fifty two patients (60.5%) had significant proteinuria (≥300mg/day), 46 had pre-eclampsia, 5 had superimposed pre-eclampsia and 1 had renal hypertension. Four women (4.7%) had severe proteinuria (>5g/day).

Spot urinary protein-creatinine ratio in a pre-24 hour urine collection sample is predictive of total urinary protein excretion in hospitalized pregnant women with hypertension.

EARLY- AND LATE-ONSET RENAL FAILURE FROM ANGIOTENSIN BLOCKADE: A COAT OF MANY COLORS – NEED FOR INCREASED PHYSICIAN AWARENESS.

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Worsening of renal failure in patients with Chronic Kidney Disease, (CKD) concurrently on RAAS blockade (AB) who have renal artery stenosis (RAS), in the presence of precipitating factors is well recognized, moreso following initiation of AB. We recently described an unrecognized syndrome of late onset renal failure from angiotensin blockade (LORFFAB) in patients on AB; this warrants drug discontinuation. Physicians remain unaware of the scope of worsening azotemia associated with use of AB in patients with CKD.

We herein report four patients seen over one weekend, in early November 2005, by a Nephrology Consult Service, for symptomatic worsening of renal failure, each concurrently on AB. AB was discontinued in three whilst an ACEI (cough) was switched for an ARB in the fourth. GFR was monitored in all four patients.

There were one male, three females; mean age was 67 years. Renal ultrasound was normal in all four patients. MRA in one was normal. Kidney function normalized within days in two patients, improved in one patient and one patient remains hemodialysis-dependent. Hyperkalemia occurred in 3, anemia in 4, with two requiring erythropoietin; secondary hyperparathyroidism was present in three. There was dose escalation of combination ACEI and ARB (1), volume depletion and UTI (1), and septicemia with hypotension (1). No precipitating factor was identified one patient.

We submit that there is an unmet and unrecognized urgent need for increased physician awareness of the scope of early- and late- onset worsening of renal failure occurring in CKD patients on AB. We submit that with the adoption of a more targeted application of AB in selected patients, with indefinite monitoring of kidney function by MDRD estimated GFR, as well as pre-emptive suspension of AB under appropriate clinical circumstances, the concept of renoprotection using RAAS blockade would have been better served.

LATE ONSET RENAL FAILURE FROM ANGIOTENSIN BLOCKADE (LORFFAB): EXTENDED OBSERVATIONS. IMPLICATIONS FOR LATE ONSET ACCELERATED LOSS OF GFR IN SUSCEPTIBLE PATIENTS ON RAAS BLOCKADE - TIME FOR A PARADIGM SHIFT IN USE OF RAAS BLOCKADE?

Macaulay Onuigbo, Midelfort Clinic, Eau Claire, WI; Nnonyelum T Onuigbo, NT Systems, eau Claire, WI

There remain concerns regarding an unrecognized syndrome of late onset RAAS blockade (AB)-associated worsening of renal failure in patients with Chronic Kidney Disease (CKD).

We followed 103 patients with increasing baseline serum creatinine, concurrently on AB, seen in a Hypertension Specialist Clinic over 30 months. Where appropriate, AB was discontinued. GFR was monitored.

Thirteen of 103 patients required hemodialysis, four have died, and six remain hemodialysis-dependent. RAS was common. Precipitating factors include systemic illness, volume depletion and post-operative states. We demonstrated statistically significant 45% increased GFR in five patients with normal renal arteries, one month after discontinuation of AB, despite absent precipitating factors. This is late onset renal failure from angiotensin blockade (LORFFAB).

With 20 million diabetics in the USA, 11 million diabetic hypertensives, and whereas only 45,000 US diabetics reach ESRD annually, the majority of our diabetics do not progress to ESRD. The worldwide ESRD epidemic, coincident with increasing use of AB, raises a scary specter of iatrogenic ESRD. LORFFAB requires further study. Given a significant potential for AB-associated renal failure, we call for a more cautious use of AB. The vastly cited RENAAL and IDNT trials failed to show any mortality benefits. A dispassionate appraisal of available data calls for a multidisciplinary approach to achieve optimal blood pressure control (with or without AB), control of hyperglycemia, dyslipidemia, etc. We propose a more targeted use of AB, in high risk diabetic and nondiabetic patients (so-called progressors), with GFR monitoring, *indefinitely*. We submit that renoprotection would have been better served, this way.

AT_1 BLOCKADE MODULATES INFLAMMATORY RESPONSE IN RENAL TISSUE OF UNINEPHRECTOMIZED SHR

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Uninephrectomized (UNX) spontaneously hypertensive rats (UNX-SHR) develop earlier glomerular hyperfiltration and interstitial damage of the remnant kidney. Therefore, UNX-SHR is a useful animal model to investigate mechanisms involved in the progression of hypertensive renal disease. Drugs which interact against RAAS have demonstrated to be useful in controlling blood pressure and proteinuria. The purpose of the present study was to evaluate whether AT1 blockade may reduce inflammatory cell infiltrate in renal tissue by controlling Monocyte Chemoattractant Protein-1 (MCP-1) and Transforming growth factor ß1($TGFß_1$) in UNX-SHR. Male SHR and Wistar Kyoto (WKY) underwent uninephrectomy at 10 weeks old and were subsequently assigned to the following schedule during six months: [G1] UNX-SHR; [G2] UNX-WKY; [G3] UNX-SHR with valsartan 50 mg/kg/day. [G4] UNX-WKY with valsartan 50 mg/kg/day. Systolic blood pressure, creatinine clearance (Crcl) and proteinuria were evaluated. MCP-1, $TGFß_1$ and monocyte/macrophage cell infiltrate (ED1) were assessed by immunohistochemistry. Results at the end of the experiment: SBP (mmHg): G1= 218 ± 17, G2= 154 ± 7; G3= 147 ± 8, G4= 121 ± 3**. Crcl (µl/min/g BW): G1=1.2 ± 0.1*, G2= 2.9 ± 0.1; G3= 2.6 ± 0.3, G4=3.9 ± 0.2**. Proteinuria (mg/day): G1= 253 ± 39, G2= 63 ± 10; G3= 67 ± 9, G4= 15 ± 7**. MCP-1 (% / mm^2): G1= 30.2 ± 2.6*, G2= 18.2 ± 3.2; G3= 21 ± 2.3, G4= 2.0 ± 0.9 **. ED1 (Células/mm^2): G1= 464 ± 32*, G2= 147 ± 16; G3= 203 ± 18***, G4= 38 ± 10**. TGFß1 (%/mm^2): G1= 24.9 ± 2.7*, G2= 9.9 ± 1.8; G3= 11.1 ± 2, G4= 3 ± 0.7**. ($p<0.01$* vs. all Gs; $p< 0.01$** vs. G2 & G3; $p< 0.01$*** vs. G2). Conclusions: AT1 blockade by valsartan reduces both MCP-1 and $TGFß_1$ immunostaining together with the inflammatory cell infiltrate (ED1 positive cells) in renal tissue not only of SHR-UNX but also WKY-UNX. These findings emphasize the valuable protective kidney role that drugs which interacts against AT1 receptor of angiotensin II present especially in hypertensive renal disease.

ALDOSTERONE ANTAGONISTS (AA) ARE ASSOCIATED WITH ACHIEVED TARGET BLOOD PRESSURE IN CHRONIC KIDNEY DISEASE (CKD).

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CKD patients require multiple medicines to adequately treat hypertension. There is little data to guide the use of add-on medications. Studies have established that plasma aldosterone increases with worsening renal function. Among patients without CKD use of spironolactone is associated with improved systolic blood pressure (SBP). There is no published data on the use of AA for the treatment of hypertension in patients with CKD. We retrospectively looked at a large CKD clinic to determine the efficacy of AA.

Our CKD clinic focuses on multiple aspects of CKD care including blood pressure (BP) control. Many aspects of care are prospectively recorded in clinical database. The cohort was composed of 837 patients with at least 90 days in the clinic (90-676, ave. 263) and at least 2 visits (2-26, ave. 5). The cohort was diverse with respect to race (24% African American), age (19-96, median 71), gender (49% female) and diabetic status (49% diabetics). BP control was defined using K/DOQI targets for SBP of ≤ 130 (except for stage V CKD, SBP ≤ 140).

We investigated whether use of specific drug classes predicted SBP control. The use of AA (N=69) was the best predictor of SBP control with 58% control. AA were particularly effective in the later stages of CKD with 90% (27/30) of patients in stages 4 and 5 at target SBP. The median spironolactone dose was 25 mg/day (range 12.5-400).

The average potassium for patients on AA was 4.55. Sixty-seven percent of patients on AA were also on an ACEi or angiotensin receptor blockers (ARB), similar to the overall prevalence of the use of ACEi or ARB (68%). A chart review was done to determine if severe CHF was the indication for AA, possibly confounding the BP results. CHF was found to be the indication for AA in 10 of 69 patients.

In this retrospective review of practice patterns in a CKD clinic use of AA was associated with best control of blood pressure. The use of AA was not associated with a high potassium, nor did they prevent the use of ACEi or ARB. A controlled trial of the safety and efficacy of AA as an add-on medication for control of BP in advanced CKD is indicated.

BLOOD PRESSURE (BP) CONTROL BY RACE, GENDER AND CHRONIC KIDNEY DISEASE (CKD) STAGE IN A CKD CLINIC

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Control of BP is fundamental to slowing progression of CKD. One recent study showed that only 35% of CKD patients had BP ≤ 130/80. Hypertension is thought to be more poorly controlled with worsening renal function, and more poorly controlled in diabetics with CKD. CKD clinics are specialty clinics that focus on the diverse medical needs of CKD patients.

Many aspects of care are prospectively recorded in our clinical CKD database. The cohort was composed of 837 patients with at least 90 days in the CKD clinic (90-676, ave. 263) and at least 2 visits (2-26, ave. 5). The cohort was diverse with respect to race (24% African American), age (19-96, median 71), gender (49% female) and diabetic status (49% diabetics). BP control was defined using K/DOQI targets for SBP of ≤ 130 (except for stage V CKD, SBP ≤ 140). We used the latest clinical visit to investigate office BP, medications, and correlates of BP control including gender, race, age, diabetic status and number of antihypertensive medications.

Average SBP was 133.5 ± 20.9 with 51.4% controlled to target BP. BP was at goal in 51.9% males, 51.0% females; 45.7% African Americans; 45.6% diabetics. By K/DOQI CKD staging: forty seven percent of CKD stage 2 patients (n=76) were controlled; 52.0% of stage 3 (n=281); 46.9% of stage 4 (n=326); 60.6% of stage 5 (n=127).

Only 3.7% of the cohort was not on any antihypertensive medications. Overall there was an average of 3.0±1.5 antihypertensives per patient. The most frequently used classes were ACEi or ARB in 68% (39% ACEi and 38% ARB individually, 9% on both), loop diuretics in 64% and beta blockers in 61%. The average number of medications among patients with SBP ≤ 130 was 2.8±1.5 compared to 3.2±1.5 in patients with SBP > 130.

This is the first study investigating BP control in the setting of a CKD clinic with significant numbers of female patients. BP control is good compared to published data. However, nearly half the patients still have elevated blood pressure predisposing them to renal and cardiovascular end-points.

THE VIEW OF SEXUAL LIFE BETWEEN MALE PATIENTS RECEIVING CONTINUOUS AMBULATORY PERITONEAL DIALYSIS AND THEIR WIVES

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The objectives of the study were to identify attitude, behaviour, problems and adaptation of sexual relationship of male patients receiving continuous ambulatory peritoneal dialysis (CAPD) and their wives. Subjects included 70 male patients and their wives receiving treatment as out patients at the nephrology clinic of 3 hospitals in Southern Thailand. Questionnaires on attitude and behaviour were used for data collection and their reliability confirmed by Cronbach's alpha coefficients of 0.92 and 0.76, respectively. Data analysis was performed by percentage, means, standard deviations and t-test.

The results revealed that attitude and behaviour regarding sexual relationship of patients and wives were at a moderate level. There was a statistically significant difference in attitude ($p < 0.05$) but not in behaviour of patients and wives.

It was also found that patients' problems were(1)erectile dysfunction 60% (2)decreased sexual desire 48.6% , and (3)lack of sexual desire 40%, while wives'problems were(1)decreased sexual desire 57.1% (2) fear to harm patients 54.3%, and(3)lack of sexual desire 42.9%.

Finally it was also found that patients' and wives' adaptations were

(1) physical mode 42.8% and 28.5%
(2)cognitive mode 8.5% in both patients and wives
(3)affection mode 37% and 45.7%,respectively.

These results indicate the importance of attitude regarding sexual relationship of patients and wives and the need for promotion of patients and wives' adaptation to sexual relationship problems by using cognitive mode.

TUMORAL CALCINOSIS & ORANGE SAND IN THE CAPD BAG

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Tumoral Calcinosis is an uncommon disorder of bone and mineral metabolism in the setting of chronic kidney disease. However, Tumoral calcinosis with extensive ectopic calcification of the small bowel and peritoneum in the setting of peritoneal dialysis is even more uncommon.

We report a 53 year old woman with ESRD secondary to lupus nephritis on peritoneal dialysis (4 x 2 Liter exchanges) for 7 years who noticed orange grit in her CAPD bag for about 1.5 years prior to admission. She also reported a slowly worsening right lower limb pain of 4 months duration. Her physical exam was unremarkable except for a palpable mass in her L gluteal area. Her BUN clearance was 52 L/week with a weekly Kt /V of 1.51. Her serum albumin was 2.7 (3.1-4.3 g/dL), serum calcium was 10.3 mg/dl; phosphorus was 5.8 mg/dl and an ICMA (whole molecule) PTH of 60 pmol/L (normal 1.0-5.2 pmol/L). Her Alkaline phosphatase was 540 U/L (Normal 81-213 U/L) while the bony fraction was 333 U/L (normal 24-146).

An analysis of the orange grit in the PD effluent revealed calcium crystals. CT abdomen revealed extensive calcification of her bowel loops, peritoneum and blood vessels in addition to two large calcific masses in her left buttock that were confirmed as tumoral calcinosis after excision.

In light of the compelling images we review her history from CKD stage I to V, highlighting the evolution of secondary hyperparathyroidism that was ignored in 1980's due to lack of persuasive evidence advocating use of vitamin D analogues and the subsequent onset of tertiary hyperparathyroidism. This vignette also underscores the changing paradigm of bone metabolic disease in CKD from the early 1990's to the current KDOQI guidelines and evidence for instituting care at each stage of her kidney disease that may have potentially averted this rare but devastating outcome.

DO CKD GUIDELINES TRANSLATE TO PRACTICE, EVEN AMONG HIGH-RISK ELDERLY PATIENTS?

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Chronic kidney disease (CKD) is a major health problem in the elderly and is associated with risk of disease progression, cardiovascular disease, and mortality.

To test the hypothesis that nationally accepted clinical practice guidelines for CKD (K/DOQI) have not been translated to the care of the elderly CKD patient, we examined medical records of 500 consecutive geriatric outpatients referred by primary care providers to Home-Based Primary Care (HBPC) Program in the Southern Arizona VA Health Care System from 1/1/2001 through 7/31/2005. We chose patients referred to HBPC because they are characterized by a high disease burden and are at high risk for CKD.

We identified 83 of 500 referred patients with both age $\geq$70 years and Stage 3 CKD or worse (estimated GFR or eGFR <60 ml/min/1.73 m^2). Among these 83 patients (S_{Cr}, mean $\pm$ s.d., 1.9$\pm$0.3mg/dl, eGFR [MDRD Levey formula] 38.3$\pm$7.2 ml/min/1.73m^2), we found failure to document the diagnosis of CKD in 39 (47%) and failure to refer to a nephrologist in 66 (79.5%). Though 52 (92.9%) out of 56 anemic patients had evidence of lab evaluation, workup for elements of metabolic bone disease was frequently missing: PTH levels were obtained in only 3 patients (3.6%), serum calcium in 67 (80.7%), and phosphate in 65 (78.3%). Proteinuria was not assessed in 61% of all patients and 52% of diabetics. Among 31 (37.3%) patients with a recorded history of diabetes, 8 (25.8%) were not receiving an ACE inhibitor or an angiotensin receptor blocker. Among 73 (88.0%) patients with a recorded history of hypertension, only 32 (43.8%) showed optimum control (SBP<130 mmHg and DBP<80 mmHg).

We conclude that primary care of elderly high-risk patients, when measured against K/DOQI guidelines, frequently fails to identify CKD, refer for nephrology evaluation, initiate work up for potential CKD-related complications, or achieve optimum disease-specific management outcomes. The breadth of the problem suggests that both systematic and educational barriers impair translation of K/DOQI guidelines into clinical practice.

THE VANCOUVER ISLAND KIDNEY CARE INITIATIVE: AN EDUCATIONAL PROJECT ON GUIDELINE-BASED KIDNEY DISEASE CARE FOR FAMILY PHYSICIANS

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The purpose of the Kidney Care Initiative was to assist family physicians to identify patients in their practices at risk for kidney disease and to assist them to use guideline-based care. Fifteen family doctors were enrolled in the project in 2004 and they entered a total of 304 patients in the project database. They were provided with various educational sessions, office management tools and one-to-one academic detailing about kidney disease.

The measures used to determine guideline-based care were screening diabetic and hypertensive patients with serum creatinine and urine ACR and the prescribing of ACE inhibitors and ARBs. Baseline data prior to the start of the project was obtained, and a control group of physicians not in the project was used for comparison during the same time period.

The results after 12 months showed a creatinine screening rate of 86% for at-risk patients of doctors in the project compared to 61% for patients of doctors not in the project. Similar results were shown for ACR screening (52% for project doctors vs. 15% for non-project doctors). ACEI/ARB prescribing was also greater in the project group (58% vs. 37%). Although the number of physicians in the project was small, we concluded that the educational program resulted in improved screening and prescribing.

ISCHEMIC AND CONGESTIVE HEART DISEASE: MORTALITY ON PATIENTS WAITING RENAL TRANSPLANTATION. A SINGLE-CENTER STUDY.

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Chronic kidney disease (CKD) is associated with a high rate of mortality due to cardiovascular disease. While the role of ischemic heart disease (IHD) in mortality of CKD patients is well described, less is known about the natural history of congestive heart disease (CHD). We used Single-Photon Emission Computed Tomography (SPECT) to identify both IHD and systolic-dysfunction derived CHD in CKD patients waiting for renal transplant.

Data on 2,521 patients who had a SPECT scan between November 1997 and December 2003 was reviewed. 402 patients (16%) were identified with CHD (LVEF <40%). 611 patients (24%) had IHD, 210 of which had LVEF <40. CHD patients were more often black (32 vs. 25% whites, p=.002), male (26 vs. 19% females, p<.001), younger (49.5 ± 0.44 vs. 50.7 ± 0.31 years, p=.03), and more likely on dialysis longer than non-CHD patients (19.5 ± 0.94 vs. 14.4 ± 0.62 months, p<.001). IHD patients were more often white (27 vs. 22% blacks, p=.04), male (28 vs. 19% females, p<.001), older (53.1 ± 0.25 vs. 50.3 ± 0.38 years, p<.001), more likely on dialysis longer than non-IHD patients (19.2 ± 1.2 vs. 15.5 ± 0.57 months, p=.006). No differences in socio-economic status were found for either CHD or IHD.

We analyzed the data on the 1675 patients listed for renal transplantation during this period and followed up to July 2004. Hazard ratios took into account several variables including diabetes, time on dialysis and age: 1.0 for LVEF 50-69% (reference), 1.27 (95%CI 1.005 – 1.608, p=.046) for LVEF 40-49%, 1.49 (1.091 – 2.033, p=.012) for LVEF 30-39%, 2.33 (1.58 – 3.441, p<.001) for LVEF <30%, and 0.68 (0.44 – 1.033, p=.07) for LVEF ≥ 70%.

In summary, CHD and IHD are associated with increased mortality of CKD patients on the transplant waitlist. A graded increase in the mortality risk was observed with worsening degrees of systolic dysfunction. The role on transplantation on survival of CKD patients with CHD and IHD should be investigated.

IMPACT OF EPOETIN ALFA (EPO) ON PROGRESSION TO DIALYSIS IN ELDERLY CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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The purpose of this analysis was to evaluate the impact of EPO therapy on progression to dialysis in elderly CKD patients.

Using health claims and laboratory data from over 35 health plans between 1/1999 and 4/2004, elderly (≥65 years) dialysis patients who had ≥1 hemoglobin (Hb) value and ≥1 glomerular filtration rate (GFR) value <60 mL/min/1.73 m^2 prior to dialysis were identified. Patients were excluded if they had an organ transplant, had received blood transfusions or darbepoetin alfa, or had received dialysis for reasons other than CKD. Each CKD patient in the EPO group was matched by Hb and GFR to one control CKD patient who did not receive EPO. The observation start date was defined as the time when the matched EPO and control patients had the same GFR value. The time from the observation start date to the first marker of dialysis was compared between the two groups.

Sixty-eight patients (34 EPO and 34 controls) formed the study population, with baseline Hb and GFR values 10.2±1.1 g/dL and 15±6 mL/min/1.73 m^2, respectively. Mean age was similar between the two groups (years; EPO: 75.0±2.7 vs. control: 75.3±2.5), with a higher proportion of men in the EPO group (68% vs. 44%). The average time to dialysis was 156 days longer for the EPO group (319±252 vs. 163± 151 days, P=0.003). Stratified analysis by CKD stages revealed that EPO therapy in less severe CKD patients offered a greater delay in time to dialysis (Stage 4, (n=32): days to dialysis; EPO: 389±227 vs. control: 176±141, difference: 213, P=0.003. Stage 5 (n=36): days to dialysis; EPO: 256±263 vs. control: 152±162, difference: 104, P=0.160).

This matched cohort study suggests that EPO therapy may have a beneficial impact on delaying progression to dialysis, especially in patients with less severe CKD. These findings need to be further validated.

FABRY DISEASE: EARLY CLINICAL MANIFESTATIONS AND AGE AT CLINICAL EVENTS IN A COHORT OF 1375 ADULT MALES AND FEMALES

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Fabry disease (FD) is an X-linked lysosomal storage disorder due to the deficiency of a-galactosidase A and accumulation of globotriaosylceramide (GL-3) in visceral tissues and body fluids. The early mortality is caused by involvement of kidney, heart and brain. Enzyme replacement therapy for FD has been shown to clear the vascular endothelial accumulation and may decrease the incidence of significant clinical events in treated patients. Early institution of therapy may prove most effective; however, failure to diagnose affected individuals based on recognition of early symptoms compromises these efforts. The Fabry Registry was analyzed to determine presenting symptoms, age at diagnosis, and age at clinical events in 1375 adults with FD (males N=755 and females N=620). The median age of diagnosis was 28 yr for males (N=669) and 35 yr for females (N=534). Males with FD presented with symptoms at a median reported age of 10 years (N = 513). Males with FD had initial presenting symptoms most commonly present in the neurologic system (46%, with pain being predominant), followed by renal (45%), skin (29%), and GI (14%). Females with FD presented with symptoms at a median age of 14 years (N=307). At presentation, females had symptoms most commonly present in neurologic (43%, specifically pain), GI (23%), ophthalmologic (20%), and skin (20%). The age at which a serious complication occurred in a target organ was recorded. The mean age (SD) was 39.2 yr (9.6) (N=119 events reported) for dialysis or kidney transplantation, 42.8 (12) (N=241) for cardiac events (MI, arrhythmia, angina, CHF or significant cardiac procedure), and 40.1 (12.7) (N=86) for cerebrovascular events (stroke). Awareness of the early course of FD and common presenting signs and symptoms in males and females may lead to improved recognition and outcome for affected individuals.

EFFECT OF ANEMIA MANAGEMENT ON THE PROGRESSON OF CHRONIC KIDNEY DISEASE

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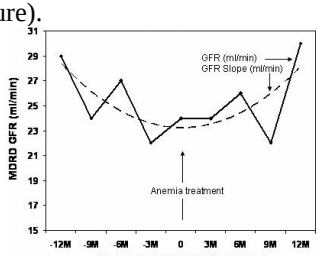
Treating anemia associated with Chronic Kidney Disease (CKD) may have several benefits including delayed progression of kidney disease. We evaluated the progression of kidney disease in anemic patients with CKD receiving darbepoetin alfa. Patients were treated in a pharmacist and nurse-directed anemia management clinic based on a protocol established with nephrologists. All patients (n=104) were anemic (Hb $\leq$ 11 g/dL) at enrollment and received darbepoetin alfa (and iron if needed). Follow-up was between 3 and 12 months. The MDRD glomerular filtration rates (GFR) were compared over a period of 12 months prior and 12 months after the initiation of anemia therapy. The average baseline Hgb was 10.1 g/dl at enrollment and 11.49 g/dl after 12 months of treatment. Most (75%) patients were in stage IV CKD with the remaining 25% in stage III. Average GFR was 29 ml/min/1.73m^2 12 months prior to starting the treatment, 24 ml/min/1.73m^2 at enrollment and 30 ml/min/1.73m^2 after 12 months of anemia therapy (Figure).



Our data shows delayed disease progression and even improvement of GFR in some patients after initiating anemia therapy. Prospective studies are warranted to further investigate the benefit of anemia management in the pre-dialysis CKD population.

HANDLING OF DIETARY PHOSPHORUS LOAD IN NORMAL VOLUNTEERS

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Excess phosphorus intake and increased serum phosphate (Pi) levels even in the normal range are associated with adverse outcomes in chronic kidney disease (CKD) patients and in health. Although the association between random Pi levels and clinical outcomes has been studied in detail, less is known about the immediate regulation of phosphorus handling following a dietary load. We hypothesized that the augmentation of urinary Pi excretion following an oral load would be mediated by an increase in the serum Pi, the magnitude of which would be related to the amount of phosphorus intake. We measured serum Pi and urinary fractional excretion of phosphate (FE_{PO4}) before and repeatedly after a standardized, 500-mg phosphorus breakfast meal in 20 healthy volunteers (mean age 45 ± 13; 14 women). We repeated the measurements in 4 subjects who consumed an isocaloric, 250-mg phosphorus meal. All meals were consumed after an overnight fast. After each meal, subjects underwent blood and urine testing every 30 minutes for 4 hours. The mean creatinine clearance was 81 ± 18 ml/min and the mean 24 hr urine Pi content was 884 ± 215 mg. Within the first 60 minutes following the 500-mg phosphorus meal, FE_{PO4} increased by 75% (95% CI 47, 103%; P <0.001), while the serum Pi actually decreased by 1.8% (95% CI −6.5, 2.8%, P=NS). Thereafter, FE_{PO4} remained elevated while serum Pi increased minimally. Similarly, within the first 60 minutes following the 250-mg phosphorus meal, the FE_{PO4} increased by 69% (95% CI 20, 158%; P=NS), while the serum Pi dropped by 7.5% (95% CI −21, 6%; P=NS). The data show that there was a significant increase in urinary Pi excretion within the first 60 minutes after an oral Pi load. Within the same time frame, however, there was no significant change in serum Pi, suggesting that the increase in the FE_{PO4} is not mediated by changes in the serum Pi level. Whether there may be a phosphaturic signal secreted from the gut remains unknown, and is the subject of further investigation.

MINERAL METABOLISM PRESCRIBING PRACTICE PATTERNS IN CKD STAGE 3 AND STAGE 4 PATIENTS

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Disorders of mineral metabolism and bone disease begin in early stages of chronic kidney disease (CKD) and can be influenced by various therapeutic approaches. The K/DOQI™ guidelines offer an outline for providing standardized care for best outcomes. It is unknown whether real-world (RW) therapeutic approaches to influence mineral metabolism starts early as recommended by the K/DOQI™ guidelines. The HeROICkd™ registry captures RW clinical data in CKD stages 3& 4, enabling evaluation of outcomes based on patient factors and therapeutic approaches, and to document RW treatment strategies. This registry has enrolled 1,620 adult patients, from 79 US centers, who have begun Hectorol® (doxercalciferol) therapy. Treatment and outcome data is collected at 4 time points (baseline and quarterly). Baseline characteristics of the 1,450 CKD stages 3 and 4 patients with data available are presented here. The 784 (54%) men and 666 (46%) women had a mean age of 70.4 yrs. Most patients were Caucasian (68%), followed by Black (21%). Hypertension (45%) or diabetes (29%) was the primary cause of renal disease. Concomitant medications included anti-hypertensive (95%), lipid-lowering (57%), glucose-lowering (45%), hemoglobin-boosting medications (43%), and phosphate binders (7%). The table depicts mean baseline iPTH, Ca, P, and CaXP product values. Findings suggest that CKD stages 3 & 4 patients need more aggressive and early treatment in order to achieve the K/DOQI™ guidelines for mineral metabolism. Earlier treatment is needed to ultimately impact these patients' outcomes. These data provide valuable insight into RW practice, suggesting the need for increased awareness of early mineral metabolism treatment and of the K/DOQI™ guidelines.

Mean (range] iPTH, Ca, P, CaXP product values at baseline - CKD Stage 3			
iPTH (pg/dL)	Ca (mg/dL)	P (mg/dL)	CaXP (mg/dL)
136.3 (2.9-1500.0)	9.37 (7.0-10.9)	3.51 (1.9-9.4)	32.94 (18.2-87.4)
Mean (range] iPTH, Ca, P, CaXP product values at baseline - CKD Stage 4			
iPTH (pg/dL)	Ca (mg/dL)	P (mg/dL)	CaXP (mg/dL)
227.1 (14.7-9624.5)	9.21 (4.4-20.2)	4.01 (1.9-9.7)	36.85 (16.9-77.6)

IMPACT OF ANEMIA CORRECTION WITH AN ERYTHROPOIESIS STIMULATING PROTEIN (ESP) ON RENAL FUNCTION IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS NOT ON DIALYSIS: A META-ANALYSIS

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Although the therapeutic use of ESPs has been established as an effective treatment for CKD-related anemia, the ability of ESPs to delay renal function decline is not well-established. We conducted a meta-analysis of the effect of anemia correction on renal function among CKD patients not on dialysis. The planned analyses focused on doubling of serum creatinine, GFR decline, and initiation of dialysis.

We systematically reviewed MEDLINE articles published between January 1980 and July 2005 in order to identify randomized controlled trials (RCTs) that evaluated the effects of an ESP on renal function among CKD patients not on dialysis. We only included RCTs that followed 50 or more patients for a minimum of 30 weeks. Since selected studies were heterogeneous, we calculated separate pooled estimates for each outcome and treatment comparison (e.g. placebo, no treatment, and deferred ESP use).

Only five studies, evaluating a total of 453 CKD patients, met our inclusion criteria. Pooled estimates from two studies showed that the number of patients with a doubling of baseline serum creatinine was significantly lower in the ESP-treated group compared to the control group (OR=0.29; 95% CI: 0.15-0.58). Early ESP use was associated with a slower decline in GFR compared to deferred ESP use (Pooled SMD from 2 studies = 0.43; 95% CI: 0.18-0.69). Pooled estimates of odds ratios for dialysis initiation, comparing ESP vs no treatment (OR = 0.59; 95% CI: 0.14-2.56) and early ESP vs deferred ESP (OR = 0.92; 95% CI: 0.19-4.51) were not statistically significant, partly due to conflicting trends in the pooled studies.

The limited number of studies examined in this analysis suggests that anemia correction with ESP treatment may delay doubling of baseline serum creatinine and slow GFR decline in CKD patients not on dialysis.

PREVALENCE OF CHRONIC KIDNEY DISEASE IN INDIVIDUALS WITH TRADITIONAL RISK FACTORS FOR CARDIOVASCULAR DISEASE

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Chronic kidney disease (CKD) is a strong independent risk factor (RF) for cardiovascular disease (CVD). There is a clustering of traditional cardiovascular RF, such as hypertension, diabetes and hyperlipidemia, and CKD. The presence of CKD may affect decisions regarding evaluation and management of these CVD risk factors. We assessed the prevalence of CKD in patients with traditional CVD RF without and with known CVD.

This is a cross-sectional study of individuals greater than 40 years of age who are enrolled in a regional medical care plan affiliated with a national managed care organization. Administrative data were collected on CKD, CVD, hypertension, diabetes and hypercholesterolemia from 2000 to 2003. We used ICD-9-CM codes to identify CKD, CVD and each CVD RF. A total of 111,361 members with at least one claim were included in the cohort. Analyses were stratified according to > and < 65 years.

Number (%*) of members with recognized CKD *Column percent

Groups	No CVD						CVD	Total
	0 RF	Chol	HTN	DM	3 RF	ALL	ALL	
< 65 years	1166 (2.3)	700 (4.4)	809 (5.4)	54 (16)	24 (21)	2294 (3.1)	539 (8.5)	2833 (3.1)
> 65 years	280 (3.8)	241 (7)	398 (7.8)	32 (15)	9 (15)	764 (5.5)	923 (15)	1687 (7.9)
Total	1446 (2.6)	941 (4.9)	1207 (6)	86 (16)	33 (19)	3058 (3.5)	1462 (12)	4520 (4.1)

As expected, older people, those with CVD RF and those with CVD are more likely to have CKD. However, even among high-risk groups, the prevalence of CKD seems lower than expected, suggesting lack of awareness by physicians. Increased awareness of CKD in patients at increased risk is necessary for appropriate management of CVD and CVD RF in patients with CKD. Limitations of this analysis include ascertainment of disease only from ICD-9-CM codes.

CARDIOVASCULAR PROTECTION IN CKD IS ENHANCED BY STRUCTURED RENAL CARE: RESULTS FROM CRIOS

S. Mujais, B. Mittal, A. Singh, C. Firanek, K. Story. Baxter, McGaw Park, IL and Harvard Med. School, Boston, Mass

Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular disease and use of prevention measures is crucial for improved outcomes. The CRIOS study was undertaken to evaluate whether a structured program with informatic support and monthly review of select parameters in an iterative care process can lead to enhancement of delivered care. 1963 patients have been enrolled in 7 North American centers. We examined the impact of this process on use of pharmacologic prevention and control of hyperlipidemia. Average follow up was 414 days. Aspirin use increased from 37% of patients at entry to 44% ($p<0.0001$) at last follow up (US from 30% to 34% ($p=0.03$); Canada from 47% to 59% ($p<0.0001$). Use of statins also increased from 52% at entry to 65% ($p<0.0001$) at last follow up (US from 46% to 56% ($p<0.0001$); Canada from 61% to 78% ($p<0.0001$)). Mean LDL declined from 101 mg/dL to 92 mg/dL ($p<0.0001$) (US from 103 to 95 mg/dL, $p<0.01$; Canada from 99 to 89 mg/dL, $p<0.01$) and the proportion of patients with an LDL greater than 100 mg/dL declined from 47% to 36% (US from 49% to 37%; Canada from 41% to 34%). Use of beta-blockers also increased during the period of observation from 48% to 62%. These results suggest that structured iterative renal care with informatic support can contribute significantly to enhancement of cardiovascular protection in CKD.

RENAL PROTECTION IN CKD IS ENHANCED BY STRUCTURED RENAL CARE: RESULTS FROM CRIOS

S. Mujais, B. Mittal, A. Singh, C. Firanek, K. Story. Baxter, McGaw Park, IL and Harvard Med. School, Boston, Mass

Patients with chronic kidney disease (CKD) are at increased risk for progression and use of renal protection measures is crucial for improved outcomes. The CRIOS study was undertaken to evaluate whether a structured program with informatic support and monthly review of select care parameters against guideline benchmarks in an iterative care process can lead to enhancement of delivered care. 1963 patients have been enrolled in 7 North American centers. We examined the impact of this process on use of pharmacologic renoprotection and blood pressure control. Average follow up was 414 days. ACE inhibitors use increased from 44% of patients at entry to 57% ($p<0.0001$) at last follow up (US from 39% to 49%($p<0.0001$); Canada from 54% to 68%($p<0.0001$)). Use of ARBs also increased from 29% at entry to 40% ($p<0.0001$) at last follow up (US from 26% to 34%($p<0.0001$); Canada from 32% to 50%($p<0.0001$)). Mean systolic BP was unchanged from 135 mmHg to 133 mmHg (US from 135 to 131 mmHg, $p<0.01$; Canada from 134 to 135 mmHg, p=ns). Mean diastolic BP declined from 75 mmHg to 73 mmHg, $p<0.05$ (US from 75 to 73 mmHg, $p<0.05$; Canada from 74 to 73 mmHg, p=ns). Use of phosphate binders increased from 19% of patients to 32% (US 8 to 12%; Canada 36 to 65%). These results suggest that structured iterative renal care with informatic support can contribute significantly to enhancement of renoprotection in CKD.

EVALUATION OF AN ANEMIA MANAGEMENT PROGRAM IN THE PRE-ESRD POPULATION

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Little is known about anemia management programs in the pre-ESRD population. An in-depth program evaluation was conducted at the University of Wisconsin-Madison Health Kidney Clinic to determine the efficacy of an outpatient nurse and pharmacist-driven anemia management program.

One hundred eight (Hb≤11g/dL) patients with chronic kidney disease (mean GFR=19.5±10 ml/min) were retrospectively evaluated. Treatment goal was a Hb level between 11 and 12 g/dL using monthly administrations of darbepoetin alfa.

Mean Hb levels were 10±1.1 g/dL at enrollment and 11.5.5±1.2 g/dL after 12 months. Fifty eight patients (84%) reached the target Hb within 58±77 days. Forty eight patients (70%) received monthly injections of darbepoetin alfa whereas twenty one patients (30%) required twice monthly dosing. The latter group had higher PTH (182 v 127 pg/L, p=0.04), lower TSAT (19% v 25%, p=0.005) and lower GFR (18.5 v. 24 ml/min, p=0.06) levels compared to the group on monthly injections. ACE (-) and ARBs use was not statistically different between the two groups (67% v 60%). A patient/provider survey specifically created for this program was administered after seventeen months and revealed 80% satisfaction among patients (n=26) with education about anemia and 100% satisfaction among providers (n=8) with quality of care given patients.

The current study demonstrates the effectiveness of outpatient nurse/pharmacist driven anemia management programs for patients with CKD stages III and IV. Most patients reach the target Hb levels with monthly darbepoetin injections. Improvements in patient teaching methods, aggressive iron replacement therapy and the implementation of a parallel bone management program may be recommended.

PRIMARY RENAL AMYLOIDOSIS IN A YOUNG MALE WITH RAPID PROGRESSION TO END-STAGE RENAL DISEASE (ESRD).

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Most patients with primary renal amyloidosis (AL) are older than 60 years of age. AL mostly presents with nephritic syndrome. Mild renal dysfunction is frequent, but rapidly progressing renal failure is rare. Here we report a case of AL, presented in a young male with very rapid progression to ESRD in less than 4 months, with normal serum and urine immunoglobulin load at onset.

A 38 year old healthy soldier returned from Iraq war. He developed puffiness in his face and swollen legs after two months of his return. He saw his doctor, who noticed him to have high blood pressure (BP) and renal insufficiency with serum creatinine (Scr) of 1.9 mg/dl. He was referred to the nephrology clinic for further evaluation where a month later, he was found to have SCr of 9.0 mg/dl, and enlarged kidneys (12.9 and 13.2 cm) by ultrasound. 24 hour urine showed 22 grams of proteinuria. Serological work-up was ordered and he was admitted to the hospital for kidney biopsy. On hospital day 1, he had chest pain and underwent cardiac catheterization with a stent placement. The renal biopsy was delayed due to this procedure. He was started on dialysis afterwards because of uremia and anuria. Serological work up revealed normal ASO titer complement levels, ANA, HIV test, hepatitis serology, antiphospholipid Antibody, anti-GBM Antibody, ANCA, cryoglobulin and anti smooth muscle Antibody. SPEP, UPEP followed by immunofixation studies were also normal initially making it a diagnostic challenge. He underwent diagnostic renal biopsy after a month of his cardiac procedure that turned positive for amyloidosis.

Serum immunofixation (SIF) was repeated which showed an elevated free lambda band this time. Bone marrow biopsy showed normal marrow and flow cytometry studies showed 5-10 % plasma cells of lambda predominance. He underwent a fat pad biopsy that was negative for amyloid. He was treated with high-dose steroids, melphalan, and autologus stem cell transplantation. Post-transplant SPEP and SIF studies were normal at six months. Patient's amyloidosis is under remission after I year and he is on long term dialysis. He is currently under evaluation for kidney transplantation.

The prognosis of patients with AL is poor with a median survival of less than two years. The median time from diagnosis to onset of dialysis is 14 months and from dialysis to death is only 8 months. The patient in this case is unusual because he progressed to dialysis in less than 4 months and is doing well on dialysis after 15 months.

LONG-TERM EFFECTS OF ANTI-PROTEINURIC AGENTS ON FABRY ASSOCIATED RENAL DISEASE IN CONJUNCTION WITH ENZYME REPLACEMENT THERAPY.

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Fabry disease is an X-linked, multisystemic lysosomal storage disease that causes a wide range of proteinuria and leads to progressive renal failure. Enzyme replacement therapy (ERT) has shown beneficial effects in phase III and IV studies.

We prospectively evaluated 3 females and 9 males with Fabry disease who were treated with anti-proteinuric therapy, Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB), in conjunction with ERT. We evaluated glomerular filtration rate (GFR) based on MDRD (Modification of Diet in Renal Disease calculation) as well as proteinuria and blood pressure initially, and at approximate follow-up intervals of 6 months, 12 months and 24 months.

Evaluation	Mean Proteinuria mg/24hrs	Mean GFR ml/min
0	1472	71
6	882	65
12	768	64
24	570	55

One of the 12 patients progressed to end stage renal disease 12 months after initial presentation.

Anti-proteinuric therapy with ACEIs and ARBs in conjunction with ERT leads to long-term reduction of proteinuria in Fabry disease. The rate of change in GFR appeared to stabilize with therapy. However, hypotension did limit anti-proteinuric therapy, especially in male patients.

SECONDARY HYPERPARATHYROIDISM (SHP) IN STAGES 3 AND 4 CHRONIC KIDNEY DISEASE (CKD) DESPITE K/DOQI TARGET PHOSPHORUS: NKF'S KIDNEY EARLY EVALUATION PROGRAM (KEEP) RESULTS.

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The objective of this study was to estimate the SHP prevalence in a large, community based, cohort generated from KEEP.

KEEP is a CKD screening program enrolling high-risk individuals $\geq$ 18 years. KEEP participants screened between 11/01/05 and 12/01/05 were included. If eGFR (abbreviated MDRD equation) was less than 60 ml/min/1.73 m^2, reflex testing for calcium, phosphorus, and intact parathyroid hormone (iPTH) was performed. Data are presented as mean $\pm$ S.E.M.

Of 2412 participants, Reflex testing was performed for 458/2412 (19 %) in stage 3, and 21/2412 (0.8 %) in stage 4. The iPTH was 76.3 $\pm$ 2.36 and 222.3 $\pm$ 51.7 pg/ml in stages 3 and 4, respectively. The phosphorus was 3.38 $\pm$ 0.022 in stage 3 and 3.65 $\pm$ 0.150 mg/dl in stage 4.

The Phosphorus K/DOQI target (2.7 to 4.6 mg/dl) was met by 94.8 % in stage 3 and 90.5 % in stage 4 CKD. The iPTH in pg/ml exceeded K/DOQI targets in 47.0 % (> 70) of stage 3, and in 61.9 % (> 110) of stage 4 CKD.

These data support the importance of iPTH testing for patients with stages 3 and 4 CKD, including those with K/DOQI target phosphorus.

RESOLUTION OF PRE-TRANSPLANT PROTEINURIA FOLLOWING KIDNEY TRANSPLANTATION

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An increasing number of kidney transplants are preformed prior to the patient needing dialysis. Some of these patients have significant pre-transplant proteinuria which makes the interpretation of post-transplant protein excretion difficult.

In this study we evaluated the change in urine protein excretion in 116 patients who had urine protein excretion measured within 3 months prior to their transplant. Proteinuria was quantified in 24 hour urine collections pre-transplant, 3 weeks and 12 months post-transplant. Pre-transplant urine protein excretion was 3645$\pm$3687 (50-20,446) mg/day. At 3 weeks post-transplant proteinuria had declined to 615$\pm$1073 (45-7612) mg/day ($p<0.0001$). Pre-transplant 48 (41%) of the patients had more than 3000 mg/day of proteinuria but only 2 (2%) had this level of proteinuria 3 weeks post-transplant. These two patients had recurrent focal segmental glomerulosclerosis. By one year, proteinuria had declined further to 494+1133 (4-7199) mg/day ($p<0.0001$ vs. 3 weeks) and 4 patients had high grade proteinuria >3000mg/day. All four had recurrent native disease. Higher levels of pre-transplant proteinuria were related to higher post transplant levels (r 0.22, $p<0.001$). However, compared to 66% of patients pre-transplant, only 10% (at 3 weeks) and 8% (at one year) post-transplant had proteinuria of more than 1500 mg/day. Examination of surveillance biopsies at one year showed that all patients, save one, with proteinuria >1500 mg/day had significant allograft pathology (either de novo or recurrent).

Conclusion, pre-transplant proteinuria, even when it is high grade, declines rapidly after transplantation. Beyond 3 weeks post-transplant, proteinuria >3000 mg/day is indicative of either de novo or recurrent allograft glomerular disease.

CREATININE PRODUCTION RATE IN DECEASED KIDNEY DONORS: A CRUCIAL YET UNMEASURED VARIABLE

Rodolfo R. Batarse[1], Sandra Leyden[2]. Paul Shragg[3], Robert W. Steiner[1], University of California, San Diego Medical Center, [1]Division of Nephrology and [3]General Clinical Research Center, San Diego, CA. USA; [2]Lifesharing Community Organ and Tissue Donation, San Diego, CA, USA. The serum creatinine (SC) is an inadequate measure of kidney function in deceased donors (DD), because creatinine production rates (CPRs) vary, as they do in the living population. As DD kidneys with very similar SC's vary markedly in quality (i.e. Creatine Clearance (CrCl)), procurement teams now use both the Cockgroft-Gault equation (CGE) and extended donor criteria (EDC) to enhance the predictive value of the SC, using demographic and epidemiologic criteria to implicitly estimate CPR. In this study, urine was collected over 6 to 24 hours in 179 sequential DDs (age 39 +/- 18.5 years, 46% traumatic death) to determine individual CPR's. A nomogram was used to calculate CrCl at the bedside ({CrCl= 16.67 [(Liters of Urine Collected)(Urine Spot Creatinine)/[(Serum Creatinine)(Hours of Collection)]. The SC that was determined while DD urine was being collected for measured CPR, was used to calculate the CPR that was imputed by the CGE for that DD. As expected, the estimated CGE-CPR correlated with measured CPR ($p<0.0001$). Even disregarding outliers, however, the standard deviation of the difference between directly measured CPR's and CGE-CPR's was over 500mg/24 hours, suggesting significant over- or under- estimation of DD kidney function in a significant number of cases. The difference between conventional CGE-CPR's and measured CPR's averaged 210mg/day. Only male gender was associated with a greater difference in the two measures ($p=0.008$). The degree of difference between CGE-CPR's and measured CPR's was not influenced by the other demographic and EDC variables. Appropriately, measured CPR's trended inversely with these renal risk factors. CGE-CPR artifactually correlated with demographic and epidemiologic factors because of statistical coupling (related variables appearing in compared groups). Measured CPR's are feasible and more accurately assess individual DD kidney quality than do current practices. Their precise applications (timing and as sensitive markers of terminal decreases in GFR) need to be explored.

THE IMPACT OF AVOIDING BOTH STEROIDS AND CALCINEURIN INHIBITORS ON POLYOMAVIRUS-ASSOCIATED NEPHROPATHY IN KIDNEY TRANSPLANATION

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Introduction: Polyomavirus-associated nephropathy (PVAN) contributes to renal allograft loss. Intensive immunosuppressant therapy is an important risk factor for PVAN. Standard protocols utilizing tacrolimus, mycophenolate mofetil (MMF) and steroids may be associated with more PVAN than newer protocols utilizing steroid-free maintenance immunosuppression and calcineurin inhibitor (CI) avoidance. In this study we evaluated the impact of sirolimus and MMF as maintenance immunosuppression on the incidence of PVAN.

Methods: Our center performed 360 kidney transplants from 1/99 through 9/05. Patients were separated into 2 groups based on immunosuppressive protocol. Group A consisted of 175 patients transplanted from 1/99 through 6/02 who received tacrolimus, MMF and steroids. Group B consisted of 185 patients transplanted between 7/02 and 9/05, who received MMF and sirolimus as maintenance immunosuppression. Patients in Group B did not receive maintenance steroids and either had CI avoidance or withdrawal and replacement with sirolimus between 3 and 6 months post-transplantation. Both groups received induction with either thymoglobulin or an IL-2 receptor blocker. A kidney biopsy was performed on any patient who had a persistent 25% rise in serum creatinine. The incidence of PVAN and acute rejection (AR) were compared between the two groups.

Results: Patients demographics, including race and transplant type were similar in both groups. 57 out of 175 patients in group A and 45 out of 185 patients in group B underwent a kidney biopsy. The incidence of PVAN was 4% (7/175) in group A vs. 0% (0/185) in group B ($p < 0.05$). There was no significant difference in AR rates between groups A and B (29/175 vs. 24/185 respectively).

Conclusions: Immunosuppressive minimization utilizing calcineurin avoidance and steroid-free maintenance immunosuppression reduces the incidence of PVAN without causing increased incidence of AR. Further prospective studies are needed to confirm these findings.

C-REACTIVE PROTEIN LEVELS DO NOT PREDICT ACUTE REJECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Purpose: A rise in serum creatinine is a relatively late sign of acute allograft dysfunction. A reliable test signaling impending allograft dysfunction due to acute rejection (AR) would be clinically useful. High-sensitivity C-reactive protein (hs-CRP) may be predictive of AR, although three previous retrospective studies have had conflicting results. One study has suggested that higher levels of CRP are predictive of AR, while 2 other studies conflict with these findings.

Methods: 89 consecutive kidney transplant recipients (KTR) from 5/02 through 8/04 were prospectively followed for 12 months after transplantation. Based on immunologic risk factors, patients received immunosuppression per institutional protocol. Hs-CRP was measured prior to surgery, 1 month and 6 months post-transplant. Repeated measures ANOVA was used to determine if increased levels of hs-CRP were predictive of AR.

Results: 13 of 89 KTR had an episode of AR. Mean pre-transplant CRP levels did not differ between the 13 patients who had AR within one year post-transplant and the 76 patients who did not have AR (12.5mg/L vs. 9.5mg/L, respectively). Two of the 13 episodes of AR occurred between 1 and 6 months post-transplant and there was no difference in mean 1 month CRP levels between those with and those without AR (14.1mg/L vs. 21.8mg/L, respectively). There were 4 episodes of AR after 6 months post-transplant. Mean 6 month CRP levels did not differ between those with AR (2.15mg/L) and those without AR (8.5mg/L). Repeated measures ANOVA did not show that CRP levels predict AR.

Conclusion: Activation of the immune system is associated with a rise in the acute phase reactant C-reactive protein (CRP). It has been proposed that a “primed immune system” may predispose to increased risk of AR. Previous retrospective studies have provided conflicting results on whether CRP is predictive of AR. We have demonstrated in a prospective observational study that neither pre-transplant CRP levels or serial CRP levels after transplant are predictive of AR.

PHASE ANGLE BY BIA ANTECIPATE RENAL OUTCOME VERY EARLY POST-TX

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Background. Phase angle (PA) studied by bioelectrical impedance analysis (BIA) correlates with morbidity and mortality among hemodialysis (HD) patients, and intracellular water (ICW) volume is a reliable surrogate of protein metabolism. We investigate the influence of body composition assessed by BIA (PA; intracellular water, ICW; extracellular water, ECW) during peri-transplant (Tx) period on renal graft function and hospitalization time. **Methods**. Thirty six patients (20 males, 16 females) with mean age 39.3 ± 10.2 years were studied. Each patient received triple-drug immunosuppressive therapy with methilprednisolone, cyclosporine, azatioprine or micophenolate of mofetil. BIA was assessed before Tx, at day 12 post-Tx and on the day of discharge. Phase angle, ECW and ICW were studied as well as plasma creatinine (Pcr) and plasma urea (Pu). **Results.** By comparing with pre-Tx, at day 12 post-Tx comparing with before Tx, ECW increased ($p < 0.0001$), ICW decreased ($p < 0.0001$) and PA decreased ($p < 0.0001$). We observed negative correlations between ECW pre-Tx with Pu at discharge ($r = - 0.435$; $p = 0.021$) and between ECW pre-Tx with the number of days on the hospital ($r = - 0.368$; $p = 0.027$); and positive correlations between both ICW and PA pre-Tx with Pu at discharge ($r = 0.435$; $p = 0.021$ and $r = 0.407$; $p = 0.031$, respectively) and with number of days on the hospital ($r = 0.368$; $p = 0.027$ and $r = 0.362$; $p = 0.030$, respectively). At day 12 post-Tx we encountered a positive correlation between ECW with Pcr ($r = 0.425$; $p = 0.022$) and between ECW with Pu ($r = 0.474$, $p = 0.009$), while ICW and PA correlated negatively with Pcr ($r = - 0.425$, $p = 0.022$; $r = - 0.420$, $p = 0.023$; respectively) and with Pu ($r = - 0.474$, $p = 0.009$; $r = - 0.471$, $p = 0.010$; respectively).**Conclusions**. Our results higlight the strengthness of the association of PA with graft function evolution during the period peri-transplant. We confirm that a slight overhydration contributes for a better and earlier graft fuction.

IS THERE ANY DIFFERENCE IN THE RECOVERY FROM DELAYED GRAFT FUNCTION IN RECIPIENTS OF ACUTE RENAL FAILURE DONOR KIDNEYS BETWEEN MYCOPHENOLATE MOFETIL AND SIROLIMUS BASED IMMUNOSUPPRESSIVE THERAPY?

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We looked at acute renal failure donor kidney transplantation whether there is an association with slow recovery from DGF and rapamune based immunosuppressive therapy.

35 patients were transplanted with acute renal failure donor kidneys between 2001 and 2004 at our transplant center. All the acute renal failure donors were between 16-50 years of age and had normal renal function at admission then had a sustained elevation of creatinine greater than 2.0mg/dl. 80% of the recipients developed delayed graft function.

Both groups were comparable with respect to donor age, donor creatinine, and cold ischemia time, etiology of acute renal failure in the donor, recipient age, race, sex and HLA mismatch and incidence of rejection. Both groups were on steroid free maintenance therapy. Trough sirolimus levels were maintained around 6-10ng/ml

	Delayed Graft Function	Creatinine Clearance (ml/min) 1 month	Creatinine Clearance (ml/min) 3 months	Creatinine Clearance (ml/min) 6 months
Sirolimus (N = 25)	22	37.4 ± 24.7	47.56 ± 22.3	53.6 ± 20.8
MMF (N = 17)	12	63.3 ± 25.3	71.6 ± 29.9	78.5 ± 36.3
P - value	0.20	0.002*	0.013*	0.039*

*p - value is significant if less than 0.05.

Creatinine clearance is estimated by Cockroft-Gault formula

We believe that MMF/calcineurin inhibitor regimen may be a better option than sirolimus /calcineurin inhibitor immunosuppressive therapy in recipients of acute renal failure donor kidneys.

LATE SUB-CLINICAL BK POLYOMA VIRUS (BKV) REACTIVATION IN KIDNEY TRANSPLANT (TX) PATIENTS.

M. Gera, MD. Stegall, TS. Larson, TF. Smith, TS. Sebo, MD. Griffin; **Mayo Clinic Rochester**. BKV has emerged as an important cause of renal allograft failure. Screening tests for BKV reactivation are urine cytology for virally loaded "decoy cells" (DC) and quantitative blood PCR for viral DNA (qPCR). During the first year post TX the reported prevalence of DC and qPCR positivity is 30% and 15% respectively. Prevalence of BKV at later time points is unknown.

We retrospectively studied the prevalence of qPCR and DC in patients coming for 3rd to 5th post TX annual exam. Of 636 patients transplanted, 470 alive patients with functional grafts came for 2nd to 5th annual follow-up. 369 of these were screened for BKV by qPCR and 362 for DC.

Table 1: qPCR positive patients

Yrs post TX	Pts screened	qPCR +ve Prevalence	Previous Reactivation Detected	No Previous Reactivation Detected	Also Urine DC +ve
5	92	11 (12%)	3	8 (8%)	7
4	133	11 (8%)	7	4 (3%)	4
3	144	17 (12%)	5	12 (8%)	4
Total	369	39 (11%)	15	24 (7%)	15 (40%)

Table 2: Urine DC positive patients

Yrs Post TX	Pts. screened	DC Prevalence	Previous Positive	DC incidence	Also qPCR +ve
5	87	17 (20%)	2	15 (17%)	7
4	137	12 (9%)	4	8 (6%)	4
3	139	16 (12%)	6	10 (7%)	4
Total	362	45 (13%)	12	33 (9%)	15 (33%)

1 Cases of BK viremia and DC shedding are present at 3 or more years post TX **2.** There is poor correlation between qPCR and DC assays late post TX. **3.** Clinical significance of late BK viremia and viruria needs further investigation.

USEFULLNESS OF PT, PTT IN PATIENTS UNDERGOING RENAL TRANSPLANT BIOPSY

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Coagulation studies are routinely done in most centers to evaluate bleeding risks before the renal transplant biopsies. The waiting for the results of these studies cause significant delay in performing the biopsies. The cost effectiveness and usefulness of time delay for these studies are not known.

Method:

We did a retrospective analysis of out patient transplant renal biopsies done from March 15 to September 15, 2005 in a university hospital. The pre-procedure coagulation profile was measured by PT and PTT on the day of biopsy. Routinely bleeding time is not measured in our institution before the biopsy. Patients who are on heparin, coumadin or aspirin were excluded from the study.

There were a total of 245 patients were scheduled for elective surveillance transplant renal biopsy in this period of time. Among the 245 patients, 103 patients were cancelled before the procedure for no show or other medical reasons, but none were cancelled for coagulation abnormalities. Total of 142 patients had renal biopsy under ultrasound guidance by the 6 renal fellows under supervisions of 3 different nephrologists and 1 transplant surgeon.

Result:

Prothrombin time was normal in all patients but partial thromboplastin time was 3 to 4 seconds higher than normal in three patients. None of the three patients had any bleeding after the biopsy. Patients who had gross hematuria had normal PT and PTT. There was no significant bleeding requiring blood transfusion in any patient.

Conclusion:

Pre-renal transplant biopsy evaluation with PT, PTT has limited use in predicting risk of bleeding when patients are not on any anticoagulants.

USE OF INTRA-OPERATIVE CVVH AND OUTCOMES IN ORTHOTOPIC LIVER TRANSPLANTATION

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ARF in the setting of orthotopic liver transplantation (OLTx) is associated with mortality rates as high as 70%. One retrospective analysis showed that pts initiated on continuous renal replacement therapy prior to OLTx had a mortality rate similar to pts without ARF. The practice of intra-operative continuous veno-venous hemofiltration (IO-CVVH) was introduced to our institution in September of 2004 with the intention of improving outcomes in this population. We assessed the influence on clinical outcomes of IO-CVVH in pts undergoing OLTx who were receiving CVVH pre-operatively or deemed to be at high risk for post-operative ARF.

We reviewed all pts who underwent OLTx at our institution between January of 2001and June of 2005. Two groups were identified: those who received IO-CVVH and those who met clinical criteria to receive IO-CVVH but did not. Criteria included pre-op initiation of CVVH, serum Cr of >1.8, anuria or oliguria, coagulopathy resistant to FFP infusion, or the presence of type 1 hepatorenal syndrome as determined by a nephrologist. The group that did not receive IO-CVVH either underwent OLTx prior to September of 2004 or did not receive IO-CVVH at the discretion of the consulting nephrologist.

Seventeen pts were identified in each group. Mean age was 53 in each group; each group had 11 males and 6 females. The mean serum creatinine and APACHE III scores were similar (3.0 vs. 2.0 and 86 vs. 70 respectively p=NS). There was no significant difference in mortality (2/17 vs. 2/17), dialysis dependence at 6 months (1/15 vs. 0/15 p=NS), time on ventilator, number of infections, ICU days, or total hospital length of stay. All surviving pts had a functioning allograft at 6 months.

This study suggests that IO-CVVH does not have a significant impact in pts undergoing OLTx with ARF or deemed to be at high risk of developing post-operative ARF. This study is limited by its small sample size and retrospective design. A larger, prospective, randomized trial would be required to adequately address this question.

RECURRENT IMMUNOTACTOID GLOMERULOPATHY IN A RENAL TRANSPLANT RECEPIENT

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Immunotactoid glomerulopathy is characterized by the presence of parallel microtubules 30-50nm in diameter deposited in the glomeruli in the presence of C3 and IgG. It is a rare primary glomerulopathy that is unresponsive to therapy.

We report a case of a 56 year old female who developed end stage renal disease secondary to immunotactoid glomerulopathy and received a cadaveric kidney transplant. She was started on mycophenolate mofetil, tacrolimus and prednisone for her immunosuppressive regime. Six weeks after transplantation, she developed proteinuria and underwent an allograft kidney biopsy. Electron microscopic images revealed fibrillary structure in the mesangium and paramesangial area and focally revealed microtubular morphology consistent with the immunotactoids. There was focal presence of microtubular deposits in the size range from 30-50 nm, in both the native kidney and the renal allograft. This was compatible with the diagnosis of immunotactoid glomerulopathy. We reviewed the native kidney biopsy from 12 years ago, which also showed features of immunotactoid glomerulopathy.

Immunotactoid glomerulopathy is a rare progressive disorder leading to end stage renal disease. Renal transplantation can be performed in these patients who progress to end stage renal disease. Recurrence of immunotactoid glomerulopathy displays the same features although the rate of progression is typically slower than in the native kidneys.

INCREASED IP-10 PRODUCTION BY PERIPHERAL BLOOD MONOCYTES DURING ACUTE REJECTION

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Acute allograft rejection represents a burden in renal transplantation, remaining a major determinant of graft survival. Most acute rejection episodes are cell-mediated processes. Chemokines are a small basic proteins implicated in the regulation of leukocyte migration. Chemokines have been implicated in inflammatory tissue destruction, including acute cellular allograft rejection.

In our study we intended to verify chemokine production by peripheral blood monocytes in the early phases of acute cellular rejection. Our study integrates 42 consecutive patients submitted to solitary renal cadaveric transplantation in the same centre, between 01/01/02 and 09/30/02. We studied IL-8, Mig (Monokine induced by interferon-gamma), RANTES (Regulated on activation, normal T-cell expressed and secreted), IP-10 (interferon-gamma inducible protein), MIP-1beta (Macrophage inflammatory protein 1 beta) and MCP-1 (Macrophage chemoatractant protein 1). Patients were monitorized immediately before transplantation, weekly during the first three months in post-transplantation and monthly between the third and sixth month. The frequency of chemokines producing monocytes were performed by flow cytometry, chemokine staining was performed after six hours of incubation with Brefeldin, both without and with the activated LPS. Statistical analysis was performed using t-Test for continuous variables and Chi-square for binomial variables. Six patients developed acute cellular rejection and 4 developed acute tubular necrosis.

In the first week after transplantation we observed a decrease in the frequency of chemokines producing monocytes, probably related to the immunossupression. There was an increase in chemokine producing monocytes in the first week in rejection patients. Only IP-10 levels reached a statistically significant increase ($p<0,01$) early in acute rejection episodes, that wasn't observed in acute tubular necrosis and in patients without graft dysfunction.

GITELMAN'S SYNDROME-FROM DONOR TO RECIPIENT

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Gitelman syndrome is a rare autosomal recessive disorder which is characterized by persistent hypokalemia, hypomagnesemia and hypocalciuria. This syndrome is caused by mutations in the SLC 12A3 gene, which encodes the thiazide-sensitive sodium-chloride co-transporter. The pathophysiology of this syndrome is similar to a thiazide diuretic acting 24 hours a day.

We report a case of a recipient who developed Gitelman's syndrome after she received a kidney from her father who had the disorder. She is a 27 yr old lady with type 1 diabetes mellitus who had developed end-stage renal disease. She received a kidney from her father, who was diagnosed with Gitelman's syndrome during the pre-transplant evaluation process.

Pre transplant evaluation did not show any of the features of Gitleman's syndrome in this young lady, who was anuric and on hemodialysis. Subsequently in the months following transplant, she started developing persistent hypokalemic metabolic alkalosis, hypomagnesemia and hypocalciuria. Her electrolyte deficiencies have been replaced appropriately.

	pre-transplant	2 months post-op	4 months post-op
K+ (3.5-5.0mmol/L)	5.3	3	2.6
HCO3 (22-28mmol/L)	20	35	29
Mg++ (1.6-2.7mmol/L)	2	1.4	1.6
Ica++ (1.17-1.33mmol/L)	1.17	1.24	1.28
Scr (0.5-1.3mg/dl)	6.7	0.8	0.8
Urinary calcium++			TLTQ**

TLTQ**=Too low to quantify

This is the first reported case of a patient who showed features of Gitelman's syndrome after receiving a kidney from a donor who had the disorder. Recipients can be transplanted from donors with Gitelman's syndrome with careful attention to their electrolytes.

MASSIVE PROTEINURIA FOLLOWING USE OF SIROLIMUS (SRL) IN A LIVER TRANSPLANT RECIPIENT

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Calcineurin inhibitor (CI) Nephrotoxicity is a major cause of renal failure in recipients of non-renal solid organ transplants. There is enthusiasm for converting to 'non-nephrotoxic' drugs like SRL. Proteinuria has been shown in renal transplants converted from CI to SRL. Case: A 65 yr old male, recipient of an orthotopic liver transplant for fulminant hepatic failure in 2000, was on Tacrolimus and Mycophenalate Mofetil (MMF). S Cr increased from a baseline of 1.3 to 2.5 mg/dL over 4 years. To preserve his renal function he was taken off Tacrolimus, and he developed acute rejection on MMF alone. SRL was then started after a baseline 24 hour urine collection for proteinuria (Table).

	Pre-SRL	After 8 wks of SRL Rx	Post-SRL Cessation 2wk	3m	6m
24h Urine Prot. (mg)	259mg	14,763	9660	6019	2178
S Alb(g/L)	4.5	2.2	2.7	3.3	4.4

After conversion, S Cr decreased to 1.3 mg/dL. 8 weeks later, the patient reported generalized swelling of his body. Exam revealed anasarca, and a 24 hr urine collection was done (Table). Kidney biopsy revealed extensive diffuse fusion of epithelial foot processes on EM. SRL was stopped and Tacrolimus was restarted. Quantification of proteinuria following cessation of SRL therapy was done after 2 weeks , 3 months, and 6 months (Table). Edema resolved, and S Cr stabilized between 2 and 2.3 mg/dL.

This is the first reported case of proteinuria following use of SRL in a liver transplant recipient. The mechanisms postulated include vasodilatation following CI withdrawal, and VEGF over-expression in podocytes. Caution is advised in conversion of transplant recipients from CI to SRL in the setting of nephrotoxicity. Further prospective trials are needed to better define this syndrome of proteinuria post conversion to SRL in liver transplant recipients.

REVERSIBLE RENAL ALLOGRAFT DYSFUNCTION AND PROTEINURIA FROM NUT-CRACKER-LIKE SYNDROME

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A 27 year old Hispanic male with hypertension and renal failure, on hemodialysis for 4 years received living donor renal transplant from his 19 year old sister. His serum creatinine (SCr) decreased to 1.7 (mg/dl), 3 weeks post transplant with a urine protein creatinine ratio (UP) of 0.1(mg/g). At 5 weeks post transplant SCr increased to 2.1. Allograft sonogram revealed a fluid collection without hydronephrosis. The UP was 0.6. At 7 weeks, SCr increased to 2.6. A bruit became audible over the allograft. Repeat sonogram showed increase in size of the fluid collection. This was drained and renal allograft biopsy was done. Interestingly, biopsy showed extensive glomerulosclerosis with interstitial fibrosis. However, SCr decreased to 2.1 following the procedure and the bruit disappeared. Review of the donor magnetic resonance angiogram showed presence of a small polar accessory renal artery, corresponding to the biopsied area. At 9 weeks SCr remained at 2.2; UP however increased to 4.2. Sonogram showed re accumulation of fluid and the bruit reappeared. A repeat biopsy from the opposite pole revealed normal renal histology. The fluid collection was drained and peritoneal fenestration with omentopexy was done. SCr decreased to 1.6 and UP decreased to 0.3. Bruit disappeared. Currently at one year post transplant, allograft function and UP remain stable.

We report this unique case of renal allograft dysfunction and proteinuria. We believe that the underlying pathophysiology is similar to ‘nut-cracker’ syndrome. Mesoaortic compression of renal vein producing renal vein hypertension is known to result in flank pain, hematuria and variable amounts of proteinuria from native kidney. The ‘night and day’ allograft biopsy findings illustrate the possibility of sampling errors resulting from local vascular variables in the allograft.

KNOWLEDGE AND ATTITUDINAL BARRIERS TO TRANSPLANTATION FOR DIALYSIS PATIENTS

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Since renal transplantation can have health and quality-of-life advantages versus remaining on dialysis, we need to understand why transplant-eligible patients are not pursuing it.

We surveyed 243 transplant-eligible dialysis patients to measure their transplant knowledge and decision-making. Of the predominantly African-American (68%) and male (56%) patients, those less likely to pursue donation were older (55 vs. 50 years, p=.003) and in poorer health (51.4% vs. 36.6%, p=.02).

Less than half of transplant-eligible dialysis patients were pursuing deceased donor (40%) or living donor (17%) transplantation. Patients not pursuing transplant were more concerned about surgical pain (21.5% vs. 5.9%, p=.001) and the disappointment they would feel if the kidney failed (33.1% vs. 18.8%, p=.01) than patients pursuing it. They were also less likely to agree that getting off dialysis (54.7% vs. 82.0%, p<.001) influenced their decision about transplant. Finally, patients not pursuing transplant were less likely to know that transplanted patients generally live longer than patients remaining on dialysis (33.8% vs. 49.0%, p=.02), that patients generally wait for a deceased donor kidney for 3-4 years (12.9% vs. 30.4%, p=.001), and that donors do not pay for donation-related costs (45.3% vs. 66.7%, p=.001) compared to patients pursuing transplant.

A majority of eligible dialysis patients not pursuing transplant have a high level of fear about the transplant surgery and a lack of awareness of important living donation benefits. Improved psychosocial education about living donation is needed to correct these misconceptions.

THE ASSESSMENTS OF RACIAL HEALTH DISPARITIES IN RENAL TRANSPLANTATION

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Multiple investigations confer the underutilization of renal transplantation; only a few investigations specify the racial disparity in transplantation of a multivariable analysis with the potentiality for interventions to alleviate racial transplant complexities. African Americans(AA) make up 12% of the US population; nevertheless, AA represents 35 % of patients with ESRD. AA are 4 times more prone to renal failure than Caucasians(C).The scientific community is aware of the high risks of ESRD that necessitate transplantation in the AA's, however, The Cleveland Clinic(CCF)Minority Men'sCenter (MMHC) observed patients to distinguish a Multivariate of disparities in renal transplantation, with the purpose of categorizing dynamics of an independent effect of race on disparities of renal transplantations.Therein, leading to a proposed intervention education curriculum of health literacy,awareness and prevention, thus eradicating disparities and equalizing transplantation rates. This investigation is a review of C and AA, [N=772,168=AA (22%),604 =C(78%)] consists of renal transplant recipients from Jan-95 to Mar-04 from the Transplant Database, a database for all transplants our performed. The follow-up was 5-yrs.The populace was assessed by demographic criteria, as well as variables known to effect renal graft function. Unpaired t-test was used to determine difference of each group($p < 0.005$). Post transplantation functions were calculated in provisions of 5-yr. graft survival rates and serum creatinine and other standards. The demographic for variables, apart were equivalent. Regardless of disparity in immunosuppressive regimens and HLA-match, AA's had an advanced rate of rejection measures (AA=19 % vs. C=13 %, p=0.05).Also prominent features of disparities in ESRD etiology (hypertension AA =32%, CA =5 %, p<0.0001) and graft type (AA =70 % CA=53 %, p=0.0003). Creatinine was outstanding compared with CA at each post-transplant time, with AA=2.8 vs. CA= 2.0(p=0.008). Distinction in living donor graft survival at 5-yrs.was not significance (AA=75%,CA=90%, p=0.5).This study demonstrates that despite controlling with a multivariate analysis, there subsist a significant racial differences in transplantation among cadaveric transplantations. Hence, we propose attentive disparity interventions for AA transplant candidates. This may facilitate and enhance living donor rates as well as strengthen donor compliance.

PREMATURE ATHEROCSCLEROSIS, ACUTE RENAL FAILURE AND SPINDLE CELL SARCOMA: A CASE PRESENTATION

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There are many known risk factors for premature atherosclerosis including family history, smoking, and an unfavorable lipid profile. Acquired renal artery stenosis commonly occurs in the setting of diffuse atherosclerosis but progression to complete occlusion is rare.

A 51 year old Caucasian male with no significant past medical problems and a 50 pack year smoking history noted lower extremity claudication and a gluteal mass. The mass was thought to be a lipoma. Two years later he required right iliofemoral stenting and was noted to have severe diffuse vascular disease. Two months after this he developed acute renal failure due to bilateral renal artery stenoses with complete occlusion. The right renal artery was successfully recanalized. Two months later he developed back pain and decreased urine output. He had re-occluded the right renal artery which again was successfully recanalized. His acute renal failure gradually improved. Testing showed that he had elevated lipoprotein (a), homocysteine, and fibrinogen.

Gluteal masses were noted while he was undergoing another revascularization procedure for worsening lower extremity ischemia. Biopsy proved them to be a grade 3 of 4 spindle cell sarcoma. Metastases were found in multiple soft tissues, bones and bone marrow. He went on to hospice care and died four months after diagnosis.

Notable is that despite the severe vascular disease and recurrent renal injury his renal function improved after each insult. We speculate that the aggressive diffusely occlusive vascular disease may have been a sarcoma associated vasculopathy.

RENAL MASS DECREASES WITH WEIGHT LOSS IN OBESITY

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Renal mass may be a marker of kidney function and a risk factor for chronic kidney disease (CKD). Obesity may also be a risk factor for CKD but it is not known how it affects renal mass. We measured renal parenchymal volume (RPV) in 8 obese patients before and 1month after weight loss and compared it to RPV in 157 normal, nonobese subjects. The nonobese subjects were potential transplant donors with body mass index (BMI) of 27.4 $\pm$ 4. Obese patients were all female with a mean weight of 124 $\pm$ 4 kg and a mean BMI of 46.5 $\pm$ 1.7. RPV was measured by tracing the kidneys, excluding sinus fat, calyces, and vessels on sequential transverse images from CT scans. In normal subjects RPV increased with increasing body surface area (BSA) with a correlation coefficient of 0.75, and was 9.4 % smaller in females ($p < 0.001$). The ratio of RPV to BSA did not differ between obese and nonobese female subjects (180 $\pm$ 5 ml/m^2 vs. 183 $\pm$ 2.5 ml/m^2). After 1 month, weight loss ranged from 5.2 to 12.9 % with a mean of 8.7 %, and RPV decreased between 2.3 and 17.3 % with a mean of 12.1 %. The decrease in RPV was greater than the decrease in BSA (mean of 12.1 % vs. 3.7 %, $p < 0.005$). Conclusion: renal mass is related to body size and this relationship is the same in obese and normal individuals. Renal mass decreases with weight loss in obesity but the fact that the decrease is greater than the decrease in body surface area suggests that the change in renal mass is related to other factors as well.

PREDICTIVE VALUE OF TROPONIN I IN HEMODIALYSIS PATIENTS PRESENTING WITH CHEST PAIN; A CASE CONTROL STUDY

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Controversy exists regarding the utility of cardiac troponin I in hemodialysis(HD) patients with chest pain. We reviewed 100 patients who presented to the emergency room with chest pain, non-ST segment elevation on EKG who subsequently underwent coronary angiography with documented one or more vessel disease regardless of troponin I levels. We determined the predictive value of troponin I among HD (n=50) and non-HD (n=50) patients using CAD as endpoint. *By t-test analysis, there were no significant differences in mean age (62.6*±10 vs 62.2 ±11), lipid profile, CK, CK-MB and LV function (48.7±12% vs 50±12%). By chi square analysis, there were no significant differences in male (60% vs 46%), CAD (64% vs 68%), hypertension, prior MI, CHF, CVA, prior coronary intervention, PVD, use of beta-blockers, calciuim channel blockers and nitrates. HD patients had higher rates of LVH (56% vs 27%, p=0.03) and are more likely to be on ACEI (100% vs 92%, p=0.041). Correlation analysis showed only the first troponin I level correlated with CAD, thus the first troponin I was stratified into <0.3ng/ml and >0.3ng/ml. By logistic regression, troponin I >0.3ng/ml was not predictive of CAD in HD patients [odds ratio 0.87,(95% CI 0.19-4.0),p=0.8]. There was an increase risk of CAD in non-HD patients if the first troponin I was >0.3ng/ml [odds ratio 3.8, (95% CI 1.01-14.52),p=0.022] after adjustment for LVH and ACEI. *In conclusion*, unlike normal population, we found that troponin I has no predictive value for angiographically documented CAD in HD patients with chest pain and normal EKG.

PREVALENCE OF SWING SEGMENT STENOSIS IN DYSFUNCTIONAL AUTOGENOUS ARTERIOVENOUS FISTULAS

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Swing segment stenosis is an observed lesion in dysfuctional autogenous AVF's but not well described. A swing segment is the segment of the native vein that is mobilized during arterio-venous surgical anastomosis. We sought to determine the prevalence of these lesions within a cohort of hemodialysis patients referred for clinical evaluation to an outpatient interventional nephrology clinic. Between January 31, 2003-June30, 2005, all records of patients referred for AVF dysfunction were reviewed (n=484). Of these, 278 patients had angiographically documented stenoses on their first visit. Among the 278 patients, 64% were males, 93% African Americans and mean age was 55$\pm$18 years. Of the AVF's, brachiocephalic (BC) comprised 42%, radiocephalic (RC) 37%, brachiobasilic (BB) 21%, others 1%. Overall, the prevalence of angiographically documented swing segment lesion (proximal, distal swing or juxta-anastomotic and cephalic arch) was 45.7%, arterial anastomosis 15.5%, puncture zone 31.2%, central vein stenosis 6.5% and arterial stenosis 1.1%. Of the Swing segment lesions, the most prevalent was juxta-anatomotic stenosis accounting for 63%, while proximal and cephalic lesions accounted for 18% and 19% respectively. The distribution of swing segment lesions was equivalent among the various fistulas (BC 35.4%, RC 33.9% and BB 30.7%). 83% of the swing segment stenoses underwent angioplasty with a 93% success rate. In our population, swing segment stenoses are the most common lesions in dysfunctional AVF's with juxta-anastomotic stenosis being the predominant lesion, independent of the fistula type. Whether the occurrence of these lesions is due to mobilization of the vein during surgery is unclear.

COMPARISON OF PRACTICE RESOURCES REQUIRED TO PROVIDE WEEKLY (QW) VERSUS MONTHLY (QM) ERYTHROPOIESIS STIMULATING PROTEIN (ESP) THERAPY

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A study was conducted to assess differences in monthly practice resources and costs associated with treating non-dialysis CKD patients (pts) on QW versus QM ESP regimens for anemia.

A time and motion study was conducted at 10 outpatient nephrology clinics (5 QW and 5 QM); with each clinic having ≥40 pts on routine ESP therapy. Trained observers (blinded to regimen) documented injection-related activities occurring from pt arrival to departure. Total monthly practice costs per pt associated with the administration of an ESP were calculated, including labor costs (average wage rates of practice staff multiplied by the time observed for the specific activity) and supply costs (based on average list prices in medical supply catalogs). QW costs were multiplied by four to calculate monthly costs. Costs of ESP drugs were not included.

Staff time was recorded for 47 QW and 44 QM ESP injections. Each month, practices spent an average of 13.4 (sd 7.3) minutes with each QM pt, compared with 35.5 (sd 30.8) minutes for each QW pt. The average total monthly practice cost of providing ESP therapy to a QW pt ($15.80, sd $20.3) was more than double that for a QM pt ($6.78, sd $6.20). Visit-related staff time accounted for the largest proportion of the observed difference in total monthly cost (approximately 50%). QM and QW sites also reported 87.5 and 150 (median) additional minutes per month, respectively, for administrative tasks related to ESP injections (not included in cost estimates).

This is one of very few studies to collect empirical data from nephrology offices on activities and resources utilized in routine ESP administration to non-dialysis CKD patients. Once monthly dosing was observed to require less staff time, on average 22 fewer minutes, and $9.02 less cost per injection per month, compared to weekly administration.

HIGH PREVALENCE OF ASYMPTOMATIC HEMATURIA IN INDIANS: The Screening and Early Evaluation of Kidney Disease (SEEK) Study. Bhatia R[1], Mittal B[1], Sridevi S[2], Sreedhara R[3], Modi KG[4], Anil C[2], Singh A[1].Brigham & Women's Hospital, Boston, MA[1], SVYM Hospital Mysore[2], Bhopal Memorial Hospital[4], Bhopal, Apollo Hospital, Bangalore, India[3]. **Background**: Data on the prevalence of CKD in India and its associated factors are lacking. We studied 680 subjects as a part of the pilot study of a larger multi-center project involving 16 academic centers in India. 2 centers contributed to the current data set - from Kote, Mysore (n=500) and Bhopal (n=180). **Methods:** Screening was done by a trained health facilitator and a questionnaire was completed in the local language to elicit a relevant history. Informed consent was taken after study approval by the Partners IRB in Boston and by local IRB's in India. Indicators for CKD, including proteinuria, hematuria, glycosuria and reduced GFR were investigated. Blood in urine was estimated with the use of *Bayer's Multistix* for dipstick analysis. eGFR was calculated using the MDRD equation. Subjects with positive results were further evaluated by an Internist. **Results:** A total of 680 patients participated in this study: In the Kote cohort (n=500), the prevalence of hematuria was 15.5 %. 75% of subjects with hematuria were females. The mean age was 42 years. On urinalysis, 16.6 % of patients with hematuria were found to have proteinuria also; the mean GFR was 65.8 (SD +/- 13.5). Average serum creatinine was 1.09 mg/dL. Hypertension (defined as >140/90 mmHg) was present in 12.5 % of these subjects with hematuria and average SBP was 117.6 mm Hg. In Bhopal (n=180), 13% subjects had asymptomatic hematuria; the mean GFR was 71.9 (SD +/-14.5). The average SBP was 129.3 mm Hg and the mean serum creatinine was 1.1 mg/dL.30.4 % of subjects with hematuria were female. Only 1 subject was also menstruating at the time of dipstick analysis. 17.3 % of subjects with hematuria also had proteinuria. **Conclusions:** Evaluation of the prevalence and risk factors for CKD was carried out as a part of a larger multi-center study. Prevalence of asymptomatic hematuria was found to be predominantly in female patients. Because hematuria can be the first sign of occult renal disease these patients need to be followed-up longitudinally. Here we have found asymptomatic isolated hematuria as well as its early association with proteinuria and CKD.

HOME HEMODIALYSIS PATIENTS: WHAT ARE THEIR CHARACTERISTICS?

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With the development of new equipment there has been an increase in the number of hemodialysis patients able to dialyze at home. The Short-Home Hemo Dialysis program was initiated in August, 2003 at a Midwestern dialysis facility and has grown to 22 patients in 25 months. It is particularly attractive to the rural, working patients living in the area. These initial patients are beginning to shape an image that can be recognized as an S-HHD patient.

In comparison, S-HHD patients are 10 years younger and four times more likely to be employed than incenter and PD patients. The dialysis vintage of S-HHD patients is 36 months compared to 39.3 on incenter and 22 months with PD. More females use NxStage and males use Aksys, matching machines to body size. 75% are in rural areas and eating better (11% higher albumins). Their SF-36 mental health composite scores are consistent with incenter scores but higher than PD scores. The SF36 physical composite scores are higher than both incenter and PD scores. The most prevalent cause of ESRD in our S-HHD population is diabetes (38%), consistent with the other modalities. Using a ratio of actual to target Kt/v, S-HHD adequacy is better than PD using the Aksys machine, but both S-HHD methods are lower than incenter hemodialysis adequacies. Medicare is the primary payor for dialysis among this group and although more are employed only 14% have employer group plans.

As this modality choice continues to increase in numbers, it will be useful to recognize appropriate candidates and plan for them.

RACE DETERMINES APPROPRIATE WEIGHT TO USE IN COCKROFT-GAULT EQUATION IN DIABETIC PATIENTS

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The purpose of this study was to determine if actual body weight (ABW), adjusted body weight (AdjBW), or ideal body weight (IBW) results in the most accurate estimates of GFR when using the Cockroft-Gault (CG) in diabetic patients.

A retrospective chart review was conducted for all diabetic patients at an academic primary care clinic. Patients with all information required to estimate GFR using the 6-variable MDRD and CG equations were included. CG GFRs (normalized for BSA) were estimated for all patients using ABW, AdjBW [IBW+0.4*(ABW-IBW)], and IBW. Accuracy of these estimates relative to MDRD eGFR was determined using 1) median prediction errors (MPE), a measure of prediction bias and 2) median absolute prediction errors (MAPE), a measure of typical prediction error size.

Patient characteristics (n=222) included [number or median (range)]: 133 F/89 M; 55 years of age (23, 93); 130 blacks/92 nonblacks; height 66" (52, 78); ABW 94 kg (48, 174); BMI 33.7 kg/m^2 (17.7, 62.1); serum creatinine 0.96 mg/dL (0.50, 9.12); albumin 3.7 g/dL (2.3, 4.7), and MDRD eGFR 84 $mL/min/1.73m^2$ (6, 216). For blacks, the MPE was lowest when ABW was used [0.29% (95% CI: -3.37%, 5.61%)], followed by AdjBW (-19.8%) and IBW (-34.8%). For nonblacks, the MPE was lowest when AdjBW was used [-6.26% (95% CI: -8.38%, -3.65%)], followed by ABW (17.4%) and IBW (-23.2%). MAPE was lowest for blacks (12.0%) and nonblacks (8.84%) when ABW and AdjBW were used, respectively.

In this population, use of ABW in the CG equation provided the most accurate estimates of GFR in blacks, while use of AdjBW provided the most accurate GFR estimates in nonblacks. Accuracy substantially decreased in both groups when alternative weights were used. This suggests that the standard practice of using the same body weight for all races substantially degrades the accuracy of CG GFR estimates.

ANEMIA MANAGEMENT IN CHRONIC KIDNEY DISEASE: PRIMARY CARE PHYSICIANS CONTRASTED WITH NEPHROLOGISTS

Paul W. Crawford, Karen Roberts, Associates In Nephrology, Chicago, Illinois, USA

PURPOSE: To evaluate anemia management in CKD patients receiving erythropoietin under the direction of primary care physicians as compared to that of the nephrologists.

METHODS: A retrospective analysis of the medical record, including laboratory results, of anemic CKD patients who were being treated with erythropoietin and were followed by both a primary care physician and a nephrologist. Using KDOQI guidelines, the effectiveness and efficiency of anemia management by the primary care physician as compared to the nephrology teams' management were measured.

RESULTS:

Hemoglobin > 14 mg/dL	
Nephrologist Managed	***Primary Care Managed***
2.0%	38.6%

Hemoglobin Target Range Met (11-12 mg/dL)	
Nephrologist Managed	***Primary Care Managed***
78%	58%

Results demonstrated that the nephrology team more consistently managed anemia as defined by the KDOQI guidelines.

CONCLUSIONS: In the observed sample, nephrology led CKD clinics are more effective than primary care led efforts for management of anemic CKD patients. With 38.6% of primary care managed patients having a Hg of >14, inefficient use of erythropoietin was demonstrated. In contrast, nephrologist managed anemia of CKD was more effective, with 78% of all patients being managed in the target Hg range of 11-12 mg/dL.

CHANGING TRENDS IN REFERRAL SOURCE OF ESRD PATIENTS IN A NEPHROLOGY PRACTICE BETWEEN 1995 AND 2005 Paul W. Crawford, Associates In Nephrology, Chicago, Illinois, USA

PURPOSE: In effort to determine relative value of work in defining a productivity formula for a large specialty group practice (25 physicians, 3 advanced practice nurses; caring for approximately 2000 patients), the source of ESRD referrals over the past 11 years (1995-2005) was evaluated.

METHODS: The billing data base was retrospectively reviewed to determine the date of initial dialysis and to determine if their first encounter with a nephrologist was as an inpatient or in the CKD clinic. Using the initial dialysis date, the percent of ESRD patients who were first seen as inpatients vs. outpatients was calculated. RESULTS:

	HOSPITAL	CKD CLINIC
1995	88%	12%
1996	91%	09%
1997	90%	10%
1998	89%	11%
1999	91%	9%
2000	88%	12%
2001	80%	20%
2002	77%	23%
2003	58%	42%
2004	52%	48%
2005	41%	59%

Over the observed period, the origin of ESRD patients has shifted from primarily hospital based referrals to outpatient referrals.

CONCLUSIONS: Findings demonstrate an increasing demand for outpatient based CKD care. The nature of nephrology practice has changed significantly over the time period observed. The value of the work performed in a Nephrology CKD clinic is greater than previously appreciated. This observation should be incorporated into the productivity formula for a large Nephrology group practice. In looking to the future of nephrology practices, there must be a paradigm shift from predominantly hospital based care to CKD clinics, with all of it's necessary multidisciplinary team and resources.

TIME ASSOCIATED WITH IN OFFICE ERYTHROPOIESIS STIMULATING PROTEIN (ESP) INJECTIONS FOR ANEMIA IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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Nephrology offices were observed to examine the activities and staff resources utilized in routine ESP administration to non-dialysis CKD patients.

A cross-sectional, time and motion assessment of CKD patients receiving routine ESP treatment was performed in 10 large community-based nephrology practices. Trained researchers observed and documented tasks and times associated with 91 ESP injections, from patients' arrival in the clinic to their departure. The time associated with each task was analyzed using descriptive statistics.

On average, patients spent a mean of 21 (sd 15.6) minutes for a routine injection visit, during which, 11 (sd 7.8) minutes were spent interacting with staff. The remaining 10 minutes were waiting time and other activities.

Staff Interaction Activities	Mean (sd) Time (Min)
Administering injection	3.2 (1.7)
Examination and consultation	6.4 (7.0)
Registration and scheduling	1.5 (1.5)

One third of patients had a consultation with a mid-level practitioner averaging 4 minutes. A small number (11%) had physician consultations averaging 7 minutes. Staff self-reports of time spent completing additional injection related activities, which were not observed, (e.g. billing) were highly variable, ranging from 7 to 85 minutes ((mean 44 minutes, sd 30).

Management of CKD patients generally includes monitoring patients' vital signs, weight, and lab results, and adjusting therapy accordingly. This study provides an overview of the activities and staff resources utilized during routine ESP injection visits. There was a notable variation in the average amount of time spent per injection.

ASSESSMENT OF EFFECTS OF LANTHANUM CARBONATE ON LIVER IN NORMAL AND UREMIC RATS

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The liver is the primary excretory organ for lanthanum (La) and recent studies have confirmed it as a site of trace La deposition. However, no toxicological endpoints were evaluated. We therefore report here, the results of a detailed histological assessment of the liver from uremic rats given p.o. $La_2(CO_3)_3$, as well as normal rats given high i.v. doses of $LaCl_3$.

Male rats were 5/6th nephrectomized and given $La_2(CO_3)_3$ at 0, 100, 500, 1000 or 2000 mg/kg/day p.o. for 12 weeks (*n*=8), or made uremic with a 0.3% adenine diet for 3 weeks and given $La_2(CO_3)_3$ at 0 or 1000 mg/kg/day p.o. for 4 weeks (*n*=10). Normal rats were similarly treated to act as controls. In a further study, male and female rats were dosed i.v. with $LaCl_3$ at 0, 3, 30 or 300 mg/kg/day for 4 weeks (*n*=10/sex), achieving average plasma La concentrations of 0.05±0.00, 3.3±0.8, 20.8±5.2 and 1575±236 ng/mL, respectively, representing up to 1400 times the C_{max} observed in dialysis patients given the maximum recommended clinical dose of $La_2(CO_3)_3$ (3 g/day).

Liver La concentration was 67226±17516 ng/g at the highest dose. At the end of treatment, serum ALP, AST and ALT activities were measured, and a detailed histological examination of H&E- and PAS-stained liver sections was carried out. Serum enzyme activities showed no changes indicative of liver toxicity. Histopathological findings in the liver were typical of the spectrum of background changes noted in laboratory rats, and incidences were not increased in lanthanum-treated compared with vehicle-treated rats.

Classical toxicology studies have also indicated no clinically relevant risk to this organ and a recent report has revealed no adverse effects of treatment on liver function or hepatobiliary adverse events in >2000 dialysis patients treated with $LaCO_3$ for up to 3 years. These studies provide further non-clinical evidence of the safety of $LaCO_3$, and support its therapeutic use as a treatment for hyperphosphatemia in ESRD patients.

STRINGENT CONTAMINATION CONTROL IS NEEDED IN TISSUE DEPOSITION STUDIES WITH LANTHANUM

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Tissue deposition studies with lanthanum in rodents carry an inherent risk of sample contamination due to low intestinal absorption of lanthanum (0.0007% of dose in rats) and fecal lanthanum concentrations up to 10,000,000 times higher than in the tissues being analyzed. Recent studies using dietary administration, rather than gavage or capsule dosing, have produced contradictory deposition profiles, particularly in respect of brain penetration. As this method may compound contamination risk, tissue lanthanum levels in rats dosed via diet, gavage or i.v. (as chloride salt) were directly compared to determine whether the presence of extraneous lanthanum might explain the discrepant profiles.

Male rats (255 g, *n*=10/group) were pair-fed to ensure that dietary and gavage doses were closely matched (0 or 838–863mg/kg as carbonate salt) or were dosed i.v. (0 or 30 mcg/kg) daily for 4 weeks. Stringent precautions were taken to reduce the risk of contamination.

Mean±SD plasma lanthanum levels were 0.084±0.015 (diet), 0.319±0.132 (gavage) and 20.8±5.2 (IV) ng/ml, compared to 0.055±0.015 (diet), 0.050±0.000 (gavage) and 0.069±0.03 (i.v.) ng/ml for the respective vehicle controls. Brain lanthanum levels were too low to be measured in the vehicle controls or after gavage or i.v dosing of lanthanum (LLoQ 2.8–8 ng/g). However, in rats given lanthanum via diet, cerebral, mid brain and cerebella concentrations were 98.7±173, 16.6±20.5 and 69.8±102 ng/g wet wt, even though this group had the lowest plasma exposure, which suggests sample contamination. Results for skeletal muscle and lung in the dietary group were also influenced by contamination, whereas concentrations in liver and bone, accepted sites of lanthanum deposition, were proportional to those in plasma.

These findings indicate a need for strict quality control in studies of lanthanum deposition, and highlight the potential for dietary administration to give misleading tissue deposition profiles.

AN UNCOMMON CAUSE OF NAUSEA AND VOMITING IN AN ESRD PATIENT

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Case Report

A 29 y/o noncompliant AA/M presented with a 6 month history of intermittent nausea, vomiting and abdominal pain. Past medical history: ESRD, hypertension, anemia, and was recently started on cinacalcet for secondary hyperparathyroidism. Asterixis was noted on PE. Lab: BUN 136 mg/dl; CR 46.2 mg/dl; CA 10.9 mg/dl; HCT 29.5%.

Uremia was suspected. His symptoms improved initially with daily dialysis but had a recurrence of nausea, vomiting and abdominal pain by the 5th day. Abdominal series was negative. A CT scan of the abdomen and pelvis demonstrated intussusception of the small bowel with partial to complete bowel obstruction. A small bowel resection with end to end reanastomosis was performed. Pathology revealed a hamartomatous polyp measuring 4.5 cm as the lead point.

Discussion

Intussusception is a rare cause of intestinal obstruction in adults, accounting for 1-5% of abdominal obstructions. The symptomatology is frequently nonspecific and elusive, which often delays diagnosis. An identifiable cause can be found in 70-90% of cases, with neoplasm accounting for 65% of cases.

Plain film radiography is commonly used for initial evaluation, but it lacks both sensitivity and specificity. The diagnosis of intussusception is made most reliably through computed tomography. The treatment in children is frequently nonsurgical, simply requiring hydrostatic reduction with barium or air. However, in adults surgical resection is often needed.

Conclusion

It is important to maintain a broad differential and a high clinical index of suspicion in an ESRD patient with nausea and vomiting, despite coexisting conditions.

CHARACTERIZATION OF GRANULOMATOUS INTERSTITIAL NEPHRITIS AT MAYO CLINIC OVER THE PAST DECADE Christoph Eggert, Donna Lager, Eric Haugen, Matthew Lewin, Mayo Clinic, Rochester, MN, USA

Granulomatous Interstitial Nephritis (GIN) is a form of interstitial nephritis that may be autoimmune or precipitated by drugs, infections, or other causes. Several series have examined patients with Acute Interstitial Nephritis (AIN) with regards to therapy and outcome, but few comment specifically about granuloma formation on the renal biopsy. Antibiotics account for around 70% of the cases of AIN in the literature, and full renal recovery with steroids has been shown in around 65%. About 12% remain on RRT after treatment.

We sought to further characterize GIN by searching the pathology and nephrology biopsy databases at Mayo Clinic for all cases of biopsy-proven GIN for the past 10 years; 30 were identified. From the patients' chart we extracted clinical data, therapy and outcome.

Average follow-up time was 26 months (0-91m). All patients presented with acute or subacute renal failure, and all except one were treated with immunosuppressives. 1 case was due to tuberculosis. 16 cases were thought to be medication related (group 1), of these, 7 were antibiotic-induced and 4 were NSAID related. 13 were not thought to be related to infection or medication (group 2); 6 of these were related to systemic sarcoidosis and 5 represented renal-limited sarcoidosis. The average presenting creatinines in groups 1 and 2 were 5.1 and 4.3 mg/dL respectively, and after treatment (in patients who had at least 2 months follow-up) fell to 2.1 and 3.0 mg/dL. 1/15 in group 1 and 4/11 in group 2 had hypercalcemia. Serum ACE level was elevated in 3/11 in group 2. 5 patients in group 2 had abnormal chest radiography, and 3 had granulomas in sites distant from the kidney. There were 2 relapses in group 1 and 4 relapses in group 2; 2 of these 4 were still on immunosuppression when the relapse occurred. Only 2 of the 30 patients (8%, both in group 1) had a creatinine <1.4 mg/dL at final follow-up. 1/16 in group 1 and 3/13 in group 2 developed ESRD.

GIN appears to have a worse prognosis than AIN with a significant chance of incomplete recovery of renal function, regardless of the suspected etiology. Careful follow-up is required, and further study of pathogenesis and optimal therapy would be useful.

THE OPTIMA STUDY: EARLIER INTERVENTION OF CINACALCET HCL (SENSIPAR®/MIMPARA®) ENABLES GREATER ACHIEVEMENT OF KDOQI™ SECONDARY HYPERPARATHYROIDISM (SHPT) TARGETS IN DIALYSIS PATIENTS.

JM Frazão,[1] F Macário,[2] M Yaqoob, [3] K Bouman,[4] J Braun,[5] B von Albertini,[6] HS Brink,[7] F Maduell,[8] H Graf,[9] H Saha,[10] V Zani[11], D Carter,[11] B Molemans,[11] P Messa;[12] Hosp S. João and School of Medicine University of Porto, Portugal[1], Diálise Aveiro, Portugal[2], Royal London Hosp, UK[3], ZNA Middelheim, Belgium[4], KfH Kuratorium für Dialyse und Nierentransplantation e. V. Nürnberg, Germany[5], Ctr Dialyse Cécil, Switzerland[6], Med Spectrum Twente, NL[7], Hosp General Castellón, Spain[8], Krankenanstalt Stadt Wien-Rudolfstiftung, Austria,[9] Tampere Univ Hosp, Finland[10], Amgen, Switzerland[11], Policlinico Milano, ltaly[12].

Cinacalcet HCl simultaneously reduces PTH, Ca, P, and Ca x P in dialysis pts. The magnitude of PTH reduction is consistent regardless of SHPT severity. In this 23-week study, 552 dialysis pts with baseline (BL) iPTH 300-800 pg/mL were randomly assigned (2:1) to receive cinacalcet HCl or conventional therapy (CT) (with unrestricted vitamin D and phosphate binder use). Cinacalcet HCl was initiated at 30 mg/day and titrated to achieve an iPTH 150-300 pg/mL; vitamin D was dosed to augment Ca and P target achievement. The effect on iPTH in pts with BL iPTH 300-500 and 500-800 pg/mL was evaluated. The proportion of pts and mean dose in pts achieving an iPTH <300 pg/mL during the efficacy phase (wks 17-23) is shown (Table).

	Cinacalcet HCl			CT
	BL iPTH 300 - 500 n=192	BL iPTH 500 - 800 n=164	Overall n=364	Overall n=184
iPTH <300 pg/mL	80%	64%	73%	22%
Ca x P <55 mg^2/dL^2	78%	79%	78%	58%
Both iPTH + Ca x P	65%	55%	60%	16%
Mean dose	42 mg	60 mg	49 mg	N/A

Simultaneous control of PTH and Ca x P was greatest in pts with lower BL PTH, and was achieved with lower cinacalcet HCl doses. Clinical studies to confirm if cinacalcet HCl use at lower iPTH levels provides more efficient treatment and prevents disease progression are merited.

PREVALENCE OF IRON DEFICIENCY IN ANEMIA OF CHRONIC KIDNEY DISEASE (CKD) STAGE 3 AND 4

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PURPOSE: To determine the prevalence of iron deficiency in patients with anemia and CKD stage 3 and 4 (i.e. Glomerular Filtration Rate (GFR) between 15 to 60mL/min calculated by modified MDRD formula). METHODS: A cross sectional analysis of 200 ambulatory chronic kidney disease patients who met the following criteria: hemoglobin (Hb) ≤ 12.5gm/dL in males and postmenopausal females and Hb ≤ 11gm/dL in premenopausal females; GFR 15 – 60mL/min; age 18 – 87 years. In these patients iron status was evaluated by standardized laboratory tests: Serum Iron, Serum Ferritin, Total Iron Binding Capacity (TIBC) and Transferrin Saturation (%TSat). RESULTS:

		Stage 3 & 4	Stage 3	Stage 4
Serum Ferritin	< 200	62%	65%	59%
	201 – 399	18%	20%	18%
	>400	18%	15%	24%
Transferrin Saturation	<15	16%	19%	12%
	15-20	21%	14%	29%
	21 -25	24%	24%	24%
	26-30	21%	24%	18%
Total Iron Binding Capacity	<250	21%	10%	35%
	251-300	42%	52%	29%
	301-350	11%	10%	12%
	351-400	13%	10%	18%

All 3 data sets point to absolute iron deficiency (Serum Ferritin <100ng/dL and TSat <20%) in 38% CKD patients with GFR (MDRD) = 15 to 60mL/min. CONCLUSION: Combination of decreased Serum Ferritin and TIBC indicate impaired iron absorption (either due to dietary iron deficiency or gastrointestinal absorption defect i.e. Hepcidin dependent). Decreased TIBC implies impaired Transferrin iron carrying ability due to deranged liver synthesis of Transferrin.

PRIMARY CARE PROVIDERS' KNOWLEDGE AND PRACTICES RELATED TO KIDNEY DISEASE

Elisa Gladstone, NKDEP, Bethesda, MD, USA

Primary care providers (PCPs) provide a vital role in reducing CKD and ESRD incidence by diagnosing, treating and preventing kidney disease. Yet no comprehensive survey of PCPs, kidney disease related knowledge and practices was available. We conducted this survey to guide the development of the National Kidney Disease Education program (NKDEP) messages for and outreach to PCPs. About 780 physicians, nurse practitioners and physician assistants in six metropolitan areas completed a survey via fax or the Internet. To be eligible, participants were required to a) work in a family, general or internal medicine practice; b) see at least 10 adult patients per week; c) work in a solo practice, group practice, HMO, hospital setting or community clinic; and d) have at least 20% of patients with diabetes and/or hypertension. PCPs indicated strong awareness for some CKD risk factors with 96% saying they would begin closely monitoring kidney function in all patients presenting with diabetes and 89% doing so for patients with hypertension. However, just 36% would do so for African American patients, and 62% for patients with a family history of kidney failure. When asked to indicate when they would diagnose CKD in response a hypothetical example, 27% indicated they would diagnose CKD at a creatinine level equivalent to later stages of the disease. Sixty-six percent indicated a level equivalent to Stage 3 and just 4% used the diagnostic standard of 1.0-1.1 mg/dl. Nearly all respondents (98%) said they routinely discuss with at-risk patients the importance of controlling hypertension and diabetes to prevent CKD progression and 91% said they routinely discuss the severity and/or possible complications of kidney disease. Yet, 12% of respondents said they always discuss ways to prevent CKD with at-risk patients, 47% frequently do and 38% occasionally do. Just 3% said they never or rarely discuss CKD with at-risk patients. Awareness of most CKD risk factors is high, yet knowledge of some factors is low. In addition, PCPs tend to diagnosis CKD at later rather than earlier stages and do not consistently discuss CKD with at-risk patients.

CALCIUM GLUCONATE INCREASES iCa, ATTENUATES PTH AND PARATHYROID (PT) HYPERPLASIA IN UREMIC RATS WITHOUT CAUSING CALCIFICATION

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Vit D sterols (e.g., calcitriol), used in treatment of secondary hyperparathyroidism (sHPT), are associated with hyperphosphatemia, hypercalcemia, and vascular calcification. Calcium-based phosphate binders may produce hypercalcemia, but the effects on soft tissue calcification are not well known. The objective of this study was to determine the effects of calcium loading on soft tissue calcification, PT hyperplasia and serum PTH, since increased iCa signals through the calcium-sensing receptor to decrease PTH. Uremia, induced in male SD rats by 5/6 nephrectomy (Nx), was followed by treatment for 40 days with Ca gluconate (3% in H_20 or 3% in diet) or deionized (DI) water. Serum chemistries monitored throughout the study are shown as terminal data below. BUN and creatinine increased >3-fold in Nx rats compared to normal rats (BUN=22, creatinine = 0.3 mg/dL). Serum iCa significantly increased (above DI water controls) in calcium gluconate-treated rats to levels produced by a dose of calcitriol (iCa=1.5±0.1 mM) that mediated aortic vascular calcification in Nx rats (*JASN* 2005;16:889-890A).

Treatment	iCa mmol/L	PTH pg/ml	PT wt mg/kg	PCNA+ cells/mm^2	Calcification	
					Renal	aorta
DI water	1.2± .0	644± 263	2.0± 0.3	66± 8	.2± .2	0
Ca 3% H_2O	1.4± .0*	33± 8 *	1.0± 0.1 *	20± 3 *	.6± .2	0
Ca 3% diet	1.4± .0*	56± 17 *	1.0± 0.1 *	19± 3 *	.6± .2	0
normal	1.3± .0	85± 10	1.1± 0.1	33± 6	0± 0	0

Values=mean±SE, n=6-9; *P<0.05 vs. DI water. Calcification scored by pathologist blinded to treatment-scale:0=none; 1=minimal; 2=mild; 3=moderate; 4=marked; 5=severe

Ca gluconate reduced serum PTH and PT hyperplasia compared to DI water-treated, uremic rats. Renal calcification was virtually absent and when present was subcapsular, likely resulting from surgical repair and inflammation in the Nx kidney rather than treatment. No aortic calcification occurred. These results suggest that Ca intake, like calcitriol, can increase iCa and control sHPT, but unlike calcitriol does not produce calcification.

COST MINIMIZATION MODEL EVALUATING RESOURCE UTILIZATION TO NEPHROLOGY PRACTICES TREATING PATIENTS WITH ERYTHROPOIESIS STIMULATING PROTEIN (ESP) ON A MONTHLY (QM) VERSUS WEEKLY (QW) BASIS

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An economic model was developed to analyze the labor and supplies utilized when administering ESP on QW versus QM dosing schedules in an Excel platform. The model compared a QW to a QM patient with the assumption that the patient can be managed on either one of the frequencies. Parameter estimates were based on weighted averages from data collected from an observational study. Fifteen generally used supplies were documented in the study. Thirty-eight labor activities, identified during focus groups of nephrology practice managers and peer reviewed medical literature, were observed. For those parameters outside of the observer's view (specifically front office, filing, and billing activities), the data were collected from a survey completed by the practice study coordinator.

Ten sites were observed (5 QW, 5 QM). The average number of patients receiving an ESP per month was 218 patients in the QW sites and 292 in the QM sites, although most sites administered ESP in various dosing regimens. Based on the observed activities QW sites spent 46.1 minutes per month per injection, while QM sites spent 14.8. The model estimated that QW sites spent 167.5 hours per month and QM offices spent 72.0 hours per month on injection related activities. QW sites consumed an average of 2.5X more supplies than QM sites.

The results from the model suggest that use of both resources and supplies are reduced when ESPs are administered on a QM regimen. Less frequent ESP dosing regimens can potentially allow for increased practice capacity through improved operational efficiencies.

PUBLIC AWARENESS OF KIDNEY DISEASE THROUGH LOCAL NEWS.

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Health information is a prominent part of local television broadcasts yet little is know about what or how health is reported. The purpose of this study was to describe and characterize how local TV news, the primary news source for the majority of Americans, reports on kidney disease.

Using our searchable database of health-related late local news segments from 2002, we identified all stories with the following keywords: kidney, hypertension, blood pressure (BP), or diabetes. This database is a representative sample of the late local news on 144 stations in the 50 largest US media markets, comprising 60% of the population. The content of each identified story was reviewed to determine if it mentioned: 1) chronic kidney disease (CKD), 2) screening for kidney disease, or 3) kidney disease as a potential complication (for BP or diabetes related stories).

Of the 1799 news stories in the database, only 2(0.11%) included "kidney" as a keyword in the summary, and neither referred to CKD, screening or complications of other diseases. One segment discussed the laparoscopic kidney donation of a daughter to her father, and the other described the effects of water consumption on kidney function. Of the 15 stories about hypertension or BP (0.83% of all stories) and the 9 stories about diabetes (0.50% of all stories), none mentioned the above criteria.

Despite efforts by the kidney community to increase public awareness of and screening for CKD, health-related news stories from local news, the primary news source for the majority of the US population, do not yet appear to help achieve these goals. Further work will be needed to evaluate if this is changing over time. It may be necessary to re-direct efforts and resources to advocate for increased representation of kidney disease public awareness in local news venues.

NON-INVASIVE CARDIOVASCULAR PARAMETERS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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The purpose of this study is to evaluate the relationship between renal function and two non-invasive methods of cardiovascular risk assessment - measurements of arterial stiffness and endothelial function.

Adult non-diabetic patients with CKD stages 2-5 are included in this study. Arterial stiffness is measured by pulse wave velocity using applanation tonometry. Endothelial function is estimated by measuring changes in skin microcirculatory blood flow in response to ischemia utilizing the laser Doppler technique. Statistically significant differences between means are calculated using Student t test; $p<0.05$ is considered statistically significant. All values are expressed as mean $\pm$ SD. SPSS software was used to determine correlations.

43 patients with CKD and 15 healthy volunteers participated in the study. Patients' average age is 57.1 ± 16.3 years; age of controls is 60.5 ± 17.2 years, p=NS. The mean creatinine clearance (CrCl) of patients with CKD is 47.3 ± 42.6 ml/min versus 95.9 ± 49.1 ml/min in controls, p=0.0006. Augmentation index (AIx75), a dimensionless measure of arterial stiffness, is 26.6 ± 9.2 in CKD group versus 24.3 ± 11.8 in the control group, p=NS. Measures of endothelial function using laser Doppler technique show a 529 ± 208% increase of blood flow in healthy controls but only 375 ± 184% in the CKD group, p=0.009. Moreover, degree of endothelial function impairment correlates with degree of kidney disease. CrCl correlates with endothelial function (r=0.388, p=0.011) but not with Aix75.

We found a difference in endothelial function measurements between CKD patients and healthy volunteers but not in arterial stiffness assessment. Arterial stiffness is known to increase with age. Older age in both patient and control groups might have accounted for lack of difference between the two. However, this study shows that endothelial function by laser doppler technique is impaired in patients with CKD and this impairment appears to correlate to the degree of GFR impairment. Further studies are needed to evaluate the etiology and prognostic significance of this dysfunction.

CONSISTENT PHARMACOKINETIC PROPERTIES OF CERA (CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR) IN HEALTHY VOLUNTEERS AND IN PATIENTS WITH CKD

Iain C. Macdougall,[1] Bruno Reigner,[2] Frank C. Dougherty[2]. [1]King's College Hospital, London, UK; [2]F. Hoffmann-La Roche Ltd, Basel, Switzerland

CERA is a new agent currently in development as a treatment for anemia with extended administration intervals in patients with chronic kidney disease (CKD) on dialysis and not on dialysis.

The pharmacokinetic (PK) properties of intravenous (IV) and subcutaneous (SC) CERA have been examined in three Phase I studies in healthy volunteers and CKD patients on peritoneal dialysis (PD).

In two parallel-group, multiple-ascending dose studies, healthy volunteers were randomized to receive CERA (either 0.4, 0.8, 1.6, or 3.2 μg/kg) by IV injection on three occasions at 3-weekly intervals (n=61), or by SC injection on four occasions at 2-weekly intervals (n=48). In a third multicenter, cross-over study, 16 stable CKD patients on PD (hemoglobin [Hb] ≤12 g/dL), received a single administration of IV CERA 0.4 μg/kg (n=8) or SC CERA 0.8 μg/kg (n=8). After 6 weeks, the route of administration was switched so that all patients received single administrations of CERA via both routes.

In healthy volunteers, the mean half-life was 133 h for IV and 137 h for SC CERA. In CKD patients on PD, half-lives of CERA after IV and SC administration were similar (134 and 139 h). CERA was generally well tolerated. The most frequent adverse events in PD patients were gastrointestinal and other general disorders.

These findings show a prolonged half-life for CERA, which is comparable for IV and SC administration and is consistent in both healthy volunteers and CKD patients on PD. The results suggest that CERA can be administered at extended dosing intervals. This is currently being evaluated further in Phase III studies.

INTERVENTIONAL NEPHROLOGY VS. INTERVENTIONAL RADIOLOGY: CAN WE WORK TOGETHER?

Ivan D. Maya, Rachel Oser, Souheil Saddekni, UAB, Departments of Medicine and Radiology, Birmingham, AL.

Background: Interventional nephrology is a relatively young subspecialty that deals with one of the most important aspects of dialysis care: vascular and peritoneal access. Training of qualified interventional nephrologists has been difficult. Majority of interventionalists have been trained by peers in an outpatient setting with few being trained in an academic environment.

Methods: The departments of medicine and radiology at UAB decided in 2004 to create a combined interventional nephrology program. The agreement gave 40% interventional time to nephrology and 60% to radiology.

Results: During the 15-month study period (July 2004 to September 2005), a total of 1306 procedures were performed. Of that total, 588 were permanent vascular access placement, 49 temporary vascular access, 423 fistulograms, 198 mechanical thrombectomies, 28 peritoneal catheter placements, and 20 upper extremity venograms for mapping. Interventional nephrology performed 39.6% of the procedures. There were no major complications accounted for in either group. Success rate was greater than 98.5% on all cases for both groups. Two new techniques were introduced to the service including the placement of femoral permanent catheters and placement of peritoneal catheters.

Conclusions: We demonstrated that in an academic center the departments of medicine and radiology could work together, and learn from each other. Interventional nephrologic procedures were done with the same quality, safety and effectiveness for both groups. It showed that with collaboration all involved parties gained from a mutual goal. Finally, a multi-disciplinary team approach to dialysis access is fundamental to provide proper medical care to the ESRD population.

RESULTS IN A LARGE SHORT DAILY HOME HEMODIALYSIS PROGRAM John Moran, Sheila Doss, Ann Robar
WellBound, Inc., Mountain View, CA USA.

We present results on 37 patients established on maintenance short daily home hemodialysis for 3.1 – 42.7 months (mean 15.3 months), providing a total of 567 patient months of experience. There were 25 males and 12 females, with a median age of 53 years (range 27 – 85 years). Twenty-nine patients were on NxStage System One (NxStage, Lawrence, MA), 5 patients were on the Aksys Personal Hemodialysis machine (PHD, Aksys, Lincolnville, IL), and 3 patients were on the Fresenius 2008K@HOME machine (Fresenius USA, Walnut Creek, CA); 1 patient changed from Aksys PHD to NxStage System One. All patients transferred from either conventional in-center HD or from PD (1 patient). Patients dialyzed for 90 - 300 minutes (mean 184 minutes). All patients initially dialyzed 6 days per week; 7 patients on NxStage converted to 5 days per week after variable periods. The vascular access was an AV fistula in 24 patients, AV graft in 8, central venous catheter in 4, and LifeSite in 1. All patients with AV fistulas used the buttonhole technique with blunt needles (Medisystems, Seattle, WA).

Laboratory indices, including serum albumin and serum phosphate, did not change significantly. The need for antihypertensive therapy was greatly reduced: the mean number of antihypertensive medications per patient fell from 2.1 to 0.9 ($p = 0.0001$ by paired t test) while the mean number of antihypertensive pills per patient per day fell from 2.9 to 1.1 ($p = 0.002$). Erythropoietin and phosphate binder doses did not change.

All patients reported greatly improved energy and quality of life, and notably lost their symptoms of post-dialysis “washout”. One patient returned to center hemodialysis after 17.3 months because of partner burnout and 1 transferred to peritoneal dialysis because of vascular access failure. One patient was transplanted after 8.3 months. There were 5 deaths: 1 myocardial infarction and 2 sudden cardiac deaths (including 1 patient with NYHA Stage 4 heart failure), 1 multiple myeloma, and 1 patient with terminal liver failure.

Patients established on short daily home hemodialysis have an excellent quality of life and a clear preference over conventional center hemodialysis.

CHRONIC KIDNEY DISEASE (CKD) CLINIC IMPROVES MANAGEMENT OF CARDIOVASCULAR DISEASE (CVD) RISK FACTORS IN CKD. **Naima Ogletree, S. Frinak, S. Soman, J.Yee, Henry Ford Health System, Detroit, Michigan, USA.**

We hypothesized that a newly implemented Nurse Practitioner (NP) driven CKD management program would benefit CKD patients by achieving goals outlined by the Kidney Disease Outcomes Quality Initiative (KDOQI). Optimizing treatment for blood pressure (BP) to a goal of less than 130/80mm Hg and LDL-cholesterol (LDL-C) to less than 100 mg/dL helps retard progression of CKD and reduce the morbidity and mortality from CVD. The purpose of this study was to evaluate the effectiveness of this program in achieving target BP and LDL-C in CKD patients.

A unique computerized database for patient enrollment was designed and implemented using Filemaker Pro 7™ software to aggregate patient data analysis. Enrollment in the CKD clinic as part of routine nephrology care began from Oct. 2003 after the patient had received prior care from their nephrologists and a diagnosis of CKD was established. The CKD clinic was managed by a licensed NP specializing in nephrology, who functioned independently and consulted nephrologists when needed. BP and LDL-C values were compared from Oct. 2003 through Oct. 2005 in 481 prevalent patients. An algorithmic approach for BP management was utilized with emphasis on implementing the appropriate K/DOQI Clinical Practice Guidelines for CKD.

Since enrollment into the CKD clinic, improvements were noted in both BP and lipid management. Average follow-up in this clinic was 18 months. At their first visit to this clinic, 52% and 71% of the patients met KDOQI guidelines for BP and LDL control respectively as compared to 56% and 73% of patients at their last available visit. There was also a 3.2% reduction in mean arterial pressure, with a 4% reduction in LDL (mg/dL) in this time period.

With the newly implemented NP driven CKD clinic, the number of CKD patients achieving target BP and LDL goals was maintained. We conclude that a targeted CKD clinic program will continue to improve CKD outcomes by optimizing healthcare resource utilization.

TACKLING THE AFRICAN AMERICAN HEALTH CRISIS VIA A PEER MENTORING CABLEVISION TALK SHOW

Erica Perry, June Swartz, Nathaniel Steed, National Kidney Foundation of Michigan, Ann Arbor, Michigan, USA.

The purpose of this project was to heighten awareness that African Americans are 4 times more at risk for CKD than Caucasians, explore causative factors and barriers, and discuss prevention options among the local broadcast community of 90,000 households in Ann Arbor/Ypsilanti, Michigan.

We utilized the oral tradition as a means to convey the problem to the television viewer. Four dialysis and transplant African American Peer Mentors hosted the 4 shows in which African American experts were guests. The studio audience consisted of churches, high school and college classes, and others who asked the panel questions during the hour long show. The topics included: "Is there really an epidemic?" "What keeps us from dealing with the problem?" "Does what we eat really matter?" "How can we get healthier?"

To prepare for each topic, the Peer Mentors worked with 4 community discussion focus groups of interested African Americans, some of whom were dialysis family members (9 times more at risk to develop CKD.)

Surveys were given to discussion group members, audiences, and the peers themselves to measure behavioral change, learning and attitude. Of the discussion group members 94% returned the surveys and 93% made behavioral changes in diet after attending the discussion groups. 82% of the studio audience returned questionnaires and 100% said they learned about barriers to getting good health care and 90% accepted the challenges given them at the end of each show to increase fruit and vegetable intake for the week.

Because 1) discussion groups wanted to continue to meet 2)peer mentors began exercise classes, 3) viewers continue to request reruns 4) 4 dialysis units have ordered the 4 part series of video tapes to show to patients and staff (for CEUs), 5) we have been invited to continue prevention programming on cable TV, 6) the series won the Philo T Farnsworth Video Festival Award, we conclude that African Americans are very interested in preventing this health crisis, and that the oral tradition is the best vehicle for education and empowerment.

TIME TO CONTROL OF SERUM PHOSPHORUS IN END-STAGE RENAL DISEASE PATIENTS IS PROPORTIONAL TO INITIAL DOSAGE OF LANTHANUM CARBONATE

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The purpose of this additional analysis was to investigate the relationship between baseline (BL) serum phosphorus (SP) and the dose of lanthanum carbonate (LC) required to achieve SP control, and to assess whether SP control is achieved more rapidly if the initial LC dosage is adjusted according to pretreatment (after a variable-duration washout from previous binder) SP levels. Two studies were conducted in men and women ≥18 y on hemodialysis (HD) 3 times/wk and with SP ≥5.6 mg/dL after washout. Study 1 was a phase II, double-blind, placebo-controlled trial of 4 fixed LC doses over 6 wks. Patients (mean age 56.4 yrs; 71% black, 25% white) receiving HD for ≥6 mo included men (n=80) and women (n=64). Doses of 1350 or 2250 mg/d (elemental lanthanum [La]) provided dose-dependent, rapid (≤14 d and 7 d, respectively) SP control (≤5.5 mg/dL) while lower doses did not. The maximum decrease in SP occurred within 2 wks of treatment for both higher dosages. At the end of treatment, 9.4% of patients on placebo had SP ≤5.5 mg/dL vs 43.3% and 46.2% of the LC 1350 mg/d and 2250 mg/d patients, respectively. The most frequent adverse events (AEs) in LC-treated patients were gastrointestinal and included nausea, vomiting, and diarrhea, with no evidence of a dose relationship among the LC-treated groups. Study 2 was a phase III, open-label study in which patients on HD for ≥3 mo received LC or calcium carbonate with 5 wks dose titration followed by 20 wks open label treatment. Patients (96.7% white) included men (n=341) and women (n=169) aged 19–87 yrs (mean ±SD; 57±14.3). Patients with BL SP of 5.5–≤7.5 (n=210), 7.5–≤9 (n=146), and >9.0 mg/dL (n=163) had final doses of 1423±577, 1688±552, and 1815±546 mg/d (La), respectively, showing a strong direct correlation between baseline SP and final dose. The incidence of AEs was similar for the 2 treatment groups. In conclusion, the dose of LC needed to achieve SP control is proportional to BL SP levels. SP levels can also be brought under control faster with higher initial doses of LC without an increase in AEs.

SUBCUTANEOUS (SC) CERA (CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR) ADMINISTERED ONCE EVERY 2 WEEKS EFFECTIVELY CORRECTS ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD) ON DIALYSIS AND NOT ON DIALYSIS

Robert Provenzano, St. John Hospital & Medical Center, Detroit, MI, USA. Frank C. Dougherty, F. Hoffmann-La Roche Ltd, Basel, Switzerland

CERA, an innovative agent acting differently at the receptor level and with a prolonged half-life, is currently in development to provide correction of anemia and stable maintenance of hemoglobin (Hb) levels at extended administration intervals in patients with CKD on dialysis and not on dialysis.

Anemia correction with SC CERA was investigated in previously untreated patients with CKD in two multicenter Phase II studies. In study 1, 65 CKD patients not on dialysis were randomized to receive CERA 1x/wk, 1x/2wk, or 1x/3wk. In study 2, 61 CKD patients on dialysis were randomized to receive CERA at the same administration intervals. After 6 weeks, individual dose adjustments were permitted according to pre-defined Hb criteria; patients were followed for a further 12 (study 1) or 6 (study 2) weeks. Response to treatment was defined as a Hb increase of >1 g/dL from baseline on two consecutive occasions and Hb ≥11 g/dL.

All doses of CERA provided increased Hb levels that were sustained until the end of each study. In total, 10/12 patients (83%) treated with CERA 0.60 µg/kg/2wk responded to treatment. The median time to response in both studies was 5 weeks. CERA was generally well tolerated. Adverse events were typical for the patient population, the most frequent being hypertension, urinary tract infections, and gout.

These Phase II results show that in CKD patients on dialysis and not on dialysis, CERA 0.60 µg/kg/2wk could provide an adequate Hb response within the timeframe recommended by current guidelines, and suggest that CERA can correct anemia when administered at extended intervals. These features could potentially offer improved convenience to CKD patients and minimize workload for healthcare professionals. Phase III studies are ongoing to confirm these findings.

ADEQUATE HEMOGLOBIN LEVELS ARE MAINTAINED WITH CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR (CERA) IN DIALYSIS PATIENTS WITH DIFFERENT RANGES OF IRON STATUS AND PRE-EXISTING CONDITIONS

M Salifu,[1] G Villa,[2] FC Dougherty.[3] [1]Suny Downstate Medical Center, NY, USA; [2]Divisione di Nefrologia e Dialisi, Fondazione S. Maugeri, Pavia, Italy; [3]F. Hoffmann-La Roche Ltd, Basel, Switzerland

CERA, an innovative agent, is currently in development to provide sustained and stable correction of anemia with extended administration intervals in patients with chronic kidney disease.

We conducted two multicenter, Phase II studies of CERA in dialysis patients previously treated with epoetin. Patients received intravenous CERA 1x/wk or 1x/2wk (study 1) or subcutaneous CERA 1x/wk, 1x/3wk or 1x/4wk* (study 2). Patients were followed for 19 weeks (*21 weeks). Thereafter, a combined total of 109 patients entered 12-month extension periods with the aim of maintaining hemoglobin (Hb) levels at 11-12 g/dL. We report on the impact of ferritin, transferrin saturation (TSAT), C-reactive protein (CRP), and albumin on mean Hb levels over the course of these 12-month extension periods. Tertiles were calculated for each of the baseline parameters, and an ANOVA of means was performed to calculate their influence on Hb levels.

Mean Hb over the 12-month extension periods for all patients was 11.3 g/dL (95% CI: 11.2, 11.5). The table shows mean (95% CI) Hb by tertile and calculated *P*-values for each of the four parameters.

	Hb, g/dL - mean (95% CI)			
	Ferritin	TSAT	CRP	Albumin
Tertile 1	11.4 (11.2, 11.7)	11.4 (11.2, 11.6)	11.1 (10.9, 11.4)	11.3 (11.1, 11.6)
Tertile 2	11.2 (11.0, 11.4)	11.3 (11.0, 11.5)	11.5 (11.3, 11.7)	11.3 (11.1, 11.6)
Tertile 3	11.3 (11.0, 11.5)	11.3 (11.0, 11.6)	11.2 (11.0, 11.5)	11.3 (11.1, 11.5)
P-value	0.41	0.75	0.08	0.97

CERA was generally well tolerated, the most common adverse events being hypotension and muscle cramp. These Phase II results suggest that CERA can maintain stable Hb levels when administered at extended intervals in patients with a range of values indicative of iron status and inflammation. Phase III studies are ongoing to confirm these findings.

SAFETY AND EFFICACY OF IV SODIUM FERRIC GLUCONATE COMPLEX IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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This study assessed the safety, efficacy and hemoglobin (Hgb) response of patients to intravenous (IV) Sodium Ferric Gluconate complex (SFGC) with that of oral iron (Fe) in patients with chronic kidney disease (CKD). Retrospective chart review of CKD patients followed in an outpatient office setting, 26 with IV SFGC therapy and 90 with oral Fe therapy was undertaken. IV SFGC 125 mg was infused at a rate of 60 minutes once a week for six weeks. Fe studies and Hgb levels were collected at baseline, eight weeks and at 12 weeks. Fe sat% in IV SFGC group were 14.2±1.3 at baseline, 26.3±3.1 at 8 weeks. In IV SFGC group, ferritin level of 123.8±35.1 at baseline increased to 278.8±51.1 at 8 weeks. Hgb values in IV SFGC group increased from 10.4±0.2 to 11.4±0.2 at 8 weeks compared to an increase from 10.8±0.1 to 11.6±0.1 in oral Fe group. IV SFGC was more efficacious in CKD patients than oral Fe and can be safely administered.

SHORT-COURSE ERGOCALCIFEROL FOR THE MANAGEMENT OF HYPERPARATHYROIDISM

Mohamed Sekkarie and Muhammad A. Ghabra. Nephrology and Hypertension Associates, Bluefield WV

Ergocalciferol (Ergo) is recommended for CKD patients with secondary hyperparathyroidism associated with sub-optimal calcidiol (25 D) stores. The optimal regimen of administration and impact on PTH are not well known.

We report our experience in treating 30 patients with stage 3 or 4 CKD who had 25D levels below 30 ng/mL together with iPTH values that exceeded the KDOQI recommended ranges. Patients received daily 50,000 IU doses of ergo for 2 to 6 days according to the degree of 25D deficiency. Renal function tests, 25D and iPTH were measured before and 6 weeks after administering ergo.

25D rose from a mean of 15.2 to 29.3 ng/mL ($p<0.001$), with an average rise +/-sd of 4.5 +/-4.3 ng/mL per 50,000 IU tablet. Intact PTH values changed from a mean of 164 to 138 pg/mL ($p=0.05$). Six patients (20%) achieved the KDOQI iPTH targets and iPTH became over suppressed in 1. Levels of 25D exceeding 30 ng/ml were seen in 11 patients (37%) with 1 value > 50 ng/ml. P and GFR did not change but Ca rose by 0.14 mg/dL ($p=0.04$).

Short-course ergo is an alternative method for optimizing vitamin D levels in CKD. The data provide information on how CKD patients respond to this agent.

OPTIMIZATION OF CKD ANEMIA MANAGEMENT IN A COMMUNITY CKD CENTER: CONVERSION FROM PROCRIT® TO ARANESP® David B. Simon, Rosella McLean, Sally Halloran, Fred Finkelstein, Metabolism Associates, New Haven, CT USA

Treatment of anemia in CKD patients in America is suboptimal. In private practice settings, coordinating appropriate erythropoiesis stimulating protein (ESP) dosing with monitoring of blood pressure, Hgb and Fe levels, and maintaining timely billing for a large CKD population, is very challenging. Using an electronic health record (EHR), we designed a form to capture critical information from encounters in our CKD clinic. Clinical data was downloaded into a database for analysis and monthly report generation. Pending charges were sent to billing electronically, for rapid submission to insurers.

To provide ESP therapy to a growing number of eligible CKD patients and minimize inconvenience to patients and their caregivers, we converted our population from Procrit to Aranesp with the specific goal of significantly increasing the percentage of patients maintaining hemoglobin (Hgb) stability with a once-monthly (qM) dosing interval. Based on the available literature, 333 patients with CKD stage 3(24%), 4(47%), and 5(29%) were converted using a ratio of Aranesp (μg) to Procrit (units) of 1:200. Dosing frequency was kept constant for the first 2 months to allow for Hgb stabilization. All patients with stable Hgb within the range of 11.5-12.5 mg/dl were extended to qM injections, with subsequent titration to maintain Hgb stability.

The proportion of patients successfully treated with qM dosing increased from 27% to 70% just 3 months after the conversion. The mean dose of Aranesp in the qM dosing group was 120 μg. Despite extending the dosing interval, mean Hgb increased with Aranesp (12.0 ± 1.4 mg/dL) compared with Procrit prior to conversion (11.6 ± 1.6 mg/dL). We observed an increase in the number of patients reaching Hgb ≥ 11.5 mg/dl: 66% in Aranesp vs. 54% in the Procrit group.

These data demonstrate that, in combination with the use of an EHR in a community CKD center, the seamless transition from Procrit to Aranesp of a large number of CKD patients can result in a significant improvement in percentage of patients on a qM dosing regimen, while at the same time increasing the proportion achieving target Hgb outcomes.

PREVALENCE OF ANEMIA IN INDIANS: THE SCREENING AND EARLY EVALUATION OF KIDNEY DISEASE (SEEK) STUDY.

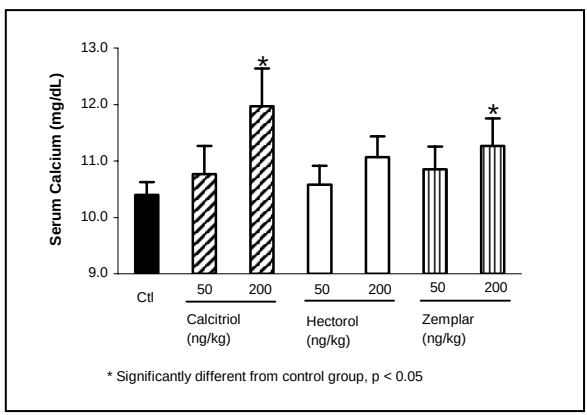
Singh A[1], Bhatia R[1], R.Sreedhara[2], Modi KG[4], Sridevi S[3], Anil C[3], Mittal B[1], Brigham & Women's Hospital, Boston MA[1], Apollo Hospital, Bangalore, India[2], SVYM Hospital Mysore, India[3], Bhopal Memorial Hospital and Research Center[4].

Background: Anemia is a widely recognized complication of CKD and is associated with high morbidity and mortality. Data on the prevalence of kidney disease in India is inadequate due to a lack of an adequate renal registry. In this rural based study, we screened for risk factors and complications of kidney disease. **Methods:** We screened 680 subjects in Mysore (n=500) and Bhopal (n=180). A standardized questionnaire was completed in local languages. Informed consent was taken from subjects after study approval by the Partners IRB in Boston and by local IRB's in India. Dipstick analyses were done for urine blood, sugar and albumin. The MDRD formula was used for eGFR. Screening data was used to estimate the prevalence of anemia in relation to other risk factors and in correlation with CKD. Serum hemoglobin, creatinine and glucose were analyzed at Ranbaxy Lab within 24 hours of collection. Anemia was defined by WHO standards. **Results:** The mean GFR in the Kote cohort was 69.2 (SD, +/- 14.4). Average hemoglobin was 12.4 gm/dL. 22.5% females and 12.8% of males were anemic. Severe anemia was seen in 11.5%. 26.4 % of patients had decreased kidney function and of these subjects, 8.8% were anemic and 16.5% were older than 60 years. Most anemic females had a BMI of < 18.5. Prevalence of other comorbidities for CKD in those with a low GFR were; Hematuria (15.8%), proteinuria (7.5%), glycosuria (3.8%). In Bhopal, mean Hb was 13.6 (SD +/-1.9) gm/dL. WHO anemia was seen in 13.6% of females and 17.9% of males. Hematuria was present in 3% of anemic subjects. **Conclusions:** The prevalence of anemia alone is high in India and can be correlated to renal insufficiency. The odds of anemia were greater in females than males and anemic women had a lower BMI. Anemia also increased with increasing age. CKD is poorly recognized in India and the early expression of anemia may be a precursor to reduced kidney function. Our data suggests the importance of considering age, BMI and hematuria for different hemoglobin levels in CKD and that correction of anemia may improve renal function.

VALIDATION OF ONLINE TRAINING OF RENAL DIETITIANS FOR PREFORMANCE OF SUBJECTIVE GLOBAL ASSESSMENT. Alison Steiber, Janeen Leon, Donna Secker, and Linda McCann. Conducting studies utilizing renal dietitians (RDs) as a source of data collection from multiple sites presents a unique challenge. The RDs need to receive consistent, high quality training on data collection techniques which is often expensive and time consuming. The purpose of this analysis was to determine whether online training to instruct RDs, in multiple facilities across the United States (US), Canada (Ca) and New Zealand (NZ), in the proper technique for performing Subjective Global Assessment (SGA) was effective. A specific webpage was designed which included reading material, flow diagrams, algorithms, and pictures of specific body parts with different degrees of somatic wasting. RDs were recruited by mail to collect data from 3 HD patients on demographics, clinical status, biochemistries, SGA, dietary intake, and quality of life (Medical Outcomes Short Form-35, SF36). All RDs who agreed to participate received instructions on entering the SGA webpage and took a pretest designed to assess their SGA knowledge. Following the pretest, RDs were required to review detailed instructions on conducting SGA and then complete a posttest. Participating RDs were from US (n=38), Ca (n=13) and NZ (n=3). The RDs (n=54) had 11$\pm$9 (mean$\pm$SD) years experience, worked an average of 34$\pm$9 hours per week, were responsible for 118$\pm$57 total dialysis patients, and 106$\pm$52 HD patients in their facilities. There were significant differences between countries in total patient load per RD (US-103$\pm$49, Ca-140$\pm$54, NZ-207$\pm$75) and total HD patients per RD (US-95$\pm$56, Ca-113$\pm$56, NZ-250$\pm$0). However, no differences were found between pre and posttest scores. The mean pretest and posttest scores for all participants were: 69$\pm$12 and 87$\pm$4 with a mean change of 17%$\pm$12; when a paired t-test was applied to the data a significant increase was found in the change from pretest to posttest scores ($p<0.05$). A positive correlation was determined between years of renal nutrition experience and posttest score ($r=0.3$, $p=0.05$). In conclusion, the online training was effective in increasing posttest scores of participants in this research project indicating the online training was effective.

EFFECTS OF ORAL HECTOROL®, ZEMPLAR®, AND CALCITRIOL IN UREMIC RATS. Stephen Strugnell and Joyce Knutson. Genzyme Corporation, Middleton, WI, USA.

Hectorol® (H), Zemplar® (Z) and Calcitriol (C) are widely used to manage elevated PTH levels in kidney patients. Little comparative data are available on the efficacy of these drugs following oral administration. To address this issue, we conducted a study in uremic rats. Six-week-old male Sprague-Dawley rats were subjected to 5/6 nephrectomy and allowed to become uremic for seven weeks. Animals were then dosed orally via gavage, 3 times/week for 2 weeks, with H, Z or C (50 or 200 ng/kg)(n=6/group). Control animals received vehicle. After the final dose, animals were placed in metabolic cages and urine collected for 24 hours. Serum was then obtained and analyzed. Both C and Z at 200 ng/kg significantly increased serum calcium. C at 50 and 200 ng/kg significantly increased urine calcium excretion. H did not significantly increase either serum or urine calcium. All three compounds caused dose-dependent decreases in serum PTH. We conclude that H, a prodrug, was less calcemic than the active compounds C and Z following oral administration and had similar effects on PTH in this model.



DIFFERENCES BETWEEN INNOVATOR AND GENERIC IRON SUCROSE COMPLEX (ISC) PREPARATIONS IN NORMAL RATS

Toblli Jorge; Cao Gabriel, Oliveri Leda; Vazquez Elba, Angerosa Margarita. Lab. Exp. Medicine. Hospital Alemán. Buenos Aires.

Several available i.v. iron formula, from innovator drugs to generic preparations are found in clinical practice. In this study we evaluate possible differences on hemodynamic and oxidative stress between the innovator and generic preparations of ISC. Four groups of SD rats: generic ISC-Feriv-group(G1); generic ISC-Hematin-group(G2); innovator ISC-Venofer-Group(G3); and Control-group(G4). G1,G2,G3 with single i.v. dose of ISC (40mg/kg) and G4 normal saline at 1,7,14, 21days. Animals were killed after i.v. dose at 1,7,28 days. In liver-heart-kidneys TBARS, GSH, GPx and CuZnSOD, LM and IHC techniques (Ferritin deposits) were performed. G1 and G2 presented a significant ($p<0.05$) decrease in SBP(mmHg)at 24hr vs. G3and G4. G1 112±1.1, G2 114±1.5, G3 116±1.6, G4 120±2. Similar findings at 7, 14 and 21 but not at 28 days. G1 and G2 presented different ($p<.01$) serum [Fe] and Sat. transf. vs. G3 and G4. Liver enzymes were dramatically increased in G1 and G2 vs. G3 and G4($p<.01$) at 24hr. and 7days. G1 and G2 presented a significant ($p<.01$) increase in TBARS, GPx and CuZn SOD and a decrease in GSH ($p<.01$) in liver-heart-kidney at 24hr. and 7days vs. G3 and G4. At 24hr: TBARS(nmol MDA/mg prot) a)liver: G1 109±10, G2 96±9, G3 75±7, G4 57±5; b)heart: G1 148±12, G2 80±18, G3 46±13, G4 30±10; c)kidney: G1 190±16, G2 132±30, G3 82±12, G4 72±9. GSH(nmol MDA/mg prot) a)liver: G1 44±5, G2 47±2, G3 56±2, G4 71±5; b)heart: G1 42±2, G2 49±3, G3 66±4, G4 69±2; c)kidney:G1 44±6, G2 53±4, G3 63±3, G4 67±2. GPx(U/mg prot) a)liver: G1 520±22, G2 351±24, G3 297±17, G4 254±11; b)heart: G1 380±16, G2 290±18, G3 172±24, G4 113±27; c) kidney: G1 207±13, G2 183±14, G3 119±24, G4 87±10. CuZn SOD(U/mg prot) a)liver: G1 20.3±1.9, G2 16.5±0.6, G3 8.9±1.1, G4 5.9±1; b)heart: G1 22.5±2.6, G2 19±2.1, G3 14±1.8, G4 9±2.1; c)kidney: G1 19.9±2.1, G2 13.5±2, G3 7.6±1, G4 4.4±1.8. Ferritin (%/area) at 28 days: a)liver G1 10.1±1.4; G2 10.9±1.3; G3 14.9±1.1; G4 2.3±0.6; b)heart G1 1.5±0.4; G2 1.3±0.3; G3 2.1±0.3; G4 0.1±0.1; c)kidney: G1 3.8±0.7; G2 3.5±0.9; G3 5.2±0.8; G4 0.3±0.1. These findings suggest that there are significant differences between the innovator ISC and the other ISC generic preparations concerning hemodynamic and tissue response in normal rats.

LANTHANUM CARBONATE ALLOWS FOR A LOWER TABLET BURDEN TO CONTROL SERUM PHOSPHORUS LEVELS

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Management of hyperphosphatemia in end-stage renal disease (ESRD) is contingent upon patient compliance, of which tablet burden is an important component, with phosphate binder therapy. A phase IV, open-label, multicenter trial was designed to evaluate efficacy and tablet burden of lanthanum carbonate (LC) vs previous therapy. This interim analysis was of a subgroup of patients whose serum phosphorus (SP) was <6.0 mg/dL (per protocol) with previous therapy at the time of LC initiation, as well as <6.0 mg/dL after 12 weeks of LC treatment. The main endpoints were efficacy and patient and physician satisfaction associated with a reduced tablet burden after switching to LC. Men (n=65) and women (n=35) ≥18 y with ESRD requiring treatment for hyperphosphatemia were enrolled. Patients (62% white; 31% black) had a mean (±SD) age of 61.1±13.4 yrs. Previous phosphate binder therapy at screening was sevelamer HCl (S; n=41) or calcium-based binders (CB; n=59). The initial LC dose was 1500 mg/d, divided between meals, titrated in 750 mg/d steps (maximum dose, 3750 mg/d) during the 12-wk titration phase to achieve SP within the K/DOQI range (3.5–5.5 mg/dL). CB patients reported taking (mean ± SD) 7.9±3.9 pills/d and S patients took 8.7±4.51 pills/d at baseline (BL), before switching to LC. At wk 12 of therapy, the average daily pill burden for previous CB patients was 5.1±2.16 (35% reduction) vs 5.2±2.41 (40% reduction) for previous S patients. Mean SP at wk 12 was 4.64±0.90 mg/dL vs 4.69±0.75 mg/dL at BL for CB patients and 4.66±0.84 mg/dL at wk 12 vs 4.76±0.75 at BL for S patients. 94% of physicians “strongly agreed” or “agreed” that patient compliance was improved with LC vs previous treatment; 96% of patients “strongly agreed” or “agreed” that tablet burden was decreased with LC. Also, 85% of patients “strongly agreed” or “agreed” that they rarely missed a dose of LC. LC was preferred to previous phosphate binder therapy by 89% of physicians and 76% of patients. LC controls mean SP within he K/DOQI range with a reduced tablet burden compared with other phosphate binders, which may help to improve patient compliance.

PREVALENCE AND PREDICTORS OF SUICIDAL IDEATION IN ESRD PATIENTS

Amy D. Waterman, Ann C. Barrett, Sara L. Stanley, Barbara H. Gradala, Karren King, Emily A. Schenk, Daniel C. Brennan, Barry A. Hong

With rates of suicide and dialysis withdrawal in ESRD patients reaching 10% nationally, understanding which patients may become suicidal can offer the opportunity for intervention through psychotherapy and medication.

We interviewed 448 transplant-eligible ESRD patients (83% on dialysis) to determine their demographics, level of suicidal ideation, perceived disease burden, health, and whether they were pursuing transplant. Patients were predominantly male (55%) and Caucasian (51%), with a mean age of 53 years (SD=12.9).

6% of ESRD patients (25/448) reported having suicidal thoughts, with one patient assessed to be in imminent risk of suicide. Compared to patients with no suicidal ideation, patients reporting suicidal ideation were more likely to be male (53% vs. 84%, p=.003) have incomes less than $20,000 (38% vs. 58%, p=.05), be very frustrated by their kidney disease (48% vs. 72%, p=.02), feel like a burden on their family (34% vs. 64%, p=.002), and report poorer health (42% vs. 72%, p=.003). Not pursuing transplant and older patient age were not associated with having higher rates of suicidal ideation.

Since underreporting of suicidal ideation is probably due to social stigma, we recommend that healthcare professionals develop a depression and suicide screening protocol. Screening patients, especially males, who express being extremely burdened by their kidney disease may be helpful in reducing the suicide rate in ESRD patients.

EXTENDED DOSING WITH DARBEPOETIN ALFA IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE (CKD) APPEARS TO BE LIMITED TO PATIENTS WITH LOW DOSE REQUIREMENTS

Jay Wish, Case Western Reserve U, Cleveland, OH, USA; Amy W Law, Roche Laboratories, Inc Nutley, NJ, USA, Kathy L Schulman, Thomson Medstat, Cambridge, MA, USA

Extended dosing (Q3W, Q4W,>Q4W) of erythropoiesis stimulating agents (ESAs) may improve compliance and quality of life for patients with CKD. This study characterizes the treatment intervals and dosing patterns with darbepoetin alfa in privately insured patients ages of 15 and older.

A total of 1,296 anemic CKD patients diagnosed between 2000 and 2005 were identified from the Medstat MarketScan Commercial and Medicare Research Databases. They were followed from the first identified diagnosis of CKD until onset of dialysis, kidney transplantation, disenrollment or study end. Dosing schedules and average weekly dose were calculated for facility-administered darbepoetin injections.

Nineteen percent of patients received their ESA only through a pharmacy while the remainder received services either exclusively in a medical setting (69%) or in combination with a pharmacy (12%). Only 23% of patients were dosed on an extended schedule of Q3W Q4W or >Q4W, while 50% were on a Q1W or Q2W schedule and 27% were classified as having a variable dosing schedule. Most variable dosing patients received a total of 2-3 injections during the study. The calculated average weekly dose decreased progressively as dosing intervals expanded from 72 and 43 mcg in Q1W and Q2W schedules to 29 and 25 mcg in Q3W and Q4W schedules.

In this study, less than a quarter of patients treated with darbepoetin alfa were on an extended schedule and the calculated average weekly dose for these patients was lower than for those on a Q1W or Q2W schedule. These results suggest that extended interval dosing is limited to patients with low dose requirements.

EXTENDED INTERVALS USING EPOETIN ALFA IN PRE-DIALYSIS PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD) APPEARS TO BE LIMITED TO PATIENTS WITH LOW DOSE REQUIREMENTS. Jay Wish, Case Western Reserve U, Cleveland, OH, USA; Amy W Law, Roche Laboratories, Inc Nutley, NJ, USA; Kathy L Schulman, Thomson Medstat, Cambridge, MA, USA

The introduction of erythropoiesis stimulating agents (ESA) has altered the treatment paradigm for anemic patients with CKD. While label recommended injection intervals for epoetin alfa suggest once to thrice weekly administration, recent publications have demonstrated that administration up to once every 4 weeks may be sufficient in some patients. This study characterizes the actual epoetin alfa treatment patterns of privately-insured patients, ages 15 years and older.

A total of 3,240 anemic CKD patients not on dialysis diagnosed between 2000 and 2005 from the Medstat MarketScan Commercial and Medicare Research Databases were treated with epoetin alfa. They were followed from the first identified diagnosis of CKD until the onset of dialysis, kidney transplantation, disenrollment or study end. Dosing schedules and average weekly dose were calculated for facility-administered epoetin injections.

Only 7.8% of patients treated with epoetin alfa were dosed on an extended (Q3W, Q4W,>Q4W) dosing schedule, while 50.1% were dosed on a BIW/TIW or Q1W schedule and 19.5% on a Q2W. Twenty-three percent of patients were classified as having a variable dosing schedule. Most variable dosing patients received 2-3 injections during the study. The calculated average weekly doses decreased as dosing intervals expanded. The average weekly dose for patients on a BIW/TIW or Q1W schedule was 14,300 U. The average weekly dose for patients on extended intervals was 7,800 U for Q3W, 8,200 U for Q4W and 5,800 U for > Q4W,

In this study, the average weekly dose for patients on an extended interval was below recommended levels of 10,000 U weekly, suggesting that only patients with low dose requirements are currently treated with extended intervals using epoetin alfa.

MULTI-METHOD ASSESSMENT OF ADHERENCE

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Medication non-adherence is known to be problematic among adolescents with kidney diseases. However, measures that provide an accurate and objective assessment of adherence are scarce. The present study used an interview and computerized method to assess adherence.

Fifteen adolescents (mean age = 15.07 years, SD = 1.99) diagnosed with renal disease or hypertension and who were taking blood pressure medications participated in this study. Participants were primarily of Caucasian descent (66.7%) and male (60%), with average household incomes in the range of $51,000-$60,000.

Participants completed the Medical Adherence Measure (MAM), a semi-structured interview that examines patient's knowledge of their medication regimen and self-reported adherence behaviors. Non-adherence was defined as the number of doses patients missed or took late during the prior week divided by the prescribed number of doses. Participants also used a Medication Event Monitoring System (MEMS) for their primary blood pressure medication over the two weeks prior to completing the MAM. MEMS cap contains a computer chip that records each time the medication bottle is opened.

On the MAM, 27% of the patients reported some non-adherence (i.e. missing more than 10% of their prescribed doses). The MEMS technology classified 50% of the patients as non-adherent. Patient rating of how adherent they were on a 1-10 Likert scale was highly correlated with the number of doses they reported taking as prescribed ($r=.77$, $p=.001$) and the number of doses missed ($r=-.63$, $p=.01$). Patient perceptions of how adherent they were also correlated with number of doses the MEMS tracked as taken on schedule ($r = .60$, $p = .023$) and number of doses as missed ($r = -.57$, $p = .03$).

An objective technological method revealed higher rates of non-adherence than patients were willing to report. However, MEMS is too expensive to use clinically. Adolescents did acknowledge adherence problems and the strong correlations between the measures suggest that a structured interview can be reliable as a screening mechanism.

THE RENAL ACIDIFICATION RESPONSE TO INSULIN IS ALTERED IN URIC ACID STONE FORMERS

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Low urine pH is the primary pathogenetic factor in the development of uric acid stones. Uric acid stone formers (UASF) demonstrate features of the metabolic syndrome including insulin resistance. The mechanism for low urine pH has been linked to insulin resistance. We previously reported that UASF exhibit an altered renal acidification response to insulin when compared with a set of historical controls. Data presented here was obtained from 22 normal subjects (NS) more closely matched by age and weight to UASF. Evaluations of these NS were obtained concurrently with those from 13 UASF.

Subjects were placed on a metabolic diet for 7 days and then underwent a 2 hour hyperinsulinemic euglycemic clamp study during which insulin was infused at 80 mU/m^2. Euglycemia was maintained with a glucose infusion. Urine collected for 2 hours prior to the clamp was compared with that collected during the study. (Results: mean ± SD)

	NS Preclamp	NS Insulin	UASF Preclamp	UASF Insulin
pH	5.67 ± 0.57	5.77 ± 0.51	5.44 ±0.60	5.56 ± 0.73
UV_{NH4} (mEq/2 hr)	2.6 ± 0.9	3.3 ± 1.5*	3.5 ± 1.7	3.7 ± 2.7
$UV_{Citrate}$ (mEq/2 hr)	0.67 ± 0.36	0.80 ± 0.38*	0.59 ±0.20	0.70 ± 0.47

**p<0.05 clamp vs. preclamp in same group*

UASF exhibited greater peripheral insulin resistance as measured by the glucose disposal rate: 2.88 ± 1.13 vs. 5.62 ± 2.55 mg/min/kg in NS. Insulin acutely increased ammonium and citrate in NS but none of the acidification parameters responded to acute hyperinsulinemia in UASF. These findings suggest that renal insulin resistance may alter proximal tubule acidification.

POST-TRANSCRIPTIONAL REGULATION OF GADD45 MRNAS IN THE MURINE RENAL INNER MEDULLA IN RESPONSE TO HYPERTONIC (GENOTOXIC) STRESS

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Hypertonicity in the renal inner medulla can cause DNA damage (via double strand breaks or oxidative stress), carbonylation of proteins and consequently apoptosis. Molecular mechanisms unique to this milieu allow renal inner medullary cells to cope effectively against hypertonicity via activation of the tumor suppressor gene p53 and upregulation of GADD153 and GADD45 proteins. GADD45 (Growth Arrest and DNA Damage-inducible) proteins are involved in many processes of cellular adaptation to environmental stress, including apoptosis, DNA repair and chromatin regulation indicating that they do contribute to cell survival. To understand how osmosensory signal transduction pathways operate in the renal inner medulla, we need to know the molecular mechanisms by which GADD45 is regulated during hypertonic stress. Biochemical and structural evidences suggest that this regulation probably occurs post-transcriptionally and resides in the 3' and 5' untranslated regions (UTRs) of the GADD45 mRNAs. Currently, three isoforms of GADD45 are known (α,β & γ), all of which are induced in response to hypertonic stress in mIMCD-3 (murine inner medullary collecting duct) cells. In this study, we show 1) that the 3'-UTRs of all three GADD45 transcripts are induced and post-transcriptionally regulated in response to hypertonicity (as evidenced by CAT reporter assays); 2) the occurrence of specific mRNA-protein interactions via complex formation(s) (as evidenced by *in vitro* UV-crosslinking studies and radiolabel transfer assays); and 3) the differential nature of interaction(s) of the three GADD45 transcripts with hypertonically-stress-induced proteins. The data clearly underscores the importance of post-transcriptional regulation in GADD45 mRNA turnover and the mechanism(s) are aptly discussed here in the light of the present data that would help reduce critical knowledge gaps in our understanding of the genotoxic stress response of the kidney.

FUNCTIONS OF THE TWO CATALYTIC SITES OF ANGIOTENSIN CONVERTING ENZYME: FROM ANEMIA TO MALE FERTILITY.

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Angiotensin converting enzyme (ACE) knockout mice have a complex phenotype including cardiovascular, reproductive and renal defects. This reflects the wide-ranging role of ACE and angiotensin II in normal physiology. ACE is a single polypeptide chain with two highly homologous catalytic domains termed the N- and C-terminal domains. To investigate the role of ACE *in vivo*, I created two new lines of mice, each having point mutations in the ACE protein that inactivate one of the two ACE catalytic domains. These mouse lines are termed N-KO and C-KO. These genetically modified mice produce normal amounts of the mutated ACE protein. The analysis of these lines shows that: 1) both strains have normal cardiovascular and renal function under basal conditions. 2) N-KO mice have markedly elevated levels of the hematosuppressive peptide AcSDKP. Despite this, these mice have a normal hematocrit. 3) Mutations in the C-terminal catalytic site inactivate the dipeptidase function of the testis isoform of ACE and the C-KO male mice are infertile. 4) Inactivation in the N-terminal catalytic site protects the animal from bleomycin-induced lung injury. This supports the idea that ACE controls both pro- and anti-fibrotic factors and as a result promotes the development of fibrosis.

THE *PKHD1* PRODUCT, POLYDUCTIN/FIBROCYSTIN, (PD1) UNDERGOES NOTCH-LIKE POST-TRANSLATIONAL PROCESSING BOTH *IN VITRO* AND *IN VIVO*.

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The longest open reading frame encoded by *PKHD1*, the gene responsible for human Autosomal Recessive Polycystic Kidney Disease (ARPKD), is contained in a 67-exon, 13kb+ transcript that is predicted to produce a >400kDa protein called polyductin/fibrocystin (PD1). However, there are lots of evidence suggesting that the gene also undergoes a complicated pattern of splicing and thus may encode a variety of additional gene products. Both the size of PD1 and the complexity of the gene splicing pattern has hindered efforts at characterizing the functional properties of the endogenous protein. Therefore, we have developed a series of cell lines with stable, inducible expression of N- and C-terminally epitope tagged forms of PD1. Using these reagents, we have shown that the N-terminal extracellular domain (NECD) is secreted into the medium while its cytoplasmic domain is cleaved from the transmembrane (TM) and released into the cytoplasm. These cleavage phenomena were detectable under standard culture conditions but appear to be regulated because they could be enhanced by treatment with PMA, a Ca ionophore. Using a cell surface biotinylation assay, we found both the expected full length product and a C-terminally tagged 80-90kDa product were present in the plasma membrane. Comparative analyses of human, mouse and canine PD1 revealed that this protein has a conserved precursor convertase(PC) sensitive sequence in its NECD and a putative gamma-secretase target sequence within its single TM domain. We showed that the large NECD is cleaved by unknown PC and tethered to the 80-90kDa products by disulfide bonds. Endogenous protein in mouse kidney tissue also undergoes the same processing. In sum, these data suggest that PD1undergoes proteolytic processing in a fashion similar to that of the key developmental protein, Notch.

CD36 MODULATES PROINFLAMMATORY PATHWAYS IN PROGRESSIVE RENAL FIBROSIS INDUCED BY URETERAL OBSTRUCTION

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Scavenger receptors play a central role in atherosclerosis by processing oxidized lipoproteins and mediating their cellular effect and by analogy are candidate mediators of renal fibrogenesis. The present study was designed to investigate the role of CD36, a class B scavenger receptor, in a model of chronic kidney disease. CD36 null mice and wildtype male mice on a C57BL/6 background were placed on a high fat Western diet (15.8% total fat, 0.5% cholate) for a run-in period of 8 weeks. Sham or unilateral ureteral obstruction (UUO) surgery was performed and groups of mice (n=6-10) were sacrificed on days 3, 7, and 14. After UUO, total kidney CD36 expression measured by immunoblotting signficantly increased at day 7 coinincident with renal infiltration of CD36+ macrophages (P<0.05, n=6-8). CD36 null mice developed significantly less fibrosis (evaluated by total collagen content and Sirius red stained interstitial area) compared to wildtype mice at days 3, 7, and 14 (P<0.01, n=8-10). CD36 null mice had signficantly reduced interstitial myofibroblast accumulation compared to wildtype mice by semi-quantitative α-smooth muscle actin immunostaining at day 7 and 14 (P<0.01). CD36 null mice had significantly more F4/80 positive macrophages at day 7 after UUO compared to wildtype (P<0.01). Levels of activated NF-κB, (measured by immunoblotting of phosphorylated IκB-α), were significantly reduced at day 7 compared to wildtype (P<0.01) despite higher macrophage numbers. CD36 null mice had significantly reduced levels of oxidative stress at day 7 compared to wildtype mice (P<0.01). These data suggest that CD36 is not only serving as scavenger receptor that processes and degrades its ligands, but that CD36-dependent cellular signaling is required to mediate fibrogenic responses potentially through modulation of oxidant and NF−κB proinflammatory pathways.

CISPLATIN INCREASES STABILITY AND TRANSLATION OF TNFα mRNA IN KIDNEY EPITHELIAL CELLS

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Cisplatin (CP) is an effective but nephrotoxic chemotherapeutic drug. Part of its nephrotoxicity is mediated through TNFα and TNFR2 pathways. The objective of the present study was to determine the mechanism whereby CP enhances TNFα production by renal epithelial cells. In vitro,CP increased the expression of TNF-α mRNA in proximal tubule cells in a time and dose dependent manner and was associated with activation of MAPKs. We studied the stability and translation of TNFα mRNA in response to cisplatin treatment. Treatment of cultured proximal tubules cells (TKPTS) with LPS induced a 5000 increase in TNF mRNA but no increase in TNF protein production. Cisplatin increased mRNA stability dramatically with a half-life of more than 3 hr. The effect on TNFα stability required pre-incubation of TKPTS cells with CP. Also, inhibitors to p38, ERK and JNK pathways did not influence the stability. Treatment with CP and LPS increased TNF protein several hundred fold without any added impact on TNF mRNA levels, indicating that CP increases the translation of TNF mRNA. We examined the role of MAPKs in CP-induced translation of TNF. LPS alone did not activate ERK, p38 or JNK in TKPTS cells whereas all three MAPKs were activated by CP+LPS. Specific inhibitors of MAPKs resulted in varying degrees of inhibition of CP+LPS-induced TNFα protein production. TNF production was reduced significantly by a p38 MAPK inhibitor (SB203580) and ERK pathway inhibitor U0126 while a JNK inhibitor (SP600125) had no effect. The translation initiation factor eIF-4E was phosphorylated in the presence of CP and phosphorylation was reduced by p38 and ERK inhibition. The eIF-4E upstream kinase, MNK, was also phosphorylated in the presence of CP. MNK phosphorylation was inhibited by SB203580 but not by U0126. Together these data suggest that: 1.cisplatin increases TNF production at the level of mRNA stability and translation; 2. The effect of cisplatin on translation is mediated through p38 and ERK; 3. The translation increase may involve the phosphorylation of eIF-4E but not mTOR pathways.

VIRAL SURVEILLANCE IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Background: Post-transplant infections have emerged as the most common reason for hospitalization in pediatric renal transplant recipients. We conducted a retrospective cohort study to evaluate if detection of subclinical EBV infection and subsequent modification of immunosuppression can decrease the incidence of PTLD.
Methods: Since 2001, patients had monthly measures of EBV by real-time quantitative PCR. At the time of subclinical infection, immunosuppression was adjusted to the lower end of the target range.
Results: Data were collected on 46 subjects with primary EBV infection from 2001 to 2004; 11 developed PTLD, 12 had symptomatic infection, and 23 had subclinical infection. Adolescents were significantly more likely to develop PTLD than younger transplant recipients (p=0.05, Chi-square). Between 1996 and 2000 (pre-viral surveillance), there were 8 cases (14%) of PTLD compared to 3 cases (4%) during the viral surveillance era (p=0.07, Chi-square). Patient characteristics in the 2 cohorts were similar with respect to demographics and recipient EBV status. There was no significant difference in calcineurin inhibitor use or rejection rates between the 2 cohorts.
Conclusion: Identification of subclinical EBV infection and the subsequent modification of immunosuppression was associated with a trend towards a decrease in PTLD in pediatric renal transplant recipients. Among patients with primary EBV infection, adolescents are at significantly higher risk to develop PTLD.

ROLE OF POLY (ADP-RIBOSE) POLYMERASE (PARP) IN DIABETIC NEPHROPATHY

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The purpose of the study: Poly(ADP-ribose) polymerase activation, an important factor in the pathogenesis of diabetes complications, is plays a crucial role in the pathophysiology of various diseases associated with oxidative-nitrosative stress. In many experimental models PARP activation lays downstream from reactive species generation, while in other cases it precedes and contributes to free radical and oxidant-induced injury.

Methods: We have examined the effect of two structurally unrelated PARP inhibitors (INO-1001, and PJ-34) on the development of diabetic nephropathy of Lepr$^{db/db}$ (BKsJ) mice, an experimental model of Type II diabetes mellitus. INO-1001 and PJ-34 were administered in the drinking water to Lepr$^{db/db}$ mice starting at 5 weeks of age. Mice were sacrificed at 17 and at 20 weeks age.

Results: We found that PARP inhibition inhibited the development of albuminuria and mesangial expansion. In addition, both inhibitors reduced hyperglycemia-induced DNA breakage in podocytes in vitro and ameliorated podocyte loss in vivo. In addition PARP inhibition reduced high glucose-induced ROS generation in podocytes via normalizing mitochondrial dysfunction.

Conclusion: Our results implicate the PARP pathway plays an important role in the pathogenesis of nephropathy associated with Type II diabetes.

POST-TRANSPLANT HYPOPHOSPHATEMIA: TERTIARY "HYPER-PHOSPHATONINISM"? Myles Wolf, Julie Holmes, Tamara Isakova,; Massachusetts General Hospital, Boston, MA.

Post-transplant hypophosphatemia is a common complication of kidney transplantation occurring in up to 93% of patients. Persistently increased PTH secretion – tertiary hyperparathyroidism – has long been thought to be the etiology but hypophosphatemia can occur despite low levels of PTH and can persist after high PTH levels normalize. Furthermore, calcitriol (1,25-D) levels are inappropriately low following transplantation despite normal allograft function, hypophosphatemia and hyperparathyroidism, suggesting mechanisms beyond PTH likely contribute to post-transplant hypophosphatemia. Fibroblast growth factor-23 (FGF-23) induces phosphaturia, inhibits renal 1,25-D synthesis and accumulates in patients with chronic kidney disease. We hypothesized that excessive FGF-23 accounts for the hypophosphatemia, urinary phosphate wasting and inappropriately low 1,25-D levels following kidney transplantation. We performed a prospective, longitudinal study of 27 living donor transplant recipients involving 119 blood and urine specimens before and repeatedly following transplant for up to 6 months. Graft function was immediate in all patients. Sample collection was discontinued if graft dysfunction developed. Mixed model linear regression for repeated measures was used to test the hypotheses. Hypophosphatemia <2.5 mg/dl developed in 85% of subjects; 37% developed levels ≤1.5 mg/dl. One patient who had undergone a subtotal parathyroidectomy prior to transplant nonetheless developed hypophosphatemia. Mean pre-transplant FGF-23 levels were 1,218 ± 542 RU/ml. Within the first week following transplantation, FGF-23 levels declined to 557 ± 579 but remained significantly above the normal range. FGF-23 was strongly associated with the serum phosphate ($P < 0.01$) and urinary fractional excretion of phosphate ($P < 0.01$), each independent of PTH. PTH was associated with phosphaturia but not serum phosphate levels. Increased FGF-23 was the only independent predictor of 1,25-D levels ($P < 0.01$). Persistently excessive FGF-23 levels in the post-transplant period contribute to hypophosphatemia and decreased 1,25-D levels. Furthermore, these results indirectly support a role for FGF-23 in the pathogenesis of secondary hyperparathyroidism *pre*-transplantation.

ß1INTEGRIN REGULATES EPITHELIAL POLARITY THROUGH RHO GTPASES

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The kidney is primarily comprised of epithelial cells. Epithelial cells are highly polarized and their plasma membrane is divided into discrete domains. The apical surface face the lumen, and the basolateral surface interact with other cells and underlying extra-cellular matrix. Establishment and maintenance of polarity is critical to the functioning of epithelial cells. Most work on epithelial polarization has used cells grown on artificial filter support. I have used a three dimensional culture system in which is closer in vivo to study how ß1integrin and Rho Gtpases coordinate to control the epithelial polarization. Individual Madin-Darby canine kidney(MDCK) cells grown in collagen gel from cyst spherical cysts comprising a monolayer of cells surrounding a hollow lumen. The cells are polarized. Addition of ß1integrin function-blocking antibody AIIB2 give rise to cysts with inverted polarity. I showed that normal polarity is restored by either expression of constitutively active Rac1or addition of exogenous laminin. I also found inhibition of ROCK, a major effector of RhoA, or myosin not only revert ß1integrin blockage induced phenotype, but also rescue the phenotypes induced by expression of dominant-negative Rac and cdc42. These findings indicate that ß1integrin orientates polarity through Rho GTPases and laminin assembly.