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EFFECT OF COLD ISCHEMIA ON THE FUNCTION AND SURVIVAL OF RENAL ALLOGRAFTS. A.K. Salahudeen, W. May, Medicine and Preventive Medicine, University of Mississippi Medical Center, Jackson, MS.

Use of kidneys from extended criteria donors (ECD) and donors after cardiac death (DCD) has increased due to scarcity of standard criteria donor (SCD) kidneys. DCD kidneys due to preprocurement ischemia and ECD kidneys due to marginal quality are likely to suffer from delayed graft function (DGF) and early graft loss. Any prolonged cold ischemia time (CIT) is likely to add to the injury, although this has not been specifically addressed. We examined the relationship between CIT and the function and survival of these kidneys and compared to SCD kidneys using the 2004 UNOS data set. In 2000, 9,469 (87%) kidneys were SCD, 165 (2%) were DCD, and 1,191(11%) were ECD. The donor age were 31 ± 14 years and 34 ± 17 years for SCD and DCD and higher at 60 ± 6 years for ECD kidneys (mean ± SD). CIT were similar: 18.6 ± 8.3 hours, 19.0 ± 8.4 hours, and 18.7 ± 8.3 hours. The HLA mismatches were not different, but the recipient age was higher for ECD (52 ± 13 years) than for DCD (48 ± 13 years) or SCD kidneys (43 ± 14 years) ($p < .001$ ECD vs the rest). DGF was higher for DCD and ECD kidneys than for SCD kidneys, eg, discharge serum creatinine was higher for DCD (4.7 ± 3.4 mg/dL) and ECD (4.1 ± 3.0 mg/dL) than for SCD kidneys (2.8 ± 2.5 mg/dL) ($p < .001$ for all interactions). Similarly, requirement for dialysis was highest for the DCD kidney recipients (46% for DCD, 37% for ECD, and 26% for SCD). Despite severe early injury in DCD kidneys, 4-year graft loss was similar between DCD and SCD kidneys ({223}25%) but was higher for ECD kidneys (38%; $p < .001$ vs the rest). In the Cox hazard analysis, CIT had significantly higher relative risk (RR) for graft failure over 30 hours for all groups combined and for each of the three groups separately. However, the preexisting injury of DCD or ECD kidneys did not add to the RR of cold ischemia on 4-year graft loss. In aggregate, despite early injury, DCD kidneys have similar graft survival as in SCD kidneys, and irrespective of donor type, CIT over 30 hours reduces renal allograft survival across the donor types. Thus, this analysis supports the wider use of DCD kidneys and the need for avoiding prolonged cold ischemia time of kidneys irrespective of donor types.

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PHYSICIAN HANDWRITING LEGIBILITY IS AS GOOD (OR BAD) AS EVERYONE ELSE'S. K.A Schnieder, C.W. Murray, R.D. Shadduck, D.G. Meyers, University of Kansas School of Medicine. Kansas City, KS.

Purpose: To compare handwriting legibility among professions. **Methods:** A convenience sample, stratified by gender, of 20 right-handed volunteers each from 7 occupations rapidly wrote the sentence "The quick brown fox jumps over the lazy dog" in < 17 seconds. Legibility was scored by two methods. The number of malformed individual letters was visually judged by a single blinded investigator. Four investigators, blinded to subject characteristics, independently rated the global legibility of the writing samples on a 4-point scale: poor, fair, good, excellent. Raters were tested with the kappa statistic. Characteristics and scores were compared using logit regression and post hoc Wilcoxon rank sum test. Scoring methods were compared by Spearman's correlation. The study was powered to detect a difference of 25% across occupations. **Results:** Among 70 males and 70 females, with ages 18 to 64 years and 12 to 28 years of education, only education differed among groups. Legibility scores did not differ significantly by occupation, age, or education, but legibility was significantly and consistently better in women.

	Accountant	*Attorney*	*AutoTech*	*Construction*	*Engineer*	*Physician*	*Scientist*	p
Age	35 ± 12	41 ± 10	29 ± 9	34 ± 7	29 ± 6	36 ± 10	42 ± 7	.31
Education	17 ± 1	19 ± 2	14 ± 2	13 ± 1	17 ± 1	22 ± 2	22 ± 2	< .01
Poorly formed letters	7.0 ± 6.7	11.3 ± 5.0	5.8 ± 3.9	9.4 ± 6.2	8.6 ± 7.9	8.5 ± 5.2	8.8 ± 3.2	.70
Score (1–4)	2.4 ± 0.5	2.0 ± 0.4	2.3 ± 0.6	2.1 ± 0.4	2.3 ± 0.6	2.4 ± 0.5	2.1 ± 0.6	.39
Illegible	15%	40%	30%	30%	35%	25%	40%	.62
Male score (*pairwise $p < .05$)	2.3 ± 0.4	2.0 ± 0.2	2.0 ± 0.6 *	2.0 ± 0.2 *	1.9 ± 0.5 *	2.0 ± 0.4 *	2.0 ± 0.4	< .01
Female score	2.6 ± 0.6	2.1 ± 0.6	2.6 ± 0.4	2.3 ± 0.5	2.7 ± 0.5	2.6 ± 0.3	2.2 ± 0.6	

There was good intra- and interrater agreement (kappa 0.35–0.56 and 0.23, respectively, $p < .001$) and good correlation between scoring methods (rho −0.75, $p < .001$). **Conclusion:** Physician handwriting legibility is not different from other occupations, although illegibility, which has been demonstrated to compromise patient care, is nonetheless prevalent. Legibility is consistently better in women.

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ENDOTHELIAL FUNCTION IN NONALCOHOLIC STEATOHEPATITIS. S.S. Shankar, P. Menon, N.P. Chalasani, H.O. Steinberg, Indiana University School of Medicine, Indianapolis, IN.

Background: Endothelial vascular function, an independent risk factor for cardiovascular disease, is impaired by insulin resistance. Nonalcoholic steatohepatitis (NASH) is associated with insulin resistance. However, the effect of NASH on endothelial function, either direct or via insulin resistance, is unknown. **Hypothesis:** NASH impairs endothelial function either directly or as a consequence of insulin resistance (IR). To test this hypothesis, we assessed endothelial function as well as insulin sensitivity in subjects with biopsy-proven NASH and BMI-matched controls. **Materials and Methods:** We studied four biopsy-proven NASH and four control subjects matched for age, gender, and BMI. We assessed lipid parameters by standard procedures and insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. We determined endothelial vascular function by measuring changes in leg blood flow (LBF) in response to graded intrafemoral arterial infusion of the endothelium dependent vasodilator methacholine (MCh). Results are expressed as mean ± SEM in NASH vs controls and compared using an unpaired *t*-test. **Results:** Total cholesterol was 224 ± 36 vs 177 ± 42 mg/dL NASH and controls, respectively ($p = .05$). LDL cholesterol was 151 ± 30 and 103 ± 29 mg/dL NASH and controls, respectively ($p = .05$). Triglyceride and HDL cholesterol levels did not differ between groups. Glucose disposal rates (insulin sensitivity) were 3.9 ± 1.3 and 6.2 ± 1.9 mg/kg/min NASH and controls, respectively (p = ns). Maximal increments in LBF in response to intra-arterial Mch, expressed as a percentage of baseline, were 34 ± 17 vs 193 ± 58% in NASH and controls, respectively ($p = .05$). **Conclusions:** NASH is associated with endothelial dysfunction over and above that associated with the obesity of NASH. Whether the endothelial dysfunction is attributable to the elevated LDL cholesterol levels, the differences in insulin sensitivity, or the intrinsic process of NASH itself requires further work and investigation.

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FOUR WEEKS OF INDINAVIR DOES NOT ALTER ADIPOGENIC TRANSCRIPTION FACTORS IN HEALTHY HIV-NEGATIVE SUBJECTS. S.S. Shankar, L.N. Bell, H.O. Steinberg, R.V. Considine, Indiana University School of Medicine, Indianapolis, IN.

Introduction and Purpose: HIV-infected patients on antiretroviral therapy have been reported to develop a lipodystrophy syndrome. Both HIV-1 protease inhibitors, as well as nucleoside analogue reverse transcriptase inhibitors, have been implicated. However, it is unclear if this is a direct drug effect or a result of an interaction between the drug and the underlying HIV infection. In order to dissect out the direct role of drug alone in this process, we studied the in vivo effect of a single protease inhibitor, indinavir, on the key adipogenic transcription factors C/EBPα, SREBP1c, and PPARγ. **Methods:** We obtained abdominal subcutaneous adipose tissue samples from seven HIV-negative subjects at baseline and after 4 weeks of daily oral indinavir at 800 mg three times a day. Adipocytes were obtained by collagenase digestion, and total RNA was isolated by standard methods. Expression of C/EBPα, SREBP1c, and PPARγ mRNA was quantitated by real time reverse transcription normalized to expression of β-actin using the delta Ct method. **Results:** The subjects had a mean age of 36 ± 3 years, with a mean BMI of 29.5 ± 9 kg/m². There was no change in BMI or waist-to-hip ratio after 4 weeks of indinavir. Indinavir treatment had no effect on expression of C/EBPα (304.0 ± 32.3 vs 359. 2 ± 43.4), SREBP1c (82.0 ± 14.0 vs 104.9 ± 34.0), or PPARγ (350.7 ± 54.0 vs 351.0 ± 48.8 relative units). **Conclusions:** Four weeks of the protease inhibitor indinavir does not alter adipogenic transcription factors in healthy HIV-negative subjects. Our findings indicate that indinavir does not appear to have a direct role in the development of lipodystrophy, suggesting that the lipodystrophy is likely either due to an interaction between drug and disease or attributable to antiretroviral agents other than indinavir.

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FOUR WEEKS OF INDINAVIR DOES NOT AFFECT BONE BREAKDOWN IN HEALTHY HIV-NEGATIVE SUBJECTS. S.S. Shankar, H.O. Steinberg, Indiana University School of Medicine, Indianapolis, IN.

Introduction and Purpose: HIV-1 protease inhibitors have been reported to increase bone breakdown in HIV-infected patients. However, it is unclear if this is a direct effect of the drug on bone or due to an interaction between drug and underlying disease. In order to assess the effect of drug alone on bone turnover, we studied the effect of a single protease inhibitor, indinavir, on markers of bone turnover. **Methods:** We studied eight healthy HIV-negative subjects with normal bone density as determined by dual x-ray absorptiometry. We measured markers of bone turnover in our subjects at baseline and after 4 weeks of daily oral indinavir at 800 mg three times a day. **Results:** We studied six male and two female subjects with a mean age of 37 ± 2 years, with a mean BMI of 29.2 ± 1.0 kg/m². All subjects had normal serum calcium, phosphorus, alkaline phosphatase, and urinary N-telopeptide levels prior to initiation of the study. There was no change in BMI after indinavir. Urinary N-telopeptide levels remained unchanged after 4 weeks of indinavir (29.6 ± 7.3 preindinavir vs 25.6 ± 2.9 nmBCE/mmol creatinine postindinavir). Urinary calcium and phophorus remained unchanged as well. **Conclusions:** Indinavir does not alter markers of bone turnover in healthy HIV-negative subjects. This indicates that the HIV-1 protease inhibitor indinavir does not appear to have a direct effect on bone breakdown.

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FOUR WEEKS OF INDINAVIR DOES NOT ALTER ADIPOGENIC TRANSCRIPTION FACTORS IN HEALTHY HIV-NEGATIVE SUBJECTS. S.S. Shankar, L.N. Bell, H.O. Steinberg, R.V. Considine, Indiana University School of Medicine, Indianapolis, IN.

Introduction and Purpose: HIV-infected patients on antiretroviral therapy have been reported to develop a lipodystrophy syndrome. Both HIV-1 protease inhibitors and nucleoside analogue reverse transcriptase inhibitors have been implicated. However, it is unclear if this is a direct drug effect or a result of an interaction between drug and the underlying HIV infection. In order to dissect out the direct role of drug alone in this process, we studied the in vivo effect of a single protease inhibitor, indinavir, on the key adipogenic transcription factors C/EBPα, SREBP1c, and PPARγ. **Methods:** We obtained abdominal subcutaneous adipose tissue samples from seven HIV-negative subjects at baseline and after 4 weeks of daily oral indinavir at 800 mg three times a day. Adipocytes were obtained by collagenase digestion, and total RNA was isolated by standard methods. Expression of C/EBPα, SREBP1c, and PPARγ mRNA was quantitated by real time reverse transcription normalized to expression of β-actin using the delta Ct method. **Results:** The subjects had a mean age of 36 ± 3 years, with a mean BMI of 29.5 ± 9 kg/m². There was no change in BMI or waist-to-hip ratio after 4 weeks of indinavir. Indinavir treatment had no effect on expression of C/EBPα (304.0 ± 32.3 vs 359.2 ± 43.4), SREBP1c (82.0 ± 14.0 vs 104.9 ± 34.0), or PPARγ (350.7 ± 54.0 vs 351.0 ± 48.8 relative units). **Conclusions:** Four weeks of the protease inhibitor indinavir does not alter adipogenic transcription factors in healthy HIV-negative subjects. Our findings indicate that indinavir does not appear to have a direct role in the development of lipodystrophy, suggesting that the lipodystrophy is likely either due to an interaction between drug and disease or attributable to antiretroviral agents other than indinavir.

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EVALUATION OF A 12-LEAD DIGITAL HOLTER SYSTEM FOR 24-HOUR Q–T INTERVAL ASSESSMENT. J.C. Somberg, Z. Molnar, V. Ranade, I. Cvetanovic, J. Molnar, Rush University, Chicago, IL, and American Institute of Therapeutics, Lake Bluff, IL.

Background: Drug-induced Q–T prolongation may precipitate life-threatening cardiac arrhythmias; therefore, evaluation of the Q–T prolonging effect of new pharmaceutical agents in a "thorough Q–T/Q–Tc study" is being mandated by the FDA. The purpose of this study was to evaluate the feasibility of a 12-lead digital Holter system for a thorough Q–T/Q–Tc study. **Methods:** Five healthy volunteers underwent 24-hour digital Holter monitoring (NorthEast Monitoring, Maynard, MA). The system provides automated Q–T analysis (AQA) and the option of onscreen manual over read (MOR) of automatic Q–T determinations. Each recording underwent a fully AQA followed by an onscreen complete MOR by an expert observer. The MOR was used as the reference standard for the validation of AQA.