of the MENQOL psychosocial domain was 32.21 (6.9). No significant correlation was obtained between the MENQOL psychosocial domain and nadir CD4 cell count. Nevertheless, we did found a significant correlation between questions 4, 7, and 9 and nadir CD4. An inverse association between question 4 (dissatisfaction with my personal life) and nadir CD4 (rho −.320. p = .028) was obtained. Noteworthy, for questions 7 (accomplishing less than I used to) and 9 (impatient with other people) there is a positive correlation (rho = .295, p = .044 and rho = .312, p = .033, respectively). In our cohort women with HIV showed more dissatisfaction with their personal life with increased immunosuppression. However, the feeling of impatience with other people could reflect other symptoms not related to depression, like anxiety. These findings demonstrate the necessity to study emotional health in women with HIV in Puerto Rico, especially the depressive symptom and how this affects infection status

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NEUROPATTERN: A NEW DIAGNOSTIC TOOL FOR PATIENTS WITH STRESS-RELATED DISORDERS. D. Hellhammer, Department of Psychobiology, Trier University, Trier, Germany.

Stress factors play an important role in physical diseases. Given the tremendous complexity of factors affecting the crosstalk between the brain and the body, there is a broad heterogeneity in the pathogenesis of stress-related disorders among patients, even sharing similar symptoms. In addition, there is a missing covariance between the psychological and biological stress response; thus, subjective patient reports are often misleading. We here introduce "Neuropattern", a newly developed diagnostic tool for clinical practice, allowing an individualized detection of stress effects in bodily diseases. Neuropattern analyzes stress effects on neurobiological interfaces, participating in the communication between the brain and the body. Functional changes of each of these interfaces are assessed by characteristic patterns of concomitant biological, psychological, and symptomatic measures, occurring in consequence of stress. Stressed patients may differentially qualify for one or more of these neuropattern, thus facilitating highly individualized indications for therapeutic treatments.

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INSULIN RECEPTORS AS WELL AS INSULIN ARE PRESENT IN SALIVA AND NASAL MUCUS. R.I. Henkin, I. Velicu, Taste and Smell Clinic, Washington, DC.

We have recently demonstrated insulin presence in saliva and nasal mucus and that levels change in response to physiological and pathological processes. Because of these findings we wished to determine if insulin receptors were also present in saliva and in nasal mucus. We measured insulin receptor concentration (in ng/mL) by colorimetric ELISA 96-plate assay in plasma, saliva, and nasal mucus in fasting and nonfasting states in patients with a variety of diseases. Insulin receptors were present in plasma, saliva, and nasal mucus. In the fasting state in control patients insulin receptor concentration in plasma was 2.3 ± 0.3 (mean ± SEM), whereas in saliva it was 7.1 ± 0.6, significantly higher than in plasma (p < .001). In the fasting state in plasma in patients with controlled diabetes mellitus insulin receptor concentration was 21.0 ± 7.4; in saliva it was 4.0 ± 0.9, significantly lower than in plasma (p < .001). In the nonfasting state plasma insulin receptors in control patients were essentially the same as in the fasting state but in diabetics plasma insulin receptor concentration was decreased in the fasting state; in saliva, in control patients and in diabetics insulin receptor concentration was essentially the same in the fasting or nonfasting state. In nasal mucus in the nonfasting state in control patients insulin receptor concentration was 9.0 ± 1.0, about three times higher than in plasma, slightly higher than in saliva and more than twice as high as compared to diabetics. Insulin concentration relative to insulin receptor concentration in saliva in control patients and diabetics was decreased significantly comparing the nonfasting to the fasting state, whereas insulin itself was increased in both control patients and diabetics. In thin and obese patients there were changes in insulin receptor concentration in plasma, saliva, and nasal mucus relative to their physiological and pathological states. These data demonstrate that both saliva and nasal mucus contain soluble insulin receptors and indicate that these biological fluids can serve as indicators of insulin receptor metabolism. Since these fluids can be obtained with greater ease than can plasma, saliva and nasal mucus can serve as simple, useful, noninvasive indicators of insulin receptor as well as insulin metabolism. This is the first demonstration of insulin receptors in saliva and nasal mucus.

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CEREBRAL PERFUSION IN NEONATES UNDERGOING REPAIR OF COMPLEX CONGENITAL HEART DEFECTS IS DETERMINED BY CARBON DIOXIDE PREOPERATIVELY BUT BY BLOOD PRESSURE POSTOPERATIVELY. J. Henson, K. Krajewski, H. Edmonds, A. Sehic, E. Austin, M. Mitchell, University of Louisville, Louisville, KY.

Background: Preoperative studies of neonates with congenital heart disease have demonstrated that increased pCO_2 results in increased cerebral perfusion, while hyperventilation with lower levels of pCO_2 results in both less cerebral perfusion and pathologic changes on MRI brain scans. However, because hyperventilation with lower levels of pCO_2 is often essential immediately post–neonatal cardiac surgery in order to correct acidosis and promote hemodynamic stability, post–cardiopulmonary bypass ventilatory strategy is both critically important and highly controversial. In order to determine the optimal management strategy in infants undergoing heart surgery, we examined the relationship between mean arterial pressure (MAP), end tidal CO_2 (ETCO2), peripheral oxygen saturation (SaO_2), and left cerebral oxygen saturation (LSaO2) pre– and post–cardiopulmonary bypass in an anatomically homogeneous cohort of neonates undergoing primary complete cardiac repair. **Methods:** 15 neonates with interrupted aortic arch and ventricular septal defect undergoing primary complete repair at Kosair Children's Hospital were enrolled in this study. Serial simultaneous measurements of MAP, SaO_2, $ETCO_2$, and $LSaO_2$ using near-infrared spectroscopy (NIRS Somenetics Inc.) were made at 5-minute intervals pre- and postseparation from cardiopulmonary bypass. Linear and parametric regression analysis was used to look for relationships between percent change in MAP, SaO_2, ETCO2, and $LSaO_2$. **Results:** Pre–cardiopulmonary bypass, changes in cerebral saturation were related to changes in ETCO2 in a linear fashion (R^2 = .421), while there was no observed relationship to MAP (R^2 = .078). Post–cardiopulmonary bypass, changes in cerebral saturation were tightly related to changes in MAP (R^2 = .357) but not to changes in $ETCO_2$ (R^2 = .086). No relationship existed between changes in cerebral saturation and changes in SaO_2 either pre– or post–cardiopulmonary bypass. **Conclusions:** Consistent with theories of cerebral autoregulation, cerebral saturation pre–cardiopulmonary bypass was determined by changes in end tidal CO_2 but not by changes in blood pressure or peripheral oxygenation. However, this relationship was obliterated post–cardiopulmonary bypass, where changes in blood pressure became the major determinate of changes in cerebral saturation. This dysautoregulation may be secondary to cerebral edema or injury occurring during the cardiopulmonary bypass run and suggests that immediately postoperatively a strategy of hyperventilation in order to maintain mean arterial pressure is justified.

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THE QUANTITATIVE VALIDATION OF NONINVASIVE DISEASE ACTIVITY INDICES IN ULCERATIVE COLITIS. P.D.R. Higgins, I. Krokos, J. Leung, M. Schwartz, J. Mapili, E.M. Zimmermann, Department of Medicine, University of Michigan, Ann Arbor, MI.

Background and Aims: There are no validated disease activity measures for ulcerative colitis. Current methods of validation are qualitative and provide no means to compare the validity of different indices. Recent data have suggested that two noninvasive indices for ulcerative colitis, the Simple Clinical Colitis Activity Index (SCCAI) and the Seo Index, can predict clinical outcomes of remission and improvement. We performed a quantitative analysis of the psychometric and performance validity of these indices in the measurement of ulcerative colitis. **Methods:** A longitudinal cohort study of 66 patients with ulcerative colitis was performed at a tertiary care center with repeated measurement of disease activity. Subjects were evaluated with the two noninvasive indices, the St. Mark's Index, and the Inflammatory Bowel Disease Questionnaire. Subjects were also asked at each visit whether they were in remission and at the return visit whether their disease activity had changed. Psychometric validity was evaluated by quantitatively measuring the content, construct, criterion-convergent, and criterion-predictive validity on a 0–1 scale. Performance validity was evaluated by measuring the reproducibility and responsiveness on a 0–1 scale. These items were totaled to provide an overall validity score for each index. **Results:** The two noninvasive indices had good criterion-convergent and criterion-predictive validity and good reproducibility. The SCCAI was weak in its content validity and in its responsiveness. The Seo Index had weaknesses in its content validity, construct validity, and responsiveness. Both indices had fair overall validity scores, and the SCCAI was superior to the Seo Index. **Conclusions:** These two noninvasive indices for ulcerative colitis have fair overall validity and are now the most rigorously validated disease activity indices for ulcerative colitis. Both indices predict the clinical end point of patient-defined remission. These noninvasive indices can lower costs and subject discomfort in future clinical trials. Quantitative evaluation of validity identifies weaknesses in disease activity indices that can be improved and can lead to better indices of disease activity in ulcerative colitis and in other disease states.

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ANTHROPOMETRIC CHARTS FOR ACHONDROPLASIA AND OTHER SKELETAL DYSPLASIAS. J.E. Hoover-Fong,[1,2] J. McGready,[1,3] K.J. Schulze,[1,3] H. Barnes,[2] C.I. Scott,[4] [1]Johns Hopkins University, Baltimore, MD; [2]McKusick-Nathans Institute of Genetic Medicine, Greenberg Center for Skeletal Dysplasias; [3]Bloomberg School of Public Health, Baltimore, MD; [4]AI DuPont Hospital for Children, Wilmington, DE.

Accurate assessment of growth parameters in skeletal dysplasia patients is problematic with current growth curves. Most were constructed from a relatively small number of patients with a paucity of longitudinal data, from multiple clinical settings, using potentially nonstandardized observational methods. Furthermore, the curves were derived from very basic parametric analysis. Of clinical significance, weight-for-age norms are currently unavailable, despite significant negative orthopedic, neurologic, and general health sequelae caused by unrecognized and untreated obesity in the short-stature population. We have collected extensive, longitudinal anthropometric data from medical records of patients with a variety of skeletal dysplasias including achondroplasia, hypochondroplasia, spondyloepiphyseal dysplasia congenita, diastrophic dysplasia, Morquio syndrome, Kniest and metatropic dysplasia. Parameters extracted include weight, length/height, head circumference, upper and lower segments, arm span, chest circumference, inner and outer canthal distance, hand and middle digit length, gender, age, and gestational age. The primary data presented here were from subjects with achondroplasia (n = 334), the most common short-stature skeletal dysplasia, with ≈2,000 data points for height, weight, and head circumference. Age-specific percentiles (5, 25, 50, 75, and 95th) for all parameters were estimated separately for males and females over 0–36 months and 2–20 years, corresponding to the CDC growth curve format for average stature individuals. A 6-month wide "moving window" (± 3 months from age of interest) was used to estimate all age-specific percentiles. Percentiles were then smoothed using a quadratic penalized smoother, with degrees of freedom and smoothing parameter estimated by a semiparametric model approach. The magnitude and longitudinal nature of this retrospective, single-observer cohort study improve the precision of the percentile estimates as compared to all previous studies. Most importantly, novel weight for age charts for patients with achondroplasia are now available for clinical use. This methodology may be easily applied to other confirmed, nonskeletal dysplasia diagnoses to assess growth in these disorders.

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USE OF PROPHYLACTIC ANTICOAGULATION AND THE RISK OF HEPATIC VENO-OCCLUSIVE DISEASE IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS. H. Imran, I.M. Tleyjeh,* A. Zirakzadeh,** V. Rodriguez, S.P. Khan, Division of Pediatric Hematology/Oncology, *Division of Infectious Diseases, and the **Division of General Internal Medicine, Mayo Clinic, Rochester, MN.

Context: Hepatic veno-occlusive disease is one of the most serious regimen-related toxicities in patients undergoing hematopoietic stem cell transplantation. The prophylactic use of anticoagulation remains controversial. **Objective:** To perform a systematic review and meta-analysis of the literature on the effect of anticoagulation in preventing veno-occlusive disease. **Data Sources:** *MEDLINE, EMBASE,* and several other databases were searched. **Study Selection:** We identified randomized controlled trials and cohort studies that compared the use of unfractionated heparin or low-molecular-weight heparin for prevention of veno-occlusive disease with a nontherapeutic control in children and adults undergoing hematopoietic stem cell transplantation. **Data Extraction:** Two investigators independently identified eligible studies and assessed their quality. **Data Synthesis:** Twelve studies were eligible, with a total of 2,782 patients. Anticoagulation prophylaxis was associated with a statistically nonsignificant decrease in the risk of veno-occlusive disease (pooled rel-

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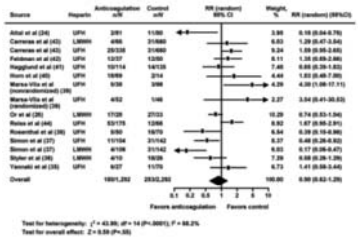
ative risk 0.90; 95% CI 0.62–1.29). Relative risk estimates differed according to the type of transplant recipient, study design, intervention, and outcome definition. However, all the cohort studies had methodologic limitations, including biases in selection and comparability. The results of 1 of 3 randomized controlled trials may have been affected by delayed introduction of anticoagulation. A second trial enrolled patients who received conventional chemoradiotherapy and were in an early stage of their disease. The relative risk was 0.18 (95% CI 0.04–0.78), but the trial had limited generalizability. The third trial was a pilot study with a small sample size (relative risk 0.74; 95% CI 0.53–1.04). **Conclusions:** Significant heterogeneity and methodologic weaknesses preclude drawing a meaningful conclusion from the pooled analysis, but the results of 2 randomized control trials suggest that prophylactic anticoagulation may help prevent veno-occlusive disease. However, a large randomized controlled trial is needed for confirmation.



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CARDIOVASCULAR SCREENING USING PULSE PRESSURE RESPONSE TO HANDGRIP. J. Iskarous, R. Barndt, N. Mina, O. Abdelmelek, J. Huang, Bethel Public Service Clinic, Downey, CA.

Our pilot studies (PS) show that pulse pressure (PP) response to isometric handgrip (IH) provides significant additional information in the prediction of cardiovascular (CV) disease. The combination of the PP and the rise in pulse pressure (RPP) during IH enabled the prediction of high systemic vascular resistance (SVR), low cardiac output (CO), degree of BP control, aortic collagen, and coronary artery (CA) risk. Prospective studies (ProS) were done using a random sample of the general population, ages 50–65, 1/1 male/female, all Caucasian, compared to normal controls (C) (matched by age/sex and race). BP was recorded (left arm) at rest and with IH (right hand at 5 psi for 3 minutes) recording RPP. Measurements were made of systolic blood pressure (SBP), PP, RPP, systolic time intervals (STI), systemic vascular resistance (SVR in standard units), and CO and aortic collagen (AC) by transthoracic 2D echocardiography. PP and RPP were used to predict right coronary artery stenosis (RS), left anterior discending stenosis (LS), and circumflex stenosis (CS) by previous PS predicted-found formula vs angiogram (r = .96, p < .001). All measurements were done by methods previously reported by our clinic. STI is a measure of adrenergic neurovascular tone (STI = PEP/LVET × 100%) that increases RPP and SVR, decreasing the central blood volume (CBV) at STI < 30. Exclusions from the study were smokers, diabetics, and LDL > 125. Group (G) 3 was treated (3Rx) with tenormin 12.5–100 mg/day for 10 years with IH measured every 3 months and all other serial measurements made annually. All data were placed into a blind matrix for analysis later. Data were grouped using PP and RPP PS criteria. **Results:** Group means are shown. X = Not measurable due to high SVR.

G	*#*	*SBP*	*PP*	*RPP*	*STI*	*CO*	*SVR*	*AC*	*LS*	*RS*	*CS*	*RBV*
C	100	110	40 (± 5)	9	53	5.5	1,120	17	0	0	0	0
1	50	92	40 (± 5)	35*	25*	2.3*	1,983*	I7	X	X	X	−32*
2	50	150*	70 (± 15)	30*	27*	2.8*	1,787*	47*	X	X	X	−29*
3	50	152*	72 (± 15)	9	33*	4.5	1,566	49*	39*	61*	48*	−3
3Rx	50	120	40 (± 5)	8	52	5	1,232	18	2	1	0	−2

*Significant difference from GC at p < .01 by t-test. RBV = reduced CBV (by hemoglobin dilution during Rx). In G1 and 2 PP and RPP (> 25) predicted low CO and low STI with high SVR, showing a need for therapy. G3 had normal RPP and required reduction of SBP with Rx. 3Rx shows regression of AC and predicts CA regression. Thus, PP and RPP screening is a rapid method to assess patient CV status.

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METABOLIC SYNDROME IN ADOLESCENTS TREATED FOR BIPOLAR DISORDER. V. Kafantaris, E. Saito, A. Berest, C. Dombrowski, J. Hirsch, North Shore-LIJ Research Institute, Glen Oaks, NY.

Background: Metabolic syndrome can be a serious complication of treatment with psychotropic medications, particularly the atypical antipsychotics. **Method:** Adolescents with bipolar I disorder who were taking at least one mood stabilizer (divalproex sodium and/or lithium) and an antipsychotic medication (aripiprazole, olanzapine, risperidone, quetiapine, or ziprasidone) were assessed at baseline and every 12 weeks thereafter. We defined the metabolic syndrome as three or more of the following five criteria: (1) triglyceride level ≥ 110 mg/dL, (2) high-density lipoprotein (HDL) ≤ 40 mg/dL, (3) body mass index (BMI) ≥ 95th percentile, (4) fasting glucose level ≥ 100 mg/dL or fasting insulin level ≥ 17 µU/mL, and (5) blood pressure ≥ 90th percentile. We present the prevalence of the metabolic syndrome among adolescents with bipolar I disorder treated with psychotropic medications and compared subjects with metabolic syndrome to those without it on certain variables using t-tests. **Results:** Thirty-seven adolescents (20 M, 17 F, mean age = 14.90 years, SD = 1.83) with mean follow-up of 36.3 weeks (SD = 18.9) had at least two fasting laboratory evaluations 12 weeks apart. Twelve of the 37 adolescents (32.4 %) met criteria for metabolic syndrome at one or more time points. As expected, BMI at week 24 was significantly higher in the group with metabolic syndrome (mean BMI = 32.8 kg/m^2) than without (mean BMI = 25.0 kg/m^2, p < .0001). We compared the 12 subjects who "ever met" criteria with those who "never met" criteria on age, gender, race, BMI, fasting glucose level, insulin, lipid profiles. The baseline BMI (p < .0185), weight (p < .0094), glucose (p < .0678) and insulin levels (p < .0793), and HOMA (p < .0432) were significantly higher in the ever-met group compared to never-met group. **Conclusions:** About one-third of our study sample developed the metabolic syndrome during treatment with a combination of a mood stabilizer and an atypical antipsychotic medication. Those subjects had significantly higher baseline weight, BMI, fasting glucose and insulin levels, and HOMA.

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CORRELATION BETWEEN HYPERTONIC SALINE PD_{20} AND METHACHOLINE PC_{20} IN ASTHMA. S. Kazani, J. Sadeh, S. Bunga, N. Khan, M.E. Wechsler, A. Deykin, and E. Israel, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

Aim: Studies have reported contradictory results on the relationship between airway hyperresponsiveness to methacholine (Mch) and that elicited by hypertonic saline (HS) inhalation. We investigated the correlation between Mch-PC_{20} and HS-PD_{20} in mild asthmatics who had performed both challenges in a research setting. **Methods:** We assembled data on mild asthmatics on prn β-agonists, with a history of positive response to Mch (PC_{20} ≤ 8 mg/mL), who had undergone a staged 3% saline challenge. Mean time between challenges was 23 months (range 0.1–74, SD 21). We also compared the bronchial reactivity to exhaled breath condensate (EBC) pH, a putative marker of airway inflammation. **Results:** Subject data:

N	24
Age (yr)	34 ± 10 (22–57)
M:F	10:14
FEV_1 (% pred)	87 ± 15 (62–112)
Mch-$PC_{20\ mg}$/mL*	0.97 (0.57 ± 1.63)
HS-$PD_{20\ mL}$*	24.97 (16.62 ± 37.51)
EBC pH	8.15 ± 0.80 (5.19–8.65)

*Geometric mean (95% CI).

Of the 24 subjects, 16 (67%) were responsive to the HS challenge. Nonresponders were assigned an HS-PD_{20} value of 74 mL. HS-PD_{20} correlated significantly with Mch-PC_{20} (r = .52, p = .0089). EBC pH did not have a significant relationship with either HS-PD_{20} or Mch-PC_{20}. **Conclusion:** HS and Mch reactivity provide similar assessments of airway reactivity in asthmatics not on controller medications. Considering the stability of the correlation, these data suggest that HS may be a substitute for Mch challenge. Neither measure of hyperresponsiveness correlates with EBC pH.

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VERIFIABLE DONOR DEATHS IN LIVING DONOR LIVER TRANSPLANTATION. J.R. Kenison, P. Adam,* C.M. Lo,# J.F. Trotter, University of Colorado Health Sciences Center, Denver, CO; *Paul Brousse Hospital, Paris, France; #University of Hong Kong, Hong Kong.

Background: In living donor liver transplantation (LDLT) the hepatic lobe donor incurs a measurable risk, the most important of which is death. The actual risk of death following a donor hepatectomy is unknown because of the absence of a sufficiently large database to allow an accurate determination of this infrequent but devastating outcome. In the absence of a definitive estimate of the risk of donor death, the medical literature has become replete with anecdotal reports of donor deaths, which in many cases are based on verbal reports, circularly referenced or unsubstantiated. Because donor death is one of the most important outcomes of LDLT, we performed a comprehensive survey of the medical and lay literature to provide a referenced source of worldwide donor deaths. **Methods:** We reviewed all published articles available from *PubMed* and from the lay literature (using <www.google.com> and <http://www.refdesk.com/paper.html>), which reported donor outcomes from 1989 to October 2005. We classified each death as definitely, possibly, or unlikely related to donor surgery. **Results:** There were a total of 16 deaths in living liver donors reported in the medical and lay literature, as shown in the Table. Ten were "definitely," two were "possibly," and three were "unlikely" related to donor surgery. The estimated total number of LDLT's performed in the United States is 2,000 and worldwide is 4,800. The estimated rate of donor death definitely related to donor surgery is 3/2,000 or 0.15% in the United States and 11/4,800 or 0.229% worldwide. The rate of donor death that is definitely or possibly related to the donor surgery is 5/2,000 or 0.25% in the United States and 14/4,800 or 0.292% worldwide. **Conclusion:** The purpose of this analysis is (1) to provide a referenced source document of living donor deaths published in the medical and/or lay literature, (2) to provide a better estimate of donor death rate associated with this procedure, and (3) to provide an impetus for centers with unreported deaths to submit these outcomes to the liver transplantation community.

Continent/Country	*# of Deaths*	*Relation to Surgery*	*Time of Death Post-Tx*
Asia	4	3 def./0 pos./1 Unl.	9 d, 10 mo, 2 yr, 3 yr
Europe	5	4 def./0 pos./1 unl.	2 d, 4 wk, 3 yr, ?, ?
USA	6	3 def./2 pos./1 unl.	3 d, 3 d, 21 d, 16 mo, 22 mo, 23 mo,
South America	1	1 def./0 pos./0 unl.	7 d

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INTERACTION OF DULOXETINE HYDROCHLORIDE WITH WARFARIN CAUSING PERSISTENT, SEVERE ELEVATION OF INTERNATIONAL NORMALIZED RATIO. Q. Khalil, C.J. Glueck, M. Winiarska, P. Wang, Cholesterol Center, Jewish Hospital, Cincinnati, OH.

To report interaction of Cymbalta (duloxetine hydrochloride) with warfarin leading to persistent, severe elevation of an INR. A 44 year old woman, homozygous for the factor V Leiden mutation, receiving warfarin (10 mg/day) for 1 year after an ischemic stroke, with a stable INR (2.17 ± 0.51) for the year, was evaluated by us 30 days after development of petechiae-purpura (day 94, Fig. 1). Serial measures were taken for INR and liver function tests (LFTs), and plasma warfarin was measured on day 85. Measures were taken on day 94 for fibrinogen, vitamin K-dependent clotting factors, and with repeat measures of factors II and X on day 98 (Fig. 1). No drugs taken daily over the previous year were changed (warfarin, atorvastatin, lamotrigine, topiramate, clorazepam, albuterol); however, Cymbalta (30 mg/day), a selective serotonin and norepinephrine reuptake inhibitor (SSNRI), was added by the psychiatrist at day 0 and was continued until day 94. Having unexpectedly high INR (5.0) on day 55, warfarin was stopped, but Cymbalta was continued. Despite cessation (documented by pill count) of warfarin, INR continued to rise to > 19 on day 85, when plasma warfarin level was 5.3 µg/mL (therapeutic range 2–8 µg/mL), 30 days after the last warfarin dose. INR was briefly reduced to 2.7 only by vitamin K (IV) on day 85. On day 94,

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