simvastatin-induced (5 μM, 16 hours) Rac activation was markedly attenuated in ECs transfected with siRNA specific for integrin β4 (38% decrease), with no change in total Rac noted. Additionally, LPS-induced (5 μg/mL, 10 minutes) Erk phosphorylation was inhibited in ECs treated with simvastatin (5 μM, 16 hours), an effect that may contribute to the antiangiogenic properties of statins, whereas Erk phosphorylation was significantly enhanced in ECs transfected with integrin β4 siRNA (100% increase). Finally, RT-PCR confirmed that IL-8 RNA was markedly increased in integrin β4–silenced ECs compared with control cells (≈threefold increase), whereas LPS-induced (5 μg/mL, 10 minutes) IL-8 expression was significantly attenuated in simvastatin-treated (5 μM, 16 hours) ECs compared with LPS alone (30% decrease), findings that may account for the anti-inflammatory properties of statins. Our results indicate a novel regulatory mechanism of Rac and Erk activities and the expression of IL-8 in ECs that is mediated by integrin β4. These data advance our understanding of the complex effects of statins on EC signaling and may ultimately lead to the identification of novel clinical targets.
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SUBCUTANEOUS INTERLEUKIN-4 FOR RELAPSED NON-HODGKIN'S LYMPHOMA: A PHASE II TRIAL IN THE NORTH CENTRAL CANCER TREATMENT GROUP, NCCTG 91-78-51. D.M. Kurtz, L.K. Tschetter, J.B. Allred, S.M. Geyer, P.J. Kurtin, W.D. Putnam, K.M. Rowland, M. Wiesenfeld, G.S. Soori, R.C. Tenglin, A.M. Bernath, T.E. Witzig, Mayo Clinic and Mayo Foundation, Rochester, MN; Sioux Falls, SD; Urbana, IL; Cedar Rapids, IA; Omaha, NE; Rapid City, SD; Danville, PA.
Purpose: Interleukin-4 (IL-4) is a pleiotropic cytokine that has in vitro antiproliferative activity against non-Hodgkin's lymphoma (NHL). This phase II study was conducted to learn the efficacy and toxicity of IL-4 on patients with relapsing or resistant NHL. **Patients and Methods:** Patients with relapsed or refractory indolent or aggressive NHL were eligible to receive either 2.5 or 5.0 μg/kg of subcutaneous IL-4 daily for 28 days of a 42-day cycle. Patients with a response and acceptable toxicity after two cycles were eligible to continue treatment for a total of six cycles followed by observation without maintenance. **Results:** Forty-one patients were enrolled and were assessable for toxicity; two patients were ineligible after histology review, leaving 39 patients for the analysis of tumor response. The median age was 65 years (range 34–79 years), and 56% were stage 4. The overall response rate was 13% (5 of 39), with one complete response and four partial responses. All five responders were in the 5.0 μg/kg group, the median time to progression in all patients was 84 days, and the median duration of response for the responders was 8.3 months (range 7.4–15.7 months). Edema was noted in 66% (27 of 41) and was the most common toxicity. **Conclusions:** Agents that target the IL-4 receptor can have therapeutic benefit in patients with relapsed or refractory NHL.

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INHIBITION OF THE HERG CHANNEL BY ASPIRIN: PH OR DIRECT EFFECT? C. Lin, X. Ke, V. Ranade, J. Molnar, J.C. Somberg, Rush University, Chicago, IL; Lake Bluff, IL.
Aspirin (ASA) has been widely used for many years for relieving pain and fever and in preventing heart attack and stroke. ASA overdose can result in an anion gap, metabolic acidosis, tinnitus, and, in severe cases, encephalopathy and cardiovascular collapse. There are studies showing the inhibitory effect of ASA on heat-evoked currents in rat dorsal root ganglion neurons and the augmented effect of ASA on the NMDA type of glutamate responses in spiral ganglion neurons. The effect of ASA on cardiac ion channels has not been studied. We evaluated the effect of ASA on cardiac IKr channel using HERG expressed on *Xenopus* oocytes. A two-microelectrode voltage clamp technique was used for recording, and the recording solution contained 96 mM NaCl, 5.0 mM KCl, 2.0 mM $CaCl_2$, 1.0 mM $MgCl_2$, and 5 mM HEPES, and the pH of the solution was adjusted with NaOH to 7.4. ASA was dissolved in the recording solution. At a concentration less than 1 mM, ASA has little effect on HERG current. ASA 1 mM and 2 mM inhibited current by 12 ± 2 and 22 ± 4%, respectively. ASA 3 mM inhibited current by 80 ± 6%. Considering the acidifying influence of ASA, the pH values of 1, 2, and 3 mM ASA solutions were determined as 7.1, 6.5, and 4.9. The pH of the recording solutions was adjusted to the corresponding pH, and the results showed that pH 7.1, 6.5, and 4.9 reduced HERG current by 6 ± 2, 10 ± 2, and 49 ± 5%. ASA 1, 2, and 3 mM caused greater inhibition of current than the recording solutions with the corresponding pH adjustment. There were significant differences in current inhibition between 2 mM ASA and the pH 6.5 recording solution ($p < .05$) and between 3 mM ASA and pH 4.9 recording solution ($p < .01$). ASA inhibits HERG current not only through acidification but also by a direct effect. The potent inhibition at 3 mM (54 mg/dL) further suggests that ASA at therapeutic doses and at doses seen with acute and chronic salicylism (40–120 mg/dL) may be arrhythmogenic owing to potent inhibition of the cardiac IKr channel.

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IS THE PH-INDUCED CHANGE IN IKR INHIBITION BY IBUTILIDE ARRHYTHMOGENIC? C. Lin, X. Ke, V. Ranade, J. Molnar, J.C. Somberg, Rush University, Chicago, IL; Lake Bluff, IL.
Ibutilide (I), a class III antiarrhythmic agent, is employed in conversion of atrial fibrillation and atrial flutter. Ibutilide inhibits the cardiac IKr channel and prolongs the Q–T interval and can give rise to ventricular tachycardia. In previous studies, we have shown that extracellular acidosis significantly attenuates the IKr inhibitory effect of proarrhythmic drugs (quinidine) and that extracellular acidosis has little impact on the inhibitory effect of less proarrhythmic drugs such as amiodarone. We hypothesized that I would behave more like quinidine than amiodarone with extracellular acidosis. Cardiac IKr was studied using human-ether-a-go-go-related gene (HERG) expressed on *Xenopus* oocytes and two-electrode voltage clamp technique. The recording solution contained 96 mM NaCl, 5.0 mM KCl, 2.0 mM $CaCl_2$, and 5 mM HEPES. The pH of the solution was adjusted to 6.2 or 7.4 to represent the acidic or normal conditions. At pH 7.4, I 0.3, 1, 3, and 10 μM inhibited current by 22 ± 5, 54 ± 5, 80 ± 3, and 93 ± 1%, respectively. When I was applied at pH 6.2, I 0.3, 1, 3, and 10 μM, I decreased HERG current by 10 ± 4, 29 ± 4, 32 ± 8, and 36 ± 5%, respectively. I 30 μM produced only a 48 ± 5% current block at pH 6.2. There were significant differences in the percentage current inhibition by 1, 3, and 10 μM I at normal pH versus pH 6.2 (p values $< .01$). The IC50 of I was 0.9 ± 0.1 μM at pH 7.4 and the IC50 was increased to 31 ± 6 μM at pH 6.2. Our results indicated that I is a potent IKr inhibitor and that extracellular acidosis markedly attenuated IKr inhibition. Diminished IKr inhibition in the ischemic region with low extracellular pH and potent IKr inhibition in the normal pH regions could result in heterogeneity in action potential duration, which may trigger and sustain arrhythmias and contribute to the proarrhythmic toxicity of ibutilide.

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SELF-MONITORING OF BLOOD GLUCOSE IN TYPE 2 DIABETES MELLITUS: USE OF AN AUTOMATED SELF-MANAGEMENT SYSTEM. K.D. Oden, T. Bomzer, P. Knudson, R. Fleming, J. Levine, E. Burns, S. Flax, The Medical College of Wisconsin, Milwaukee, WI.
Purpose: Type 2 diabetes mellitus (T2DM) requires that a patient assume volitional control of a biologic process that is normally regulated automatically in the healthy individual (ie, serum glucose). Regular self-monitoring of blood glucose (SMBG) provides an objective feedback measure of glycemic control and a way to assess the effectiveness of self-management behaviors (medication dosing, diet, exercise). Patients must be shifted away from invalid, subjective cues to objective readings as indicators of disease control to maintain a valid behavioral control system. For older adults with T2DM, the high prevalence of cognitive impairment, depression, and other chronic illnesses that cause somatic symptoms makes this process even more challenging. We report the results of a clinical trial of an automated self-management system (ASMM) intended to assist in patient-centered management of T2DM by reminding older diabetic individuals to focus on SMBG as the primary indicator of glycemic control. **Methods:** The study was a randomized trial with "delayed intervention controls," with half of participants randomized to immediate use of the ASMM and half to a delayed group, which continued usual care for 6 months before and then using an ASMM. The ASMM provided audio reminders to perform SMBG and take medication and user-friendly feedback about the pattern of glycemic control on a "real-time" basis. Participants were recruited from low-income senior housing and retirement communities in Milwaukee. Home visits were made every 3 months to measure HbA_{1c} and collect other study measures. **Results:** Forty-four diabetic men and women completed the 12-month trial. Sixty percent were Caucasian, 32% African American, and 8% Hispanic, and the mean age was 70 years. Mean baseline A_{1c} was 8.1% ± 1.0, and baseline cognition was 85 ± 2.5 on the 3MSE-R. A_{1c} dropped to 7.3 ± 1.0 by 9 months ($F = 3.56$, $p < .004$), with a 3-month lag observed in the DG. There was no relationship between 3MSE-R, depression scores, or A_{1c}. **Conclusion:** Our results indicate that providing older diabetic individuals with audio reminders and feedback led to significant improvement in glycemic control over a 12-month trial period. This effect was independent of baseline cognitive status and mood.

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SEVERE ANEMIA CAUSED BY MULTIPLE INTESTINAL HELMINTH INFESTATION. N. Paul, L. Delgado-Sanchez, S. Niranjan, Coney Island Hospital, Brooklyn, NY.
Introduction: Intestinal helminth infestations are usually asymptomatic, but serious infestations may cause symptoms ranging from abdominal discomfort to severe pain. Anorexia, nausea, diarrhea, pruritus, rectal prolapse, bowel obstruction, and death may occur. Hives and eosinophilia may develop, and the worms may sometimes spontaneously exit the body through the anus. This is a case report of intestinal helminth infestation harboring the human intestine with four different parasites at the same time. **Case Report:** A 53-year-old male patient, a recent immigrant from Bangladesh, was admitted with progressively worsening generalized weakness and exertional dyspnea. Physical examination was unremarkable except for severe pallor. Rectal examination revealed brown stool, guaiac positive. Laboratory values were indicative of severe anemia, with hemoglobin 5.6 g/dL and hematocrit of 18.5%. Mean corpuscular volume was 56 fl. The patient also had significant eosinophilia (42%) on differential diagnosis, with an absolute eosinophil count of 42%. Iron studies revealed anemia consistent of iron deficiency. On further interview, the patient admitted abdominal discomfort associated with diarrhea and passage of worm through the anus in the past. Stool for ova and parasite revealed four different helminthes: *Ascaris lumbricoides*, *Trichuris trichura*, *Strongyloides stercoralis*, and *Anchylostoma duodenale*. The patient was treated with a 1-week course of albendazole. He received blood transfusion and was started on iron supplements. A follow-up examination of stool for ova and parasite was performed and was negative for ova and parasite. The patient also underwent a colonoscopy and upper endoscopy during the course and was negative for any lesions. The patient significantly improved during the hospital course, and hemoglobin reached to 10.4 mg/dL and hematocrit 31.1 with a mean corpuscular volume of 82.7. **Discussion:** Intestinal helminth infestations most commonly affect travelers, migrant laborers, refugees, children of foreign adoptions, and the homeless. Parasitic infections may be associated with daycare centers and overseas travel. Clinicians should have a high index of suspicion for parasite infestation as a cause of anemia in the immigrant population. A very simple test of stool for ova and parasite helps in the diagnostic workup of anemia.

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FAST VENTRICULAR TACHYCARDIA AT PROGRAMMED ELECTRICAL STIMULATION AS A RISK FACTOR FOR SPONTANEOUS VENTRICULAR ARRHYTHMIAS IN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR PATIENTS. K. Phatak, J. Goldberger, R. Passman, Northwestern University, Feinberg School of Medicine, Chicago, IL.
Background: Implantable cardioverter defibrillators (ICDs) reduce mortality in high-risk individuals by preventing sudden cardiac death owing to ventricular tachyarrhythmias. Programmed electrical stimulation (PES) is useful for risk-stratifying patients for sudden cardiac death (SCD). However, the prognostic value of induced fast ventricular tachycardia (FVT) (cycle length ≤ 230 msec) is uncertain. The purpose of this study is to compare the risk of appropriate shock for ventricular tachycardia (VT) or ventricular fibrillation (VF) in ICD recipients induced into FVT, monomorphic VT (MVT) (cycle length > 230 msec), polymorphic VT (PVT)/VF, and no ventricular tachyarrhythmias at the time of PES. **Methods:** A single-center retrospective review was performed on patients who underwent PES, ICD implantation, and follow-up between 1992 and 2003. The primary end point was time to first appropriate ICD shock. Baseline variables were compared using appropriate tests of significance. Time-to-appropriate shock was compared for each type of induced rhythm using survival analysis. Cox regression was used to assess the impact of baseline variables on the primary end point. **Results:** A cohort of 289 patients with a mean age of 64 ± 14 years, ejection fraction (EF) 33 ± 15%, 65% with ischemic cardiomyopathy, and 50% with secondary prophylaxis indications was studied. Inducible FVT was present in 18%, MVT in 40%, and PVT/VF in 21%, and 20% were noninducible. The mean cycle length was 212 ± 15 msec for FVT and 286 ± 59 msec for MVT ($p < .001$). Compared with patients inducible into FVT, MVT patients had a lower EF (31% vs 36%; $p = .013$) but otherwise had no significant differences in other baseline variables. Patients were followed for 2.2 ± 2.3 years, during which time 26% received appropriate ICD therapy for VT/VF, with 16% of the FVT patients, 39% of MVT patients, 11% of PVT/VF patients, and 21% of noninducible patients receiving appropriate therapy. Patients induced into MVT had a significantly increased risk of appropriate ICD therapy (hazard ratio 2.6; 95% CI 1.2–5.5; log rank $p < .001$), whereas patients induced into FVT had a similar risk of shocks as PVT/VF patients and noninducible patients ($p > .05$ for all comparisons). After adjusting for baseline differences, only MVT and EF remained as significant predictors of appropriate ICD therapy (adjusted hazard ratio 2.2 for MVT; 95% CI 1.01–4.84; $p = .048$ and adjusted hazard ratio 0.98 for each 1% increase in EF; 95% CI 0.96–0.99; $p = .008$). **Conclusion:** FVT induced on PES is a nonspecific finding with a similar long-term risk of spontaneous VT/VF as induction into PVT/VF or a lack of induction of ventricular tachyarrhythmia at the time of PES. However, noninducible patients